Pre-stimulus Spontaneous Brain Activity Predicts the Subjective Assessment of Subject's-Own-Name

by

Evan Houldin

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Evan Houldin

Abstract

This project analyzed fMRI data from an experiment which sought to identify pre-stimulus spontaneous brain activity that could be used as predictors of the subjective assessment of noise as the subject's own name (SON). Subjects were asked to distinguish SON from other names after being cued by fully masked auditory stimuli.

A pre-stimulus contrast successfully identified possible predictors: more activation in the TPJ and R/LSTG when subjects thought they heard SON as compared to other names. A comparable contrast for the evoked-response indicated insula and dmPFC activation.

Results from; behavioural data, a contrast based on objective stimuli and an interaction-effect ANOVA all confirmed that subjects could not identify names in the stimuli, thus supporting the assertion that subjects were indeed making subjective assessments. Reaction times were also found to be faster when subjects thought they heard other names as compared to SON.

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Table of Contents

Abstract	ii
Acknowledgements	iii
Chapter 1: Introduction	1
Chapter 2: Background	3
2.1 Behavioural Data Processing	3
2.2 fMRI Data Acquisition	3
2.3 fMRI Data Processing	8
Chapter 3: Review of the State of the Art	15
Chapter 4: Research Question	17
Chapter 5: Source of Data	18
5.1: Subjects	18
5.2: Experimental Design	18
Chapter 6: Method	21
6.1: Behavioural Analysis	21
6.2: fMRI Analysis	22
Chapter 7: Results	25

7.1:	Behavioural Results	25
7.2:	fMRI Results	27
Chapter 8:	Discussion	30
8.1:	Source of Data	30
8.2:	Behavioural Results	32
8.3:	fMRI Results	34
Chapter 9:	Conclusions	39
9.1:	Behavioural Results.....	39
9.2:	fMRI Results	40
9.3:	Summary of Contributions.....	40
9.4:	Future Research	40
References		42

List of Tables

Table 1: Signal detection results 25

Table 2: Subjective and objective reaction times, in ms 26

List of Figures

Figure 1: Qin study experimental design	19
Figure 2: Contrast for pre-stimulus spontaneous activity (subjective response)	28
Figure 3: Contrast for post-stimulus activity (subjective response)	29

Chapter 1: Introduction

A precise account of the nature of the interaction between the brain and an external stimulus has long been sought. For example, Behaviourist accounts dictated that a known stimulus was sufficient to determine behaviour. Later theories posited internal mechanisms capable of generating behaviour in the absence of a stimulus (Friedenberg and Silverman, 2012). The existence and operation of such internally-driven capability is now commonly accepted and brain activity in the absence of a stimulus is known as spontaneous activity. Spontaneous activity has been identified with a range of brain recording techniques including electroencephalography (EEG) and functional magnetic resonance imaging (fMRI).

In addition to the obvious link between spontaneous activity and non-stimulus related behaviour (e.g. mind wandering), recent brain-imaging research is concerned with an additional connection; that between spontaneous activity and stimulus induced behaviour. Although it seems counter-intuitive to link brain activity that is by definition stimulus-free to stimulus-induced brain activity, early research with animals concluded that a link exists (Arieli et al., 1996). Later EEG studies extended this principle to the human brain.

More recently, functional brain imaging studies have confirmed that the activity of specific networks of cortical regions (relevant to a given activity) immediately prior to a stimulus is predictive of post-stimulus brain activity (Fox et al., 2006). Current research is devoted to identifying the temporal and spatial properties of these cortical networks (Sadaghiani et al., 2010).

The influence of pre-stimulus activity becomes particularly pronounced in the case of near-liminal stimuli. A 2009 study by Sadaghiani et al. found that auditory stimulus detection was a function of pre-stimulus activity in the auditory cortex as well as networks identified during resting state activity. The variability in the detection of a near-liminal stimulus was found to be dependent on the state of the brain pre-stimulus, not the variability of the strength of the stimulus itself (Sadaghiani et al., 2009).

This phenomenon has yet to be extended to scenarios involving the self, for example the identification of one's own name. Specifically, is one's tendency to associate an indeterminate auditory stimulus with one's own name dependent on brain activity immediately prior to the stimulus?

Chapter 2: Background Information

2.1 Behavioural Data Processing

Signal Detection Theory

Signal detection theory (SDT) is used as a means to assess the ability of a signal detector to distinguish a signal from surrounding noise. In the case of human behavioural studies, one can consider, for example; the signal detector to be the human subject, the signal to be the presentation of the subject's-own-name (SON), and noise to be the presentation of a name other than SON.

Sensitivity Index

One of the statistics used in SDT is the sensitivity index, d' (d prime). d' compares the signal and noise distributions to determine the likelihood of mistaking a signal for noise and vice versa. When d' is zero, it is impossible for a signal detector to distinguish signal from noise.

2.2 fMRI Data Acquisition

Functional Magnetic Resonance Imaging Principles

Functional Magnetic Resonance Imaging (fMRI) is a brain imaging technique that uses the Blood Oxygen Level Dependent (BOLD) contrast to determine the supply of oxygenated blood to different areas of the brain. The brain does not store energy internally and is dependent on a continual supply of oxygen and glucose in order to

facilitate neuronal information processing. As such, the BOLD contrast is an indirect measure of neuronal activity (Huettel et al., 2009).

The BOLD signal is very weak and heavily compromised by noise, so statistical techniques and tailored experimental design are critical for its detection.

BOLD Principles

Neurons use Adenosine Triphosphate (ATP) to power their metabolic activity, which primarily includes the restoration of electrical potentials following action potentials, excitatory postsynaptic potentials and inhibitory postsynaptic potentials. ATP is generated in-house, by the continual supply of oxygen and glucose to the neurons via blood cells arriving from the capillaries distributed throughout the brain.

Within blood cells, oxygen is transported by a protein called hemoglobin. When the cell body of the neuron has stripped hemoglobin of its oxygen, the hemoglobin molecule is used to transport waste carbon dioxide away from the cell. At this stage, it is called deoxygenated hemoglobin.

Deoxygenated hemoglobin has magnetic properties that reduce the nuclear magnetic spin of nearby hydrogen nuclei (specifically the hydrogen in water, which is plentiful throughout the brain). When freshly oxygenated hemoglobin is supplied to a neuron in order to replenish its depleted ATP following its data-processing activity, the result is a restoration of the magnetic spin (called magnetic re-polarization) in the surrounding water molecules. The BOLD contrast measures this

return of nuclear magnetic spin and so indirectly measures the activity of the neuron (Huettel et al., 2009).

MRI Technology

The measure of magnetic re-polarization is only possible within the special conditions created by an MRI machine. Specifically, an MRI machine generates an enormously powerful magnetic field that magnetically aligns the axis of rotation of the nuclei present within the brain (or whatever substance happens to be in the machine). Without this alignment, the axis of rotation would be randomly oriented, and there would be no baseline against which to measure a deviation from a nuclei's initial alignment.

During a scan, the machine emits a pulse at the specific nuclear magnetic resonant frequency of the nuclei of interest (in this case, hydrogen). Every element has a resonant frequency at which it will absorb (and subsequently re-emit) energy. This resonant frequency also determines the rate at which the nuclei will return to their original undisturbed alignment, thus defining a nuclear magnetic signature for every element. It so happens that hydrogen has a resonant frequency within the radio spectrum, so the electromagnetic coils within the machine are called radiofrequency coils. Shortly after absorption of the radiofrequency pulse's energy, the nuclei will re-emit this energy: the re-emitted energy is the signal that the radiofrequency coils will detect.

MRI machines also contain gradient coils, to ensure that the strength of the magnetic field is slightly different at each point within a three dimensional grid. This variation

in field strength ensures that the frequency of rotation of a target nucleus will be slightly different at each point in space and thereby gives the machine a means for distinguishing the dimensional origins of each MRI signal (Huettel et al., 2009).

The Hemodynamic Response Curve

The influx of oxygenated blood to a collection of recently activated neurons follows a characteristic pattern of flow. This pattern is known as the hemodynamic response (HDR) curve. In the classic model of this curve, blood flow increases to a recently active region and peaks approximately 5 seconds after the actual activation. Blood flow subsequently returns to baseline (following a temporary undershoot) after approximately twelve to fifteen seconds. The exact shape of this curve varies widely among brain regions as well as individuals and is also highly dependent on the length and type of stimulus presented.

The shape of the HDR curve is important for the processing of fMRI data, as it will be used as a model to be identified within the raw data and thereby assist in differentiating signal from noise (Huettel et al., 2009).

Anatomical Data

fMRI data indirectly measures neural activation, however, in order for this data to be interpreted correctly, it must be mapped onto anatomical data of the brain.

Without such mapping, one cannot tell which areas of the brain are active.

Anatomical data is recorded by the MRI machine using different contrast mechanisms from the BOLD contrast. The most common anatomical contrast

mechanism used is known as T_1 –weighted imaging. This imaging mechanism targets the recovery of the T_1 magnetic spin (spin whose axis is parallel to the direction of the magnetic field) of the nuclei in the tissue of interest (Huettel et al., 2009).

Terminology

Voxels: A voxel can be thought of as a three-dimensional pixel. It represents the spatial resolution of the MRI scan. Functional data will have a lower resolution than anatomical data.

Timecourse: A timecourse is the complete signal for a given voxel.

Repetition Time: The Repetition Time (designated as one ‘TR’) is the time between each full BOLD scan of the brain. Functional imaging scans are performed one slice at a time, with all slices completed within the length of one TR (anatomical data is also gathered one slice at a time). Although the length of a TR typically represents the limiting temporal resolution for brain functional data acquisition, this resolution can be improved by jittering the trials in the experimental design (discussed below).

Jittering: The HDR necessitates an inter-trial-interval (ITI) consistent with the temporal length of the HDR curve, at a minimum, so that the signal can return to baseline prior to the onset of successive stimuli. Where it is important to identify the shape of the HDR curve as much as possible, it is an effective strategy to vary the ITI by temporal increments that are fractions of the TR length. This allows the experimenter to sample functional data for the timecourse of a given voxel from

multiple timepoints that are incremented by temporal lengths with higher resolution than the TR length, rather than the same ones repeatedly (i.e. the same timepoints in a trial, separated by one TR). Consequently, there is more data available for defining the shape of the HDR curve. It should be noted that this technique necessitates more trials to gain sufficient statistical significance, however. The technique of varying the ITI for these purposes is called “jittering”. Where the experimenter is interested only in the peak of the HDR curve, however, jittering is not necessary (Huettel et al., 2009).

2.3 *fMRI Data Processing*

As mentioned, fMRI signal data is initially collected as activations representing the recovery of nuclear magnetic spin in hydrogen nuclei, as influenced by the presence of oxygenated hemoglobin. This signal is extremely weak and is difficult to isolate from noise. A statistical technique called regression analysis can be used to help identify the desired signal. Prior to performing this analysis, the data must be preprocessed, for the purposes of realigning it due to head movements, mapping it to the separate anatomical scan and standardizing it so that data from subjects with differently shaped brains can be compared (Huettel et al., 2009).

Preprocessing

The first preprocessing step involves assigning the same start point to activation data gathered within the same TR. Data for each slice is shifted temporally by a small amount of time (e.g. data for 30 slices within a TR of two seconds would be $1/15^{\text{th}}$ of a second apart, with each voxel within a given slice also at different times),

so this step helps simplify later processing by standardizing to the same TR. Next, signals above a certain amplitude are removed as likely outliers. Data is also examined for headshift in six different dimensional measures; the three dimensional axes and also three rotational shifts along orthogonal axes of rotation. Shifts in excess of two mm are flagged as indicating poor experimental control and data from these sessions is not used for further analysis. Data which passes this criteria is then shifted.

Generalizing experimental conclusions to the population requires combining data from multiple subjects. Brain morphology differs widely between subjects, however, and this necessitates the standardization of brain data. Two universal standards are the Montreal Neurological Institute (MNI) standard and the Talairach standard. Each of these standards uses different reference points for their coordinate systems and a different reference brain, however, both are popular. The next step in preprocessing involves the conversion of all fMRI data maps to one of these standards. Anatomical data is converted first, followed by conversion of the fMRI data in accordance with the same conversion algorithm used for the anatomical data. This step will typically also involve the standardization of fMRI data into a perfectly cubic voxel, as the slice thickness may not be the same width as the voxel width in other dimensions. Doing so helps the functional data map better onto the anatomical data.

Data is then spatially smoothed, such that nearby voxels have their values averaged out. This helps to differentiate the signal from noise in later steps. A mask is also

applied, to eliminate data points which lie outside of the skull. This helps save on processing time later, as such data can be safely ignored as noise (Huettel et al., 2009).

General Linear Model

The general linear model (GLM) assumes that the raw data signal can be broken down into a model of the expected signal, plus an error term representing the mismatch between the model and the raw signal, as per the following equation:

$$Y = \beta X + \epsilon;$$

Y represents the raw data signal, X represents a series of regressors/signal models which the experimenter expects to be contained within the data, β represents a series of magnitude modifiers corresponding to each of the regressors and ϵ represents the error/mismatch between the model and the data

The model is defined a priori by the experimenter and consists of a set of regressors (described in more detail below) that combine linearly. Note that this technique is also called multiple linear regression analysis. A computer runs the regression analysis iteratively, such that the error term is minimized and the regressors come closest to representing the raw data signal.

The output of the GLM is a set of β values. There is one (or more, depending on the program command used) unique β value for each regressor, for each voxel, for each brain imaged in the study. Each β value represents the degree to which the regressor/signal model must be modified so that it best fits the raw data (Huettel et al., 2009).

Regressors

Regressors can be categorized as task regressors or nuisance regressors. A task regressor is a signal model comprised of idealized HDR curves/functions with onset times that correspond to the trials in which a given stimulus of interest was presented. For example, if an experiment consisted of ten experimental trials in which faces were presented as stimuli and ten neutral trials in which a fixation cross was presented as stimuli, then the experimental task regressor would consist of a signal with ten model HDR functions with onsets occurring each time a face was presented to a subject. An example of a nuisance regressor is a signal consisting of variability corresponding to head shifts along the x-axis (Huettel et al., 2009).

Finite Impulse Response function

The idealized default HDR function is commonly replaced with more flexible models of the HDR such as a finite impulse response (FIR) function which uses multiple functions staggered by incremented time intervals to model the unknown HDR curve present within the signal. The ideal number of functions corresponds to the number of TRs within the ITI. The FIR function is especially useful if the specific shape of the HDR is of interest to the experimenter, for example when one would like information on pre-stimulus brain activity (Huettel et al., 2009).

Contrasts

As mentioned, the output of a GLM is a set of β values corresponding to the regressors defined by the experimenter. Regressors which explain much of the raw

signal for a given voxel will have high β values for that voxel. For example, in an experiment seeking to identify cortical areas relevant to facial recognition, one might have a task regressor in which HDR functions were modeled for each onset of face stimuli. One might expect that this regressor would have a relatively high β value in the voxels corresponding to the fusiform face area (FFA). fMRI does not measure the absolute value of activation, however, so on its own, this β value is meaningless. To give meaning to the β value, it must be contrasted against another β value in a statistical context. For example, another task regressor might contain a series of HDR functions that correspond to each onset of a neutral fixation cross. If it were the case that the FFA does not respond to fixation crosses, then the β value representing the correspondence of this regressor to the raw data signal would be lower than that of the face task regressor. A t-test is used to compare the likelihood that the two β values are different. The t-tests for all the voxels of interest (e.g. across the entirety of the brain or in a region of interest such as the FFA) can then be displayed in a three-dimensional map. Such a map represents the output of the contrast.

Note that this usage of the term “contrast” is different from the one used above in reference to imaging mechanisms that initially acquire the functional signal. Both usages are found in discussions of fMRI, with meaning implied by context.

When a FIR function is used to improve the model of the HDR, β values can be compared for each timepoint corresponding to the functions used to represent the HDR curve (Huettel et al., 2009).

Corrections for Multiple Comparisons

Statistical tests for fMRI are performed on a per-voxel basis. Given the high number of total voxels in a scan, there is a correspondingly high probability of making a Type I error (false positive). This probability is called the familywise error rate (FWER). There are a number of ways to control for the FWER and a common technique is to make use of cluster-size thresholding. While there is a relatively high likelihood that isolated voxels distributed across a scanning volume will pass a statistical significance threshold by random chance, the likelihood of a contiguous cluster of voxels doing so by chance is much lower. Cluster-size thresholding involves the determination of the minimum contiguous-voxel-cluster size necessary to avoid making a Type I error, in accordance with a probability of error set by the experimenter. The threshold is then applied by eliminating (from the contrast map) voxels that are not a part of a voxel cluster that is at least as large as the threshold (Heuttel et al., 2009).

Image presentation

fMRI software can present brain images according to 'neurological convention' or 'radiological convention'. In neurological convention, the left hemisphere is presented on the left side of the screen and the right hemisphere is presented on the right. Radiological convention presents brain images as a radiologist would see them; as if the patient were standing before them face-to-face. Consequently, the left hemisphere appears on the right side of the image.

Brodmann Areas

Brodmann areas (BA) are a set of neocortical regions defined by their cellular structure, each with a numerical designation. Note that these regions do not correspond to the boundaries of neocortical sulci or gyri. The differences in cellular structure were originally identified by neurobiologist Korbinian Brodmann using a cellular staining technique. It is thought that this structural difference corresponds to a functional difference. Brodmann identified 47 BAs in total (Huettel et al., 2009).

Chapter 3: Review of the State of the Art

Behavioural variability evoked by identical stimuli has long been unexplained (Boly et al., 2007). Earlier studies with electroencephalography suggested that this variability could be accounted for by variation in pre-stimulus spontaneous brain activity (Arieli et al., 1996). Spontaneous activity is any brain activity present in the absence of an external stimulus. As such, it was long ignored as being irrelevant with respect to post-stimulus brain activity. More recently, however, spontaneous activity has gained in importance as an explanation for the variance in post-stimulus brain activity. It is now thought that the state of activity in the brain immediately prior to a stimulus has an impact on how a stimulus is perceived. Specifically, pre-stimulus spontaneous activity can be used as a predictor of post-stimulus brain activity.

In an early EEG experiment (Arieli et al., 1996), it was found that the total evoked response could be reasonably predicted by adding the average incremental evoked response to the measured spontaneous activity immediately prior to stimulus onset. This idea has gained more recent support in functional brain imaging research. For example, in an fMRI attention paradigm, it was found that lapses in attention are preceded by reduced activity (pre-stimulus) in regions of the anterior cingulate cortex and right prefrontal cortical areas (Weissman et al., 2006).

In the case of stimulus detection paradigms, the degree to which pre-stimulus spontaneous activity influences the post-stimulus brain response depends on the salience of the stimulus. Highly salient stimuli would be less influenced by

spontaneous activity. Consider a hypothetical experiment in which a name is spoken clearly and directly to a subject, without other distractions. One would expect the subject to respond (i.e., correctly identify the stimulus) regardless of prior mental states. In contrast, subliminally presented stimuli, or stimuli embedded in distracting noise would understandably result in more variable responses dependent upon pre-stimulus spontaneous activity.

For example, in a 2005 study (Pessoa and Padmala), target faces with a fearful, happy or neutral expression were presented briefly to subjects for 67ms, followed by a mask consisting of a neutral face. It was found that a subject's decision to identify the target face as a fearful one (irrespective of the actual target face presented) could be predicted by pre-stimulus activation in a network consisting of four cortical regions.

In another study (Boly et al., 2007), pre-stimulus activity in the medial thalamus and lateral frontoparietal network was found to predict the ability to consciously detect low-intensity somatosensory stimuli.

An imaging study performed in 2009 (Sadaghiani et al.) extended this principle to the prediction of liminal auditory stimuli detection (specifically, tones). It was found that auditory stimulus detection was a function of pre-stimulus activity in the auditory cortex as well as activity in networks identified during the resting state.

Chapter 4: Research Question

Prior research has successfully established spontaneous activity as a predictor of post-stimulus activity in several domains, beginning with the 1996 EEG study by Arieli et al. As mentioned above, a study by Sadaghiani et al. (2009) extended this principle to the prediction of auditory stimuli detection. The current study used an experimental paradigm that was similar to the Sadaghiani et al. study, but instead of presenting tones, it asked subjects to identify their own name or other names when they were presented with names embedded within (yet completely masked by) auditory noise. In doing so, this study hopes to extend the scope of response-prediction research to subjective assessments of the subject's-own-name (SON).

Specifically, this research hopes to determine whether it is possible to identify pre-stimulus brain activity that can be used as predictors of the subjective assessment of noise stimuli as being SON.

Chapter 5: Source of Data

This thesis analyzes fMRI data from an experiment performed at the Free University of Berlin in 2011 by Dr. Pengmin Qin of the Mind, Brain Imaging and Neuroethics Research Unit at the Institute of Mental Health Research in Ottawa (led by Dr. Georg Northoff). The details of this experiment are outlined below.

5.1 *Subjects*

The study consisted of 18 subjects (15 female, 3 male), aged 20-34, with a mean age of 27.1. All subjects had first names consisting of two syllables.

5.2 *Experimental Design*

The experiment consisted of 180 trials per subject (broken into four 10 minute sessions) organized in an event-related design. Each trial lasted between 12-16 seconds, as shown in Figure 1. The two-second pre-stimulus period indicated in Figure 1 only existed for the first trial. The following trials had a pre-stimulus period consisting only of the prior trial, for an ITI of 12-16 seconds. The stimuli consisted of auditory-presented names that were fully masked with noise, such that the underlying name could not be consciously distinguished. Names belonged to one of three categories; the subject's own name (SON), a familiar name (FN) belonging to a friend of the subject and an unfamiliar name (UN), belonging to someone not personally known to the subject, yet considered common in Germany. All names consisted of two syllables. A male researcher unknown to the subjects recorded all names.

Stimuli were presented for one second. Following the stimulus presentation, there was a one to three second 'jitter' period prior to the self-evaluation. In the self-evaluation stage, subjects were asked to press one of two buttons, corresponding to *yes* and *no* responses, in answer to the question "Is this your name?". This stage lasted one second. Responses recorded outside of this one-second time-period were not considered in subsequent analysis. The self-evaluation stage was followed by a nine to eleven second period during which subjects were asked to stare at a fixation cross present in a display in front of them. Response times and fMRI data were also recorded.

The order of the trials was pseudo randomized. 60 trials were presented in total for each category of name (i.e., SON, FN and UN). In 20 of these 60, the subjects were not asked to respond during the self-evaluation (i.e., there were 20 passive listening trials).

Figure 1 Qin study experimental design

Imaging data was generated on a Siemens 3.0T MAGNETOM Trio, A Tim system scanner located at the Free University of Berlin. TR = 2 seconds.

Chapter 6: Method

Data analysis consisted of two stages; behavioural analysis followed by fMRI analysis.

It is worth noting here that portions of the analysis are solely concerned with controlling for the possibility that subjects heard the names present within the noise, despite efforts to ensure that all names were completely masked by the noise. Specifically, these portions are the first part of the behavioural analysis (concerned with signal detection), the third fMRI contrast and the ANOVA. These analyses could have been avoided if noise (only) were presented to subjects, in place of names masked by noise. This complication in the experimental design is further discussed in section 8.1 (Discussion: Source of Data).

6.1 Behavioural Analysis

There were two objectives in the behavioural analysis:

- 1) Determine whether subjective name-identification was truly random, for the purposes of confirming that subjects could not identify the names present in the noise.
- 2) Determine whether differences in response time exist between trials (as categorized by the subjective response and by the objective presentation of masked names).

In the first part of the behavioural analysis, signal detection theory was used to determine the sensitivity index, d' .

In the second part of the behavioural analysis, three t-tests were performed on the reaction time data. The first t-test compared reaction times for all trials in which the subjects identified the stimuli as SON against reaction times for stimuli which they identified as another name (irrespective of the actual name embedded within the noise). The last two t-tests compared the reaction times for trials in which SON stimuli were presented against the FN-stimuli trials and also against the UN-stimuli trials.

The behavioural analysis was performed using the SPSS software package¹.

6.2 *fMRI Analysis*

Preprocessing

Data was preprocessed using the AFNI² software package. Preprocessing included the removal of outlier data (“de-spiking”), head motion correction, masking for skull removal, spatial smoothing and conversion to Talairach space.

GLM

The AFNI function 3dDeconvolve was used to implement the GLM. Further, the FIR function TENT was used to generate multiple β values across the HDR, in order to

¹ Statistical Package for the Social Sciences, IBM proprietary software.

² Analysis of Functional NeuroImages, supported by the National Institute of Mental Health in Bethesda, MD, USA.

more flexibly identify the shape of the HDR curve across multiple timepoints (seven in total, including one each for the pre-stimulus and stimulus).

Two GLMs were implemented. The first enabled comparison of trials as categorized by the subjective results (i.e., trials in which subjects identified the stimuli as SON vs. trials in which subjects identified the stimuli as FN and UN). Accordingly, regressor HDR onset times corresponded to trials categorized in this way. This is referred to below as the “subjective GLM”. The second enabled comparison of trials as categorized by the actual stimuli presented (i.e., trials in which SON was presented vs. trials in which FN and UN were presented). Accordingly, regressor HDR onset times corresponded to trials categorized in this way. This is referred to as the “objective GLM”.

Contrasts

Three contrasts were performed in the fMRI data analysis.

To generate each contrast, t-tests were performed using the AFNI software package to identify regressor β value differences on a per-voxel basis, for all subjects. Family-wise error correction was also performed via cluster-size thresholding. The first two contrasts were performed using β values generated by the subjective GLM whereas the third contrast was performed using β values generated by the objective GLM.

Contrasts are described below, with the time of brain activity noted:

1) Pre-stimulus spontaneous activity (one TR prior to stimulus onset): Trials in which subjects identified the stimuli as SON were tested against trials in which subjects identified the stimuli as other names (either FN or UN).

2) Post-stimulus activity (third TR following stimulus onset): Trials in which subjects identified the stimuli as SON were tested against trials in which subjects identified the stimuli as other names (either FN or UN). Note that the third TR was identified as the time of the peak BOLD signal (i.e. the peak of the HDR curve) after also investigating other TRs. Given that the HDR typically peaks around 5 seconds after the stimulus, it was hypothesized that either the second, third or fourth TR would correspond to the peak BOLD signal. Contrasts for the second and fourth TRs yielded no results, however.

3) Post-stimulus activity (third TR following stimulus onset, as identified in the preceding contrast): Trials in which SON were presented as stimuli were tested against trials in which other names (either FN or UN) were presented as stimuli.

ANOVA

A 2 X 2 ANOVA was performed with the β values to identify a possible interaction effect between the subjective responses and the objective stimuli, as follows:

(SON, Other Names) x (correct, incorrect)

The ANOVA was performed with the AFNI software package.

Chapter 7: Results

7.1 Behavioural Results

Signal Detection Results

Table 1 presents the signal detection results. The leftmost table is provided as a legend to assist in interpreting the data presented in the rightmost table. The data presented is the mean number of responses among participants.

Table 1 Signal detection results, mean number of responses among participants

		Name Presented				Name Presented	
		SON	Other Name			SON	Other Name
Subjective Assessment	SON	Hit	False Alarm	Subjective Assessment	SON	14.28	14.58
	Other Name	Miss	Correct Rejection		Other Name	21.61	21.47

Note 1: Hits = subject correct when SON presented, Miss = subject incorrect when SON presented, False alarm = subject incorrectly assessed another name as SON when another name was presented, Correct rejection = subject correctly identified another name as such when another name was presented

Note 2: Table data for false alarms and correct rejections are presented as the averages of the familiar and unfamiliar name results

From this data, the sensitivity index, $d' = 0.0266$ (one sample t-test, compared with 0: $t=0.203$, $p=0.841$)

Reaction times

Table 2 presents average reaction times along with their standard deviations.

Subjective results were averaged for all trials in which the subjects identified the stimuli as being their own name and all trials in which they identified the stimuli as being another name (irrespective of the actual name embedded within the noise).

Objective results were averaged for trials in which SON, FN and UN stimuli were presented.

Table 2 Subjective and objective reaction times, in ms

<i>Subjective</i>	<i>M</i>	<i>SD</i>
SON	532	116
Other name	485	112
<i>Objective</i>	<i>M</i>	<i>SD</i>
SON	510	111
Other name 1	515	116
Other name 2	501	123

T-tests

Subjective results; $p = 2.9E-5$.

Objective results; $p = .70$ (SON vs. Other name 1); $p = .51$ (SON vs. Other name 2).

7.2 *fMRI Results*

Pre-stimulus Spontaneous Activity: SON vs. Other Names, according to the subjective response

Figure 2 presents a series of brain cross sections spaced 7mm apart in the horizontal plane. Images are presented according to the radiological convention, such that the right hemisphere of the brain appears on the left side of the image. Voxels in red are those in which there was a statistically significant difference in β values, where β values were larger for regressors in which subjects thought they were hearing SON, as compared to those in which they thought they were hearing a name other than SON. These voxels therefore correlate with brain regions in which there was greater hemodynamic activity (in a statistically significant sense) when subjects thought they heard SON, as compared with a name other than SON. These regions correspond approximately to the right and left superior temporal gyrus (RSTG, LSTG) as well as the temporoparietal junction (TPJ).

The contrast that generated these images was performed with β values from 1 TR prior to stimulus onset. All voxels present passed the cluster-size threshold; FWER correction ($p < 0.05$).

Figure 2 Contrast for pre-stimulus spontaneous activity (subjective response)

Post-stimulus activity: SON vs. Other names, according to the subjective response

Figure 3 presents two images. The image on the left presents a horizontal cross section. The image on the right presents a sagittal cross section. Once again, images are presented according to the radiological convention. Voxels in red are those in which there was a statistically significant difference in β values, where β values were larger for regressors in which subjects thought they were hearing SON, as compared to those in which they thought they were hearing a name other than SON. These voxels therefore correlate with brain regions in which there was greater

hemodynamic activity (in a statistically significant sense) when subjects thought they heard SON, as compared with a name other than SON. These regions correspond approximately to the insula and orbitofrontal cortex (OFC), as well as the dorsomedial prefrontal cortex (dmPFC).

The contrast that generated these images was performed with β values from 3 TRs after stimulus onset. All voxels present passed the cluster-size threshold; FWER correction ($p < 0.05$).

Figure 3 Contrast for post-stimulus activity (subjective response)

Post-stimulus activity: SON vs. Other names, according to the trial stimuli

No significant activation found.

ANOVA

No interaction effect found.

Chapter 8: Discussion

8.1 *Source of Data*

The importance of fully masking the names with noise becomes apparent when one considers the two alternatives: unmasked, explicitly presented names and near-liminally presented names. An explicit stimulus would not be useful in revealing a connection between the state of the brain immediately prior to and following the stimulus. The answer to the question “Is this your name” would always be “yes” irrespective of the pre-stimulus brain state. Pre-stimulus spontaneous activity may well predispose the brain to identify noise as SON in various trials, however there would be no way of identifying such trials because they would be grouped with all others. The only way to reveal predictive spontaneous activity is to identify trials in which subjects thought they heard SON and then examine the HDR signal immediately prior to the stimulus onset. The behavioural response data serves to help in this identification.

With respect to near-liminally presented names, it is imperative to note a key difference in the design of this study as compared to the other predictive-response studies mentioned in Chapter 3. The objective of this experimental design is to place the subjects into a state in which they think they hear their own name. It is not relevant whether their name is actually embedded within the noise when they think they hear it. This is in contrast to the other studies because they focused on behavioural performance, i.e. determining which pre-stimulus networks of cortical

activation improved the subjects' chances of detecting the signal from the noise. In this study, improved signal detection actually detracts from the ability to derive conclusions from the results because it would imply that subjects were actually hearing their own name, instead of believing that they heard their own name. Signal detection theory is used in the behavioural analysis, but only to ensure that subjects have chance levels of signal detection success, rather than a greater than chance level success rate.

In considering this point, an immediately salient suggestion with respect to the experimental design is that pure noise would be preferable to masked names as a stimulus. Noise devoid of any embedded signal would have a clear advantage in that it would be known that the subjects were guessing when they heard their own name, without the need for further signal detection testing. This was brought up with Dr. Qin, who explained that fully-masked names were employed as a consequence of constraints set by other experiments being performed in conjunction with this one.

Another issue is that subjects were not asked to complete a confidence scale following each trial, indicating their confidence in having heard their own name. This makes it more difficult to assert that the fMRI results indeed reflect pre-stimulus predictors of subjectively identifying the stimuli as SON, as it is possible that subjects did not believe that any of the stimuli contained name content and could simply have been guessing at random. This is further complicated by the sensitivity index results, which indicate chance levels of signal detection. Although

chance-level signal detection results are desirable for the reasons mentioned earlier, such results are also consistent with purely random guessing on the part of the subjects. If the subjects were guessing randomly, then pre-stimulus activity would have no bearing on the subjective assessment of SON. Fortunately, the fMRI results are helpful in dismissing this conclusion. If subjects were truly guessing at random, then one would not expect that contrasts based on trial data defined by the subjective reports would bear any results at all. The fact that these subjective contrasts did generate results in the form of significant activations indicates the existence of more complex processing (although it could be equivalently argued that the pre-stimulus activations only indicate a predisposition to guess!).

Dr. Qin further explained that such a confidence scale was omitted as a consequence of limited time available on the fMRI machine.

8.2 Behavioural Results

Signal Detection – Sensitivity Index

Table 1 demonstrates that the number of hits (averaged across subjects) was very close to the number of false alarms, where it is assumed that SON is the signal that subjects are trying to detect. In other words, for every time that subjects correctly identified the signal present in the noise, they also incorrectly identified the signal as present when it was not. Similarly, the number of misses was very close to the number of correct rejections; i.e., for every time they correctly identified the fact that the signal was not present, they also incorrectly stated that it was not present when in fact it was. These results demonstrate that the likelihood that subjects could

correctly identify the signal was very close to chance levels of probability. Such likelihood of detection means that the signal detectors (i.e., the subjects) cannot be trusted to identify the signal, as their accuracy is little different from guessing. This supports the idea that subjects could not hear anything (at least on a conscious level) beyond the noise presented to them.

The sensitivity index summarizes this assessment in a single datum, after taking hits and false alarms as its input. That d' is very close to zero also supports the premise that subjects were unable to consciously distinguish the signal (i.e., SON) from the noise. The signal detection results were an important finding, as any indication that the subjects could perceive their name would reduce the likelihood that pre-stimulus spontaneous activity could influence post-stimulus activity, for the reasons discussed above.

Reaction Times

Subjective Results:

There was a highly significant difference in the subjects' reaction time when they thought they heard their own name as compared to when they thought they heard someone else's name. This could imply more cognitive processing, possibly as a consequence of the involvement of networks associated with the self, although this is merely speculation. Such networks would not be called upon to facilitate the processing of other names, thus speeding up the response.

It is important to note, however, that the one- to three-second jitter introduced after the stimulus of every trial casts at least some doubt on such a conclusion. It is possible that such a delay between stimulus and response could overshadow any genuine difference in cognitive processing related to the decision to identify the stimulus as SON. The difference in reaction time, although found to be significant, could reflect a causal factor completely unrelated to the processing of self-related information. The advantage of including the jitter outweighs its exclusion, however, given its importance in improving detection of the HDR curve within the fMRI raw data signal and thereby improving the identification of pre-stimulus spontaneous activity.

Objective Results:

There was no significant difference in the reaction times for the presentation of SON as compared with FN or ON. This result is expected, given that the results of the sensitivity index strongly suggest that the subjects were genuinely unable to distinguish signal from noise. As a consequence, reaction times should be randomly distributed amongst all trials, irrespective of the stimuli present in a given trial.

8.3 fMRI Results

Pre-stimulus Spontaneous Activity: SON vs. Other Names, according to the subjective response

These results were most central in answering the research question stated in chapter 4. That any significant activation was discovered in this contrast at all is a

direct indication that predictors of the subjective assessment of SON exist. That these areas of activation also correspond to prior research on the self (as discussed below) supports such a claim even more strongly.

The cortical areas identified in the contrast correspond roughly to BA22, 41 and 42, (which can also be identified as the RSTG, LSTG) and also to the TPJ.

The STG contains Wernicke's Area³, which is known to be involved in processing speech so that it can be perceived as language (Demonet et al., 1992). The involvement of Wernicke's area could illuminate some of the behavioural results; specifically why reaction times were longer for the subjective perception of SON. It's possible that subjects were considering the noise in the subjective SON trials to be language (or at least to contain language), whereas the remaining trials were disregarded as complete noise, or at least non-language. Given that this activation is pre-stimulus, it could be an indication of some readiness or bias to perceive incoming sounds as language. This is conjecture, however, as subjects were never asked to rank the quality of the noise as it pertains to language.

Ideally, subjects would have been asked to complete a confidence scale following each trial (one that is slightly more comprehensive than the one suggested above). In such a confidence scale, a "5" could correspond to having heard SON clearly; "4" less clearly. A "1" could correspond to having heard another name (either FN or UN) clearly; "2" less clearly. A "3" ranking could correspond to having heard neither SON

³ Wernicke's area is typically found in an individual's dominant hemisphere; most commonly the left. There isn't full agreement on the exact location of Wernicke's Area within the STG, however.

nor another name and might by default be non-language. If the aforementioned conjecture (regarding non-subjective-SON trials as non-language) were correct, then one would expect no activation of the STG in trials that subjects ranked as 1-3.

More generally, BA41 is associated with the primary auditory cortex (Morosan et al., 2001) and thus the processing of all sound. It's unclear why subjects would be more predisposed to perceive SON rather than other names following auditory cortex activation, however.

It is important to note that one should not necessarily expect the regions identified in the pre-stimulus contrast to be correlated with the self, despite the fact that there may be a later causal relationship between these regions and a percept involving the self (insofar as SON reflects the self, which is highly dependent on definitions of the self). Nevertheless, it can be argued that such a relationship exists. A 2009 review of investigations into the self identified the TPJ as one of four key regions that were consistently active across studies (Legrand and Ruby, 2009). Additionally, the bilateral anterior temporal gyrus (Brodmann area 22) showed up across many of the studies.

Post-stimulus activity: SON vs. Other Names, according to the subjective response

The cortical areas identified in the contrast correspond roughly to the Insula/OFC and the dmPFC. All of these regions have been found to be involved in functions related to the self (Legrand and Ruby, 2009, Shany-Ur et al., 2014). The dmPFC in particular is one of four key regions that were consistently active across studies in the aforementioned Legrand and Ruby meta-analysis. Such an association helps in

challenging the possibility raised in section 8.1 that subjects might have been guessing at random when they chose to identify noise as SON and that the activations identified in these contrasts might only indicate the cortical areas associated with guessing and with the predisposition to guess. The fact that the regions identified in the post stimulus subjective contrast happen to have strong links to self-related functions makes it unlikely that subjects were guessing in this experiment and were in fact subjectively assessing the stimuli as SON or not-SON.

Post-stimulus activity: SON vs. Other Names, according to the trial stimuli

That no significant activation was found is to be expected, given the results of the sensitivity index. As these results indicate that subjects were unaware of any content underlying the stimuli, then it would be surprising to find any preferential cortical activation. Nevertheless, these results were important because a positive result would have cast doubt on all other results presented here. For example, it could have indicated that, at some level of cognitive processing, subjects were aware of the underlying name embedded within the noise.

ANOVA

The lack of an interaction effect was a positive result, given that an interaction effect would have cast doubt on the conclusion that the subjective-assessment contrast results were purely a consequence of the subjective assessments of names based on noise. Instead it would have implied that subjects were somehow sensitive to the actual name present within the noise.

Although such a result might be expected, given the results of the sensitivity index, it is important to note that brain activity does not necessarily translate directly to behavioural activity. While the behavioural results may indicate an insensitivity to names embedded in the noise, it is not impossible that subjects were detecting the names at some level of cognitive processing. Such brain activity could influence the results and thus it was important to rule it out in the functional analysis.

Cocktail Party Effect

The results of this experiment can perhaps contribute to an explanation for the “cocktail party effect”, in which (for example) an individual engaged in a conversation at a party is able to identify their own name being spoken elsewhere at the party, despite their attention being focused on the conversation and the noise present elsewhere in the room (Wood and Cowan, 1995).

In the context of the results presented in this paper, one’s ability to detect their own name (signal) within the chatter of a party (noise) would not be a case of improved signal detection on account of a preferential ability to recognize the auditory pattern of one’s own name. Rather, the noise of the party would simply be that: noise. The signal/one’s own name would not necessarily be present within this noise, but would instead arise from a bias imposed by the state of the brain immediately prior to consciously hearing one’s own name. Thus, one of the secrets to the cocktail party effect may be that when we are predisposed to subjectively believe that there is a signal associated with our own name, we will *impose* such a signal upon incoming noise stimuli.

Chapter 9: Conclusions

9.1 *Behavioural Results*

Two conclusions can be drawn from the results of the behavioural analysis:

The results of the sensitivity index indicated that subjects were unable to distinguish SON from UN and FN embedded within the noise. As a direct consequence of this, it can be asserted that the subjects' identification of SON stimuli was a subjective assessment only. Accordingly, the variability in subjects' responses is most likely a product of pre-stimulus spontaneous activity, as insufficient information was identifiable in the stimuli themselves. This result was important for setting up later conclusions based on the fMRI results, as a higher d' result could indicate that subjects' responses were biased by an ability to distinguish the signal present within the noise.

The reaction time results indicated that subjects were slower in making their assessments that the stimuli contained SON. The extra time could be accounted for by extra cognitive processing related to the assessment of SON, although it is difficult to speculate what this extra processing might be. Such a conclusion is further complicated by the fact that a one- to three-second delay was present following the stimulus of every trial. It is possible that this delay could negate the effects of additional cognitive processing.

9.2 *fMRI Results*

The fMRI results were all positive with respect to the research goals of this project. It can be concluded from the results of the pre-stimulus activity contrast that pre-stimulus spontaneous activity can predict post-stimulus subjective (auditory) assessments of SON. More specifically, activity in the RSTG, LSTG and TPJ predict such a response. The results of the post-stimulus contrast (according to subjective response) indicate that activity in the insula and the dmPFC are associated with the subjective assessment of SON. Finally, the results of the last contrast and the ANOVA helped to confirm that the prior conclusions were sound, given that there was a lack of post stimulus activation when the contrast compared the objective stimuli and that there were no interaction effects between the subjective assessments and the objective stimuli.

9.3 *Summary of Contributions*

In line with the research question posed in chapter 4, this project successfully identified pre-stimulus cortical areas that could be used as precursor indicators of the subjective assessment of auditory noise stimuli as SON. Specifically, it was found that pre-stimulus activity in the RSTG, LSTG and TPJ predict that subjects will identify auditory noise as SON.

9.4 *Future Research*

The most obvious direction for future research is to extend the paradigm from this study to other sensory domains. For example, visual noise could be presented with

the expectation that the subjects' responses would be influenced by their pre-stimulus spontaneous activity. Subjects could be told that their own face was embedded within some of the images and that familiar and unknown faces were embedded in others. It would be interesting to determine whether similar pre-stimulus spontaneous activity could predict subjects' subjective assessment of seeing their own face in the noise. If some of these pre-stimulus regions coincided with the brain areas reported in this study, then it would lend support to a hypothesis that activity in such areas acts as generic precursor activity to the subjective assessment of self. Extension of this research to a multiplicity of domains with reference to different identifiers of self would help consolidate an understanding of the networks involved in defining the self.

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