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**BIOCULTURALISM REVISITED,
THE NEUROGNOSTIC HELIX UNCOILED**

by

Barbara Anne Lindsay White, B.A.

A dissertation submitted to
the Faculty of Graduate Studies and Research
in partial fulfillment of
the requirements for the degree of

Master of Arts

Department of Sociology and Anthropology

Carleton University
Ottawa, Ontario
October 23, 1995

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Bioculturalism Revisited, The Neurogenostic Helix Uncoiled

submitted by Barbara Anne Lindsay White, B.A.

in partial fulfillment of the requirements

for the degree of Master of Arts

Chair, Department of Sociology and
Anthropology

Thesis Supervisor

Carleton University

September 29, 1995

ABSTRACT

This thesis re-interprets the process of human brain and cognitive evolution from the operationally precise standpoint of the effects of nutrition on the synthesis and release of the precursor-dependent neurotransmitters: dopamine, norepinephrine, acetylcholine and serotonin, in functionally-specified regions of the brain known to have exhibited allometric increases in size in members of the genus Homo. The nature of this inquiry is warranted on the basis of prior speculations. It is also supported on the basis of the a priori assumption that the costs of brain growth and maintenance are essential to understanding the conditions under which the process of hominid encephalization could occur. In the process of comparing the content and activity patterns of the precursor-dependent neurotransmitters in cortical and subcortical regions of the brain known to have exhibited significant allometric increases in size in members of the genus Homo, the hypothesis that the effects of nutrition on brain neurotransmitter synthesis may have represented another metabolic constraint on the process of hominid encephalization - independent of the role previously ascribed to caloric energy and dietary fatty acids - is advanced. The position that culturally- and technologically-templated shifts in hominid diet may have interacted with the structural and functional potentials inherent in the protohuman genome to "co-produce" the development and evolution of the brain and the cognitive capacities of our species is also developed.

"THE MIND IS A STRANGE MACHINE WHICH CAN COMBINE THE MATERIALS OFFERED TO IT IN THE MOST ASTONISHING WAYS."

-BERTRAND RUSSELL, *THE CONQUEST OF HAPPINESS* (1930).

"WHAT WE THINK AND FEEL AND ARE IS TO A GREAT EXTENT DETERMINED BY THE STATE OF OUR DUCTLESS GLANDS AND OUR VISCERA."

**-ALDOUS HUXLEY "MEDITATION ON EL GRECO,"
MUSIC AT NIGHT (1931).**

"IT TAKES A LONG TIME TO UNDERSTAND NOTHING."

**-EDWARD DAHLBERG, "ON WISDOM AND FOLLY"
REASONS OF THE HEART (1965)**

**"A TEACHER AFFECTS ETERNITY;
HE CAN NEVER TELL WHERE HIS INFLUENCE STOPS."**

-HENRY ADAMS, *THE EDUCATION OF HENRY ADAMS* (1907)

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PART ONE

INTRODUCTION, METHODS, AND FIRST SOJOURNS

1.0 INTRODUCTION

The fossil record provides us with evidence that the cranial capacity of our hominid ancestors¹ increased in size from approximately 425 to 1330 cubic centimetres (cc) over the span of some 4 million years (Eccles 1989:15; Jerison 1973, 1979, 1990; Blumenberg 1983). The question that has perplexed many researchers is WHY ? Why did the forces of natural selection favour significant increases in the size of the brain ? What accounts for the fact that human beings are, vis à vis our closest living relatives the chimpanzees with whom we share 97.5% genetic affinity and a common ancestor approximately 6 million years ago (MYA) so phenotypically distinct ? That is, endowed with much greater cognitive flexibility than the minimal 2.5% differences in base nucleotide sequences between hominids and pongids would seem to predict or allow ? These are philosophically and thus scientifically compelling questions. Blind Forces and Infinite Wisdoms notwithstanding it is left to us mere mortals, clad only in the trappings of a dominant epistemology (interpretive paradigms in hand) to try and thrust and parry our way out of this enigma.

In this thesis I will examine the anthropological relevance of the observation that nutrition affects brain neurotransmitter synthesis and release (e.g., Wurtman & Fernstrom 1972, 1975;

¹ Which includes (subject to an ongoing debate) *Australopithecus afarensis*, *Australopithecus africanus*, *Homo habilis*, *Homo erectus*, and archaic *Homo sapiens* (see Chapter 3).

Fernstrom & Wurtman 1974; Dakshinamurti 1977; Wurtman & Growdon 1978; Plaitakis et al. 1978; Feller & O'Dell 1980; Wurtman 1981, 1982; Mair et al., 1985; Micheau et al. 1985; Lieberman & Abou-Nader 1986; Witt & Goldman-Rakic 1983; Thurmond & Brown 1984; Leathwood & Heinrich 1986; Milner & Wurtman 1986; Acworth et al. 1988a,b; Fernstrom 1988; Raleigh et al. 1988; Wurtman 1988; During et al. 1988, 1989; Ulus et al. 1989; Schaecter & Wurtman 1990; Chafetz 1990; Kaplan et al., 1991). I will refer specifically to the effects of tryptophan, tyrosine, phenylalanine, choline, thiamine, niacin, vitamin B6, vitamin C, iron, copper, pantothenic acid, fat, and protein:carbohydrate ratios on dopamine (DA), norepinephrine (NE), serotonin (5HT), and acetylcholine (ACh) synthesis (Part 3).

My central agenda is to re-interpret the evolution of the brain and the cognitive capacities of our species from the operationally very precise standpoint of the effects of nutrition on the content and activity patterns of the precursor dependent neurotransmitters (p.d.NTs) in [as I will seek in an original effort to emphasize] functionally specified regions of the brain known to have exhibited significant allometric increases in size in members of the genus *Homo*. Methodologically, this is a unique strategy (discussion see Chapter 2).

In the process of demonstrating that the p.d.NTs are particularly active in those very regions that underwent

significant increases in size I will argue that the effects of nutrition on brain neurotransmitter (NT) synthesis may have represented another metabolic constraint on the process of brain evolution - independent of the role previously ascribed to caloric energy (Martin 1981, 1983; Foley & Lee 1992; Leonard & Robertson 1992; Speth 1992) and dietary lipids (Crawford & Marsh 1989). Less conservative hypotheses will also be advanced.

A co-evolutionary model of the dialectical interaction between "biology" (operationalized in terms of specific aspects of structural, functional, and chemical neuroanatomy) and "culture" (operationalized in terms of specific nutrients relevant to brain NT synthesis) will be fully developed. Far from denying the controlling influence of genetics, I will simply examine how nutritional factors can interact with genetic ones to "co-produce" the development of the cognitive potentialities inherent in the brain/genome. Heuther's (1988) research on the transgenerational phenotypic effects of developmental variations in amino acid availability will provide me with a significant opportunity to bridge the gap between ontogeny and phylogeny without being accused of advancing a specious form of Lamarckism.

My overall theoretical orientation is supported on the basis of the *a priori* assumption that "there is perhaps more to be learned in concrete terms about hominid brain evolution by asking how our ancestors could afford (in energetic terms) to develop

large brains than by speculating about why they needed them" (Martin in reply to Blumenberg 1983:607; italics in the original). In other words **"the costs of brain growth and maintenance are essential to understanding the conditions under which [the process of hominid] encephalization could occur"** (Foley & Lee 1992:223). The fact that amino acid availability (vis à vis its effects on p.d.NT synthesis) represents one such cost of brain growth and maintenance augurs well for the merits of this inquiry. My overall methodological orientation is supported on the basis of "the principle of proper mass" (Jerison 1973) and "optimal foraging theory" (Stephens & Krebs 1976; Pulliam 1974, 1975) as discussed in Chapter 2.

Particular attention will be paid to the summary observation that the prefrontal cortex (PFC), which is an area of the frontal cortex that has undergone the most significant allometric increases in size (Passingham 1973), exhibits a particularly high density of dopaminergic activity markers (Brown et al., 1979; Goldman-Rakic 1994; Berger & Trotter 1986), is curiously devoid of "synthesis modulating autoreceptors" (Bannon et al., 1981), and is moreover "unusually dependent on precursor availability" (Deutch & Roth 1990). In this thesis I will ask why, or rather how, our hominid ancestors could afford (in energetic terms) to develop large brains when they were, by default of the unique electrophysiological properties of the PFC, unusually dependent on amino acid precursor availabilities. Obviously I will be exploring the evolution of the

brain and the cognitive capacities of our species from a decidedly ecological perspective.

1.1 Signposts on the Road

Upon archival inspection it is apparent that the interpretive significance of Wurtman and colleagues' research has not escaped the attention of several anthropologists interested in exploring the evolution of the brain (Blumenberg 1983) and (with greater emphasis) foraging theory (Gaulin & Konner 1977; Armelagos 1987). In 1977 Gaulin & Konner observed that

...tryptophan-free diets deplete brain serotonin... choline has been shown to affect brain acetylcholine synthesis...catecholamine synthesis may be similarly affected by brain levels of their precursor the amino acid tyrosine. These direct effects of dietary components on brain neurotransmitter synthesis in both acute and chronic models open a broad path for the investigation of possible neurobehavioral facultative adaptations to dietary variation. **It is even possible that some differences in the observed behaviour of people in various human groups is attributable to differences in dietary composition affecting brain** (Gaulin & Konner 1977:73; emphasis mine).

In 1983 Blumenberg suggested that

new emphases in foraging behaviours and the concomitant alterations in dietary biases and priorities...could have had important effects on neurotransmitter molecules and brain activity. The amino acids tryptophan and tyrosine, which are found at high levels in meat protein, and lecithin, which is a rich component of egg yolks, legumes, and liver, are precursors of neurotransmitters.

However, the relationship is not a simple one, and dietary increase of these molecules may not necessarily result in neurotransmitter synthesis...These few observations provide a fascinating window into the way in which new dietary regimes can affect neurotransmitter synthesis and thereby broad-based activity patterns in the brain...[A] simple loop can be described (Blumenberg 1983:598 in reference to Wurtman (1982)). **See Figure 1.1**

And in 1987 Armelagos argued that "the discovery that diet can affect neural transmitters has implications for biocultural models [of food choice]" (Armelagos 1987:587)².

I find it interesting that Gaulin and Konner's ambiguously worded interpretation comes close to asserting, and yet studiously avoids admitting, the more profound cognitive implications of Wurtman and colleagues' research. Likewise, too, I find it interesting that Blumenberg's model clearly admits, but does not define, what 'other behavioural' effects might be associated with foraging-related variations in NT precursor availability.

Blumenberg's (1983) model (my Figure 1.1) provides us with a useful 'neurochemically-driven' version of what Haraway (1988) would call a "self-making productionist dialectic". However it begs the question: what are the other behavioural effects his model clearly admits but does not define ? Might diet have the capacity to exert an effect on behaviours not strictly in the service of

² This was stated in the context of interpreting Wurtman's (1982) discussion on the complex relationship between carbohydrate consumption, 5HT synthesis, and appetite.

Figure 1.1 Blumenberg's (1983:598) model of the dialectical interaction between foraging activities, diet, neurotransmitter synthesis, and behaviour.

foraging ? Or rather (and this is my point): is it possible that technologically-facilitated shifts in hominid foraging practices and dietary biases had the capacity to exert an effect on foraging and other related behaviours and cognitive functionalities by way of their pre- and post-natal metabolic effects on the activities of the p.d.NTs exhibiting high content and activity patterns in those very brain regions that underwent significant increases in size in members of the genus *Homo* ? Therein, of course, lies the hidden interpretive potential, and profound theoretical significance of, Wurtman and colleagues' research.

Stated quite simply then: these several anthropologists' efforts at generalizing the merits of Wurtman and colleagues' research onto various paradigms of interpretive significance are noteworthy. They could, however, be greatly enriched if they adopted, as I will here, a more broad-based interdisciplinary approach. In the process of confronting specific aspects of structural, functional, developmental and chemical neuroanatomy, electrophysiology, comparative neurology and paleoneurology, and the interpretations accorded an understanding of phylogenetic changes in chemoarchitecture, I will offer a more complex interpretation of the anthropological relevance of Wurtman and colleagues' research on the relationship between nutrition and brain NT synthesis.

1.3 'Lest We Forget

I hasten to remind even the neuroscientifically sophisticated reader' that

ideas about the monoamine cortical afferent systems have evolved from the operational concept of a rather diffuse, unspecified group of afferents to one of a widely projecting, yet highly organized system in mammalian cerebral cortex. It is clear that important phylogenetic changes have occurred in these cortical afferent systems... (Levitt et al., 1984:55-56; see below).

Moreover,

...just as we have seen anatomically that neurotransmitter innervation of cortex becomes more extensive and variable as one ascends the phylogenetic scale, neurotransmitter release may come to take on more specific roles... Since, in man, patterns of degeneration of the DA, NA, and ACh innervation of cortex and subcortex are observed in patients dying of neuropsychiatric diseases which all include severe cognitive deficits... [i.e., Parkinson's, Huntington's, Alzheimer's] **it seems likely that during evolution neurotransmitters in cortex come to play an increasingly important role in neural integration** rather than the purely permissive functions ascribed to neurotransmitters in the basal ganglia and limbic system" (Iversen 1984:335, emphasis mine).

In other words, despite the fact that the monoaminergic neurons represent by some estimates "0.05% of all CNS neurons" (Glowinski 1984:231) they are nonetheless very important in the expression of the cognitive functionalities that make us so uniquely human. As

' Witness, for example, Eccles' (1984) suggestion that "the various monoaminergic inputs into the neocortex are too diffuse in operation for [his theoretical] purposes" (1984:12).

Glowinski (1984) quite rightly emphasizes, perhaps this is because they "have the amazing ability to regulate many if not all [executive] functions of the CNS due to their extended spatial, temporal, and energy domains" (p.231).

1.4 Overview

To achieve the many aims of this thesis I have divided it into into four parts. They are labelled in such a way that respects, and at the same time attempts to reconcile, the stylistic demands of the actualistic versus paleosciences. I wrap up **Part 1** by delineating my overall methodology and related aspects of theory (Chapter 2). Then I provide both the neuroscientifically and anthropologically trained readers with some preparatory concepts, terms, and insights of (shall I say) The Other (Chapters 3 and 4).

In **Part 2** I review the anthropological literature on the process of Plio-Pleistocene hominid encephalization, with reference to archaeologically, phylogenetically, statistically, ecologically, and theoretically derived models of brain evolution (Chapter 5 & 6). Special attention is given to the ecological approach to brain evolution (e.g., Martin 1981, 1983; Gibson 1986; Milton 1988) because it provides indirect evidence that this thesis, limited as it is to being anything other than (as yet) mere theoretical significance, is consistent with previous data.

In **Part 3** I review neuroscientific and nutritional biochemical research on the role of various amino acids, vitamins and minerals in the synthesis of 5HT (Chapter 7), ACh (Chapter 8), NE (Chapter 9) and DA (Chapter 10). Within each of these chapters I also develop an understanding of the cognitive functions the p.d.NTs have been implicated in by virtue of the brain regions they exhibit high content and activity patterns in. For the sake of clarity and consistency, I will deal with each p.d.NT separately but according to the same descriptive criteria (e.g., synthesis, release, synthesizing cell bodies and major targets, distribution throughout the brain, cortical and subcortical content and activity patterns, phylogenetic differences, and functional significance).

In **Part 4** I will discuss my major theoretical position. In Chapter 11 I will focus on six select aspects of developmental neurobiology including Heuther's research on the transgenerational phenotypic effects of developmental variations in amino acid availability. Amongst other things, I will also examine the postnatal development profiles of the content and activity patterns of the p.d.NTs in major cortical regions. In Chapter 12 I develop two theoretical models to convey the substance of my thesis.⁴

⁴ That I do not endeavour to reconstruct hominid diet as originally intended is an unfortunate consequence of the necessary depth and breadth of this groundwork analysis.

This, then is the task of the present inquiry: to interpret the evolution of the brain and the cognitive capacities of our species from the operational standpoint of the effects of nutrition on the content and activity patterns of the p.d.NTs in functionally specified regions of the brain known to have exhibited significant allometric increases in size in members of the genus *Homo*. Once again, it is understood that "the costs of brain growth and maintenance are essential to understanding the conditions under which [the process of hominid] encephalization could occur" (Foley & Lee 1992:223).

2.0 METHODS

Given the diverse readership it seems reasonable to emphasize that "physical anthropology does not serve to bridge a gap between the purely biological and the purely social studies of man. Its function is rather to demonstrate that no such gap exists" (Little 1995:262 quoting Frederick Hulse 1971. See text for original reference). Currently, "the eclectic use of a wide range of techniques, data and ideas, and a willingness to embrace interdisciplinary approaches, has provided the basis for the current lively status of research into hominid evolution" (Foley 1987:78). In the context of the present thesis I am grateful that

anthropology is rapidly realizing its need for "plus factors". And we suspect that it will not be long before a new breed of anthropologist will arrive on the scene as conversant with sulci, neocognitrons, and transmitter substances as they are with demes, mythemes, and patrilineal cross-cousin marriage. It may take longer for a cadre of transpersonal ethnographers to emerge from graduate schools and to enter the field to pursue the meaning of the Vision Quest, and still longer for a cadre of mature contemplatives to inform the epistemic foundation of the discipline. However long it takes, these changes will come - and they will be welcome (Laughlin et al., 1990:348).

2.1 Research Methods in Anthropology

While it is true, "imaginative reconstruction was [once] explicitly legitimated as part of the scientific craft" (Haraway

1988:230)⁶, the current methods employed by anthropologists are not so dissimilar to the methods employed by neuroscientists. As Foley (1987) interprets

the study of the past and the present is often contrasted by stating that the former depends on indirect observation whereas the latter can be observed directly. Social anthropologists, ethologists and ecologists can all study populations and individuals alive today, and draw conclusions from their direct observations. Paleoanthropologists, on the other hand, must observe the systems of the past indirectly, through the material relics - fossils, artifacts etc. This might mean that knowledge in the 'actualistic sciences' is more certain than the 'paleosciences'.

This contrast, though, is probably not as marked as might appear at first sight...All knowledge whether of the present or the past, is based upon inferences...that is, **structured deductions** made on the basis of principles that link phenomena together...

The difference...between knowledge about the present and the past is not so much the difference between direct and indirect observation, but differences in the length of a chain of inference, and the strength of the links that make up that chain. It may well be that any knowledge about the past must be based on a longer, and less easily investigated, set of inferences than knowledge of the present, but the epistemology is essentially the same. In either case, advances in the discipline rest on the extent to which the chains of inference have been scrutinized and tested (Foley 1987:79, emphasis mine).

I agree with this assessment for many reasons, not the least of which is because it effectively summarizes what I am trying to do here.

⁶ Primarily because behaviour doesn't fossilize and yet that is precisely what needs explaining (ibid.).

In this thesis I will forge some links between an archaeologically, statistically, and theoretically informed understanding of the process of hominid encephalization and cognitive evolution, with a neuroscientifically-derived understanding of the relationship between the effects of nutrition on NT synthesis and release in structurally and functionally specified regions of the brain. To do this I will build some lengthy "chains of inference" comprised of details selectively apprehended from structural, functional, and chemical neuroanatomy, developmental neurobiology, comparative and paleoneurology, nutritional biochemistry, and even neurophilosophy. Ultimately this will enable me to advance some carefully 'structured deductions' on the basis of principles (e.g., structural/functional, developmental, chemoarchitectural and ecological principles) that link phenomena together. Rest assured, I will make a concerted effort to render the weak links and lingering equivocalities evident so as not to distort or over-interpret the neuroanthropological relevance of Wurtman and colleagues' research.

This, then, is the methodological impetus of the present work. I do not deny the imperatives of the dominant epistemology. Rather, I accept, by default of the nature of the inquiry, a license to develop a speculative thesis that warrants further scrutiny and testing in ways that I conscientiously seek to render wholly and critically apparent.

2.2 Levels and Units of Analysis

From a methodological standpoint it is apparent we can try and understand the evolution of the brain and the cognitive capacities of the genus *Homo* from a number of paradigmatic perspectives. In common parlance, we can take a "top-down" or "bottom-up" approach. I advocate the latter investigative strategy and demonstrate why by discussing the various *a priori* assumptions and ensuing operational approaches we could conceivably make and thus adopt.

The central dogma of anthropology is 'Culture Maketh the Man' (see Haraway 1988 in historical review, and Chapter 6). By way of definition, culture

refers to the non-biological aspects of the human species, incorporating such features as language, tool-making, increased behavioural flexibility, symbolic thought and expression, and it is transmitted through learning and teaching rather than through any genetic system...With the development of these characteristics human evolution became separated from the mainstream of biological evolution (Foley 1987:3).

We are reminded, however, that the heuristic utility of the concept of culture is limited precisely because

most of what is known as culture occurs elsewhere in some form in the animal kingdom. Use of the term culture in paleoanthropology obscures this continuity...Culture is a composite term...[and] there is little advantage in using a term that bestows the advantage of a descriptive shorthand if it begs the very question we are asking and so occurs at the expense of analytic precision (Foley 1987:4).

One could, therefore, argue that

behavioural, not cultural, evolution is an adequate term, making the fewest assumptions...This does not remove the characteristics that make humans unique...but deals with them in ways that make comparisons between species feasible (Foley 1987:5).

And yet, when we encounter the theoretical sophistication of the Biogenetic Structuralists (e.g., Laughlin & d'Aquili 1974; Laughlin et al., 1990) we are forced to reconcile our methods with the fact that "behavior itself does not evolve or develop; rather it is the structure mediating behavior that evolves" (Laughlin et al., 1990:47). In other words,

understanding a patterned change of behaviour over time requires examination of the structural changes that subserve the behaviour, as well as the principles producing or causing the changes at the structural level (Laughlin et al., 1990:48).

This, then, leads us to a crucial methodological juncture.

2.2.1 Beyond the Structures Mediating Behaviour

It is my position that we can capitalize on the various insights of the Biogenetic Structuralists, and at the same time be even more fruitfully reductionistic, if we look at (1) the content and activity patterns of the p.d.NTs in the structures that evolved to mediate critical aspects of human behaviour, as well as (2) the amino acids that subserve the synthesis of the p.d.NTs that are particularly active in the structures that expanded during the

course of the human evolution to mediate adaptive aspects of behaviour. This strategy necessarily draws attention to aspects of hominid diet, and in turn the paleoecology or 'environment' of our hominid ancestors. This seems only fitting given the fundamental importance of the dialectical interaction between culture and the environment that comprises yet another sacred tenet in anthropology.

By way of summary (see Figure 2.1), the methodological strategy I advocate necessitates moving from: (1) 'Culture', to (2) 'behaviour', to (3) 'the structures mediating behaviour' to (4) 'the content and activity of the p.d.NTs in the structures mediating behaviour'⁸, to (5) 'the amino acids, vitamins, and minerals that subserve the synthesis of the p.d.NTs that are particularly active in the structures mediating behaviour', to (6) the foods that supply the amino acids (etc.) that subserve the synthesis of the p.d.NTs that particularly active in the structures mediating behaviour', to (7) 'the Environment', which provides the range of foods that supply the amino acids that subserve the synthesis of the p.d.NTs that are particularly active in the structures that evolved to mediate the expression of the clusters

⁷ Subcategories of which include the development and ongoing maintenance of the structures mediating behaviour.

⁸ which includes (a) phylogenetic changes in their patterns of distribution, (b) developmental alterations in their activity-related profiles, and (c) lifelong metabolic contingencies

of critical human behaviours we traditionally (by way of a descriptive shorthand) call 'Culture'.

The fact that I purposefully avoid the 'rules governing behaviour' (e.g., terrestriality, body size, home range, foraging patterns, maternal metabolic turnover and diet⁹) does not mean to suggest that they are not relevant to the aims of this thesis. Indeed, many of these rules may be re-interpretable in the context of the thesis advanced.

2.3 Jerison's Principle of Proper Mass

My bias in favour of examining the content and activity patterns of the p.d.NTs in functionally specified regions of the brain must be subjected to the critical scrutiny of Jerison's (1973) 'Principle of Proper Mass'¹⁰. This principle holds that

the mass of neural tissue controlling a particular function is appropriate to the amount of information processing involved in performing the function. This implies that in comparisons among species the importance of a function in the life of each species will be reflected by the absolute amount of neural tissue for that function in each species. It also implies that, within a species, the relative masses of neural tissue associated with different functions are related to the relative importance of the functions in each species (Jerison 1973:8-9).

⁹ pursued more fully in Part 2.

¹⁰ I am indebted to Charles Laughlin for clarifying the merits and necessity of this approach; (see also Laughlin et al., 1990:121).

Figure 2.1 Methodological flow chart showing levels and units of analyses, and the dialectical interaction between aspects of 'culture' and 'the environment' that this interpretive strategy implies. See text for discussion.

In essence, this principle contends that whatever it is that makes us human must surely be revealed to us through an analysis of the absolute and relative sizes of functionally specified regions in the brain of members of the genus *Homo*.

Accordingly, while I will discuss the content and activity patterns of the p.d.NTs in a number of cortical and subcortical structures, ultimately my analyses will focus on only those regions that underwent significant allometric increases in size. This explains why I will pay particular attention to the activities of DA in the prefrontal cortex (PFC)¹¹. The PFC is the region of the brain that has exhibited the most significant relative increases in size. By way of the application of the principle of proper mass we may very easily conclude that it was critical to the evolution of the cognitive capacities, and indeed culture (Laughlin et al., 1990), of our species.

This, then, is one of my main tasks: to assess [where data permit] the quantitative importance of DA, 5HT, ACh, and NE in the brain regions known to have exhibited statistically significant allometric increases in size.

...

¹¹ I am grateful to professor Charles Laughlin for suggesting that I look at DA in the PFC.

2.4 A Question of Operationalization

Methodologically, the question still remains: how can I operationalize the absolute and relative importance of the various p.d.NTs in the brain regions known to have undergone allometric increases in size in the genus *Homo*? As the neuroscientifically-inclined reader will appreciate, we can, and will, look at a variety of bio- and histochemical measures: (1) endogenous NT levels [a measure of content]; (2) in vivo NT synthesis [a measure of metabolic activity]; and (3) regional differences in the content and activity patterns of DA, NE, 5HT and ACh. In other words, just as we will confront the operationally and thus theoretically crucial distinction between the effects of nutrition on NT synthesis versus release, so too will I address the very important distinction between brain NT content versus activity. What we conclude on the basis of these distinctions will reveal much about the relationship between methodology and theory. Rest assured, I will render the larger theoretical ramifications of these finer distinctions quite clear in Parts 3 and 4.

2.5 Methodological Restrictions

It has been suggested that

neither the special characteristics of humans, nor the limiting nature of the fossil record, must be allowed to limit the questions we seek to ask about the evolution of our own species...The main task facing paleo-anthropologists...[is to show how human] uniqueness can

be the product of processes that are themselves general to all living matter (Foley 1987:274).

For the purposes of clarification: the importance of the transformation of amino acids into chemical agents of information transfer in the central nervous system (CNS) is not unique to humans but is, rather, general to all living matter. Indeed, it is a very old relationship.

Evolutionally, the appearance of transmitters precedes that of the nervous system, with several of these substances occurring within single celled organisms, such as Protozoa, as well as in simple multicellular organisms...In these instances, the "neurotransmitters" may act as intracellular regulators of metabolism...With further evolutionary progression, it has been proposed that these same substances advanced from intracellular to intercellular messengers, culminating eventually with their participation in the rapid intercellular communication mediated by nerves (Wallace 1988:431).

My interest, then, in assigning NTs (or more precisely, their amino acid substrate precursors and related biosynthetic cofactors) the status of "independent variables" in the process of hominid encephalization and neurocognitive evolution satisfies this methodological prerequisite. Given the relative antiquity of NTs vis a vis the actual development of the nervous system proper, this seems an eminently persuasive position to adopt. It goes without saying that amino acids were the building blocks of life on earth.

...

2.5.1 In Terms of Formal Logic

While it is true, I am assigning NTs amino acid precursors the status of independent variables in the process of hominid brain and cognitive evolution, I must emphasize the fact that I can only assign them a "necessary but not sufficient" role. My position is best summarized with reference to the work of the biogenetic structuralists:

...for every event in consciousness there is a corresponding and causally interrelated physiological event. However, the opposite does not hold true. A physiological event may or may not be matched by an event in consciousness. A more technical way of saying this is that, whereas an event in consciousness is a sufficient condition for a physiological event, a physiological event is merely a necessary condition for an experiential event...(Laughlin et al., 1990:92).

In other words, I cannot assign NTs and their amino acid precursors causal significance. I can at best invoke the concept of a "co-producer". This recognizes the paramount importance of genetic factors governing CNS complexity. Amino acids could at best interact with genetic mechanisms to co-produce the process of change. This would occur as a consequence of positive feedback effects, i.e., autocatalysis.

2.6 Conclusions and Summary

To place this thesis in a larger historical context I admit: just as the classical interpretive paradigms of the 1950s were

developed as a partial response to the human rights and anti-racist struggles of the day (see Haraway 1988 in historical review), and later re-interpretations reflected the abhorrently very necessary (if only partially realized) self-correcting mechanisms of the Euro-American feminist movement of the '70s (ibid). So too is this thesis a product of contemporary intellectual forces. We refer to (1) the theoretical legacy of two decades of neuroscientific research on 'the biological basis of behaviour' as suggested by an understanding of the neurochemical and cognitive deficits associated with such neuropsychiatric conditions as stress, Parkinson's, Alzheimer's, Schizophrenia and Huntington's. And (2) very recent attempts within the confines of anthropology to establish the metabolic, energetic, nutritional and ecological constraints on brain evolution (i.e., Clutton-Brock 1977; Clutton-Brock & Harvey 1977, 1980; Eisenberg & Wilson 1978; Martin 1981, 1982, 1984; Gibson & Parker 1982; Armstrong 1983; Blumenberg 1983; Gibson 1986, 1993; Milton 1988; Crawford & Marsh 1989; Foley & Lee 1992; Speth 1992; Southgate 1992; Leonard & Robertson 1992; Oftedal 1992).

By superimposing (in a manner consistent with Jerison's "principle of proper mass") the chemical neuroanatomies and cognitive functionalities of DA, NE, ACh, and 5HT onto contemporary models of hominid brain and cognitive evolution, I hope to demonstrate how the general biological principle of NT synthesis in functionally-specified regions of the brain known to have exhibited

significant increases in size can account (in an admittedly 'necessary but not sufficient' manner) for the evolution of higher-order cognitive capacities of the genus *Homo*.

This, then, is my methodological impetus. I do not deny the imperatives of the dominant epistemology. Rather, I accept, by default of the nature of the inquiry, a license to develop a speculative thesis that warrants further scrutiny and testing.

3.0 A PRIMER FOR NEUROSCIENTISTS

In this chapter I will acquaint the neuroscientifically trained reader with some of the issues dealt with by anthropologists. I will begin by debunking a popular myth and deconstructing a scientific one. Then, in the spirit of ensuring a common baseline of understanding, I will provide some basic details regarding the classification of primates, major primate divergence dates and degrees of genetic relatedness, and current debates concerning hominid phylogenesis. The discussions pertaining to "optimal foraging theory" and "bioculturalism" are particularly important.

3.1 Popular and Scientific Myths

The first thing the non-anthropologically trained reader needs to know is that there is no such thing as a "missing link". Granted, "there is an almost complete fossil gap from 8 to 4 myBP [million years before present]" (Eccles 1989:13), but this in no way challenges the idea that hominids and pongids (that is, chimpanzees) last shared a common ancestor 5 to 9.2 mya (Eccles 1989:14). It only means some questions about the transitional form[s] remain, as yet, unanswered.

The next thing the non-anthropologically trained reader needs to know is that the thinking in our discipline has likewise been

conditioned by the theoretical initiatives of pioneers in our field.

For Sherwood Washburn in 1950, what distinguished hominids from apes was a decisive difference in the shape of the ilium and its gluteal muscles. The recent discoveries and analyses of the pelvises of the South African man-apes had established that modern humans and the small brained australopithecines both walked upright; for Washburn, that meant that bipedalism was a behavioural complex fundamental to the meaning of being human...**Examining the foundation of the human way of life would mean deriving the consequences of a great primary adaptation** (Haraway 1988:223).

Not surprisingly, then, the story of human evolution usually begins with a discussion of the advent of bipedalism. This we know was accomplished first by *Australopithecus africanus* some 3.6-3.7 mya (Leakey & Hay 1979; Eccles 1989:52)¹².

The third understanding of critical importance is the knowledge that in the popular as well as scientific imagination "technology has...an extraordinary scientific mythic significance" (Haraway 1988:223)¹³. This relates to the assumption that one of the main consequence of bipedalism was the freeing of the hands to make tools. As Haraway quite insightfully provides:

With the primary humanizing adaptational complex [of bipedalism], **the animal adopted the behavior to remake itself. This is the key mythic element of evolutionary scientific humanism.** In this framework, culture means,

¹² See discussion below.

¹³ Witness, for example, the beginning for the movie 2001: A Space Odyssey.

first of all, tools. Culture remakes the animals; the persistent Western dualism between nature and culture is resolved through a self-making productionist dialectic...Man is his own product; that is the meaning of the human way of life (Haraway 1988:223; emphasis mine).

This thesis is not immune to these historical forces. In fact, the idea that gradual increments in technological ability may have enhanced the range of foodstuffs and hence nutrients available to our hominid ancestors is central to my thesis.

The fourth insight of some value is that

it has long been assumed that many of the unique biological and behavioural characteristics of modern humans evolved in response to the selective pressures of a predatory existence (Trinkaus 1986:107).

However, the importance of meat eating and systematic hunting in the early stages of human evolution is not supported on the basis of the archaeological record (e.g., Isaac 1971; Hladik 1981; Isaac & Crader 1981; Teleki 1981; Mann 1981; Blumenschine 1987, 1992; Behrensmeyer 1986; Trinkaus 1986; Potts 1988; Blumenschine & Cavallo 1992). Neither has the uniqueness of human tool use stood up against the careful scrutiny of non-human primate foraging behaviour. Chimpanzees use tools in ways that effectively challenge the view that technology was an exclusive and therefore critical aspect of human uniqueness (see various articles in Gibson & Ingold 1993). These findings have prompted investigators to consider other factors that may have been critical in the process of human

evolution. In Chapter 6 I will review the theories of brain evolution that have enjoyed or have gained special prominence.

3.2 Everything You Need To Know But...

This section is devoted to bringing the reader up to speed regarding the way in which physical anthropologists have come to view the process of human evolution. It is by no means a comprehensive treatment but it will establish a common baseline of understanding. Later, when we look at statistical models of brain evolution that compare the sizes of various brain regions between human and non-human primates we will be able to refer back to these details.

3.2.1 The Short Story of Inexorable Ascent

By way of a loose but standard interpretation, after we climbed out of the trees and stood on two feet, we evolved many behaviours that - either in kind or degree - served to distinguish us from the apes. We made baby slings, carrying containers, digging sticks, stone tools, and eventually weapons for hunting and defense. We also engaged in co-operative forms of gathering and hunting, learned to communicate complex ideas with symbols in the form of language, and evolved fire, art, and burial rites. Ultimately we created home bases, formed seasonally variable but [matrilineally ?] stable social groups, divided up our labour

according to hierarchical notions of gender, status, age, and power, and advanced beyond the confines of sub-Saharan Africa into Europe and Asia. In the inexorably long process of achieving this level of organizational complexity we grew brains [as Foley (1987:1) suggests with a singular wit] "far too big for comfort"!

The standard argument is that the reason we came out of the trees was because the tropical forests were receding. This was a result of environmental changes that began at least 10 mya in the late Miocene (Foley 1987:Chapter 5). As global temperatures declined, the vast expanses of the African tropical rainforest were broken up. These changes were further compounded by the effects of glacial/interglacial cycles [as many as eight in the middle and late Pleistocene alone, occurring every 100,000 years (Foley 1987:108)]. To escape the more intense levels of competition in the tropical refugia, our ancestors slowly moved into various savanna mosaic environments. This we can formally define as diverse and continuous set of tropical habitats comprised of wooded savanna, bush savanna, and grass savanna (Foley 1987:100). The common denominator is that, unlike the tropical rainforest, these environments were seasonal. That is, they received between 250 and 2000 mm of rain per annum. This translates into a dry season of anywhere from 2.5 to 10 months a year (Foley 1987:197). This significant axis of variability created new selection pressures for our ancestors. That is, they created new reasons for our ancestors to innovate in ways they had never needed to before given the

steady climate and plentiful food supplies in the tropical rainforest.

When they walked upon the open savannas they encountered much larger predators and prey in the form of carnivores and roaming herds of ungulates. This so-called 'meat on the hoof' would have provided our ancestors with a valuable alternative source of protein. This need (even if not persistent) would have been rendered acute in the long dry season when resource competition and depletion was high. In other words, the reduced energetic yields associated with the dry season would have provided our ancestors with ample incentive to explore the use of this alternative source of energy. Scavenging for bone marrow, fat, and animal flesh probably have arisen in this context: out of sheer caloric necessity.

We can very easily predict, then, that the extent to which our hominid ancestors were more or less adept at surmounting the challenges of a seasonal environment would have been a significant factor in the process of human evolution. This, then, is exactly why technology possesses such extraordinary scientific mythic significance (Haraway 1988). The use of wood, bone, and stone tools enabled us to exploit a progressively wider range of food resources than we would have been able to access had we been restricted to using our hands, nails and teeth. The implication is that technology enabled our ancestors to enhance their net caloric

energy yields. This in turn would have conferred positive benefits for our ancestors' survival and reproductive abilities (not to mention our ability to sustain larger social groups which were the foundation of the human way of life).

This, then, is the short story of the inexorably long process of human evolution¹⁴. Quite simply: "the success of *Homo sapiens* had a great deal to do with how well humans exploited the dietary resources of their environments" (Katz 1987:42). As we will see below, implicit in this formulation is the idea that it was our ancestors' ability to maximize net energetic returns in the face of decreasing seasonal and competitive odds that was the defining criteria of human evolution. Current theories on brain evolution reinforce the idea that metabolic factors are limiting (Martin 1981, 1983; Armstrong 1983) and thus probably highly significant (Foley & Lee 1992; Leonard & Robertson 1992). The unique focus of this thesis will complement and extend this level of analysis.

3.2.2 Classification of Living and Extinct Primates

Figure 3.1 provides a summary description of the phylogenetic relationships and classifications of living and extinct primates. The purpose of this figure is four-fold: (1) to draw the readers'

¹⁴ For a more indepth discussion on these and related issues the reader is referred to the highly intelligent and comprehensive synthesis of Foley (1987).

Figure 3.1 Phylogenetic relationships and classifications of living and extinct primates (based on Richard 1985; Foley 1987; Eccles 1989; and Jones et al., 1990). Shaded areas in dispute. Numbers 1-5 refer to genetic relationships in Figure 3.4b

attention to the human family tree (lighter shading; boldfaced-terms); (2) to provide the reader with the option of positioning the degrees of genetic relatedness between humans and other primates I will discuss in section 3.2.4¹⁵; (3) to provide an opportunity to understand the phylogenetic significance of the degrees of CNS complexity encountered in various models of brain evolution in Chapter 5; and (4) to ensure a working understanding of the controversy surrounding the inclusion of chimpanzees and gorillas in the family Hominidae (as opposed to Pongidae; darker shading)¹⁶.

I will begin with a discussion of the order of primates.¹⁷ It is helpful to know that living primates fall into "six natural groups...(1) the lemurs of Madagascar; (2) the lorises and bushbabies; (3) the tarsiers; (4) the New World monkeys; (5) the Old World monkeys; and (6) the apes and humans" (Jones et al., 1992:19). This simplifies the necessary complexities of the following discussion.

Living primates can be divided into two main groups: the Prosimi and the Anthropoidea. Prosimians are the more ancient

¹⁵ Ignore, then, the numbers 1-5 because they only have meaning with reference to Figure 3.4b.

¹⁶ Which has necessitated the creation of a new subfamily called Homininae that many authors (including myself) are reluctant to use for purely pragmatic reasons.

¹⁷ This information in this section is based on Foley (1987:8-14) and Jones et al., (1992:19-21).

lineage comprised of lemurs, lorises and tarsiers. Anthropoids can be subdivided into Catarrhini (Old World primates) and Platyrrhini (New World primates), the latter of which has remained an almost entirely arboreal group. The infraorder Catarrhini gives rise to the Cercopithecoidea (or monkeys) and the Hominoidea (apes and humans). The fruit-eating (occasionally omnivorous) baboons and Rhesus macaques¹⁸, and the leaf-eating colobines, are all members of the superfamily Cerceopithecoidea. The superfamily Hominoidea is comprised of humans and their closest relatives the greater and lesser apes. Traditionally, the gibbons (Hylobatide) are referred to as the 'lesser apes', and the Asian orang-utan, pygmy and common chimpanzee, and the gorilla are referred to as the 'greater apes'.

Significantly, the label 'great apes' used to be synonymous with pongids (referring the family Pongidae). Recent genetic evidence has, however, forced researchers to be self-conscious of their use of the latter term¹⁹. This leads us directly into the debate concerning the recent classification of the great apes as *hominids* as opposed to *pongids*.

Originally, orang-utans, gorillas and chimpanzees used to be classified as belonging to the family of Pongidae. Only humans and

¹⁸ Groups whose brains have provided neuroscientists with a basis for extrapolating the human neural condition.

¹⁹ For that reason we draw the readers' attention to the fact that they encountered the term earlier in the phrase the 'hominid-pongid split', and will yet again encounter the term pongid on the X-axis of various bar graphs in Chapter 5.

their direct ancestors had membership in the family Hominidae. Recently, however, it was determined that humans, chimpanzees and gorillas shared a much closer genetic relationship to one another than any of them did to the Asian orang-utan (Foley 1987:10-13). In formal classification terms, this meant that (1) the great apes would have to be included in the family Hominidae, and (2) a new name would have to be invented to refer exclusively to humans and their direct ancestors. The subfamily name Homininae (hominines) was thus created. Hominines, then, has come to replace the more traditional referent hominids in the more recent literature.

In this thesis, however, I strictly avoid the usage of the term hominines. This is justified on the grounds that my purposes are best served with reference to the original term. The various comparative neurological models of brain evolution that we will encounter in Chapter 5 suggest the necessity of this approach. For the sake of consistency, I will allow the term pongid to include chimpanzees and gorillas, preferring instead the term hominid for humans and their direct ancestors. Quite simply, the use of the term hominine "would lead to considerable confusion given that the term hominid has been used extensively to describe humans and their direct ancestors" (Foley 1987:13).

The controversy surrounding the creation of new subfamilies notwithstanding, hominids can be divided into two major genera (*Australopithecus* and *Homo*) and as many as seven related species.

The boldfaced terms in Figure 3.1 (highlighted on the basis of their direct ancestral relationships to humans) convey the taxonomic complexities of this observation. These phylogenetic complexities are best understood, however, with reference to two separate discussions. In section 3.2.3 I will discuss the temporal occurrences of various hominid species in the fossil record. In section 3.2.4 I will provide the reader with a brief description of the various competing phylogenies that have been constructed to explain the process of hominid phylogenesis.

3.2.3 A Temporal Analysis of Hominid Phylogenesis

The earliest stages of human evolution occurred in Africa during the late Pliocene and early Pleistocene (i.e., 2.5 - 1 million years ago; a period commonly referred to as the Plio-Pleistocene because it straddles two geological epochs). This period in geological time saw the emergence of two hominid genera: Australopithecines and Homo, and as many as seven related species: the "gracile" or lightly built (1) *Australopithecus afarensis* and (2) *Australopithecus africanus*; the very large or "robust" (3) *Australopithecus robustus*, (4) *Australopithecus boisei*, and (5) *Australopithecus crassidens*, and finally (6) *Homo habilis* and (7) *Homo erectus*. Then, in the late Pleistocene we saw the emergence of *Homo neanderthalensis* and archaic as well as modern *Homo sapiens*. All of these hominid groups were - with the clear exception of the robust australopithecines, and the ambiguous exception of the

neanderthals - ancestral to modern humans. Many of these late Pliocene and early Pleistocene species overlapped in time and space; that is, were sympatric. In fact, between 4 and 1 million years ago all of these species were represented at one time or another in the fossil record (Foley 1987:239 in review). What remains to be determined, however, is the extent to which these species coexisted and overlapped ecologically.

Archaeological evidence to date suggests that whereas *Homo habilis* and the robust australopithecines may have coexisted, so too did *Australopithecus boisei* and *Australopithecus africanus*. Both of these conclusions derive from studies of the East African archaeological site at Omo. Studies at Koobi Fora and Olduvai (East Africa) also reveal the coexistence of *Homo erectus* and *Australopithecus boisei*. I find these observations particularly fascinating in light of the interpretations accorded an understanding of the differences in dental and craniofacial architecture exhibited by the gracile and robust australopithecines and *Homo habilis* (Robinson 1954 cited in Mann 1981; Grine 1984; Sakka 1984; Wood 1984; Ryan & Johanson 1989).

Parenthetically, the molars, jaws and masticatory apparatus of the robust and hyper-robust australopithecines were very large in comparison to those of the so-called gracile lineage (which includes *Australopithecus afarensis*, *A.africanus*, and *Homo habilis*). By comparison, then, to the robust lineage, the relative

sizes of the gracile members' incisors and canines were much larger than their molars and premolars. This selective reduction in the so-called tooth-grinding complex of the gracile lineage suggested distinct differences in the type - and perhaps quality - of their diet relative to that of the robust line. The consensus seems to be that the robust lineages' lack of association with stone tools may have restricted them to a hard-covered pulpy fruit, nut, and other coarse diet that would have required a heavier masticatory apparatus (e.g., Mann 1981). On the other hand, it is assumed that our ancestors' use of tools enabled them to access a much wider range of foods; that is, opportunistically foraging or otherwise systematically consume bone marrow, animal flesh and fat. This idea is reinforced in the context of the assumption that their technological ability to first access then pre-masticate otherwise inaccessible foods (that is, render them texturally and compositionally accessible and digestible) would have favoured a selective reduction in their posterior tooth-grinding complex and related masticatory apparatus.

Clearly, the robust australopithecines were occupying a distinctly different dietary niche than our ancestors. And this was no doubt reinforced in the context of their failure to be associated with any stone tools (Mann 1981). While they were probably specializing on hard food items (see footnote number 8), our ancestors were increasingly engaging in a form of dietary eclecticism that bordered on (and eventually became) established

omnivory. This, of course, was a strategy borne of the advantages of using various wood, bone and stone tools to surmount the nutritional difficulties of living in a highly seasonal environment²⁰. As problematic as this sounds, it would be tempting to try and model the potential neurochemico-metabolic differences of these alternative foraging strategies (i.e., by way of application of the principle of optimization as discussed in section 3.5.1.). For the moment this remains a tangential aside.

Two major events occurred during the early Pleistocene: habilis was replaced by erectus (1.8-1.6 MYA) and australopithecines became extinct (approximately 1 MYA). So, from about 1.6 to about 400,000 years ago *Homo erectus* was the only living member of the genus *Homo*. Curiously, *Homo erectus* exhibited few changes during this period despite the fact that this is when our ancestors moved beyond the confines of sub-Saharan Africa into Asia and Europe. Significantly, it was not until approximately 400,000 years ago that this pattern of morphological stasis begins to break down. Then we see a whole series of complex multi-regional events that scholars are still having difficulty interpreting the phylogenetic significance of²¹. The nature of this confusion is

²⁰ Where 'meat on the hoof' and underground storage organs would have provided a valuable source of energy, and essential amino acids, in times of heightened resource competition and depletion.

²¹ Witness, for example the debate between various prominent advocates of the so-called "African Genesis" versus "multi-regional hypothesis of human evolution" documented fully in The Yearbook of Physical Anthropology (1992).

clearly evident in the construction of the various hominid phylogenies depicted in Figures 3.3 and 3.4 (discussion see section 3.2.6).

This period from 400,000 to 200,000 years ago witnessed the transition from *Homo erectus* to our species, *Homo sapiens*. The transitional forms that first appeared in the archaeological record some 300,000 years ago are referred to as archaic *Homo sapiens*²². Cro-Magnon Man refers to the archaic species appearing in the fossil record around 100,000 years ago. Neanderthal, of course, refers to the "morphologically distinct group of hominids found in Europe and parts of Asia between 100,000 and 50,000 years ago" (Foley 1987)²³. These were the curiously large (transitional ?) forms that I referred to in Figure 3.1 as *Homo neanderthalensis*. While their status in relation to humans is far from clear, their presence in the fossil record from, say, 50,000 years ago has fuelled even the popular imagination.

'Lest we get embroiled in unnecessary complexities, however, I remind the reader quite simply that "the replacement of the archaic forms of *Homo sapiens* by anatomically modern *Homo sapiens sapiens* is one of the longstanding problems in paleoanthropology"

²² We will encounter this term in some ecological models of brain evolution in Part 4.

²³ 150,000 to 30,000 years by other estimates (Jones et al., 1992:251).

(Foley 1987:32). In other words, much of this summary is for information content alone.

Whereas the family Hominidae appeared 6 MYA, members of the genus *Homo* did not appear in the fossil record until approximately 2 mya. Then, 200,000, years ago we witness the birth of our species, *Homo sapiens*. Only 100,000 years ago our unique subspecies *Homo sapiens sapiens* appear in the fossil record. The period of temporal and possible ecological overlap with the neanderthals ended abruptly approximately 30,000 years ago. This is the point in the archaeological record where only the fossilized remains of anatomically modern humans (that is, *Homo sapiens sapiens*) can be found. In other words, by 30,000 years ago we were the only representatives of the hominid family left alive on the globe. It was "one long argument"²⁴ in which our ancestors appear to have triumphed.

While I cannot offer any resolution to the archaeologically complex problems of upper Pleistocene hominid phylogenesis²⁵, I can draw the readers' attention to the fact that the morphological differences between the curiously large neanderthals and other archaic *Homo sapiens* may suggest subtle dietary differences. This

²⁴ A pithy description of the process of human evolution that was coined by a prominent anthropologist whose name I cannot recall.

²⁵ As effectively summarized in the "African Eve/Genesis" versus "multi-regional hypothesis" debate which I do not herein intend to pursue.

A

B

Percentage difference in base nucleotide sequences of DNA between selected pairs of primates

(1) Human/chimpanzee	2.5
(2) Human/gibbon	5.1
(3) Human/green (Old World) monkey	9.0
(4) Human/capuchin (New World) monkey	15.8
(5) Human/lemur	42.0

Figure 3.4 (A) An evolutionary tree for primates based on globin and mitochondrial gene sequences (redrawn from Jones et al., 1992:320). The pattern represents a consensus, although the relationship between humans, chimpanzees and gorillas remains the subject of continued debate. Bars indicate the ranges of estimates for the branch points. (B) Table comparing the percentage differences in base nucleotide sequences of DNA between selected pairs of animal species (from Stebbins 1982 cited in Eccles 1989:9). Numbers in parentheses can be understood with cross-reference to Figure 3.1. This permits direct comparison of taxonomic and genetic relationships. See text for discussion.

them with an optimal metabolic "solution" to the "problem" of a newly inherent genetic potential ?

For the present purposes it is enough to recognize that in the course of human evolution our ancestors jostled for evolutionary supremacy with a number of sympatric groups. And that "for a period of at least 2 million years there was more than one hominid species, probably living sympatrically" (Foley 1987:223). Interestingly, the differences that separated these groups were most pronounced, it seems, in the areas of dental and craniofacial morphology, technology and diet²⁷. I will return to these and related issues in Part 4.

3.2.4 Models of Hominid Phylogenesis

This section picks up where the last one left off: in the area of hominid phylogenesis. In this section, however, I am preoccupied with explaining the various phylogenies that have been constructed to account for the temporal and spatial complexities observed in the archaeological record. I will restrict myself to explaining only the most salient points (Figure 3.2).

To paraphrase Foley (1987:36): *Australopithecus afarensis*, the earliest known hominid taxon, is generally thought to be ancestral

²⁷ We will not speculate on the importance of language or various forms of social organization in this thesis.

Figure 3.2 Alternative phylogenies for early hominid evolution (redrawn from Foley 1987:34, Figure 2.11). (a) Walker & Leakey 1978; (b) Johanson & White 1979; (c) Skelton, McHenry & Drawhorn 1986; (d) a model showing early divergence of the robust australopithecines and speciation within *Homo*. *Homo sp.* = *homo indeterminate*. Whereas all models agree *Homo habilis* and *erectus* are ancestral to humans, and the robust australopithecines are not, the contribution of the gracile australopithecines (*afarensis* and *africanus*) are still hotly debated. See text for discussion.

to all later forms. However some models argue for earlier divergence (that is, some models argue that while *afarensis* was ancestral at least in part to *A.africanus*, it may also have given rise to other species). *Australopithecus africanus* is considered by some to be ancestral to both the robust australopithecines and the genus *Homo* (Figure 3.2c). Interestingly, the fossil record has also been interpreted as suggesting a split between the australopithecines and *Homo* before the appearance of *A.africanus* (Figure 3.2b). The fact, however, that the robust australopithecines diverged from the line leading to humans is not in dispute. The only question that has surfaced is one pertaining to the actual number of robust species. Finally, Figure 3.2d provides us with the added understanding that while the status of *Homo habilis* as the first member of the genus *Homo* is somewhat misleading because it belies the possibility that there may have been more than one taxon of *Homo* before the appearance of *erectus*.

Turning now to Figure 3.3, we see (a) a simple unilineal model; (b) a classic view with neanderthals as a side branch; and lastly (c) a model that attempts to reconcile the evidence for our African origins with the multi-regional complexities of the archaeological record. Interestingly, the first model positions neanderthals between archaic and modern *Homo sapiens*. This complements what some researchers have argued (i.e.) that neanderthals, far from being genetically isolated and extinct, genetically drifted (as it were) into the sapient pool (i.e.,

Figure 3.3 Alternative phylogenies for later hominid evolution (redrawn from Foley 1987:35, Figure 2.12). (a) simple unilinear model; (b) classic view with neanderthals as a side branch; (c) based on Andrews 1984a. The latter model attempts to take into account the multiregional nature of human evolution while at the same time giving preeminence to the hypothesis that our ancestors evolved out of Africa. See text for further discussion.

interbred with ancestral forms). The second model denies this possibility. This last model, while in agreement with the second, insists that the European, Indonesian and Asian erectus finds were all extinct sidebranches.

Very obviously, I cannot say for sure what phylogenetic scenarios were most likely to have occurred. But I can draw attention to the fact that anthropologists are increasingly sensitive to their obligation to construct phylogenetic models that take into account the multi-regional nature of human evolution. For neuroscientists, then, it should be clear: just as we can detect only that which the 'power' of our methods, techniques, and interpretive paradigms allow us to see, so too do we observe that even within the confines of physical anthropology "as goes archaeology, so goes evolutionary theory".

3.2.5 Divergence Dates and Degrees of Genetic Relatedness

In the continued spirit of ensuring a common baseline of understanding I refer the reader to Figure 3.4. This provides a quick summary of the divergence dates of the major hominoids (Figure 3.4a) as well as the degrees of genetic relatedness between humans and selected primates (Figure 3.4b). It is understood that some of these primates will be encountered in later chapters.

A

B

**Percentage difference in base nucleotide sequences of DNA
between selected pairs of primates**

(1) Human/chimpanzee	2.5
(2) Human/gibbon	5.1
(3) Human/green (Old World) monkey	9.0
(4) Human/capuchin (New World) monkey	15.8
(5) Human/lemur	42.0

Figure 3.4 (A) An evolutionary tree for primates based on globin and mitochondrial gene sequences (redrawn from Jones et al., 1992:320). The pattern represents a consensus, although the relationship between humans, chimpanzees and gorillas remains the subject of continued debate. Bars indicate the ranges of estimates for the branch points. (B) Table comparing the percentage differences in base nucleotide sequences of DNA between selected pairs of animal species (from Stebbins 1982 cited in Eccles 1989:9). Numbers in parentheses can be understood with cross-reference to Figure 3.1. This permits direct comparison of taxonomic and genetic relationships. See text for discussion.

Figure 3.4a is an evolutionary tree for primates based on globin and mitochondrial DNA analysis (redrawn from Jones et al., 1992:320). Significantly, humans, chimpanzees, and gorillas diverged from one another between 4 and 10 million years ago (mya). And the orang-utan lineage diverged from all three approximately 12-19 mya. Also, whereas the gibbon lineage diverged between 13 and 22 mya, the Old World monkeys (OWM) split off from the human evolutionary tree somewhere between 24 and 33 million years ago. The bars indicate the range of estimates provided for these divergence dates.

Figure 3.4b provides us with the added understanding (enhanced more fully with reference to the numbers 1-5 superimposed on Figure 3.1) that humans and chimpanzees possess an almost identical genetic blueprint. With the exception of a mere 2.5% difference in base nucleotides between humans and the chimpanzee, we are the same genetically. This is the most perplexing problem of human evolution. Once again: what accounts for the fact that human beings are endowed with a much greater degree of cognitive and behavioural flexibility than their minimal genetic differences would seem to predict or allow? The theoretical perspectives that have thus far been developed to explain this paradox (e.g., Laughlin et al. 1990 with reference to the work of Changeux) provide clear, albeit indirect, support for my interest in the structural and functional effects of neurochemical activities (discussion Part 4).

3.3 Anthropological Approaches to Questions of Diet

While I will never be able to reconstruct hominid diet as precisely as my preoccupation with NT amino acids (etc.) requires, partial theoretical recourse is provided by way of the application of "optimal foraging theory" (e.g., Smith 1983; Stephens & Krebs 1986; Kurland & Beckerman 1985) and the tenets of bioculturalism (Katz 1987; Armelagos 1987).²⁸

Optimal foraging theory is a *predictive* model based on the fundamental importance of maximum caloric energy acquisition. Bioculturalism, on the other hand, is an *adaptive* model based on an understanding of the fundamental importance of food to the success of the interaction between biological and cultural mechanisms of adaptation (Katz 1987). Both seek to understand the adaptive logic of certain dietary practices. However, whereas optimal foraging theory does so from the operational standpoint of the importance of energetic/metabolic returns, bioculturalism does so from the operational standpoint of the effects of specific nutrients on the expression or suppression of certain genetically inherited phenotypic potentialities (e.g., Katz 1987). In effect, then, just as optimal foraging theory is interested in predicting "the degree of best fit" between energetic expenditures (vis à vis foraging activities) and caloric returns, so too is bioculturalism is

²⁸ I am once again indebted to Charles Laughlin for suggesting the merits of the optimal foraging paradigm.

interested in modelling the degree of best fit between biological and cultural mechanisms of adaptation. The latter definition provides a clear statement of my own theoretical interests - hence the title of this thesis. I will expand on these definitions below.

3.3.1 Optimal Foraging Theory

Optimal foraging theory is an interpretive paradigm used by anthropologists to "predict behaviours related to the acquisition of specific nutrients" (Chafetz 1990:10). It assumes, on an *a priori* basis, that all organisms seek to maximize calorie intake and minimize energetic expenditures. It is, you might say, the pleasure/pain principle of foraging: Pleasure:caloric consumption::Pain:energetic expenditure. Another way of defining this anthropological paradigm is to compare it to the neurologic "principle of proper mass" (Chapter 2). The principle of proper mass allows us to predict what regions and structures of the brain may have played a more significant role in the life of any organism - based on a comparison of absolute and relative sizes. In an analogous manner, so too does optimal foraging allow us to predict what hominid dietary biases would most likely have been selected for in a Darwinian sense - based on a cost/benefit analysis of the net energetic gains associated with the consumption of specific classes of foods (i.e., prey versus patch). The relevance of optimal foraging theory to the construction of my own thesis can

best be understood with reference to what the theory both stresses and advocates.

Optimal foraging theory stresses the comparative method. It insists that we must first identify the problems facing an organism. Then it asks that we predict the one "optimal solution" to the problem we identify. That is,

the one among a **range of alternatives** [the range being the "phenotypic set"] that maximizes benefits and minimizes costs. This in a way amounts to making a prediction about what should evolve. It consequently provides a template of the 'perfect adaptation' [the optimal phenotype] against which we can measure what actually did occur. In effect this is way of modelling the selective pressures operating on an organism... (Foley 1987:65).

If we view, for instance, the unusual precursor dependence of the prefrontal cortex (Deutch & Roth 1990:375) as a "problem", and enhanced precursor acquisition as the "optimal solution", optimal foraging theory then allows us to predict the following: the hominid group whose foraging strategy was optimally suited to the task of satisfying the unusually high precursor demands we know the PFC makes on the amino acid/protein content of diet would be selected for in a Darwinian sense. So too might we allow this analyses of the high content and activity patterns of the p.d.NTs in those very brain regions that exhibited significant allometric increases in size to suggest other such arguments. Very obviously the internal logic of the paradigm has helped me construct various

hypotheses that can perhaps one day be tested against the archaeological record.

The only aspect of optimal foraging theory that is not compatible with this thesis is the paradigm's traditional emphasis on the acquisition of caloric energy to the exclusion of all other nutritional requirements. Fortunately, however, the insights of two prominent anthropologists help me justify my current preoccupation with dietary amino acids²⁹.

As Casimir observes

Special, seasonal hunting and gathering activities should not be viewed as aspects of primary energy acquisition. It can be very meaningful to expend large amounts of energy in order to obtain small quantities of [say] vitamin C, certain essential amino and fatty acids, or specific minerals (Casimir in reply to Smith 1983:643).

Indeed,

a diet which maximizes calories per unit time might only be adaptive at times of extreme food shortage. A partially satiated predator might do better to specialize on a prey with a high amount of some needed nutrient rather than stick to the diet which maximizes caloric intake. **The diet which maximizes fitness may not be the diet that maximizes the rate of caloric intake** (Pulliam 1974:70).

²⁹ That is, the manner in which the development and ongoing maintenance of the brain imposes significant neurochemico-metabolic demands on the essential amino acid content of diet (Wurtman and colleagues; and by extension of Brown et al., 1979; Goldman-Rakic & Brown 1982; Deutch & Roth 1990. Discussion Part 3).

This is exactly my point - i.e., with reference to the effects of variations in amino acid availability on brain NT synthesis. In Part 3 I will provide structural, functional, developmental, neurochemical, and electrophysiological evidence in favour of the possibility that (all things being equal but caloric factors aside) the hominid foraging strategy that maximized an individuals' access to NT amino acid (and related nutrient co-enzyme) supplies - especially at critical developmental stages - may in fact have been the one that maximized adaptive fitness!

3.3.2 Bioculturalism

Bioculturalism can loosely be defined as an attempt by anthropologists to understand how specific nutrients affect the nature of the interaction between biological and cultural mechanisms of adaptation. Witness, for example, (1) the paradoxically positive benefits of inherently toxic fava bean consumption in heterozygous female carriers of the glucose-6-phosphate dehydrogenase deficiency (G-6PD) gene who are also susceptible to parasitic malarial infection; (2) bitter manioc consumption in relation to the incidence of sickle cell anemia; and (3) the more commonly understood relationship between alkali treatment of maize consumption and the pellagra-preventative benefits associated with the consequent liberation of otherwise bound niacin (Katz 1987). This knowledge has been developed under the aegis of bioculturalism.

What this paradigm effectively establishes is that "food consumption provides a clear interface between biological and cultural mechanisms of adaptation" (Katz 1987:44). As Katz would argue, this is because food is endowed with the unique capacity to influence the maintenance of genetic systems. That is, confer adaptive advantages to genetic systems harbouring, for instance, paradoxically fatal but beneficial phenotypic traits. The relevance of this insight to the construction of this thesis is clear: it justifies, in a strictly anthropological context, an interest in the transgenerational phenotypic effects of developmental variations in NT amino acid availability. It provides, in other words, a clearly anthropological framework in which to discuss the many ways in which subtle aspects of diet may have conferred adaptive advantages to genetic systems harbouring, for instance, "positive" mutations favouring the expansion and structural, functional and neurochemical reorganization of particular cortical and subcortical structures in the brain (e.g., neocortex, hippocampus, amygdala, striatum, prefrontal cortex).

I can also express this point in the very terms that Katz (1987) used to convey the substance of his biocultural evolutionary approach (which, by the way was centred on the relationship between nutrition and deficiency diseases). Katz equates the "the full nutritional potentials" of foods with a "lock", and the cultural knowledge necessary to liberate this knowledge as the "key" (Katz 1987:57). I find his emphasis on "the full nutritional potentials"

of foods quite stimulating because it has encouraged me to construct one of my own theoretical concepts: that of a "neurochemical potential". This, I would argue, is comprised of the essential amino acids, vitamins, and minerals we discuss in Part 3.

I also find his "lock and key" metaphor quite useful because (putting aside the strictures of his definition) it encourages me to argue that it is precisely those kinds of foods that contain optimal "neurochemical potentials" that are able to unlock the "cognitive potentials" inherent in the brain/genome. This recalls the "safe generalization...that genetic templates transmit potentialities or capacities rather than adult behavioural traits, which is for cultural templates" (Stebbins 1982 quoted in Eccles 1989:222). The benefits, then, of Katz's specific co-evolutionary model to the construction of this thesis is that it encourages me to conceive of the cognitive capacities inherent in the brain/genome as a "lock", and the amino acids necessary for brain NT synthesis as a "key".

As the perceptive reader can appreciate, then, I am using the term **bioculturalism** in the title because it is a descriptive shorthand for an anthropological paradigm that recognizes the quintessential importance of food to the nature of the interaction between cultural and genetic templates. I am appending the term **revisited** because I am operationalizing the biocultural dialectic from a unique interdisciplinary standpoint that emphasizes aspects

of structural, functional, developmental, and especially chemical neuroanatomy. The value of this position can once again be understood with reference to the work of Solomon Katz.

Katz (1987) argues that human evolution is all about a population's "genetic information pool" interacting with its "cultural information pool". These pools, he argues, are characterized by both gradual and saltatory changes in their "information content" over time - which, by definition, is biocultural evolution. In this thesis I too will operationalize the "cultural information pool" in terms of specific nutrients - although in this case it will be reference to the amino acids, vitamins and minerals that mediate the synthesis of the DA, NE, 5HT, and ACh. In contradistinction to Katz, however, I will operationalize the concept of the "genetic information pool" not in terms of deficiency disease states but, rather, in terms of specific brain structures, functions, developmental constraints, and neurochemical anatomies.

This, then, effectively summarizes my interest in optimal foraging theory and bioculturalism. The reader can anticipate that I will use many of their terms of reference (e.g., optimization, phenotypic set, optimal phenotypes, biological and cultural information pools, etc.) to develop my theoretical position.

4.0 A PRIMER FOR ANTHROPOLOGISTS

In this Chapter I will provide the reader with some terms and concepts used by neuroscientists to understand the workings of the brain. It is the task of neuroanthropologists to determine how best to use these findings to develop grand theories to explain the evolution of humanity, culture and the cognitive capacities of **Homo sapiens sapiens**. In the spirit of establishing a common baseline of understanding I will provide some basic details regarding (1) neurotransmitter release and the cellular basis of learning and memory; (2) the homeostatic properties of neurons (based on Zigmond 1994); and (3) the trophic theory of neural connection (Purves 1986, 1988). The impact the work of the biogenetic structuralists (e.g., Laughlin et al., 1990) has had on my thinking will also become apparent. In the first section I will introduce eight issues of interpretive significance.

4.1 Popular and Scientific Myths

4.1.1 Mind As Emergent Property

The first thing the reader needs to know is that, contrary to popular opinion, "understanding the mind may not be as intricate as our vanity hoped or our intellect feared" (Rodolfo Llinas 1986 cited in Churchland 1986:99). Mind appears very likely to be an "emergent property of the brain's electrical and metabolic

activity" (Fischbach 1992:57 stated originally in the form of a rhetorical question). This we know from studying PET scans that provide us with dramatic images of circumscribed patterns of electrical and metabolic activity in various regions of the brain of awake subjects performing a variety of cognitive performance tasks (e.g., hearing words versus seeing, speaking, or generating words¹⁰). Such evidence suggests, in effect, that

mind and brain are two views of the same reality - mind is how the brain experiences its own functioning, and brain provides the structures of mind (Laughlin et al, 1990:13).

This reinforces the view that the ability to experience specific cognitive/emotive states is contingent upon the likelihood of being able to create and/or re-create specific patterns of electrochemical activity in the distributed structures that mediate the structure of the experience.

The emphasis on *metabolic* ability is well placed in the context of our own interest in the limits nutritional factors might place on neurochemico-metabolic activity patterns in the brain. **Might nutritional factors relevant to brain NT synthesis place limits on the range of functions the mind can experience the adaptive structure of?**

...

¹⁰ See images in Fischbach (1992:54-55).

4.1.2 Brain As Metabolic Organ

The second thing the reader needs to know is that the brain is a metabolic organ comprised of hierarchically organized components that interact according to the "bipolar demands of growth and adaptation" (Laughlin et al. 1990:56). This we can begin to understand with reference to Figure 4.1 which depicts the processes of divergent and convergent innervation (redrawn from Purves 1988). As Laughlin et al., (1990) argue, cells that comprise the foundation of all brain work are "intrinsically motivated" (p.43) to expand their temporal and spatial domains of influence (as in the case of divergence). However, they must also adapt themselves to the electrochemical-metabolic barrage of stimuli they receive from other neurons in the "community of cells" (Laughlin et al., 1990:34-36) they physically associate with over both short and long distances (as in convergence). It is the outcome of this metabolic dialogue between cells "competing" (Purves 1988) for trophic and other focused neural attentions that determines, in a manner analogous to the Darwinian notion of survival of the fittest (Rakic et al., 1994) the ultimate organization of the brain and hence the very structure of mind and consciousness (Laughlin et al., 1990).

Another way of expressing this relationship is by way of the understanding that

the target dependent death of innervating neurons, the normal rearrangement of connections in development, and the maintenance of adult connections are all affected by

Figure 4.1 Divergent and convergent innervation (redrawn from Purves 1988:68, Figure 4.8). (A) Each nerve cell axon usually innervates many divergent target cells [in, for instance, different cortical and subcortical structures, regions, and/or laminae of the same or opposite hemisphere]. This one-to-many relationship is called divergent innervation. (B) From the postsynaptic perspective, each target cell may be innervated by many different neurons [which release the same or different neurotransmitters as in the case above]. This relationship is called convergent innervation. Epigenetic modulation of these events (i.e., the selective stabilization of a subset of the particularly active connections) determines the spatial and temporal domains of influence of the NT-specific fibre systems and thus the structural and functional architecture of the brain. See text for further discussion.

the level of electrical activity in the target cells. Thus, the regulatory signals for neuron survival and terminal outgrowth, whatever they may be, are themselves susceptible to the influence of neural activity (Purves 1988:149).

What I am are interested in is how the effects of nutrition on NT synthesis might affect its activity patterns and hence the outcome of the competitive interactions that determine the functional circuitry of the brain. Later I will pursue the idea that variations in amino acid (etc.) availability may constrain or potentiate the ability of some NT-specific pharmacosystems (that is, their worker neurons and related communities of cells) to compete effectively with other neural networks for expanded spatial and temporal domains of influence across the brain. In this sense, then, I am interested in examining how nutritional variables might modulate the outcome of genetically templated but labile processes of divergent and convergent innervation (Figure 4.1). Stated in the extreme, I am interested in **how nutrition affects the development of the structure of the brain and hence the very structure of the mind**. In an anthropological context, I am interested in how our hominid ancestors' diet affected the evolution of the structure of the brain and mind of members of the genus *Homo*, and hence (indirectly) the evolution of culture.

...

4.1.3 Mind As Structural/Functional Hierarchy

The third thing the reader needs to know is that the components that make up the brain can be described as: (1) **synapses**: the smallest unit of information transfer; (2) **neurons**: cell bodies and their fibrous axonal and dendritic processes which send and receive chemically-coded bits of information from other cell bodies that reside in proximal and distal regions of the brain; (3) **neural networks**: that is, the society or "community of cells" (Laughlin et al. 1990:34-36) whose bipolar demands of growth and adaptation interact with those same properties in other neurons to "co-produce...the organization of neural networks" (Laughlin et al., 1990:43); (4) **"neurognostic models"** (Laughlin et al., 1990:57-59): that is, Piagetian-like "schematic structures" of the hypothetical world determined *initially* by genetic instructions but refined in the process of interaction with the world; And (5) **"paleo- and neo-neurognostic structures"** (Laughlin et al., 1990): that is, groups of neural networks and models whose cell bodies reside principally within either subcortical limbic or neocortical regions whose activities mediate the experience of affective and cognitive states (that cannot readily be dissociated except heuristically). This, then, effectively provides us with some working terms and definitions.

...

4.1.4 Biogenetic Structuralism

The fourth thing the reader needs to know is that "any cell or network of cells that has synaptic connections to the target cell or network can potentially **penetrate** the target and influence its current and future activity by exercising positive or negative feedback" (Laughlin et al., 1990:42). This we can envision once again with reference to Figure 4.1 and the process of convergence. Cells that converge on a neuron all influence its current and future activity.

The fifth thing the reader needs to know is conceptual:

this linking up of neurons to form networks, and networks to form even more complex networks and models is a process known as *entrainment*. As the term implies, systems become hooked up (much like railroad cars) to form "trains". Entrainments may be relatively enduring or momentary depending on the function being performed (Laughlin et al., 1990:52).

PET scans provide us with dramatic examples of these kinds of spatial and temporal entrainments. These previously established concepts of "penetration" and "entrainment" will help us invigorate the language and substance of our own theoretical discourse.

Later I will hypothesize that variations in amino acid availability affecting brain NT synthesis (especially but not exclusively at critical developmental stages) may affect the metabolic ability of some NT specific systems to "penetrate" and

thus "entrain" the metabolic machineries of the various members of the communities of cells that make up the hierarchy of the brain. That is, penetrate and entrain the productive activities of the various components of the CNS so as to maximize their own trophic fitness! This could have profound cognitive consequences if we recognize that the cell (or community of cells) in question may reside principally in limbic or cortical regions and will thus be in a position to effectively impose their own metabolically vested interests - their own functional and cognitive agendas - on the rest of the brain.

The sixth thing the reader needs to know is perhaps obvious: the biogenetic structuralists (Laughlin & d'Aquili 1974; Laughlin et al., 1990) have much to teach us. In the context of the present thesis I am fortunate in that I was able to depend on their interdisciplinary thesis to provide me with many significant starting points for my own theoretical discourse. By way of example, I have been heavily influenced by the idea that "the structure of experience is that part of the nervous system mediating experience. And...the structure of experience, being living tissue, develops" (Laughlin et al., 1990:43; italics in the original). This has prompted me to re-examine the implications of the observation that

...factors that influence levels of CA [,ACh] or 5HT in adult neuronal systems must also be assumed to have the potential of altering these same transmitter systems in early embryos. Changes in neurotransmitter levels induced by variations in amino acid availability...may possibly

have long range effects on the morphology, survival or differentiation of cells within the CNS. (Wallace 1988:438).

As suggested above, later I will hypothesize that variations in amino acid availability at critical developmental stages might affect the development of the structures of the nervous system mediating experience and the very structure of experience. I will also pursue the point that these structural and functional changes would accumulate in the "cultural information pool" (Katz 1987) and thus determine (amongst other things) the range and type of behavioural and neurocognitive entrainments its' resident members were both subjected to, as well as able to transmit to, succeeding generations via the effects of observational learning (Part 4).

4.1.5 Methodological Reductionism as Heuristic

The seventh proviso that warrants emphasis is the idea that

it seems quite futile to attempt to account for a particular emotional [or cognitive] state in terms of the activity of one or more biogenic amines...Amines may function separately or in concert at crucial nodes of the complex neuronal networks which underlie emotional [and cognitive] states...(Kety 1972 cited in Eccles 1989:101))

This red flag is well placed in the context of the present thesis. In Chapter 12 the reader will encounter some simplified schematics that attempt to convey the relationships between nutritional

biochemistry and structural, functional, and chemical neuroanatomy. The casual reader may assume I am advocating what the preceding cautions against, but I am not. Clearly, my efforts at fully satisfying (1) the application of the "principle of proper mass" (Chapter 2) to aspects of both structure and chemistry, and (2) the application of the "principle of optimization" (Chapter 3) to aspects of nutrition and developmental neurobiology renders any such assumption false. My interests in constructing a view of the brain that happens to focus on specific NTs, specific neural structures, and specific (attendant) cognitive functions is for purely heuristic reasons. These efforts will merely establish the empirical building blocks of my larger theoretical model.

Our eighth point is clear: no preliminary effort at ensuring a common baseline of understanding can do justice to the many theoretical complexities of the neurosciences.

4.2 Neurotransmitter Release and the Cellular Basis of Learning

Figure 4.2 provides a summary of (A) the process of NT release, and (B) several practical examples of how this process subserves the cellular basis of learning and memory. Figure 4.2A is self-explanatory and in all probability (given the calibre of the

A

B

Figure 4.2 Model (A) provides an image of the process of neurotransmitter release (redrawn from Stevens (1979). When a NT-filled vesicle (1) fuses with the presynaptic lipid membrane (as in 2) it releases its contents (3) into the synaptic cleft. They in turn interact with receptor molecules on the postsynaptic membrane (4). Whether or not the receiving cell propagates the signal (that is, releases NTs from its own distal terminals) depends on whether or not the sum of excitatory and inhibitory inputs on that cell depolarize it sufficiently for an action potential to occur. In model (B) we see several practical examples of how the process of NT release subserves learning and memory (redrawn from Kandel & Hawkins 1992). The left and middle panels depict two cellular mechanisms proposed to subserve neuroassociative conditioning: the 'Hebb synapse' and 'activity-dependent facilitation'. The far right panel depicts the cellular basis of 'long-term potentiation': a neuroassociative process believed to contribute to learning in the hippocampus of mammals. Lighter shade denotes neurons in which coincident activity must occur to produce associative changes in synaptic strength during learning. See text for further discussion.

readership) need not have been provided³¹. The benefits of Figure 4.2B (redrawn from Kandel & Hawkins 1992) is that it helps us understand how the selective stabilization of some synapses can occur. Metaphorically speaking, just as this thesis stands on the shoulders of giants, so too do the activities of associated neurons help one another establish themselves as meaningful participants in a community of living cells. In many respects it is an enlightened form of self-interest operating at the cellular neuronal level.

In the bottom left panel (the Hebb synapse) we see that associative learning can be produced by repeated and coincident activity in both pre-and post-synaptic neurons. In the middle panel we see that associative learning can also occur when there is repeated and coincident activity between the modulatory and presynaptic neuron. The modulatory neuron produces activity-dependent enhancement of NT release from the presynaptic neuron. This also facilitates the selective stabilization of the pre- and post-synaptic neurons (hence the term "activity dependent facilitation"). The far right panel depicts the cellular basis of long-term potentiation (LTP) - a neuroassociative process hypothesized to subserve learning in the hippocampus of mammals. As we can see, not only must coincident activity occur between the pre- and post-synaptic neurons, but retrograde transport of effector (i.e., second messenger or trophic) molecules must also

³¹ For a thorough discussion of the process of NT release the interested reader is referred to, for instance, Stevens (1979).

occur (as indicated by the arrows). As Kandel & Hawkins (1992) explain, "this retrograde factor then diffuses to the presynaptic terminals to activate one or more second messengers that **enhance transmitter release** and thereby maintain LTP" (p.85).

While this represents the broadest of surveys, the point is this: nutrition can affect NT synthesis and release and thus create the metabolic preconditions for learning to take place. Learning takes place at the level of the synapse and moves its way up (via the metabolic aftereffects of NT release) various structural and functional hierarchies. Memory resides in the strength of the connections between the components of that hierarchy (Laughlin et al., 1990). In this sense, then, memory is the product of NT release. Very obviously, then, so too is the structure of "behaviour" (in all its forms) associated with the metabolic aftereffects of NT release in particular structural and functional hierarchies. In technical terms,

both learning and memory are somehow expressed through changes in nerve cells...Memory persisting for weeks can result from changes in the strength of already existing contacts...Prolonged changes in synaptic strength can be achieved by changing the amount of chemical transmitter released by the presynaptic terminals of specific neurons...[In short], biochemical processes can be casually related to functional (plastic) changes in specific nerve cells, and these plastic changes in turn can be casually related to the behavioral modification (Kandel & Schwartz 1982:433).

...

4.3 Homeostatic Properties of Neurons

We are fortunate in that Zigmond (1994) provides us with a valuable series of portraits that explain the dynamics of NT release and the functional implications of their homeostatic properties. As Figure 4.3 reveals, there are several categories of feedback loops that can influence the dynamics of transmitter release. In panel "A" the number 1 is used to distinguish the local from the multisynaptic (#2) feedback loop. In the first condition the terminal fiber communicates with itself. In the second condition the receiving cell communicates with the sender. In both instances the net effect of NT release is to provide the cell, and its community of cells, with an opportunity to modulate the activities of the original sending cell. Ultimately this boils down to providing mechanisms whereby the rates of NT synthesis and release in various cells can be modified according to the functional demands being placed on the cell or system. These modulatory events are achieved through interaction with (as shown in panel B) "synthesis-modulating" (3) versus "release-modulating" (4) receptors³². As Zigmond explains

whereas regulation of release presumably maintains some constancy in the availability of extracellular transmitter, regulation of synthesis ensures that intracellular transmitter stores are constant even if release is not (1994:116).

³² However in the case of local feedback loops, they are generally referred to as "autoreceptors".

Figure 4.3 Categories of feedback loops that can influence the dynamics of transmitter (T) release (redrawn from Zigmond 1984:116, Figure 1). A = Local (1) versus multi-synaptic loops (2). B = synthesis-modulating (3), versus release-modulating (4), influences. C = rapid versus slow acting feedback loops (e.g. activation of enzyme activity from E_i to E_a , left panel, versus induction of enzyme levels and synthesis of new receptors, right panel). See text for discussion.

In panel "C" we see that the regulation of NT synthesis occurs both in the short as well as long term. As Zigmond explains:

For example, whereas tyrosine hydroxylase, the rate limiting enzyme in catecholamine biosynthesis, can be modulated by phosphorylation of the tyrosine hydroxylase [TH] molecule, it is also subject to genomic regulation via induction of new tyrosine hydroxylase protein (Zigmond 1994:116).

This is what he meant to convey with the use of the "Ea/Ei" [enzyme activation, enzyme induction] loop interior to the presynaptic cell in the "short-term" panel. The images in the "long-term" panel are meant to convey both the genomic induction of new TH and the synthesis of postsynaptic receptors (see Lynch & Baudry 1984).

In Figure 4.4 we explore the functional implications of the homeostatic properties of neurons. This is where the story gets interesting. In panel "A" we see that

the capacity of a neuron to adjust its rate of release to the concentration of transmitter in the adjacent extracellular fluid may permit a few neurons present in early development **to exert a disproportionately greater influence on brain function** (Zigmond 1994:116).

And this influence might be greater than would be predicted by the initial [genetically templated] density of innervation. In panel "B" we see that, theoretically, "the coupling of synthesis to release should enable a neuron to function over a broad range of

A

B

C

Figure 4.4 Implications of the homeostatic properties of neuronal systems (redrawn from Zigmond 1994). (A): During development a small number of initial "pioneer" neurons (left panel) might release transmitter at a higher rate so as to influence a wider field of target neurons than would be predicted by the density of innervation. (B): Coupling synthesis to release should enable a neuron to function over a broad range of firing rates without running out of transmitter (T) or generating an excess (until limits of regulation are exceeded, see arrow). (C): Short-term processes for increasing the capacity of transmitter biosynthesis (left panel) may permit neurons to respond rapidly to changing demands (S1) but preclude an additional response to still further demands imposed simultaneously (S2), whereas long term processes (right panel) may allow more permanent adjustments when the increased demand becomes long-lasting (S1), thereby facilitating a rapid response to still greater challenges (S2). Zigmond's insights help us understand the structural (A), metabolic (B), and behavioural (C) significance of ontogenetic and phylogenetic differences in the quality of diet. See text for further discussion.

firing rates without running out of transmitter or generating an excess" (Zigmond 1994:116). In panel "C" we see that

the availability of both short- and long-term processes for increasing the capacity for transmitter biosynthesis should permit neurons to respond rapidly to changing demands [S2 left], and to make more permanent adjustments when the increased demands becomes longer-lasting [S1 right], thereby facilitating a rapid response to still greater challenges [S2 right] (Zigmond 1994:116).

Figure 4.4A helps us understand how developmental variations in amino acid availability might affect the ability of some brain cells to establish complex relationships with other cells and networks. It will, therefore, prove invaluable when I build my larger theoretical model (Chapter 12). Figure 4.4B allows us to understand how dietary variations in NT precursor availability might affect the type or range of metabolic activities specific cells and NT-specific pharmacosystems are able to effectively engage in. In other words, Figure 4.4B is broadly applicable to the aims of this thesis and will help me pre-establish the general significance of Wurtman and colleagues' research. What their research suggest is that variations in dietary NT precursor availability will determine whether or not a neuron can indeed keep pace with the functional demands being made upon it. Figure 4.4C allows us to appreciate that lifelong aspects of diet might affect the ability of some individuals to cope (neurochemically and thus behaviourally) with successive layers of environmental stress. Thus Figure 4.4C will prove invaluable when the reader is called upon in Chapter 9 to conceptualize the neurochemically selective effects of

stress on NE turnover and the beneficial effects of increased tyrosine availability (e.g., Raleigh et al., 1988).

Turning now to Figure 4.5, we see that there are several ways to conceptualize neural dysfunction resulting from a breakdown in synaptic homeostasis. In the top panel "A" we see what the process of aging is all about. By way of a conceptually loaded explanation³³: if there is a reduction in the number of active connections in a "community of cells" (Laughlin et al., 1990), and the remaining members are unable to mount a compensatory response necessary to effectively maintain the prior established commitments of the original cell, the original receiving cell(s) will atrophy and die - as in the case of aging (Figure 4.5A right panel) - or (as would be the case under normal circumstances) simply withdraw their "trophic support" mechanisms and "conscientiously" refrain from participating in that cell's communal activities. Necessarily lengthy explanation aside, the point is this: "deficits in the ability to invoke such compensations may exist in circumstances such as senescence [and protein deficiency, I might conjecture], **leading to accelerated rates of behavioural decline**" (Zigmond 1992:119).

³³ Obviously influenced by the language of the biogenetic structuralists (Laughlin et al., 1990) and the ideas of Purves (1986, 1988).

Figure 4.5 Models of dysfunction resulting from a breakdown in synaptic homeostasis (redrawn from Zigmond 1994:120, Figure 7). (A) = Absence of compensation to the loss of neurons as might occur during senescence (compare with the adaptation postulated to occur during development, shown in Figure 4.3A). (B) = Reduced compensation of transmitter synthesis and release during a period of increased activity (mania ?) compared to the normal case (dashed line). (C) = Overcompensation of transmitter synthesis and release during a period of increased activity resulting in (anhedonia?). Zigmond's models help us conceptualize the functional significance of Wurtman and colleagues' research on the relationship between nutrition and brain NT synthesis. See text for further discussion.

In Figure 4.5B (left panel³⁴) we see that reduced compensation of NT synthesis and release during a period of increased activity [brought about by a deficiency in the autoregulation of NT release] might induce behavioural changes such as that characteristic of mania. This is to be compared to the right panel which depicts the normal synthesis/release response curve over time³⁵. In model "C" we are provided with an image of a behavioural outcome Zigmond (1994) hypothesizes is a consequence of overcompensation of NT synthesis and release: "anhedonia" [which is a mild form of depression characterized by general lethargy and a vague disinterest in previously satisfying personal pursuits].

The models in Figure 4.5 are quite useful because they help us visualize the microstructural basis of behavioural impairments resulting from a dysfunction of homeostatic mechanisms. The fundamental emphasis on the necessity of striking and maintaining a balance between NT synthesis and release helps us conceptualize the theoretical implications of Wurtman and colleagues' research on the relationship between nutrition and NT synthesis.

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³⁴ With minor adjustments for the sake of clarity.

³⁵ Missing dashed line supplied by way of estimate.

4.4 The Trophic Theory of Neural Connection

To appreciate the significance of this theory it is necessary to understand that the functional wiring diagram of the brain is not "hard-wired" and can change throughout the life of an organism. This only makes sense given that the genotype cannot ever be expected to fully anticipate the precise nature of the functional demands a given environment will place upon an organism (Greenough 1984). Because of these limitations, experience is "allowed" to modify the functional wiring diagram of the brain according to the functional demands being placed on the organism. This means the CNS is effectively endowed with the capacity to **re-organize itself** according to the ever changing profile of various environmental demands (both within and across time). This is called "neural epigenesis". As is perhaps by now apparent "one of the most powerful epigenetic effects on cortical development appears to be neuronal activity" (Jones 1990:348).

By way of clarification, the functional demands being placed on an organism manifest themselves in the brain as differential patterns of neurochemical activity in particular neuronal arrays. These chronic patterns are etched into the functional wiring diagram of the brain (at the level of the synapse) via the metabolic aftereffects of NT release. By metabolic after-effects I mean minimally second messenger systems capable of activating, modifying, and selectively stabilization of a subset of synapses

and neuronal networks (i.e., whose perceptual, behavioural, sensorimotor and cognitive functionalities are appropriate to the demands of the environment). But let there be no confusion on this point: the terms activation, modification, and selective stabilization carry with them certain mechanistic connotations that highlight the significance of the trophic theory of neural connection.

By way of explanation: NT release activates a biochemical cascade on events in the postsynaptic surface (Kandel & Schwartz 1982). Given the repeated expression of the kinds of "coincident activity" patterns seen in Figure 4.2, postsynaptic receptor densities will increase (Lynch & Baudry 1984). Typically, this is what researchers mean by "modification": the exposure of previously hidden postsynaptic receptors (ibid.). The concept of "selective stabilization", however, implies the **retrograde transport** of trophic support molecules (hence the arrows in Figure 4.2B, far right panel). Nerve growth factor (NGF) is thus far the best candidate for providing trophic support (Purves 1986:486), however nitric oxide (Kandel & Hawkins 1992) may also exert some similarly positive benefits.

Expanding on our definition of the trophic theory of neural connection, we would suggest that its theoretical significance reflects the development of the following idea: the extent to which a cell can successfully compete with other neurons impinging on

that same cell"¹⁶ for "target derived molecules in limited supply" (such as NGF) will determine whether or not that cell's future relationship to the "target cell" will be selectively stabilized and maintained relative to the status of (shall I say) the other "suitor" cells. In other words, the suitor cells that are most successful in currying trophic favours from the target cell will be the ones that literally "survive" in the classic Darwinian sense. It is the outcome of this process of competition which determines the very structure of the "community of cells" (Laughlin et al., 1990:34) that makes up the brain - and thus the very structure of mind and consciousness.

The relevance of the trophic theory to the aims of our thesis will become clear once I have established an understanding of Wurtman and colleagues' research on the relationship between amino acid availability and brain NT synthesis and release. As suggested earlier I will later pursue the idea that variations in NT precursor availability might affect the ability of some cells to compete effectively with other cells for target derived trophic molecules. This would effectively endow some cells with the capacity to impose their own metabolic agenda on the development of the structural and functional architecture of the CNS. Once again, this could have profound cognitive consequences if we recognize that their cell bodies (and their associated community of cells) might reside principally in, say, limbic versus prefrontal regions

¹⁶ As in the case of "convergence" (Figure 4.1 above).

- or left versus right hemispheres! One of our more speculative hypotheses will be the idea that developmental variations in amino acid availability might ultimately result in the selective stabilization of different "cognitive styles" rooted in different patterns of entrainment between the left and right hemispheres. Evidence for the selective lateralization of DA (Slopsema 1982) will be used to support this argument.

Details aside, if we remove the lens of hyper-reductionism we can see that ultimately the individual is the phenotypic outcome of all the environmental demands that have been placed on the activities of its' constituent cells and structural and functional hierarchies. In other words:

the vast complexity of symbolic expression and behaviour observed among humans beings may be accounted for by considering a relatively simple and finite neurocognitive system in interaction with a rich and ever-changing environment. In this case it is a simple genotype in interaction with an environment that produces a relatively complex array of phenotypic expressions (Laughlin et al., 1990:41-42).

In Chapter 12 I will argue (following Katz 1987) that nutrition is a significant aspect of the environment. In this sense, then, Laughlin et al's insight quoted directly above provides me with a valuable alternative explanation of my major theoretical position. Theoretically, it was a simple protohuman genotype in interaction with a nutritionally variable cultural environment that co-produced (along with other environmental factors) a relatively complex array

of phenotypic expressions in members of the genus *Homo*. All things being equal, our hominid ancestors' diet would, therefore, have been of profound adaptive significance.

PART TWO

THE ANTHROPOLOGY OF HOMINID BRAIN AND COGNITIVE EVOLUTION

5.0 BRAIN EVOLUTION - FACTS AS KNOWN

In this chapter I will review the process of human brain evolution from the standpoint of paleo- and comparative neurology, allometry, behavioural ecology, and what might reasonably be called statistical neuro-ecology. By paleoneurology I mean "the study of fossil endocasts" (Edinger 1949 cited in Holloway 1966:104) - endocasts being molds made of the interior surface of the cranial bone. By allometry I mean "an empirical approach concerned with the recognition of overall correlations between individual parameters and body size and with the interpretation of individual or group departures from the identifiable common trend" (Martin 1984:75). By behavioural ecology I am referring to studies which reveal the statistically significant behavioural correlates of brain size. By statistical neuro-ecology I am referring to two very important research papers that calculate the metabolic costs associated with the development (Foley & Lee 1992) and ongoing maintenance (Leonard & Robertson 1992) of the fossil hominid brain.

The findings of the paleoneurologists will allow us to appreciate the fact that "the challenge of trying to understand human brain evolution requires a constant synthetic integration between comparative neuroanatomy and paleoneurology" (Holloway 1985:215). The findings of the comparative neurologist will provide us with a basis for comparison with the content and activity patterns of the p.d.NTs in particular cortical and subcortical structures of the brain examined in Part 3. The findings of the

behavioural ecologists will illustrate the use of correlational statistics in anthropology (e.g., the detection of a correlation between diet and brain size that provides indirect support for the thesis herein advanced). The findings of the statistical neuro-ecologists will reinforce the view that the process of hominid encephalization was a metabolically costly venture with obvious implications for hominid foraging patterns and diet.

Periodically very necessary theoretical forays aside, it remains for Chapter 6 to formally summarize the major theories on brain evolution that have been advanced to date.

5.1 Four Phenotypic Windows on Brain Evolution

We have much ground to cover in this chapter. Figure 5.1 provides a good place to start. I will begin by structuring a discussion of brain evolution around this model. It defines four "phenotypic windows" through which we can view the process of hominid encephalization: (1) size only, (2) reorganization, (3) hierarchy or maturation, and (4) hemispheric asymmetry (based on Holloway 1983). While "empirical paleoneurological evidence does exist for models A,B, and D...model C can only be inferred from comparative neurology" (Holloway 1983:225).

The argument for looking at size is quite simple: brain size provides a rough estimate of the information processing capacity of

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**PM-1 3 1/2"x4" PHOTOGRAPHIC MICROCOPY TARGET
NBS 1010a ANSI/ISO #2 EQUIVALENT**

PRECISIONSM RESOLUTION TARGETS

Figure 5.1 Holloway's (1983:225) interpretation of the four kinds of brain changes that can occur through time (T₁ to T₂). In A, the brain is shown with two hemispheres (left and right), and two transverse dotted lines which represent the central and lunate sulci respectively. The change from T₁ to T₂ is simply an increase in size (absolute) without any change between the size of components or connections between them. This change could occur isometrically or allometrically.

In B, the change from T₁ to T₂ does not allow any change in absolute brain size, but rather a change in components, such that the lunate sulcus is placed more posteriorly, thus expanding the posterior position of parietal association cortex. This is a reorganizational model.

Model C depicts changes in hierarchical development without any change in absolute in brain size from T₁ to T₂. The arrows represent fibre systems, maturing at different rates and/or increasing in number between different cortical regions through the corpus collosum, although other brain structures and fibre systems could be involved.

In model D, absolute brain size remains the same from T₁ to T₂, but a more human type of hemispheric asymmetrical petalal pattern has emerged (i.e. left-occipital, right frontal).

It is important to note that these four models do not exhaust the possibilities of brain changes through time when size, reorganization or heirarchy are considered in different combinations. It is most probable that all four of these possibilities have been realized in human brain evolution at various times. Empirical paleoneurological evidence does exist for models A, B, and D, but model C can only be inferred from comparative neuroanatomy, although it must have lawful relationships with A, B, and D. It is hopefully obvious that any plot of brain size vs. time ignores possibilities B, C, and D, each of which could have had very profound effects on cognition, social behaviour, or adaptation. Indeed, the shift from T₁ to T₂ in model B could represent a true case of "punctured equilibrium," as could C or D. Model A could be considered as a "P.E.," but in fact might simply be due to a slight increase in size, e.g., allometry.

a species (Jerison 1973). The argument for looking at hemispheric asymmetry is heuristic: theoretically, it provides us with a way of assessing the cognitive, behavioural, linguistic, social, and even cultural complexities of our hominid ancestors. The argument for looking at aspects of both neural reorganization and changes in hierarchy or maturation is likewise profoundly cautionary:

behaviour might be fragmented into modes of cognitive functioning, such as "memory", "foresight", "planning", "delay between stimulus and response," etc., etc. Any differences between brains in either cerebral organization or hierarchal development would not be included in the plot, and thus significant selection points possibly missed (Holloway 1983:218).

In other words **"it is not the size, per se, that is responsible for the evolution of higher cognition, but rather the complexity and organization within the brain"** (Laughlin & d'Aquili 1974:37).

Keep in mind, all of these axes of variability could combine in complex ways to confound our ability to interpret the significance of brain changes (or lack thereof) over time. In practical terms, this means that the gracile australopithecines may have been endowed with a much greater degree of cognitive flexibility than the comparability of their brain size estimates with the great apes would seem to suggest (see discussion below). So too does this suggest that the curiously long period of morphological stasis exhibited by *Homo erectus* (Chapter 3) may not have been as uneventful as standard interpretations would seem to suggest.

Figure 5.2 Mean cranial capacity and 95 percent population limits of each of five fossil hominids (redrawn from Tobias 1983 cited in Eccles 1989:21). See text for discussion

5.2 The Fossil Record

5.2.1 Brain Size Only

Figures 5.2 provide a readily comprehensible images of the dramatic trebling of hominid cranial capacity (cc) in the past 3 million years. It also draws our attention to the high degrees of variability observed in the fossil record. Table 5.1 provides a text-based summary of these details (which includes mean cranial capacity estimates for all the fossil hominid species introduced in Chapter 3, time of appearance, time of extinction, associated lithic technologies, and important ecological/dietary differences between hominid groups). Table 5.1 also provides cranial capacity estimates for the greater apes (chimpanzee, gorilla, and orang-utan).

The first thing we notice is that brain size increased approximately 3-fold in the span of some 3.5 million years - that is, since our earliest ancestors, *Australopithecus afarensis*, stood on two feet. This explains why bipedalism is seen as so significant to the process of hominid encephalization: it occurred prior to any significant increases in cranial capacity and was presumably, therefore, a causal factor.

Table 5.1 The fossil record of human ancestry (with non-human primate comparisons)

Species or genus	Time of appearance (years ago)	Time of extinction (years ago)	Average cranial capacity (cc)	Other characteristics
<i>Homo sapiens</i>				
Modern races	30,000	still living	1330	Magdalenian, Aurignician and modern cultures.
Cro-Magnon				
Neanderthal	100,000	30,000	1470	Mousterian culture. Earliest rites and ceremonies.
Archaic	300,000	200,000	1300	Late Acheulian culture.
<i>Homo erectus</i>	1,600,000	400,000	950	Acheulian culture. First use of fire.
<i>Homo habilis</i>	2,000,000	1,600,000	700	Oldovan culture. First use of chipped stone tools.
<i>Australopithecus robustus</i>	3,000,000	2,000,000	550	Walked erect, no known tools.
				Vegetarian (?), not ancestral.
<i>Australopithecus africanus</i>	3,000,000	2,000,000	500	Walked erect. No known tools.
				Omnivorous (?), possibly ancestral.
<i>Australopithecus afarensis</i>	3,500,000	2,500,000	425	Walked erect, probably ancestral.
<i>Ramapithecus</i>	14,000,000	10,000,000	?	Walked on all fours. Teeth approach hominid type.
Dryopithecines	22,000,000	12,000,000	?	Knuckle walker ? Possible common ancestor of apes and humans.
chimpanzee			394	
orang-utan			506	
gorilla			411	

Source: Eccles (1989: Table 2.2. and p.17).

The second thing we notice is that *Homo habilis*, who was the first tool maker, exhibited a 44% increase in cranial capacity over *Australopithecus africanus* (Eccles 1989:23). This explains why technology has such extraordinary scientific mythic significance. It seems to have "developed more or less concurrently with the human brain"¹⁷, and was presumably, therefore, a causally-related factor.

The third thing we notice is that *Homo erectus* presents a mean cranial capacity intermediate in value between that of our earliest australopithecine ancestors and anatomically modern *Homo sapiens sapiens*. We cannot, however, on the basis of brain size alone, deduce anything other than what Figure 5.2. depicts: gradual increases in cranial capacity over the span of some 3 million years. To infer anything else would be tantamount to adopting the use of a "cerebral rubicon" which is clearly arbitrary and therefore of little explanatory power. It is only when we model the energetic costs associated with the process of hominid encephalization (section 5.4.1 below) that we can really appreciate the significance of what is being seen here.

Comparisons with the great apes are perhaps more revealing. The human brain is almost four times larger than the chimp brain. Much to our confusion and delight, this can only be accounted for on the basis of a mere 2.5 percent difference in base nucleotide

¹⁷ But see Wynn (1988) in critical review.

sequences (Chapter 3). How we can understand the basis of this difference is a matter of ongoing debate. But perhaps dietary differences may be casually implicated (as suggested on the basis of a related comparison).

If we adopt (as is the practice) the gorilla as a model of the hominoid that evolved into the earliest hominid³⁸ we can see that "though the brain sizes are comparable [411 and 500 cc, Table 5.1], there is a great difference in the face and jaws. There is a reduction in tooth size and a great decrease in the size of the canines" (Eccles 1989:18). This suggests our ancestors experienced changes in their diet *before* they exhibited any significant increases in brain size. The ordering of these events is clearly suggestive of the focus of this report: the antecedent necessity of dietary changes that can fully support increases in cranial capacity before they occur. (This recalls the lengthy aside in Chapter 3 regarding the presumed dietary differences between the robust australopithecines and members of our gracile lineage).

We also note that the mean cranial capacity of the robust australopithecines does not appear to have exceeded 550 cc despite the fact that members of this group endured for quite some time in the fossil record (for a period of about 1 million years). Once again, I am inclined to question the energetic constraints their "vegetarian diet" (Table 5.1) may have imposed on their ability to

³⁸ By Eccles' (1989) definition, *Australopithecus africanus*.

sustain the kinds of increases in cranial capacity omnivorous ancestors gradually came to enjoy the disquieting benefits of.

5.2.2 Neural Reorganization

Another kind of information that can occasionally be obtained from fossil endocasts are convolutional details. There are three convolutional details of interpretive significance: (1) the positioning of the lunate sulcus in *Australopithecus*; (2) a Broca's area convolution in *Homo habilis* and *Homo erectus*; and (3) a possible asymmetry in the Sylvian fissure in Neanderthal Man (for the present purposes, archaic *Homo sapiens*). All of these neural reorganizational markers have implications for our understanding of the evolution of language and all that that entails (e.g., socially, technologically, nutritionally, and culturally).

The lunate sulcus is the anterior boundary of the primary visual striate cortex. It separates the posterior visual cortex from the parietal lobe. Significantly, the position of the lunate sulcus in the brains of the great apes versus humans is different. And in humans this difference is associated with expansion of the adjacent parieto-temporal association cortex - which includes Wernicke's area. This is an area of the brain that mediates speech comprehension and production. What is debatable is the position of the lunate sulcus in *Australopithecus*.

Dean Falk (e.g., 1982) has argued that the lunate sulcus in *Australopithecus* is in the anterior "pongid position". Ralph Holloway (e.g., 1983, 1985), on the other hand, has argued that it is in the posterior "hominid position". Assuming a methodological resolution is forthcoming, researchers may yet be able to determine (1) whether or not "natural selection **did** operate on the **organization** of cortex, as well as its size, early in hominid evolution" (Holloway 1983:221; emphasis in the original), and (2) "whether the brain systems for human language that are anterior to the lunate sulcus (e.g., Wernicke's area) could have begun their enlargement in the australopithecines" (Jerison 1990:288).

Another controversy that persists in the literature relates to the detection of some sulcal markings in the region of the left inferior frontal lobule (i.e., Broca's area) in *Homo habilis* and *Homo erectus*. As Jerison (1990:289) explains, "Falk (1983a) has been able to recognize this convolution in *Homo habilis*, but is it Broca's area?". If we were to examine this finding critically we might argue that it is "impossible to reason from increased fissurization in a Broca's area that a language area had evolved. Increased fissurization is one of the effects of increased brain size" (Jerison 1990:289). However, the most reasonable conclusion seems to be this:

The increases in brain size between the australopithecines and early *Homo* increased the numbers of folds in all parts of the cerebral cortex. These new folds may simply be an effect of this overall size increase rather

than a specific change. These hominids may have been the first to use Broca's area for language, but endocasts alone are not enough to prove it (Deacon commenting in Jones et al., 1992:117).

Finally, we also note that an asymmetry observed in the Sylvian fissure of the Chappelle aux Saints specimen of Neanderthal man (*Homo sapiens*) suggests the likelihood of Wernicke's area development. While it is true, we cannot base any firm conclusions on but one fossil find, "it would, of course, be surprising if language areas had not evolved by that stage of human history, about 40,000 years ago" (Jerison 1990:289).

5.2.3 Hierarchy or Maturation

One of Holloway's stronger statements explains more fully the importance of aspects other than size.

By cathecting on size alone, all evolutionary paradigms become reduced to natural or genetic selection operating on incremental size increases and behavioral efficiency, which always has the underlying implicit structural argument that 'intelligence' equals 'brain size'...In other words, all of individual variation, the very stuff that evolution works on, is reduced to a single dimension of either small or large. In fact, it is likely that the selection events in any animal's life depend more on the timing of maturational events, epigenesis within the central nervous system (CNS), and everyday events - that is, the 'nitty-gritty' life-death 'selection walks' - are matters of hierarchical organization, differentiation, and development, of which the outcomes through time can only be measured (thusfar) as size increments. We should and can demand richer explanations (Holloway 1979:85 cited in Holloway 1983:216).

What Holloway essentially argues is that mutant genes may occasionally come along that code not only for increases in brain size but also for **ontogenetic changes in the timing and/or sequencing of maturational events**. Natural selection would then act on the phenotypic outcomes of these events. This is where our thesis fits in.

What interests Holloway is the manner in which such genetic mutational events could produce behavioural outcomes of **social** significance. This reflects his long-standing contention that "the most significant evolutionary changes leading from an apelike hominoid to humankind were in the area of social behavior" (Holloway 1981:287). Our interest in the epigenetic effects of nutrition does not deny the merits of Holloway's formulation. Rather, it provides a neuroscientifically-grounded explanation of the epigenetic mechanisms responsible for activating and maintaining these axes of ontogenetic and phylogenetic variability. I will explain my meaning.

Preliminary to the discussion in Part 4, Jones (1990) suggested that

a genetically determined morphological variant occurring in development could thus be reinforced by the strong epigenetic influence of arriving afferent and developing neural activity (Jones 1990:348).

What seems apparent to us is that this is a mechanistic explanation for the expression of the kinds of developmental changes Holloway's model C is interested in. Later I will examine how developmental variations in amino acid availability affecting CNS NT **activities** could conceivably affect the maintenance of morphological variants occurring in development. Just as mutant genes may code for ontogenetic changes in the timing and/or sequencing of maturational events (Holloway 1983), so too might developmental variations in amino acid availability interact with these events to selectively stabilize and reinforce them by the strong epigenetic influence of arriving afferent and developing neurochemico-metabolic activity.

Fundamentally then, both Holloway and I agree that

when and how various neural systems develop and mature through interaction and transaction with a material, social and nurturant milieu is one of the most important questions facing neurobiologists today (Holloway 1981:292).

My interest in the effects of nutrition compliments and extends his original emphasis on the material, social, and nurturant milieu.

5.2.4 Hemispheric Asymmetry

What physical anthropologists look for when they try to detect hemispheric asymmetries in the brains of our fossil hominid ancestors is the attainment of the more human type of left-occipital, right frontal petalial asymmetry in the fossil record.

According to Holloway & De La Coste-Lareymondie (1982) we can see this pattern perhaps beginning with *Australopithecus*. But certainly by the time of *Homo* we see this pattern "with such frequency as to be indistinguishable from modern *Homo sapiens*..." (Holloway 1983:222 in reference to Holloway & De La Coste-Lareymondie 1982). This suggests that

to the degree that gross petalial patterns are correlated with cognitive tasks specialization...[we may deduce that] human cognitive patterns evolved **early** in hominid evolution and were related to selection pressures operating on both symbolic and spatiovisual integration... (Holloway & De La Coste-Lareymondie 1982:101; added emphasis).

The interpretive significance of this pattern is perhaps obvious: theoretically, we can infer much about the potential cognitive, behavioural, linguistic, social, and even cultural complexities of our hominid ancestors on the basis of the presence or absence of petalial asymmetries. This recognizes, of course, that the two hemispheres are specialized for different "gnostic functions" (Sperry 1982 cited in Eccles 1989:208) and thus possess different "cognitive styles" (Cohen 1969 cited in Paredes & Hepburn 1976:123). This can be seen with reference to Figure 5.3. The dominant left hemisphere specializes in "logical-analytical" operations on perceptual material. The minor right hemisphere specializes in "gestalt-synthetic" operations on perceptual material. Other distinct differences are also apparent with regards

DOMINANT HEMISPHERE	MINOR HEMISPHERE
<p>Auditory:</p> <p>Speech sounds. Processing consonant-vowel syllables. Symbol recognition and analysis. Recall of auditory images of visual objects.</p> <p>Visual:</p> <p>Perception recognition of conceptual similarity.</p> <p>Tactile and Motor:</p> <p>Contralateral control of motor functions. Fine hand skills. Hand gestures during speech.</p> <p>Conceptual:</p> <p>"Logical-analytical" operations on perceptual material. Temporal sequential ordering.</p>	<p>Auditory:</p> <p>Melody recognition. Vocal nonspeech sounds (coughing, laughing, crying). Steady-state vowels.</p> <p>Visual:</p> <p>Drawing, building models from a picture. Space relations in two- and three-dimensional space. Perceptual recognition of identity.</p> <p>Tactile and Motor:</p> <p>Contralateral control of motor functions Tactile pattern perception</p> <p>Conceptual:</p> <p>"Gestalt-synthetic" operations on perceptual material.</p>

Figure 5.3 Neurognostic functions associated with the activities of the "dominant" (left) and "minor" (right) hemispheres (redrawn from Laughlin & d'Aquili 1974:61). See text for discussion.

to auditory, visual, tactile and motor information processing and output.

Later I will pursue the functional and developmental significance of the observation (Figure 5.4) that "DA levels of the medial prefrontal subarea are lateralized, the left hemisphere being significantly higher than the right hemisphere" (Slopsema 1982:197, added emphasis). This I will relate to the insights of Galaburda (1991).

Asymmetry results from the absolutely lesser development of one side, rather than the phrenological greater development of the other...[This suggests asymmetry is a result of] development by selection, reduction, inhibition, and/or pruning rather than by induction, instruction, stimulation, and/or building up (Galaburda et al., 1991:271).

What his analysis serves to remind us is that hemispheric asymmetry is something that is achieved developmentally. And that, as a result, it is susceptible to epigenetic influences - with implications for "differential survival of individuals with one or another type of asymmetry..." (Galaburda et al., 1991:266). I will endeavour to respond creatively to his ideas by examining the developmental effects of variations in amino acid availability.

Fundamentally I will argue that developmental variations in amino acid availability might affect the maturation of cognitive task specializations. Expressed differently: technologically and culturally-templated shifts in hominid diet may have - as Paredes

Figure 5.4 Regional catecholamine concentrations in left and right prefrontal neocortical areas of male WEzob rats (from Slopesma et al., 1982:199, Table 1). While PFC NE content (right panel) is not lateralized, DA in the medial subarea of the PFC (left panel) is ($p < 0.02$, Student's t test, two tailed). See text for discussion.

& Hepburn (1976:126) argue all cultures invariably do "differentially reinforce[d] right- and left-hemisphere dominated cognitive processes". Stated more simply: aspects of hominid diet may have interacted with lateralized neurochemical mechanisms to "co-produce" the evolution of hemispheric specialization. This once again recognize the importance Galaburda places on the concept of development vis a vis hemispheric specialization. It may be genetically given, but it can be epigenetically modified on the basis of the selectively stabilizing effects of neurochemico-metabolic activity patterns.

5.3 Comparative Neurology

In this section I will discuss what, from the methodological standpoint of this thesis, constitutes the most valuable information on brain evolution.

Figure 5.5 provides in visual form what Table 5.2 documents: the size indices of various extant primate brain regions relative a basal insectivore³⁹. Figure 5.6 depicts phylogenetic differences in the percentage of prefrontal to total neocortex for various primate species. Figure 5.7 provides a dramatic image of the significant (and non-significant) differences in the size of various regions of the human brain (expressed as a percentage of

³⁹ for a more complete description of all brain changes the reader is referred to Eccles (1989).

A

B

Figure 5.5 Size indices of various brain regions (A) and the neocortex in particular (B) relative to a basal insectivore (based on Eccles 1989:146, Tables 7.1 and 7.2). Basal ins.=basal insectivore; O+NWM= Old and New World monkeys. See text for discussion.

Table 5.2 Size Indices of Various Brain Regions Relative to a Basal Insectivore

	Tenrecinae		Prosimians		Gibbon		Gonilla		Homo
	Insectivora		Old and New World Monkeys		Chimpanzee		Average Pongid (gibbons, chimpanzees and gonilla)		
Cerebellum	1.00	1.64	4.64	6.20	9.76	8.71	7.95	8.81	21.75
Diencephalon	1.00	1.56	5.56	8.00	10.90	8.39	6.43	8.57	14.76
Striatum	1.00	1.80	5.99	10.12	15.41	11.51	8.41	11.78	21.98
Amygdala	1.00	1.10	1.73	2.24	n/a	n/a	n/a	1.85	4.48
centromedial group	1.00	1.08	1.16	1.30	1.20	1.11	0.88	1.06	2.52
corticobasolateral group	1.00	1.13	2.23	3.05	3.24	2.28	1.94	2.49	6.02
Septum	1.00	1.22	1.91	2.09	n/a	n/a	n/a	2.16	5.45
Hippocampus	1.00	1.75	2.91	2.64	5.07	2.18	1.72	2.99	4.87
area CA1	1.00								6.6
Neocortex	1.00	2.65	20.37	48.41	65.58	71.73	48.32	61.88	196.41
Encephalization Index	1.00	1.43	4.24	8.12				11.19	33.73
	N=4	N=50	N=18	N=23	N=1	N=1	N=1	N=3	N=1

Source: Eccles (1989:42, 105 and 146).

Figure 5.6 Percent prefrontal to total neocortex for various primate species (based on Passingham 1973:350, Table V). Pan= chimpanzee; Hylobates = gibbon; Papio cyn.= cynocephalus; Papio hamad.= hamadryas. See text for discussion.

Figure 5.7 A simplified schematic of the human brain showing deviations of the sizes of various regions of cortex based on scaling of brain structures in other primates, expressed in percentage of the predicted size for a typical primate with a human sized brain (redrawn from Deacon cited in Jones et al., 1992:123). See text for discussion.

the predicted size for a typical primate with a human sized brain). The reader will forgive the omission of Brodmann's cytoarchitectural map of the human brain (e.g., as cited in Eccles 1989:84), and Paul McLean's (more fully elaborated in 1990) concept of the triune brain (composed of the reptilian, paleomammalian, and neomammalian brains corresponding roughly to the brain stem, limbic cortex, and neocortex respectively).

What is strikingly apparent is that the size of the human neocortex (Figure 5.5b, Table 5.2), prefrontal neocortex (Figures 5.6 and 5.7), striatum, cerebellum (Figure 5.5a, Table 5.2), and to a lesser extent superior temporal gyrus (Figure 5.7), diencephalon (thalamus and hypothalamus - Table 5.2), amygdala, septum, and hippocampus (Figure 5.5a, Table 5.2) all exhibited statistically significant increases in relative size. Clearly (as we can appreciate by way of the application of the principle of proper mass) the functional attributes associated with the activities of these cortical and subcortical regions conferred significant adaptive advantages on our hominid ancestors. That is, of course, why we see changes in these neural parameters. The problem, however, is in interpreting the significance of these comparative neurological differences.

As a first approximation I might apply the principle of proper mass (Chapter 3) and rank-order the significance of these differences. In doing so we can appreciate that while the cognitive

functions associated with the activities of the hippocampus may have made at best a moderate contribution to the overall success of our species (Eccles 1989:157, but see discussion below), the cognitive functions associated with the activities of the prefrontal cortex were very obviously crucial to the evolution of culture (Laughlin et al., 1990:114) and thus humanity itself. In between these two extremes exist a range of interpretive possibilities that reflect the statistical importance of various cortical and subcortical structures. I will explore these below with reference to some additional lines of inquiry.

5.3.1 Evolution of the Neocortex

If we compare the human neocortical size index of 196.41 to the chimpanzee value of 71.73, and the average pongid value of 61.88, it can be seen that much of what makes us distinctly human is orchestrated by the activities of the neocortex. In general terms, these significant differences imply increased information processing capacity on the part of humans (Jerison 1973). I recognize, however, that just as the thalamus is too large a mass to indicate where important shifts have occurred (Armstrong 1982, see below), so too have the major subdivisions of the neocortex expanded at different rates during hominid evolution (Figure 5.7).

Only the prefrontal cortex and the superior temporal gyrus have expanded to a size that is larger than would be predicted for

an ape with a human sized brain. Significantly, it has also been observed that the motor premotor, and somatosensory cortices have expanded at different rates, with greater relative development seen in the somatosensory cortex. Conversely, while the occipital cortex has expanded in absolute terms, it is smaller (relatively speaking) than would be predicted on the basis of scaling of brain structures in other primates. All of these changes provide further evidence that brain evolution is a "mosaic" process (Armstrong 1982) characterized by quantitative and hence *qualitative* shifts between the activities of the major subdivisions of the neocortex. This has been called, by way of a descriptive shorthand, "neural reorganization" (Holloway 1966, 1983).

How we interpret the significance of these mosaic changes depends on whether or not we adhere to convention. Any area of cortex that is not primary motor, sensory, visual, or auditory is traditionally referred to as "association cortex". By way of an oversimplification:

1. motor and premotor cortex = control of movement
2. somatosensory cortex = sensory information from body
3. occipital cortex = primary visual information processing
4. superior temporal gyrus = primary auditory cortex
5. frontal, prefrontal, parietal, inferior temporal, rostral occipital cortex = association cortex
6. Broca's and Wernicke's = language areas (discussion see below)

Clearly, however,

...we should not restrict ourselves by prematurely characterizing and categorizing the information, e.g., as sensory or associative..The vocabulary to describe the

processing is likely to involve words like "perception", "cognition", "memory", and so forth, and in handling its neural information the brain may be translating it into "knowledge". The words are important because they imply a level of analysis for which the normal vocabulary of physiology may be inadequate (Jerison 1990:306).

This seems an eminently reasonable position to take, and I will enhance my vocabulary accordingly.

By referencing, for instance, the functional attributes associated with the activities of the PFC, I hope to provide a more complex interpretation of the significance of evolutionary changes in this cortical region. We know that the PFC mediates planning, foresight, intentionality, sociality, time-binding, imaginal thinking, selective attention, memory, symbolic manipulation, symbolic reasoning, and self-consciousness (e.g., Laughlin et al., 1990:116; Laughlin & d'Aquili 1974; Berger & Weinberger 1990; Fuster 1984, 1990, 1991; Bertolucci-D'Angio et al., 1990; deBruin 1990; Uylings & van Edem 1990; Goldman-Rakic 1984, 1990, 1992). This seems a more satisfactory explanation for the evolution of the human PFC than one which merely emphasizes increased associative information processing capacity.

Later I will pursue the functional implications of the absolute and relative differences in the distribution patterns of NE, DA, ACh and 5HT. Not only will I respond to the conventionally-worded observation that the "machinery for biosynthesis of catecholamines may have developed *pari passu* [by an equal progress]

with the evolution of the primate neocortex, particularly in relation to the expansion of association cortex" (Brown et al., 1979:146). But I will also pursue the ecological and nutritional implications of the fact that the PFC is densely innervated by DA (Brown et al., 1979), has a particularly high rate of basal discharge and spike firing activity (Bannon et al., 1981; Bunney & Chiodo 1984), is uniquely devoid of DA synthesis-modulating autoreceptors (Bannon & Roth 1981; Roth et al., 1988) and is, moreover, "unusually dependent on precursor availability" (Deutch & Roth 1990:375). Naturally we will want to consider why natural selection would favour rendering the human PFC, and its attendant role in human symbolic reasoning and consciousness, so curiously susceptible to the vagaries of food choice.

5.3.2 Evolution of the Cerebellum and Striatum

If we compare the size index of the human cerebellum and striatum (21.75 and 5.45) to that of an average pongid (8.81 and 11.78 respectively) it can be seen that some of what separated the hominids from pongids must also have been orchestrated by the activities of these regions. It is significant that both of these structures control the expression of motor abilities (e.g., Eccles 1989).

Eccles (1989:60) relates the significance of these changes to the requirements of bipedalism. The unstated implication is that phylogenetic increases in the relative size of the cerebellum may have been related to the evolution of tool manufacture and use (Laughlin et al., 1990:128) as well as manual dexterity and throwing ability in general (Calvin 1983, 1993). Recent articles in Gibson & Ingold (1993, Part 3) might also prompt us to assign a portion of these changes to the evolution of language.

5.3.3 Evolution of the Amygdala and Septum

If we compare the size index of the human amygdala (4.48) and septum (5.45) to that of an average pongid (1.85 and 2.16 respectively), it can be seen that the success of *Homo* also had something to do with the functional attributes of these limbic structures.

In examining the relative significance of these changes Eccles (1989) argues that "...evolution tended to enhance those components related to pleasurable and enjoyable experience (septum and corticobasolateral amygdala), while the components related to aggression and rage (centromedial amygdala) remained underdeveloped" (Eccles 1989:106).⁴⁰ This provides some empirical support for Holloway's (e.g., 1966) long-standing contention that

⁴⁰ The many articles in Aggleton (1992) provide further support for the role of the amygdala in aspects of emotion.

the evolution of positive sociality was critically important to the evolution of our species (a point made also by Laughlin et al., 1990:128). Later I will find it significant that serotonergic mechanisms have long been implicated in aspects of sociality and aggression (e.g., see references cited Kaplan 1991; Botchin et al., 1993).

Parenthetically, it has also been observed that the pathways from the septum and amygdala go to the medial dorsal nucleus of the thalamus, which then project to the PFC (Eccles 1989:98). Eccles (1989) suggests that "these pathways presumably are of great significance in the reciprocal exchange of information between the neocortex and the limbic system, which is concerned in the development and expression of emotion" (Eccles 1989:99).

I defer to the assumption that the amygdala was an important structure in the process of human evolution because it facilitated the coordination of emotional responses. Likewise, too, I am inclined to agree that because "the amygdala is an important nodal point in the adaptive response to an environment with constantly changing affective contingencies...[it] undoubtedly plays a large role in a wide range of behaviours" (Amaral 1992:57). At the same time, however, I recognize an opportunity to extend the interpretation of the phylogenetic significance of the amygdala beyond the boundaries of common convention.

Murray & Mishkin (1985) reported that "the amygdala is also essential for associations that have no obvious emotional content...Cross modal association could be one of the amygdala's major functions" (pp.604-605). This can also be understood with reference to Amaral et al's (1992) efforts in documenting a veritable cascade of information from unimodal and polymodal visual, auditory, and somatosensory association cortices flowing into the amygdala. What strikes me, however, having read Rozin's (1976) theory on the evolution of intelligence, is that an effort to wed the thrust of these two papers might prove useful.

Rozin (1976) argues that the evolution of intelligence involved increased levels of accessibility between modality-specific subprograms developed initially to serve behaviourally and environmentally circumscribed needs. But "in the course of evolution these programs became more accessible to other systems and, in the extreme, may rise to the level of consciousness and be applied over the full realm of behaviour or emotional function" (Rozin 1976:246). It is tempting to argue that the amygdala may have been a crucial "nodal point" in this process. Stated in the extreme: phylogenetic increases in the size of the amygdala may have facilitated cross-modal information transfer and thus, in humans, access to the so-called "cognitive unconscious". I will pursue this idea in Chapter 12.

Commensurate with, and independent of, this creative exercise, later I will find it significant that the amygdala contains both a moderate to high density of monoaminergic content and activity markers (Brown et al., 1979) and the highest density of ACh content and activity markers found anywhere in the brain (Mesulam 1990).

5.3.4 Evolution of the Thalamus

Table 5.2 also documents changes in the size index of the human diencephalon (which includes the thalamus and hypothalamus). Whereas the average pongid presents us with a diencephalic size index of 8.57, humans exhibit a significant increase to 14.76. What we make of this depends on what we know about the functions of the thalamus and hypothalamus.

Iversen's (1984) well received synthesis allows us to appreciate that the evolution of the hypothalamus must have had something to do with its role in processing "interoceptive cues of biological significance for the species-specific behavior essential for survival" (Iversen 1984:328). Natural selection would surely have favoured enhanced interoceptive discriminative capacities. Later we will find it significant that the highest densities of subcortical NE content and activity markers are found in the hypothalamus (Brown et al., 1979).

As for changes in the thalamus, first we must confront the fact that "not all parts of the thalamus changed at the same rate during hominid evolution" (Armstrong 1982:153). And that while "the thalamus itself has enlarged, in part as a result of the additions of numbers of neurons in its different nuclei...[it is] too large a mass to indicate where important shifts have occurred" (Armstrong 1982:155). This serves as yet another reminder that brain evolution is a "mosaic process" (ibid) and can be operationalized as such.

As Armstrong (1982) reports,

two nuclei appear divergent on the criterion of numbers of [predicted versus observed] neurons. These two nuclei [anterior principal (AP) and lateral dorsal (LD)] are limbic nuclei according to their connections with the cingulate gyrus, subiculum, and mammillary bodies...The increases in these limbic neurons [can be] speculatively interpreted as supporting art of the human ability to symbolize and have a cultural way of life (Armstrong 1982:155).

We can complexify this interpretation if we expand our definition of the functional significance of the thalamus.

According to McCormick (1989) the thalamus "is critical for the generation of certain types of forebrain rhythmic activity **and serves as an intermediary between the external world and the neocortex**" (pp.216-217, added emphasis). As anthropologists, we might be inclined to view this through the philosophical lens of Popper & Eccles (1977 cited in Eccles 1989:73) "three worlds that comprise all existence and all experience". This would prompt us to

suggest that the evolution of the thalamus may have facilitated the exchange of information between World 1 ("physical objects and states") and World 2 ("states of consciousness") with implications for the development of World 3 (i.e., culture or "knowledge in an objective sense").

Later I will pursue the related significance of the observation that ACh and NE combine with the activities of the thalamic relay neurons to ensure the faithful transfer of phasically imperative extero- and interceptive information to the cerebral cortex (McCormick et al., 1989; McCormick 1991). The unstated implication is that NE and ACh serve as neurochemical intermediaries between the external world and the neocortex through their actions in the thalamus.

5.3.5 Evolution of the Hippocampus

The difference in the size index of the human versus average pongid hippocampus is small: 4.87 and 2.99 respectively (Table 5.2). Eccles (1989) suggests that this difference implies a modest contribution on the part of the hippocampus to the evolution of human cognitive capacities in general and memory capacities in particular. By way of application of the "principle of proper mass" (Chapter 3) I might be inclined to agree with this assessment. The rather large size of the gibbon hippocampus (with a size index 5.07

relative to a basal insectivore) reinforces the merits of this assumption. Parenthetically (by extension of the ongoing debate between O'Keefe & Nadel 1978 and Olton and colleagues) I might conjecture that the gibbons' foraging strategy places heightened demands on the spatial working memory and cognitive mapping skills of its hippocampus (i.e., more so than humans).

Significantly, though, we do see larger size increments in area CA1 of the hippocampus (6.6 relative to a basal insectivore) than the hippocampus overall. No one knows what to make of this except that

the functional consequences of the changes in the balance of the hippocampal subdivisions occurring with increasing hippocampal size should be borne in mind when considering the possible differences in the contribution of hippocampus to behaviour of humans versus smaller brained animals (Gall 1989:173-174).

In other words, we cannot rule out the significance of the hippocampus altogether. Important mosaic changes were occurring in this region that defy simplistic interpretations. As a first approximation I might conclude that because area CA1 contains the pyramidal cells that participate in a uniquely mammalian form of learning called "long-term potentiation" (Kandel & Hawkins 1992 defined in Chapter 4), natural selection was favourably disposed to operating on the integrity of this learning mechanism more specifically through area CA1 rather than the hippocampus as a whole. Certainly this would be a metabolically less expensive

strategy - one born of the logic of building on prior established patterns of functional significance.

Later I will find it significant that NE participates in long-term potentiation in the hippocampus (Hopkins & Johnston 1984). So too will I respond to the indisputable fact that ACh is crucial to the integrity of hippocampal memory functions in general (e.g., Olton & Samuelson 1976; Olton et al., 1977; O'Keefe & Nadel 1978; Olton et al., 1979a,b; Olton & Feustle 1981; Morris et al., 1982; Deutsch 1983; O'Keefe 1983; Olton 1983; Walker & Olton 1984; Bartus et al. 1985a,b).

One final note under the heading of the hippocampus:

the massive hippocampal commissural system proves to be more variable across species than once suspected...[Most] remarkable is the great reduction in hippocampal commissural projections in primates...It is of interest in this regard that field CA3, the source of the commissural projections to pyramidal subfields, does **decrease** in size in proportion to CA1 in bigger-brained animals (Gall 1989:186, added emphasis).

This seems particularly interesting in light of the observation that

whereas both infrahuman hippocampi are wholly dedicated to the construction of maps of the physical environment, only the right hippocampus performs this in humans. Damage to the left hippocampus leads to a loss of memory for verbal material. The **left hippocampus** in humans appears to function as a semantic map for the storage and manipulation of narratives (O'Keefe 1985:92).

It would be interesting if we were to observe neurochemical asymmetries in the hippocampus. This would suggest the additional speculative possibility that nutritional factors might also co-produce functional asymmetries in the hippocampus. As I have yet to investigate this possibility I will simply pursue the functional implications of the activities of ACh, NE, and 5HT in the hippocampus. Interestingly, DA exerts no significant role in the hippocampus (Figure 10.2A).

In addition, I will also pursue the interpretive implications of the hypothesis that "the neural system which generates hippocampal theta rhythm may be related to the neural substrate for consciousness" (O'Keefe 1985:84). This I will endeavour to relate to the significance of Vanderwolf's findings that both 5HT and ACh mediate the generation of the hippocampal theta rhythm (Vanderwolf 1987, 1989; Vanderwolf et al., 1989, 1990).

5.3.6 Evolution of the Language Areas

While I regret to say I have not provided a copy of Brodmann's cytoarchitectural map, I will nonetheless discuss the evolution of the language areas in terms of his labelled reference points. Wernicke's area corresponds to regions 39, 40, the posterior parts of areas 21 and 22, and part of area 37. Broca's area corresponds to parts 44 and 45 (see Eccles 1989:85 in review). If we compare

the development of these cytoarchitectural regions in the human versus orang-utan brain [there are no Brodmann-type maps for chimpanzees] we see that whereas Wernicke's areas 39 and 40 are barely visible, Broca's areas 44 and 45 are missing. Further evidence along these lines comes from an analysis of the patterns of myelination on the brain (see Eccles 1989:90). Significantly, areas 39 and 40 are the latest cortical regions to myelinate. This has been taken as evidence that "areas 39 and 40 are phylogenetically developed as new regions of the cortex" (Eccles 1989:89). This necessarily recalls some aspects of the fossil record. The australopithecines appear to have exhibited some modest development in the region of the inferior frontal lobule (Broca's area). *Homo habilis*, on the other hand, exhibited development in both the anterior (Broca) and posterior (Wernicke) speech areas. *Homo erectus* exhibited progressive development in these areas. And of course "with Neanderthal Man the large brain presumably had full development to the *Homo sapiens sapiens* level" (Eccles 1989:91).

This, then, paints a picture of the gradual evolution of human language capacities. I recognize, however, that the issue is far from resolved. There are as many advocates of the position that human language evolved early and gradually (e.g., beginning with *Homo habilis*) as there are proponents of the position that it appeared rather late and suddenly (e.g., only with our species 40,000 years ago). Following Aiello & Dunbar (1993) I may suggest the following: how we define language, (i.e., whether we emphasize

similarities or differences with ape vocal communication styles, rely on the fossil hominid record, or agree that lithic technologies are valid indications of the linguistic and cognitive competencies of our ancestors) will determine what interpretation we advance. This debate is not, however, crucial to the present discussion. The reader is referred to the many and various articles in Gibson & Ingold (1993) as well as Aiello & Dunbar (1993) which we will examine briefly in the next chapter.

5.4 Allometry

No chapter on brain evolution would be complete without discussing the concept of allometry. This can be defined as both "the term given to describe the change in proportions brought about by changes in size" (Foley 1987:119) and

an empirical approach concerned with the recognition of overall correlations between individual parameters and body size and with the interpretation of individual or group departures from the identifiable common trend (Martin 1984:75).

A classic example of the application of this principle comes to us by way of Jerison's original (1973) efforts at determining the correlation between brain size and body size.

...

5.4.1 Relative Brain Size

Using regression analysis Jerison (1973) determined that the correlation between mammalian brain and body size was 0.67. What interested him was the extent to which various species (in particular humans and their fossil representatives) deviated from this observable common trend. This he argued had implications for assessing the extent to which a given species had a quantity of "extra neurons" that were in all probability devoted to higher-order cognitive functions (or more precisely: "increased information processing capacity" which was his working definition of intelligence). This he conveyed through the use of an "encephalization quotient" (EQ) - a statistical variant of which we encountered in Table 5.2 as the "encephalization index" (EI). Notice the human EI is three times that of the average pongid. The functional implications are clear by way of the more appropriately explicit definition that

brain/body allometry can be used to estimate a body-control component in brain size, and the 'residual' (in the statistical sense) component, which can be taken as a measure of encephalization, can be used to estimate the amount of processing capacity related to the evolution of mind (Jerison 1985:13).

Jerison's research has had a profound theoretical legacy. The use of EQs (and statistical variants thereof) are still used today as indicators of the degree to which a given species approximates the cognitive capacities of modern *Homo sapiens sapiens*. And this

in spite of the most telling original criticism: the calculation of EQs depends on accurate measurement of body weights, and yet "we have scarcely a single accurate body weight to associate with any particular hominid cranial capacity" (Holloway 1983:216). As is the nature of science, though, Jerison's estimates have since been revised.

5.4.2 Maternal Metabolic Turnover

Martin (1981, 1984) later determined that the exponent for the relationship between increases in body size and brain size was in fact 0.75 with body size. In other words, **an increase in one unit of body mass is associated with a 0.75 unit increases in brain size**. What rendered this such an uncompromising challenge to the validity of Jerison's model was that this relationship could be re-interpreted in terms of Kleiber's curve. Kleiber's curve is a measure of oxygen consumption on the basis of body weight. This statistical parallel suggested to Martin that brain size was correlated not with a portion of body size *per se* but rather basal energetic requirements; (understand that the interpretation in boldface text above also provides an exact definition of the Kleiber principle - substituting, of course, the term "metabolic rate" for "brain size"). This lead Martin to propose the following:

it is widely accepted that brain size is scaled to keep pace with changes in body surface area (rather than

volume), and this provides the basis for many interpretations of relative brain size. Re-examination of brain-body size relationships for large samples of species from three major vertebrate groups (mammals, birds, reptiles) now shows that **there is no empirical foundation for the concept of scaling to body surface area. Instead, it seems that brain size may be linked to maternal metabolic turnover.** This has implications not only for assessment of relative brain size in particular species, but also for pursuing links between brain size and 'life strategies' (Martin 1981:57; emphasis mine).

This finding was to have profound theoretical consequences, triggering what some might reasonably call a dramatic paradigmatic shift.

Martin's findings have not only provided incentive to re-examine the previously observed correlations between brain size and diet (e.g., Jerison 1973; Milton & May 1976 cited in Milton 1988:285; Eisenberg & Wilson 1978; Clutton-Brock & Harvey 1977, 1980), but his research provides additional theoretical support for the interests expressed here. Stated quite simply:

the coefficient of [Martin's] allometric equation is close to 0.75, similar to the relationship between body size and basal metabolic rate (BMR)...This implies that brain size and BMR are isometrically related, from which the further inference may be drawn that the size of an individual's brain is closely linked to the amount of energy available to sustain it (Foley & Lee 1990:223)

In an analogous manner I will also argue that the size of an individual's brain may be closely linked to the amount of dietary amino acids available to sustain the high rates of p.d.NT activity

seen in the regions that exhibited significant allometric increases in size.⁴¹ In other words, amino acid availability relevant to brain NT synthesis - and not just caloric energy per se - are important costs associated with the growth and development of the brain. As such they too have significant implications for our understanding of hominid foraging patterns and diet and (more generally speaking) the ecological constraints on the process of hominid brain evolution. I will expand on this position in Chapter 12.

5.4.1 Behavioral Ecology

Relative brain size (or degree of encephalization) appears to correlate with a number of aspects of behavioural ecology including body size, terrestriality, home range, and feeding strategies (Milton & May 1976 cited in Milton 1988:285; Eisenberg & Wilson 1978; Clutton-Brock & Harvey 1977; Milton 1988), as well as (more specifically) "omnivorous extractive foraging" (Gibson 1986), and the quality of diet (Foley & Lee 1992). As is the nature of correlational studies, however, it is often hard to separate the facts from theory. For the purposes of the present chapter it is sufficient to realize the following chronology of events.

⁴¹ I will often append the term "in the regions that exhibited significant allometric increases in size" because where I cannot quantify phylogenetic differences in neurochemical activity, I can extrapolate them by way of the application of the principle of proper mass.

In the mid-to-late 1960s Bauchot & Stephan observed an association between brain size and diet (see references cited in Clutton-Brock & Harvey 1980:321). They did not, however, demonstrate this statistically. Likewise too, while Jerison (1973) observed that brain size tended to increase more rapidly among carnivores than it did among herbivores, he did not pursue this line of thinking. It remained for Milton & May (1976, cited in Milton 1988:325) to statistically determine that body size, diet, and home range were correlated. They interpreted their findings as follows: larger primates feeding on young leaves patchily distributed in space and time needed a larger supplying area to satisfy their relatively greater caloric needs. This favours brain expansion. This idea has since spawned many similar observations and arguments.

In 1978 Eisenberg and Wilson provided additional evidence supporting a correlation between home range, diet, and brain size. In that study they compared the relative brain size of various bat species classified according to a wide array of dietary statuses: frugivores, insectivores, nectarivores, carnivores, piscivores, sanguivores and foliage gleaners (as discussed in Martin 1984:84). They determined that the relative brain size of the frugivores was almost twice as large as the brain size of the insectivores, and that the remaining bats exhibited relative brain sizes of intermediate values. They concluded that foraging-related

differences in the requirements for storing spatial information was a key explanatory factor in brain evolution.

In 1980 Clutton-Brock & Harvey conducted a similar study of 118 primates. What they too observed was that "within the primate family, folivores have comparatively smaller brains than frugivores and insectivores" (1980:321). They too assigned spatial and temporal differences in the distribution patterns of leaves versus fruits a causal status with implications for neocortical memory storage capacity. Other studies have been conducted along similar lines. As Martin (1984:87-88) explains, the relationship

between relative brain size and diet/feeding strategy has also been investigated in a selection of small mammals (Harvey et al., 1980; Mace et al., 1980, 1981), with a similar result. Folivores have significantly smaller brains than species with frugivorous, insectivorous, granivorous or generalists dietary habits. Mace et al. (1980)...concluded:

differences in relative brain size arise through variation in either the range of stimuli that need to be processed for feeding or information storage and retrieval systems, **rather than through the nature of the food source** (Martin 1984:87-88; emphasis mine).

In a similar fashion, Gibson (1986) later observed that

moderately large brains tend to be found in primate omnivores or frugivores who engage in extractive tasks requiring somewhat less complex sensorimotor coordinations...such as cracking nuts with the teeth, peeling fruit, opening bean pods and unrolling leaves to obtain hidden insects...Small brains are found among insectivores, frugivores, omnivores and folivores who eat exposed rather than hidden foods and who manipulate foods

using only typical primate eye-hand mouth coordination (Gibson 1986:99-100).

She concluded that "extraction per se does not appear to be the critical variable with respect to brain size. Rather, neocortical size correlates with the complexity of and variety of the sensorimotor coordinations needed for the finding and processing of foods" (Gibson 1986:100).

With the recent and welcome exception of Foley & Lee (1992), no one investigated the actual nature of the food source that, for instance, Mace et al., 1980 (quoted above) categorically rejected the potentially confounding significance of. It remained for Foley & Lee (1992) to pursue the implications of the fact that whereas "leaves constitute a relatively low level of nutritional quality...fruits supply relatively easily digested energy as well as protein and fatty acids" (p.224).

Much to the benefit of our own theoretical interest, Foley & Lee (1992) conducted a pairwise comparison of phylogenetically comparable species of primates with the most extreme preference for high-quality versus low-quality foods (Figure 5.8). What they discovered was a negative correlation between folivory and EQ ($r=0.74$) and a positive correlation between both faunivory and EQ ($r=0.709$) and frugivory and EQ ($r=0.686$). I find their conclusions most intriguing.

Figure 5.8 A phylogenetically based pairwise comparison of the most extreme folivores and frugivores (in each of a number of primate clades) exhibiting the most extreme preference for high quality and low quality foods (redrawn from Foley & Lee 1992). Number above bars indicate percentage of feeding time on leaves, fruits and animals. See text for discussion.

Although high EQs are not invariably associated with high quality diets, low quality diets do not appear to permit or be associated with high EQs. Fruit and animal diets appear to be able to fuel larger primate brains, whereas the low energy and high toxicity of folivorous diets may constrain the available energy and basal metabolic rates (Foley & Lee 1992:225).

This reinforces the idea that brain evolution is correlated with dietary factors. The question, is: which group of factors?

The standard interpretation focuses on caloric energy to the exclusion of all other nutrients. This is understandable, of course, because the brain consumes roughly 87% of resting metabolic energy at birth, 44% in the five-year old child, and approximately 20-25% in adult humans (see references cited in Leonard & Robertson 1992:179). But what of the demands particular brain regions (exhibiting high content and activity patterns of the p.d.NTs) make on the amino acid content of diet - at critical developmental stages as well as throughout the life of the organism?⁴²

Parenthetically, I have to wonder if (in the slightly awkward but necessarily condensed terms of this thesis) Foley & Lee's "low quality" diets seen in Figure 5.8 could reasonably be associated with low "neurochemical potentials" (loosely defined in Chapter 4). Or if perhaps some of the statistical "noise" in this study (recall the observation that high quality diets are not invariably

⁴² Static and dynamic profiles of which we will examine in Chapters 7-11.

associated with high EQs) might be reduced by efforts to control for amino acid content! It would indeed be interesting to pursue this line of research. For the moment I must contend myself with the observation that brain evolution is constrained by dietary (most probably caloric but possibly other nutritional) factors. This is clearly established in the context of the findings discussed in the next section below.

5.5 "Statistical Neuroecology"

Two very important research papers calculate the metabolic costs associated with the development (Foley & Lee 1992) and ongoing maintenance (Leonard & Robertson 1992) of the fossil hominid brain. Both of these papers examine the dietary implications of hominid encephalization, and are, therefore, highly compatible with the aims of this thesis.

5.5.1 Ecology and Energetics of Encephalization

Responding to the challenges of Martin's (1981, 1984) groundbreaking research, Foley & Lee (1992) suggested the following:

the flexible and sophisticated cognition and behavior resulting from a large brain have been sufficient for explaining the marked rate of increase since the appearance of the hominid clade. From an ecological perspective...it is perhaps more interesting to ask what

the costs of encephalization are and how they can be afforded...[T]he costs of brain growth and maintenance are essential to understanding the conditions under which encephalization may occur (Foley & Lee 1992:223)⁴³.

Then they set out to establish just what those costs were. (Later I will do the same by examining the content and activity patterns of the p.d.NTs in particular regions of the brain known to have undergone significant allometric increases in size.).

As shown in Figure 5.9, Foley & Lee (1992) estimated the percentage increases in energy requirements of different brain sizes above those of a chimpanzee for hominid infants from birth through 18 months. They determined that

australopithecines (basal hominids) have energetic costs approximately 1% higher than chimpanzees, but that for *Homo* the additional costs vary from 5-17% depending on brain size and age (Foley & Lee 1992:229).

This is unique and valuable research because "it could be argued that these models indicate the extent to which different hominids require different levels of energy intake" (Foley & Lee 1992:229). Foley & Lee pursued the dietary implications of these findings.

Just as Foley & Lee argue that "the energetics of encephalization are a significant factor in human foraging and dietary strategies" (p.228), so too will I argue that the evolution

⁴³ The reader will recall from Chapter 1 that this is the exact phrase we used to describe the a priori assumptions of our own theoretical interests.

Figure 5.9 Estimates of the percentage increase in energy requirements of different brain sizes above those of chimpanzees for hominid infants from birth through 18 months (redrawn from Foley & Lee 1992, Figure 4 with minor corrections). See text for discussion.

of the machinery for catecholamine biosynthesis in the neocortex and especially primate association cortex (Brown et al., 1979) must have been significant factors in the evolution of certain dietary biases (e.g., meat eating and the pursuit of otherwise high protein foods). Hopefully it goes without saying that protein supplies amino acids, and hence dietary proteins may have some effect on brain neurotransmitter synthesis.

5.5.2 Nutritional Requirements of Encephalization

Leonard & Robertson (1992) recognized that one of the implications of Martin's research was that "the energetic costs associated with the evolution of a large brain must have been facilitated by important changes in the composition of the diets of our ancestors" (p. 179). It was against the backdrop of this realization that they set out to provide "estimates of energy needs for fossil hominids [that could] provide an additional source of data for developing and/or evaluating alternative hypotheses regarding human evolution" (1992:180). Figure 5.10 provides a summary of their estimates of the percentage metabolic energy devoted strictly to brain metabolism for selected hominid species.

Whereas the percentage of metabolic energy devoted to brain metabolism in *Australopithecus afarensis* can be estimated in the range of 8.3-9.0, the neurometabolic needs of the brain of *Homo*

Figure 5.10 Estimates of the percentage of resting metabolic energy devoted to brain metabolism ($100 \times \text{brain MR/RMR}$) for selected hominid species (based on Leonard & Robertson 1992, Table 4). BM= brain metabolism. RMR = resting metabolic rate. See text for discussion.

erectus increased to 13-14.6. This represents, according to their estimates, a 35-55% increase in caloric needs. They concluded on the basis of these and related estimates that

within the fossil record, it appears that both total energy expenditures and energy required by the brain increased substantially with the emergence of *Homo erectus*...The high total metabolic needs and the large proportion of energy required by the brain imply that important dietary changes occurred with *H.erectus* (Leonard & Robertson 1992:179).

Perhaps this is why we see *Homo erectus* selectively scavenging the livers of carnivores at Koobi Fora (Upper Member) some 1.6 mya (Walker et al., 1982). As Blumenberg (1983:598) likewise independently conceived, such behaviours may have had consequences for neurotransmitter synthesis and thus "broad based activity patterns in the brain" (recall Figure 1.1). I will pursue this idea at greater length in Chapter 12.

One aspect of Leonard & Robertson's research that is clearly not compatible with our thesis is revealed in the following quote. Paradoxically, however, they illustrate their conclusions with reference to an 1969 paper that perhaps I can use to provide indirect support for my position.

The clear implication is that the diet of *H.erectus* was not simply an australopithecine diet with more meat; rather, there were important changes in both animal and vegetable components of the diet. In fact the need for protein per se probably had very little to do with the evolution of the hunting and gathering economy. Protein requirements, like energy needs, scale to the 3/4th power of body weight across all mammals (Munro 1969). Therefore the protein needs for *H.erectus* should have been

proportionally the same as for earlier hominids. **What made meat an important resource to exploit was not its' high protein content, rather, its high caloric return (i.e., larger proportion of metabolizable energy and higher lipid content than most plant foods)...** (Leonard & Robertson 1992:191, added emphasis).

The suggestion in boldface terms poses a challenge to our own theoretical agenda because it denies the relative importance of protein/amino acid acquisition. And yet the prior insight helps us understand why Brown et al. (1979) would have observed that "machinery for biosynthesis of the catecholamines may have developed *pari passu* [by an equal progress] with the evolution of the primate neocortex, particularly in relation to the expansion of the association cortex" (Brown et al., 1979:146). I will explain my meaning.

Let us assume for the moment that NT synthesis scales to 3/4th's of body weight. In Chapter 10 we will confront evidence that will suggest the unique electrophysiological properties and unusual precursor dependence of the PFC (Deutch & Roth 1990:375; Bannon et al. 1981; Bunney & Chiodo 1984) may provide a unique and potentially profound exception to this general rule. In that sense then, we may yet be constrained to interpret Leonard & Robertsons's conclusion with some degree of scepticism. Just as Commissiong (1988:185) will later be quoted as saying "the role that catecholamine precursors (phenylalanine and tyrosine) play in regulating the synthesis of DA and NA in different brain regions of

the CNS will have to be explored on a case by case basis", so too might I suggest that a more thorough examination of the developmental, electrophysiological, microstructural, and functional properties of some specific regions of the brain (that is, the ones that underwent the most significant allometric increases in size in members of the genus *Homo*) is warranted. This effort may yet provide evidence in favour of Pulliam's original (1974) insight that

a diet which maximizes calories per unit time might only be adaptive at times of extreme food shortage. A partially satiated predator might do better to specialize on a prey with a high amount of some needed nutrient rather than stick to the diet which maximizes caloric intake. **The diet which maximizes fitness may not be the diet that maximizes the rate of caloric intake** (Pulliam 1974:70, added emphasis).

In Chapter 12 I will explore the idea that (all things being equal) the diet that may have maximized the adaptive fitness of our hominid ancestors may have been the one that maximized intake of the amino acids necessary to effectively satisfy and maintain the unusually high precursor demands of the evolving PFC.

6.0 BRAIN EVOLUTION: THEORIES AS GIVEN

Many theories have been advanced to explain the proximal causes for, or otherwise significant factors in, human brain evolution. By way of a rather long list: "hunting" (Dart 1953, Ardrey 1961, Washburn and Lancaster 1968); "gathering" (Tanner and Zihlman 1976, Zihlman & Tanner 1979, Tanner 1981); "tool making" (Washburn 1960, Lancaster 1967, Tobias 1981); "information processing capacity" (Jerison 1973, 1979, 1982; Parker & Gibson 1979; Gibson & Parker 1982, Gibson 1993); "food sharing" (Isaac 1978) and "central place foraging" (Isaac 1983); "heat-stress" under conditions of primitive hunting (Fialkowski 1986, 1987); "cold-stress" under conditions of reduced climatic temperature (Beals et al., 1984); the cognitive/mnemonic requirements of foraging spatially and temporally distributed foods (Bauchot & Stephan 1966, 1969; Milton & May 1976; Eisenberg & Wilson 1978; Clutton-Brock & Harvey 1980; Milton 1988); the cognitive requirements of extracting foods from complex hidden matrices or so-called "omnivorous extractive foraging" (Gibson 1986); the mnemonic (foraging related) requirements of increased longevity (Allman 1990); maternal energetics (Martin, 1981, 1982, 1984); "language" (Shepartz 1993; Bickerton 1990); group size and the evolution of "vocal [in lieu of physical] grooming" (Aiello & Dunbar 1993); positive sociality (Holloway 1966, 1981); social manipulation, "scenario-building" and deception (Alexander 1989) or so-called "Machiavellian intelligence" (see various articles in

Byrne & Whiten 1988), and, interestingly, long-chain fatty acid availability (Crawford & Marsh 1989) have all variously been proposed as prime movers of hominid evolution.

In this chapter I will endeavour to discuss the essential features of all of these theories. I will divide them up according to their perceived historical, contemporary, or directly relevant theoretical status. I will not pursue the first importance of bipedalism because that would be redundant over the interpretations offered in Chapter 3. Suffice it to say: "the best, and perhaps single uncontested candidate for a feature critical to hominid origins is bipedalism. Aside from bipedalism, no other 'uniquely hominid' behaviours are currently agreed upon" (Shepartz 1993:94).

6.1 Historical Perspectives on Brain Evolution

6.1.1 Hunting

Historically it was assumed that our ancestors were blood-thirsty carnivores whose killer instincts were responsible for human evolution (e.g., Dart 1953). It was thought that everything that made us uniquely human devolved from the social and technological requirements of "the so-called hunting way of life" (see Haraway 1988 for a brilliantly sardonic historical review). In its most extreme formulation hunting was seen not as "...a mere

subsistence category, but a way of life that served as the "integrating schedule" of the nervous system" (Haraway 1988:233). There was only one small glitch: the fossil record failed to support the view that our early ancestors were systematic hunters (Behrensmeyer 1987; Speth 1987; Blumenschine 1987, 1992; O'Connell et al., 1988; Blumenschine & Cavello 1992). They were at best "opportunistic scavengers" who had last access to what generally remained: long bone marrow and fat (Blumenschine 1992). In all probability, therefore, "foods such as tubers, roots, fruits, nuts, eggs, insects, and other small animals were quantitatively the main items of early hominid diet" (Isaac & Crader 1981:94). The search for the "prime mover" continues with the full recognition that "the earlier, too literal approach [to the fossil record] sometimes gave rise to unjustifiable conclusions which we now try to avoid as we realize that knowledge of the processes and agencies involved in the formation of a site is essential to its interpretation" (Clark 1985:69-70).

6.1.2 Tool Making

We mentioned the "scientific mythic significance of technology" (Haraway 1988) in Chapter 3. Tools were assigned causal status for basically two reasons: (1) the ideological supremacy of the hunting hypothesis and (2) on the archaeologically-based assumption that the human brain evolved more or less concurrently

with technology (Wynn 1988:281-282). One caveat applies: it was not the tools themselves that were significant but the fact that they were "the fulcrum for a complex of behaviours, including language and hunting, that levered intelligence onto a higher plane" (Wynn 1988:272).

In 1983 Holloway argued that "the appearance of stone tools made to a standard pattern preceded any really clear demonstrable change in the brain (as measured by its volume)" (Holloway 1983:288). Somewhat ironically Wynn (1988) later argued that (1) "it is not until the appearance of *Homo erectus* that we have evidence of a technology that is well outside of what is known for apes" (Wynn 1988:280); (2) "hominids made and used more or less the same range of tools at 300,000 years as they used at 1.5 million...and from the perspective of spatial concepts and Piagetian theory, the record after 300,000 years shows no developments" (Wynn 1988:281-282). And (3) "most of our technology developed after the evolution of modern brains and modern intelligence. Therefore it seems an unlikely selective factor in and of itself" (Wynn 1988:282). While Holloway and Wynn may disagree on timing, the point is still made: the evolution of human technology (exhibiting significant periods of conceptual stasis) did not co-evolve with the human brain. This is not to suggest that technology has lost its mythic appeal. As Wynn observes "the concepts and terms of ecology and ethology now elaborate the earlier and simpler notion of 'tool maketh the man.' It is

unfashionable to focus on tools themselves, but very fashionable to focus on the natural systems in which tools play a central role [e.g., extractive foraging (Gibson 1986)]" (Wynn 1988: 272).

6.1.3 Gathering

The term "gathering" is a descriptive shorthand for a theoretical position that has as its origins a feminist reaction to the masculinism of the then dominant interpretive paradigm, the so-called hunting hypothesis. Historically, anthropologists were so enamoured with the biases of the archaeological record⁴⁴, and so enamoured by the idea that our male ancestors were bonding and hunting and killing, that they virtually denied women a role in human evolution. If women were apprehended at all it was only vaguely - i.e., through the lens of the still popular assumption that women were breeding machines cowering helplessly in caves waiting to trade sex for scraps of meat. Feminist anthropologists rendered quite clear the several related facts that: (1) women were very obviously quite self-reliant (as suggested on the basis of the cross-cultural observation that women provide on average 80% of the calories of contemporary gather-hunter societies); (2) the first tools were in all probability baby slings, carrying containers, and digging sticks; and (3) the first social groups were in all probability formed by females (around a core of dependent

⁴⁴ Plants do not fossilize.

offspring) whose birth spacing was probably 2-4 years apart (Lee & DeVore (1976) and Tanner & Zihlman (1976) cited in Haraway (1988)). In effect, these scholarly initiatives served to "undercut the fundamental organizing axis of male dynamism in hominization" (Haraway 1988:252). Clearly this was a very necessary (if only partially realized) historical event.

6.1.4 Information Processing Capacity

As we saw in Chapter 5, Jerison (1973) championed the view that by controlling for the influence of body on brain size we can produce measures of relative brain size [conveyed though the use of an EQ] that enables estimates of the degree to which various species might possess a quantity of "extra neurons" that are in all probability devoted to higher-order cognitive functions. It was thought that the higher the EQ the more "information processing capacity" the species possessed. This was taken as an indicator of "intelligence" (so defined) and later as a property of mind (Jerison 1990). In this sense then natural selection was seen to have been acting on the "information processing capacity" of our hominid ancestors by way of selection for increases in brain size.

Holloway (1966, 1981) was instrumental in generating concern for a strict reliance on such "distal phenotypic manifestations" as "brain size only". We encountered the specifics of his position in

Chapter 5. One point, however, I did not render clear. The most basic criticism of Jerison's legacy (i.e., the use of EQs and the like) is that they create the impression that brain size is somehow correlated with "intelligence". And yet, as Holloway observes,

progressing from an Oldowan pebble tool to that of a Mousterian point involved perhaps as much as two to three million years, and the respective makers show a growth in cranial capacity amounting to about 900-1000 cm³, which is, incidentally, the total range of variation of cranial capacity in normal modern *Homo sapiens* (1981:296).

We must remember, however, to separate out the wheat from the chaff. Perhaps EQs are suspect because we do not have reliable postcranial estimates to work into the denominator of the formula, but certainly the idea that natural selection favoured increases in information processing capacity is a reasonable one.

6.1.5 "Food Sharing" and "Central Place Foraging"

Isaac (1978) championed the view that human "food sharing" (which can be contrasted with the non-human practice of "tolerated scrounging") was a critical selective factor in human evolution. Later (1983) he shifted the emphasis to "central place foraging" because it more readily conveyed the substance of his thesis: i.e., that food sharing was intimately related to technology and hunting and had implications for the evolution of human sociality including (amongst other things) stable social group formation, pair bonding, and the sexual division of labour. In his words:

food sharing [is] the behaviour central to a novel complex of adaptations that included as critical components hunting and/or scavenging, gathering and carrying...[that] could only have functioned through the use of tools and other equipment. For example, without the aid of a carrying device primates such as ourselves or our ancestors could not have transported from the field to the home base a sufficient amount of plant food worth sharing" (Isaac 1978 cited in Isaac 1989:306).

The major criticism is that the archaeological record does not support the assumption that our early ancestors were skilled enough hunters to have acquired sufficient plant food to have supported the kinds of social interactive dynamics that Isaac's model is predicated on. As Blumenschine (1992) explains:

the crux of the debate between Isaac and Binford on the socio-economic function of early archaeological sites is not whether hominids hunted or scavenged, but rather whether the nutritional yield (i.e., tissue types and regularity of carcass acquisition by hominids was adequate to promote food transport and sharing (1992:212).

In an effort to solve this debate Blumeschine (1992) analyzed "carcass consumption sequences" at early archaeological sites. He concluded the following: (1) early hominids were probably restricted to scavenging carcasses and long bones containing marrow that were largely defleshed before our ancestors could access them (Blumeschine 1992:215); and (2) "rather than promoting cooperative sharing, such small amounts of easily defended, energy-dense bone marrow might instead encourage intragroup competition" (Blumenschine 1992:218).

6.1.6 Positive Sociality

Ralph Holloway (e.g., 1983) has been instrumental in raising our consciousness about the importance of social factors in human evolution. Responding to the mythic-proportioned significance of technology, Holloway argued that

the growth of the brain reflects selection pressures for increased behavioural adaptability. But perceptual, cognitive, and motor aspects of stone tool-making were only an aspect of social behavioural adaptability and evolution during the Plio/Pleistocene. Rather than seeing stone tools and the makers' motor skills as the primary focus for pressures of natural selection. I regard them as clues to the more complex social processes that were under direct selection pressures. In other words, it was not the tools themselves that were the key factors in successful evolutionary coping. Rather, the associated social, behavioral and cultural processes, directing such activities as tool-making, hunting and gathering were basic (Holloway 1983:288).

This can be contrasted with the position of the (dare I say) "machievellian intelligentsia" discussed in section 6.2.3 below. While Holloway stressed the positive aspects of human sociality, proponents of the latter stressed the negative. They both agree, however, that the greatest challenges facing humans were in the area of social control, and as such would have created the selective pressures necessary for brain expansion.

6.1.7 Language

While "language" per se may not be unique to humans, the symbolic complexities of human language are clearly evolved over

that of the non-human primates. In this sense, then, language can still be seen to have provided a significant selective impetus for the evolution of the brain. As Chomsky (1980:439 quoted in Eccles 1989:80) explains:

...human language which develops even at very low levels of human intelligence and despite severe physical and social handicaps, is outside the capacities of other species, in its most rudimentary properties...The difference appears to be qualitative: not a matter of 'more or less', **but of a different type of intellectual organization.**

This can be illustrated with reference to Eccles' (1989) discussion on the functional components of language.

Citing Popper, he lists four properties or rather "levels" of human language: (1) the "expressive or symptomatic function" characterized by the utterance of affective states of experience; (2) the "releasing or signalling function" characterized by an attempt to elicit a reaction in the receiver; (3) the "descriptive function" characterized by efforts to describe objects and experiences holding out the unique potential for lying; and (4) the "argumentative function" characterized by efforts to engage in rational thought and discourse. This is language at its highest level. Implicit is the idea that "each level of language is permeated by the lower levels" (Eccles 1989:72). Once again we confront the notion of functional hierarchies (Laughlin et al., 1990).

Eccles concludes that while "there is no doubt that apes are adept at learning symbolic languages at level 2, i.e., as signals...it is doubtful if they ever manage to rise to level 3, descriptive language, and of course level 4 is not in question" (Eccles 1989:80). So it would seem, then, that the uniqueness of human language remains fundamentally intact when analyzed from a functionalist perspective. By way of clarification, it is understood that the evolution of language contributed significantly and uniquely to the evolution of culture and all that that entails.

For an up to date discussion on the many ways in which anthropologists are currently endeavouring to extrapolate an understanding of the linguistic and cognitive competencies of our early hominid ancestors by analyzing the levels of predetermined complexity worked into various lithic technologies the reader is referred to the many articles in Gibson & Ingold (1993).

6.2 Contemporary Theories of Brain Evolution

6.2.1 "Heat Stress"

Fialkowski's (1986) position devolves somewhat ironically from the assumption that "human brain capabilities definitely exceeding those required for hunting constitute the key problem of hominid

evolution" (Fialkowski 1986:288). I say ironically because he then concludes that

the increase in size and complexity of the hominid brain (at any rate, the early stages of the process) was largely a side effect of an evolutionary response to considerably increased heat stress under conditions of primitive hunting (Fialkowski 1986:288).

Heat stress, he hypothesizes, would have been redundancy producing [because brain cells are especially vulnerable] hence the increases in cranial capacity observed in our hominid ancestors. How he reconciles the functional implications of his model - i.e., that "reliability adaptation should tend to support mainly the vital functions" (Fialkowski 1986:289) - is quite clever. He states quite simply that

the brain we observe now is the result of at least 100,000 years towards abstract thinking...therefore it is possible that the cerebral association areas have changed their function, originally in having been mainly oriented to the vital (Fialkowski 1986:290).

6.2.2 "Cold Stress"

Beals et al.'s (1984:301) position is also quite parsimonious (if somewhat more cautious):

hominid expansion into regions of cold climate produced changes in head shape. Such change in shape contributed to the increased cranial volume...This thermoregulatory model is taken not as exclusionary or competitive with other approaches but rather as an adjunct toward understanding the distribution of cranial morphology over time and space.

Their "clinal depiction of cranial capacity at heterographic present" is most interesting. So too are their related efforts at developing clinal maps of the Pleistocene. By way of explanation, their position is predicated on the ability to establish the occurrence of climatic shifts that would have provided the preconditions necessary for both changes in cranial morphology and attendant increases in cranial capacity. For a critique of this theoretical perspective the reader is referred to the comments of various authors provided at the end of his original article (Beals 1984).

6.2.3 Machiavellian Intelligence

This is an interesting theory if for no other reason than it is sensationalistic. Proponents argue that the process of hominid encephalization was punctuated by an adaptive premium placed on such skills as social manipulation and deception. Alexander (1989) provides us with an example of their deductive reasonings:

The most unpredictable and demanding aspects of the environment of evolving humans have always been its social aspects, not the physical climate or food shortages, as is often implied. The human psyche was designed primarily to solve social problems within its own species...This hypothesis rejects the notion that complex intellects evolved because they saved early humans from starvation, predation, climate, weather, or some combination of such challenges. All other organisms solved these kinds of problems...without complex human-like intellects...

The central evolved function of the human psyche...is to yield an ability to anticipate or predict

the future - explicitly the social future - and to manipulate it in the (evolutionary, reproductive) interest of self's genetic success...all other effects or properties of the psyche are secondary to this strategic functions (Alexander 1989:457-459, added emphasis).

The most serious challenge to this hypothesis comes to us by way of Milton's (1988) efforts at defending the alternative position of the foraging theorists. Quite simply: "since no other primate species shows cerebral expansion similar to that of the human lineage, sociality, in itself, is not a sufficient explanation for the evolution of large brain size in humans" (Milton 1988:296). Parenthetically, this be also be construed as a caveat that applies to Holloway's position discussed in section 6.1.6.

6.2.4 Group Size and "Vocal in Lieu of Physical Grooming"

Aiello & Dunbar (1993) contribute significantly to our understanding of the relationship between the evolution of human language and the evolution of the human brain. They relate both to the social consequences of group size, or more specifically, increases in group size (that would invariably come about as a consequence of defense-related needs associated with increasing environmental aridity). According to Aiello & Dunbar (1993) group size has implications for the evolution of vocal in lieu of physical grooming. Their basic argument is that human groups need mechanisms to ensure social cohesion, and language picks up where

physical [or as they say, "social"] grooming leaves off. Theoretically, the selective pressures favouring this shift become increasingly acute as group size eclipses the ability of individual members to service their social relationships in conventional physical ways.

As the original authors explain and conclude:

the need for large groups among our early ancestors was the driving force behind not only the evolution of language **but also hominid encephalization**...The close relationship between encephalization and group size allows us to predict the point in time at which groups became so large that language would have been necessary to maintain social cohesion. When this model is applied to the fossil record it suggests that the necessity for both large groups and (at least rudimentary) language appeared early in the evolution of the genus *Homo* and began to increase rapidly in the second half of the Middle Pleistocene [i.e., 250,000 years ago] (Aiello & Dunbar 1993:184, emphasis added).

Methodologically, "this hypothesis is based on a close statistical relationship between relative neocortex, group size, and the amount of time devoted to social grooming among non-human primates" (Aiello & Dunbar 1993:184). Their basic argument is that "language evolved as a form of bonding mechanism in order to use time more efficiently" (p.184). As such, the requirements of group size and language created the selective pressures that ultimately came to favour increases in hominid cranial capacity.

The archaeological record provides support for Aiello and Dunbar's (1993) correlational model. That they calculate the

beginnings of a shift in group size with the first appearance of *Homo* is only appropriate given that this is, of course, when we see the first signs of a cerebral departure from the great apes.

6.3 Relevant Theoretical Perspectives

6.3.1 The Foraging Strategy Hypothesis

In Chapter 5 we examined the factual basis of the foraging strategy hypothesis of brain evolution (Milton & May 1976; Clutton-Brock 1977; Clutton-Brock & Harvey 1977, 1980; Milton 1988). Once again, what all these prominent anthropologists share is a strong conviction that brain evolution arose as a consequence of the behavioural and cognitive demands of foraging spatially and temporally distributed foods. As Milton (1988) explains, there are five issues that provide the foundation for this theoretical framework: (1) body size, diet, and home range size; (2) spatial distribution of potential plant foods; (3) temporal distribution of potential plant foods; (4) predictability in space and time; and (5) food search efficiency. I will define each issue in turn.

Under "body size, diet, and home range size" it has been observed that

primates eating primarily young leaves should have larger supplying areas than those specializing on more mature leaves, while fruit specialists should have larger

supplying areas than leaf specialists (with body size and all other considerations being equal) (Milton 1988:285).

Under "spatial distribution of potential plant foods" it has been observed that while plant food sources in the tropical forest are quite diverse, they do, nonetheless, exhibit very low densities that could be characterized as "patchy in space" (Milton 1988:286). Under "temporal distribution of potential plant foods" it has been observed (on the basis of Milton's invaluable 1980 research) that

young leaves were available on particular species for a mean of 6.8 months of an annual cycle, green and ripe fruits for 3.7 months, and flower buds and flowers for 2.7 months. Ripe fruits, however, were available on particular species for only 1.1 months. Further, these times were available on individual trees for even shorter periods of time: new leaves for a mean of 5.3 months, green and ripe fruit for 2.1 months, and flower buds and flowers for 1.8 months. Ripe fruits were available for individual trees for only 0.8 months. Examination of the nutrient content of some of these dietary items showed that in individual cases some of these apparently were optimally edible for no more than 72 hours per annum (e.g., flush leaves for *Cebia pentandra*) (Milton 1980). Thus, **potential foods for primates in such forests can be described as patchy in time and generally ephemeral in terms of optimal nutritional quality** (Milton 1988:286, emphasis added).⁴⁵

Under "predictability in space and time" it has been observed that once a primary consumer establishes the location and timing of a preferred food item it can use it for the rest of its lifetime. This "may have served as a critical stimulus in the development of cerebral complexity in higher primates for it places them under

⁴⁵ I will return to the issue of temporal constraints on the acquisition of foods containing "optimal nutritional qualities" in my major theoretical chapter in Part 4.

somewhat different selective pressures than secondary consumers" (Milton 1988:287).

Lastly, under "food search efficiency" we confront the neurological implications of "optimal foraging theory" discussed in Chapter 3. Milton asks: "how might selection function to improve food search efficiency when dealing with patchily distributed plant foods ?" (Milton 1988:287). She concludes the following:

Increasing mental complexity with a strong emphasis on learning and retention is one direction selection could take. This would accomplish the dual purpose of improving an animal's ability to recognize and remember the locations and timing of a variety of preferred foods as well as provide the required behavioural flexibility. In time, 'wise' primates that could seek out the most nutritious foods with the least expenditures of time and energy should outcompete 'less wise' primates relying primarily on a strategy of chemosensory cues or random search (Milton 1988:287-288).

Noteworthy too is the fact that Milton (1988) provides evidence in support of the hypothesis that "all else being equal, those primate species dependent on the most hyper-dispersed and patchy foods should show greater evidence of mental development than primates eating more uniform dietary resources" (p.288).

In section 6.3.3 I will discuss one of the major challenges to the theoretical position of the foraging theorists (i.e., with reference to Martin 1984).

...

6.3.2 "Omnivorous Extractive Foraging"

An interesting variation on the finding that EQ is higher in frugivores than it is in folivores (discussed in Chapter 5) is the observation that "small brains are found among insectivores, frugivores, omnivores and folivores who eat exposed rather than hidden foods and who manipulate foods using only typical primate hand-eye coordinations" (Gibson 1986:100). This provides an exception to the general rule as it suggests that "cortical enlargement may have arisen as an adaptation to feeding on varied foods which are difficult both to procure and process" (Gibson 1986:94). This differs from the other applications of foraging theory insofar as it places the emphasis not on spatial or temporal aspects of food distribution, but, rather, on the variety and complexity of cognitive operations required in order to obtain "extractive foods" once found. Several examples of extractive foods are provided in the following:

nut-meat, shellfish, snails, eggs, brains or bone marrow which must be removed from hard outer coverings, seeds and beans that must be removed from pods, tubers or roots that must be dug from the ground, ants and termites that must be removed from mounds or hills, insect larvae or pith that must be extracted from bark, and meat that is extracted from its hide prior to ingestion (Gibson 1986:96).

As Gibson (1986:100) stresses:

extraction per se does not appear to be the critical variable with respect to brain size. Rather, neocortical size correlates with the complexity of and variety of the

sensorimotor coordinations needed for the finding and processing of foods.

Equally interesting is the observation that

extractive foods tend to be premium foods, high in both energy and protein. Many are readily available during the dry seasons. Consequently, animals who can utilise these foods may gain access to the year-round high-calorie diet essential for the support of a large brain (Gibson 1986:96).

This suggests an indirect relationship between EQ and the quality of the foods. Depending on your viewpoint, this could be construed as either complementing Foley & Lee's (1992) findings regarding the relationship between the quality of diet and EQ (recall Figure 5.8). Whereas Foley & Lee (1992) detect a **direct** relationship between the quality of diet and EQ, Gibson (1986) detects an indirect one, confounded (as it were) by the type of cognitive tasks required to obtain those high quality "premium" foods. While I can offer no resolution to the debate, I agree with Martin (1984:76, quoting Peters 1976) that

considerable caution must...be exercised in proceeding from the recognition of correlations (or deviations from a trend) to the inference of underlying casual processes.

There may be as many causalities suggested here as there are interested observers, and there may be no foolproof way to distinguish 'correct' from 'erroneous' suggestions [cited in McNab 1980].

...

6.3.3 The Energy Strategy Hypothesis

Martin (1981) observed that brain size is correlated with maternal metabolic turnover. Some of the specifics of his model were encountered in Chapter 5. Recognizing the competitive preeminence of the so-called foraging strategy hypothesis, Martin (1984) responded as follows:

maternal metabolic turnover sets certain constraints for fetal brain development and broadly determines neonatal brain size in accordance with Kleiber's Law...One can [therefore] inquire whether grade differences in relative brain size between dietary categories - e.g. between primate folivores and frugivores - might be correlated with grade differences in metabolic rate...

[I]t can be concluded that some species exhibit **"high-energy strategies"**...[e.g., frugivores], while other exhibit **"low energy strategies"**...[e.g., folivorous primates]...Species with "high-energy strategies" are typically found to have significantly larger brains than their ecological relatives with "low energy strategies". Accordingly, it is quite reasonable to postulate...that brain size largely reflects maternal metabolic turnover during gestation **and that the correlation between dietary habits and relative brain size is secondary rather than indicative of a direct causal relationship** (Martin 1984:90-92).

He concludes with the rejoinder that

instead of postulating that mammals with "high-energy strategies" need larger brains in order to locate their food in the environment (e.g., because it is patchy and unpredictable in distribution) one might simply propose that such mammals can afford larger brains because of the higher level of metabolic turnover in pregnant females (Martin 1984:92).

Martin does concede, however, that

in reality it is likely that the two competing hypotheses advanced to explain the correlation between relative

brain size and diet (which can be termed the "foraging strategy hypothesis" and the "energy strategy hypothesis", respectively) must to some extent be combined in order to produce a valid theory (Martin 1984:92).

As an example of how this might be the case he suggests that "differential feeding strategies have direct implications for metabolic turnover which have indirect repercussions for relative brain size" (Martin 1984:93).

The position of the Allman (1990) is interesting because it reflects a vague attempt to reconcile the differences between the foraging and energy strategy hypotheses.

6.3.4 Longevity

Allman's (1990) position is similar to that advanced by the proponents of the foraging strategy hypothesis. His hypothesis is that "neocortex evolved in tandem with the higher energy metabolism characteristic of mammals so as to assure a continuous localization of food resources" (Allman 1990:278). His position is unique, however, with respect to the emphasis he places on the cognitive/mnemonic requirements of increased longevity.

Neocortex is most expanded relative to body size in species with the greatest life span. The expanded neocortex enables metabolically active mammals to store the necessary experiences, foraging strategies, and cognitive processes to cope with periods of food shortage that will inevitably occur during a long life span (Allman 1990:279).

This seems a reasonable position to take - especially insofar as it attempts to reconcile the competitive imperatives of the foraging and energy strategy hypotheses of brain evolution by invoking a third variable emphasis on increased longevity.

6.3.5 Long-Chain Fatty Acid Availability

This theory comes to us from outside the realm of anthropology. It is predicated on the understanding that

the most important new group of chemicals investigated in recent years is that of the essential fatty acids. These are used to build structural lipid in a similar way in which essential amino-acids build protein. Structural lipids construct cell membranes...they are quantitatively the most important structural components in the brain and nervous system...They account for 50-60% of the materials used to construct the brain (Crawford & Marsh 1991:119).

This observation has obvious implications for our understanding of the relationship between diet and brain evolution.

Crawford & Marsh hypothesize that brain evolution was "substrate driven" by dietary fatty acid availability factors relevant to CNS structural complexity. According to their interpretation, animals (including ancestral hominids !) who were more adept at acquiring pre-formed structural lipids would benefit not only metabolically but neurologically. As they surmise:

the process of building up these long-chain fatty acids is tedious. Any animals that can bypass even a part of it

can switch off the mechanism, save on effort and time and possibly on genetic 'disk space'. The same argument applies as with vitamin A: **the direct supply of preformed neural fatty acids could allow development of biological systems dependent on or stimulated by these nutrients** (Crawford & Marsh 1989:128, emphasis added).

Clearly, this is highly compatible with our own theoretical agenda - only in this thesis I am interested in dietary amino acids and their effects on NT synthesis as opposed to fatty acids and their effects on lipid membrane construction. In either case the same caveat applies: "the test of nutrition or substrate driven change is that a biological expression of change would follow a significant alteration in food structure" (Crawford & Marsh 1989:204). Crawford & Marsh satisfy this requirement within the context of their own inquiry. So too will I endeavour to demonstrate this with respect to the activities of the NT amino acid precursors at critical developmental stages.

Crawford & Marsh (1989:12) argue that

just as the beginning of life was determined by chemistry so its later forms and expressions were also chemically shaped: not exclusively - sometimes chemistry would operate independently, sometimes in tandem with selection, and sometimes selection would operate alone.

This is something I will explore in Part 4 from the standpoint of my own theoretical interests. In many respects this is the most reasonable position to take because it satisfies the same theoretical and methodological requirements I am imposing on my own thesis: "there is perhaps more to be learned in concrete terms

about hominid brain evolution by asking how our ancestors could afford (in energetic terms) to develop large brains than by speculating about why they needed them" (R.D. Martin commenting in Blumenberg 1983:607).

PART THREE

THE NEUROSCIENCE OF BRAIN CHEMISTRY, STRUCTURE AND FUNCTION

7.0 SEROTONIN

In this chapter I will examine the process of serotonin (5HT - 5-hydroxytryptamine) synthesis and release, its content and activity patterns across various cortical and subcortical structures, and some select aspects of the behavioural/cognitive functions serotonergic mechanisms have been implicated in. This will establish the many ways in which serotonin activities contribute to the ongoing maintenance of brain function. Tangential references to the food sources that provide both adequate and inadequate supplies of the nutrients implicated in 5HT synthesis will also be provided. In Chapter 11 I will examine the developmental profiles of 5HT content and activity patterns in many of the same structures examined below.

7.1 Tryptophan and 5HT Synthesis

The steps involved in 5HT synthesis are depicted in Figure 7.1. The amino acid tryptophan is converted into 5-hydroxytryptophan (5HTP) by the enzyme tryptophan hydroxylase. This is the rate limiting step in 5HT synthesis (Fernstrom 1988:137). The enzyme aromatic amino acid decarboxylase then converts 5HTP to 5HT. Monoamine oxidase (MAO) breaks liberated 5HT down into its principle metabolite 5-hydroxyindoleacetic acid (5-HIAA).

Figure 7.1 Serotonin (5HT- 5hydroxytryptophan) synthesis. A = minor pathway of tryptophan metabolism. B = anthranilic acid pathway of niacin production. See text for discussion.

The reason the relationship between tryptophan and 5HT synthesis is so interesting is because "serotonin-releasing neurons will virtually **always** produce more or less of their transmitter when they are provided with more or less of its precursor" (Milner & Wurtman 1986:880). And this doesn't just apply to experimental settings. As Acworth et al. (1988:121) emphasize: "brain tryptophan levels - and serotonin synthesis - are influenced by *normal* meal-to-meal variations in what one eats...".

The implications of these findings are quite profound from a functionalist perspective. As Acworth et al. (1983) have quite boldly suggested, "the participation of serotonergic neurons in a large number of brain functions might have the effect of making these functions '**hostages to eating**'" (Acworth et al. 1988:125). It remains for sections 7.4 and 7.6 and parts of Chapter 11 (aspects of chemical neuroanatomy, psychopharmacology, and developmental neurobiology, respectively) to establish just what kinds of 'brain functions' serotonergic mechanisms might conceivably be implicated in. In Chapter 12 I will pursue the neuroanthropological implications of this theoretical deduction.

Parenthetically, while the daily requirements for tryptophan are not yet firmly established, 82-630 mg/day constitute the low-to-high range (Burton 1976:51). Plant foods (such as corn, potatoes, rice) are poor to marginally adequate sources of

tryptophan. The best sources of tryptophan are **beef** (300 mg/100g), **liver** (246 mg/100g) and **fish** (228 mg/100g) (Burton 1976:54-55).

7.1.1. Niacin and 5HT Synthesis

As seen in Figure 7.1 (left portion of drawing) tryptophan can also be diverted into *niacin* production via the *anthranillic pathway* (Bender 1992:247). This places a heavy burden on the tryptophan content of diet because even

under normal conditions almost all of the dietary intake of tryptophan, apart from the small amount that is used for **not** new protein synthesis, is metabolised by this pathway...About 1% of tryptophan metabolism is by way of [serotonin synthesis] (Bender 1992:199, emphasis in the original).

The importance of this observation is underscored by the fact that "even when tryptophan intake is limited, part of it appears to be diverted into the niacin pathway" (Dakshinamurti 1977:287. See also Bender 1992:199 and 247).

Whether or not a niacin deficiency can cause impairments in 5HT-mediated cognitive functions remains to be empirically established in a controlled experimental setting. The clinical symptoms associated with *pellagra* (the most conspicuous disease associated with a niacin deficiency) are, however, suggestive of this possibility. The symptoms include "depression, apprehension,

hyperirritability, emotional instability, and an impairment of recent memory" (Dakshinamurti 1977:281-282). All of these symptoms have been variously equated with an underfunctioning of serotonergic mechanisms (Anisman et al. 1990; Richter-Levin & Segal 1989; Young 1988).

Parenthetically, the recommended daily allowance (RDA) for niacin is 13-18 mg/day (Burk & Solomans 1985 cited in Chafetz 1990:257). And

although present in small amounts in virtually all biological materials, it is ~~meat~~ (with 5-15 mg (100g)⁻¹) that is the richest source...Fruits and vegetables, particularly legume seeds, are [also] quite useful sources [0.7-2.0 mg (100g)⁻¹] (Coulter 1989:198, emphasis added).

7.1.3 Protein, Carbohydrates, and 5HT Synthesis

The synthesis of 5HT is a little more complicated than the preceding would suggest. All of the large neutral amino acids (LNAAs) tyrosine, phenylalanine, histidine, leucine, isoleucine, valine, threonine, and methionine compete with one another for transport to the brain. The facilitated diffusion system which carries them across the blood-brain barrier (BBB) has various affinities for these LNAAs (Table 7.1).

Table 7.1 Affinity constants for the transportation of various large neutral amino acids across the blood-brain barrier *

Amino acid	Valine	Isoleucine	Leucine	Tyrosine	Phenylalanine	Tryptophan
Km (uM)	168	145	87	86	32	52

* Source: Moller (1988:357).

The benefits of carbohydrate consumption to 5HT synthesis is that it gives tryptophan a competitive BBB transport advantage over the other LNAAs that have higher affinities for the facilitated diffusion system. This is because carbohydrate consumption causes insulin release and the preferential sequestering all LNAAs except tryptophan into the skeletal muscles. This has the net effect of reducing the tryptophan:LNAAs ratio which in turn facilitates increased BBB transport and preferential synthesis of 5HT.

The net effect of consumption of a diet relatively high in protein is the opposite. As Wurtman (1988) explains:

the ability of circulating tryptophan molecules to enter the brain is...diminished when the other LNAAs rise. Since all dietary proteins are considerably richer in the other LNAAs than in tryptophan (only 1.0%-1.5% of most proteins), consumption of a protein rich meal decreases the "plasma tryptophan ratio" (the ratio of the plasma tryptophan concentration to the summed concentrations of its major competitors) for brain uptake...This, in turn, decreases tryptophan's transport into the brain and slows its conversion to serotonin (p.76).

Paradoxically then, while tryptophan is obtained from proteins, 5HT synthesis best proceeds under conditions that enhance the carbohydrate:protein ratio in the diet.

As to the significance of this mechanism, Wurtman assumes

the responses of serotonergic neurons to food-induced changes in the relative concentration of plasma amino acids allow [5HT] neurons to serve a special function, as "sensors", in the brain's mechanisms governing nutrient choice (Wurtman 1988:77).

Fernstrom (1988:144) disagrees, and suggests "the search for the ultimate significance of linking 5HT synthesis rate to the supply of tryptophan to the brain must...continue in new and/or renewed directions" (see also Leathwood 1988:280). Perhaps I can provide an alternative hypothesis grounded in evolutionary and behavioral ecology (see section 7.6.1 below).

In Chapter 12 I will dovetail an understanding of the effects of variations in tryptophan and fat availability on social contact aggression and social dominance patterns (section 7.6.1 below) with an examination of seasonal variations in the protein, fat, and sugar/carbohydrate content of a typical primates' diet (provided by Richard 1985). Results of this comparison will lead to the kinds of structured theoretical deductions advanced in section 7.6.1 below.

7.1.4 Thiamine and 5HT Synthesis

Thiamine (vitamin B1) is also implicated in 5HT synthesis. This we know on the basis of the observation that a thiamine deficiency can cause decreases in brain stem, midbrain, and thalamic 5HT and associated impairments in various measures of learning and recent memory (Witt & Goldman-Rakic 1983, Plaitakis et al., 1978). How principally brain stem effects can produce higher order cognitive deficits is attributable to "depletion of serotonin in forebrain structures as a secondary consequence of the thiamine

deficiency-induced brainstem lesions" (Witt & Goldman-Rakic 1983:400).

Parenthetically, the daily requirements for thiamine range from 1-1.4 mg/day (Burk & Solomans 1985 cited in Chafetz 1990:257). Significantly,

although it is extremely widespread in small amounts, only a few foodstuffs can be regarded as good sources. As a general rule it is present in greatest amounts [0.1-1.0 mg (100g)⁻¹ in foodstuffs that are rich in carbohydrate and/or associated with high levels of carbohydrate metabolism in the original living material. Examples are legume seeds and the embryo component of cereal grains (the germ)...The reason why pork should contain about ten times the amount of thiamin [about 1 mg (100g)⁻¹ that beef, lamb, poultry, and fish contain has yet to be established (Coultate 1989:188).

Interestingly, "fruits and vegetables...are **not** important sources of dietary thiamine" (Coultate 1989:191, emphasis added).

7.1.5 Vitamin B6

Ebadi (1978) provides us with a lengthy but apt description of the critical importance of vitamin B6 in brain function.

Vitamin B6 deficiency results in lowered concentrations of coenzyme A in blood, in reduced absorption and storage of vitamin B12, and in increased excretion of vitamin C. Furthermore, vitamin B6 acts synergistically with vitamin E to control metabolism of unsaturated fats, with vitamin C in tyrosine metabolism, and with niacin in its action and participates in niacin synthesis. In addition, vitamin B6 deficiency results in insufficiency of insulin

and alteration of the functions of adrenal and pituitary glands, since it is involved in the synthesis of growth hormone, follicle-stimulating hormone, luteinizing hormone, aldosterone, glucagon, cortisol, estradiol, testosterone, and epinephrine. These above-mentioned hormones, whose metabolism is vitamin B6-dependent, play decisive roles in maintaining the functional integrity of the peripheral and central nervous systems.

Vitamin B6 participates in the metabolism of amino acids in the decarboxylation, transamination, deamination, racemization, and desulfhydration reactions...The crucial roles that these coenzymes play in the maintenance of functional integrity of the brain becomes evident when one realizes that **all the compounds implicated as neurotransmitters are synthesized and/or metabolized by the aid of the vitamin B6-dependent reactions. These include dopamine, norepinephrine, and serotonin...tyramine, tryptamine... taurine... histamine... gamma aminobutyric acid...and even acetylcholine indirectly** (Ebadi 1978:129-130, added emphasis)

Very obviously I will refer back to this quote when I discuss the relationship between vitamin B6 and DA, NE and ACh synthesis.

With regards to the relationship between 5HT synthesis and vitamin B6, it is a consequence of the fact that aromatic amino acid decarboxylase (Figure 7.1) is a pyridoxal phosphate-dependent enzyme (Dakshinamurti 1977:298). Thus the conversion of 5HTP to 5HT is dependent on the availability of vitamin B6. Dakshinamurti (1977:304) cites evidence in favour of the proposition that reduced vitamin B6 is associated with serotonergic deficits and related behavioural impairments.

Parenthetically, the RDA for vitamin B6 is 2-2.2 mg/day (Chafetz 1990). Interestingly, while vitamin B6 "has been found in

at least small amounts [around 10ug (100g)⁻¹] in almost all biological materials in which it has been sought...**meat** and other animal tissues, egg yolk, and wheatgerm are particularly rich sources (around 500ug (100g)⁻¹)" (Coultate 1989:195). Significantly, fruits and vegetables are low in pyridoxine (Dakshinamurti 1977:299). The implication here is that meat eating on the part of our hominid ancestors would have been very beneficial in a biosynthetic/neurochemical sense.

7.1.6 Fats

Kaplan et al. (1991) reported that cynomolgus monkeys maintained for 22 months on low fat diets exhibited more socially-contingent "contact aggression" than did their regularly maintained control counterparts. In the first 3 months of the experiment (but not thereafter) the main effect was status-linked. This meant that the dominant fat-deprived monkeys initiated more contact aggression than did their low ranking but equally nutritionally-deprived counterparts. But after the first three months all fat-deprived primates were equally aggressive regardless of their social status. Kaplan et al. (1991:640) cited a body of evidence in favour of the interpretation that 5HT mechanisms were in all probability causally implicated. Botchin et al. (1993) later provided empirical support for this conclusion. The reader is referred to section 7.6.1 for a lengthier discussion of this very important research.

Having established the effects of various nutritional variables on 5HT synthesis I will now endeavour to clarify the effects of diet on 5HT release.

7.2 5HT Release

Schaechter & Wurtman (1990:203)

...demonstrate for the first time that both precursor-dependent elevations and reductions in brain serotonin levels produce **proportionate changes** in serotonin release, and that the magnitude of the tryptophan effect is unrelated to neuronal firing frequency. The data support the hypothesis that **serotonin release is proportionate to intracellular serotonin levels** (emphasis added).

The astute reader might very well ask: are these increases sustained or transient ? Do homeostatic mechanisms render the observed increases in 5HT release of dubious physiologic significance ? Acworth et al., (1988:121) report that

food-induced changes in serotonin synthesis are, in fact, "allowed" to modulate the amount of serotonin released from raphe neurons per firing **without activating a compensatory mechanism to slow the neurons firing frequency** (emphasis added).

This means 5HT is under **open-loop** control.

Just why 5HT is under open loop control is at present unknown.

Indeed,

it seems contrary to homeostatic principles for variations in nutrient intake to be able to dictate brain

composition and even function. One is left pondering **the evolutionary advantages** in having such an open loop system, and one for which there are no obvious endocrine counterparts (Acworth et al., 1988:118).

In Chapter 12 (as well as in section 7.6.1 below) I will pursue the evolutionary advantages of this open-loop system. One implication, however, seems clear:

variations in the amounts of neurotransmitter that are released will, presumably, cause parallel changes in the amount of information flowing across the synapse (i.e. the number of postsynaptic receptors that are activated when the neuron fires). Ultimately, such alterations should modify the net impulse traffic through brain networks containing the affected neurons, and should presumably be reflected as changes in the behavioral or physiologic brain outputs under their influence (Fernstrom 1977:208).

Let us now examine what 'behavioural or physiologic brain outputs' are subserved by serotonergic mechanisms.

7.4 5HT Distribution Throughout the Brain

It is a well established fact that "serotonergic neurons in the brain stem are provided with highly branched fibres which innervate virtually the entire central nervous system, thus comprising the most expansive central neuronal network yet described" (Nieuwenhuys 1985:35-36). The functional implications are quite profound. Because 5HT neurons

project diffusely to virtually every region of the central nervous system...[they] appear to be in a position to exert an important influence on the activity of **the entire cerebral cortex** as well as activity on the diencephalon, basal ganglia, brainstem, cerebellum and spinal cord (Vanderwolf et al. 1989:181).

This can also be understood with reference to the necessary complexities of the next few sections.

7.4.1 5HT Synthesizing Cell Bodies

There are a total of 9 serotonin-synthesizing cell groups, numbered (according to the nomenclature of Dahlstrom & Fuxe (1964) cited in Nieuwenhuys 1985:33): **B1-B9**. They are distributed across various regions of the mesencephalon, pons and medulla oblongata. By way of interpretation and simplification:

- B1 = nucleus raphes pallidus (50%)
- B2 = nucleus raphes obscuris (35%)
- B3 = nucleus raphes magnus (15%)
- B4 = dorsal to the nucleus prepositus hypoglossi
- B5 = nucleus raphes pontis (10%)
- B6 = nucleus centralis superior (35%)
- B7 = nucleus raphes dorsalis (70%)
- B8 = nucleus centralis superior (35%)
- B9 = midbrain area close to the medial lemniscus

The numbers in parentheses represent the proportion of serotonergic neurons [where provided] in various raphe nuclei (of the cat, from Nieuwenhuys 1985:35).

As Nieuwenhuys (1985:36) interprets,

the following mainly - or at least partly - serotonergic projections may be distinguished: (a) the ventral ascending pathway, (b) the dorsal ascending pathway, (c) projections to various rhombencephalic centres, (d) the cerebellar pathway, (e) bulbospinal pathways, and (f) the supra-ependymal plexus.

For the present purposes I will focus on the median and dorsal raphe nuclei which between them account for about 80% of forebrain 5HT (Azmitia 1978:233).

7.4.2 5HT Targets

Serotonin innervation of the cerebral cortex arises in the midbrain raphe region from the dorsal (DR) and median (MR) nuclei. These serotonergic fibres, which comprise the so-called "ventral ascending pathway" (described by Nieuwenhuys 1985) join the medial forebrain bundle (MFB) and give off axonal branches to (for instance) the substantia nigra, caudate-putamen, various thalamic nuclei, the hypothalamus, hippocampus, amygdala, and lateral and caudal parts of the neocortex (Nieuwenhuys 1985:33-41). I am fortunate in that I can quantify many of these relationships in a manner that will later serve my own theoretical and methodological interests.

...

Figure 7.2 Serotonin (5HT) content in various cortical regions of the young adult Rhesus monkey (redrawn from Brown et al., 1979). See text for discussion.

Figure 7.3 Serotonin activity based on the hourly accumulation rates of 5HTP (ng/gr/hr) in various areas of cortex of the young adult Rhesus monkey (redrawn from Brown et al., 1979). See text for discussion.

3

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Figure 7.4 Concentrations (ng/g tissue) of 5-hydroxyindoleacetic acid (5HIAA) in various cortical regions of the young adult Rhesus monkey (redrawn from Brown et al., 1979). See text for discussion.

Figure 7.5 5HT content (ug/g tissue) and "activity" (synthesis rate constant: $k=1/h$) in various regions of subcortex of the young adult Rhesus monkey (based on Brown et al., 1979). See text for discussion.

7.4.3 5HT Content and Activity Patterns in Cortex

Brown et al.'s (1979) landmark studies provide us with some valuable insights into the content and activity patterns of 5HT in various cortical and subcortical regions of the young adult Rhesus monkey brain [there are no comparable studies with humans].

Figure 7.2 profiles the content of 5HT in various cortical regions. This illustrates that while the topographical distribution is fairly uniform, the higher concentrations occur in the anterior inferotemporal cortex, superior temporal gyrus, and somatosensory cortex (Brown et al., 1979:139).

Figure 7.3 looks at the 5HT synthesis (based on the hourly accumulation rates of 5HTP) in those same regions. Note: 5HTP can be taken as "a reliable estimate of turnover...and a convenient measure of *in vivo* synthesis rates" (Brown et al., 1979:140). As is apparent, there appears to be a rostral to caudal gradient in 5HTP accumulation, with the highest 5HT activity in the superior temporal and occipital cortex.

Figure 7.4 depicts the ng/g concentration of the major 5HT metabolite 5HIAA. Interestingly, the lowest 5-HIAA concentrations are found in the prefrontal cortex. High levels are found in the occipital cortex. The highest levels are observed in the superior

temporal gyrus and the anterior portion of the inferior temporal gyrus.

The functional implications of the high 5HIAA activities in the occipital cortex are as both Brown et al. (1979) and later Levitt (1984) succinctly observed:

the 5HT system in primate visual cortex is extremely active, and in contrast to the virtually non-existent NA system in this same region, may participate to a large extent, **in visual information processing...** (Levitt et al., 1984:57).

It is regrettable that so many operational distinctions (5HTP accumulation versus 5HIAA levels) muddle our ability to make definitive statements regarding 5HT **activity**. I will rely on the original authors' conclusion that "the most rapid serotonin **turnover** occurs in the **posterior parietal [association] cortex** where a synthesis rate constant of 0.66/h was calculated compared to k values of 0.35 and 0.41/h in orbital and dorsolateral prefrontal areas, respectively" (Brown et al., 1979:140).

7.4.4 5HT Content and Activity Patterns in Subcortex

Figure 7.5 reproduces Brown et al's findings regarding the content and activity patterns of 5HT in selected subcortical regions. It should be mentioned that, in contrast to the activity

pattern estimates depicted in Figures 7.3-5 for cortex (which are based on separate provisions of 5HTP and 5HIAA values), the activity estimates depicted in Figure 7.6a are based on Brown et al.'s actual calculations for "synthesis rate constants" (k -which combines both 5HTP and 5HIAA values as provided in their Table 2).⁴⁶

With regard to subcortical **content**, we can see that

the concentration of 5HT was found to be about the same in each of the subcortical areas examined. However, 5HT concentrations are somewhat higher in the thalamus, hypothalamus and brain stem than in the putamen, caudate and hippocampus...[T]he highest concentration of 5HIAA is found in the thalamus and the lowest in the hippocampus (Brown et al., 1979:140-141).

With regard to subcortical **activity**, we can see that

the accumulation of 5HTP is most rapid in the caudate, putamen, and amygdala; intermediate accumulations occur in hypothalamus and brain stem, and lowest rates are in thalamus and hippocampus...Caudate and putamen showed a k value of 0.93 and 2.19/h, respectively, while brain stem and hypothalamus had rate constants of 0.31 and 0.28/h, and the lowest value is calculated for thalamus, 0.17/h... (Brown et al., 1979:141-142).

I am surprised (perhaps as a consequence of my trained biases) to be confronted with this evidence because it suggests that 5HT participates in motor functions. As Brown et al., (1979) admit,

⁴⁶ This is a rather annoying distinction, but one that is forced upon us by Brown et al.'s failure to provide all their data. It would have been most helpful if they included a table documenting the synthesis rate constants observed in cortex as they did for subcortex.

few studies exist on serotonin content in the subcortical structures of the subhuman primates...serotonin content is more uniform from structure to structure. Serotonin activity, on the other hand, is notably high in neostriatum, higher in fact than in any structures so far measured in the rhesus monkey. This finding is in agreement with the recent observation that the highest tryptophan hydroxylase activity in human brain occurs in neostriatum. Although the role of the nigrostriatal dopaminergic pathway has received major emphasis in studies of extrapyramidal function, the present observations on serotonin call attention to the potential importance of this monoamine in motor function (Brown et al., 1979:145-146).

7.4.6 Hemispheric Lateralization of 5HT

Although I have yet to investigate this area as thoroughly as my own theoretical interests would warrant, it is fascinating to observe that

Rosen et al., (1984) have reported that there is a greater 5HT content in the left striatum and right accumbens of the rat, and that there is a higher concentration of 5HT metabolites (5HIAA) in the left cortex...**Such findings may be important in our understanding of functional asymmetries in the forebrain** (Fallon & Loughlin 1987:73, added emphasis).

Later I will be tempted to pursue the possibility that pre- and postnatal variations in dietary tryptophan availability might interact with genetic mechanisms governing the development of lateralization of function to "co-produce" the kinds of cognitive task specializations associated with hemispheric asymmetries (Figure 5.3).

7.5 5HT in Phylogenesis

The most dramatic phylogenetic changes in the distribution patterns of 5HT have thus far been observed in the laminar and sublaminal components of the visual areas at mesencephalic, diencephalic, and telencephalic levels (Morrison & Foote 1986; Berger & Trotter 1988). Many of these complexities are beyond the scope and comprehension of this report. My larger theoretical interests are best served in the context of some comprehensibly general observations.

As Bloom (1986) explains,

the remarkable heterogeneity of NA and 5HT innervation observed in monkey neocortex is highly ordered and is systematically related to the cytoarchitectonic region, lamina, age, species, and functional nature of the particular area of the neocortex being examined. In addition, there are important differences in the NA and 5HT innervation in each of these 'dimensions'. In each case, **the different innervation patterns point to functional distinctions between these two transmitter-specific systems and point towards a substantial and independent role for each of these monoamine systems in neocortical information processing** (Bloom 1986:299-301; emphasis added).

To this we can add the following:

Work in primates has shown regional variations in terms of the density and laminar distribution of the 5-HT axons...These studies suggest **a greater degree of organization of the serotonergic innervation in animals with more highly developed cortices**... (Parnavelas 1990:18; emphasis added).

More specifically, we may also observe that

in contrast the relative homogeneity of the 5HT innervation of rat neocortex, the 5HT innervation of the primate is more laminated and complex...The 5HT innervation of area 17 in the squirrel monkey is less dense than in the macaque monkeys...[D]uring advancing phylogenetic development from rodent to New World monkeys to Old World monkeys, both the geniculocortical and 5HT projections to layer IV [of the neocortex] specialize in their sublaminal distribution (Fallon & Loughlin 1987:72 in review).

Bloom (1986) helps us understand the more general significance of this research (which in most cases involves comparative analyses).

The old world monkeys receive an even denser 5HT innervation of primary visual cortex than do squirrel monkeys..., whereas the overall density of the NA innervation is equivalent, or even slightly decreased in the old as compared to new world monkey. These variations correlate with the further specialization in the old world species.

These observations suggest that coincident with the extensive phylogenetic development and functional differentiation of neocortex in the primate there is a parallel elaboration and differentiation of the ascending NA and 5HT projections (Bloom 1986:299-301, emphasis mine).

This provides a sampling of the findings thus far culled from the neuroscience archives.

The most useful message we can take away from this discussion is one of general significance:

...just as we have seen anatomically that neurotransmitter innervation of cortex becomes more extensive and variable as one ascends the phylogenetic scale, neurotransmitter release may come to take on more specific roles...Since, in man, patterns of degeneration

of the DA, NA, and ACh innervation of cortex and subcortex are observed in patients dying of neuropsychiatric diseases which all include severe cognitive deficits...[ie., Parkinson's, Huntington's, Alzheimer's] **it seems likely that during evolution neurotransmitters in cortex come to play an increasingly important role in neural integration** rather than the purely permissive functions ascribed to neurotransmitters in the basal ganglia and limbic system (Iversen 1984:335, emphasis added).

7.6 The Functional Significance of 5HT

As quoted above, Acworth et al. (1988) suggested that "the participation of serotonergic neurons in a large number of brain functions might have the effect of making these functions '**hostages to eating**'" (Acworth et al. (1988:125). While I could conceivably examine 5HT from the perspective of its role in visual information processing (Brown et al., 1979; Morrison & Foote 1986; Berger & Trotter 1988), motor functions (Brown et al., 1979), and hippocampal and forebrain mechanisms in learning and memory (Vanderwolf et al. 1987, 1989, 1990; Plaitakis et al., 1978; Fallon & Loughlin 1987; Young 1986), I will focus on but one heuristic: the role of 5HT in social behaviour. This discussion will give a clear indication of the way in which I intend to interpret the anthropological relevance of serotonergic mechanisms.

...

7.6.1 5HT and Social Behaviour

It is commonly understood that "dominance relationships are an important axis of social organization" (Raleigh et al., 1988:300). And that they determine (amongst other things) who produces offspring and thus contributes to the evolution of the genetic information pool. It has also been suggested that, in all likelihood, "the most significant evolutionary changes leading from an apelike hominoid to humankind were in the areas of social behaviour" (Holloway 1983:287 as discussed in Chapter 5). It is in both of these respects that the following insights seem so theoretically compelling.

Raleigh et al. (1988) observed that

repeated acute tryptophan (20mg/kg/day) administration induced changes in many behaviours. **Social grooming**, approaching, resting, and eating increased while locomoting, avoiding, being solitary, and being vigilant decreased (Raleigh et al., 1988:301, added emphasis).

So too did Kaplan et al., (1991) observe that

monkeys consuming a relatively low fat, low cholesterol [prudent] diet for 22 months initiated **more contact aggression** than did monkeys eating a relatively high fat, high cholesterol [luxury] diet (Kaplan et al., 1991:639).

That serotonergic mechanisms were implicated in the main effect of reduced fat on social contact aggression was later confirmed by Botchin et al., (1993). As Kaplan (1993) explained:

CSF⁴⁷ 5HIAA concentrations were significantly lower in the animals consuming the low cholesterol diet than in their high cholesterol counterparts ($p < 0.001$). Importantly the low cholesterol animals were **more aggressive [and] less affiliative...These results were not confounded by age or gender differences.**

Most profoundly of all, Raleigh et al., (1988) observed that

when a dominant male is removed from his troop the remaining subordinate males compete to become dominant. The initial phase of this competition involves the formation of alliances with females and is sensitive to tryptophan and other serotonergic agonists...**Treatment of one of the remaining subordinate males with tryptophan is uniformly associated with that animal becoming dominant. Conversely, reduction of serotonergic function is uniformly associated with the treated subject remaining subordinate** (Raleigh et al., 1988:300).

As an anthropologist, naturally I am inclined to reflect on the sociocultural, reproductive, and genetic implications of these findings. It seems reasonable to question the relationship between dietary tryptophan availability and social cohesion - as well as the impact the status-linked effects of dietary variations in tryptophan and fat might have (by way of their inevitable reproductive effects) on the content and evolution of the "genetic information pool" (Katz 1987).

In Chapter 12 I will pursue the possibility that serotonergic mechanisms might (1) interact with seasonal variations in nutrient availability to co-produce patterns of group fission and fusion; and (2) determine the outcome of efforts to become socially

⁴⁷ Cerebral spinal fluid.

dominant and thus indirectly affect the qualities that find their way into the genetic information pool. So too will I argue (by extension of Armelagos 1987) that (3) those foraging strategies and dietary biases that had the added benefit of enabling fat and tryptophan replete males and females to acquire and/or maintain dominant social status with reproductive benefits would be selected for in a Darwinian sense.

Once we have apprehended the details of Chapter 11 we will be in a better position to appreciate the subtleties of the following much more complex hypothesis: 5HT may act as a physiological sensor of broad-based ecological patterns and trigger cycles of social fission and fusion according to the abilities of the environment to sustain the metabolic demands of reproduction - as well as [and this is the important point]: the fine-grained neurochemical demands of the developing foetus at critical developmental stages of neurophysiological preparedness for interaction with the larger world. In others words: **the unique open loop status of 5HT may be comprehensible in terms of its ability to provide an exquisitely environmentally sensitive interface between biological and cultural mechanisms of adaptation.**

One way of expressing this relationship is to suggest that by providing a mechanism that is uniquely sensitive to the effects of diet, natural selection strives to ensure that the developing foetus is exposed to an optimal mix of seasonally available

nutrients necessary to effectively ensure the integrity of the tight sequential timing of various pre- and postnatal developmental events. In other words, perhaps the open loop status of 5HT is comprehensible in terms of its ability to create the optimal conditions for reproduction given the downstream nutritional effects of seasonality on the mother's diet. Perhaps the role of 5HT is to ensure that social fusion and reproduction occur at the same time that the mother is able to provide the developing foetus with an optimal supply of "seasonally available nutrients" (Chapter 6, section 6.3.1) necessary to effectively facilitate the tight sequential timing and development of crucial structural and functional maturational events.

The "miniature biochemical preparedness profiles" in Chapter 11 will allow us to appreciate the importance of striving for a "degree of best fit" between the "optimal neurochemical potentials" inherent in the environment and the "optimal structural and functional potentialities" inherent in the genome.

I will expand on these arguments in Chapter 12. They serve as but examples of the ways in which we can interpret the significance of the relationship between nutrition and NT synthesis from an anthropological perspective. Others will follow (in the same preliminary fashion) in the text of the next three chapters.

8.0 ACETYLCHOLINE

Consistent with the general format of Part 3, it will be the goal of this chapter to establish just what factors affect ACh synthesis and release; ACh distribution throughout the brain; and the cognitive functions cholinergic mechanisms have been implicated in. In Chapter 11 I will discuss some select aspects of ACh development in cortex.

8.1 ACh Synthesis

As summarized in Figure 8.1, ACh is synthesized from the precursors choline (Ch) and acetyl coenzyme A (acetyl-CoA). Choline acetyltransferase (ChAT) catalyzes the production of ACh via the acetylation of choline by acetyl CoA. Once ACh is released from the synapse it is hydrolyzed by acetylcholinesterase (AChE). The action of this enzyme produces the two major ACh metabolites: acetate and choline. By some estimates, 30-50% of the choline liberated by AChE is taken back up by the neuron (Ordenez 1977) and may be used preferentially for ACh synthesis (Ulus et al., 1989).

8.1.1 Rate-Limiting Factors: Choline and Acetyl CoA

Unlike most biosynthetic pathways whose rate of end-product synthesis is controlled by the activities of one rate-limiting

enzyme, "...ChAT activity in the cholinergic neurons is **not** rate-limiting, the rate of synthesis depends on the availability of the two precursors, Ch and acetyl-CoA" (Pepeu et al., 1990:275. See also Tucek 1990). This is unique among the p.d.NTs. This uniqueness is a consequence of the simple fact that ChAT is not fully saturated with substrate at physiologic concentrations. In technical terms

the estimated intracellular concentrations of free choline and of extramitochondrial acetyl-CoA (50 and 5 μM , respectively...) are below their K_m ⁴⁹ for ChAT (400-1200 μM for choline and 7-18 μM for acetyl-CoA...). Thus, it seems that the enzyme *in situ* is not saturated with substrate and altered delivery of precursors should change the amount of product generated (Collier 1988:265).

As can be seen, this provides dietary variations in choline a physiologic "window of opportunity" to control the rate of ACh synthesis.

The picture is, however, slightly more complicated than this. It is compounded by the fact that ACh synthesizing neurons can obtain choline from potentially four sources (three of which are indicated in Figure 8.1):

...that stored as PC [phosphatidylcholine] in their own membranes; that formed intrasynaptically from the hydrolysis of acetylcholine (taken back up into the presynaptic terminal by a high affinity process estimated

⁴⁹ Note: "the k_m is the concentration of substrate necessary for the enzyme to function at half maximal rate" (Azmitia 1978:277).

to be 30-50% efficient in the brain); and that present in the blood stream (and taken into the brain by a specific blood-brain barrier transport system) (Wurtman 1988:83).

The fourth source is the liver: "in certain mammalian organs (e.g., liver) choline is synthesized *de novo* by the stepwise methylation of phosphatidylethanolamine... [which is] derived from the nonessential amino acid serine..." (Ordenez 1977:210-211).

When and how any of these conditions prevail is a matter of ongoing scrutiny. Apparently, "a significant fraction of plasma and, therefore, brain choline is of dietary origin" (Cohen & Wurtman 1976:561). Ulus et al. (1989) provide us with a valuable explanation as to why researchers have had so much difficulty establishing the precursor sensitivities of ACh neurons.

Whether or not dietary choline affects ACh synthesis depends on the dual and competitive necessities of (1) maintaining intracellular ACh stores (in the form of phosphatidylcholine (PC)) versus (2) satisfying the immediate metabolic demands of particularly active ACh-releasing neurons (Ulus et al., 1989). These mutually exclusive events are made manifest by the fluctuating activities of choline kinase and ChAT (Figure 8.1). Whereas neuronal depolarization selectively enhances the activity of ChAT - "thus possibly shunting the choline into ACh synthesis" (Ulus et al. 1989:224), the activation of choline kinase results in the storage of free choline as PC (ibid). We may conclude, therefore, that only when enhanced ACh activity preferentially

Figure 8.1 Acetylcholine synthesis. A,B = alternative sources of choline. C,D = acetyl CoA producing pathways (dashed pathway contributes significantly less). HAU = high affinity choline uptake. See text for discussion.

activates ChAT we will be able to detect a main effect of increased choline availability on ACh synthesis and release.

Once again, however, we must return to the fact that other biosynthetic options exist. In short, our ability to detect this main effect is confounded by the fact that ACh neurons can theoretically compensate for inadequate dietary supplies by "autocannibalizing" (Blusztajn & Wurtman 1983) choline stored as phosphatidylcholine (PC) in the structural lipid membranes. As the term implies, this is a potentially harmful form of resource mobilization because of the cumulative deleterious effects on the structural and functional integrity of the brain (i.e., as perhaps seen in Alzheimer's disease. See also Wurtman 1985 cited in Wurtman 1988). This renders all the more profound the summary observation that

physiologic variations of choline content in the diet (that is, variations within the range that **omnivorous animals or humans** might consume from day to day) are associated with parallel changes in brain ACh concentrations, especially in the caudate nucleus (Cohen & Wurtman 1976:561; emphasis added).

The emphasis here is two-fold: even human diets exhibit the potential to control CNS ACh stores. And secondly, the brain regions most likely to be adversely affected by inadequate dietary supplies of choline would be those very regions that exhibit high densities of cholinergic markers. In section 8.3.2 I will explore these relative density profiles.

Parenthetically,

choline is present in some foods normally consumed by man (for example, egg yolks, 1.7 percent by weight; meat, 0.6 percent by weight; fish, 0.2 percent by weight; cereals and cereal products, 0.1 percent by weight; and legumes, 0.2 to 0.35 percent by weight), but largely absent from others (for example, most fruits and soft vegetables)... Day-to-day or long term variations in food choice can thus cause marked variations in the amounts of choline ingested. Hence, **the six- to eightfold range in daily choline consumption examined in our studies may reflect variations normally encountered in human diets** (Cohen & Wurtman 1976:562).

Of additional significance is the observation (more properly understood in the context of the details examined in Chapter 11) that

there are at least three sources of choline present for infants in human milk: lecithin, sphingomyelin, and choline itself. This is an important finding; **the mother's intake or deficiency of choline could be reflected in the developing infant's metabolism and behavior** (Chafetz 1990:100).

I will pursue the implications of all of these findings in Part 4. For the present purposes it is enough to understand that hominid meat eating may have conferred significant adaptive benefits vis à vis choline supplies and the potential for increased brain ACh synthesis.

8.1.2 Acetyl-CoA and Thiamine

As can be seen in Figure 8.1C and D, acetyl-CoA is provided by way of both glucose and pyruvate metabolism (Tucek 1990:472-473).

Examining the contribution of the pyruvate pathway to acetyl-CoA production, it can be seen that pyruvate decarboxylase (the enzyme that converts pyruvate to acetyl-CoA) is a **thiamine-dependent reaction**. It is in this sense, then, that thiamine is indirectly implicated in ACh synthesis. This can be assessed quantitatively.

Studies reveal that a thiamine deficiency can cause a **66%** decrease in pyruvate decarboxylase (Dakshinamurti 1977:268), a **42%** reduction in brain acetyl-CoA, and a resultant **35%** reduction in ACh levels in the brain (Heinrich et al. 1973). This is associated not only with "a reduction in **both** the pool size and rate of turnover of acetylcholine...[but] functional impairments" (Bender 1992:146-147). The kinds of functional impairments I am talking about here are those associated with the functional attributes of the regions densely innervated by ACh fibres. That is why memory functions are most often impaired in thiamine deficiencies status (e.g., Wernicke's-Korsakoff's syndrome⁴⁹): ACh activity is particularly high in the hippocampus which is a subcortical structure implicated in mnemonic functioning (e.g., Olton 1983).

Finally, a thiamine deficiency can also impair ACh synthesis **indirectly** by way of its effects on the activities of the alternative glucose pathway (Figure 8.1C). If a dietary thiamine deficiency exists, this will impair cerebral glucose metabolism and

⁴⁹ See references in Hakim & Pappius (1981).

thus acetyl-CoA formation. And of course because acetyl-CoA is a rate limiting factor in ACh synthesis (see comments above), this too will cause deficits in ACh synthesis (Hakim & Pappius 1981). Thus decreased ACh synthesis observed under conditions of a thiamine deficiency is a consequence of its effects on pyruvate as well as glucose metabolism.

Parenthetically, the daily requirements for thiamine range from 1-1.4 mg/day (Burk & Solomans 1985 cited in Chafetz 1990:257). Significantly,

although it is extremely widespread in small amounts, only a few foodstuffs can be regarded as good sources. As a general rule it is present in greatest amounts [0.1-1.0 mg (100g)⁻¹ in foodstuffs that are rich in carbohydrate and/or associated with high levels of carbohydrate metabolism in the original living material. Examples are legume seeds and the embryo component of cereal grains (the germ)...The reason why pork should contain about ten times the amount of thiamine [about 1 mg (100g)⁻¹ that beef, lamb, poultry, and fish contain has yet to be established (Coultate 1989:188).

We also note that **"fruits and vegetables... are not important sources of dietary thiamine"** (Coultate 1989:191).

8.1.3 Coenzyme A, Pantothenic Acid and Vitamin B6

Pantothenic acid (inappropriately known as Vitamin B5) also plays a role in the stepwise biosynthesis of ACh. It does so as the functional moiety of coenzyme A (Bender 1992:341). It will be

recalled that coenzyme A is the precursor to acetyl-CoA (Figure 8.1C and D). Thus, while pantothenic acid is two biosynthetic steps removed from ACh synthesis, it is nonetheless indirectly implicated by virtue of the fact that it is a structural component of CoA, which is the acetyl carrier for acetyl-CoA, which is one of the two rate-limiting factors in ACh synthesis (see Coultate 1992:204-205).

With regards to the role of vitamin B6 in ACh synthesis, we can deduce that it too affects ACh synthesis on the basis of the simple observation that "a vitamin B6 deficiency results in lowered concentrations of coenzyme A in blood..." (Ebadi 1978:129). Given, once again, that coenzyme A is the precursor to acetyl-CoA, which is the precursor to ACh, the point is clear: a vitamin B6 deficiency may indirectly affect ACh synthesis according to the same chain of events discussed above. In both instances, however, we are reminded that "whether it is possible to stimulate ACh release in vivo by **enhancing** acetyl-CoA formation needs to be demonstrated" (Pepeu et al 1990:275 in review). Whether or not a pantothenic acid or vitamin B6 deficiency can cause impairments in ACh synthesis has yet to be firmly established. This is but a 'structured deduction' made on the basis of biosynthetic principles that await further clarification.

Parenthetically, the RDA for pantothenic acid is 4-7 mg/day (Burk & Solomans 1985 cited in Chafetz 1990:257). Moreover,

pantothenic acid is extremely widely distributed, mostly at around $0.2\text{-}0.5\text{ mg (100g)}^{-1}$, levels generally assumed to give a more than adequate dietary intake. As with so many vitamins, liver contains especially high levels, in this case about 20 mg (100g)^{-1} . Quite high losses of pantothenic acid have been reported to occur during food processing, mostly due to leaching, but some decomposition is known to occur especially during heating under alkaline or acid conditions (Coultate 1989:205).

As the reader may recall, I already commented on the dietary sources of vitamin B6 in Chapter 7 (section 7.1.5).

8.1.4 Vitamin B6 and Lipid Metabolism

We also note that "pyridoxal phosphate has a clear role in lipid metabolism as the coenzyme for phosphatidylserine decarboxylation, leading to the formation of phosphatidylethanolamine, and thence to **phosphatidylcholine**" (Bender 1992:229). Phosphatidylcholine, the reader may recall, is the sequestered form of choline that can be "autocannibalized" in the all too likely event that an omnivorous animal's or human's diet fails to provide adequate supplies of choline. It is in this sense, then, that vitamin B6 can be construed as being a significant dietary factor in ACh synthesis: it catalyzes *de novo* production of PC by way of serine metabolism in the liver. This provides ACh neurons with an alternative (if less than ideal) source of choline.

It has also been observed that "choline deficiency is exacerbated by deficiency of methionine, folic acid or vitamin B¹² which further impairs the capacity for *de novo* synthesis" (Bender 1992:405). Interestingly, vitamin B12 is only obtained from meat (Mann 1981).

We will now turn to a formal discussion of the mechanisms involved in ACh release.

8.2 ACh Release

The simple and elegant fact is: "...the number of ACh molecules released when a neuron fires may vary with nutritional status" (Cohen & Wurtman 1976:561; emphasis added). This is confirmed on the basis of more recent evidence that reveals

when choline is made available (in concentrations bracketing the physiologic range), a clear dose relationship is observed between its concentration and acetylcholine release (Wurtman 1988:82, emphasis added).

Very obviously this is significant from a functionalist perspective because it implies that nutritional status will determine the amount, and duration, of ACh release across all those spatial and temporal domains that ACh is characteristically active in. This could have profound implications for the selective stabilization

and hence functional integrity of neurons and networks with strong cholinergic components.

We caution, however: this level of metabolic sensitivity is characteristic only of particularly active but not otherwise quiescent ACh releasing neurons (Wurtman 1988; Ulus et al., 1989). In Chapter 4 I discussed some critical homeostatic properties of neurons (based on Zigmond 1992). The metabolic contingencies governing the effects of choline availability on ACh synthesis and release can be taken as but another example of neuronal homeostasis. Summarily speaking, "acetylcholine synthesis and release can...be amplified, **in physiologically active neurons**, by consumption of PC-rich foods" (Wurtman 1988:84, emphasis added).

8.2.1 Open- Versus Closed-Loop Status

We have observed that the precursor dependence of ACh is evident only in particularly active - but not otherwise quiescent - neurons. On this basis alone I might conclude that ACh is under closed-loop control. This label does, however, refer exclusively to the effects of precursor availability on ACh **release**.

Recognizing that "elevations in serum choline increase ACh synthesis in the brain **without inducing end-product inhibition of either ACh synthesis or release**" (Ulus et al. 1978 cited in Wurtman

1979:75, emphasis added), we might be tempted to conclude that ACh (in active but not quiescent neurons) is under open-loop control (Wurtman 1988 and Tucek 1990). And yet we have to confront the fact that ACh-releasing neurons exhibit an array of receptor properties that defy simplistic descriptions as to their physiologic status.

Pepeu et al. (1990) observe that

in each brain area the cholinergic nerve endings are equipped with qualitatively and/or quantitatively different sets of presynaptic receptors, making possible a differential regional modulation (Pepeu et al., 1990:275).

We may conclude, therefore, [by extension of Commissiong (1988)] that the "open" or "closed loop" status of ACh will have to be explored on a "case-by-case basis" because ACh neurons exhibit different tendencies towards autoreceptor mediated feedback inhibition in different regions of the brain (see Pepeu 1990:275-276). We do note, however, that even while [conservatively speaking] "all presynaptic receptors inhibit ACh release...**this inhibition is never complete** but only reduces by approximately 50% the release [of ACh]" (Pepeu et al., 1990:276). This suggests the ACh system - even if closed - is not under tight controls. IN any event, because I cannot reconcile the unpredictable properties of ACh-releasing neurons with the strict imperatives of the terms "open" or "closed-loop", I will assign it an indeterminate status.

8.2.2 Clinical Caveats

I would be remiss if I did not point out that the experimental findings that increased choline availability in animals can enhance ACh synthesis and release contrasts markedly with the generally poor results of human trials (Sahakian 1988). These trials are generally designed to test the clinical effects of choline supplementation in Alzheimer's patients known to suffer from an 80% loss of functioning cholinergic neurons (see references cited in Bartus et al., 1985). Or as Wurtman (1988) observes: "most well-controlled studies have treated subjects for relatively short intervals (6-8 weeks or less) and have focused on younger subjects, with little or no success" (p.83). I can best explain the discrepancies between the results of human clinical versus experimental (i.e., animal) trials with reference to the insights of Lieberman & Abou-Nader (1986).

Arguably, the fact that ACh precursor loading cannot ameliorate the cognitive deficits associated with Alzheimer's disease is comprehensible in the terms that have rendered problematic the ability of researchers to detect an effect: It depends on heightened neuronal activity in the very ACh neurons that are damaged in the typical experimental subject. Quite simply: "Alzheimer's disease is accompanied by a profound decrease in the activity of ChAT in brain cortex and in the ability of cortical tissue to synthesize ACh" (Tucek 1990:470). This suggests the

typical clinical subject is neurophysiologically ill-equipped to respond favourably to enhanced choline availability. In this sense, then, it can be argued that the poor results of human clinical trials are misleading, and not at all indicative of how an otherwise healthy population would respond to the neuroprophylactic benefits of long-term choline supplementation.

We turn now to an examination of the distribution of ACh across the brain. This will establish the functional significance of cholinergic mechanisms as well as the potential functional significance of differences in nutritional status affecting brain ACh synthesis and release.

8.3 ACh Distribution Throughout the Brain

While it is true, "acetylcholine is one of the most ubiquitous neurotransmitters in the mammalian central nervous system" (Mesulam 1990:231), it still exhibits regional and laminar differences which may be functionally significant.

...

8.3.1 ACh-Synthesizing Cell Bodies and Targets

Cholinergic synthesizing cell bodies, known collectively by the designations **Ch1-Ch8**, are found in several regions of the brain⁵⁰. Cell bodies Ch1-Ch4 are found in the basal forebrain whereas Ch5-Ch8 are found in the brain stem. As Nieuwenhuys (1985) explains:

the **Ch1** group corresponds to the medial septal nucleus; about 10% of its neurons are cholinergic. The **Ch2** group corresponds to the cortical limb of the nucleus of the diagonal band of Broca; at least 70% of its neurons are cholinergic. The **Ch3** group most closely corresponds to the horizontal limb of the nucleus of the diagonal band of Broca; only 1% of the neurons of this nucleus are cholinergic. The **Ch4** group, which is very extensive in the human brain [and can be further subdivided into anteromedial (Ch4am), anterolateral (Ch4al), anterior (Ch4a) and posterior (Ch4p) components], most closely corresponds to the nucleus basalis of Meynert [nbM]...At least 90% of the neurons in the [NBM] are cholinergic (Nieuwenhuys 1985:9).

Ch5 neurons correspond most closely with the lateral rhombencephalic tegmental area. **Ch6** neurons are associated with the adjacent central grey. **Ch7** corresponds to the medial habenula; **Ch8** to the parabigeminal nucleus (Nieuwenhuys 1985).

From the perspective of this thesis it is interesting to observe that

⁵⁰ For a detailed image of the following complexities the reader is referred to Nieuwenhuys (1985:8).

Ch1 and, particularly, Ch2 provide a substantial cholinergic projection to the hippocampus...Cholinergic neurons located in the anterolateral portion of the Ch4 project...to the amygdaloid complex...The remaining parts of Ch4 provide a major cholinergic projection to the entire neocortex (Nieuwenhuys 1985:10, emphasis added).

In Chapter 12 I will pursue the fact that these brain regions exhibited increases in relative size in members of the genus *Homo*.

These relationships may be summarized as follows:

Ch1 (10%)	--> hippocampus
Ch2 (70%)	--> hippocampus via the fimbria-fornix pathway
Ch3 (1%)	--> olfactory bulb
Ch4 (90%)	--> amygdala
	--> cerebral neocortex
Ch4am	--> medial aspects of the cerebral hemispheres
Ch4al	--> frontoparietal opercular cortex and amygdala
Ch4i	--> dorsal prefrontal, insular, posterior parietal, inferotemporal, and peristriate
Ch4p	--> superior temporal gyrus and adjacent areas
Ch5/6 ⁵¹	--> superior colliculus
	--> numerous regions of the thalamus

Given the aims of the current thesis, an overly detailed description of chemical neuroanatomy is not necessary⁵². I am fortunate in that Mesulam et al., (1986) examined 33 cytoarchitectonic regions of cortex and subcortex for differences in ACh content and activity. I will rely on his findings to help me rationalize my approach to these chemoarchitectural complexities.

⁵¹ Lewis & Shute's "dorsal tegmental pathway".

⁵² The interested reader is referred to the research of Lewis & Shute (1978), Nieuwenhuys (1985), and Mesulam (1990).

3.3.2 Relative Densities

Mesulam et al. (1986) examined 33 cytoarchitectonic subregions of the cerebral cortex of two Rhesus monkeys for 2 markers of ACh activity: ChAT and AChE. The benefits of the ChAT analysis is that it possesses the specificity AChE does not:

Only cholinergic neurons and their processes contain ChAT. This enzyme is therefore a specific marker for the presynaptic component of cholinergic pathways...Unlike ChAT, AChE is not a specific marker of cholinergic neurons...AChE is also found within the postsynaptic cholinceptive neurons... (Mesulam et al. 1986:148).

Table 8.1 summarizes their findings. Figure 8.2 shows the location of 31 of the 33 regions they sampled (the numbers correspond to those areas described in Table 8.1). Figure 8.3 graphs the mean values obtained for each of the 6 structurally defined groups listed in Table 8.1: association areas, primary sensorimotor regions, cingulate gyrus, isocortical paralimbic areas, nonisocortical paralimbic zones, and core limbic structures.

Comparison of the values in Table 8.1 suggests there are significant regional differences in the content and activity patterns of ACh across various regions of the brain. According to Mesulam et al., (1986), these regional differences are as high as **seven-fold**. Granted, we have to question the generalizability of results obtained from any study where $N=2$, but clearly different methods serve different purposes. In this case it serves the

Figure 8.2 Location of the 31 cytoarchitectonic areas (grouped into 6 functionally distinct regions) sampled by Mesulam et al., (1986). (A) Lateral view of hemisphere. (B) Medial and ventral view. (A= arcuate sulcus; C= central sulcus; CA= calcarine sulcus; CC= corpus callosum; CG= cingulate gyrus; INS= insula; IP= intraparietal sulcus; L= lunate sulcus; LOF= lateral orbitofrontal sulcus; MOF= medial orbitofrontal sulcus; OT= occipitotemporal sulcus; P= principal sulcus; R= rhinal sulcus; S= sylvian fissure; ST= superior temporal sulcus; STP = boundaries of supratemporal plane - not a true sulcal marking; T= thalamus). Sample numbers correspond to those in Table 8.1. See text for discussion.

Table 8.1 Enzyme Specific Activities in 33 Cytoarchitectonic Subregions of the Cerebral Cortex of Two Rhesus Monkeys (a,b,c)

Sample No., Area	Case 1		Case 2	
	ChAT*	AChE**	ChAT	AChE
A. Association areas	3.465	0.898	7.202	0.832
1. Peristriate visual association	3.467	1.165	3.938	0.260
2. Temporal visual association	1.820	1.046	5.560	0.600
3. Somatosensory association	3.213	0.688	4.327	1.004
4. Auditory association	4.357	1.064	9.081	1.170
5. Dorsal premotor association	3.990	1.034	9.708	1.120
6. Dorsolateral prefrontal	2.740	0.418	6.096	0.950
7. Principalis cortex (prefrontal)	3.680	0.926	6.758	0.720
8. Frontopolar cortex	4.157	1.194	5.827	1.190
9. Caudal inferior parietal lobule	2.070	0.501	4.092	0.290
10. Rostral inferior parietal lobule	2.867	0.708	11.320	0.390
11. Banks of superior temporal sulcus	4.157	0.977	11.707	0.830
12. Caudal inferotemporal cortex	5.047	1.068	8.002	1.460
B. Primary sensorimotor regions	4.394	0.979	9.820	0.546
13. Dorsal primary motor	4.013	0.988	6.335	0.540
14. Ventral primary motor	5.443	0.863	7.191	0.535
15. Primary somatosensory	5.503	1.566	10.511	0.540
16. Primary auditory	4.653	0.778	21.307	1.100
17. Primary visual	2.367	0.702	3.762	0.016
C. Cingulate gyrus	3.170	0.662	7.600	0.755
18. Anterior cingulate	3.040	0.656	9.043	1.144
19. Caudal cingulate	3.300	0.672	6.156	0.370
D. Isocortical paralimbic areas	5.405	1.015	14.358	1.125
20. Medial inferotemporal visual association	5.523	1.144	11.268	1.550
21. Temporopolar auditory association	7.247	0.890	23.366	1.240
22. Granular insula	5.387	1.134	13.870	0.920
23. Granular anterior orbitofrontal	3.457	0.892	8.933	0.790
E. Nonisocortical paralimbic zones	8.686	1.809	17.282	1.951
24. Parolfactory areas	6.670	1.566	9.574	1.706
25. Dysgranular midorbitofrontal	5.147	0.964	14.282	0.950
26. Agranular caudal orbitofrontal	13.733	3.050	28.754	3.260
27. Dysgranular insula	5.703	1.430	15.358	1.240
28. Agranular insula	7.717	1.624	22.827	1.820
29. Dysgranular temporopolar	5.767	1.326	18.418	2.640
30. Agranular temporopolar	13.817	2.872	16.850	1.870
31. Entorhinal-prorhinal	10.927	1.700	12.206	2.070
F. Core limbic areas	21.675	3.960	39.730	5.220
32. Midhippocampus	8.883	1.799	27.878	2.870
33. Amygdala	34.470	6.122	51.582	7.570

(a) The anatomical locations of the sampled areas 1-31 are shown in Figure 8.2

(b) Values in bold type indicate group means (plotted in Figure 8.3).

(c) See original text for standard errors.

Source: Mesulam et al., (1986).

* Choline acetyltransferase (nmol/15 min/mg protein).

** Acetylcholinesterase (umol/hr/mg protein).

Figure 8.3 Choline acetyltransferase (ChAT) activity in various regions of cortex and subcortex of two rhesus monkeys (based on Mesulam et al., 1986:147 Table). See text and companion Table 8.2.

purpose of establishing the fact that within-species differences in ACh content and activity are quite pronounced. This in itself is significant.

As Mesulam et al. (1986) interpret, these inter-animal differences in ACh content and activity may be functionally significant.

Interanimal variations of cholinergic enzymes have been shown in mice...These experiments also demonstrated that mice with higher levels of cholinergic markers performed better in learning tasks. **It is conceivable that there are substantial individual variations in the quantity of cortical cholinergic innervation in primates, including humans, and these variations reflect individual differences in learning abilities** (Mesulam et al., 1986:149, emphasis mine).

This 'structured theoretical deduction' will later provide an opportunity to ask how inter-animal differences in diet might interact with genetic mechanisms governing the development of normal cholinergic architecture to "co-produce" these apparent structural **and functional** differences (Chapter 12).

It can also be seen that whereas the association areas of prefrontal, posterior parietal, and occipitotemporal cortex exhibit the **lowest** densities of cholinergic markers, the core limbic regions displayed the **highest** ones - the amygdala being the highest of all 33 regions sampled in their study (Figure 8.2). The primary motor and sensory regions displayed intermediate values. These

observations are consistent with the patterns observed in human cortex:

...histochemical preparations in the neurologically normal human brain show...paralimbic areas such as the caudal orbitofrontal cortex⁵³, insula, temporopolar cortex, entorhinal cortex, and parts of the cingulate gyrus contain a more intense concentration of presynaptic cholinergic markers than immediately adjacent sensory areas...Core limbic areas such as the hippocampus and amygdala also display a very high intensity of cholinergic markers (Mesulam 1990:237).

These observations lead Mesulam et al. (1986) to suggest that cortical cholinergic mechanisms may be in a unique position to regulate the access of modality-specific sensory (as well as neuroassociative) information into the limbic system (Figure 8.4).

As Figure 8.4 suggests:

sensory information is likely to come under progressively greater cholinergic influence as it approaches the core limbic structures. Moreover, the paralimbic areas that provide a neural matrix for widespread sensory-limbic interactions also contain a particularly rich cholinergic innervation. This anatomical distribution suggest that **cortical cholinergic synapses are in a position to regulate the access of sensory information into the limbic system** (Mesulam et al., 1986:149).

They expand on this position by adding that

sensory-limbic interactions are considered essential for the processes of storage and retrieval...The widely recognized contribution of central cholinergic pathways to memory could therefore reflect, at least in part, their role in **regulating the transfer of information**

⁵³ An aspect of the PFC.

Figure 8.4 The amygdalopetal flow of sensory information across cortical association areas in three major modalities (redrawn from Mesulam 1986:149, Figure 3). Numbers in parentheses refer to mean choline acetyltransferase (ChAT) activities (nmol/15 min/mg protein) in several of the 33 cytoarchitectonic regions examined in their study. Numbers in circles correspond to those depicted in Figure 8.2. See text for further discussion.

between sensory association cortex and the limbic system
(Mesulam et al., 1986:149).

In Chapter 12 I will relate these findings to both Rozin's (1976) theory on the evolution of human consciousness, and Murray & Mishkin's (1985) observations regarding the cross-modal associative capacities of the amygdala (both mentioned briefly in Chapter 5). In Chapter 12 I will pursue the obvious parallels that can be drawn between (1) the ability of cortical ACh to regulate the access of modality-specific sensory information into the amygdala (Mesulam et al., 1986); (2) the ability of the amygdala to mediate cross-modal information processing (Murray & Mishkin 1985); and (3) the ability of cross-modal information processing capacity to subserve the evolution of human consciousness (Rozin 1976).

8.4 ACh in Phylogenesis

As Mesulam (1990) explains, in a very precise language that complements the substantive preoccupations of my own research,

the human brain has a unique anatomy that underlies a behavioural repertoire not found in other species. So far our observations show that the overall plan of organization for ascending cholinergic pathways in the human brain displays many similarities to that of other primates. However, it is important to realize that the cholinergic pathways in the human brain may also possess distinctive and unique features...It is essential to obtain this information in order to understand further how this pharmaco-system is organized in the human brain, how it differs from the organization of the cholinergic

pathways in other animals **and in what ways these differences contribute to the unique behavioral repertoire of the human brain** (Mesulam 1990:239-240).

This is the fundamental question I am asking of all the precursor-dependent neurochemical networks, with an additional bias in favour of asking how differences in nutritional status might interact with genetic mechanisms to "co-produce" these very obviously functionally significant phylogenetic differences.

Unfortunately research in this area is in its infancy, and I can provide but two summary observations. The first is rather curious but simple: the cortices of primates (unlike rodents) do not contain intrinsic cortical cholinergic neurons (Mesulam et al., 1984 cited in Nieuwenhuys 1985:11). This is, as Tucek (1990:469) remarked, an "unclarified piece of the puzzle". The second finding is by way of summary:

the Ch4, Ch5, Ch6 cell groups are particularly extensive in the primate brain...[But] of all the cholinergic cell groups in the primate brain, the Ch4 cell group...is the largest. This is in keeping with the marked cortical development in the primate line of evolution...In addition to its larger size, it also appears that the human Ch4 displays a greater level of differentiation than the Ch4 complex in monkey brain. Previous observations already noted that the nucleus basalis of Meynert [Ch4] shows a gradual increase in size and differentiation in the course of phylogenetic evolution (Mesulam 1990:232-233).

This reinforces the idea that brain evolution is a mosaic process (Armstrong 1983) characterized by subtle chemical neuroanatomical changes that [as I am attempting to emphasize] carry with them the implication that dietary factors other than sheer caloric energy may have been implicated in the process of hominid encephalization.

In Chapter 12 I will pursue the ecological and paleodietary implications of the general observation that Ch4 has undergone significant increases in size in the course of hominid phylogenesis.

8.5 The Functional Significance of Cholinergic Mechanisms

ACh has been implicated in a number of significant neurologic properties: "neural plasticity" (Bear & Singer 1986 cited in Jasper et al. 1988:601); non-specific "cortical activation, arousal and attention" (Okaichi & Jarrard 1982; Sillito & Murphy 1987); thalamocortical information processing (McCormick et al., 1989, 1990); generation of the hippocampal theta rhythm (Vanderwolf 1987; Stewart & Fox 1990); "learning", or more precisely, post-lesion task acquisition (Hepler et al., 1985); "spatial working memory" (Olton et al. 1977; Olton & Samuelson 1979; Olton & Papas 1979; Morris et al 1982; Wirsching et al., 1984; Beatty & Bierley 1985; Barnes 1988); "non-spatial working memory" (Olton & Feustle 1981); "cognitive mapping" (O'Keefe & Nadel 1978; Nadel & MacDonald 1980);

"reference memory" (Hagan et al, 1988); "layer 1 event holding" (Vogt 1991:69) and, of course, Alzheimer's disease (e.g., Coyle 1983; Bartus et al., 1985a,b).

For the purposes of the present inquiry we can put aside these fine-grained operational distinctions and recognize, quite simply, that "if there is a key transmitter for memory, and perhaps for other aspects of cognitive function, the best bet for that transmitter would be acetylcholine" (Davies 1985:215). This clearly provides a parsimonious example of the way in which the significance of dietary factors in human cognitive evolution can be conceptualized.

In Chapter 12 I will explore the more conservative possibility that any dietary strategy that had the added benefit of enhancing hippocampal and forebrain cholinergic components of learning and memory (in an environment that placed an adaptive premium on such skills) would be selected for in a Darwinian sense. More speculative hypotheses will also be advanced. This provides another indication of the way in which I can conceptualize the importance of cholinergic mechanisms and related dietary factors beyond the strictures of Mesulam et al.'s (1986) interpretations. Other ideas will follow once we have examined some unique aspects of ACh development in the cortex (Chapter 11).

9.0 NOREPINEPHRINE

It will be the goal of this chapter to review the same objective criteria established in Chapters 7 and 8: the steps involved in CA synthesis and release⁴, NE distribution throughout the brain, and the cognitive functions noradrenalin has been implicated in. What little there is known about phylogenetic differences in the distribution of NE will also be discussed. In Chapter 11 I will look at NE from a strictly developmental perspective.

9.1 NE Synthesis

On the surface, the steps involved in NE are quite simple (Figure 8.1.). NE is synthesized from the non-essential amino acid tyrosine by a series of enzyme-catalyzed reactions. While tyrosine is generally regarded as the substrate precursor of CA synthesis, *de novo* tyrosine synthesis can occur via hepatic or CNS intraneuronal hydroxylation of phenylalanine (During et al. 1988 in review). This is why the conversion of phenylalanine to tyrosine is conceptualized as the first step.

⁴ NE and DA are synthesized along the same biosynthetic pathway; therefore it is, for all practical purposes, impossible to separate them.

Figure 9.1 Catecholamine biosynthesis. HVA = homovanillic acid. MHPG = 3,4-methoxyhydroxyphenylglycol. See text for discussion.

Tyrosine is converted into dihydroxyphenylalanine (DOPA) by tyrosine hydroxylase. Aromatic amino acid decarboxylase then acts upon DOPA to produce DA. The enzyme dopamine- β -hydroxylase converts DA to NE. Liberated NE is broken down by the activities of monoamine oxidase (MAO) and catechol-O-methyltransferase into its two major metabolites: 3-methoxy-4-hydroxyphenylglycol (MHPG-SO⁴) and 3,4-dihydroxyphenylglycol (DOPEG). Parenthetically, NE can also be converted into epinephrine via the action of phenylethanolamine-N-methyltransferase (PNMT).

9.1.1 Tyrosine and NE

The rate-limiting enzyme (RLE) governing NE synthesis is tyrosine hydroxylase (see Fillenz 1990:79-83).⁵⁵ **Under basal conditions** its pharmacokinetic properties limit the extent to which increases in tyrosine availability can increase CA synthesis. This can be explained in technical terms. Whereas the estimated K_m for tyrosine hydroxylase is 50-125 μM , the physiologic substrate concentration of tyrosine is 100-200 μM (Morgenroth et al. 1978; Joh et al. 1978 cited in Milner & Wurtman 1986:875). This suggests a level of **75% enzyme saturation** (Carlsson & Lindquist 1978 cited in Spring 1986:35). Theoretically, this provides increased tyrosine

⁵⁵ Parenthetically, molecular oxygen and reduced pterine cofactor are absolute requirements for the activity of this enzyme (Fillenz 1990:79) and thus constitute additional rate limiting factors in CA synthesis (ibid:120).

with a small "window of opportunity" to cause increases in the rate of CA synthesis - under basal conditions.

These precursor sensitivities are heightened in metabolically active neurons. This is because

increases in firing frequency of the catecholaminergic neurons cause allosteric changes in tyrosine hydroxylase, thereby increases its affinity for its cofactor tetrahydrobiopterin, reducing its susceptibility to end-product inhibition...and enhancing its dependence on its saturation with tyrosine (During et al. 1989:1449)⁵⁶.

Theoretically, the allosteric changes in tyrosine hydroxylase would expand the "window of opportunity" tyrosine had to exert an affect on the rate of NE synthesis. The reduced susceptibility to end-product inhibition is more properly pursued in the section on NT release.

This explains how we can reconcile the observation that 'NE may become rate limiting under certain metabolic conditions' with the first principle of nutritional biochemistry that states that the activities of the RLE in any biosynthetic pathway control the rate of end-product synthesis. Put simply: "catecholaminergic neurons become tyrosine sensitive when they are physiologically active, and lose this capacity when quiescent" (Acworth et al.,

⁵⁶ See also Acworth et al., (1988), Spring (1986:35), and Fillenz (1990:79-81).

1988:127). In all respects, then, "firing frequency predicts tyrosine responsiveness" (During et al., 1989:1453).

We must recognize, however, that even in metabolically active neurons the upper pharmacokinetic limits of tyrosine hydroxylase would place constraints on the ability of increases in tyrosine to effect any significant change. This explains the summary observation that

the ability of supplemental tyrosine to enhance catecholamine synthesis would be explained not so much by its ability to increase substrate-saturation of tyrosine hydroxylase but **by blocking the decrease that would otherwise occur** (Milner & Wurtman 1986:878).

This speaks to the "neuroprotective" benefits of increased precursor availability.

Theoretically, enhanced precursor availability would protect CA-releasing neurons from dangerous depletions of their NT reservoirs that might otherwise occur if the functional demands being made on the individual exceeded their capacity to replenish their intracellular stores. In the last section of this chapter we will encounter some practical examples of this metabolic likelihood.

The caveat that "it is necessary to consume pure tyrosine, separate from other amino acids, in order to obtain **major** increases in brain tyrosine levels" (Milner & Wurtman 1986:880, emphasis

Table 9.1a Ranges of Daily Requirements of Essential Amino Acids

	low (mg/day)	high (mg/day)
phenylalanine	400	1180
tyrosine	82	630
methionine	175	1100
leucine	170	1100
valine	230	800
lysine	400	1200
isoleucine	70	700
threonine	103	1500

Source: Burton (1976:51).

Table 9.1b Essential Amino Acid Composition of Protein Foods (mg/100g) *

	arginine	histidine	threonine	valine	leucine	isoleucine	lysine	methionine	phenylalanine	tryptophan
egg	700	240	560	780	1015	700	630	360	640	130
mother's milk	50	23	59	87	154	80	75	22	64	22
beef	1090	410	875	980	1380	790	1150	530	1000	246
meat, beef	1220	620	845	975	1480	980	1630	515	740	300
fish, muscle	1410	500	890	1140	1800	1235	1710	810	835	228
rice	440	100	230	360	500	320	195	205	300	80
wheat	560	275	430	560	910	520	350	325	685	155
potatoes	100	44	140	110	190	75	170	50	120	40
oats	775	260	410	615	910	560	410	230	625	150
barley	610	260	480	610	840	510	420	190	620	190
corn	380	200	300	425	1200	510	180	250	400	48
rye	590	250	370	560	670	440	450	180	470	140
peas, beans	1610	500	885	1265	1610	1270	1480	460	1150	185

* listed in decreasing order of biologic value.

Source: Burton (1976:54-55).

added) does not render the real-world significance of Wurtman and colleagues' research any less profound. It simply means that competition occurs at many levels in the CNS - including the blood brain barrier (recall Table 7.1), and we must keep this in mind when trying to construct arguments pertaining to the neurochemical effects of differences in nutritional status. Table 9.1a provides the range of estimates for the daily requirements of all the essential amino acids. Table 9.1b lists the essential amino acid composition of various protein foods listed in decreasing order of biologic value. Tyrosine is not an essential amino acid, therefore it is not listed. But do not be misled. Tyrosine is so important that the body has retained its capacity to synthesize it from phenylalanine (with the help of iron as will be discussed below).

The low-to-high range of estimates for the daily requirements of phenylalanine are 400-1180 mg/day for the average adult. Figure 9.2 graphs several of the examples provided in Table 9.1b and compares them with the tryptophan content of various protein foods (mg/100g). As can be seen, **liver** (next to dried peas and beans at 1150 mg/100g) is the best source of phenylalanine, providing 1000 mg/100g. Meat (740 mg/100g), fish (835 mg/100g), and eggs (640 mg/100g) are also good sources. Plant foods such as corn, rice, and potatoes are very poor sources of phenylalanine, containing no more than the low requirement of 400 mg/100g of food. I will comment on the amino acid composition of mother's milk in Chapter 11.

Figure 9.2 Phenylalanine and tryptophan content (mg/100g) of selected dietary sources of protein (based on Burton 1976:54-55). We recall from Table 9.1a that the low-high ranges of recommended daily intakes is 400-1,180 mg/day for phenylalanine and 82-630 mg/per day of tryptophan. See text for discussion.

9.1.2 Iron as Biosynthetic Cofactor

Tyrosine and phenylalanine are not the only nutrients that affect NE synthesis. "Iron plays a key role for three of the enzymes of amino acid metabolism... namely the aromatic amino acid hydroxylases" (Youdim quoted in Lajtha & Balazs 1988:466). This includes phenylalanine and tyrosine hydroxylase.

Lehmann & Heinrich (1986) focused on the role of iron (Fe) in the conversion of phenylalanine to tyrosine. They demonstrated that "the iron content of phenylalanine hydroxylase has been shown to **correlate directly** with its enzymatic activity" (Lehmann & Heinrich 1986:468). Moreover they also observed that

in subjects with mild-to-medium severe iron-deficiency anemia, the metabolic conversion of dietary L-phenylalanine to L-tyrosine by the iron enzyme phenylalanine hydroxylase, is **reduced to about 56% of the normal value**, returning to within normal range after successful treatment with oral iron (Lehmann & Heinrich 1986:473).

Whether an iron deficiency can actually cause a reduction in NE synthesis or related functional impairments remains to be seen. The fact, however, that an iron deficiency affects CA receptor density (Youdim quoted in Lajtha & Balazs 1988:466) is suggestive of this possibility. By way of application of the concept of denervation supersensitivity, I might suggest that the observed increases in receptor density were a compensatory (homeostatic) consequence of

reduced CAergic activity. Clearly, however, the precise effects of iron on CA synthesis await further clarification.

Parenthetically, the recommended daily requirement of iron for men, women, and a 1 year old infant respectively is 10, 18, and 15 mg/day (Burk & Solomans 1985 cited in Chafetz 1990:257). On the surface it appears

iron is generally abundant in most foodstuffs, of plant as well as animal origin. Lean meat contains between 2 and 4 mg (100g)⁻¹...Liver has rather more, around 9 mg (100g)⁻¹. Leafy green vegetables, legumes, nuts, and whole cereal grains lean meat contains 2-4 mg (100g)⁻¹. Most fruit, potatoes, and white fish such as cod have between 0.3 and 1.2 mg (100g)⁻¹...eggs have around 2 mg (100g)⁻¹ (Coultate 1989:283).

These values are, however, woefully misleading because they fail to reflect the differences in absorption rate of the iron obtained from plant versus animal foods.

When haem iron, e.g. the myoglobin of meat or fish skeletal muscle tissue, is the dietary source, 15-20% is absorbed. No more than 8% of the iron in plant foods, including cereals, legumes, and leafy vegetables, is found to be absorbed...**The iron in plant foods is mostly present as insoluble complexes** of Fe¹¹¹ with phytic acid, oxylates, phosphates, and carbonates (Coultate 1989:285, emphasis added).

9.1.3 Thiamine and NE

Mair et al.'s (1985) research demonstrates that even 13-15 weeks after a mere two-week period of acute thiamine deficiency,

rats exhibited significant impairments in various measures of learning and memory. These cognitive deficits were correlated with reduced levels of NE in the hippocampus, olfactory bulbs, and especially neocortex. Given the absence of any deleterious effects on serotonergic and dopaminergic mechanisms⁵⁷, Mair et al. (1985) concluded that the NE system may be selectively vulnerable to the effects of a thiamine deficiency (Mair et al. 1985:281. See also McEntee & Mair 1978).

Mair et al.'s (1985) observation that "...a bout of thiamine deficiency can produce **persistent** deficits in brain norepinephrine and concomitant decrements in behavioural measures of learning and memory" (p.273, emphasis added) is fascinating, although not comprehensible in simple neurophysiological terms. This is because the primary biochemical lesions associated with a thiamine deficiency have not yet been established.

Mair et al. (1985) speculate on well-reasoned grounds that the deleterious effect of an acute thiamine deficiency is associated with the rate-limiting role it occupies in the hexomonophosphate (HMP) pathway of glucose metabolism (see also Dakshinamurti 1977:258). The HMP pathway provides the metabolic energy necessary to shunt NE from the brain stem locus coeruleus (see below) to midbrain and neocortical structures (ibid:281). The HMP pathway is,

⁵⁷ But see Chapter 7 (section 7.1.4).

however, transketolase-limited, and transketolase is especially vulnerable to thiamine depletion (see also Dakshinamurti 1977:258).

Provisionally, then, I may conclude that a thiamine deficiency can metabolically impair the ability of the LC HMP pathway to shunt NE to more rostral brain structures. This in turn can cause significant impairments of the kinds of cognitive and mnemonic functions subserved by midbrain and neocortical noradrenergic mechanisms.

I discussed thiamine requirements and sources in Chapter 7 (section 7.1.4). Tables 9.2 and 9.3 provide a more comprehensive profile of the thiamine (as well as vitamin B6 and pantothenic acid) content of common foods. As can be seen, **plant foods are very poor sources of thiamine**, whereas foods of animal origin are exceptionally high (e.g., liver contains 2.5-3.0 ug/100g).

9.1.4 Vitamin B6 and NE

As I have already established in Chapter 7

all the compounds implicated as neurotransmitters are synthesized and/or metabolized by the aid of the vitamin B⁶-dependent reactions. These include dopamine, norepinephrine...and serotonin...gamma aminobutyric acid...and even acetylcholine indirectly (Ebadi 1978:129-130).

Table 9.2 Dietary intake recommendations for daily intakes of the micronutrients by the food and nutrition board (National Research Council)*

	adult women	adult men	1 yr old infant
thiamine	1	1.4	0.5
niacin	13	18	8
vitamin B6	2	2.2	0.6
vitamin C	60	60	35
iron	18	10	15
pantothenic acid	4 to 7	4 to 7	2
copper	2 to 3	2 to 3	0.7 to 1.0

* Source: Burk & Solomons (1985; cited in Chafetz 1990:257).

Table 9.3 Vitamin B6, thiamine, and pantothenic acid contents (ug/g) of common foods*

	vitamin B6	thiamine	pantothenic acid
liver	6.5 to 8.4	2.5 to 3.0	64 to 77
beef	3.3	0.9	4.7
fish	2.3 to 3.3	0.3 to 1.0	2.8 to 5.5
chicken	3.3 to 6.8	0.5 to 0.8	8 to 10
eggs	1.1	1.1	16
peanuts	4	3.2	21
walnuts	7.3	3.3	9
avocados	4.2	1.1	11
bananas	5.1	0.5	2.6
potatoes	2.5	1	3.8
squash	0.8	0.5	3.6
apples	0.3	0.3	1
oranges	0.6	1	2.5
tomatoes	1	0.6	3.3
peas	1.6	3.5	7.5
lettuce	0.6	0.6	2

* Source: Linder (1985:68).

We might well assume that any cognitive deficits associated with a vitamin B6 deficiency status are, in all probability, attributable to its effects upon GABAergic mechanisms. I would tend, on substantive grounds, to agree with such an assumption. This is because GABA represents, quantitatively speaking, a much more important NT in brain function (e.g., Glowinski 1984; Jasper et al., 1988). Indeed, "in most cortical areas GABA-containing cells form approximately 25% of the neuronal population" (Parnavelas 1990:22). It has also been observed that "glutamic acid decarboxylase [the enzyme which synthesizes GABA] is more susceptible to vitamin B6 deficiency in comparison to other vitamins requiring enzymes such as aromatic L-amino acid decarboxylase" (Ebadi 1990:195).

While current evidence suggests the effects of a pyridoxine deficiency might be restricted to serotonergic and GABAergic mechanisms (Dakshinamurti 1977:304), **we cannot rule out the possibility that noradrenergic mechanisms are also implicated.** This is, however, a speculative suggestion that awaits empirical verification (if, indeed, such could be achieved given the inevitable physiological 'noise' any such experiment would obviously encounter given the spectrum of pyridoxine's effects).

...

9.1.5 Copper and NE

It is an established fact that

dopamine- β -hydroxylase is a copper-containing enzyme involved in the synthesis of the catecholamines noradrenaline and adrenaline from tyrosine in the adrenal medulla and central nervous system. The active enzyme [DBH] contains Cu^{+} ... (Bender 1992:369, added emphasis).

It is not surprising, therefore, to observe that "brain levels of norepinephrine and dopamine are significantly depleted in copper-deficient rats and copper repletion restores norepinephrine levels" (Bhathena et al., 1986:42).⁵⁸ This appears to establish the importance of copper (Cu) in CA synthesis.

The findings of Chafetz & Bernard (1984, cited in Chafetz 1990:199) provide some support for the hypothesis that dietary variations in copper may be functionally significant. As Chafetz (1990) explains, "error scores of animals performing on a radial maze were correlated with hippocampal copper content: Animals with large numbers of errors tended to have lowest concentration of copper" (1990:199). This suggests copper plays a significant role in maintaining the functional integrity of the hippocampal component of working memory perhaps through its effects on

⁵⁸ It is, however, not quite clear how Cu could affect DA levels unless, of course, we are talking about a 'compensatory decrease' that might result from an excess accumulation of DA metabolites.

noradrenergic mechanisms (see Olton 1983 for a discussion of the role of the hippocampus in working memory).

Parenthetically, the recommended daily intake of copper is 2-3mg/day (Table 9.2). Interestingly, while copper is widely distributed in various foods

at levels between 0.1 and 0.5 mg (100g)¹...milk is notably low in copper, at around 0.2 mg (100ml)¹, and mammalian **liver** is exceptionally high, at around 8 mg (100g)¹...As with iron, it appears nature expects newborn infants to get by on the reserves built up before birth until they are weaned (Coultate 1989:286, emphasis added).

9.1.6 Vitamin C and NE

It can also be argued that variations in dietary ascorbate can affect CA synthesis by way of its indirect and direct effects on the activities of the two biosynthetic enzymes phenylalanine hydroxylase and DBH.

The observation that "the presence of ascorbic acid in the duodenum greatly enhances the extent of iron uptake" (Coultate 1992:24) can be combined with the evidence provided in section 9.1.3 to create a lengthy chain of inference. This line of reasoning is predicated on the understanding that iron mediates the conversion of phenylalanine to tyrosine. I will adopt as my working assumption the idea that because vitamin C can enhance Fe uptake it

may also enhance the likelihood of the conversion of phenylalanine to tyrosine - and thereby levels of CA synthesized (albeit only under conditions of increased neuronal activity).

An equally tortured but more persuasive argument could be based on the technical understanding that "the active enzyme [DBH] contains Cu^+ , which is oxidized to Cu^{2+} during the hydroxylation of the substrate; reduction back to Cu^+ specifically requires **ascorbate**" (Bender 1992:369, emphasis mine). Or as Coultate (1992) states:

another important reaction requiring ascorbate is the hydroxylation of 3,4-dihydroxyphenylethylamine (dopamine, a derivative of tyrosine) to noradrenaline... This may be the origin of the disturbances of the nervous system that accompany scurvy (Coultate 1992:207-208).

The implication is that a vitamin C deficiency may cause reduced levels of CA synthesis in the brain with attendant global functional impairments.⁵⁹

Parenthetically, the recommended daily intake of vitamin C is 60 mg/day for the average adult (Table 9.2). As is commonly known, the richest sources are fruits. But as Coultate (1989:207) notes, wide variations do occur (e.g., in mg (100g)¹: apples and carrot =6; peas and tomato =25; new potatoes =30; citrus fruit =50;

⁵⁹ See also Chafetz (1990:211-226) for a lengthier discussion of the possible significance of ascorbate in CNS and periphery.

cauliflower =60; broccoli =110; parsley =150; blackcurrent =200; rose-hip =1000).

This exhausts the list of nutrients that are directly or indirectly implicated in CA synthesis. Let us now turn to a discussion of the factors that affect CA release.

9.2 Factors Affecting NE Release

As is perhaps to be expected on the basis of the information contained in section 9.1.1,

the effects of tyrosine appear to be more in the realm of pharmacology, **sustaining and even amplifying transmitter release** in response to increased activity at catecholaminergic cells (Milner & Wurtman 1988:880).

In other words, it is only in metabolically active neurons, but not quiescent ones, that tyrosine is able to affect NE release. As in all cases examined thusfar the question still remains: are these increases sustained or transient ? Do homeostatic mechanisms render the effects of diet on CA release functionally insignificant ?

Acworth et al. (1988) reported that

supplemental tyrosine - given in doses which need not elevate plasma tyrosine beyond its physiologic range - can indeed enhance the release of dopamine in nigrostriatal neurons in otherwise-untreated animals. **But...this effect is transient**, probably because it

triggers receptor mediated feedback mechanisms that slow neuronal firing and/or act presynaptically to diminish transmitter release per firing. These hypothetical mechanisms⁶⁰ would be expected to bring net dopamine [and NE] release per neuron, per unit time, back to levels existing before the amino acid was given (Acworth et al., 1988:475).

During et al. (1988) drew similar conclusions when they examined the effects of phenylalanine availability on CA release.

The change in dopamine release with both the low and high doses of phenylalanine is transient, **probably** because autoreceptor feedback mechanisms influence neuronal firing frequencies and the amounts of transmitter released per firing...the net effect being to stabilize dopamine release at the levels existing before the amino acid was administered (During et al., 1988:94).

Both these reports indicate **NE is under closed-loop control**.

What does this mean in terms of our understanding of the effects of nutrition on brain CA activities ? If we want to conceptualize the ongoing functional significance of dietary variations in amino acid availability on NT release we must do so **indirectly** through its effects on NT **synthesis**. Zigmond's (1994) hypothetical models of neural homeostasis discussed in Chapter 4 (Figures 4.3-4.5) can help us understand the general importance of this relationship. Inevitably, however, we must return to a point made earlier:

⁶⁰ The reader is referred to Zigmond's (1994) models of the homeostatic properties of neurons discussed in Chapter 4.

the ability of supplemental tyrosine to enhance catecholamine synthesis would be explained not so much by its ability to increase substrate-saturation of tyrosine hydroxylase but **by blocking the decrease that would otherwise occur** (Milner & Wurtman 1986:878).

To the extent, then, that I can construct plausible examples of the likelihood that the functional demands being made on an individual may exceed their ability to replenish their intraneuronal CA stores, is the same extent to which I can make a case for the ongoing functional significance⁶¹ of various nutrients affecting CA synthesis. I will question my ability to do so.

Preliminary to the discussion in section 9.5.1 below, it can be seen that an "uncontrollable stressor" can cause a selective decrease and eventual depletion of central NE (Reinstein et al. 1984). This in turn results in behavioural disturbances "in locomotor and exploratory behaviour" (Reinstein et al. 1984:2225). Significantly though, **pre-treatment administration of tyrosine can attenuate the neurochemical and behavioural deficits associated with the stressor** *ibid*). Theoretically, this establishes the functional significance of optimal dietary supplies of tyrosine/phenylalanine even in the absence of its effects on NE release.

In the next section I will examine the chemical neuroanatomy of NE on the assumption that if metabolic imbalances were to occur,

⁶¹ Development is a different matter entirely (see Chapter 11).

they would most likely manifest themselves in the kinds of behavioural and cognitive impairments associated with the unique content and active patterns of NE in neocortex and subcortex.

9.3 Distribution Throughout the Brain

In this section I will examine the distribution of NE throughout the CNS. First, I endeavour to put two controversies to rest. Then I will define the location of NE-synthesizing cell bodies, the major target structures of their terminal fibres, and the content and activity patterns of NE in various regions of cortex and subcortex.⁶²

9.3.1 Controversies Put to Rest

Without a doubt "the way in which noradrenergic axons communicate with the neuronal elements in the cerebral cortex and the issue of whether these fibers form conventional synapses has been the source of controversy" (Parnavelas 1990:15). Previously it was thought that NE was released "more diffusely than classical neurotransmitters... [However] systematic analysis of serial

⁶² For a more comprehensive discussion the reader is referred to Lindvall & Björklund (1978), Loy et al. (1980), Levitt et al, (1984), and Nieuwenhuys (1985).

ultrathin sections has shown that **90%** of noradrenergic terminals in the cortex form conventional synapses" (Fillenz 1990:192). So too do we observe that, contrary to the assumption that NE innervation of cortex was

diffuse and uniform throughout...recent investigations have revealed regional variations in pattern and density of cortical noradrenergic innervation, adhering to cytoarchitectonic boundaries... (Nieuwenhuys 1985:23 references cited).

The latter point is brought home forcefully in section 9.3.3. These two controversies put to rest indicate that NE participates in CNS information processing, and does so in a structurally and thus potentially functionally significant manner. This renders all the more profound the metabolic implications of variations in amino acid availability affecting NE synthesis.

9.3.2 NE Synthesizing Cell Bodies & Targets

There are seven noradrenergic cell groups designated (according the nomenclature of Dahlstrom & Fuxe 1964) **A1-A7** (see Nieuwenhuys 1985:21 & 27 for detailed schematics). Cell groups A1, A2, A5, and A7 give rise to Ungerstadt's ventral noradrenergic pathway/bundle (VNB).

The terminal areas innervated by this system are strictly subcortical, including the motor nuclei of the brainstem, substantia nigra, and ventral tegmental areas, raphe

nuclei, the amygdala, and lateral septum. The densest innervation is to the hypothalamus (Iversen 1984:322).

The remaining groups³, A4 and A6, contain about 50% of the total number of NE-synthesizing neurons. They are therefore "quantitatively by far the most important noradrenergic centre of the brain" (Nieuwenhuys 1985:19-20). Together they comprise the "**locus coeruleus**" (LC) complex. The LC gives rise to the dorsal noradrenergic bundle (DNB). Significantly,

structures innervated by the DNB include sensory nuclei of the brainstem, the raphe nuclei, the substantia nigra, cerebellum, limited regions of the hypothalamus, striatum, amygdala [mainly the central and basal nuclei⁴], and septum. The richest innervation is, however, to hippocampus and neocortex (Iversen 1984:322).

The VNB and DNB are also known collectively as the central tegmental tract (CTT) (Lindvall & Bjorklund 1978). The CTT has a major route of projection along the medial forebrain bundle (MFB) - "a highly heterogenous system of CA fibres [that] ascends from the brainstem reticular formation toward diencephalic and telencephalic regions" (Lindvall & Bjorklund 1978:169).

I am fortunate in that I can quantify many of these relationships with reference to Brown et al., (1979).

³ A3 is conspicuously absent in primates (Nieuwenhuys 1985).

⁴ Nieuwenhuys (1985:22).

Figure 9.3 Norepinephrine (NE) content (ng/g/tissue) in various cortical regions of the young adult Rhesus monkey (redrawn from Brown et al., 1979). See text for discussion.

Figure 9.4 A measure of catecholamine (CA) activity based on the hourly accumulation rates of DOPA (ng/gr/hr) in various cortical regions of the young adult Rhesus monkey (redrawn from Brown et al., 1979). See text for discussion.

9.3.3 NE Content and CA Activity in Cortex

While it is true "there appears to be no brain areas completely devoid of noradrenaline" (Fillenz 1990:181), the content and activity patterns of NE do exhibit uneven distribution profiles across cortex and subcortex.

With regards to cortical **content** of NE (Figure 9.3), it can be seen that it is **highest** in somatosensory cortex and **lowest** in the occipital cortex. Intermediate values are observed in the remaining regions (e.g., prefrontal cortex, superior and inferior temporal gyrus, etc.). These findings have since been confirmed by Levitt et al. (1984) and Lewis & Morrison (1989).

Most areas of the frontal lobe and anterior regions of superior and inferior temporal gyri are densely innervated by NA axons. NA innervation is highest in somatosensory cortex and least dense in posterior parietal and occipital cortical regions (Levitt et al., 1984:51).

These regional differences in cortical NE content may be functionally significant. As Brown et al. (1979) interpret, "the high quantities of norepinephrine in somatosensory cortex suggest that this monoamine may play an unexpected role in supporting **somesthetic function**" (Brown et al. 1979:143). The role of NE in sensorimotor integration finds additional support in Lewis & Morrison's (1989) research on the dopamine-B-hydroxylase content of

the PFC, and Morrison & Foote's (1986) analysis of the distribution patterns of noradrenergic fibres in visual cortex.

With regards to cortical CA activity⁶⁵ (Figure 9.4), it is **highest** in orbital and dorsolateral prefrontal cortex, and **lowest** in occipital cortex (Brown et al., 1979). Intermediate levels of CA activity are observed in the other seven regions. This indicates the CAs are particularly important in maintaining the ongoing activities of the prefrontal cortex (see especially chapter 10).

9.3.4 NE Content and CA Activity in Subcortex

With regards to NE **content** in various subcortical regions (Figure 9.5A), it appears **highest** in the hypothalamus and **lowest** in the amygdala and hippocampus (Brown et al., 1979; caudate and putamen not sampled). The functional significance of these absolute and relative differences are a matter of informed speculation. Iversen's (1984) research supports the interpretation that NE in the hypothalamus mediates interoceptive sensory cue processing, or rather "interoceptive cues of biological significance for the species-specific behavior essential for survival" (Iversen 1984:328).

⁶⁵ DOPA is a non-specific indicator of CA activity in general.

Figure 9.5 Norepinephrine (NE) content (ug/g/tissue):A , and catecholamine (CA) activity based on the hourly accumulation rates of DOPA (ng/gr/hr):B , in various subcortical regions of the young adult Rhesus monkey (redrawn from Brown et al., 1979). See text for discussion.

With regards to **CA activity** in subcortex (Figure 9.5B), it appears **highest** in the amygdala, brain stem, and thalamus, and lowest in the hypothalamus, with intermediate values in the hippocampus, caudate and putamen. The marked contrast between Figures 9.5A versus B is confounded by the fact that DOPA is a non-specific indicator of CA activity that does not permit us to differentiate between noradrenergic and dopaminergic components.

9.4 NE in Phylogenesis

We have already seen that the NE-synthesizing cell group A3 is conspicuously absent in primates (Nieuwenhuys 1985:19). If we compare phylogenetic differences in activities of the CAs in cortex versus subcortex we confront one of the more profound observations of this thesis:

Catecholamine turnover in the monkey is thus as a rule higher in cortical structures than in subcortical structures; in the rat, however, catecholamine activity in cortical regions is quantitatively similar to that in subcortical loci. These findings indicate that **machinery for biosynthesis of catecholamines may have developed pari passu [by an equal progress] with the evolution of the primate neocortex**, particularly in relation to the expansion of association cortex (Brown et al., 1979:146).

This is as significant in its paleodietary implications as was Martin's (1981) demonstration that EQ is correlated with maternal metabolic turnover. Both Foley & Lee (1992) and Leonard & Robertson (1992) recognized that the energetics of encephalization have

important implications for our understanding of hominid diet (as discussed briefly in Chapters 5 and 6). So too would I suggest that Brown et al.'s (1979) findings - when combined with the details of Wurtman and colleagues' research - suggests the importance of NT amino acid availability factors in brain evolution **independent of** the role previously ascribed to caloric energy. I will pick up this thread in Chapter 12.

Other findings from the frontiers of comparative neurology are also relevant. I will begin by expressing them in general terms.

Lewis & Morrison (1989) observed that "the NA innervation of the human cerebral cortex...is widespread, similar to what has been documented extensively in rodents...but its regional and laminar differentiation seems to be more elaborate in man" (Lewis & Morrison 1989:257-259). Bloom (1986) also observed that "coincident with the extensive phylogenetic development and functional differentiation of neocortex in the primate there is a parallel elaboration and differentiation of the ascending NA and 5HT projections" (Bloom 1986:301). What this implies is perhaps obvious: "the primate and human cerebral cortices exhibit far greater regional and laminar differences in the density and patterns of innervation than the rat neocortex" (Parnavelas 1990:14).

More specifically, out of the 21 distinct cytoarchitectonic areas of both Rhesus and Squirrel monkey cortex examined by Levitt et al., (1984), the visual areas exhibited the most significant differences. Apparently, whereas the rat visual cortex receives a dense plexus of noradrenergic fibres, the human visual cortex is sparsely innervated. As the authors conclude: "this difference appears to be a phylogenetic pattern, as visual cortex in cat, although innervated by NA axons, appears to be intermediate in density between rat and monkey" (Levitt et al., 1984:51)⁶⁶ They concluded that

while the density of innervation of each cortical region in the rat is uniform, both the NA and 5HT systems in the primate have changed to become much more variable between regions. Secondly, while the laminar distribution for each afferent system is the same across rat cortex, distinct innervation patterns are evident between primate cortical regions. In addition, cortical layers that receive the heaviest innervation in rat, I and IV, receive much less input in many areas of the primate cortex (Levitt et al., 1984:56).

It remains to be established what the functional significance of these subtle laminar differences are. The same applies to Lewis & Morrison's recent (1989) research on NE innervation patterns in the human cortex.

⁶⁶ Phylogenetic differences in NE axon orientation and branching patterns are also discussed (pp.52-53), but these are beyond the comprehension of this report.

Discussing phylogenetic differences in the laminar distribution patterns of NE fibres, Lewis & Morrison (1989:260) observe that "the most striking difference in humans by comparison with other species is the relative paucity of NE fibers in the molecular layer." Examining various regions of the human prefrontal cortex, they also observed that "noradrenergic fibres are most dense in those regions, areas 8B and 9, which are perhaps most clearly involved in sensorimotor function" (p.325). This supports Brown et al.'s (1979) original suggestion that NE participates in sensorimotor integration. Morrison & Foote's (1986) interpretation regarding the striking differences seen in the visual cortex also support this view:

Within the [primate] visual system, NA fibers [relative to 5HT] preferentially innervate those regions involved in **spatial analysis and visuomotor response** rather than those involved in feature extraction and pattern analysis (Morrison & Foote 1986:117).

Very obviously researchers are struggling to interpret the functional significance of phylogenetic differences in chemoarchitecture. At this point in time all we can say for sure is that "the NA and DA innervations of the human cortex have a highly specific organization that is markedly different from that in lower mammalian species" (Lewis & Morrison 1989:269). And that while these differences may very obviously be functionally significant, researchers are a long way from being able to say in what ways they contribute to the fundamental uniqueness of *Homo sapiens sapiens*.

9.5 The Functional Significance of NE

NE has been implicated in a dizzying array of brain functions. To begin, NE has been implicated in selective attention (Sara 1985); sensory-gating and stimulus filtering (Waterhouse et al., 1978, 1980; Woodward & Waterhouse 1978; Zornetzer et al., 1978; Woodward et al., 1979; Harley 1991); enhanced reactivities of hippocampal cells to afferent stimuli (Segal et al., 1991:323); enhanced distal environmental cue coupling to the hippocampal network (Harley 1991:319); and enhanced cortical responsiveness during periods of waking, attentiveness, and cognition (McCormick et al., 1991).

In addition, NE has also been implicated in: memory consolidation and recall (Zornetzer et al., 1978; Quartermain 1983; Zornetzer 1985; Liang et al. 1986; Palmer et al., 1987; Haroutunian et al., 1990); age-related memory losses and cognitive decline (Vijayashankar & Brody 1979; Bondareff et al., 1982; Zornetzer 1985; Decker & Gallagher 1987; Decker & McGaugh 1989; Decker et al., 1990; Pappas et al., 1992); and neural plasticity in all areas of cortex (Kasamatsu et al., 1984) - which implies and includes "the capacity of the brain to undergo modification due to experience" (Murtha et al., 1990:249).

Finally, it has also been observed that NE has been implicated in exploratory motivations (Ellison 1977); stress and depression

(Reinstein et al. 1984; Anisman 1984; Raleigh et al., 1988; Anisman et al., 1991); modulation of thalamocortical processing (McCormick 1989; McCormick et al. 1991); behavioural switching between intero- and exteroceptive sensory events (Iversen 1984); hippocampal states of reactivity - including long-term potentiation (Hopkins & Johnson 1984; Harley 1991; Segal & Bloom 1986; Segal et al. 1991); and prefronto-cortical sensory motor integration (Lewis & Morrison 1989). We may also be surmise that NE is implicated in cross-modal information transfer (Murray & Mishkin 1985) given its actions in the amygdala (Liang et al. 1986).

Without a doubt, this spectrum of effects is partially attributable to the role of NE in enhancement of the "signal-to-noise ratio" in the brain. This is a descriptive shorthand for its seeming ability to bias "subthreshold sensory stimuli to a detectable level" (Sara 1985:181-182⁶⁷). That is, "differentially suppress...background excitation more than stimulus-evoked excitation" (Phillis 1984:179). Perhaps not surprisingly (recall Figure 9.3) this is especially pronounced in the somatosensory cortex. Indeed, NE can "potentiate responses in the somatosensory cortex" to **subthreshold** sensory input (Sara 1985:181-182). The net effect of this action on the part of NE is to "facilitate the transfer of afferent information in the cerebral cortex" (Phillis 1984:179).

⁶⁷ See also Marshall & Finlayson (1988) for a more general discussion.

This explains a good portion of the functional significance of noradrenergic mechanisms. So too does it explain the electrophysiological basis of the functionally more restrictive term "neuromodulation" that used to be applied to noradrenergic mechanisms - inclusive of every other effect. It was not until such time as certain controversies were put to rest (section 9.3.1 above) that researchers felt free to pursue other interpretive possibilities. If we recall some of the details in Chapter 4 (i.e., Figures 4.1 and 4.2) perhaps we can construct an image of NE that accommodates the more traditional emphasis on neuromodulation while at the same time respecting recent evidence for the presence of conventional synapses.

On a structural and functional level we might well imagine a preponderance of NE-releasing neurons "positioning themselves (as it were) in various "communities of cells" (Laughlin et al., 1990) so as to "penetrate and entrain"⁶⁸ and thus influence broad-based activity patterns in the brain. This would invariably be achieved through a combination of premodulatory coincidences (Figure 4.2B) and second messenger systems capable of both enhancing the signal-to-noise ratio and inducing postsynaptic changes in receptor densities"⁶⁹ that result in the "selective stabilization" (Changeux 1987) of particularly active neurons. Figure 4.3B also provides a concrete image of how NE might be implicated in LTP in the

⁶⁸ Laughlin et al., (1990) discussed in Chapter 4.

⁶⁹ recall Lynch & Baudry (1984) mentioned in Chapter 4.

hippocampus with the added participation of trophic support molecules transported retrogradely to the NE-releasing neuron.

Many of the functional correlates of NE listed above will be used as empirical links in the various "chains of inference" I plan to construct in Chapter 12. For that reason an extended interpretation is warranted. I will briefly explain why the stress paradigm provides a useful heuristic. Then I will end this chapter with a more broad-based definition of the functional significance of noradrenergic mechanisms (that includes its role in selective attention, behavioural switching and memory).

9.5.1 NE and Stress

Reinstein et al. (1984) reported that

exposure to an uncontrollable stressor can increase brain NE turnover and decrease locomotor and exploratory behavior. **Uncontrollable stress caused NE to be released from some neurons more rapidly than it could be restored by synthesis or reuptake**, thereby impairing noradrenergic transmission and NE-dependent exploratory behaviors. Tyrosine administration presumably enhanced the transmitter's synthesis in stressed animals, thereby preventing both the neurochemical and the behavioral deficits (Reinstein et al., 1984:2225).

These findings are consistent with those of Raleigh et al., (1988), Brady et al. (1980, cited in Spring 1986:37) and Lehnert et al. (1984, cited in Milner & Wurtman 1986:880). This research suggests

that increased tyrosine availability exerts "neuroprophylactic" or so-called "neuroprotective" benefits.

The importance of adequate amine supplies is reinforced in the context of the understanding that stress pro-actively engenders a heightened noradrenergic response to either the cues associated with a stressor or the actual stressor itself (Anisman et al. 1991:5 in review). Whereas associated cue exposure can trigger increased NE synthesis and utilization, re-exposure to the actual stressor can "readily re-induce the NE reductions" (Anisman et al. 1991:5).⁷⁰ This is why an enhanced rate of NE synthesis persists for up to 48 hours following the cessation of a stressor (Fillenz 1990:212): it assures "that adequate amine supplies will be present in order for the animal to deal effectively with impending stressors...reduc[ing] the occurrence of behavioural pathology" (Anisman et al 1991:7). This places great importance on the NE precursor and related cofactor content of diet.

The far-reaching implications of this research are clear. As Spring (1986) explains, the relationship between stress and NE "raises important questions about whether tyrosine supplementation might prove beneficial to human subjects exposed to severe uncontrollable stressors" (Spring 1986:37). In an analogous manner, this research also raises the important question as to whether

⁷⁰ This suggests that biologically significant stimulus configurations become associated in the CNS with particular neurochemical responses. That is, operantly conditioned !

tyrosine "supplementation" - in the form of technologically facilitated consumption of meat (which contains amino acids in the form of proteins as well as many of the cofactors implicated in NE synthesis) - might have proven beneficial to our hominid ancestors who were no doubt experiencing "severe uncontrollable stressors" to an extent not readily generalizable to the contemporary [read cultural] human condition.

This, then, is our point: whether or not we can readily equate an "uncontrollable stressor" with any lived-in contemporary human experience remains to be seen. We can, however, liberate our thinking by realizing that life on the open savanna may have provided our hominid ancestors with some uniquely stressful challenges that we cannot quite imagine in this wholly cultural environment. In other words, while we may (as reflective scientists) question our ability to generalize the results of the stress/NE paradigm onto the contemporary cultural condition, perhaps we can more readily generalize these findings onto the ancestral **pre-cultural** condition.

By way of analogy: what I talking about here is the "the life-dinner principle" (Foley 1987:131) in experiential and neurochemical terms: "in a hunting episode a rabbit is running for its life, a fox just for a single meal." So too might I suggest that the contemporary versus ancestral human condition was qualitatively different.

In Chapter 12 I will pursue the possibility that meat eating may have enhanced our ancestors' capacity to (in effect) better "neuroprotect" themselves from the uniquely stressful experiences of their culturally incipient lives. I will argue that the neuroprotective benefits of increased protein consumption helped further rationalize meat eating in an adaptive Darwinian sense - i.e., in a manner that transcends the seeming all importance of caloric energy and costs benefit analyses.

9.5.2 NE and Selective Attention

In assessing the functional significance of locu coeruleus (LC) discharge activity, Iversen (1984) observes that

LC neurons display biphasic responses to a range of physiologically relevant stimuli in the auditory, visual and tactile modalities. In monkeys, more vigorous responses to complex novel stimuli were generally seen. Thus, by selectively augmenting CNS activity engaged by rapidly changing exogenous stimuli, robust NA-LC discharge may bias the global orientation of behavior towards coping with **phasically imperative events in the external environment** (Iversen 1984:329; emphasis added).

This seems an especially interesting interpretation given the understanding that consciousness is, by definition, a function of phasically imperative, i.e., **novel** or otherwise schematically mismatched events being elevated to the level of the "sensorium"⁷¹.

⁷¹ As used by Laughlin et al., (1990:106).

Perhaps this helps explain the functional significance of the high levels of NE seen in the PFC (Figure 9.3).

Nieuwenhuys (1985) reminds us that

locus coeruleus cells are activated by stressful, threatening stimuli...[They] may function as part of an 'alarm' system...[and exert] a 'stress dampening function'...[I]n the monkey these cells respond vigorously to complex arousing stimuli such as preferred food...[T]he generalization may be made that in the waking state the locus coeruleus exerts an 'attention function', i.e. continuously 'monitors' the environment for important stimuli/events, and prepares the organism to cope with emergency situations (Nieuwenhuys 1985:25-26).

So too do we observe that NE, at the thalamic level, "most densely innervates the visual (or polymodal) area that mediates orientation towards and manipulation of the external environment" (Morrison & Foote 1986:136). We also note that NE acts in concert with ACh at the thalamic level to "fine tune cortical neuronal responsiveness, perhaps to allow processing to occur in the most efficient manner possible" (McCormick 1989:217). This is because

increased release of ACh and NE will...increase the likelihood that phasic EPSPs [excitatory postsynaptic potentials] will trigger action potentials in a one-to-one manner...and thus result in the faithful transfer of incoming spike trains to cerebral cortex (McCormick 1989:220)⁷².

⁷² This adds to our understanding of what is meant by the suggestion that NE enhances the "signal-to noise ratio" and "facilitates the transfer of afferent information to the cerebral cortex".

All of these interpretations reinforce the merits of examining the functional significance of nutritional variables affecting NE synthesis.

The role of NE in selective attention (which, fundamentally, means the biasing of salient subthreshold sensory input to a detectable level) seems particularly relevant because, while we know NE is found in high concentrations in the prefrontal cortex (Figure 9.3), we also observe that "human consciousness is largely the product of forebrain processes and that afference must reach a level threshold of intensity to enter consciousness" (Laughlin et al., 1990:106). In Chapter 12 I will question whether NE may be participating more fully in certain critical aspects of human consciousness than the other pharmacosystems exhibiting different modulatory and chemoarchitectural patterns. And if so, what implications this has for our understanding of the evolution of hominid foraging strategies.

9.5.3 NE and Behavioural Switching

Iversen's (1984) "behavioural switching" hypothesis is interesting because it focuses on the functional significance of noradrenergic mechanisms in the hypothalamus. And as we know from Chapter 5 (Table 5.2) the diencephalon did exhibit statistically significant increases in size in members of the genus *Homo*.

Iversen (1984) defines attention accordingly:

'Attention' is a much used psychological term...To cite some of these meanings, attention may be focused 1) within a stimulus complex, e.g., to one or more features of a visual pattern but not to all features; 2) between competing stimuli in the environment, e.g., two or more discrete visual events or two or more sensory events in different modalities; 3) between interoceptive and exteroceptive sensory events, put most simply between stimuli eliciting instinctive or voluntary acts; and 4) between sensory events and irrelevant background noise... In the original formulation of the attention hypothesis of the DNB lesion effect, Mason & Iversen (1979) were thinking in terms of mechanisms 1 and 2...[however] hypotheses 3 and 4 [also] look interesting from the point of view of behavioral and neurophysiological experiments on the NA neurons (Iversen 1984:328-329).

Her "behavioural switching hypothesis" extends the effects of NE into the 3rd and 4th domains of experience.

Iversen (1984) argues that whereas exteroceptive sensory events (e.g., auditory, visual, tactile) are processed by the noradrenergic fibres innervating the cortex and hippocampus, interoceptive cues "of biological significance for the species-specific behavior essential for survival" (Iversen 1984:328) are processed by the noradrenergic fibres innervating the limbic-hypothalamic axis. Her model is based on the observation that

LC firing decreases during sleep and increases during waking. Particularly interesting is the finding that spontaneous activity and sensory-evoked activity in the LC is tonically reduced when instinctive behaviors such as grooming or feeding occur (Iversen 1984:329).

In the words of Iversen (1984:329):

this suggests that as well as enhancing the coding of sensory cues in limbic system and cortex, the LC also serves a permissive function dampening the response to external sensory cues during the performance of essential motor acts, **thus facilitating transitions between behavioral states** (emphasis added).

Accordingly she predicts that

lesions to the dorsal NA system would reduce the neurophysiological impact of sensory signals and impair the ability to switch between relevant responses to changing sensory input (Iversen 1984:329).

The specifics and predictions of her model are particularly compelling when viewed through the lens of Wurtman and colleagues' research.

While I would not presume to endow inadequate dietary supplies of tyrosine with the capacity to effect the kind of lesion her model requires, I am, nonetheless, tempted to question the impact culturally and technologically templated differences in diet might have on the integrity of these subtle mechanisms. In Chapter 12 I will be pursue the possibility that aspects of hominid diet may have **created the preconditions for** subtle interindividual and interspecies differences in the ability to attend rapidly to phasically imperative visual, auditory and tactile sensory events in the intero- and exteroceptive fields of experience. As split second timing might mean the difference between life or death, natural selection would be given another axis of variability to act upon. If it can reasonably be argued that the proximal cause .f

such differences might be variations in NE synthesis in the cortex, hippocampus, and limbic-hypothalamic axis, I might also argue that natural selection would be obliged to operate on the noradrenergic potential of hominid diet - independent of its caloric content. Once again, the diet that maximizes fitness may not be the one that maximizes caloric intake at the expense of other nutrients (Pulliam 1974).

9.5.4 NE and Memory

It is perhaps obvious why NE should be implicated in memory consolidation and retrieval as a logical extension of its role in selective attention. As Squire (1987) states,

locus coeruleus neurons, the source of the forebrain NE system, fire in relation to an animal's level of vigilance and they can be phasically activated by stimuli such as lights, tones, and mild skin contacts... This suggests that the locus coeruleus helps alert the forebrain for the processing of important external stimuli. NE might therefore be expected to influence learning and memory, insofar as increased vigilance or attention at the time of learning can make information processing more efficient. Moreover, because memory is not fully formed at the instant of learning, it is possible at least in principle that NE might influence learning and memory shortly after the moment of learning by also producing a vigilant or attentive-like state (Squire 1987:44, emphasis added).

This is the position Sara (1985) adopted in the context of explaining the memory retrieval deficits seen in Korsakoff's patients: The assumption is they suffered an "impairment in

information processing at the time of the acquisition due to [a noradrenergically-mediated] attention deficit" (Sara 1985:191).

Harley (1991) reinforces the view that the role of NE in memory is a logical extension of its role in selective attention.

It seems fitting that a mechanism which can produce transient potentiation of cellular responses to a putative sensory input should also, **on an apparent continuum of degree or duration of activation**, be linked to an increased future response to that input. The short term effect would presumably increase the intensity of experience or promote attention to input, while the long-term effect could be viewed as the promotion of memory.

The two processes of attention and memory have long been functionally linked in the psychological literature. It now appears that they are linked at the mechanistic level as well...The picture of LC function which emerges... supports the hypothesis that the LC is part of a [facilitator-] system which increases the likelihood of the physiological changes which underlie the functions of 'noticing' and 'remembering'" (Harley 1991:318)

We see, then, that the integrity of the noradrenergic system is necessary for both the acquisition, and subsequent retrieval, of memories that are most often elicited under discriminative stimulus conditions.

The prediction that "pharmacological or physiological interventions that enhance NE activity to a certain **optimal level** should facilitate memory retrieval" (Sara 1985:183, emphasis added) seems particularly intriguing. In Chapter 12 I will pursue the added understanding that seasonally-, technologically-, and culturally-templated differences in NE precursor and related

cofactor availability might have been significant factors in human evolution insofar as they can be seen to be significant factors in enhancing NE activities to a certain optimal level with implications for enhanced memory retrieval.

10.0 DOPAMINE

In this chapter I will discuss the same objective criteria established in the prior chapters: DA synthesis, release, chemoarchitecture (including cortical and subcortical content and activity markers), and functional attributes. Some details regarding phylogenetic differences in chemoarchitecture will also be provided. Given the fact that NE and DA are both catecholamines (that is, constituents of the same biosynthetic pathway) most of the evidence relevant to an understanding of the effects of nutrition on DA synthesis and release has already been provided in Chapter 9. Accordingly, the first two sections provide but a brief recapitulation of only the most salient details. That I don't just refer the reader back to Chapter 9 is because under the heading of DA synthesis we confront one of the more critical building blocks of this thesis. In Chapter 11 I will examine developmental aspects of DAergic activity in the CNS.

10.1 DA Synthesis

As summarized in Chapter 9 (Figure 9.1) DA is synthesized from the amino acids phenylalanine and tyrosine by a series of enzyme-catalyzed reactions. Phenylalanine is converted into tyrosine with the help of iron (section 9.1.2). Tyrosine is then converted into dihydroxyphenylalanine (DOPA) by the action of the RLE tyrosine hydroxylase (TH). Interestingly, TH is a vitamin B6-dependent

reaction implicating B6 in CA synthesis (section 9.1.4). DOPA is converted to DA by the action of aromatic amino acid decarboxylase (which is also vitamin B6-dependent reaction). Liberated DA is then broken down into its major metabolites, 3,4-dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA) in the presence of one of two metabolic enzymes: monoamine oxidase (MAO) and catechol-O-methyltransferase.

Deutch & Roth (1990) provide us with a succinct explanation as to why small physiologic changes in precursor availability affect brain DA synthesis.

While all catecholamine neurons are ultimately dependent upon tyrosine as a precursor substance, the degree to which relatively small changes in precursor availability are rapidly reflected by changes in metabolism of dopaminergic neurons has only recently been determined. **The relationship between local tyrosine concentration and catecholamine synthesis appears to be operative only under conditions in which tyrosine hydroxylase (TH) is in an activated state** (Deutch & Roth 1990:375, emphasis added).

And as we have seen in Chapter 9, this is because

increases in firing frequency of the catecholaminergic neurons cause allosteric changes in tyrosine hydroxylase, thereby increases its affinity for its cofactor tetrahydrobiopterin, reducing its susceptibility to end-product inhibition...and enhancing its dependence on its saturation with tyrosine (During et al. 1989:1449).

What makes this worth repeating is the simple and exciting fact that tyrosine hydroxylase in the PFC is - by virtue of its anomalously high basal discharge rates, burst firing activity, and

enhanced DA turnover (Bannon et al. 1982a,b; Bannon & Roth 1983; Bunney & Chiodo 1984) - electrophysiologically predisposed to being in a predominantly activated state ! Perhaps this explains the significance of the additional observation that DA neurons in the prefrontal and anterior cingulate cortices do not (unlike virtually all other regions of the brain) possess "synthesis-modulating autoreceptors" (Bannon et al., 1981)³. No doubt a unique mechanism was necessary to enable the PFC to maintain its homeostatic properties (recall Zigmond's models discussed in Chapter 4). In Chapter 12 I will speculate on the adaptive significance of the absence of synthesis-modulating autoreceptors on PFC DA neurons.

As to the dietary significance of these several findings, Deutch & Roth (1990) said it best when they observed that

the higher basal firing rate of mesoprefrontal DA neurons and the greater frequency with which burst firing is observed in these neurons presumably contribute to a greater proportion of TH being in the activated form in the PFC than in other mesotelencephalic regions. Such a relative predominance of phosphorylated enzyme in the PFC may contribute to the enhanced responsiveness of the cortical DA innervation to precursor (tyrosine) availability.

The DA innervation of the prefrontal and cingulate cortices, but not other mesotelencephalic sites, respond to administration of tyrosine by increasing synthesis...[This suggests] **increased activity of the PFC DA innervation renders this system unusually dependent upon precursor availability** (Deutch & Roth 1990:375).

³ The reader may recall we encountered synthesis-modulating autoreceptors back in Chapter 4 (Figure 4.3B).

What we must confront, then, is the exciting possibility that **"precursor availability becomes an important factor in controlling transmitter output from these [PFC] neurons"** (Roth et al. 1988:199).

Given the fact that the PFC has exhibited the most significant allometric increases in size in our members of the genus *Homo* (Chapter 5, Figures 5.6 and 5.7), and as a result performs an executive role in human cognitive functioning (Laughlin et al., 1990), Roth et al.'s observation seems a profound insight indeed. What it effectively implies is something rather bold that Acworth et al., (1988) said in the context of the open-loop status of 5HT: that all the cognitive functionalities dependent on the activities of the PFC may in effect be "hostages to eating". One has to wonder about the liberating benefits of technologically-driven shifts in our Plio-Pleistocene hominid ancestors' diet (Chapter 12).

As we can see, then, even if the closed-loop status of NE prevents us from making only the most carefully structured theoretical deductions (as to the ongoing functional significance of CA precursor availability) DA in the PFC provides us with a unique and liberating exception. More to the point: the unique electrophysiological properties of PFC DA neurons (which include increased burst firing activity, increased DA turnover, etc.) hits home the point that we cannot make blanket statements about the functional significance of dietary precursors affecting CA

synthesis. Indeed, "the role that catecholamine precursors (phenylalanine and tyrosine) play in regulating the synthesis of DA and NA in different brain regions of the CNS will have to be explored on a case by case basis" (Commissiong 1988:185) precisely because not all regions exhibit the same activity-related profiles.

10.2 DA Release

As for the effects of dietary precursor on DA release, Fallon & Loughlin (1987) explain:

cortical D₂ receptors are present presynaptically as autoreceptors in pirifrom cortex, entorhinal cortex...and subcortical sites, such as the caudate-putamen, olfactory tubercle, and nucleus accumbens...These autoreceptors are absent in prefrontal and anterior cingulate cortices...which helps to explain why there is a higher ratio of DA turnover in these cortices as opposed to DA-rich subcortical sites. However, recent studies suggest that in the prefrontal/lateral cingulate cortex, **synthesis-modulating autoreceptors are absent but release modulating autoreceptors may be present**; thus long-term (synthesis) regulation of DA may be lacking, but short-term (release) regulation of DA may exist... (Fallon & Loughlin 1987:54-55; emphasis added).

In other words, despite the occurrence of such theoretically provocative structural anomalies as the curious absence of synthesis-modulating autoreceptors on DAergic neurons in the PFC, release-modulating autoreceptors are in all probability present. We may conclude, therefore, that DA release is also under closed-loop control.

11.4 Distribution Throughout The Brain

The DA system is quite complicated. I will provide a brief overview of DAergic synthesizing cell bodies and their major cortical and subcortical targets. Then I will focus on developing an understanding of regional differences in the content and activity patterns of DA in the cortex and subcortex.

11.4.1 DA Synthesizing Cell Bodies

DA is synthesized by eight different neuronal groups, designated A8 through A15. These cell groups are found in mesencephalic [midbrain], diencephalic [basal forebrain], and telencephalic [forebrain] regions. **A11-A14** are found in the diencephalon and project to subcortical regions. **A15**, the only DA synthesizing cell body in the telencephalon, resides in the olfactory bulb and forms part of a set of interneurons (Nieuwenhuys 1985:14). As Nieuwenhuys (1985) explains, the mesencephalic DA cells **A8-A10**

have been described as forming three cell groups...but the boundaries between these groups is indistinct... [These regions] give rise to a massive ascending projection which Ungerstedt (1971) divided into two systems: the nigrostriatal dopaminergic system, which (as its name implies) originates mainly from the substantia nigra or A9 group, and the mesolimbic dopaminergic system, which arises mainly from the A10 group. In the more recent literature...it has been emphasized that the dopaminergic neurons in the midbrain constitute a single

group projecting in at least crude topographic order to striatal, limbic and cortical telencephalic regions. The entire forebrain projection is, accordingly, now commonly referred to as the 'mesotelencephalic dopaminergic system' (Nieuwenhuys 1985:14-15).

Nieuwenhuys (1985:18) advocates a parcelling of the mesotelencephalic system into 3 subsystems: (1) the *mesostriatal*, (2) *mesolimbic*, and (3) *mesocortical* projections.

By way of clarification, the mesostriatal DA subsystem arises from DA neurons in the A8, A9, and A10 cell groups, whereas both the mesolimbic and mesocortical subsystems arise from cell bodies originating in A10 and the most medial part of the A9 substantia nigra. Collectively, the A8-A10 cell groups are known as the "mesotelencephalic dopaminergic system". It is, however, still common to encounter references to the 'substantia nigra-ventral tegmental area' (SN-VTA) which provides DAergic innervation of forebrain structures in an analogous manner⁷⁴. Significantly, the mesolimbic and mesocortical DA fibres merge with the ascending '*medial forebrain bundle*' (MFB). The MFB is a very important fibre tract comprised of "a highly heterogenous system of CA fibres [that] ascends from the brainstem reticular formation toward diencephalic and telencephalic regions" (Lindvall & Bjorklund 1978:169). For a detailed discussion refer to Nieuwenhuys (1985). I will simply add that A14 is "small and inconspicuous in primates" and A10 is "poorly developed in man" (Nieuwenhuys 1985:17).

⁷⁴ We will encounter this term in Chapter 11 when we model the prenatal development of the monoamine systems.

11.4.2 Dopaminergic Targets

The *mesostriatal* projections originating from cell groups A8, A9 and A10

fan out in the caudate nucleus and the putamen where they form an extremely dense terminal network. The nucleus accumbens, which is often considered a ventromedial extension of the caudate nucleus occupying an intermediate position between the 'extrapyramidal' and 'limbic' systems, is also richly supplied with mesostriatal dopaminergic fibres...Collaterals of the mesostriatal projection constitute a rather sparse plexus of dopamine-containing terminal axons throughout the globus pallidus (Nieuwenhuys 1985:16).

The *mesolimbic* projections, which arises from cell group A10 and from the most medial part of the substantia nigra, traverses the MFB and innervates the

bulbus olfactorius (scattered terminals in all layers), anterior olfactory nucleus (a sparse to moderate innervation), olfactory tubercle or anterior perforated substance (a very dense input), lateral septal nucleus, bed nucleus of stria terminalis (a dense plexus...) and the amygdaloid complex (concentrated in the central and basal nuclei...) (Nieuwenhuys 1985:17).

The *mesocortical* projections which (like the mesolimbic subsystem) arises from cell group A10 and from the most medial part of the substantia nigra, innervates the following cortical (and, strictly speaking, limbic) regions:

the medial part of the frontal lobe, the pre-piriform and piriform cortices, the entorhinal cortex and the anterior cingulate cortex... In most of these areas the

dopaminergic fibres constitute dense and well-delineated fields of termination (Nieuwenhuys 1985:17).

As to the subcortical structures receiving DAergic input from the A11-A14 diencephalic nuclei, the following labels and relationships apply:

- :tubero-infundibular DAergic projection
= A12 --> median eminence, pituitary stalk
- :incerto-hypothalamic DAergic projection
= A11 and A13 --> dorsal and rostral hypothalamic regions
- :diencephalo-septal DAergic projection
= A11, A13 and A14 --> lateral septal nucleus
- :DAergic hypothalamo-spinal projection
= A11 --> e.g., dorsal horn of spinal cord

I am fortunate in that I can quantify many of these relationships with reference to the landmark research of Brown et al., (1979).

10.4.3 Relative Densities of DA in Cortex

With regards to DA content in the cortex (Figure 10.1), we see that it is **highest** in orbital and dorsolateral prefrontal cortex and **lowest** in the occipital cortex. High-to-intermediate levels are observed in the premotor and motor cortex and superior and inferior temporal gyrus (anterior). Low-to-intermediate levels are observed in the inferior temporal gyrus (posterior), somatosensory cortex, and posterior parietal cortex. As Brown et al. (1979) state

the dopamine concentration appears to decrease as an almost linear function of distance along the fronto-occipital axis. **The highest concentrations of dopamine are found in the two prefrontal cortical regions;** decreasing concentration are observed in the premotor, precentral, postcentral, and parietal cortices with **the visual cortex at the occipital pole containing the lowest concentrations of dopamine**, less than 10% of that found in the prefrontal cortex...Within the temporal lobe, the anterior inferotemporal cortex, the posterior inferotemporal cortex, and the superior temporal gyrus all contain substantial concentrations of cortical dopamine which are still less than that found in prefrontal cortex (Brown et al., 1979:137, emphasis added).

The observation that the highest DA content in the primate cortex is found in the orbital and dorsolateral PFC is consistent with the histochemical findings of Levitt et al. (1984). It does, however, contrast with those of Berger et al. (1988) who examined the relative density of DAergic afferents. As Berger et al. (1988:105) report:

DA axons were present in every cortical region examined: rostral prefrontal cortex (sulcus principalis, area 46 and areas 9, 10, 11, 12)...medial dorsal parts of the motor areas: primary (area 4), premotor (area 6), and supplementary motor (medial area 6) cortices; parietal (areas 1, 2, 3a, 3b, 5, 7), temporal (areas 21 and 22), anterior (area 24), and posterior (area 23) cingulate, and visual (areas 17 and 18) cortices... The regional density of innervation followed a general rostrocaudal decreasing gradient, with a very low density in the visual cortex. **However, in the rostral part of the brain, the greatest number of DA fibers was observed not in the granular prefrontal but in the agranular motor cortices** (emphasis added).

...

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PM-1 3½"x4" PHOTOGRAPHIC MICROCOPY TARGET
NBS 1010a ANSI/ISO #2 EQUIVALENT

PRECISIONSM RESOLUTION TARGETS

Figure 10.1 Dopamine content (ng/g tissue) in various cortical regions of the young adult Rhesus monkey (redrawn from Brown et al., 1979). See text for discussion.

This and related research has lead to the more general conclusion that the terminal projection sites of DAergic axons innervate

all cortices, with a preferential innervation of motor versus sensory cortices, agranular versus granular cortices, association versus primary sensory regions, and auditory association versus visual association. Correlated with this are-to-area specialization is the general finding that layer IV is always poorly innervated. These patterns of innervation suggest that DA regulates the activity of cortical output rather than thalamocortical input projections (Fallon & Loughlin 1990:52).

Recognize, however, on the basis of more recent evidence, that "the dichotomy between granular and agranular cortices in the frontal cortex is not necessarily the best predictor of the density of DA-IR [dopamine immunoreactive] processes" (Williams & Goldman-Rakic 1993:213); and that the challenge Berger et al.'s (1988) results pose to Brown et al.'s (1979) observations graphed in Figure 10.1 is not as serious as it first seems. As Williams and Goldman-Rakic (1993:210) report, some areas of the PFC (e.g., the medial granular areas 8Bm and 9) are indeed more densely innervated by DAergic fibres than some agranular regions (e.g., agranular dorsal precentral cortex area 6D). In other words some areas of the PFC are indeed more densely innervated by DA than the motor cortices - but not all.

Given our interest in assessing the functional significance of cortical DA, it is also quite interesting to recognize that

recent electron microscopic evidence in monkey and human clearly demonstrates that DA synaptic contacts onto

cortical neurons are located almost exclusively on the distal dendrites and spines of distal dendrites...a finding that widely expands the range of potential targets of dopaminergic inputs...It is evident that nearly every cell within a cortical module may potentially receive a DA input...Thus, our data suggest that **all regions, and possibly all neurons, of the primate frontal lobe are influenced by the modulatory actions of midbrain dopaminergic neurons** (Williams & Goldman-Rakic 1993:221, emphasis added).

Having already established the fact that "precursor availability becomes an important factor in controlling transmitter output from these neurons" (Roth et al. 1988:199) I am most intrigued. These several lines of evidence suggest that dietary variations in precursor availability may have, as an indirect consequence of their ability to alter PFC DA activities, the capacity to control the output of possibly all neurons of the frontal lobe! This renders the precursor content of diet all the more functionally significant.

10.4.4 Relative Densities of DA in Subcortex

Figure 10.2A profiles what Brown et al., (1979) observed regarding subcortical DA **content**.

Not unexpectedly, the **highest** concentration of dopamine were found in putamen and caudate. Intermediate values for dopamine concentration are found in hypothalamus, thalamus, and amygdala. The **lowest** amounts are found in brain stem and hippocampus (Brown et al., 1979:140).

The high content of DA in the caudate/putamen implicates DAergic mechanisms in the ascribed functionalities of this region, namely motor output.

As regards subcortical CA **activity** (Figure 10.2B), we see again that it is **highest** in the amygdala, brain stem, **lowest** in the hypothalamus, and of intermediate significance in the caudate, putamen and hippocampus. This implicates CA activity in limbic functions.

10.5 DA in Phylogenesis

While many of the subtleties pertaining to comparative neurological differences in NT distribution throughout the brain are beyond the scope or comprehension of this report (because they refer to laminar and sublaminar distinctions that researchers are still trying to interpret the meaning of), I am fortunate in that Berger et al. (1988) provide a succinct appraisal of the DAergic system.

The expansion and differentiation of the primate neocortex is accompanied by a regional- and laminar-specific redistribution of the DA input, which suggests an involvement of this amine in the functions of additional cortical targets... **[T]here are extended cortical zones that receive very few or no DA projections in the rat...but that become innervated in primates; these include most of the parietal and temporal cortices and layer I of most areas.** Indeed, in the rat only the anterior cingulate cortex receives a rich contingent of

Figure 10.2 A measure of (A) dopamine (DA) content (ug/g/tissue), and (B) catecholamine (CA) activity (based on the hourly accumulation rates of DOPA (ng/gr/hr)), in various subcortical regions of the young adult Rhesus monkey (redrawn from Brown et al., 1979). See text for discussion.

DA terminals in the molecular layer; however, in the primate, layer I is the most densely innervated cortical lamina in all areas, and is virtually the only target of DA afferents in the primary visual cortex. **It is tempting to speculate that the cortical DA targets, which have appeared more recently in phylogeny, are of particular functional importance** (Berger et al., 1988:117).

This is a particularly fascinating observation. In Chapter 12 I will explore the paleodietary implications of this significant insight.

As to the functional significance of phylogenetic changes in chemoarchitecture, again we return to the broadly applicable insights of Iversen (1984):

just as we have seen anatomically that neurotransmitter innervation of cortex becomes more extensive and variable as one ascends the phylogenetic scale, neurotransmitter release may come to take on more specific roles...It seems likely that during evolution neurotransmitters in cortex come to play an increasingly important role in neural integration (Iversen 1984:335, emphasis mine).

From this standpoint it is interesting to observe that

among the three monoamine systems innervating the cerebral cortex, **the DA system undergoes the greatest transformations from rodent to primate**, which is characterized essentially by expanded terminal fields and by more highly differentiated laminar distribution (Berger et al., 1988:118, emphasis added).

This suggests that of all the NTs examined in this report, DA may play an especially pronounced role in the evolution of neural integration. This much is also suggested on the basis of the

previously discussed evidence that DA is found in its highest concentrations in the PFC.

As to other phylogenetic changes, the observation was made that the "machinery for biosynthesis of catecholamines may have developed *pari passu* [by an equal progress] with the evolution of the primate neocortex, particularly in relation to the expansion of association cortex" (Brown et al., 1979:146). Clearly, the fact that CA synthesis parallels the evolution of the neocortex, and especially association cortex, is as profound in its paleodietary implications as was Martin's (1981) observation that brain size is correlated with maternal metabolic turnover.

10.6 The Functional Significance of DA

The functional significance of DA in cortex has been clearly established in the context of Brosowski et al.'s (1979) demonstration that impairments in PFC-related cognitive functions can be brought about using only DA-specific pharmacologic techniques. The implications of this research are quite profound. Put simply: *"dopamine in frontal cortex [may be] essential for the kinds of cognitive functions dependent on the integrity of the frontal cortex"* (Iversen 1984:334). Brosowski et al.'s (1979) paper generated as much enthusiasm in the neurosciences as did Martin's (1981) research within the field of anthropology.

By way of explanation, Brosowski et al. (1979) examined the effects of DA lesions in the PFC on "spatial delayed alternation" performance which is the operational equivalent of the concept of "working memory". By way of definition:

working memory is the term applied by cognitive psychologists and theorists to the type of memory that is active and relevant only for a short period of time, usually on a scale of seconds...This criterion - useful or relevant only transiently - distinguishes working memory from the very different process that has been called reference [or long-term associative] memory (Goldman-Rakic 1990:325).

As Goldman-Rakic (1990) explains:

the significance of working memory for higher cortical functions is not necessarily self-evident. Perhaps even the quality of its transient nature misleads us into thinking it is somehow less important than the more permanent archival nature of long-term memory. However, the brain's working memory function, i.e., the ability to bring to mind events in the absence of direct stimulation, may be its inherently most flexible mechanism **and its evolutionarily most significant achievement**. Thus, working memory confers the ability to guide behaviour by representations of the outside world rather than by immediate stimulation, and thus to base behaviour on ideas and thoughts.

The difference between guidance of behavior by symbols, concepts, or ideas and guidance by external stimuli cannot be overemphasized (Goldman-Rakic 1990:333).

This implies that DA is critical for the expression of the brain's inherently most flexible cognitive mechanism and evolutionarily most significant achievement. That DA is found in its highest

concentrations in the PFC suggests the merits of expanding this definition.

The PFC has been implicated in cross-temporal information processing or so-called "time-binding", planning, foresight, intentionality, symbolic reasoning, social discriminations and behaviour, stress, and of course the evolution of human consciousness (Goldman-Rakic & Brown 1982; Goldman-Rakic 1984, 1990, 1992; Glowinski et al., 1984; Iversen 1984; Reader & Jasper 1984; Thierry et al., 1984, 1990; Fallon & Loughlin 1987; Robbins & Everitt 1987; Descarries et al., 1988; Berger & Weinberger 1990; Fuster 1984, 1990, 1991; Laughlin & d'Aquili 1974; Roth et al., 1988; Packard & White 1989; Laughlin et al., 1990; BertGlucci-D'Angio et al., 1990; deBruin 1990; Deutch & Roth 1990; Kaas 1990; Kostovic 1990; Parnavelas 1990; Uylings & van Edem 1990). By far, however, the most comprehensive description of the functional significance of the PFC is as follows:

the prefrontal cortex in humans is intimately involved in mediating: (1) superordinate control and monitoring of lower-order, relatively autonomous functions and systems; (2) anticipatory and attentional functions relative to sensory stimuli already constituted by secondary sensory and multimodal association areas; (3) augmentation of intended sensory and cognitive "objects" and inhibition of competitive objects, sense modalities, and cognitive functions; (4) planning, initiating, implementing, and monitoring the effects of complex adaptive behavior; (5) production and imposition of redundancy upon sensorial space; (6) facilitation of memory, but not actually involved in primary sensory memory storage; (7) focusing arousal energy to appropriate objects or goals; (8) construction of temporal cognitive plans, and maintenance of continuous concentration and behavioral response; (9) integration of the sensory world relative to internal

states and motor responses, especially when confronted by novelty in the environment; (1) initiation of and motor control of speech, and comprehension of textual material; and (11) control of affect, emotion, and mood relative to sensorial events (Laughlin et al., 1990:116).

This is achieved on the basis of the myriad connections many neural systems have with the PFC (ibid). Interestingly, Laughlin et al., (1990) precede their discussion on the functional significance of the PFC with the observation that

prefrontal processes may function to produce redundancy in otherwise novel sensorial space, processes that have been shown to exhibit lateral asymmetry and to be associated with dopaminergic (sic) systems; that is, prefrontal systems whose synapses secrete the chemical dopamine (Laughlin et al., 1990:115).

They too recognized the importance of DAergic activity in mediating the functional integrity of the PFC.⁵

In Chapter 12 I will pursue the paleodietary implications of the critical position DA occupies in overall brain functions vis a vis the PFC. Naturally I will be constrained to ask how our ancestors could have afforded, in energetic terms, to have evolved larger brains that were - by virtue of the unique electrophysiological properties of the PFC - unusually dependent on precursor availability. I will also question why natural selection would have favoured rendering the PFC - and its' attendant role in human consciousness - so susceptible to the vagaries of food

⁵ Indeed, it was Charles Laughlin who suggested I focus on DA in the PFC!

choice. This has significant implications for our understanding of the nutritional and ecological constraints on the process of brain and cognitive evolution.

PART FOUR

WHERE ANTHROPOLOGY AND NEUROSCIENCE MEET

11.0 The Frontiers of Developmental Neurobiology

The goal of this chapter is to discuss some aspects of pre- and postnatal developmental neurobiology that will establish the structural and functional significance of dietary variations in amino acid (etc.) availability affecting brain. As has been established in Chapters 7-10, several amino acids, vitamins, and minerals mediate the biosynthesis of the p.d.NTs. I have summarized these relationships in Table 11.1. They are significant for many reasons, the most important of which is:

factors that influence levels of CA or 5HT [or for that matter ACh] in adult neuronal systems must also be assumed to have the potential of altering these same transmitter systems in early embryos. Changes in neurotransmitter levels induced by variations in amino acid availability...may possibly have long range effects on the morphology, survival or differentiation of cells within the CNS (Wallace 1988:438).

I will begin by comparing and contrasting anthropological and neuroscientific definitions of the process of development. To this I will add a formal definition of the stages of neuronal development. Then I will focus on the six overlapping agendas of this chapter: (1) the time of origin of monamine synthesizing cells in early embryogenesis; (2) data on postnatal changes in the content and activity patterns of DA, 5HT, and NE in 6 areas of the non-human primate cortex from birth through 24-36 months; (3) the process of synaptogenesis in the human prefrontal and striate cortex, as well as 6 areas of the non-human primate cortex, from

birth through to maturity; (4) the development of ACh in the prefrontal cortex; (5) the transgenerational phenotypic effects of developmental variations in amino acid availability; and (6) the transgenerational phenotypic effects of observational learning.

The first four agendas will serve to establish the sweep of pre- and postnatal susceptibilities of certain brain regions to the nutritional variables summarized in Table 11.1.⁷⁶ The fifth initiative is the most valuable because it helps establish my major theoretical position without being accused of advancing a specious form of Lamarckism. The sixth provides me with an equal (if theoretically more complex) opportunity to further develop an understanding of the neuroevolutionary implications of culturally-templated differences in diet. Very obviously, I will touch on some major theoretical issue in this chapter that I will expand upon in Chapter 12.

11.1 Anthropology and Neuroscience on Human Development

Figure 11.1A provides a "model of adaptation at genetic, developmental, and short-term levels throughout the life span" (redrawn from Little 1995:131). This presents a very reasonable

⁷⁶ Appendix 1 suggests the way in which we should adjust our thinking when we endeavour to relate these findings to the human condition. Clearly, all of the developmental phases in humans are significantly prolonged relative to that observed in other species.

Table 11.1 Relationship between macro- and micronutrient availability and brain NT synthesis.

	SHT	ACh	DA	NE
carbohydrates	facilitator			
fat	facilitator			
phenylalanine			precursor	precursor
tyrosine			precursor	precursor
tryptophan	precursor			
LNAAs	competitor			
choline		precursor		
thiamine	cofactor	cofactor		cofactor
niacin	competitor			
"B5"		cofactor		
Vit B6	cofactor	cofactor	cofactor	cofactor
Vit C				cofactor
zinc				
iron			cofactor	cofactor
copper				cofactor

interpretation of developmental events. It draws our attention to a very simple but crucial fact:

developmental adaptation during intrauterine and extrauterine growth modifies the genetic base, and modifies the range of adaptation, probably reducing it somewhat...Adult adaptation capacity or adaptability, then, is a narrowed range of the original genetic potential, and this range of adaptability becomes further limited during the course of aging or senescence (Little 1995:130).

This can also be expressed in terms which have the added advantage of establishing my position with respect to such models. Simply put:

the conclusion that the consequences of early nutritional deprivation, for example, can be reversed in later life is wrong. There is no way to reverse any processes during brain development, once it becomes manifested in terms of structural changes. It is the change of structure that, on the one hand, represents an irreversible final stage of a developmental process and that, on the other hand, becomes the starting point - the basis of all future developmental events (Heuther 1988:422).

I am fortunate in that I can draw on the images and insights discussed in Chapter 4 (i.e., Figure 4.1 and 4.4A) to establish what this process is all about on a neuronal population level. The images in Figure 11.1B remind us that the range of adult adaptations is the developmental outcome of the competitive interactions between convergent and divergent neurons and associated "communities of cells" (Laughlin et al. 1990). The reader may recall that Zigmond (1994) suggested that in the process of early development some "pioneer neurons" might be able to adjust

Figure 11.1 A= a model of adaptation at genetic, developmental, and short-term levels throughout the life span (redrawn from Little 1995:131, Figure 4). The images in B (seen previously in Figures 4.4 and 4.5) serve to remind us what the lifelong process of development is all about on a neuronal population level. The "environmental influences" seen in the bottom panel are the synaptic and other inputs that converge on a cell (as discussed in Chapter 4). See text for discussion.

their rate of NT synthesis and release according to the extracellular supply of NT amino acids precursors, and in so doing exert a disproportionately greater influence on neural development than their initial density of innervation would predict (p.116). When combined with the tenets of trophic theory (Purves 1986, 1988) this suggests one of our major hypotheses: *developmental variations in amino availability may give some "pioneer neurons" a competitive metabolic advantage to expand their spatial and temporal domains of influence and thus (in effect) impose their own physiologically vested interests and associated cognitive functionalities on the development of the rest of the CNS.*

As to the difference between a strictly anthropological versus neuroscientific definition of development, I am likewise fortunate in that I can draw on the image in Figure 11.1A to help establish what the process of neuronal development is all about on a macro-behavioural (i.e., adaptive) level. The images in Figure 11.1A remind us that developmental variations in amino acid availability will interact with **and modify** the genetic base (shaded panel) and in so doing modify the range of adaptations the individual is effectively able to engage in later in life (middle and right panels). Expressed in terms of this thesis: developmental variations in amino acid availability will interact with the cognitive potentials inherent in the genome (left panel) and thus determine the limits of individual cognitive capacity in later

life. In this sense then the image in Figure 11.1A can also be construed as an image of the process of **cognitive** development.

11.1.1 Stages of Neural Development

Kostovic (1990:223-224) defines four broad phases in cortical histogenesis (Table 11.2): **(1)** the early fetal phase characterized by "intensive progressive histogenetic events: proliferation, migration, and neuronal differentiation" (Kostovic 1990:224); **(2)** the late fetal phase characterized by transient patterns of cortical organization; **(3)** "the early postnatal phase of reorganization and overproduction of cortical circuitry elements" (ibid), and **(4)** the late postnatal phase (childhood, puberty and adolescence) characterized by the prolonged structural and chemical maturation of the brain. It is unfortunate that "very few data are available on the last 3 phases of the human cortical development...[given that] these are the very periods that hold the key to the understanding of onset, timing, and nature of the cognitive development in man" (Kostovic 1990:224). Naturally I am very interested in how pre- and postnatal variations in amino acid availability might affect the integrity of these four phases of cortical histogenesis which lead ultimately to the human patterns observed in Figure 11.1A.

Table 11.2**Cortical Histogenesis in Humans**

Developmental phase	Major histogenetic feature
1. Early fetal	Progressive histogenetic events (proliferation, migration and differentiation)
2. Late fetal	Transient patterns of cortical organization
3. Early postnatal life and infancy	Reorganization & overproduction of cortical circuitry elements
4. Late postnatal (childhood, puberty and adolescence)	Prolonged structural and chemical maturation

Source: Kostovic (1990:224).

Kostovic recognizes that "naturally occurring neuronal death and reorganizational histogenetic events...lead to the more advanced level of functional organization of the cerebral cortex" (Kostovic 1990:233). I have to wonder how aspects of nutrition might interact with this process to co-produce this process of neural reorganization. My response to Zigmond (1994) directly above explains my position. Kostovic also observes that the functional reorganization of the brain is achieved "by means of a profound structural **and transmitter-related** reorganization and not exclusively by progressive elaboration of fetal patterns" (Kostovic 1990:235). This suggests neural and cognitive development is an *epigenetic* process that is susceptible to virtually any influence on the synthesis of the NTs whose activities characterize and shape the competitive processes of neural reorganization.

In the next three sections I will discuss when and where variations in amino acid (etc.) availability might theoretically exert significant developmental effects.

11.2 Time of Origin of MA Synthesizing Cell Bodies

As Levitt & Rakic (1982) observed

the precocious genesis and onset of differentiation of MA neurons, including the early and rapid maturation of their terminal innervation, has lead to speculation that they may be involved in the regulation of various aspects

of the development and plasticity responses of their target neurons (1982:36).

With that *a priori* assumption in hand they set out to compare the time of origin of the substantia-ventral tegmental area (SN/VTA), locus coeruleus (LC) and raphe dorsalis/centralis superior (RD/CS) with the time or origin of their major synaptic targets in the Rhesus monkey (Figure 11.2). Their investigations revealed that

the widely projecting brain stem MA neurons are formed more than a month before the peak of neurogenesis in areas that receive noradrenergic and serotonergic afferents such as neocortex and hippocampus (Levitt & Rakic 1982:50).

These findings provide support for the idea that the early differentiation of primate MA synthesizing cell bodies may control critical aspects of development in their target structures (i.e., hippocampus, striatum, prefrontal cortex). By 'critical aspects of development' I mean morphological, biochemical, physiological, and ultimately functional properties. This renders all the more profound the developmental effects of amino acid availability. When viewed through the lens of Wurtman and colleagues' research we can see that adequate prenatal supplies of all the nutrients summarized in Table 11.1 would very obviously be necessary for optimal structural and functional development of the monoamine target structures seen in Figure 11.2. An examination of postnatal changes in the content and activity patterns of the p.d.NTs in cortex allows us to be even more specific.

Figure 11.2 Diagram comparing (1) the time spans of neuronal origin of the locus coeruleus (LC), substantia nigra/ventral tegmental area (SN/VTa) and raphe dorsalis/centralis superior (RD/CS) with (2) the time of neuron origin of their major synaptic targets in the rhesus monkey (redrawn from Levitt & Rakic 1982). Arrowheads indicate the approximate time when cell genesis for each nucleus or cortical area reaches its peak. As is evident, peak production of monoamine (MA) cells occurs from 1 week to 1.5 months prior to the peak periods in their respective targets. This data suggests the early differentiation of primate MA synthesizing cell bodies may control critical aspects of development in their target structures (i.e., their morphological, biochemical, and physiological properties). See text for further discussion.

11.3 Postnatal Development of Monoamines In Cortex

It has been suggested that "there are certain periods during brain development when the brain, or better: the developmental processes that take place in certain areas of the brain, are particularly vulnerable to changes of their nutritional supply" (Heuther 1988:421). I am fortunate in that Goldman-Rakic & Brown's (1982) research provides us with **a very precise** understanding of the kinds of events that might be particularly susceptible to developmental variations in amino acid availability.

Previously they established that the content and activity patterns of the monoamines in cortex are regionally heterogenous (Brown et al., 1979 as discussed fully in Part 3). They deduced that these differences must have been functionally significant. As a logical extension of this earlier work they set out to determine the postnatal content and activity patterns of DA, NE and 5HT in 6 regions of cortex (prefrontal, premotor, precentral, postcentral, parietal, and occipital) of the Rhesus monkey from birth through 24-36 months of age. They assumed developmental differences in the content and activity patterns of the p.d.NTs in cortex might be as functionally significant as the adult levels were presumed to be. In this sense then they sought to demonstrate the likelihood that cognitive maturation is subserved by neurochemical factors. I endeavour to summarize their findings below. For the sake of clarity I will boldface those terms that provide readily

comprehensible indications of the kinds of protracted susceptibilities NT specific systems in particular regions might have to post-natal amino acid (etc.) supplies.

11.3.1 Developmental Changes in Monoamine Content

Figure 11.3 documents postnatal changes in the content of NE, DA and 5HT in 6 areas of cortex.

With regards to cortical NE, we see it **increases steadily from birth through 24-36 months of age in most regions examined**. Between birth and 24-36 months there is a statistically significant difference in NE content in prefrontal, posterior parietal, and visual cortex (all $P < 0.001$). **NE in the PFC exhibits its greatest increase between 15-18 and 24-36 months**. This is similar to the profile seen in premotor cortex where NE content nearly doubles between this same period. This contrast with the earlier more pronounced development of NE content in the precentral motor, postcentral somatosensory and posterior parietal cortices during the first 15 months. NE in occipital cortex appears to develop in two stages: it rises from birth to 2 months, remains steady until 15 months, then rises again. The finding that NE content in precentral motor cortex at 8 months exceeds the level observed in adults apparently has to be interpreted with caution given that it might reflect individual variability.

Figure 11.3 Varying concentrations of DA, NE, and 5HT in 6 regions of the cortex of the Rhesus monkey at various developmental stages from birth (NB) to 24-36 months. Redrawn from Goldman-Rakic & Brown (1982, Figures 1-3). See text for discussion.

With regards to cortical DA, we see that "in the frontal lobe DA develops according to a somewhat more complex pattern" (p.342). **While the content at birth versus adulthood is not significantly different, the periods in between are characterized by significant fluctuations.** It appears that DA levels decrease during the first 8 months and then gradually increase to adult levels. DA in the premotor cortex exhibits similar oscillations. In motor cortex, DA content peaks at 5 months and declines steadily thereafter, reaching the adult level by 15-18 months. Interestingly, DA levels in somatosensory and posterior parietal cortex are considerably lower than those observed in the frontal lobe. As well, the developmental patterns in these regions are much less variable. Finally, "at all developmental stages DA content of the occipital cortex is the lowest of all cortical regions measured" (Goldman-Rakic & Brown 1982:342).

With regards to cortical 5HT, we can see that by comparison with the other monoamines

5HT content matures the earliest and exhibits the least dramatic fluctuations. The main significant comparisons were between newborns and 24-36-month-olds in prefrontal ($P < 0.01$) and visual ($P < 0.001$) cortex. In these areas and in somatosensory, posterior parietal and motor cortices as well, **5HT content appears to reach adult values by 2 months of age and to show little change after this point** (Goldman-Rakic 1982:342).

The fluctuating activities of 5HT in prefrontal and premotor cortex provide us with the only exceptions to this general conclusion. The

content of 5HT in PFC parallels that of DA, with a statistically significant fall in concentration between 5 and 8 months relative to the adult level.

As can be seen, NE in all regions presents a protracted developmental profile. DA is more complicated. 5HT is the least remarkable of all [using prolonged development as a descriptive criteria].

11.3.2 Monoamine Activity in Cortex

Figure 11.4 summarizes Goldman-Rakic's findings regarding the activity patterns of the monoamines in 4 regions of primate cortex: prefrontal, premotor, parietal, and occipital. Several findings seem particularly noteworthy. For instance, **"in prefrontal cortex, DOPA accumulation exhibits a nearly 3-fold linear increase from birth to 36 months of age ($P < 0.001$)"** (p.343). Equally interesting is the finding that **whereas DA activities in the posterior parietal cortex remain steady for the first 15-18 months they rise sharply and dramatically thereafter**. Somewhat parenthetically, we also note that CA activities in the premotor cortex achieve their adult level by 8 months of age. The developmental activities of the CAs in the occipital cortex are rather unremarkable.

Figure 11.4 Monoamine activity levels in 4 cortical areas of the Rhesus monkey brain at various developmental stages from newborn (NB) through 24-36 months of age based on hourly accumulation rates (nmoles/gm/h) of 3,4-dihydroxyphenylalanine (DOPA) and 5-hydroxytryptophan (5HTP) (redrawn from Goldman-Rakic & Brown 1982, Figure 4). See text for discussion.

Results of their comparison of DOPA accumulation rates in association areas (PFC and posterior parietal cortex) between two age groups (8 months and 24-36 months) are also noteworthy.

Catecholamine synthetic activity in the association areas...increases dramatically (70% and 167%, respectively) between 8 and 24-36 months of age ($P < 0.001$)...Over the same period catecholaminergic synthetic activity in premotor, motor, and somatosensory cortex shows only slight or modest changes ranging from 1-28% (Goldman-Rakic & Brown 1982:343).

This clearly reveals that the normal development of CAergic activities in the PFC would be particularly susceptible to dietary variations in amino acid etc. availability for many years after birth. Rakic et al.'s (1994) studies on synaptogenesis in the PFC extends this time frame well into adulthood (section 11.5). So too does Kostovic's (1990) research (section 11.4) encourage similar conclusions regarding the protracted susceptibilities of PFC neurons to dietary supplies.

Goldman-Rakic & Brown's (1982) study also reveals that there is a complementary relationship between the activities of NE and DA and 5HT in rostral and caudal regions. This can be seen with reference to Figure 11.5 which documents the topographical distribution of the DOPA and 5HTP over 4 developmental periods. These additional findings indicate that

Prefrontal = +70%; premotor = +1%; motor = +21%; somatosensory = +28%; parietal = 167%; visual = +46% (Goldman-Rakic & Brown 1982:Table 1).

Figure 11.5 Topographical distribution (nmol/gm/hr accumulation rates) of DOPA and 5HTP in 6 functionally distinct regions of the dorsal neocortex of the rhesus monkey (redrawn from Goldman-Rakic & Brown 1982, Figure 6). Whereas DOPA accumulation is highest in rostral regions and lowest in caudal areas, the reverse is true for 5HTP accumulation at every age examined. See text for discussion.

there is a complementary relationship between rates of catecholamine and indolamine synthesis throughout development... Simply stated, DOPA accumulation is highest in rostral regions and lowest in caudal areas while the reverse is the case for 5HTP accumulation at every age examined (Goldman-Rakic & Brown 1982:345).

The complementary nature of these content and activity patterns (Figures 11.3-11.5) are no doubt functionally significant. Clearly, developmental variations in amino acid (etc.⁷⁹) availability might alter the very nature of these functional interactions (Chapter 12).

11.3.3 Topographical Differences in Monoamine Content in Cortex

Figure 11.6 provides yet another useful way in which the significance of diet can be conceptualized: on the basis of an analysis of the topographical distribution patterns of NE, DA, 5HT and 5HIAA⁷⁹.

Several patterns in Figure 11.6 are noteworthy: (1) NE is fairly evenly distributed across cortex at 2 months of age, but (as would be expected on the basis of Brown et al.'s (1979) findings discussed in Chapter 9) "becomes increasingly concentrated in the somatosensory cortex over the subsequent **2-3 years** of postnatal

⁷⁹ See Table 11.1 for additional nutrients.

⁷⁹ The reader will recall from Figure 7.1 that this is a 5HT metabolite.

Figure 11.6 Topographical distribution of NE, DA, 5HT and the serotonin metabolite 5HIAA in 6 functionally distinct regions of the dorsal neocortex of the rhesus monkey (redrawn from Goldman-Rakic & Brown 1982, Figure 5). See text for discussion.

development...[By young adulthood] NE reaches its highest point, more than twice that of any other cortical region examined" (Goldman-Rakic & Brown 1982:344). (2)

At 2 months DA is evenly distributed in prefrontal, premotor and motor cortex, but at 5 and 8 months, the DA concentration increases selectively in motor cortex. **Between 8 months and 2-3 years, the DA content decreases in the motor cortex area and increases in prefrontal cortex** to produce the rostral caudal gradient characteristic of this neurotransmitter in adult cortex (Goldman-Rakic & Brown 1982:344-345).

And (3) "the highest 5HT and/or 5HIAA concentrations are generally found in the posterior cortical regions such as the somatosensory or visual cortex" (ibid:345).

11.3.4 The Concept of Preparedness

If there is one message we can take away from this review of Goldman-Rakic & Brown's (1982) research it is the following: developmental changes in the content and activity patterns of the p.d.NTs in cortex are genetically-templated "optimal solutions" to the "problem" of adaptation. They are carefully timed sequential developmental events that subserve the process of functional maturation. They are orchestrated in such a way as to ensure that development occurs in an orderly and efficient manner. In an ecological sense, though, the **images in Figures 11.3-11.6 are genetic "problems" requiring an "optimal nutritional solution".**

Figure 11.7 Three different developmental courses that may be taken by neural structures relative to preparedness (redrawn from Laughlin et al., 1990:65). See text for discussion.

This is precisely because of their precursor-dependent status. Whether or not an optimal nutritional "solution" to these neurochemical "problems" of adaptation is forthcoming depends on the dietary biases reflected in the cultural information pool (Chapter 12). The potential cognitive consequences of such culturally-determined variations are comprehensible in the very terms the biogenetic structuralists used to respond to Martin Seligman's preparedness paradigm.

As Laughlin et al. (1990) explain:

development of a complex neural network mediating an advanced response may require completion of a previous series of developments before it becomes prepared to mediate the advanced response...

In our account preparedness is the degree to which neural models are at optimal readiness for adaptive interaction with the environment at some particular point in ontogenesis. The pattern of development of neurognosis will be highly variable depending on the nature and complexity of the environmental stimulus **and the progressive sequence of the requisite neural tissue**. As depicted in [our Figure 11.7], the neural model may be at optimal preparedness in utero or at birth, and decrement to relative unpreparedness thereafter (curve a). On the other hand, the model may not be prepared until later indevelopment, but once the activated, it increases in preparedness throughout the remaining developmental period (curve c). Or their might occur a relatively more precise period of optimal readiness before which the model is contraprepared, during which it is prepared, and after which there is a rapid decrement to unpreparedness, even contrapreparedness (curve b). These three types of readiness are offered merely as examples; there will actually be many variations as models and systems of models move through their developmental phases (Laughlin et al., 1990:65-66, emphasis added).

Their last point is well taken in the context of the evidence provided in Figures 11.3-11.6. What seems apparent is that all the images in these four figures are essentially miniature portraits of the preparedness paradigm as seen through the lens of dynamic differences in the content and activity patterns of the p.d.NTs in functionally specified regions of the brain. They not only reveal the point in time at which environmental stimuli will be able to developmentally entrain the receptive field properties of certain cortical neurons, but they also reveal the precise neurochemical mix of mechanisms through which this can and ideally should be achieved.

Witness, for example, Goldman-Rakic & Brown's (1982) observation that

the most striking increases in catecholamine synthetic activity were found in the prefrontal and parietal association areas as compared with sensory and motor cortex...It may not be coincidental that the dorsolateral prefrontal cortex assumes its mature role in cortical function only gradually over the course of 2-3 years and does not attain physiological maturity until the stage of puberty...**The timetable of maturation of prefrontal catecholamines corresponds to the protracted development of prefrontal function and provides another source of evidence that catecholamines may play an important role in mediating prefrontal cortical activity** (Goldman-Rakic & Brown 1982:346-347, emphasis added).

Conveniently, the prolonged maturational timetable for CA activities in prefrontal and parietal association areas provides us with a concrete example of Laughlin et al's "curve c" (Figure

11.7), as does maturational profile of ACh in the PFC (see discussion below).

All of this suggests that postnatal aspects of nutrition may interact with the timing and/or sequencing of these developmental events to "co-produce" varying degrees of contra- or optimal readiness for interaction with the larger world of experience. This suggests the following: in the absence of requisite nutritional supplies the state of optimal readiness or "preparedness" for information assimilation in particular neurognostic structures and models may not (all things being equal) be fully achieved. Developmental variations in amino acid availability at critical pre- and postnatal stages might therefore affect the degree of "optimal readiness" of various neurognostic structures for adaptive interaction with the larger world of coordinating entrainments.

As the reader can see, far from denying the controlling influence of genetics, I am simply hypothesizing that developmental variations in NT precursor availability would interact with genetic factors governing the optimal profiles seen in Figures 11.3-11.6 to "co-produce" varying degrees of physiological preparedness for neurognostic interaction with the larger world. In this sense then Goldman-Rakic & Brown's (1982) research also provides us with several exquisite examples of **the most fundamental interface between biological and cultural mechanisms of adaptation**. I will pursue this at greater length in Chapter 12.

11.4 Development of ACh in Cortex

While I cannot offer as comprehensive a review of the cholinergic system as that pertaining to the catecholamines as provided by Goldman-Rakic and Brown (1982), I can draw the reader's attention to one small detail of interpretive significance.

Kostovic (1990) observed that after the first three phases of neuronal development (recall Table 11.2)

the major histochemical change...is the appearance of "cholinergic" innervation of layer III associative pyramidal neurons. This late developmental event, which seems to be [uniquely] characteristic of the human cortex, has its onset after the first postnatal year, proceeds gradually, and reaches its peak intensity in young adults (Kostovic 1990:236).

Given that the pyramidal neurons of layer III "are the major source of associative and commissural projections...and are important neuronal elements underlying cognitive processing in the cerebral cortex" (Kostovic 1990:235), this seems quite significant indeed. What it suggests is that cognitive maturation is subserved in part by cholinergic mechanisms (see also comments in Mrzljak et al. 1990). Interestingly, these mechanisms may be unique to humans. As Kostovic (1990:235) observed: "the AChE-rich innervation of layer III pyramidal neurons has so far been documented only in the human cortex, and this late developmental process seems to be a unique feature of the human, and possibly of the primate brain." These

findings provide us with another example of the preparedness paradigm as seen through the lens of developmental biochemistry.

As the details in Chapter 8 allow us to appreciate, this protracted phase of ACh development in layer III pyramidal cells of association cortex would have placed sustained demands on the choline (etc., Table 11.1) content of our hominid ancestors' diet. Theoretically (i.e., with reference to optimal foraging theory discussed in Chapter 4), this would have placed an adaptive premium on any foraging strategy that was optimally suited to fulfilling these protracted demands.

11.5 Synaptogenesis in Human and Non-Human Primate Cerebral Cortex

As Rakic et al., (1994:227) observed

the formation of appropriate synapses is the ultimate step in the construction of brain circuitry. Synaptic architecture defines the limits of individual mental capacity...It is surprising, therefore, how little we know about synaptogenesis in the cerebral cortex and how poor our understanding is of the relationship between synaptic maturity and functional development.

Figure 11.8 provides a summary of their findings collected over an 8 year period. Figure 11.8A plots the synaptic densities observed in human prefrontal and striate cortex from before birth through infancy, childhood, puberty, adulthood, and into maturity. The four models in Figure 11.8B reveal data from non-human primates (Rhesus

macaques) in the primary visual (area 17), prefrontal association (area 46), primary motor (area 4) and primary somatosensory (area 1) from before birth, through infancy, childhood, puberty, and young adulthood (20 years).

What is at first readily apparent is the fact that synaptogenesis occurs very rapidly after birth in all regions. By way of explanation, the exponential phase "coincides with the so-called 'sensitive period' of both sensory and association areas" (Rakic et al., 1994:230). Conversely, the period of peak synaptic density in adolescence - the so-called "plateau phase" (which involves neither a net accretion or net loss of synapses) is "the period in human development that coincides with intellectual growth and the achievement of adult levels of competence in language and logical thought" (Rakic et al., 1994:230).

Interestingly,

many modifications in the morpho-functional maturation of the cerebral cortex have been proposed to explain dramatic behavioural change in [adolescence]...including reorganization and turnover of synaptic circuitry (Purves 1988), synaptic vesicle proliferation (Miller 1988), axonal myelination (Gibson 1970), and biochemical differentiation (Goldman-Rakic & Brown 1982). **Most of these cellular events occur during the plateau phase of synaptogenesis and any and all of these parameters could contribute to the functional maturation of the cerebral cortex** (Rakic et al. 1994:231, emphasis added).

Figure 11.8 Model A: Synaptic density in the human striate area (open, large circles) and prefrontal cortex (black, small circles) (redrawn from Rakic et al., 1994 Figure 4). Model B: Histograms of the density of synapses per 100 μg^3 of neuropil in the primary visual (area 17), prefrontal association (area 46), primary motor (area 4) and primary somatosensory (area 1) at various ages of the Rhesus macaque. MAB: months after birth; DAC: days after conception; B: birth; P: puberty (redrawn from Rakic et al., 1994, Figure 3). See text for discussion.

As the reader may recall, I examined both Purves (1988) and Goldman-Rakic & Brown (1982) above.⁹⁰

Summarizing Rakic et al.'s (1994) findings (Figure 11.8B), it can be seen that

the highest density of synapses in motor, somatosensory, and visual cortex is reached at 2-3 months of age and then declines, at first gradually (up to 3 years), and then more sharply after that point...[However] **a somewhat different time course is emerging for the prefrontal cortex, where the highest level of synaptic density appears to be sustained from the second postnatal month until the third year after birth before declining very gradually to the adult level** (Rakic et al., 1994:230).

This can also be seen in the human data plotted in Figure 11.8A, only here **"the plateau phase for prefrontal cortex [in humans] would correspond to the entire period of childhood through puberty, roughly 13 years"** (Rakic et al., 1994:231). The dietary implications of such protracted phases of development - especially in the PFC - are readily apparent.

Rakic et al. (1994) conclude that "factors which improve synaptic efficiency may be more critical than shifts in synaptic density as a neural basis for behavioural maturation and plasticity during this prolonged postnatal phase" (Rakic et al., 1994:231). This points to the significance of dietary factors. Given the

⁹⁰ It is unfortunate we have yet to pursue the significance of Miller (1988) cited in Rakic et al., (1994).

implications of both Wurtman and colleagues' research - and the models of synaptic homeostasis discussed at length in Chapter 4 (Figures 4.2-4.4 from Zigmond 1992) - we can see the logic in assigning variations in amino acid availability a special and distinctive role improving "synaptic efficiency" - and thus a special and distinctive role in supporting the neural basis of behavioural maturation and plasticity during the prolonged postnatal phase.

Another important finding of their research is that whereas

individual variability in the density of synaptic contacts during the rapid phase of production in the macaque monkey is relatively small in all areas examined...in the phases of synaptic eliminations...the densities synaptic junctions begin to display considerable intra- and interindividual variability (Rakic et al., 1994:234-235).

By extension of the relationship between nutrition and NT synthesis, this suggests intra- and interindividual differences in amino acid availability might interact with these developmental differences to both reinforce **and co-produce** them. This would give natural selection another axis of phenotypic variability on which to act. In this sense, then, natural selection could be seen to be acting on the neurochemical consequences of diet as a way of operating on the proximal causes of whatever distal phenotypic manifestations might ensue as a result of these outcomes of intra- and interindividual differences in the phase of synaptic elimination.

11.6 Transgenerational Phenotypic Effects Of Nutrition

Heuther's (1988) research on the **transgenerational** phenotypic effects of developmental variations in NT amino acid availability at critical developmental stages provides us with some exciting *a priori* assumptions and generalizable conclusions I can use to invigorate the thrust and substance of my own analysis.

Heuther begins from the persuasively worded position that

one cannot deny the possibility that shifts in the nutritional supply in a given population will cause shifts in the amount and proportions of available essential substrates (e.g. Trp) made available to the descendants by their parents. It is possible that these shifts during early ontogenesis will influence and modify all those processes of metabolic and phenotypic maturation which are dependent on a well defined availability of a particular amino acid...(Heuther 1988:426).

This provides me with a clear statement I can use to explain one of the major components of my major theoretical position regarding the neurocognitive significance of hominid diet. Stated quite simply:

One cannot deny the possibility that culturally-templated shifts in the diet of our Plio-Pleistocene hominids may have caused shifts in the amounts or proportions of NT amino acids made available to our ancestors and thus possibly shifts in the development of all the cognitive functionalities subserved by the metabolic activities of the p.d.NTs that depend on a well defined availability of amino

acid precursors and biosynthetic cofactors. I will expand on this in the context of Heuther's specific findings.

Heuther (1988) exposed several generations of rats to 3.8 fold increases in prenatal tryptophan availability by way of the maternal diet. Then he measured the tryptophan (Trp), 5HT and 5HIAA content in the brains of each generation's offspring at 5, 10, 15, and 20 days postpartum.

In the first generation (offspring of normal rats placed on the Trp-enriched diet two weeks before mating) the concentration of Trp in the brain was significantly reduced until 20 days of age (i.e., during the whole suckling period), and so was the brain concentration of serotonin. In the offspring of the F2 generation a recovery from the depletion of Trp and serotonin in the brain was observed. In the third generation the serotonin concentration in the forebrain was no longer different from controls. However, in this generation, the initial brain weight and the postnatal growth of the body and brain was significantly decreased. The adult rats of the third generation were significantly smaller than the control rats bred on normal diets, and so was their daily food intake relative to body weight.

These results indicate that an altered nutritional supply of tryptophan during the development of an individual may induce a sequence of metabolic adaptations. **Such responses seem to last and to become continuously modified through several generations - until a new steady state is finally achieved. In the course of this adjustment, the expression of certain phenotypic parameters may be activated or suppressed** (Heuther 1988:426-427, added emphasis).

Heuther's research demonstrates that variations in NT amino acid availability interact with the phenotypic potentials inherent in the developing brain/genome to **co-produce** the behavioural and cognitive potentialities of successive generations. This too is our

central theoretical position, only ours is couched in operationally more precise terms that reflect the unique methodological constraints of this thesis (e.g., the principle of proper mass). That we are obliged to add "until a new steady state is achieved" is only fitting given our understanding of the anthropological principle and archaeological reality of "punctuated equilibrium" !

When we examine Heuther's (1988) research, we are essentially seeing a reductionist version of punctuated equilibrium rooted in dietary practices affecting brain NT synthesis and thus the "activation or suppression" of certain phenotypic parameters. I cannot help but wonder what the cumulative phenotypic outcomes would be. If we plotted the outcome of such changes over time how would they compare to the more traditional images of punctuated equilibrium associated with plotting brain size over time ? It is tempting to speculate that NT-specific aspects of hominid diet may have interacted with genetic mechanisms to co-produce the evolution of the cognitive capacities of our species both commensurate with and independent of changes in brain size over time. This recalls Holloway's original emphasis on the significance of "neural reorganization" (Chapter 5).

Fundamentally, I am interested in how aspects of hominid nutrition may have interacted with genetic mutational events to co-produce the process of neural reorganization so very obviously crucial to the process of cognitive evolution. However, because I

see this process in neurochemical terms (being associated with the activities of particular brain regions), I am inclined to assign nutritional variables proximal causal status. With these qualifications in hand, I wholeheartedly agree that

it is likely that the selection events in any animal's life depend more on the timing of maturational events, epigenesis within the CNS, and everyday events - that is, the 'nitty-gritty' life-death selection walks' - are matters of hierarchical organization, differentiation, and development (Holloway 1979 quoted in Holloway 1983:216).

In Chapter 12 we will encounter some "chains of inference" comprised of the summary details apprehended in Part 3 that will provide some specific examples of the kinds of phenotypic parameters that could conceivably have been "activated or suppressed" in our hominid ancestors (i.e., by virtue of the transgenerational effects of their foraging strategies of dietary biases).

11.7 Transgenerational Effects of Observational Learning

Neuroscientists and anthropologists are already in full agreement on many issues relating to human uniqueness; they just don't know it yet. Both neuroscientists and anthropologists agree that humans possess the capacity to "remake ourselves" in a kind of "self-making productionist" (Haraway 1988) "autocatalytic" dialectic. However, whereas anthropologists assert that this is

species-distinctive with reference to the use of technology, neuroscientists assert this is species-general with reference to selective stabilization and trophic theory. Allman's (1990) viewpoint helps us appreciate how fundamentally compatible these two approaches to the question of human uniqueness are.

Cortical organization is linked to behavior and has some capacity to change throughout the life of a mammal. The neocortex may participate in epigenetic evolution. **Changes in behavior that resulted in changes in cortical organization could be transmitted by observational learning from one generation to the next.** For example, a foraging technique might require a type of difficult discrimination which would result in use-dependent changes in cortical organization. **This behaviour and its attendant cortical manifestations could be propagated through the generations through observational learning** (Allman 1990:277-278, emphasis in the original).

At the same time, however, this calls into question some other important issues.

In the same manner that I questioned the "other behavioural" implications of Blumenberg's (1983) autocatalytic model in Chapter 1, we might also ask: what of the behaviours not strictly in the service of foraging ? Might Allman's insights have general applications beyond the heuristic limitations of "foraging behaviours" ? If there is one point I should make clear before I end this chapter it is that the neural reorganizational effects of observational learning apply with equal force to the full spectrum of behaviours. That is what is meant by the concept of neural epigenesis: it is use-dependent and activity contingent.

Our point, however, is this: if we accept the idea that developmental variations in amino acid availability may affect the structural, functional, cognitive, and "behavioral" development of individuals, we are obliged to accept the fact that this would have implications for the cognitive structure⁸¹ of the group. In other words, cultural differences in diet might eventually produce variations in the range and type of "behaviours" that accumulate culturally, and thus the range and type of indoctrinating influences that can be used to interorganismically coordinate the neural reorganizational patterns of succeeding generations through the medium of observational learning. This is another way in which I can conceivably construe the transgenerational phenotypic effects of diet. It is one step removed from the concept of development - but only insofar as it implies the agency of other actors. It is still firmly rooted in the principles of developmental neurobiology.

So too does our position respect the fact that

the modification and development of neurogenesis into adult structures within a social frame is obviously a complex process and will involve at least 3 factors: (1) the development of the nervous system proper; (2) the intraorganismic and interorganismic coordination of entrainment patterns and cognitive functions; and (3) the transmission of patterns of cognition, adaptively coordinated with the environment, to subsequent generations (Laughlin et al., 1990:67).

⁸¹ Or "cognitive style" (Paredes & Hepburn 1976).

The emphasis here is on the fact that developmental variations in NT amino acid availability may conspire to produce phenotypic and behavioural outcomes that accumulate not only over the life time various individuals (multiplied by Figure 11.1) but culturally as well. In other words, the structural and functional effects of developmental variations in NT amino acid (etc.) availability may ultimately conspire to produce original effects in the other two domains of influence (that a strict reliance on development will obscure the significance of). More to the point: the relationship between nutrition and CNS NT synthesis may have profound implications for our understanding of the evolution of the brain and the cognitive capacities of our species. This implies that the evolution of culture may have been constrained, or indeed potentiated, by nutritional and ecological factors interacting with varying degrees of CNS complexity.

12.0 BIOCULTURALISM REVISITED, THE NEUROGNOSTIC HELIX UNCOILED

I will begin this chapter by providing four "chains of inference" which effectively summarize all the details in Chapters 7-11. My *a priori* assumption that "the costs of brain **growth** and **maintenance** are essential to understanding the conditions under which [hominid] encephalization could occur" (Foley & Lee 1992:223) will influence the way in which I construct these arguments. So too will the application of my overriding methodological axiom: the principle of proper mass (Chapter 2).

While I will discuss each of the precursor-dependent neurotransmitters in the theoretical terms I was persuaded on empirical grounds to do, ultimately I will try to systematically eliminate all those relationships that fail to satisfy the strict application of the law of proper mass. At the end of this chapter I will endeavour to convey the general thrust of my thesis by constructing some original schematic models that reflect the overall theoretical impetus of this inquiry.

12.1 The Contribution of Serotonin

Figure 12.1 provides a summary depiction of all the empirical relationships discussed in Chapter 7 and 11. It is tempting to pursue the highest densities of 5HT content in the occipital

cortex, and make some argument about the significance of tryptophan, vitamin B6, niacin (etc.) to the evolution of hominid visual information processing capacity. However, because this capacity was already well developed in primates, and because the occipital cortex has **not** exhibited significant allometric increases in size in humans relative to chimpanzees (Figure 5.7) I will ignore this interpretive possibility (even though it might be residually significant in a developmental sense). The same holds true for the high 5HT content and activity patterns observed in the somatosensory (SSCtx) cortex (Figures 7.2-7.4). While the somatosensory cortex has exhibited some reorganizational changes in humans relative to motor and premotor cortex (Figure 5.7), this region is not significantly larger in humans than in the chimpanzee to warrant further consideration.

As to the anthropological significance of the remaining relationships, it will be recalled that the caudate/putamen, superior temporal gyrus, amygdala, and diencephalon (thalamus and hypothalamus) have all exhibited allometric increases in size in humans (Table 5.2). As such, I might very well impute a significant degree of adaptive value to foraging strategies that had the added advantage of enhancing 5HT synthesis though increased acquisition of dietary tryptophan, fat, thiamine, and vitamin B6 coupled with favourable protein:carbohydrate (LNAA) ratios as well as adequate niacin. It is interesting to note in this regard that virtually all of the nutrients that are implicated in 5HT synthesis

Figure 12.1 "Chain of inference" linking aspects of nutrition with brain chemistry, structure, function, and development (based on details in Chapter 7 and 11). See text for discussion.

are found in absolutely greater abundance in the very kinds of foods that our hominid ancestors devoted their lithic technologies to the selective pursuit of (e.g., meat, nuts, bone marrow. See section 6.3.2).

The most persuasive argument to make for the evolutionary significance of serotonergic mechanisms relates to the pre-existing theoretical framework. Holloway (e.g., 1983) suggested that the evolution of sociality was a critical selective force in human evolution. Eccles (1989) agreed, and interpreted the mosaic changes in the amygdala (Table 5.2) accordingly. In an analogous manner I would also emphasize the importance of sociality in human evolution.

As mentioned in Chapter 7, reduced tryptophan is associated with heightened contact aggression and reduced social grooming. Significantly, it is also associated with the outcomes of various competitions for social supremacy in primate dominance hierarchies. Recall:

when a dominant male is removed from his troop the remaining subordinate males compete to become dominant. The initial phase of this competition involves the formation of alliances with females and is sensitive to tryptophan and other serotonergic agonists...**Treatment of one of the remaining subordinate males with tryptophan is uniformly associated with that animal becoming dominant. Conversely, reduction of serotonergic function is uniformly associated with the treated subject remaining subordinate** (Raleigh et al., 1988:300).

It is of no small significance that these effects would have reproductive consequences and hence transgenerational implications for the kinds of attributes that would seep into the genetic information pool.

Figure 12.2 depicts seasonal variations in the protein, sugar [read also carbohydrate] and fat composition of a typical primates' diets over the span of a year. The serotonergic implications of such nutritional patterns seem obvious at first glance. We know tryptophan is an amino acid that comes from protein. And we know reduced fat - like reduced tryptophan - causes heightened contact aggression and reduced social grooming. We also know food scarcity prompts social fission. It seems reasonable, therefore, to conclude that such reoccurring nutritional stresses might provoke seasonal patterns of social fission and fusion through their behavioural effects traditionally associated with serotonergic mechanisms.

Minimally, I could argue that heightened contact aggression and reduced sociality would be adaptive in times of food scarcity. The added benefit of this is that groups would re-combine in times of plenty, bringing with them potentially new and adaptive genetic characteristics of value to the diversity and fitness of the gene pool. In this sense, then, I would argue that serotonergic mechanisms - by triggering patterns of fission and fusion appropriate to the nutritional carrying capacity of the environment

Figure 12.2 Seasonal variations in the protein, sugar, and fat composition of the purple-faced (solid line) and gray (dashed line) langurs' diets (redrawn from Richard 1985:157). See text for discussion.

· would indirectly serve to promote gene flow. I can expand on this speculative proposition.

Looking back at Figure 12.1 we see that 5HT reaches its adult levels in cortex in most regions by about 2 months of age. This implies that the activities of 5HT are crucial to the first foundational stages of postnatal development. This means inadequate immediate postnatal supplies of tryptophan could have serious structural and functional consequences for all the reasons discussed in the context of Figure 11.1. This places great importance on the tryptophan content of the mother's milk/diet. [Parenthetically, the tryptophan content of mother's milk is well balanced relative to the other amino acids (Table 9.1b)]. It would only be adaptive, then, for 5HT to be sensitive to the presence of the very properties in the environment that it absolutely required in adult-like quantities soon after birth. Theoretically, this would place an adaptive premium on any foraging strategy (technological, social, or otherwise) that had the added benefit of enhancing tryptophan acquisition at *precisely the same time* that the developing infant was making tryptophan-related demands on the mother's milk.

By facilitating social cohesion and creating the conditions for mating, 5HT would be in the unique position to determine the kinds of nutritional influences the foetus was exposed to as a result of the downstream effects of seasonality on the mother's

diet. This could have profound functional consequences depending on how well the short-lived temporal profiles of "optimal nutrient availability" (Chapter 6, section 6.3.1) interacted with the tight sequential timing of pre- and postnatal developmental events. In this sense we are tempted to argue that the open-loop status of 5HT might be a genetically programmed "initiator sequence" of the social conditions for reproduction that would result in optimal foetal brain development. In this way 5HT would provide a exquisitely sensitive interface between biological and cultural mechanisms of adaptation. It would serve, in effect, to create a "degree of best fit" between the optimal downstream effects of seasonality (Figure 12.2) and the temporally discrete phases of neurochemical preparedness in the developing foetus' CNS (Figures 11.3-11.6).

Perhaps, then, we can interpret the unique "open-loop status" of 5HT in broad ecological terms. Perhaps 5HT is a physiological sensor of the very properties in the environment that are optimally well suited to reproduction and pre- and postnatal brain development ? We might conclude as much given our understanding of how tryptophan and related 5HT activities interact with social and reproductive parameters.

...

12.2 The Contribution of Acetylcholine

Our argument for the evolutionary significance of dietary factors affecting ACh synthesis in regions of the brain known to have undergone significant allometric increases in size in members of the genus *Homo* is far less provocative, but no less important.

Figure 12.3 summarizes the aspects of structural, functional, chemical, and developmental neuroanatomy discussed in Chapters 8 and 11. Significantly, **all** of the regions specified as exhibiting moderate to high densities of ACh content and activity markers also exhibited significant allometric increases in size in members of the genus *Homo*.

Although I cannot quantify my reasons for including the thalamic ACh component in this methodologically self-conscious summary, I would simply remind the reader that ACh acts in concert with NE to promote the best abilities of the thalamus to act as "an intermediary between the external world and the neocortex" (McCormick et al., 1989:216-217. Persuaded, as I am, by an interest in the "three Worlds of experience" (recall tangential reference to Popper's model cited on page 117 of this thesis), I cannot resist such terms of reference - especially when they help us understand not only the functional but **ecological** implications of such phylogenetic changes. This is, after all, what I am interested in: the ecological and nutritional implications of brain evolution.

Figure 12.3 "Chain of inference" linking aspects of nutrition with brain chemistry, structure, function, and development (based on details in Chapters 8 and 11). Arrowhead refers to development. See text for discussion.

Similarly, while the hippocampus may have exhibited less remarkable increases in size in members of the genus *Homo* (Table 5.2), I am inclined, by sheer volume of research on the functional significance of hippocampal ACh, to include it. The commonly ascribed role of ACh in learning and memory justifies my interest in this limbic structure.

Coupling an understanding of ACh in both hippocampus and cortex with the significance of both these mechanisms in memory, I would suggest the following: if it can be seen that natural selection placed an adaptive premium on learning and memory skills, it likewise too would have to have been 'obliged' to favour all those foraging strategies that enhanced choline (etc.) availability. Interestingly, all the foods that contain high lecithin/choline levels (e.g., meat, liver, eggs) are, once again, the very kinds of foods that our hominid ancestors would have required technologies more sophisticated than those used by the great apes to access the nutritional benefits of.

Referring once again to Figure 12.3 we see that we have also been persuaded by Mesulam's (1986) observations to focus on ACh in the amygdala. The reader will recall this phylogenetically expanded limbic region exhibits **the** highest ACh content and activity patterns of all the 33 regions examined. I have already reviewed Mesulam's interpretations regarding the functional significance of cholinergic architecture. The suggestion that "cholinergic synapses

are in a position to regulate the access of sensory information into the limbic system" (p. 216 above) is quite provocative - especially when assessed against an anthropologist's knowledge of Rozin's (1976) theory on the evolution of human consciousness.

Rozin (1976) reminds us very simply that

intelligence [is] a phenotype subject to the same biological principles and evolutionary forces as any other phenotype. As is the case with virtually all complex biological systems, intelligence should be organized in a hierarchical manner, out of component "subprograms." Within an evolutionary framework, these subprograms, which we call adaptive specializations, usually originate as specific solutions to specific problems in survival, such as prey detection. These specializations, functionally defined, may be simple programs or circuits⁷⁶, or clusters of these⁷⁷, and may contain both plastic and prewired elements. They form the building blocks for higher level intelligence.

At the time of their origin, these specializations are tightly wired into the functional system they were designed to serve and are thus inaccessible to other programs or systems in the brain. I suggest that in the course of evolution these programs become more accessible to other systems and, in the extreme, may rise to the level of consciousness and be applied over the full realm of behaviour or mental function. Accessibility can be gained by establishment of a physical connection of one system to another⁷⁸ or any duplication of one system's circuitry in another part of the brain by use of the appropriate genetic blueprint. I maintain that the notion of accessibility, or levels of accessibility is useful in understanding the development and dissolution of intelligence, as well as its evolution (Rozin 1976:245-246; italics in the original).

⁷⁶ Analogous with Laughlin et al's (1990) "community of cells".

⁷⁷ Analogous with Laughlin et al's (1990) "neurognostic models".

⁷⁸ Laughlin et al.s (1990) concept of "penetration" defined in Chapter 4.

I also agree that cognitive functions (and their NT and related nutrient concomitants) are phenotypes that can be selected for in a Darwinian sense. While this summary observation is more relevant in terms of my interests in the *developmental* effects of nutrition (i.e., vis à vis hierarchy), it also seems relevant here - in this discussion on ACh in the amygdala - precisely because ACh controls certain "levels of accessibility" of sensory and associative information access up to the level of the limbic system. This is perhaps significant given the inevitabilities of subsequent information transfer to (e.g.) executive prefrontal regions.

At the very least, Mesulam's interpretations of the actions of ACh in the amygdala provide us with a clear example of how some pharmacosystems might come to exert disproportionately greater controls on various "levels of accessibility" within the CNS, and in so doing exert a decided influence on the evolution of human consciousness - of which sensory-limbic components are an important part." So, too, am I inclined to point out that there are some obvious parallels between (1) the ability of cortical ACh to regulate the access of modality-specific sensory information into the amygdala (Mesulam et al., 1986); (2) the ability of the amygdala to mediate cross-modal information processing (Murray & Mishkin 1985); and (3) the ability of cross-modal information

¹⁹ Recall, for instance, the chosen emphases of the so-called "machievellian intelligentsia" discussed in Chapter 5. In that interpretive framework, social-affective states loomed large and were assigned causal significant status.

processing capacity to subserve the evolution of human consciousness (Rozin 1976).

By far, however, the most persuasive case I can make for the evolutionary significance of all those nutrients related to ACh synthesis is based on the observation that the ACh content of association cortex layer III pyramidal cells develop very slowly over a number of years corresponding to the attainment of young adulthood in humans (Chapter 11, section 11.4). We dovetail this with Mesulam's (1986) observation regarding the striking inter-individual differences (Figure 8.3) in cortical ACh content - with implications for cognitive functioning. It also seems reasonable to recall the very important observation that the kinds of quantities of choline Wurtman and colleagues were experimenting with were within the physiological range that "an omnivorous animal or human" might consume from day-to-day. All of this evidence makes me wonder if natural selection might also have in some sense been operating on the abilities of our ancestors to acquire those nutrients that would sustain the requirements of their prolonged phases of structural and functional maturation. It is interesting to recall the fact that this late maturing feature of ACh in the cortex is unique to humans.

The kinds of developmental profiles observed by Kostovic (1990) are obviously significant from an ecological perspective. They provide, in essence, various kinds of genetic "problems" of

CNS development (other examples of which we saw in Goldman-Rakic & Brown's 1982 research summarized in Figures 11.3-11.6) that must be solved within an ecological framework. This places great emphasis on various aspects of diet, and not just sheer caloric energy as in most standard anthropological applications of optimal foraging theory to problems of brain evolution (e.g., Foley & Lee 1992 and Leonard & Robertson 1992 as discussed in Chapter 5).

The merits of the argument for the evolutionary significance of ACh-related aspects of hominid diet are further reinforced in the context of the observation that the CH4 ACh synthesizing cell body exhibited unique allometric increases in size in members of the genus *Homo*. Theoretically, CH4 would not have evolved in the absence of a dietary strategy appropriate to satisfying the heightened demands this ACh synthesizing cell body would invariably (as a result of its expanded temporal and spatial domains of influence achieved through the increases seen in the neocortex and amygdala) make on the choline (etc.) content of our ancestors' diet. This is another way of saying brain and diet co-evolve. This is something the proponents of the so-called foraging strategy hypothesis of brain evolution have also demonstrated on the basis of other data sets (see Part 2).

...

12.3 The Contribution of Norepinephrine

Precisely because NE is a closed-loop system, the only way in which I can construct a plausible argument for the ongoing functional significance of dietary variables affecting brain NE synthesis is to invoke the powers of the stress/NE paradigm introduced in Chapter 9. And yet because I am obliged to make so many qualifications of my my position, the effort becomes progressively suspect.

Young (1986) observed that the relationship between stress and NE "raises important questions about whether tyrosine supplementation might prove beneficial to human subjects exposed to severe uncontrollable stressors" (Spring 1986:37). I responded to this with the suggestion that this research also raise the important question as to whether or not tyrosine "supplementation" in the form of technologically facilitated consumption of high protein/amino acid sources such as meat might have proven especially beneficial to our hominid ancestors who were no doubt experiencing "severe uncontrollable stressors" to an extent not readily generalizable to the contemporary human condition. And yet clearly we must be chastened by the fact that it often takes pure doses of tyrosine to effect any significant changes in NE synthesis. These are not readily generalizable conditions. As to whether or not enhanced protein acquisition enabled our ancestors to (in essence) "neuroprotect" themselves from the deleterious

noradrenergic effects of their perhaps uniquely stressful lives is possible, but vaguely suspect in the degree of operational specificity it requires.

While I might be tempted to pursue the implications of the observation that one of the behavioural concomitants of stress-related NE reductions is an impaired motivation to exhibit all the signs of "curiosity" and the desire to explore the environment (behaviours of decided adaptive significance in any setting), I will forego such arguments. They are unnecessarily tenuous - especially when confronted with other more persuasive possibilities rooted firmly in the requirements of the principle of proper mass (Jerison 1973).

Figure 12.4 depicts various structural, functional and neurochemical relationships of interpretive significance. With the partial exception of the somatosensory cortex (SSCTx) which exhibits the highest content of NE in cortex (Figure 9.3), all of the other regions have undergone significant allometric increases in size. In view of the high content of NE in these regions, it seems reasonable to impute a degree of adaptive significance to any hominid foraging strategy that had the added benefit of enhancing NE precursor acquisition (thus sustaining the ongoing functional integrities of these regions). This much I can suggest on the basis of not only the law of proper mass (Chapter 2), but basic

Figure 12.1 "Chain of inference" linking aspects of nutrition with brain chemistry, structure, function, and development (based on information contained in Chapters 9 and 11). HMP = hexomonophosphate. See text for discussion.

homeostatic principles (Figures 4.3.-4.5) and the application of optimal foraging theory (Chapter 3).

Ultimately, however, it appears best to return to the time-honoured relationship between ontogeny and phylogeny, and the more persuasive interpretive possibilities that devolved from an understanding of the effects of dietary variations on neural development. This is because pre- and postnatal aspects of nutrition affect the attainment of the structural and functional hierarchies (i.e.) Rozins' (1976) extended quote [cited above] deals specifically and eloquently with. WE might also recall Little's (1995) diagram (Figure 11.1A) and the added understanding that is gained from the images in Figure 11.1B.

Returning to Figure 12.4, it can be seen that cortical NE increases steadily from birth through 24-36 months (Goldman-Rakic & Brown 1982). And, moreover, NE in PFC exhibits its greatest increase between approximately 1.5 and 3 years in the PFC. This corresponds in the human to a much more protracted period (Appendix 1). This speaks clearly as to the functional significance of dietary variations affecting NE synthesis in the cortex and PFC (e.g., for all the reasons implied by Rozin's quote above). Theoretically, an optimal supply of required nutrients (Table 11.1) would enable the prolonged development in the cortex and PFC to proceed as genetically planned and according to the tight sequential timing of all the other interdependent neurochemico-

developmental events suggested in Figures 11.3-11.6. If, however, inadequate amino acid (etc.) supplies were (for whatever seasonal, technological, or sumptuary reasons) encountered at these critical periods, we would expect to see subtle reorganizational changes **that there would be no turning back upon - no reversing in later life.** This recalls the summary observation that

the conclusion that the consequences of early nutritional deprivation, for example, can be reversed in later life is wrong. There is no way to reverse any processes during brain development, once it became manifested in terms of structural changes. It is the change of structure that, on the one hand, represents an irreversible final stage of a developmental process and that, on the other hand, becomes the starting point - the basis of all future developmental events (Heuther 1988:422).

It is in this sense, then, that I can very easily create some reasonable arguments for the long-range adaptive significance of pre- and postnatal NT amino acid (etc.) supplies. If we want to conceive of this symbolically we can do so (once again) with reference to Figure 11.1.

12.4 The Contribution of Dopamine

Turning now to Figure 12.5, it can be seen that the DA content and activity profiles are quite high in the cortical and subcortical regions subserving motor functions (i.e., caudate/putamen and motor/premotor cortex). With the exception of the motor and premotor cortices, all of the regions included in

Figure 12.4 have exhibited significant allometric increases in size (Table 5.2).

My interest in DA stems first and foremost from a knowledge of its unique functional (Brosowski et al. 1979), structural (Bannon et al., 1981), electrophysiological (Bunney & Chiodo 1984), and precursor-dependent (Deutch & Roth 1990) status in the PFC. The PFC is the region of the human brain that has exhibited **the** most significant increases in size. It seems rather curious that natural selection would have favoured rendering the PFC, and its attendant role in the evolution of human consciousness and culture so "unusually dependent on precursor availability" (Deutch & Roth 1991:375). And this pertains to the maintenance of its *ongoing* functions!

In a developmental sense we can also appreciate the nutritional pressures our hominid ancestors must have been under. Witness the prolonged rate of DOPA accumulation (a non-specific marker of CA activity) in the PFC over the protracted three year period. Once again, this corresponds to a much lengthier period in humans. Not surprisingly, this implicates the CAs in significant aspects of cognitive maturation. We might also question the significance of the profile seen in the posterior parietal area given that this region mediates language (a very significant feature of human evolution). All of these examples provide further "proof" that the ancestral hominid diet that maximized genetic

Figure 12.5 "Chain of inference" linking aspects of nutrition with brain chemistry, structure, function, and development (based on information contained in Chapters 10 and 11). See text for discussion.

fitness may **not** have been the one that maximized sheer caloric intake at the expense of the NT precursors (especially at crucial developmental stages in the PFC).

12.5 Genetic Problems and Ecological Solutions

The benefits of optimal foraging theory and bioculturalism to the construction of this thesis are that they ask us to identify the most fundamental problems between the biological and cultural interfaces. Then they compel us to examine the best ecological solutions to those problems. Table 12.1 provides a sampling of some of the "genetic problems" our ancestors had to face. In the right column I provide some suggestions as to the optimal ecological solutions we might reasonably use to predict, at the very least, that the requirements of various hominid foraging strategies - beyond the strict necessities of obtaining ample caloric energy supplies. Now let us compare this to Foley's (1987) ecological approach to the nutritional implications of seasonality.

In Figure 12.6A we see that our hominid ancestors basically had two choices in times of scarcity: (1) expand the diet to include low-quality but plentiful resources, or (2) withdraw to those resources providing the highest returns. It is interesting that in model B we confront the distinct possibility that (as mentioned in Chapter 3) the robust and gracile hominids were very

Table 12.1 Biological Problems and Cultural Solutions

Genetic "Problem"	Optimal "Solution"
unusually high DA precursor requirements of prefrontal cortex	optimal dietary supplies of tyrosine, phenylalanine, iron, copper, thiamine, Vitamins C and B1
prolonged postnatal development of ACh layer III pyramidal cells in association cortex	sustained optimal intake of choline, pantothenic acid, thiamine, methionine, folic acid, Vitamin B12
prolonged development of cortical CA activity patterns	optimal dietary supplies of tyrosine, phenylalanine, iron, copper, thiamine, Vitamins C and B1
selection for increased memory capacity	e.g., adequate dietary supplies of choline (etc.) necessary to maintain the activities of ACh in hippocampus and neocortex
reproduction through social dominance	increased dietary typtophan, and fat
selection for increased positive sociality (e.g., through serotonergic mechanisms)	increased dietary typtophan, fat, thiamine, and vitamin B6 coupled with favourable protein:carbohydrate (LNAA) ratios, and adequate niacin
expansion of the neocortex	increased machinery for CA biosynthesis, especially in association cortex
evolution of the hominid brain (i.e., all the structures listed in Table 5.2)	optimal supplies of all the nutrients listed in Table 11.1 (with additional cross-reference to Figures 12.1-12.4)

likely consuming different diets with, as I would argue here, different "neurochemical potentials". This model implies that low-quality diets would not support the dramatic rates of cranial expansion observed in members of the gracile lineage. This was later demonstrated by Foley & Lee (1992) who modelled the limitations high versus low quality diets place on the attainment of higher EQs in various dietarily diverged primate species (Figure 5.8).

As I can perhaps conjecture, the hominid group that diverged to the low quality foods in times of scarcity may ultimately have been at a long-term (Figure 11.1) adaptive disadvantage vis à vis an inability to provide sustained solutions to the various genetic problems summarized in Table 12.1. These differences might, for instance, be especially pertinent to the unusual precursor demands of the PFC **and** the prolonged structural maturation of layer III pyramidal cells. Interestingly, **all of the optimal solutions offered in Table 12.1 would best be achieved by adopting the gracile hominid strategy depicted in Figure 12.6B.** As the reader may recall, most of the nutrients implicated in brain NT synthesis are found in greater abundance in **animal**, not plant foods. Perhaps this in some small way further explains (all things except technology being equal) the eventual supremacy of the gracile lineage over the once (and for along time) sympatric robust australopithecines.

Figure 12.6 These models of (A) competition in a temporarily variable (i.e., seasonal, environment and (B) alternative early hominid responses to seasonal stress (redrawn from Foley 1987:193 and 212 respectively) call into question the neurochemical and related neurocognitive ramifications of seasonal and phylogenetic variations in diet. We would predict that those individuals/groups and species who withdrew to the highest amino acid-return resources in times of seasonal nutritional stress would be at a neurochemical and ultimately long-term neurocognitive advantage. See text for further discussion.

At very least we can envision such dietary differences creating distinctly different developmental outcomes. This we can suggest with reference to Zigmond's (1994) valuable insights that some pioneering neurons in development might be able - given enhanced amino acid precursor availabilities - to exert a disproportionately greater influence on the structural and functional development of the brain (i.e., through its effects on synaptic architecture as depicted in Figure 4.4A) than would be predicted on the basis of the density of innervation patterns. In an analogous manner, I would also argue that seasonally and especially technologically shifting aspects of hominid diet may have, at one point in time, provided a necessary impetus to the development of new functional hierarchies in the brain!

Perhaps, then, diet really was the defining criteria of human brain evolution - i.e., insofar as it can be seen to have provided the "neurochemical potential" to activate and selectively maintain newly inherent "cognitive potentials" perhaps at one point in time only latent in the genetic information pool!

12.6 Bioculturalism Revisited, The Neurognostic Helix Uncoiled

My larger theoretical position, which does not deny the controlling influence of genetics (recall, we assign nutrition a necessary but not sufficient role in human brain evolution), can

best be summarized with reference to two models. Figure 12.7 depicts the fundamental interaction between (1) the metabolic demands associated with the development of the structural and functional potentialities inherent in the brain/genome at particular ontogenetic and phylogenetic stages with (2) the nutritive and related neurochemical potentialities inherent in the diet at different points within and across time. This is exactly the relationship I posit as being significant. No more and no less.

I hypothesize that pre- and postnatal variations in the amino acid (etc.) availability of our hominid ancestors' diet may have interacted with the metabolic demands associated with particular ontogenetic and phylogenetic stages of CNS complexity to "co-produce" the development and evolution of the brain and the cognitive capacities of our species. My thinking has been profoundly influenced by the interpretive rigors of biogenetic structuralism (Laughlin et al., 1990, as discussed in Chapter 4). This explains the use of the term "neurognosis" in the title of this thesis. It is a conceptually-loaded term used by the biogenetic structuralists to explain the structural, functional, developmental, experiential, and cross-cultural complexities of the basis of mind. The title of this thesis is meant to suggest the relevance of this term. In addition, the use of the term 'neurgnosis' also reflects my modest attempt to pay homage to the significant influence Charles Laughlin has had on the development of this thesis.

Figure 12.7 Mind as a product of the interaction of (A) the metabolic demands associated with the structural and functional development of the cognitive potentials inherent in the brain/genome (both within and across time) with (B) the nutritive and related neurochemical potentials inherent in the culturally-templated diet both within and across time (e.g., environmentally given, seasonally variable, phylogenetically-typical, culturally-templated, socially-shared, technologically-determined, and evolutionally-shifting aspects of diet). In this model the yin/yang symbol is meant to convey the indivisibility of brain structure and function. The exaggerated size differences in all icons are meant to convey the precarious nature of brain/nutrient interactions both within and across time (e.g., at particular ontogenetic as well as phylogenetic junctures). Once again, it is our contention that pre- and post-natal variations in the amino acid (etc.) content of our ancestors' diet interacted with the neurometabolic demands associated with particular ontogenetic and phylogenetic stages to 'co-produce' the evolution of the cognitive capacities of our species. See text for further discussion.

Figure 12.8 provides a biocultural perspective on brain evolution. It models the heuristic specifics of this inquiry. The relationship between nutrition and brain NT synthesis (i.e., in functionally specified regions of the brain known to have exhibited significant allometric increases in size in members of the genus *Homo*) is posited as providing **the** most fundamental interface between biological and cultural mechanisms of adaptation. Variations on Kostovic (1990) phases of cortical histogenesis (Table 11.1) are superimposed on various segments of the winding helix. The use of the yin/yang symbol is meant to convey the relationship between aspects of brain structure, function **and** chemistry. These provide the shifting contents of the "genetic information pool" (Katz 1987). The various nutrients in the shaded circles can be construed as "complimentary base pairs" insofar as they are absolute requirements for the development and ongoing maintenance of the cortical and subcortical regions depicted. These nutrients provide the shifting contents of the "cultural information pool" (ibid). It is important to remind ourselves that

all human groups, through the medium of culture, are actual or potential occupants of the same dietary niche, each group may distance itself from potential dietary rivals through cultural conventions (Milton 1992:253).

While it is true, these systems might be in "dynamic equilibrium" (Katz 1987) over time, natural selection is predetermined to select the optimal phenotype that these transgenerational cycles produce. It goes without saying that the

Figure 12.8 Bioculturalism Revisited, The Neurognostic Helix Uncoiled. A: "cultural information pool" (Katz 1987) operationalized in terms of nutrients required for brain DA, 5HT, NE, and ACh synthesis. B: "genetic information pool" (ibid) operationalized in terms of the structural, functional, and associated neurochemical properties of the brain. The neurochemical potentials in diet interact with the structural and functional potentialities inherent in the brain/genome to "co-produce" human neurocognitive evolution. While the informatic content of these genetic and cultural information pools may ultimately be in 'dynamic equilibrium' (Katz 1987), they are periodically punctuated by informational changes. Natural selection acts upon the phenotypic outcomes of the interactions between these periodic changes in nutritional and genetic parameters. Selection for the 'optimal phenotype' implies selection for the optimal foraging strategy capable of satisfying the metabolic demands associated with the activities of the p.d.NTs in various regions of the brain during critical stages of ontogeny and phylogeny. PFC = prefrontal cortex; NCtx = neocortex; C/P = caudate/putamen; STG = superior temporal gyrus; HIPP = hippocampus; Phe = phenylalanine; Tyr = tyrosine; Trp = tryptophan; Fe = iron; Cu = copper; LNAAs = large neutral amino acids. See text for further discussion.

nature of the optimal phenotype will depend on the nature of the environment. Fortunately, I have partial recourse by way of the archaeological and comparative neurological record (i.e., by way of extrapolation).

Clearly, the greatest adaptive premium was placed on the evolution of the PFC and its attendant cognitive functionalities. So too would I argue that the greatest adaptive premium must have been placed on the hominid foraging strategy that was optimally suited to satisfying the electrophysiologically unique demands that the PFC places on the DA precursor content of diet. In this sense, then, I would argue that our ancestors may truly have been "hostages to eating" (recall Chapter 7).

My central point is this [recalling Heuther (1988) quoted in Chapter 11]: one cannot deny the possibility that culturally-templated shifts in the diet of our Plio-Pleistocene hominids may have caused shifts in the amounts or proportions of NT amino acids made available to our ancestors and thus possibly shifts in the development of all the cognitive functionalities subserved by the metabolic activities of the p.d.NTs that depend on a well defined availability of amino acid precursors and biosynthetic cofactors. This is our central theoretical position. What the images in Figure 12.8 attempt to convey is that variations in the NT amino acid content of our hominid ancestors' diet may have interacted with the

cognitive potentialities inherent in the brain/genome to **co-produce** the behavioural and cognitive potentialities of our species.

At a future date it will be most rewarding to dovetail these kinds of analyses with the concept of hemispheric specialization (mentioned briefly in Chapter 5, Figures 5.3-5.4). Conceivably, culturally-, seasonally-, and technologically-templated variations in Plio-Pleistocene hominid diet, at critical developmental stages, may have co-produced the evolution of hemispheric asymmetry in profoundly significant ways in which we can (as yet) only partially apprehend through the application of trophic theory.

Acknowledgements

The development of this thesis would not have been possible without the advice, support, and encouragement of Charles Laughlin Jr.. So too was the wise and kindly influence of Brian Given crucial to the realization of this project. Special thanks also to the following individuals for their many gestures of kindness and support: Bruce Cox, Denis Olsen, Terry Nosanchuk, Kim Mitchell, Nazira Conroy, Norris Durham, David Niehaus, Mike Anderson, Josef Dlouhy, Mark Tyrell, Jared Keil, Ken McGillvray, Jane Jordan-White and G.Russell White.

Appendix 1

A model of the progressive prolongation of life phases and gestation in selected primates *

* Source: Lovejoy (1981) cited in Eccles (1989:109, Figure 5). Note the proportionality of the four indicated phases.

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PRECISIONSM RESOLUTION TARGETS

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