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**LANGUAGE DYSFUNCTION IN NEGATIVE AND MIXED
SYMPTOMATIC SCHIZOPHRENIC SUBGROUPS
AS EVIDENCED BY THE N400 EVENT-RELATED POTENTIAL:
A COMPARISON WITH NORMAL CONTROLS**

by

Duncan R. de Lugt

**Thesis submitted to
the Faculty of Graduate Studies and Research
in partial fulfilment of
the requirements for the degree of**

Master of Science

Department of Psychology

Carleton University

Ottawa, Ontario

August 1992

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of Canada

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"LANGUAGE DYSFUNCTION IN NEGATIVE AND MIXED SYMPTOMATIC
SCHIZOPHRENIC SUBGROUPS AS EVIDENCED BY THE N400 EVENT-RELATED
POTENTIAL: A COMPARISON WITH NORMAL CONTROLS

submitted by Duncan R. de Lugt, B.A.Hons.
in partial fulfilment of the requirements for
the degree of Master of Science

Thesis Supervisor

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September 10, 1992

ABSTRACT

As negative symptoms in schizophrenia have been associated with both language and frontal lobe disturbances, the semantically-sensitive N400 event-related potential (ERP) was examined as a putative correlate of these pathologies in medicated schizophrenic patients. The N400 component was investigated in thirty medicated schizophrenic patients; 15 suffering from predominantly negative symptoms (NS), and 15 suffering from a mix of both positive and negative symptoms (MS). The results from these two groups were compared to 15 normal controls (NC), who were matched for age and sex. In the N400 lexical decision paradigm, subjects were asked to indicate whether pairs of words were semantically related or unrelated to each other. Recording sites included the midline positions Fz, Cz and Pz. Amplitude and latencies were examined for artifact, error free ERP components elicited by the second word in each word pair. Although visual inspection of waveshape morphology suggested more varied and less stable ERPs of schizophrenic patients compared to normal controls, for all three groups the unrelated word pair condition elicited the negative N400 component which was also visible, however reduced, in the related word pair condition. Despite non-significant group differences in the amplitude of the N400 at any of the recording sites, the N400 latencies were significantly more prolonged in both of the patient groups as compared to the normal controls. NS and MS groups did not differ with respect to latency measures. These results are discussed in relation to previous findings and directions for additional research are suggested.

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1. INTRODUCTION

Research into the pathophysiological indices associated with schizophrenia has produced a plethora of data that has increased our understanding of the type, location and behavioral correlates of brain abnormalities. While postmortem studies and neuroimaging strategies such as BEAM, CT, PET, MRI and cBFA have documented a variety of brain irregularities including; cerebral atrophy (Doran et al., 1988; Shelton et al., 1988), ventricular enlargement (Weinberger, Torrey, Neophytides & Wyatt, 1979), and cerebral, metabolic and electrical disturbances (Berman, Zec & Weinberger, 1986; Geraud, Arne-Bes, Guell & Bes, 1987; Geunther, Breitling, Banquet, Marcie & Rondot, 1986); scalp recorded averaged evoked electrical potentials still remain one of the most direct, non-invasive methods for monitoring the timing (much faster than PET and MRI imaging techniques - McCarley, Faux, Shenton, Nestor & Adams, 1991), of discrete neuronal events associated with variations in brain functioning.

1.1 Event-Related Potentials (ERP's)

Event-related potentials (ERP's) are time locked changes of the brain's electrical activity that are associated with a physical or psychological event (Picton, Hink, Perez-Abalo, Linden & Wiens, 1984; Picton & Hink, 1974). ERP's can be thought of as "early" (0 to 50 msec post-stimulus), "middle" (50 to 250 msec post-stimulus), or "late" (more than 250 msec post-stimulus), all of which provide information on the nature and timing of neuronal events. Early and middle ERP's are described as "sensory" or "exogenous" potentials, and can be evoked by discrete physical stimuli, either auditory, visual or somatosensory; while late or slow potentials are described as "cognitive" or "endogenous" potentials, and are elicited by discrete sensory or task-related events requiring mental activity, and are relatively independent of the physical characteristics of the stimulus. ERP's are analyzed by measuring the amplitude, latency and consistency or variability of the positive and negative deflections of the post-stimulus evoked waveform.

The amplitude and latency of early ERP's are relatively non-susceptible to changes in mental state, but are more dependant on stimulus characteristics such as modality,

intensity and rate (Amadeo & Shagass, 1973; Hankoff & Peress, 1981; Shagass, Straumanis, Roemer & Amadeo, 1977). The initial nanovolt, short-latency positive peaks occurring within 10 milliseconds after acoustic stimulus onset implicate origins in the peripheral and brain stem portions of the auditory system and as such are labelled as brain stem auditory evoked potentials or BSAEP's (Jewitt & Williston, 1971).

Middle latency ERP's or cortical potentials as they are sometimes called, are elicited by auditory, visual or somatosensory stimuli, and are made up of a series of positive and negative deflections commonly labelled as P100, N100, P200, and N200. The letters used in the naming of the deflections refer to the polarity of the peak, and the numbers refer to the approximate post-stimulus latency where the peak is typically found (ie: P100 refers to a positive peak with a post-stimulus latency of approximately 100 msec). The amplitude of the N100 and P200 components is considered to be affected by the amount of attention that is paid to the stimulus, with increased attention resulting in an increase in the amplitude of the potential (Picton, Hillyard, Kraus & Galambos, 1974). Results from studies conducted specifically to assess the relationship between the N100 amplitude and

attention have determined that either increased attention to target auditory stimuli, or increased intensity of the stimuli, consistently resulted in augmentation of the N100 peak (Schwent & Hillyard, 1975; Schwent, Hillyard & Galambos, 1976a, 1976b).

Late or cognitive ERP's are thought to reflect cognitive or information-processing operations, and include the late positive component (LPC), the contingent negative variation (CNV), the post imperative negative variation (PINV) and the N400. The LPC is a generic term referring to any positive shifting components occurring later than 250 msec post-stimulus, but typically refers to the P300 ERP. The P300 is a late positive deflection that occurs between 250 and 500 msec after a rare, task relevant stimulus has occurred. This late positive wave is widely distributed across the scalp, and is maximally recorded from the parieto-central regions (Picton & Hink, 1974). The CNV is a relatively long lasting and steady negative deflection that occurs after a warning stimulus and before an imperative stimulus. CNV findings have been accounted for by two different psychological functions: the "attention" hypothesis which states that the magnitude of the CNV has a positive linear relationship to attention (Teece, 1972); and the "arousal" hypothesis which suggests that the

magnitude of the CNV displays a non-linear (inverted "U") relationship to the level of arousal (Teece, 1972). The distribution of this negative potential appears to differ, depending on the task involved (Jarvileto & Fruhstofer, 1970) and therefore, it is possible that the negativity is representative of some sort of sustained activation of the cortical areas concerned with the task. The PINV is believed to be a measure of the time that it takes a waveform to return to the basal level following the imperative stimulus (Picton et al., 1984). Finally, the N400 is a measure of semantic incongruence that occurs when an individual is presented with either word pairs or with sentence completion whereby the second or last word is either unrelated, or a nonsense word, based on the previous word(s) presented (Kutas & Van Petten, 1988). When this incongruous presentation occurs, a negative ERP shift occurring at about 400 msec post-stimulus is enhanced. The N400 is believed to represent an individuals cognitive processing of semantic anomalies in both the visual and auditory modalities, with an augmented and faster N400 representing better processing mechanisms (Kutas & Van Petten, 1988).

These ERP's have all been employed in the evaluation of various psychopathological disorders, and have proven to be

effective tools as they activate central response mechanisms, both sensory and cognitive, thereby providing an evaluation of possible functional deficits within the brain.

1.2 *Schizophrenia and ERP's: General Findings*

A predominant ERP finding is that potentials occurring between 0 and 100 msec post-stimulus have larger amplitude, longer latency and greater wave-shape stability in schizophrenic patients as compared to normal controls (Chapman, 1979; Romani, Zerbi, Mariotti, Callieco & Cosi, 1986). Post 100 msec potentials in schizophrenics, however, have been found to have attenuated amplitudes and lower stability compared to those found in normal controls (Chapman, 1979; Romani et al., 1986).

Research on early ERP's and schizophrenia has, nevertheless, not always been consistent. While some studies have failed to demonstrate any differences in BSAEP's between normals and schizophrenics (Pfefferbaum, Horvath, Roth, Tinklinberg & Kopell, 1980; Szelenberger, 1983), others have found that chronic schizophrenics suffering from auditory hallucinations had abnormal latency characteristics (Josiassen, Shagass & Roemer, 1988; Lindstrom, Klockhoff,

Svedberg, & Bergstrom, 1987), attenuated amplitudes, or an absence of specific components of the BSAEP (Hayashida et al., 1986). Also, it has been shown that chronic schizophrenics, when given electrical stimulation, display a unique negative potential occurring 60 msec post-stimulus (Roemer, Shagass, Straumanis & Amadeo, 1978; Shagass, Roemer, Straumanis & Amadeo, 1978; Shagass et al., 1977; Shagass, 1975, 1976), which was not observed in the normal controls. Shagass has suggested that this negative potential indicates underactivation of a pre-cortical "gating" or "filtering" mechanism which may act on sensory input at the subcortical level. This putative impaired filtering capacity, and the resultant sensory overload and its impact on available sensory resources at the cortical level (Shagass et al., 1978), is thought to contribute to reduced amplitudes of the subsequent middle and late cortical ERP's to task stimuli. Other studies (Braff & Judd, 1986; Franks, Adler, Waldo, Alpert & Freedman, 1983; Freedman, Adler, Waldo, Pachtman & Franks, 1983), have demonstrated, using a two-stimulus conditioning test ERP paradigm, that in schizophrenic patients, a P50 ERP component evoked by the second stimulus is not inhibited by the effects of the first stimulus as is typically observed in normal controls. This increased amplitude of the P50 component in

schizophrenic patients, is thought to reflect a lack of normal central inhibition, or gating, of sensory stimulation of the cortex (Freedman et al., 1983), thus supporting the previous interpretation put forth by Shagass (1977).

Studies on middle latency ERP's and schizophrenia have typically found attenuated amplitudes of these components (Buchsbaum, 1977; Landau, Buchsbaum, Carpenter, Strauss & Sacks, 1975; Pfefferbaum, Wenegrat, Ford, Roth & Kopell, 1984; Pfefferbaum et al., 1980; Schooler, Buchsbaum & Carpenter, 1976). In particular, the amplitude of the N100 component, which is considered to vary as a function of the selective attention of the subject (Hillyard & Picton, 1979), has been found to be reduced in schizophrenic patients compared to normal controls (Baribeau-Braun, Picton, Gosselin & Quan, 1980; Buchsbaum, 1977; Roth, Pfefferbaum, Kelly, Berger & Kopell, 1981; Roth, Horvath, Pfefferbaum & Kopell, 1980; Roth & Cannon, 1972; Shagass et al., 1978; Shagass et al., 1977). In a study designed to assess the N100 potential in schizophrenics and controls during a dichotic listening task, it was found that the normal controls exhibited larger N100 amplitudes than the schizophrenic patients when stimuli were presented at a slow rate, and when attention was divided between the left and right ears (Baribeau-Braun et al., 1980).

Normalized N100 amplitudes were observed in the schizophrenics only under conditions of focused attention whereby the stimuli were presented at a faster rate, which indicated to the authors that the difficulty the schizophrenics were experiencing may be in the "sustaining" of selective processing strategies, rather than an absence or slowness of attention selectivity. Buchsbaum (1977), suggested that the attenuation of the middle latency ERP components may reflect a neurophysiological mechanism whereby the cortex attempts to compensate for the stimulus overload resulting from subcortical "gating" deficiencies, possibly arising from limbic system dysfunction.

Schizophrenia also affects components of late ERP's including the P300, CNV, PINV and N400. Chronic schizophrenics appear to exhibit attenuated P300 amplitude components (Brecher & Begleiter, 1983; Duncan, Morihisa, Fawcett & Kirch, 1987; Duncan-Johnson, Roth & Kopell, 1984; Mirsky & Duncan, 1986; Pass, Klorman, Salzman, Klein & Kaskey, 1980; Roth, 1987; Roth et al., 1979; Roth, 1977; Steinhauer & Zubin, 1982; Verleger & Cohen, 1978), and delayed P300 latencies (Baribeau-Braun, Picton & Gosselin, 1983; Blackwood et al., 1987; Pfefferbaum, Ford, White & Roth, 1989; Pfefferbaum et al., 1984; Romani et al., 1987; St. Clair, Blackwood & Muir, 1989),

possibly indicating an abnormal cerebral process associated with "response set" attention. Baribeau-Braun, Picton & Gosselin (1983), using a dichotic listening task, found that the P300 remained abnormally small, even when the target stimuli were detected accurately, therefore suggesting that schizophrenics suffer from "a general inefficiency in obtaining information from significant stimuli", and that this deficit is not related to arousal since the abnormality was not shown to decrease when the stimuli were presented more rapidly. The CNV component, measured in forewarned reaction time (RT) paradigms, has been found to be attenuated in schizophrenic patients (Briling, 1980; Pritchard, 1986; Strandberg, Marsh, Brown, Asarnow & Guthrie, 1984; Timsit-Berthier, Delaunoy, Kominck & Rouseau, 1973; Timsit-Berthier et al., 1984; Van den Bosch, 1983). Research has also correlated specific sub-types of schizophrenia with specific CNV characteristics (Bachneff & Englesmann, 1983; McCallum & Abraham, 1973; Rizzo, Spadaro, Albani & Morocutt, 1984). Closely related to the CNV is the PINV, a measure of the resolution of CNV negativity after the imperative stimulus, which has been shown to have prolonged negativity in schizophrenic patients compared to normal controls (Bachneff & Englesmann, 1980; Pritchard 1986; Timsit-Berthier et al.,

1973). Finally, while there has been little research done on the N400 and schizophrenia, preliminary data suggests that the amplitude of this component is attenuated in the schizophrenic population (Adams, Faux, McCarley, Marcy & Shenton, 1989; Grillon, Ameli & Glazer, 1991).

2. LANGUAGE DYSFUNCTION IN SCHIZOPHRENIA

Perhaps one of the first and most striking clinical signs that someone suffers from schizophrenia is the linguistic disturbance commonly noted in schizophrenic's speech patterns. This disorder of communication, characterized by low complexity, low integrity and dysfluency, may be biologically related to language processing and cognitive disturbances. These disturbances have been attributed to an inability of the schizophrenic to organize linguistic elements into meaningful structures (Chaika, 1974; Patterson, 1987), and to demonstrate relatively poor judgement or perspective on the appropriateness of their own speech patterns (Harrow, Lanin-Kettering & Miller, 1989; Thomas, King, Fraser & Kendall, 1990). This disordered perspective suggests that the schizophrenic patients may suffer from either an impairment in the development and planning of ideas used to formulate their speech patterns (Thomas et al., 1990), a marked increase in their vulnerability to distraction (Grillon, Courchesne, Ameli, Geyer & Braff, 1990), or an impairment in the monitoring of their speech as it occurs; thus allowing it to deviate from the external social context and demands of the existing situation (Harrow et al., 1989).

One symptom of linguistic dysfunction is the tendency to make perseverative errors which is defined as behaviour that cannot be terminated, or whereby strong associations to previous tasks or behaviours interfere with, or supplant ongoing contextually appropriate activity (Kwapil, Hegley, Chapman & Chapman, 1990; Luria, 1980). These verbal perseverations observed at the phonemic, semantic, and syntactic levels, have been demonstrated in schizophrenic patients (Barr, Bilder, Goldberg, Kaplan & Mukherjee, 1989; Bilder and Goldberg, 1987; Chaika, 1982), and may represent a breakdown of language ability at various levels of the neurolinguistic hierarchy (Barr et al., 1989). It has been suggested that these perseverations are due to dysfunctional executive frontal lobe mechanisms that monitor language output (Barr et al., 1989; Novoa & Ardila, 1987). Verbal perseveration has been attributed a disturbance of the executive functions of the frontal lobes (Barr et al., 1989), possibly indicating a failure of the switching mechanisms believed to be related to attentional disturbances (Chaika, 1982), and the impairment of an individual's planning or monitoring of their linguistic productions (Andreasen & Grove, 1979). A two-process theory proposed by Posner and Snyder (1975) suggests that the active association between words or

ideas formed by normal individuals, decay rapidly or are inhibited, which limits their potential to disrupt ongoing discourse. This theory suggests that schizophrenics may have a defect either in the decay or in the inhibitory process, which subsequently results in the intrusion of already activated associations into ongoing speech (Maher, 1983).

Cloze probability analysis, whereby a single word is left out of a sentence and the reader is asked to supply the appropriate missing word, has been used to assess the ability of schizophrenics to predict the missing component of the sentence. Schizophrenics have been found to have significantly lower cloze probability scores than normal controls (Ragin & Oltmanns, 1987), suggesting to the authors that schizophrenics do not effectively plan and edit their speech in order to create predictable sentences, and therefore, make less comprehensible sentence output for the listener. Although schizophrenic patients frequently make errors in their communications, there is often little if any effort on their behalf to correct these problems. Thus it has been suggested that schizophrenics suffer from an impaired perspective of their speech patterns, indicating they do not possess the ability to monitor and recognize the inappropriateness of their communication, as do normal

controls (Chaika, 1974; Harrow et al., 1989).

2.1 Frontal Lobe Dysfunction in Schizophrenia

A variety of language dysfunctions have been attributed to frontal lobe pathology including; decreased verbal output, improper use of syntax, and failure to comprehend proper word sequencing (Stuss & Benson, 1984). The use of neuropsychological measures including the Newcombe Word Fluency Test whereby the subject is asked to give orally the names of as many animals and objects as possible in a given time period; and the Chicago Word Fluency Test whereby the subject is asked to write down as many words as possible in a given time period that begin with a particular letter, have also suggested that schizophrenics suffer from language related frontal lobe deficits as schizophrenics appear to have a much greater difficulty generating appropriate word responses as compared to normal controls (Kolb & Wishaw, 1983).

The Wisconsin Card Sorting Test (WCST) is another neuropsychological test commonly used to assess frontal lobe dysfunction (Braff et al., 1991; Heaton, 1981). For this test, subjects are presented with four target cards bearing

designs that differ in colour, form or number. They are then instructed to sort a pack of 128 cards that vary along these dimensions. The correct matching criteria used (colour, form or number) is changed without warning once subjects complete 10 correct matches in a row; and continues until the subject has completed six categories (colour, form, and number - twice), or until all 128 stimulus cards have been placed under the target cards. This has been shown to be particularly sensitive to frontal lobe dysfunction (Braff et al., 1991; Milner, 1963; Robinson, Heaton, Lehman & Stilson, 1980; Heaton, 1981), and has been used to support the concept of a dysfunctional frontal lobe system in the progression of schizophrenia (Seidman et al., 1991). Schizophrenic patients have been found to be impaired on the WCST, having increased number of errors, and percent perseverative responses, as compared to normal controls (Berman et al., 1986; Weinberger, Berman & Zec, 1986). Also included in these studies was concurrent rCBF analysis which showed relative frontal lobe hypoactivity in schizophrenic patients during the WCST, compared to relative frontal lobe hyperactivity in the normal controls. The authors interpreted these results as reflecting dysfunction of dorsolateral prefrontal cortical activity in schizophrenia. Other studies have also supported this finding

of low relative frontal metabolism in schizophrenia (Cohen et al., 1987; Wolkin et al., 1988; Cleghorn, Zipursky & List, 1991).

Frontal lobe dysfunction has been implicated in the manifestation of negative symptoms associated with schizophrenia as evidenced by clinical cognitive and behavioral, neurochemical, and brain imaging strategies (Levin, 1984). Levin (1984) suggests that negative symptoms such as emotional withdrawal, blunted affect and lack of spontaneous conversation, are clinical manifestations of frontal lobe damage, and that these observable cognitive deficits may be a reflection of a fundamental defect of attentional mechanisms controlled primarily by the frontal lobes. This conclusion is supported by another study (Crow, 1980), where it was suggested that the negative symptoms such as emotional withdrawal and apathy, are related to cell damage and loss, which has been localized to the frontal lobes of schizophrenic patients through the use of CT scans (Tanaka, Hazaman, Kawahara & Kobayashi, 1981), and rCBF analysis (Weinberger et al., 1986; Ingvar and Franzen, 1974). Additional support has also come from Volkow, Wolf and Van Gelder (1987), who suggested that schizophrenics suffering from predominantly negative symptoms are metabolically

hypofrontal as compared to positive symptomatic patients. It has also been reported that patients suffering from enduring negative symptoms show significantly reduced glucose utilization in both frontal and parietal cortices, as well as in the thalamus (Buchanan et al., 1991).

Additional research assessing regional cerebral blood flow in response to tasks that either do or do not require frontal lobe activation has revealed that both medicated and unmedicated schizophrenic patients failed to activate frontal blood flow when they were required to perform the WCST, a test believed to activate frontal lobe functioning (Weinberger et al., 1986; Berman, Illowski & Weinberger, 1988). On tests not designed to activate frontal lobes, the rCBF distribution for patients was no different to that found for the normal controls. Work done by Resnick, Gur, Alavi, Gur and Reivich (1988) employing PET scans, also found lower cortical glucose metabolic rates in schizophrenic patients as compared to normal controls, suggesting to the authors that schizophrenics may have relative hypermetabolism in structures that have been implicated in dopamine pathways. Findings of reduced frontal lobe activation in schizophrenic patients has also been supported by other studies employing computerized EEG measures during performance on the WCST (Williamson, Kutcher & Cooper,

1989), and during performance on a continuous performance task (Buchsbaum, 1990).

The role of the frontal lobes in the complex planning and editing of speech components into comprehensible communication is essential for normal discourse to occur (McGrath, 1991). Impairment of frontal lobe functioning could therefore possible lead to distractibility and perseveration errors. Alexander, Benson and Stuss (1989), found that frontal lobe lesions lead to reduced social and contextual organization of language, and poverty of speech, which suggests that these symptoms found in schizophrenic patients, may likely be related to frontal lobe pathology. These findings are especially relevant to schizophrenia, as frontal lobe dysfunction in schizophrenia has received empirical support from various neuroimaging strategies including PET and SPECT scans (Buchsbaum et al., 1982; Farkas et al., 1984), rCBF analysis (Weinberger et al., 1986), and computerized electroencephalography (Morihiya & McAnulty, 1985).

2.2 *Negative Symptoms in Schizophrenia*

Schizophrenic symptoms can readily be broken down into those considered to be "positive" such as hallucinations,

delusions, and paranoia; and those considered to be "deficit" or "negative" such as blunted affect, social and emotional withdrawal, loss of drive, and poverty of speech (Walker & Lewine, 1988). Both blunted affect and poverty of speech have been described as key symptoms for the definition of a negative symptom subtype of schizophrenia, as these symptoms are believed to be both primary and enduring (Crow, 1985). Negative symptoms are thought to predominate in the chronic phase of the illness, and are possibly related to structural brain abnormalities (Crow, 1980; Andreasen & Olsen, 1982). Therefore, it is conceivable that those patients exhibiting negative symptoms, and who appear to be resistant to neuroleptic treatment, may have suffered some degree of irreversible frontal lobe damage.

Negative symptoms appear to be related to the frontal lobes, as patients with known focal prefrontal lesions have been reported to suffer from diminished social drive, blunted affect and poverty of speech (Blumer & Benson, 1975; Fuster, 1980; Stuss & Benson, 1986). Using an intracarotid xenon technique, Ingvar and Franzen (1974) showed that schizophrenic patients were hypofrontal (ie: having reduced blood flow to the anterior cortical areas of the brain), relative to normal controls showing hyperfrontality. In addition, these

investigators found that the degree of hypofrontality was positively correlated with the severity of negative symptoms the patients displayed. This finding has been confirmed by another study (Volkow et al., 1987) where it was found, using PET scans to measure cerebral glucose metabolism, that patients suffering from increased severity and number of negative symptoms, displayed increased hypofrontality than did patients with fewer and less severe negative symptoms.

Research on language processing in schizophrenia suggests that deficits in the processing of auditory verbal information is correlated with positive symptoms (Cornblatt, Lenzeweger, Dworkin & Erlenmeyer-Kimling, 1985; Green & Walker, 1985; Harvey, Earle-Boyer & Levinson, 1988; Harvey & Serper, 1990), whereas the processing of visual verbal information is correlated with negative symptoms (Green & Walker, 1985; Neuchterlein, Edell, Norris & Dawson, 1986). Therefore, as generally poor linguistic performance in schizophrenia has been associated with negative, rather than positive symptoms (Ragin & Oltmanns, 1987; Thomas et al., 1990), it is important to separate specific types of language processing dysfunctions in schizophrenic patients because of the possibility that these problems may be differentially produced.

It has been suggested by Morice and Ingram (1983), that

schizophrenics suffering from low complexity of speech and dysfluency tend to have an earlier onset of the illness than patients with delusional and psychotic symptomatology, which is also widely regarded as indicative of poor outcome. The belief in a subgroup of schizophrenics suffering from predominantly negative symptoms has received support from Thomas, King & Fraser (1987) who found that speech of first onset, negative symptomatic schizophrenics was syntactically less complex than that of schizophrenics with no negative symptoms. Measures assessing "paucity of verbalization" and "impoverished thinking" have also been used to differentiate out-patient chronic schizophrenics from hospitalized chronic schizophrenics, with the hospitalized patients displaying greater negative symptomatology and reduced responsiveness to treatment (Siegel, Harrow, Reilly & Tucker, 1976).

In an article by Thomas et al. (1990), the authors suggested that differences between acute and chronic schizophrenics are unlikely influenced by the duration of time spent in hospital, and that low complexity and reduced linguistic output is indicative of a negative symptomatic schizophrenic, and is strongly related to the chronicity of the illness. The authors suggest that first onset schizophrenics displaying negative symptoms, including low

complexity of speech will have a poor prognosis regarding the course of their illness , than later onset patients suffering fewer negative symptoms.

2.3 Neuroleptic Medication and Schizophrenia

While it has been argued that reduced linguistic complexity and poverty of speech are a result of neuroleptic medications (de Alarcon & Carney, 1969), more recent research suggests that this is not the case. In a study by Ragin, Pogue-Geile & Oltmanns (1989), the authors conducted within group comparisons of medicated and non-medicated schizophrenic patients, once at hospital admission, and again seven months after discharge, and found no difference in the occurrence of poverty of speech based on neuroleptic medication. In another study designed to assess the language of schizophrenic patients, the authors suggested that linguistic differences cannot be explained by medication effects. In a related article, Hymowitz and Spohn (1980) reported no decrease in either the complexity or coherence of speech as a result of neuroleptic medication.

King, Fraser, Thomas & Kendall (1990) also suggested that language deterioration in schizophrenia is not matched by a

similar deterioration in the language of manic patients, although the two patient groups had continued on equivalent doses of maintenance medication during the intervening three years of the study. The authors concluded that this progressive deterioration of verbal output is unresponsive to, and not a result of, the neuroleptic medication that the patient was receiving.

The view of negative symptoms being unresponsive to neuroleptic medication has been supported by other studies as well (Taylor, Greenspan & Abrams, 1979), however Crow (1985), suggested that a more subtle distinction between primary and secondary negative symptoms may be required in order to adequately evaluate the association between medications and these symptoms. Therefore, while neuroleptic medications appear not to have a significant effect on negative symptomatology, caution must still be exercised when stating this assumption conclusively.

3. LANGUAGE DEVIANCE AND THE N400 ERP

While almost any unexpected stimulus deviation in the stream of constant events in a testing paradigm can result in the P300 ERP (Snyder, Hillyard & Gallambos, 1980), Kutas and Hillyard (1980a, 1980b & 1980c) discovered that while expected sentence completions are associated with late positivity between 300 and 600 msec poststimulus, incongruous sentence completions produced an additional negative component occurring in the same range at about 400 msec poststimulus (Figure 1). When the semantically anomalous word is also physically deviant (eg: "I take coffee with cream and ENGINE."), both a P300 and an N400 are elicited, suggesting that the physical and semantic attributes of a word are processed in parallel, and not interactively (Kutas & Hillyard, 1980c). This new N400 ERP elicited by semantic anomalies in the visual and auditory modalities has proven to be a very robust component (Holcomb, 1986; McCallum, Farmer & Pocock, 1984).

Although both the P300 and N400 ERP's are considered as endogenous cognitive responses to deviance, the N400 is thought to result from expectancies of one's long-term memory store specific to language, and the expectancy that a series

FIGURE 1

N400 EVENT-RELATED POTENTIAL: AN EXAMPLE

Grand averaged event-related potentials (ERPs) to the best sentence completion (EAT), anomalous and related sentence completion (DRINK), and anomalous and unrelated sentence completion (CRY); Recorded from scalp site: Pz. (Figure taken from Kutas, Lindamood & Hillyard, 1984)

of words will either make sense or be related, whereas the P300 is more responsive to short-term expectancies related to a deviation of physical parameters such as a high pitched tone occurring within a series of low tones (Kutas & Van Petten, 1988). The amplitude of the N400 appears to be negatively related to word expectedness or predictability within a given context (Kutas & Hillyard, 1984).

When presented with predictable and unpredictable endings to stimuli sequences using: visually presented sentences, well known melodies, geometric figures ordered in increasing sizes, and notes of the musical scale in ascending order, only the semantically anomalous words used for sentence completion elicited the N400 ERP (Besson & Macar, 1987). All the other incongruous stimuli produced the P300, suggesting that both the context and deviation must be linguistic in order to elicit the N400 ERP. It has also been proposed that while the P300 occurs in response to a signal that can be readily interpreted using short-term memory, the N400 appears to occur when the interpretation of the linguistic information requires access to long-term memory (Stuss, Picton & Cerri, 1986). This suggests that the amplitude of the resulting N400 component may be related to the extent of the memory search.

While semantic incongruity has been demonstrated to

elicit the N400 (Kutas & Hillyard, 1980a & 1980c), it is not restricted to this process. In another study subjects were presented with simple semantic propositions employing true affirmatives, false affirmatives, true negatives, and false negatives, only the final words of the false affirmative (ie. "a cat is a hammer"), and true negative statements (ie. "a cat is not a hammer"), produced the N400 ERP (Fishler, Bloom, Childers, Roucos & Perry, 1983). The authors concluded that the N400 ERP is more sensitive to the association between entries in the mental lexicon than to the propositional content of the statement.

The N400 ERP has also been shown in response to both intermediate and terminal semantic anomalies, suggesting that stimulus words are integrated with the preceding context on a moment to moment basis, rather than being held in a buffer until the sentence is completed (Carpenter & Daneman, 1981). Related to this work is research suggesting that the amplitude of the N400 arising from a given stimulus word, is directly related to the degree to which the preceding word(s) have "prepared the way" or "primed" that particular stimulus word (Kutas, Lindamood & Hillyard, 1984; Underwood & Bargh, 1982). Results from these studies also suggest that although N400 amplitude changes with the expectancies set up by sentence

context, it is also related to the association between single lexical items, not all of which need to be present to elicit the N400 waveform.

Semantic priming is said to occur if the speed and accuracy of target word recognition is improved when that word is preceded by semantically related words rather than unrelated or nonsense words (Johnson-Laird, Hermann & Chaffin, 1984). Semantic priming can be thought of as consisting of two separate sub-processes, including a fast acting component based on word association learned as a part of one's language, and a slower component reflecting one's conscious expectancies (Kutas & Van Petten, 1988).

Using the N400 ERP to investigate the semantic priming effect, it has been found that while both primed and unprimed words displayed the N400 component, the peak amplitude was significantly larger for the unprimed words (Bentin, McCarthy & Wood, 1985; Harbin, Marsh & Harvey, 1984; Kutas, 1985; Kutas & Hillyard, 1984). Unfortunately, both the P300 and N400 components tend to occur in the 300 to 600 msec poststimulus time frame, thereby making it difficult to assess their relative contributions to the resultant waveform. Therefore, if the overlapping P300 component can be removed from the waveform, the morphology and distribution of the N400, as it

relates to semantic priming, can be better visualized and measured. One way to achieve this is to instruct subjects to indicate if a letter following the stimulus word pair (by at least one second), was presented in either, or both of the words in that word pair (Kutas, 1985). By doing this, the subject's task decision, and therefore the associated P300 component, is delayed well beyond the N400 ERP elicited by the target word (Kutas & Van Petten, 1988).

Kutas and Van Petten (1988), suggest that the ERP difference between primed and unprimed words tend to be smaller than the difference between anomalous and best completion words of sentences. The authors suggest that this difference may be due to a stronger more constrictive context found in a sentence fragment, than that found in a single word. It was also suggested that antonym pairs may yield larger N400 waveforms, as these comparisons are considered to be stronger and more constrained than comparisons made using word pairs taken from the same category. The subject's level of attention given to the experimental task, as well as the degree of semantic analysis of the word pairs, have also been suggested as being important factors underlying the amplitude of the N400 ERP (Holcomb, 1986; Kutas, 1985).

Although the N400 is a relatively new ERP component

discovered a little more than a decade ago (Kutas & Hillyard, 1980a), a substantial amount of research to date has demonstrated the strong relationship between this component and linguistic processes. This research indicates that the N400 is a sensitive and useful tool for assessing the timing and organization of certain information and linguistic processes.

44. THE N400 ERP AND SCHIZOPHRENIA

While numerous studies have reported that schizophrenics display reduced P300 amplitude for both visual and auditory stimuli, as well as attenuated CNV responses (Pritchard, 1986; Roth et al., 1986), very few have examined what changes occur to the N400 in this patient population. Although it is well known that schizophrenics suffer from impaired speech patterns (Barr et al., 1989), and that the N400 ERP has been shown to physiologically reflect contextual effects of language processing in normal controls (Kutas & Van Petten, 1988), there has as yet been only a few studies on the relationship between the two.

In one such study, a lexicon decision task was used in which subjects were presented with stimulus pairs whereby the second stimulus of each pair was either a related word, unrelated word, or a non-word (Koyama et al., 1991). Subjects were instructed to hit a "yes" key if they felt the second item of the stimulus pair was a word, and to hit a "no" key if they felt it was a non-word. All subjects produced the N400 ERP when the second stimulus was either an unrelated word or a non-word, which supports the previous findings of studies using normal controls (Koyama, Nageishi & Shimokochi, 1988;

Kutas & Van Petten, 1988). While no difference was found in the amplitude between the schizophrenic group and the normal controls under the unrelated and non-word conditions, the morphology of the N400 was less clear and the latency was delayed. The authors of this study concluded that while the lexical memory of the schizophrenic group was intact, and they seemed able to use contextual cues properly, the delay in the latency of the N400 appears to indicate that schizophrenics suffer from a deficit in their ability to search their memory to adequately select an appropriate response.

In another study (Adams et al., 1989), sentence ending words were used whereby the final word in each sentence was considered to be either a highly constrained best completion word (cloze probability > 0.85, ie. "He takes coffee with cream and *sugar*"), or an anomalous completion word (cloze probability < 0.01, ie. "He takes coffee with cream and *paper*"). The results indicated that while both the schizophrenic group and normal controls displayed the N400 ERP to the anomalous completion word, the amplitude of the N400 peak was significantly more attenuated in the schizophrenic group as compared to the normal controls. Unfortunately, due to the small sample size of this study (8 schizophrenics and

8 normal controls), these results are preliminary, and need to be confirmed using a larger sample size.

Finally, Grillon et al. (1991), compared 14 schizophrenic patients with 14 age matched normal controls, using word pair stimuli whereby subjects were to press a "yes" key if they believed the second word in the pair to be related to the first, and to press a "no" key if they believed it was not. Although the N400 ERP was found to be both attenuated and delayed in the schizophrenic group, as compared to the normal controls, these findings were not consistent for all subjects in the patient group. While some schizophrenics had a normal N400, others had either a reduced ERP, confirming the results of Adams et al. (1989); a delayed ERP, confirming the work of Koyama et al. (1991); or a combination of the two.

In the study by Grillon et al. (1991), the authors suggest that their findings of N400 variability may yet be another aspect of the heterogeneity of the schizophrenic disorder, which seems likely given that subgroups of schizophrenics have been shown to differ in their linguistic ability (Manschreck et al., 1988; Thomas et al., 1990). Precisely how N400 variability is related to linguistic performance has yet to be determined, possibly through the use of measures which assess more specific correlates of the

disorder such as positive and negative symptomatology (Andreasen, 1982).

4.1 Research Question

At present, there have only been a few studies on the language of schizophrenia and the N400 ERP (Adams et al., 1989; Koyama et al., 1991; Grillon et al., 1991). In a non-experimental paper, Patterson (1987) had initially hypothesized that schizophrenics should have a reduced N400 because they typically have difficulty generating appropriate linguistic expectancies. Although this result was found by Adams et al. (1989), the study done by Koyama et al. (1991), did not find any difference in the amplitude of the N400 between schizophrenics and normal controls. The study conducted by Grillon et al. (1991), however, found that while some schizophrenics had normal N400 amplitude, others had either reduced amplitude, or delayed latency.

Research has suggested that negative symptomatology is typically correlated with reduced language output in schizophrenia, while negative symptoms and language deficits appear to be related to the dysfunctional frontal lobe processes deemed necessary for language production. The

purpose of this present study therefore, is to compare the N400 amplitude and latency of predominantly negative symptomatic schizophrenics, with that of mixed, positive and negative symptomatic schizophrenic patients, in order to characterize which symptomatic subgroups may be associated with the reduction and delay of the N400 ERP noted in previous studies.

4.2 Study Hypotheses

It is hypothesized that the results of this study will indicate schizophrenic patients have both reduced amplitude and delayed latency of the N400 component, as compared to normal controls, suggesting possible linguistic impairment as well as delayed information processing. Also, it is expected that these deficits found in the schizophrenic group will be more pronounced in patients suffering from predominantly negative symptoms, as compared to those suffering from a combination of both negative and positive symptoms, as certain language deficits in this group appear to be characteristic of negative symptomatology (Thomas et al., 1990). Finally, it is believed that patient group differences will be maximal in the frontal, rather than posterior regions of the scalp as frontal

lobe dysfunction is believed to be associated with both language deficits (Stuss & Benson, 1984), and with negative symptoms in schizophrenia (Levin, 1984).

5. METHODOLOGY

5.1 *Experimental Subjects*

A total of 45 subjects were included in this study in order to provide adequate power analysis (Streiner, 1990); with 15 subjects in each of the three testing groups: medicated schizophrenics, which were divided into two subgroups; one consisting of 15 patients displaying predominantly negative symptoms (NS), and one consisting of 15 patients displaying a mix of both positive and negative symptomatology (MS); and the third group consisting of 15 normal controls (NC). All subjects signed a standard consent form prior to enrolment in the study (please see Appendix A). The schizophrenic patients were diagnosed as suffering from schizophrenia based on DSM-III-R diagnostic criteria (APA, 1987); and were subgrouped into negative and mixed-symptomatic patients based on scores from the Positive and Negative Syndrome Scale for schizophrenia (PANSS; Kay, Opler & Fiszbein, 1987). The scoring form of the PANSS was modified however, such that it employed a scale of "0" (denoting that the symptom was 'not present'), to "6" (denoting an 'extremely severe symptom'), rather than the "1" to "7" scale originally

included in the PANSS (please see Appendix B). This modification to the scoring form was made, in order that the absence of symptoms would not result in a higher positive score; thus making the 2:1 negative to positive symptom ratio more difficult to achieve. The psychiatric population was drawn from the neuroleptic clinic of the Royal Ottawa Hospital (the local psychiatric hospital). The normal controls were comprised of non-hospital employees (n=9), and Royal Ottawa Hospital staff (n=6) volunteers. Subject groups were matched for age and sex.

5.1.1. *Inclusion Criteria*

Both schizophrenic patients and normal controls between the ages of 18 and 65 were eligible for inclusion in this study. Patients satisfied the DSM-III-R criteria (APA, 1987) for chronic schizophrenia, and were in a stable phase of the illness as assessed by the clinician's judgement of positive and negative symptoms, and general psychopathology, over the four week period prior to study enrolment. Neuroleptic and adjunct medication dosages, course (episodic or chronic), subdiagnosis, duration of illness, and years of formal education were recorded for each patient at the time of study

participation (please see Appendix C). Also, an Extrapyramidal Symptom Rating Scale (ESRS) was completed for each patient in order to provide an indication of the severity of side effects the patients were experiencing as a result of their neuroleptic treatment (please see Appendix D). The neuroleptic medications and dosages, and the ESRS were included in order to determine whether either medications, or their side effects, were related to the obtained ERP data. To be included in the negative symptom subgroup, patients had to exhibit a score of 3 (indicating moderate) or more, on at least three of the negative items (N1-N7), and fewer than three moderate ratings on the positive items (P1-P7) of the PANSS and, had a negative to positive symptom ratio score of two or more. For inclusion into the mixed symptomatology subgroup, patients had to show a score of less than three moderate ratings on the negative scale, and a negative to positive symptom ratio score of one or less.

5.1.2. Exclusion Criteria

Patients were excluded if they suffered from a primary psychiatric disorder other than schizophrenia (ie: major depression, schizoaffective disorder, etc.). Control subjects

were excluded if they were taking any central nervous system (CNS) altering drugs, or if they had any psychiatric history. Also, neither schizophrenic patients, nor control subjects were included if either had, or were suspected of having abused of alcohol or illicit drugs, had received electroconvulsive therapy (ECT) in the previous month, or had suffered a head injury that resulted in a loss of consciousness, within the previous year.

5.2 Task Stimuli

This study employed similar task parameters used by Grillon et al. (1991). The stimuli were word pairs, presented one word at a time (for a duration of 289 msec) on a computer screen in a four X six inch rectangle. The priming word (W1 - eg: colour), was presented first followed 1020 msec later by the stimulus word (W2) which was either related (eg: green) to the priming word (R), or unrelated (eg: house) to the priming word (U). All of the words used to make up the word pairs in this study were easily comprehensible (Carrol & White, 1973), and were chosen based on their high frequency of occurrence in the English language (Thorndike & Lorge, 1944). For a complete list of the word pair stimuli used, please see

Appendix E.

5.3 *Testing Procedure*

Prior to the ERP recording, subjects were asked to complete the Revised Peabody Picture Vocabulary Test (PPVT-R; Dunn & Dunn, 1981), and the Controlled Oral Word Association (COWA; Spreen & Benton, 1969) test in order to provide measures of individual linguistic intelligence and verbal fluency (please see Appendices F and G, respectively). These tests were followed by the Wisconsin Card Sorting Task (WCST; Grant & Berg, 1948) to supply an objective measure of cognitive frontal lobe functioning (please see Appendix H). For the ERP portion of testing, subjects were seated in a comfortable chair in a sound attenuated, electronically shielded testing chamber which was adjacent to the control room housing the amplifiers, computers and recording devices. A computer screen was positioned one meter in front of the subjects, and lights dimmed so as not to interfere with the subjects viewing of the word pairs. Subjects were told that words would be sequentially presented in the middle of a rectangle, situated at the centre of the screen, and that, using their dominant hand, they were to press the left button

on a key pad if the second word of the word pair was related to the first, and the right button on the key pad if the second word of the word pair was unrelated to the first. The buttons on the key pad were correspondingly labelled "yes" on the left key, and "no" on the right key. Subjects were also asked to refrain from blinking as much as they were able to during the period when the word pairs were presented on the screen, and were given the opportunity to blink as needed between word pair presentations thus allowing them to control the initiation of each word pair trial. These instructions were incorporated into the computer program, so that subjects were always aware of the appropriate times, during the testing procedure, in which to blink. They were also instructed that accuracy was very important for the study, and to take their time when pressing down on the response keys, as speed was not a factor of interest in the experiment. This last instruction was emphasized so that the Late Positive Component (LPC), or P300 did not overlap the N400 waveform (Grillon et al., 1991). There was a 1020 msec stimulus onset asynchrony between the first and second word of each word pair. Prior to actual recording, subjects were given one practice trial of ten word pairs (that were not included in the test word pair array), to familiarize themselves with the task requirements. In order

to continue in the study, subjects had to respond appropriately, and without artifact, to at least six of these ten word pair presentations. A total of 90 word pairs were presented; 45 in each of the two stimulus conditions.

5.4 *ERP Recording*

The ERP's were recorded using tin electrodes, from the mid-line vertex (Fz, Cz, Pz) positions based on the 10-20 system of electrode placement (The ten-twenty electrode system, 1958). These electrodes were referenced to linked earlobes. Electro-ocular artifacts were monitored via electrodes placed on the supra-orbital and medial-orbital ridges of the right eye, in order to monitor both horizontal and vertical eye movements, so that trials contaminated by excessive artifact could be excluded from the analysis. EEG segments were visually inspected off-line, and those segments that were contaminated by excessive EOG artifact were removed from the analysis. Electrode impedance did not exceed 5 Kohms. Electrical activity was recorded using the Grass Model 12 Neurodata Acquisition System amplifiers with a band-pass of 0.1 and 30 Hz. Signals were digitized at a rate of 256 Hz for a 1000 msec "recording window" after presentation of the

stimulus word (W2), which included a 100 msec pre-stimulus baseline period. The artifact rejection level was set at +/- 50 uv for both EEG and EOG recordings, with trials exceeding this level being excluded from the final averaging. Also, only those trials whereby the subject's response ('yes' or 'no'), correctly matched the stimulus word pair ('related' or 'unrelated'), were included in the analysis. A minimum of 20 correct response and artifact free trials per stimulus condition was required for that subject's data to be included in the analysis. Correct response, artifact-free ERP recordings were separately averaged according to which stimulus condition they belonged.

5.5 Data Reduction

Peak amplitudes (relative to the 100 msec pre-stimulus baseline), and peak latencies of the ERP components were computed using visual inspection based on the following "windows": N100, 75-150 msec; P200, 150-250 msec; P300, 250-500 msec; N400, 300-550 msec; and LPC, 400-700 msec.

5.6 Data Analysis

Peak amplitude and latency values were statistically analyzed using BMDP statistical software (BMDP, 1990) and an IBM compatible personal computer. Between groups analysis of variance (ANOVA) tests were conducted to determine the presence of significant main, and interaction effects, of the following comparisons: - separate three way ANOVAs: Group (3) X Stimulus Condition (2) X Site (3), for each amplitude and latency measure for the N100, P200, P300, N400, and LPC components.

Significant interactions were followed up with the Newman-Keuls test to determine which comparisons were significant, as this test holds the experiment-wise error rate to acceptable levels and was therefore, the preferred choice for post-hoc analysis. The one-tailed, .05 level of significance was used to determine if a given comparison was statistically significant.

Scores on the WCS1, the PPVT-R, and the COWA tests were compared, using one-way ANOVAs whereby subject group was the between group variable; followed up, if necessary, by Newman-Keuls post-hoc analysis. The neuropsychological test scores were also correlated with the amplitude and latency measures

of the N400 component in order to determine if the two different measures were related across groups, or within any one specific group.

In order to assess the possible confounding effects of antipsychotic medications and the extrapyramidal side effects associated with those medications, additional analyses were conducted correlating both the chlorpromazine (CPZ) equivalents of the neuroleptic medications and ESRS scores with the obtained ERP results. The CPZ equivalencies were calculated based on published dose equivalency scales (Davis, 1984; Jonnson, 1982; Remington, 1991).

6. RESULTS

6.1 Subject Measures

Subject parameters including: age, sex, education, reaction time to related and unrelated word pairs, and percent accurate response to related and unrelated word pairs can be found in Table 1. A total of 52 subjects were enrolled in this study, seven of which had to be excluded as they responded incorrectly to five or more word pairs (2 NSs and 2 MSs), or had excessive EOG artifact (1 NSs and 2 MSs) in the practice session. A total of 45 subjects (15 per group) remained for inclusion in the study analysis. Age differences between groups were analyzed using a one-way ANOVA, which indicated no significant differences between subject populations. A Chi-Square was conducted on the frequency of males and females in each of the three subject groups, and was not significant. A one-way ANOVA on the years of formal education received by subjects, found a significant difference [$F(2,35) = 26.56$, $p < .001$], which when followed up with Newman-Keuls analysis indicated that NCs had significantly more formal education than either NSs or MSs ($p < .01$). The NS and MS groups did not differ significantly.

TABLE 1: SUBJECT PARAMETERS

Subjects...	NC		MS		NS	
Total n	15		15		15	
Males n	12		13		13	
Females ... n	3		2		2	
-----	mean	s.e.	mean	s.e.	mean	s.e.

Age (years)	38.7	3.00	37.3	2.60	36.9	2.40
Education (years)	16.4	.62	12.6	.44	11.0	.40
RT: Related Words (msec)	1010.0	56.4	1274.7	62.7	1371.3	89.9
RT: Unrelated Words (msec)	1124.7	79.4	1229.3	51.5	1402.7	67.0
% Correct: Related Words	96.0	0.98	88.0	3.20	87.0	3.70
% Correct: Unrelated Words	96.0	1.20	93.0	1.70	92.0	2.50

Subject parameters for: age, sex, education, reaction time (RT) and percent (%) correct response to related and unrelated word pairs; Broken down by subject group: normal controls (NC), mixed symptomatic schizophrenics (MS), and negative symptomatic schizophrenics (NS).

Note: s.e. stands for standard error.

Additional information regarding the patient population, including the course of the illness (chronic or episodic) and sub-diagnosis, can be found in Table 2. T-tests between the mixed and negative symptomatic patient groups for scores on the: PANSS and ESRS scales, chlorpromazine equivalency dosages, and duration of the illness, found that negative symptomatic schizophrenics had a significantly higher negative symptom score [$t(28) = 9.20, p < .05$], and a significantly lower positive symptom score [$t(28) = 6.25, p < .05$], compared to the mixed symptomatic schizophrenics. Patients did not differ with regards to general psychopathology and total score on the PANSS, nor on any of the additional subject measures. The means and standard errors of patients' scores on the PANSS and the ESRS, as well as the averaged chlorpromazine (CPZ) equivalent of their neuroleptic medication and length of their illness, can be found in Table 3.

6.2 Psychometric Measures

A one-way ANOVA conducted on the PPVT-R analyzing the standard score, found no significant differences between groups. Analysis on the COWA test indicated a significant main effect for the total number of words subjects produced in

TABLE 2: PATIENT PARAMETERS

Subjects...	MS	NS
Course of Illness:		
Chronic	10	13
Episodic	5	2
-----	-----	-----
Sub - Diagnosis		
Catatonic	0	0
Disorganized	1	1
Paranoid	7	3
Residual	6	4
Undifferentiated	1	7

Patient population parameters for their course of illness (chronic or episodic), and for their sub-diagnosis under schizophrenia. Broken down by subject group: mixed symptomatic schizophrenics (MS), and negative symptomatic schizophrenics (NS).

TABLE 3: CLINICAL MEASURES

Subjects...	MS		NS	
	mean	s.e.	mean	s.e.
Positive and Negative Syndrome Scale:				
Negative Symptom Subscale	5.5	0.9	16.8	0.8
Positive Symptom Subscale	9.8	0.7	4.4	0.5
General Psychopathology Subscale	13.7	1.8	12.5	1.2
Total Score	29.0	3.0	33.7	1.9
Extrapyramidal Symptom Rating Scale	10.2	2.6	15.1	3.0
Averaged Chlorpromazine Equivalencies	517.0	69.6	585.0	94.2
Length of Illness (years)	17.0	2.2	16.6	2.4

Clinical measures including means and standard errors (s.e.) for the Positive and Negative Syndrome Scale (PANSS), the Extrapyramidal Symptom Rating Scale (ESRS), the averaged chlorpromazine (CPZ) equivalent of daily neuroleptic medication dosages, and the length of the illness, for each patient subgroup: mixed symptomatic schizophrenics (MS), and negative symptomatic schizophrenics (NS).

the total three minute test period [$F(2,42) = 3.41, p < .05$]. Further investigation revealed that the NC group produced significantly more words than the NS group ($p < .05$), however, there were no differences found between the number of words produced by the MS and either of the other two groups (Figure 2).

Analysis of group differences based on the WCST revealed significant group main effects for all subcategories of interest in this study including: the number of categories completed [$F(2,42) = 8.46, p < .001$], the number of total errors committed [$F(2,42) = 9.44, p < .001$], and the percentage of perseverative errors committed [$F(2,42) = 7.96, p < .002$]. Subsequent analyses indicated that the NC group completed significantly more categories than the NS group ($p < .01$), made fewer errors than both the MS group ($p < .05$) and the NS group ($p < .01$), and had a lower percentage of perseverative errors than the NS group ($p < .01$) (Figure 3). The NS and MS groups did not differ on any of the three measures.

Group means and standard errors for these three psychometric tests (PPVT-R, COWA and WCST), can be found in Table 4.

Figure 2
Total Word Output for the Controlled Oral Word
Association (COWA) Test

Number of Words Produced

NC greater than NS ($p < .05$)

Normal Controls (NC), Mixed Schizophrenics (MS),
and Negative Schizophrenics (NS)

Figure 3: Wisconsin Card Sorting Test (WCST)

Figure 3a
WCST: Categories Completed

Figure 3b
WCST: Total Errors

Figure 3c
WCST: Percent Perseverative Errors

TABLE 4: PSYCHOMETRIC TEST RESULTS

Psychometric Test ...	NC		MS		NS	
	mean	s.e.	mean	s.e.	mean	s.e.
Controlled Oral Word Association:						
'F' Category	15.2	0.95	11.7	0.90	11.1	1.90
'A' Category	11.7	1.03	10.6	0.80	8.3	1.20
'S' Category	16.9	1.30	12.7	0.95	12.1	2.90
Total Score	43.8	2.80	35.0	2.20	31.5	4.80
Peabody Picture Vocabulary Test-R						
Raw Score	160.7	4.8	161.7	1.9	155.0	5.0
Standard Score	109.4	5.5	104.3	2.5	100.5	5.9
Wisconsin Card Sorting Task						
Categories Completed	5.1	.41	3.8	.54	2.0	.64
Total Errors	25.3	5.96	50.7	7.5	69.2	7.9
% Perseverative Errors	14.6	2.9	28.2	22.7	44.9	6.7

Psychometric test results including means and standard errors (s.e.) for the three psychometric tests [Controlled Oral Word Association (COWA), Peabody Picture Vocabulary Test - Revised (PPVT-R), and the Wisconsin Card Sorting Task (WCST)] Broken down by subject group: normal controls (NC), mixed symptomatic schizophrenics (MS), and negative symptomatic schizophrenics (NS).

Note: s.e. stands for standard error.

6.3 Behavioral Measures

6.3.1 Correct Responses

A repeated measures between group ANOVA was carried out on the total number of correct responses made for: related word pairs, unrelated word pairs, and combined related and unrelated word pairs. No significant group differences were observed.

6.3.2 Reaction Time For Correct Responses

Although reaction times were recorded for each correct response subjects made to word pair presentations, they are not considered a valid measure for assessing the speed of information processing as subjects were informed that response speed was not of interest in this study, but rather they were to take their time in order to ensure that they made correct responses. Reaction times for all correct responses were, however, analyzed in order to see if group differences were still occurring. A 3 (group) by 2 (condition) ANOVA with group as a between subjects factor and condition as a within subjects factor showed a significant effect of group [$F(2,42)$

= 6.61, $p < .004$], but no difference between word pair types. Follow up analysis indicated that NCs responded more quickly than NSs ($p < .01$), but that there were no differences between the reaction times of the MS group and either of the NC and NS groups (Figure 4).

Reaction times were also analyzed for only those correct responses that were also associated with artifact free EEG epochs (the same trials that were included in the ERP analysis). This analysis also produced a significant main effect for group [$F(2,42) = 7.85$, $p < .002$], as well as a significant interaction between group and condition [$F(2,42) = 3.27$, $p < .05$]. Additional analysis showed that NCs had faster response reaction times than NSs for the unrelated word pairs ($p < .01$), and had faster reaction times than both NS and MS groups for the related word pairs ($p < .01$). There was no significant differences between the reaction times for the MS and the NS groups (Figure 5).

6.4 Event-Related Potential Measures

A repeated measures between group ANOVA was carried out on the number of rejected ERP trials based on a combination of response accuracy and EOG artifact criteria. Trials were

Figure 4

Word Pairs: Reaction Time for Correct Trials
Reaction Time (msec)

NC less than NS ($p < .01$)

Normal Controls (NC), Mixed Schizophrenics (MS),
Negative Schizophrenics (NS)

Figure 5
Word Pairs: Reaction Time for Correct
and Artifact Free Trials

NC less than MS and NS ($p < .01$) for Related Pairs
 NC less than NS ($p < .01$) for Unrelated Pairs

rejected if subjects responded incorrectly or exhibited EOG artifact. Results indicated significant group effects for: unrelated word pairs [$F(2,24) = 3.51, p < .04$], related word pairs [$F(2,24) = 4.03, p < .03$], and combined related and unrelated word pairs [$F(2,24) = 4.06, p < .03$]. These results were followed up with Newman-Keuls analyses. No significant between group differences were observed for unrelated word pairs. The NC group had fewer rejected trials to the related word pairs than the NS group ($p < .05$), and had fewer rejected trials to the combined (related and non-related) word pairs than both NS and MS groups ($p < .05$) (Figure 6). No group differences were found when separate analyses were carried out on the number of artifact contaminated responses alone.

The grand average ERPs to related and unrelated words at each site (Fz, Cz and Pz) are presented individually for NCs, MSs and NSs in Figures 7, 8 and 9 respectively. Both related and unrelated word pairs elicited a negative component (N100: 70-160 msec), and then a positive component (P200: 120-250 msec), followed by another positive component (P300: 220-450 msec). The N400 component came next (280-500 msec), and was followed by a sustained positivity (LPC: 400-720 msec), which appeared to be more pronounced in the NC group. Each of the ERP measures were subjected to a 3 (group) by 3 (site) by 2

Figure 6
Word Pairs: Total Incorrect and
Artifact Contaminated Trials

Total Trials

NC fewer than MS and NS ($p < .05$)

Normal Controls (NC), Mixed Schizophrenics (MS),
Negative Schizophrenics (NS)

FIGURE 7
GRAND AVERAGED ERPs FOR THE NORMAL CONTROL GROUP

Grand averaged event-related potentials (ERPs) for the normal control (NC) group; at frontal (Fz), central (Cz), and posterior (Pz) scalp locations. The lighter shaded line [_____] is for the unrelated word pair condition, and the darker line [_____] is for the related word pair condition. Note that the Pz waveform is labelled with the N100, P200, P300, N400 and LPC event-related potentials.

FIGURE 8
GRAND AVERAGED ERPs FOR THE MIXED SCHIZOPHRENIC GROUP

Grand averaged event-related potentials (ERPs) for the mixed schizophrenic (MS) group; at frontal (Fz), central (Cz), and posterior (Pz) scalp locations. The lighter shaded line [] is for the unrelated word pair condition, and the darker line [] is for the related word pair condition.

FIGURE 9
GRAND AVERAGED ERPs FOR THE NEGATIVE SCHIZOPHRENIC GROUP

Grand averaged event-related potentials (ERPs) for the negative schizophrenic (NS) group; at frontal (Fz), central (Cz), and posterior (Pz) scalp locations. The lighter shaded line [_____] is for the unrelated word pair condition, and the darker line [_____] is for the related word pair condition.

(condition) ANOVA with group as a between subject factor, and condition and site as within subject factors. Follow up comparisons were made with Newman-Keuls analysis. For all analyses, alpha was set to .05.

6.4.1 N100: There were no significant differences between groups in either the amplitude or the latency of the N100 ERP.

6.4.2 P200: For the P200, there was a significant group x condition interaction for the latency of the wave form [$F(2,42) = 4.42, p < .02$]. Follow up analysis indicated that NCs had a shorter latency than NS for the related word pairs ($p < .05$), and had a shorter latency than the MS group for the unrelated word pairs ($p < .01$) (Figure 10). There were no significant differences between the three experimental groups for the amplitude of the P200.

6.4.3 P300: A three-way ANOVA of the P300 amplitude revealed a significant main effect for condition [$F(1,42) = 11.12, p < .002$] whereby the related word pairs had larger P300 amplitudes than did the unrelated word pairs; and a significant site x group interaction [$F(4,84) = 2.48, p < .05$], which when further analyzed, indicated that NCs have a larger

Figure 10
P200 Latency

NC less than NS for Related Word Pairs ($p < .05$)
 NC less than MS for Unrelated Word Pairs ($p < .01$)

P300 amplitude than NSs at Pz ($p < .05$) (Figure 11). Analysis of the P300 latencies also produced a significant main effect for condition [$F(1,42) = 11.55, p < .002$] whereby the latencies to the unrelated word pairs were shorter than to the related word pairs; and a significant site $\times$ group interaction [$F(4,84) = 3.31, p < .02$]. Follow up analysis suggested that at Fz, NCs have an earlier P300 than both MSs ($p < .01$) and NSs ($p < .05$), and at Cz and Pz, NCs have an earlier P300 than MS ($p < .01$), (Figure 12). No differences were found between the MS and NS groups for either amplitude or latency measures.

6.4.4 N400: Analysis for the amplitude measure of the N400 wave form produced a significant condition main effect [$F(1,42) = 35.13, p < .001$] whereby the unrelated word pairs elicited a larger N400 amplitude than the related word pairs; and a significant site $\times$ condition interaction [$F(2,84) = 3.53, p < .04$]. No significant group effects were found.

For latency measures of the N400, significant main effects for both site and group were found [$F(2,84) = 6.99, p < .002$; and $F(2,42) = 17.98, p < .001$ respectively]. Follow up analysis determined that the NC group had a shorter latency N400 than either the MS or NS groups ($p < .01$). The two patient groups, however, did not differ significantly (Figure 13).

Figure 11
P300 Amplitude

Amplitude (μv)

Normal Controls (NC)

Mixed Schizophrenics (MS)

Negative Schizophrenics (NS)

NC is greater than NS at Pz ($p < .05$).

Normal Controls (NC), Mixed Schizophrenics (MS),
Negative Schizophrenics (NS)

Figure 12
P300 Latency

NC is less than MS and NS for Fz ($p < .01, p < .05$)

NC is less than MS for Cz ($p < .01$)

NC is less than MS for Pz ($P < .01$)

Figure 13
N400 Latency

N400 Latency (msec)

NC is less than MS and NS ($p < .01$)

Normal Controls (NC), Mixed Schizophrenics (MS),
Negative Schizophrenics (NS)

Analysis on the N400 difference waveform (acquired from each subject by digitally subtracting related waveforms from unrelated waveforms), found no significant differences between groups.

6.4.5 LPC: Analysis of the LPC amplitude following the N400 ERP revealed a significant site x group interaction [$F(4,84) = 5.66, p < .001$]. Further analysis determined that NCs had a significantly larger LPC amplitude at Pz than either of the MS or NS groups ($p < .01$). There were no significant amplitude differences between the patient groups (Figure 14).

Latency analysis of the LPC produced a significant site x condition x group interaction [$F(4,84) = 2.87, p < .03$]. Subsequent ANOVAs on the data for each condition revealed a significant site x group interaction [$F(4,84) = 4.78, p < .002$], and a significant main effect for site [$F(2,84) = 3.51, p < .04$] under the related word pair condition. No significant differences were found for the unrelated condition (Figure 15).

Figure 14
LPC Amplitude

Amplitude (μV)

Normal Controls (NC)

Mixed Schizophrenics (MS)

Negative Schizophrenics (NS)

NC is greater than MS and NS for Pz ($p < .01$)
Normal Controls (NC), Mixed Schizophrenics (MS),
Negative Schizophrenics (NS)

Figure 15: LPC Latency

Figure 15a Related Word Pairs

Normal Controls (NC) Mixed Schizophrenics (MS) Negative Schizophrenics (NS)

Main Effect of Site, $F(2,84)=3.51$, $p<.05$
 Site x Group Interaction, $F(4,84)=4.78$, $p<.05$

Figure 15b Unrelated Word Pairs

Normal Controls (NC) Mixed Schizophrenics (MS) Negative Schizophrenics (NS)

No Significant Effects

6.5 Data Correlations

All correlations were carried out on combined group data, as well as on the data for each group individually.

6.5.1 N400 ERP Measures and Neuropsychological Test Scores

The first set of correlations compared the N400 amplitude (difference scores) and latencies for all subjects combined, with the three measures of the WCST: categories completed, errors committed, and percent perseverative errors committed. Significant combined group correlations were found between the total number of errors made on the WCST and the N400 latency at Cz ($R = .305$, $p < .05$). No significant correlations were found with the separate correlated analysis carried out in each of the three subject groups.

Significant combined group correlations of the total COWA test score include the N400 latency at Fz, Cz and Pz sites ($R = -.391$, $p < .008$; $R = -.420$, $p < .004$; and $R = -.347$, $p < .02$ respectively). These results indicated that reduced verbal output, as measured by the COWA test, was negatively correlated with a delayed latency of the N400 ERP.

There were no significant correlations between the COWA

total score and the N400 amplitude and latency measures for either MS or NS groups, however the COWA total verbal output for the NC group was negatively correlated with the N400 latency at Cz and Pz sites ($R = -.575$, $p < .03$; and $R = -.674$, $p < .006$ respectively).

6.5.2 N400 ERP Measures and Clinical Rating Scores

There were no significant correlations for either the MS group, the NS group, or for both patient groups combined.

6.5.3 N400 ERP Measures and Medication Related Data

At the time this study was conducted, all of the patients (with the exception of one negative symptomatic schizophrenic) were being treated with antipsychotic medications (Table 5). Most patients were receiving one or more adjunct medications at the time of testing (Table 6). The CPZ equivalent of each subjects' daily dosage of neuroleptic drug therapy was correlated with N400 amplitudes and latencies at each electrode site for each of the two patient groups, in order to assess the effect of neuroleptic treatment on the obtained ERP results. None of the correlations were statistically

significant.

Similar correlations were conducted on ESRS symptoms with the N400 amplitudes and latencies at each electrode site, in order to see if the side effects of the neuroleptic medication were affecting the ERP waveforms. Once again, none of the correlations reached significance.

TABLE 5:
ANTIPSYCHOTIC MEDICATION DOSAGES
FOR SCHIZOPHRENIC PATIENT GROUPS

MIXED SYMPTOMATIC GROUP:			NEGATIVE SYMPTOMATIC GROUP:		
Subject No.	Type of Medication	Dose	Subject No.	Type of Medication	Dose
1	Methotrimeprazine Flupenthixol	10mg/day(10) 35mg,IM/2wks(1000)	1	Remoxipride	300mg/day(500)
2	Haloperidol	150mg,IM/2wks(500)	2	Haloperidol	300mg,IM/2wks(1000)
3	Methotrimeprazine	75mg/day(75)	3	Remoxipride	450mg/day(75u)
4	Flupenthixol	6mg/day(300)	4	None	------(000)
5	Fluanxol	12mg/day(600)	5	Stelazine Chlorpromazine Fluphenazine	10mg/day(250) 100mg/day(100) 20mg,IM/4wks(200)
6	Fluphenazine	12.5mg,IM/4wks(125)	6	Fluphenazine Chlorpromazine	67.5mg,IM/4wks(675) 50mg/day(50)
7	Pipotiazine Palmitate Chlorpromazine	75mg,IM/2wks(375) 200mg/day(200)	7	Haloperidol	200mg,IM/4wks(350)
8	Remoxipride Haloperidol	150mg/day(250) 5mg/day(250)	8	Pipotiazine Palmitate Chlorpromazine	200mg,IM/2wks(1000) 200mg/day(200)
9	Fluanxol	12mg/day(600)	9	Methotrimeprazine Fluphenazine	200mg/day(200) 100mg,IM/4wks(1000)
10	Flupenthixol	25mg,IM/4wks(250)	10	Fluphenazine	25mg,IM/4wks(250)
11	Flupenthixol Chlorpromazine	30mg,IM/3wks(350) 300mg/day(300)	11	Pimozide	3mg/day(100)
12	Haloperidol	150mg,IM/2wks(500)	12	Clozapine	300mg/day(600)
13	Clozapine	500mg/day(1000)	13	Risperidone	5mg/day(800)
14	Fluphenazine Perphenazine	60mg,IM/4wks(600) 8mg/day(70)	14	Fluphenazine Methotrimeprazine	30mg,IM/4wks(300) 50mg/day(50)
15	Clozapine	200mg/day(400)	15	Pipotiazine Palmitate	80mg,IM/2wks(400)

The antipsychotic (neuroleptic) medications and dosages that both mixed and negative symptomatic schizophrenic patients were taking at the time of study enrolment. Dosages include both depot medications (taken daily), and intramuscular (IM) medications (typically administered every 2,3 or 4 weeks). Chlorpromazine (CPZ) equivalencies are given in brackets beside the medication dosages.

TABLE 6:
ADJUNCT MEDICATION DOSAGES
FOR SCHIZOPHRENIC PATIENT GROUPS

MIXED SYMPTOMATIC GROUP:			NEGATIVE SYMPTOMATIC GROUP:		
Subject No.	Type of Medication	Dose	Subject No.	Type of Medication	Dose
1	Rivotril Procyclidine	2mg/day 10mg/day	1	Cogentin	2mg/day
2	Clonazepam Cogentin	1mg/day 2mg/day	2	Carbamazepine Depakene	20mg/day 500mg/day
3	None	-----	3	Cogentin	2mg/day
4	Procyclidine Serax	5mg/day 15mg/day	4	None	-----
5	Flurazepam Imipramine Prozac	30mg/day 125mg/day 20mg/day	5	Cogentin	2mg/day
6	Lorazepam	1mg/day	6	Cogentin	2mg/day
7	Cogentin	2mg/day	7	None	-----
8	Cogentin	2mg/day	8	Procyclidine	10mg/day
9	Cogentin	2mg/day	9	Cogentin Tegritol	2mg/day 300mg/day
10	None	-----	10	Flurazepam	30mg/day
11	Lithium Procyclidine	1500mg/day 5mg/day	11	Clonazepam	1mg/day
12	Cogentin Clonazepam	4mg/day .5mg/day	12	None	-----
13	Mitoprolol Cogentin	50mg/day 2mg/day	13	Clonazepam	1mg/day
14	Procyclidine	15mg/day	14	None	-----
15	Prozac	20mg/day	15	Procyclidine Rivotril Ranitidine	5mg/day 0.5mg/day 150mg/day

Adjunct medications and dosages that both mixed and negative symptomatic schizophrenic patients were taking at the time of study enrolment. Normal controls were not taking any medication at the time of testing with the exception that 2 of the 3 female controls were on birth control pills

7. DISCUSSION

The contextual effects of the related and unrelated word pairs were observed in the ERPs of all three experimental groups and at each recording site. This N400 potential is therefore believed to reflect the semantic incongruencies found between the words used in the word pair stimulus conditions, and is consistent with previous findings (Harvey & Marsh, 1983; Harbin et al., 1984; Bentin, 1987).

The fact that no between group differences were found either for performance accuracy or for the N400 amplitude suggests that schizophrenic patients may not suffer impairments in semantic processing as was hypothesized. This finding of normal amplitude N400s in schizophrenia is consistent with data from Koyama et al., (1991), and has received conditional support from other studies whereby amplitude differences between normal controls and schizophrenics were found for some patients, and not for others (Adams et al., 1989; Grillon et al., 1991). While subtle differences may have been obscured by the large amount of variability within each of the three testing groups, sample sizes were sufficiently large enough to detect a moderate effect, if significant differences were actually present

(Streiner, 1990).

The amplitude results obtained in this study may differ from those of other studies as a result of different methodologies employed, such as the use of sentence completion versus the use of word pair stimuli, different amplifier settings, instructions and equipment. Also, variations in subject populations, such as chronic versus episodic or paranoid versus residual schizophrenics, may have differentially affected study results. In this study, there was considerable heterogeneity within the subdiagnosis of the schizophrenic patients (please see Table 2). This may have obscured possible differences between patient groups by having large numbers of residual (MS=6, NS=4), and undifferentiated (MS=1, NS=7) patients. Future studies may wish to include only specific patient subtypes in order to assess differences between homogeneous subgroups of schizophrenic patients.

Both MS and NS groups however, had significantly delayed N400 latencies compared to normal controls which may suggest that schizophrenic patients suffer a slowing of their semantic processing mechanisms (Yates, 1966). This conclusion is supported by the significantly slower reaction time of patients (for correct and artifact free responses) compared to normal controls. This support is conditional, however, as all

subjects were instructed to take their time in responding to stimuli, in order to reduce possible confounding effects on the P300 waveform.

If schizophrenic patients actually do process semantic information more slowly than normal controls, this could explain many of their overt symptoms including disorganized thought and disrupted speech patterns. Interference caused by verbal stimuli that have not been fully processed may lead to

disruption in the normal flow of processing (Braff & Saccuzzo, 1981). As it is believed that the timing and accuracy with which thoughts are processed are dependant upon the speed of semantic processing, processing delays could have serious negative effects on language-related functions (Grillon et al., 1991). Normal amplitudes and delayed latencies of the N400 potential in schizophrenic patients are consistent with the results of Koyama et al. (1991).

It has also been suggested that the N400 ERP is related to the memory search processes that are required to identify contextual stimuli (Stuss et al., 1986). According to this hypothesis, shorter latencies for the N400 potential would reflect faster stimulus identification given appropriate (related word pairs) rather than inappropriate (unrelated word pairs) contextual cues. The delayed N400 in the schizophrenic

groups therefore, might also reflect a prolonged memory search in this population. Although schizophrenics as a group had delayed latencies compared to normal controls, there were no differences found between the negative and mixed symptomatic subgroups for either latency or amplitude measures. This finding fails to support the hypothesis that patient differences would be significantly more pronounced in the negative symptomatic group as compared to the mixed symptomatic group.

While it may be argued that schizophrenic patients have a delayed processing of all ERP components, no group differences were observed for either the amplitude or latency of the N100 component. The latency of the P200 component however, was delayed in the MS group for unrelated word pairs, and in the NS group for related word pairs, compared to NCs. This may suggest that group differences are related to both sensory processes as well as to semantic processes.

Analysis of the P300 component found that the NC group had larger amplitude than the NS group at Pz, while analysis of group latencies suggests that the processing of the second word in each word pair occurs more quickly in NCs than in either of the patient groups. These findings are similar to that of previous studies on the P300 ERP, and may be

indicative of a general slowing of cognitive functioning in schizophrenic patients (Braff & Saccuzzo, 1981).

The Pz LPC in the control group was significantly larger than that of either of the two patient groups for both related and unrelated word pair conditions. This finding is contradictory to that of Tadaï et al. (1987), where it was reported that the LPC for schizophrenic patients did not differ over the central-parietal region compared to normal controls, but was smaller in the frontal region. This non-significant trend of reduced frontal amplitude of the LPC and N400 components within the schizophrenic group reported by Koyama et al. (1991), may suggest possible frontal lobe abnormality in that patient population. This study however, failed to confirm these findings with respect to LPC or N400 potentials, and as such do not implicate frontal deficits as hypothesized.

Although electrocortical indices failed to uphold a frontal lobe deficit in NS patients, neuropsychological data evidenced partial support for this contention. It is particularly interesting to note that the NC group did significantly better than the NS group on all three WCST measures, and better than the MS group on the WCST measure of total errors committed. This suggests that NCs were better

able to form abstract concepts and to shift and maintain abstract sets, all of which are believed to reflect frontal lobe functioning (Bronstein, 1986; Robinson et al., 1980). Heaton (1981) suggests that subcategories such as "categories completed" and "percent perseverative errors" provide information on problem solving behaviour beyond the basics of success and failure, and are useful in predicting the presence or absence of frontal lobe dysfunction. Sullivan et al. (1991), has also suggested that perseveration errors on the WCST likely reflect poor functioning of the dorsolateral prefrontal cortex. Thus the poor performance by the NS group suggests that these patients may exhibit impaired frontal lobe processes. It is unlikely that these group differences are attributable to education level, as previous studies have found that schizophrenics have average overall intellectual abilities (Braff et al., 1991; Seidman, 1983), and that differing test results are not correlated with education level.

The finding that NCs were able to produce more words in the COWA test than the NSs, but not more than the MSs, lends support to the ubiquitous belief that a primary symptom or characteristic of a "negative-symptomatic" schizophrenic is poverty of speech (Crow, 1985). These combined findings of

poor NS performance on the WCST, and reduced verbal fluency as measured by the COWA test, are consistent with the literature suggesting negative symptoms are closely related to deficits of frontal lobe functioning (Crow, 1980; Stuss and Benson, 1986).

Correlational analysis found that for all subjects, increased total errors committed on the WCST is correlated with a prolonged latency for the N400 ERP at Cz. Increased total word output for the COWA test was correlated with shorter N400 latencies at all recording sites for all groups combined, and at Cz and Pz for the individual control group analysis. The results from these correlations taken together, suggest that better performance on these tests is related to shorter latency measures of the N400 ERP.

The possibility that the effects of the antipsychotic medications which patients were receiving at the time of testing somehow contributed to the observed group differences in the latency of the N400 potential appears unlikely. First, the CPZ equivalencies of the patients daily neuroleptic treatment, as well as any side effects of the neuroleptic medications as measured by the ESRS, did not correlate with any of the N400 measures. Second, research has suggested that antipsychotic medication does not contribute to, and may

actually reverse the slowness of information processing believed to occur in schizophrenic patients (Braff and Saccuzzo, 1982). Finally, the article by Grillon et al. (1991) also found there to be no correlation between CPZ equivalencies, and the associated ERP results.

It could also be argued that ERP differences were somehow related to the number of years of formal education subjects had received, however this too appears unlikely. First of all, the word pairs that were chosen for use in this study were easily comprehensible (Carol and White, 1973), occur frequently in the English language (Thornlike and Lorge, 1944), and were used originally in a study designed to assess language processing in children (personal correspondence with C. Grillon, 1992). Second, subject groups were not found to differ on the basis of their scores on the PPVT-R, a test believed to reflect verbal intelligence (Dunn & Dunn, 1981), and therefore, it appears that differences in ERP results cannot be attributed to differences in intellectual status.

In this attempt to differentiate between predominantly negative and mixed symptomatic schizophrenic patients, no significant differences were found. Future studies might endeavour to use more homogeneous groups of schizophrenic patients such that the positive symptom subgroup would suffer

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few, if any, negative symptoms and the negative symptom subgroup would suffer few, if any, positive symptoms. Testing predominantly positive symptomatic patients may, however, prove to be problematic in view of their overt behavioral symptoms, and excessive EOG artifact.

Another direction for future research would be to analyze within subject dynamic changes following the course of an acute episode of schizophrenia. Patients would be tested during the acute period, and again upon successful treatment with neuroleptic medication. Groups would be divided up between those patients suffering from predominantly negative symptoms, and those who are virtually symptom free. It is within reason to suggest that for differing reasons, positive and negative symptoms contribute to language deficits in schizophrenia, and it may be that the monitoring of the fluctuations in these symptoms over time would be a more sensitive approach to unravelling the role of these pathological processes in schizophrenic language disturbance.

In the future, research might also include left and right recording sites in order to assess possible hemispheric asymmetries of the N400 potential, as initial work in this area has shown promising results (Grillon et al., 1991; McCarley et al., 1991). This would give a more complete

topographical representation of the N400 ERP, and perhaps give further insight into differences in the distribution of this potential between schizophrenics patients and normal controls. The inclusion of an additional psychiatric population such as depressed patients, would also be useful in assessing whether differences found between schizophrenic patients and normal controls are unique to schizophrenia, or more related to psychopathology in general.

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9.1 APPENDIX A: CONSENT FORM

CONSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY

TITLE OF PROJECT: LANGUAGE DYSFUNCTION IN NEGATIVE AND MIXED SYMPTOMATIC SCHIZOPHRENIC SUBGROUPS AS EVIDENCED BY THE N400 EVENT-RELATED POTENTIAL: A COMPARISON WITH NORMAL CONTROLS

PRINCIPLE INVESTIGATOR: DUNCAN DE LUGT, B.A.Hons.

THESIS SUPERVISOR: VERNER KNOTT, D.Phil., C.Psych.

STUDY COLLABORATORS: SCOT PURDON, Ph.D. - consultant for neuro-psychological testing
BARRY JONES, M.D. - subject referral source
ALAIN LABELLE, M.D. - subject referral source

INTRODUCTION:

We invite you to take part in this research study at the Royal Ottawa Hospital. It is important that you read and understand several general rules that apply to all who take part in this study:

- a) taking part in this study is voluntary;
- b) there will be no personal benefit from taking part in this study, but knowledge may be gained that will improve our understanding of schizophrenia;
- c) you may withdraw from this study at any time
- d) your name and any personal information will be kept strictly confidential, and will not be revealed without your expressed written consent

The nature of this study and other important information are discussed below. You are urged to discuss any questions you have about this study with any of the investigators listed above.

APPENDIX A: CONTINUED...

PURPOSE OF THIS STUDY:

Language problems are a recognized symptom of schizophrenia and patients with a diagnosis of schizophrenia are known to have problems in relating words, understanding sentences and producing logical coherent speech. These problems can be assessed by tests carried out in the laboratory, and it is the purpose of this study to examine whether certain language problems are seen in certain types of schizophrenic patients and not in others; and to determine whether these problems are associated with measures of brain function.

Brain function can be measured by placing sensors on the scalp which record electrical activity referred to as an electroencephalogram (EEG). In this study, the EEG will be recorded during a language test, and the results from the EEG and the test collected from schizophrenic patients will be compared to results from the same tests administered to non-patients.

PROCEDURES INVOLVED:

You will be asked to attend the hospital for one 90 minute session to fill in several questionnaires and some paper and pencil tests that will provide us with information on general and specific psychological abilities and on language comprehension.

Following these tests, you will be asked to sit in a chair while the research assistant places sensors on your scalp and explains the language test to you. During the language test you will be asked to watch a computer monitor for words appearing on the screen and you will be required to press a response button after the presentation of some of these words. There are no associated risks with this testing except for some minor scalp irritation when sensors are placed on the scalp.

APPENDIX A: CONTINUED...

CONSENT FORM

I, _____ have read the explanation of the study, have had the opportunity to ask questions and agree to participate in the above described research project, the nature of which has been explained to me.

I also consent that any data collected as a result of my participation in this project may be utilised for education and/or scientific purposes, and that my identity and personal information will be kept strictly confidential.

I have received assurances that my participation in this study is voluntary, and that I may withdraw from participation at any time, without affecting any treatment that I may be receiving.

I further understand that my legal rights, regarding negligence and the liability of the institution or its agents, are not waived.

If I have any further questions about this study, I can contact any of the above named investigators, through the Royal Ottawa Hospital, 1145 Carling Avenue, Ottawa, Ontario, K1Z-7K4, Phone: 722-6521.

DATE

SIGNATURE OF RESEARCH SUBJECT

DATE

SIGNATURE OF WITNESS

9.2 APPENDIX B: PANSS FOR SCHIZOPHRENIA

POSITIVE AND NEGATIVE SYMPTOM SCALE FOR SCHIZOPHRENIA

Instructions: Circle the appropriate rating for each item following the specified clinical interview. Refer to the Rating Manual for item definitions, description of anchoring points and scoring procedure.

0 = not present, 1 = very mild, 2 = mild, 3 = moderate,
4 = moderate severe, 5 = severe, 6 = extremely severe

1) POSITIVE SUBSCALE

P1 Delusions.....	0	1	2	3	4	5	6
P2 Conceptual disorganization.....	0	1	2	3	4	5	6
P3 Hallucinatory behaviour.....	0	1	2	3	4	5	6
P4 Excitement.....	0	1	2	3	4	5	6
P5 Grandiosity.....	0	1	2	3	4	5	6
P6 Suspiciousness/persecution.....	0	1	2	3	4	5	6
P7 Hostility.....	0	1	2	3	4	5	6
Subtotal							

2) NEGATIVE SUBSCALE

N1 Blunted affect.....	0	1	2	3	4	5	6
N2 Emotional withdrawal.....	0	1	2	3	4	5	6
N3 Poor rapport.....	0	1	2	3	4	5	6
N4 Passive social withdrawal.....	0	1	2	3	4	5	6
N5 Difficulty in abstract thinking.....	0	1	2	3	4	5	6
N6 Lack of spontaneity/conversation.....	0	1	2	3	4	5	6
N7 Stereotyped thinking.....	0	1	2	3	4	5	6
Subtotal							

3) GENERAL PSYCHOPATHOLOGY SUBSCALE

G1 Somatic concern.....	0	1	2	3	4	5	6
G2 Anxiety.....	0	1	2	3	4	5	6
G3 Guilt feelings.....	0	1	2	3	4	5	6
G4 Tension.....	0	1	2	3	4	5	6
G5 Mannerism and posturing.....	0	1	2	3	4	5	6
G6 Depression.....	0	1	2	3	4	5	6
G7 Motor retardation.....	0	1	2	3	4	5	6
G8 Uncooperativeness.....	0	1	2	3	4	5	6
G9 Unusual thought content.....	0	1	2	3	4	5	6
G10 Disorientation.....	0	1	2	3	4	5	6
G11 Poor attention.....	0	1	2	3	4	5	6
G12 Lack of judgement and insight.....	0	1	2	3	4	5	6
G13 Disturbance of volition.....	0	1	2	3	4	5	6
G14 Poor impulse control.....	0	1	2	3	4	5	6
G15 Preoccupation.....	0	1	2	3	4	5	6
G16 Active social avoidance.....	0	1	2	3	4	5	6
Subtotal							

9.3 APPENDIX C: SUBJECT RECRUITMENT QUESTIONNAIRE

SUBJECT RECRUITMENT QUESTIONNAIRE

1. Psychiatrist: _____
2. Patient Name: _____
Chart Number: _____
Age: _____
Sex: _____
Primary Diagnosis: _____
Age of Onset: _____
Episodic/Chronic course: _____
Sub-Diagnosis: (ie. differentiate whether the
schizophrenic sub-type is catatonic; disorganized;
paranoid; residual; or undifferentiated)

3. Medications Subject is Currently Taking:
 1. Name: _____ Dose: _____
CPZ equivalent: _____ Duration: _____
 2. Name: _____ Dose: _____
CPZ equivalent: _____ Duration: _____
 3. Name: _____ Dose: _____
CPZ equivalent: _____ Duration: _____

APPENDIX C: CONTINUED...

4. Adjunct Medications:

1. Name: _____ Dose: _____
Duration: _____
2. Name: _____ Dose: _____
Duration: _____
3. Name: _____ Dose: _____
Duration: _____

5. Has the patient received E.C.T. in the last month?

Yes _____ / No _____

6. What is the maximum level of education achieved by the patient?

	<u>YES</u>	<u>NO</u>	<u>YEAR OBTAINED</u>
a) Grade School	_____	_____	_____
b) High School	_____	_____	_____
c) College	_____	_____	_____
d) University	_____	_____	_____

Also, please include the Experimental Symptom Rating Scale (ESRS)

9.4 APPENDIX D: ESRS SCORING FORM

Extrapyramidal Symptom Rating Scale (ESRS)

I PARKINSONISM, DYSTONIA AND DYSKINESIA:

Questionnaire and behavioral scale

Answer questions by checking the appropriate box for each item.

	Absent	Mild	Moderate	Severe
1. Impression of slowness or weakness, difficulty in carrying out routine tasks	___	___	___	___
2. Difficulty walking or with balance	___	___	___	___
3. Difficulty swallowing or talking	___	___	___	___
4. Stiffness, stiff posture	___	___	___	___
5. Cramps or pains in limbs, back or neck	___	___	___	___
6. Restless, nervous, unable to keep still	___	___	___	___
7. Tremors, shaking	___	___	___	___
8. Oculogyric crisis, abnormal sustained posture	___	___	___	___
9. Increased salivation	___	___	___	___
10. Abnormal involuntary movements (dyskinesia) of extremities or trunk	___	___	___	___
11. Abnormal involuntary movements (dyskinesia) of tongue, jaw, lips or face	___	___	___	___
12. Dizziness when standing up (especially in the morning)	___	___	___	___

APPENDIX D: CONTINUED...

II PARKINSONISM - Physician's examination

Enter the appropriate score for each item

1. Expressive automatic movements (facial mask/speech):
 - 0: Normal
 - 1: Very mild decrease in facial expressiveness
 - 2: Mild decrease in facial expressiveness
 - 3: Rare spontaneous smile, decrease blinking, voice slightly monotonous
 - 4: No spontaneous smile, staring gaze, low monotonous speech, mumbling
 - 5: Marked facial mask, unable to frown, slurred speech
 - 6: Extremely severe facial mask with unintelligible speech
2. Bradykinesia:
 - 0: Normal
 - 1: Global impression of slowness in movements
 - 2: Definite slowness in movements
 - 3: Very mild difficulty in initiating movements
 - 4: Mild to moderate difficulty in initiating movements
 - 5: Difficulty in starting or stopping any movement, or freezing on initiating voluntary act
 - 6: Rare voluntary movement, almost completely immobile
3. Rigidity: Right arm / Left arm / Right leg / Left leg
 - 0: Normal muscle tone
 - 1: Very mild, barely perceptible
 - 2: Mild (some resistance to passive movements)
 - 3: Moderate (definite resistance to passive movements)
 - 4: Moderately severe (moderate resistance but still easy to move the limb)
 - 5: Severe (marked resistance with definite difficulty to move the limb)
 - 6: Extremely severe (nearly frozen)
4. Gait and Posture:
 - 0: Normal
 - 1: Mild decrease of pendular arm movement
 - 2: Moderate decrease of pendular arm movement, normal steps
 - 3: No pendular arm movement, head flexed, steps more or less normal
 - 4: Stiff posture (neck, back), small step (shuffling gait)
 - 5: More marked, festination or freezing on turning
 - 6: Triple flexion, barely able to walk

APPENDIX D: CONTINUED...

5. Tremor:

right arm	___	head	___
left arm	___	jaw/chin	___
right leg	___	tongue	___
left leg	___	lips	___

None:	0
Borderline:	1
Small amplitude:	Occasional: 2
	Frequent: 3
	Constant or almost so: 4
Moderate amplitude:	Occasional: 3
	Frequent: 4
	Constant or almost so: 5
Large amplitude :	Occasional: 4
	Frequent: 5
	Constant or almost so: 6

6. Akathisia:

- 0: None
- 1: Looks restless, nervous, impatient, uncomfortable
- 2: Needs to move at least one extremity
- 3: Often needs to move one extremity or to change position
- 4: Moves one extremity almost constantly if sitting, or stamps feet while standing
- 5: Unable to sit down for more than a short period of time
- 6: Moves or walks constantly

7. Sialorrhea:

- 0: Absent
- 1: Very mild
- 2: Mild
- 3: Moderate: impairs speech
- 4: Moderately severe
- 5: Severe
- 6: Extremely severe: drooling

8. Postural stability:

- 0: Normal
- 1: Hesitation when pushed but no retropulsion
- 2: Retropulsion but recovers unaided
- 3: Exaggerated retropulsion without falling
- 4: Absence of postural response, would fall if not caught by examiner
- 5: Unstable while standing, even without pushing
- 6: Unable to stand without assistance

APPENDIX D: CONTINUED...

III DYSTONIA - Physician's examination

Enter the appropriate score for each item

1. Acute torsion dystonia:

Right arm	___	Head	___	0: Absent
Left arm	___	Jaw	___	1: Very mild
Right leg	___	Tongue	___	2: Mild
Left leg	___	Lips	___	3: Moderate
				4: Moderately Severe
				5: Severe
				6: Extremely Severe

2. Non-acute or chronic or tardive dystonia:

Right Arm	___	Head	___	0: Absent
Left arm	___	Jaw	___	1: Very Mild
Right leg	___	Tongue	___	2: Mild
Left leg	___	Lips	___	3: Moderate
				4: Moderately Severe
				5: Severe
				6: Extremely Severe

IV DYSKINETIC MOVEMENTS - Physician's examination

Enter the appropriate score for each item

1. Lingual Movements (Slow lateral or torsion movement of tongue)

None: 0

Borderline: 1

Clearly present within oral cavity: O:2 F:3 C:4

With occasional partial protrusion: O:3 F:4 C:5

With complete protrusion: O:4 F:5 C:6

2. Jaw Movements (Lateral movement, chewing, biting, clenching)

None: 0

Borderline: 1

Clearly present, small amplitude: O:2 F:3 C:4

Moderate amplitude, but without mouth opening: O:3 F:4 C:5

Large amplitude, with mouth opening: O:4 F:5 C:6

3. Bucco-Labial Movements (Puckering, pouting, smacking, etc.)

None: 0

Borderline: 1

Clearly present, small amplitude: O:2 F:3 C:4

Moderate amplitude, forward movement of lips: O:3 F:4 C:5

Large amplitude, marked, noisy smacking of lips: O:4 F:5 C:6

APPENDIX D: CONTINUED...

4. Truncal Movements (Rocking, twisting, pelvic gyrations)
None: 0
Borderline: 1
Clearly present, small amplitude: O:2 F:3 C:4
Moderate amplitude: O:3 F:4 C:5
Greater amplitude: O:4 F:5 C:6
5. Upper Extremities (Choreoathetoid movements only: arms, wrists, hands, fingers)
None: 0
Borderline: 1
Clearly present, small amplitude, movements of one limb: O:2 F:3 C:4
Moderate amplitude, movement of one limb or movement of small amplitude involving two limbs: O:3 F:4 C:5
Greater amplitude, movement involving two limbs: O:4 F:5 C:5
6. Lower Extremities (Choreoathetoid movements only: legs, knees, ankles, toes)
None: 0
Borderline: 1
Clearly present, small amplitude, movements of one limb: O:2 F:3 C:4
Moderate amplitude, movement of one limb or movement of small amplitude involving two limbs: O:3 F:4 C:5
Greater amplitude, movement involving two limbs: O:4 F:5 C:6
7. Other Involuntary Movements (Swallowing, irregular respiration, frowning, blinking, grimacing, sighing, etc.)
None: 0
Borderline: 1
Clearly present, small amplitude O:2 F:3 C:4
Moderate amplitude O:3 F:4 C:5
Greater amplitude O:4 F:5 C:6

APPENDIX D: CONTINUED...

V CLINICAL GLOBAL IMPRESSION OF SEVERITY OF DYSKINESIA

Considering your clinical experience, how **severe** is the dyskinesia at this time?

Absent:	0	Moderately severe:	5
Borderline:	1	Marked:	6
Very mild:	2	Severe:	7
Mild:	3	Extremely severe:	8
Moderate:	4		

VI CLINICAL GLOBAL IMPRESSION OF SEVERITY OF PARKINSONISM

Considering your clinical experience, how **severe** is the parkinsonism at this time?

Absent:	0	Moderately severe:	5
Borderline:	1	Marked:	6
Very mild:	2	Severe:	7
Mild:	3	Extremely severe:	8
Moderate:	4		

9.5 APPENDIX E: WORD PAIR STIMULI

WORD PAIR STIMULI

Similar Word Pairs

truck/jeep
horse/donkey
winter/summer
wagon/train
colour/green
knee/leg
milk/cow
fire/hot
carrot/corn
bus/car
house/home
peach/grapes
teacher/student
ketchup/mustard
dresser/couch
man/woman
door/window
water/rain
dog/cat
salt/pepper
lion/tiger
doctor/nurse
bow/arrow
fireman/police
hat/coat

Dissimilar Word Pairs

ketchup/street
fireman/pig
hat/gun
clown/tree
bottle/school
food/number
water/box
ice/black
pear/glove
uncle/wall
arm/cherries
house/star
cake/lamp
chicken/moon
guitar/dress
map/celery
door/lemon
sister/road
horse/blue
moon/bicycle
spoon/flower
queen/rabbit
orange/baby
shirt/wood
eagle/cup

APPENDIX E: CONTINUED...

Similar Word Pairs

ice/cold
clown/circus
bottle/glass
food/bread
shirt/pants
eagle/parrot
socks/shoes
pear/banana
chair/table
bed/desk
uncle/aunt
arm/hand
cake/pie
orange/apple
chicken/egg
guitar/trumpet
sister/brother
moon/sun
spoon/fork
queen/king

Dissimilar Word Pairs

bus/turkey
wagon/tea
milk/movie
knee/juice
fire/sleep
colour/head
dresser/mouth
elephant/chair
bed/fruit
lion/basket
dog/book
winter/butter
carrot/piano
peach/finger
teacher/fish
socks/lettuce
truck/dinner
salt/bridge
doctor/plane
bow/drink

9.6 APPENDIX F: REVISED PPVT SCORING SHEET

Plate			Plate		
Number	Word	Key Response	Number	Word	Key Response
1	bus	(4)	49	faucet	(2)
2	hand	(1)	50	group	(3)
3	bed	(3)	51	stem	(3)
4	tractor	(2)	52	vase	(3)
5	closet	(1)	53	pedal	(1)
6	snake	(4)	54	capsule	(2)
7	boat	(2)	55	surprised	(4)
8	tire	(3)	56	bark	(2)
9	cow	(1)	57	mechanic	(2)
10	lamp	(4)	58	tambourine	(1)
11	drum	(3)	59	disappointment	(4)
12	knee	(4)	60	awarding	(3)
13	helicopter	(2)	61	pitcher	(3)
14	elbow	(4)	62	reel	(1)
15	bandage	(4)	63	signal	(1)
16	feather	(1)	64	trunk	(2)
17	empty	(3)	65	human	(2)
18	fence	(4)	66	nostril	(1)
19	accident	(2)	67	disagreement	(1)
20	net	(2)	68	exhausted	(2)
21	tearing	(4)	69	vine	(4)
22	sail	(1)	70	ceremony	(4)
23	measuring	(2)	71	casserole	(2)
24	peeling	(3)	72	vehicle	(4)
25	cage	(1)	73	globe	(3)
26	tool	(4)	74	filing	(3)
27	square	(4)	75	clamp	(2)
28	stretching	(1)	76	reptile	(2)
29	arrow	(2)	77	island	(1)
30	tying	(2)	78	spatula	(3)
31	nest	(1)	79	cooperation	(4)
32	envelope	(2)	80	scalp	(4)
33	hook	(3)	81	twig	(2)
34	pasting	(4)	82	weasel	(2)
35	patting	(1)	83	demolishing	(4)
36	penguin	(1)	84	balcony	(1)
37	sewing	(2)	85	locket	(1)
38	delivering	(1)	86	amazed	(3)
39	diving	(2)	87	tubular	(1)
40	parachute	(3)	88	tusk	(1)
41	furry	(4)	89	bolt	(3)
42	vegetable	(4)	90	communication	(4)
43	shoulder	(3)	91	carpenter	(2)
44	dripping	(2)	92	isolation	(1)
45	claw	(4)	93	inflated	(3)
46	decorated	(3)	94	coast	(3)
47	frame	(1)	95	adjustable	(2)
48	forest	(3)	96	fragile	(3)

APPENDIX F: CONTINUED...

Plate			Plate		
Number	Word	Key Response	Number	Word	Key Response
97	assaulting	(1) _____	141	wrath	(3) _____
98	appliance	(1) _____	142	incandescent	(4) _____
99	pyramid	(4) _____	143	arrogant	(2) _____
100	blazing	(1) _____	144	confiding	(3) _____
101	hoisting	(1) _____	145	rhombus	(3) _____
102	arch	(4) _____	146	nautical	(3) _____
103	lecturing	(4) _____	147	tangent	(1) _____
104	dilapidated	(4) _____	148	inclement	(4) _____
105	contemplating	(2) _____	149	trajectory	(1) _____
106	canister	(1) _____	150	fettered	(1) _____
107	dissecting	(3) _____	151	waif	(3) _____
108	link	(4) _____	152	jubilant	(2) _____
109	solemn	(3) _____	153	pilfering	(4) _____
110	archery	(2) _____	154	repose	(2) _____
111	transparent	(3) _____	155	carrion	(3) _____
112	husk	(1) _____	156	indigent	(2) _____
113	utensil	(2) _____	157	convex	(1) _____
114	citrus	(3) _____	158	emaciated	(2) _____
115	pedestrian	(2) _____	159	divergence	(4) _____
116	parallelogram	(1) _____	160	dromedary	(2) _____
117	slumbering	(3) _____	161	embellishing	(2) _____
118	peninsula	(4) _____	162	entomologist	(3) _____
119	upholstery	(2) _____	163	constrain	(1) _____
120	barricade	(4) _____	164	infirm	(1) _____
121	quartet	(4) _____	165	anthropoid	(3) _____
122	tranquil	(3) _____	166	specter	(4) _____
123	abrasive	(1) _____	167	incertitude	(2) _____
124	fatigued	(3) _____	168	vitreous	(1) _____
125	spherical	(2) _____	169	obelisk	(1) _____
126	syringe	(2) _____	170	embossed	(4) _____
127	feline	(2) _____	171	ambulation	(2) _____
128	arid	(4) _____	172	calyx	(2) _____
129	exterior	(1) _____	173	osculation	(3) _____
130	constellation	(4) _____	174	cupola	(4) _____
131	cornea	(2) _____	175	homunculus	(4) _____
132	mercantile	(1) _____			
133	ascending	(3) _____			
134	filtration	(1) _____			
135	consuming	(4) _____			
136	cascade	(4) _____			
137	perpendicular	(3) _____			
138	replenishing	(1) _____			
139	emission	(3) _____			
140	talon	(3) _____			

CALCULATING RAW SCORE:

ceiling item..... _____
 minus errors..... _____
 equals..... _____
 (raw score)

9.7 APPENDIX G: COWA SCORING SHEET

CONTROLLED ORAL WORD ASSOCIATION - (FAS) - 60sec/letter

I will say a letter of the alphabet, and I want you to give me as many words that begin with that letter as quickly as you can. You will have 60 seconds in which to respond. I don't want you to use proper names such as 'Boston' or 'Bob' etcetera, and I don't want you to use the same words with different endings such as 'eat', 'eats', 'eating' etcetera.

Do you have any questions?

O.K. Lets begin ...

" F "

Total score: _____

" A "

Total score: _____

" S "

Total score: _____

Overall Total Score: _____

WISCONSIN CARD SORTING TEST: SCORING AND RECORDING FORM
University of Colorado School of Medicine: Robert Heaton Ph.D.

TRIALS: C,F,N,C,F,N

CORRECT _____ ERRORS _____ PERSEVERATIVE RESPONSES _____
NONPERSEVERATIVE ERRORS _____ PERSEVERATIVE ERRORS _____
CATEGORIES _____

END

2|5| 0|5| 93|

FIN