Identification of Proper and Common Names in the Anterior Temporal Lobe: An FMRI Study

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IDENTIFICATION OF PROPER AND COMMON NAMES IN THE ANTERIOR TEMPORAL LOBE: AN FMRI STUDY

by

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ABSTRACT
IDENTIFICATION OF PROPER AND COMMON NAMES IN THE ANTERIOR TEMPORAL LOBE: AN FMRI STUDY

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Temporal lobe epilepsy is a neurological disease that affects millions of individuals worldwide. They are usually treated through surgical resection of portions of the anterior temporal lobe (ATL). Surgical resection is effective for seizure control, but produces language and verbal memory deficits such as anomic aphasia, which adversely affects an individual's quality of life. The purpose of this study was to develop a functional MRI protocol for mapping the function of ATL in healthy subjects, and to better understand the role of the ATL and other regions of the semantic system. Such a protocol may ultimately be used by surgeons to predict and reduce or prevent side effects of cognitive decline that occur after ATL resection in epilepsy patients. The aims were: (1) To study the ATL response to associations with abstract and concrete concepts and (2) To study the ATL response to names of people and places, and the information associated with these names. Our results indicated that ATL and inferior parietal areas are modulated by the amount of information associated with proper names. ATL is activated for abstract and concrete words relative to nonwords but is not modulated by associative measures. Angular and posterior cingulate gyri, on the other hand, are modulated by information associated with both common and proper names, underlining their role in semantic representations. A very high degree of overlap between person- and word-specific networks suggests that a common semantic system underlies both types of knowledge, rather than segregation of social and non-social knowledge. These results also demonstrate robust activation of ATL by proper and common names, and point to their potential use in mapping eloquent and functionally relevant cortex in epilepsy patients.

DEDICATION

To my late grandmother Smt. Tadimeti Seetaramamma garu

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Usha Tadimeti, B.E.

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ABBREVIATIONS

ACG	Anterior Cingulate Gyrus
AED	Anti-Epileptic Drug
AFNI	Analysis of Functional Neuro Images
AG	Angular Gyrus
ATL	Anterior Temporal Lobe
BOLD	Blood Oxygen Level Dependent
CARET	Computerized Anatomical Reconstruction and Editing Tool
CNC	Concreteness
CS	Central Sulcus
EPI	Echo Planar Images
ER	Emotional Response
ESM	Electrocortical Stimulation Mapping
FG	Fusiform Gyrus
fMRI	functional Magnetic Resonance Imaging
FOV	Field Of View
FWHM	Full Width Half Maximum
IE	Interactive Experience
IFG	Inferior Frontal Gyrus

IMG	Imageability
IPS	Intra Parietal Sulcus
ITG	Inferior Temporal Gyrus
KN	Knowledge
LG	Lingual Gyrus
MCG	Middle Cingulate Gyrus
MOG	Middle Occipital Gyrus
MPBF	Mean Positional Bigram Frequency
MTG	Middle Temporal Gyrus
ON	Orthographic Neighborhood
OTS	Occipito-Temporal Sulcus
PCG	Posterior Cingulate Gyrus
PET	Positron Emission Tomography
PHG	Para Hippocampal Gyrus
POS	Parieto-Occipital Sulcus
QMC	Mean Connectivity
QPR	Probability
QRSG	Resonance Strength
QSS	Set Size
RT	Response Time
SD	Semantic Dementia
SE	Sensory Experience

SMG	Supra Marginal Gyrus
SPGR	Spoiled Gradient Echo
STG	Superior Temporal Gyrus
STS	Superior Temporal Sulcus
TE	Echo Time
TLE	Temporal Lobe Epilepsy
Tpole	Temporal Pole
TR	Repetition Time
TTG	Transverse Temporal Gyrus

1. INTRODUCTION

Epilepsy is a common neurological disorder affecting approximately two million people in America (Hirtz et al. 2007)□. It is usually characterized by seizures, which are episodes of excessive, uncontrolled and abnormal neuronal activity in the brain. Temporal Lobe Epilepsy (TLE) is a form of epilepsy that has epileptogenic tissue localized to the temporal lobe, most commonly the middle temporal lobe (Engel 1992)□. The seizures associated with TLE are either simple partial seizures or complex partial seizures. Simple partial seizures do not result in loss of awareness whereas, in complex partial seizures, there is loss of awareness. This loss of awareness is because the seizure spreads to involve both temporal lobes, which causes impairment of memory. Seizures that involve small areas of the temporal lobe, such as amygdala or hippocampus cause sensations of familiarity (déjà vu) or unfamiliarity (jamais vu), or amnesia.

The treatment of epilepsy involves the use of antiepileptic drugs (AEDs), as a first step. Medications generally work well with patients and they may remain seizure free, provided that they strictly follow the medication regimen. In 20% of the cases, the frequency of seizures decreases greatly. About 30% of the patients continue to experience seizures (intractable) in spite of AEDs (Cramer et al. 1999; Kwan P, sills, GJ 2001)□. Neurosurgery for the resection of the seizure onset zone may a viable option in some cases. Although surgery is still commonly viewed as a last-resort procedure (Engel 1999)□□, the results of ATL resection have been significantly positive. In the first randomized, controlled study, 38% of patients remained seizure free after the surgery, compared to 3% who stayed on medical treatment (Wiebe et al. 2001)□.

The surgery is effective for seizure control, but it produces language and verbal memory deficits (Engel 1992)□ such as anomic aphasia, which adversely affects the patients' quality of life (Perrine et al. 1995; Stroup et al. 2003)□. The purpose of this study is to design a functional MRI protocol for mapping the function of ATL in healthy subjects, and to better understand the role of the ATL and other regions of the semantic system. Such a protocol may ultimately be used by surgeons to predict and reduce or prevent side effects of cognitive decline that occur after ATL resection in epilepsy patients.

2. BACKGROUND

2.1 ATL damage and theories related to ATL functions

A handful of conditions that cause ATL damage are TLE surgery (Wiebe et al. 2001)□□, herpes encephalitis (Noppeney et al. 2007)□ and semantic dementia (SD)(Warrington 1975)□. These conditions have contributed to our understanding of ATL function, because they present a direct evidence of linking loss of brain tissue with functional deficits.

Left ATL resection often produces anomia (also known as anomic aphasia), which is characterized by problems in recalling people or words. However, the underlying reason for this deficit is unclear. Patients with severe anomia have no problems in reading or repetition tasks, but are unable to report the meaning of stimuli. For example, given a hammer as a stimulus, they were able to draw it but were not able to report its function (Patterson, Nestor, and Rogers 2007)□, or patients with SD were unable to choose the correct color for object drawings (Rogers, Patterson, and Graham 2007)□. It is possible that anomia is related to impairment of semantic memory, that is, memory for the meaning of words, objects and events. According to this view, loss of semantic memory produces a variety of associated cognitive deficits, of which anomia is simply the most obviously apparent and readily detected (Bell et al. 2001; Lambon Ralph et al. 2001)□.

Previous functional imaging studies have implicated the role of left ATL in semantic processing. Areas most commonly identified in these studies are in the ventral ATL, anterior portions of the Middle Temporal Gyrus (MTG), Inferior Temporal Gyrus (ITG), fusiform gyrus, and parahippocampus (Humphries et al. 2006; Patterson, Nestor, and Rogers 2007; Rogers, Patterson, and Graham 2007) especially for concrete or imageable concepts. In contrast, more dorsal aspects of the ATL i.e., anterior Superior Temporal Gyrus (STG) and Superior Temporal Sulcus (STS) are often implicated in abstract semantic analysis (Sabsevitz et al. 2005; Stowe et al. 1999). This localization of concrete semantic processing to the ventral and middle ATL is consistent with a wide range of pathological data from patients with SD, herpes simplex encephalitis, and ATL surgery (Mummery et al. 2000; Noppeney et al. 2007; Rogers et al. 2006; Rosen et al. 2002; Schmolck et al. 2002).

Imaging studies have also reported the role of ATL, especially bilateral temporal pole areas, and anterior MTG in personally familiar and famous name retrieval (Sugiura et al. 2006; Sugiura et al. 2009). Other areas of the brain in addition to ATL involved in processing of personally familiar and famous names and places are bilateral angular gyri, supramarginal gyri, left precuneus (Sugiura et al. 2009), posterior cingulate cortex (Sugiura, Shah, Zilles, and Fink 2005a).

Several theories have been proposed regarding the specific role of the ATL in semantic processing. Based on empirical studies in patients with SD and computational models of semantic memory, Patterson and colleagues have proposed that the ATL acts as a "hub" that binds distributed, modality-specific representations of object attribute knowledge (e.g., knowledge about shape, color, motion, sound, actions, and uses of objects) (Patterson, Nestor, and Rogers 2007; Rogers et al. 2004; Rogers et al. 2006)□□. The main role of this hub is to integrate various modality-specific features into a single concept (Patterson, Nestor, and Rogers 2007; Rogers et al. 2006; Tyler et al. 2004)□. A related theory proposes that the ATL processes unique concepts, such as specific individuals and places (Damasio, A.R. 1990; Damasio, H. et al. 2004; Gorno-Tempini, Cipolotti, and Price 2000)□. Given that the dorsal ATL responds strongly to abstract language (Binder et al. 2005; Sabsevitz et al. 2005)□, it has also been proposed that it is involved in computing associations between words, which are necessary for understanding abstract words but not for concrete words (Paivio 1986)□. Other authors have proposed that the ventral ATL, due to its location at the anterior end of the ventral visual stream, plays a particular role in representing knowledge about the visual attributes of concrete objects (Noppeney and Price 2003; Wise et al. 2000)□.

The lateral temporal lobe is also thought to be involved in representation of semantic memory. The current project focuses on semantic memory and the lateral temporal lobe structures. Building on these theories, we propose to develop an fMRI activation protocol optimized to detect semantic memory networks in the left lateral ATL. We will test the effects of several variables that have been hypothesized to modulate ATL activation. We predict that this optimized semantic paradigm will produce activation in the left lateral ATL, and that specific naming deficits can be predicted by the extent of damage to these activated regions in patients undergoing left ATL resection.

2.2 Clinical methods used in predicting the outcome of ATL surgery

This project focuses on the potential of fMRI in understanding the role of ATL in the semantic system. This ATL mapping protocol may be used by surgeons in predicting and preventing of language and verbal memory deficits in epileptic patients who will be undergoing surgery. Common clinical methods used for predicting ATL surgery outcome include neuropsychological testing, Electrocortical Stimulation Mapping (ESM), Wada testing and Functional Neuroimaging.

2.2.1 Neuropsychological tests

Neuropsychological tests are tasks that are specifically designed to measure a psychological function known to be linked to a particular brain structure and are generally used with ESM, fMRI or other such clinical modalities to predict the outcome of ATL surgery.

2.2.2 Electrocortical Stimulation Mapping

ESM is an in vivo procedure that is used to determine the eloquent function of cortex. ESM works on the observation that electrical stimulation of certain parts of the cortex can disturb ongoing language and speech functions in awake patients. Thus, it assumes that these areas of cortex when resected, would produce post-operative apahsia. While the patient performs the task, a particular area of the cortex is stimulated and important regions can be mapped out (Cannestra et al. 2004)□.

2.2.3 The Wada test

The Wada test is another in vivo procedure that is used to determine which side of the brain is responsible for language and memory functions. It is administered by first injecting sodium amobarbital (barbiturate) into one brain hemisphere through a catheter placed in the carotid artery via the femoral artery. The purpose is to shut the effects of one hemisphere of the brain to study the activity of the other. A series of neuropsychological tests are then presented to the patient (Simkins-Bullock 2000)□. Any deficits observed while the barbiturate is in effect can be attributed to functions residing in the anesthetized hemisphere.

2.2.4 Functional Neuroimaging

fMRI is one of the popular functional neuroimaging modalities used for studying brain function. It is based on the increase in blood flow to the local vasculature that accompanies neural activity in the brain. This increase in neural activity results in reduction of deoxyhemoglobin because the increase in blood flow occurs without an increase of similar proportion of oxygen extraction (Roy and Sherrington, 1890; Plum, Posner & Troy, 1968; Posner, Plum & Poznak, 1969; Fox and Raichle, 1985).

As deoxyhemoglobin is paramagnetic, it alters the T2* weighted MRI signal (Ogawa et al. 1990a, Ogawa et al. 1990b, Ogawa et al. 1993) and thus, deoxyhemoglobin is sometimes also referred to as an endogenous contrast enhancing agent, and serves as the source of the signal for fMRI. Using an appropriate imaging sequence, human brain functions can be observed without using exogenous contrast enhancing agents on a clinical strength (1.5 T) scanner (Bandettini et al. 1992; Bandettini et al. 1993; Schneider, Eschman, and Zuccolotto 2002). Functional activity of the brain determined from the magnetic resonance signal has confirmed known anatomically distinct processing areas in Broca's area of speech and language-related activities (Hinke et al. 1993).

2.3 Correlation between fMRI and Wada

Although Wada is extensively used across many centers in assessing the level of risk of cognitive morbidity, it has the disadvantage of being an invasive method. This has led to recent studies by Tivarus (Tivarus et al. 2009) and Trenerry that have centered around the debate whether fMRI can replace the Wada test. Many studies have also focused on comparisons between fMRI and Wada language lateralization (Bahn et al. 1997; Benke et al. 2006; Rutten, Ramsey, Van Rijen, Alpherts, et al. 2002; Sabbah et al. 2003; Woermann et al. 2003). Most have shown relatively high levels of agreement between the two tests (on the order of 80-90% concordance), and a view has emerged recently that fMRI is adequate for assessing language dominance (Abou-Khalil 2007; Baxendale, Thompson, and Duncan 2008).

2.4 Advantages of using fMRI in predicting cognitive decline following TLE surgery

One of the main advantages of using fMRI as a technique to image brain activity is that it is not invasive, which means that it does not require the injection of radioactive isotopes. Also, it requires a short scan time (about 2.0 min per run depending on the experimental paradigm). In addition to these advantages, spatial resolution less than 1mm for functional images is possible. However, with Positron Emission Tomography (PET), the technique requires injection of radioactive isotopes, multiple acquisitions of images, and therefore extended imaging times. Further, the pixel size of images obtained from PET is much larger than fMRI pixel size. Additionally, with PET, information from a single subject is limited to a finite number of imaging sessions because PET usually requires that multiple individual brain images be combined in order to obtain a reliable signal. Even though these limitations do not hinder the use of PET in many neuroscience applications, it is not suitable to assist in a pre-surgical treatment plan for an individual.

2.5 Role of fMRI in preventing cognitive decline

In addition to its potential use is predicting risk fMRI has also been suggested to have a role in preventing cognitive decline by allowing the surgeons to spare critical brain areas during resection. As the activated areas in brain observed by fMRI are necessary for normal function, these areas should be spared if possible. Many medical centers have already started adopting this approach (Kamada et al. 2006; Kho et al. 2007; Rutten, Ramsey, Van Rijen, Noordmans, et al. 2002; Ulmer et al. 2004). However, using fMRI maps for tailoring ATL resections will only be possible if the contrasts obtained from these fMRI experiments are sensitive enough to detect the critical functions of ATL. The most widely used clinical fMRI protocols for mapping language function are word generation and passive listening to speech. These protocols however, produce very little activation in ventral ATL (Binder et al. 2008; Fiez et al. 1996; Wise et al. 1991)□. As the rate of anomic aphasia after ATL resection is significant (30-60%), it can be concluded that these activation protocols are insensitive in mapping critical functions of ATL.

2.6 Significance and Novelty of this research

The ATL is sensitive to abstract concepts more than concrete concepts (Binder et al. 2005; Sabsevitz et al. 2005)□. One hypothesis is that ATL is involved in computing associations between words. According to the Dual Coding Theory (Paivio 1991)□, there are two systems for encoding words into semantic memory: verbal and nonverbal. Abstract words are coded into the semantic memory with only verbal or linguistic information whereas concrete words are coded with both verbal and nonverbal information because of their direct links to sensory-motor domains. Abstract words on the other hand do not have such links and thus have to be understood through associations with other words (Paivio 1986)□. If the nature of these associations can be understood, then the sensitivity of ATL activations can be maximized. Different associative measures like number of associated concepts and associations due to concept similarity in the semantic neighborhood were studied. Our first specific aim was to study the ATL response to associations with abstract and concrete concepts. We hypothesized that ATL response will be modulated by these measures and different areas of ATL will be modulated by abstract and concrete words.

A selective deficit in retrieving proper people has been observed in patients with TLE and temporal lobectomy patients (Glosser, Salvucci, and Chiaravalloti 2003)□. Activation of ATL for famous people relative to unfamiliar people that have used famous people or face images as stimuli has also been reported (Grabowski et al. 2001; Sugiura et al. 2006)□. In a review of studies reporting patients with impairment in famous people recognition, Gainotti (2007)□ found that patients with right ATL damage had impairments in retrieving person specific information and loss of familiarity feelings, while left ATL patients were impaired in recalling people. It is not clear whether ATL activation observed in imaging studies is due to the fact that there is information associated with a name or just due to recognizability. If ATL is involved in combining different kinds of information associated with that name, then greater activation would be observed for people with more knowledge associated with them relative to people with lesser knowledge. However, if ATL is involved in representing a name as a unique entity and does not combine information associated with it, then the activation should not be modulated by the amount of knowledge associated with that name. Our second specific aim was to study the ATL response to proper people and the information associated with those people. We hypothesized that ATL activation will be modulated by the degree of information associated with the people.

3. MATERIALS AND METHODS

3.1 Subjects

Twenty-two healthy right-handed native English speakers with no history of neurological illness participated in this study. All subjects were screened to make sure they met the safety requirements for MRI prior to scanning. A written informed consent was obtained from them prior to the experiment in accordance with the protocol sanctioned from Medical College of Wisconsin as well as Marquette University Institutional Review Boards. They were compensated for their participation.

3.2 Scanning Parameters and Image acquisition

MR images were acquired with a 3.0 Tesla long bore scanner (GE Medical Systems, Milwaukee, WI). Structural T1 weighted images were collected using SPGR sequence (TR= 8.2ms TE=3.2ms, flip angle=12, FOV= 240mm, 256x224 matrix, slice thickness = 1mm). Functional data consisted of gradient echo planar images (EPI) (TR= 2500ms, TE=20ms, flip angle=80, FOV=192mm, 96 x 96 matrix, slice thickness=2mm, functional voxel size=1.5x1.5x2mm^3, anatomical voxel size=.938x.938x1mm^3). 34 oblique slices covering the temporal lobe, inferior frontal and supramarginal gyri were collected as shown in Figure 2.1. Oblique acquision, combined with low TE and small voxel size were chosen to minimize signal loss in the anterior temporal lobes.

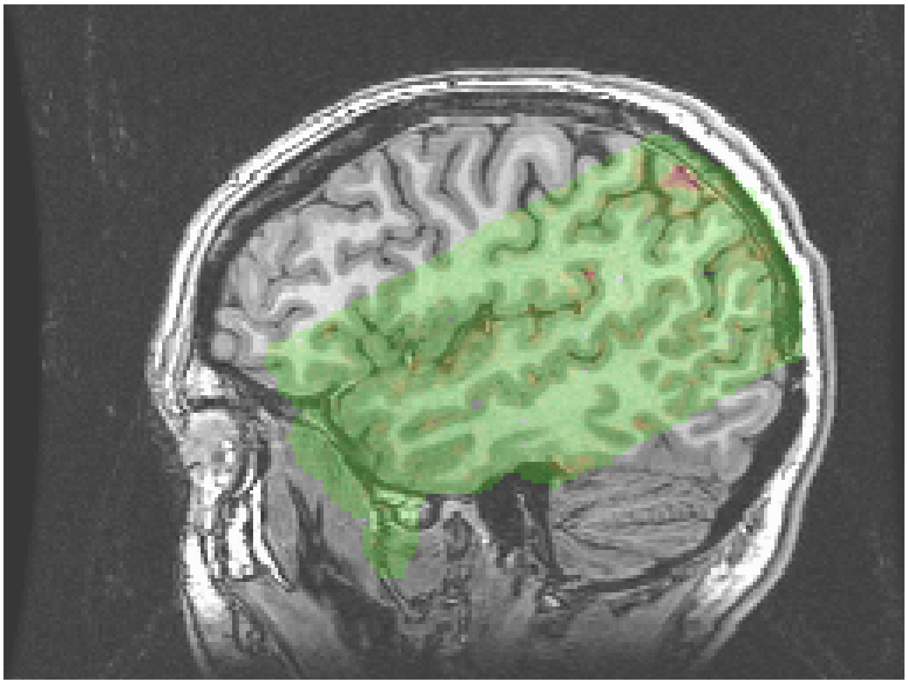

Figure 3.1: Areas of the brain covered in image acquisition. Oblique acquisition covering temporal, inferior frontal and inferior parietal lobes.

Two experiments were conducted using the same subjects and scanning parameters during a single imaging session. Experiment 1 used common names, while Experiment 2 used proper names.

3.3 Stimuli

The stimulus set consisted of 50 concrete words (*potato, chair etc*), 50 abstract words (*gain, virtue etc*) and 100 pronounceable non-words (*odomay, flooz etc*). A list of all the stimulus items used in Experiment I is provided in Appendix I. These three stimulus conditions (concrete, abstract and non-words) were matched on letter length, phoneme length, mean positional bigram frequency (MPBF) and orthographic neighborhood size using phonological data and frequency counts from English Lexicon Project database (Baayen, Piepenbrock, and Van Rijn 1993; Balota et al. 2007)□. Words (concrete and abstract) were matched to ensure that there were no significant differences between categories on any of the matched characteristics mentioned above. However, concreteness and imageability were significantly different for concrete and abstract words. A two sample t-test with equal variance was performed at $p<0.05$ to verify the significance. Concrete and abstract words differed significantly on concreteness and imageability conditions. Summary statistics for each of these conditions are given in Table 3.1.

Condition	*#Letters*	*MPBF*	*ON*	*#Phonemes*	*Frequency*	*CNC*	*IMG*
Concrete	5.45 (1.05)	1335 (641.74)	1.54 (3.08)	4.60 (1.02)	57.03 (67.60)	557.13 (76.57)	5.76 (0.78)
Abstract	5.53 (1.20)	1325 (851.42)	1.28 (2.74)	4.59 (1.32)	47.85 (51.50)	311.47 (66.24)	3.56 (0.75)
Nonwords	5.44 (0.77)	846 (606.76)	1.90 (3.17)				

Table 3.1: Summary statistics for word variables. Mean and standard deviation (in parenthesis) of different characteristics of stimulus words like number of Letters, Mean Positional Bigram Frequency (MPBF), Orthographic Neighborhood (ON), number of Phonemes, Frequency, Concreteness (CNC), Imageability (IMG)

Furthermore, for each word, several variables estimating its semantic associative neighborhood were obtained from the University of South Florida Free Association Norms (Nelson, McEvoy, and Schreiber 2004)□. We hypothesize that these associative measures will modulate the activation in the semantic system, including that in the ATL. These measures were Neighborhood

Set Size (QSS), Mediated Strength (QRSG), Mean Connectivity (QMC) and Probability (QPR), briefly described below.

Set Size (QSS)

This variable provides a relative index of how many near neighbors (free associates) the stimulus word has. It is calculated by counting the number of different responses given by two or more participants.

Resonance Strength (QRSG)

This measure is calculated by cross multiplying cue-to-associate strength by associate-to-cue strength for each associate in the set and then summing the result. Thus, it measures total “resonance” between the word and its associates.

Mean Connectivity (QMC)

This variable is a measure of mean connectivity between associates of the stimulus word. It is obtained by norming the associates of the stimulus word with a separate group of participants, counting the number of connections among the associates in the set, and then dividing by the size of the set. Thus, it estimates the density of the neighborhood of a word by calculating the mutual connectivity between the neighbors, normalized by the number of neighbors.

Probability (QPR)

This variable defines the probability of the associate word producing the stimulus word as an associate. It is calculated by counting the number of associates in the set that produce the stimulus word as an associate and then dividing it by associate set size. This measure is similar to QRSG, except it is normalized with respect to set size.

Table 3.2 describes the summary statistics of these covariates.

Condition	*QSS*	*QRSG*	*QMC*	*QPR*
Concrete	16.64 (6.08)	0.09 (0.09)	1.66 (0.67)	0.43 (0.24)
Abstract	16.53 (6.92)	0.04 (0.06)	1.52 (0.59)	0.27 (0.19)

Table 3.2: Summary statistics of covariates used in Experiment I. Mean and standard deviation (in parenthesis) of different covariates. QPR and QRSG are significantly different for concrete and abstract words. This is verified by performing a two sample t-test of equal variance at $p<0.05$.

For Experiment 2, the stimulus set consisted of 40 Famous people (*Barack Obama, Nelson Mandela etc*), 40 Famous places (*Hollywood, Statue of Liberty etc*), 40 Personally familiar people, 40 Personally familiar places, 40 Unknown people and 40 Unknown places. The famous people and places list, which was used for all subjects, was constructed such that most items were familiar to the subjects. The subjects provided a list of personally familiar people and places a few days before the experiment. The unknown people and places were which were also common for all the subjects were collected from the telephone directory and the web and were verified using ratings (see Data Collection Procedure below). Refer Appendix II for a list of famous and unknown people and place names used in this experiment.

3.4 Data collection procedure

After the consenting procedure, the subjects were instructed to remove all metallic objects from their body and clothing (jewelry, watches, coins, cell phones etc.). Subjects requiring eye-glasses were provided with special MR compatible pairs. The subjects were then asked to lie down on the scanner bed and their head is placed in a head coil, which allows the measurement of changes in magnetic field. They were instructed to keep their head as still as possible to avoid motion artifacts in the MR images. They were also provided with earplugs to protect their ears from acoustic noise from the scanner. A projector is used to display the stimuli on a screen located inside the MR scanner. The stimuli were presented at the center of the screen in white on a black background. The font used was Arial and the size was 12. Each stimulus is presented for 1 second. A button box is provided to the subjects to collect their responses.

The stimuli were presented visually in a pseudo-random order in jittered event related design. In an event related design, stimuli are presented for short duration with timing and order that can be randomized. In addition to being less sensitive to head motion (Birn et al. 1999)□, event related designs can detect variations in hemodynamic response and allow for analysis of individual response to trials (Schacter et al. 1997)□. The interval was 2.5-12 seconds.

Each subject underwent the scanning procedure for one session and each session had 8 runs (4 runs for Experiment 1 and 4 runs for Experiment 2). Each run in Experiment 1 had 12 (or 13) Abstract words, 13 (or 12) Concrete words, 25 Non-words and fixation (“+”) points in between. Each run in Experiment 2 had 20 Famous people, 20 Personally familiar people, 20 Unknown people or 20 Famous places, 20 Personally familiar places, 20 Unknown places. The people and places were not used together in the same run. The order of the stimuli was randomized using Optseq (Burock et al. 1998). E-Prime (Schneider, Eschman, and Zuccolotto 2002) was used on a Windows PC for presenting the stimulus and collecting the response times of the subjects during the task.

For Experiment 1, the subjects were asked to make a lexical decision, i.e., decide whether the presented stimulus was a real word or not and for Experiment 2, they had to decide whether they knew the person name/place and respond as quickly as possible without making mistakes, by pressing one of the two keys on the button box with index or middle finger. The finger and hand used for a positive response were counterbalanced across subjects. The subjects were trained with a sample test on a laptop computer prior to performing the task inside the scanner.

After the scanning procedure, the subjects were provided with a laptop computer to rate the people and place names that they saw inside the scanner (Experiment II) on four different variables.

The “Emotional Response” (ER) rating describes the emotion associated with a particular person or place. This rating is used for all people and places (Famous, Personally familiar, Unknown). The scale for this rating is from -10 to +10. A strong positive emotion towards a person/place is rated +10 while a strong negative emotion is rated -10. For example, if imagining that a person met with an accident causes worry or sadness, or imagining that the person won a lottery causes happiness, then that person’s name is rated on a positive scale. Similarly, for places, if imagining a place being destroyed in a bomb blast causes deep regret, that place is rated positively. Whereas, if there is a negative emotion associated with a person or place, then the rating is on the negative scale. For persons/places for whom there is neutral response, a rating of 0 is used.

The “Amount of Knowledge” (KN) rating describes the amount of information known about a person or place. This rating is also obtained for all people and places. A scale of 0 to +10 is used for this rating (0 signifying no knowledge and 10 signifying a lot of knowledge).

The “Amount of Interactive Experience” (IE) rating is obtained for personally familiar and unknown people and places. On scale of 0 to +10, if a lot of time is spent with a person or at a place, like daily or for years, then that person or place is rated 10. If moderate amount of time was spent; like meeting that person once in a few months or visiting a place often but not daily, then that person or place can be rated somewhere between 4 and 7. If there is no interaction, then that person or place is rated 0.

The “Amount of Sensory Experience” (SE) rating has Famous people and places. The scale for this rating is also from 0 to +10. This rating describes the amount of experience gained by seeing that person’s or place’s photographs, videos, documentaries or any form visual or auditory experience.

3.5 fMRI Image analysis

The AFNI software package (Cox 1996) was used for image analysis. C shell scripts were used for pipe lining the AFNI commands. Various pre-processing steps are necessary in fMRI analysis in order to take raw data from the scanner and prepare it for statistical analysis. The pre-processing steps apply numerous image and signal processing techniques to the raw data to reduce noise and artifacts. These steps were crucial for improving the power of subsequent analyses and also for making the statistical analyses valid.

The processing steps were used in the following order:

1. Converting anatomical image files into 3D+time datasets

   The AFNI command ‘to3d’ is used to convert 2D brain images into AFNI .BRIK format (3D volume datasets). The align_epi_anat.py command is then used to align EPI images to the anatomical datasets.

2. De-spiking the runs

   De-spiking is the process of removing extreme outliers from the dataset. The AFNI command 3dDespike is used for this purpose. It takes the aligned EPI dataset as input and writes a new dataset with the “spike” values removed. 3dDespike identifies spikes on a voxel-by-voxel basis and uses interpolation to replace this voxel's value with a value based on neighboring voxels.

3. Motion Correction

Also known as re-alignment or co-registration, motion correction is done to correct for differences in images due to head movements. This is implemented by first using 3dToutCount command to calculate the number of outliers in the 3D+time dataset in the brain region.

The number of outliers is proportional to the number of voxels in the image. A threshold value of 10% is then specified in a C shell script to remove outliers that were greater than the threshold value. A file is then created which contains head translation in three directions (x, y, z) and head rotation in three directions (roll, pitch, yaw). This file is referred to as “motion parameter” file.

4. Masking

The purpose of masking is to

i. Specify which areas in the image were brain and which were not

This is achieved by using the AFNI command 3dAutomask. The input is a skull-stripped image (done using 3dSkullStrip command) and the output is a brain only mask.

ii. Measure signal in ventricles, white matter areas and regions outside the brain, which can be considered as noise. This “noise” is then used as a covariate in the next step so that any signal that correlates with this “noise” signal can be partialled out. Creating masks for ventricles and white-matter regions, and calculating the average signal in these masks accomplished this.

5. Multiple Linear Regression analysis

The 3dDeconvolve and 3dREMLfit commands are used for multiple linear regression analysis of the voxel response data. Multiple linear regression is used to test for differences in blood oxygen level dependent (BOLD) signal among different conditions at each voxel. Square-wave functions represent various stimulus presentation blocks being used. This square wave is then convolved with a gamma variate function using parameters that approximate the BOLD hemodynamic response. This function that results from the convolution is a close approximation of the hemodynamic response observed in the brain. These functions were then entered into a multiple regression of the fMRI data, along with the motion and noise parameters derived from previous pre-processing steps. Contrasts between different stimulus conditions were performed under general linear model to identify voxels in which BOLD response differed between conditions and the resulting amplitude response and t statistic were stored in the functional output bucket.

For Experiment 1, contrasts were obtained between Abstract-Nonwords, Concrete-Nonwords, Concrete-Abstract conditions. In addition to these, contrasts were also obtained with different covariates like QMC, QSS, QRSG and QPR. For Experiment 2, contrasts were obtained between Famous-Unknown, Personally familiar-Unknown, People-Places, Famous-Personally familiar conditions. Contrasts with KN, IE, ER and SE as covariates were also calculated.

6. Beta Scaling

The response amplitude or the betas that resulted from multiple linear regression were scaled in proportion to the raw signal difference between the subjects.

7. Spatial filtering (blurring)

There were two reasons for applying spatial filtering as a pre-processing step. Firstly, blurring can increase signal to noise ratio in the data. The signal of interest, in this case, is the change in image intensity of a specific voxel resulting from the stimulus-induced activation via the BOLD effect. The noise is the unavoidable random variations in image intensity which were present even when no stimulation is applied. The main reason for performing spatial filtering of the fMRI data is to reduce the noise level whilst retaining the underlying signal. The blurring function is effectively a local averaging method in which unrelated noise values in the local neighborhood will tend to cancel each other out. However, in order for the underlying signal to not be reduced along with the noise, it is required that the extent of the blurring is no larger than the size of the activated region. Therefore, if it is likely that the activated regions will be very small, then spatial filtering should not be carried out.

The secondary reason for spatial filtering is to account for structural and functional differences in anatomy between brains. The most common method of carrying out spatial filtering is to convolve each volume with a Gaussian filter. The width of this filter, usually expressed in mm, determines the extent of the blurring that takes place. A width of 6 mm full-width-half-maximum (FWHM) was used, where the term FWHM refers to the full width of the kernel at the points, which were half of the value of the central maximum.

8. Group level analyses

The smoothed coefficient BRIKS from all subjects' data were then used for group level analysis. 3dttest++ command is used to perform a t-test to compare different stimulus conditions to see if the activation due to one stimulus condition in a region was significantly different from the activation due to other stimulus condition or not. –zskip option is used with 3dttest++ to exclude voxels that were zero in the analysis. This is mainly used when all subjects' brain images do not overlap perfectly due to small differences in the oblique acquisition plane.

9. Cluster correction

When conducting voxel wise test statistics, false positive error inflation is a problem. A common approach to correct these multiple comparisons is to use a clustering method that determines how big a contiguous set of voxels needs to be at an uncorrected threshold P_u, in order to be significant at a corrected threshold P_c. A value of 0.01 was used for P_u and Monte Carlo simulations are run using this value. This resulted in a cluster size of 790 for the whole brain. Clusters smaller than 790 are removed to achieve a corrected alpha level of 0.05. Similarly separate Monte Carlo simulations were run for left and right temporal and inferior parietal regions that included superior, middle and inferior temporal gyri, temporal pole, angular gyrus, supramarginal gyrus. This was done to increase sensitivity in these regions. Monte Carlo Simulations on left temporoparietal region resulted in a cluster size of 476 and 464 on the right. Therefore clusters smaller than these values (476 and 464) were removed to achieve the corrected alpha level of 0.05.

10. Overlaying the cluster corrected data on inflated brain images

The cluster corrected maps are then mapped to the brain surface using 3dVol2Surf and overlaid on inflated brain images using CARET (Van Essen et al. 2001) for displaying the results in a better format.

4. RESULTS

4.1 Experiment I

4.1.1 Behavioral Results

The subjects were more accurate in categorizing concrete words as words as compared to abstract words. There was a significant difference in accuracy between abstract-concrete and concrete-nonwords conditions as shown in the Figure 4.1. A t-test was performed between conditions to test for significance at $p<0.05$.

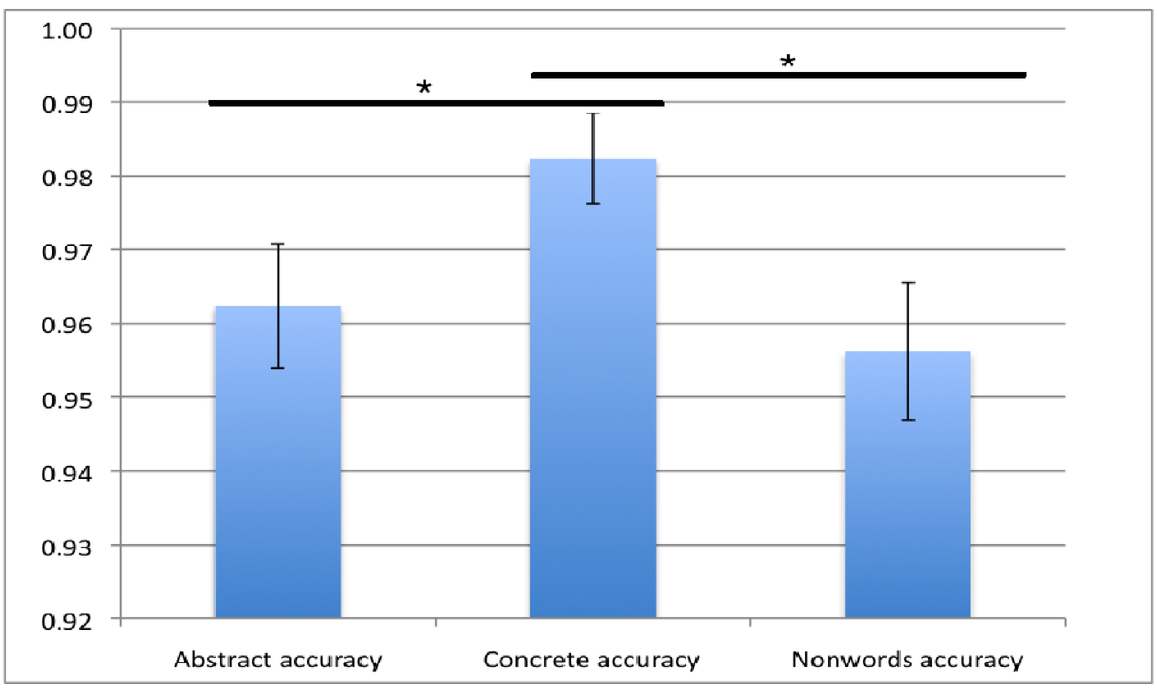

Figure 4.1: Accuracy statistics for different conditions from Experiment I. The error bars show the standard error of the mean. The asterisk (*) shows the significance value of 0.05.

Nonwords had the greatest response time (RT) followed by abstract words and concrete words. A significant difference in RT was observed between abstract-concrete, concrete-nonwords and abstract-nonwords conditions as shown in the Figure 4.2. A t-test was performed between conditions to test for significance at $p<0.05$.

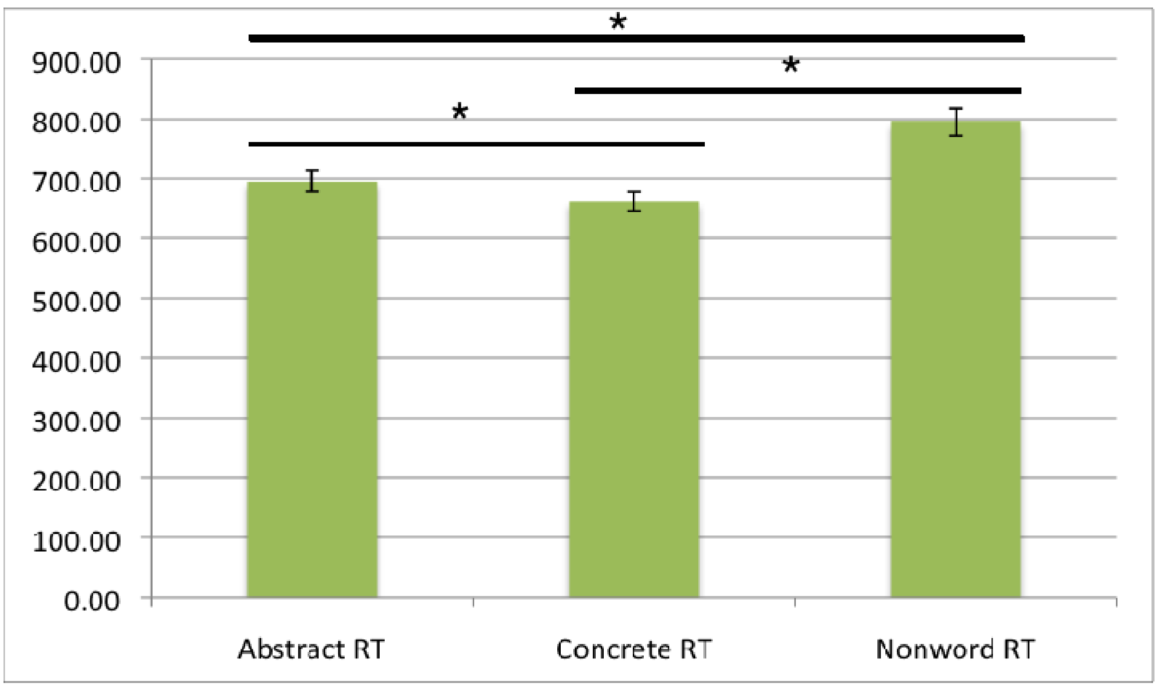

Figure 4.2: Response time statistics for different conditions from Experiment I. The error bars show the standard error of the mean. The asterisk (*) shows the significance value of 0.05.

4.1.2 fMRI Results

Figure 4.3 shows different cortical regions of the brain on an inflated brain map created using freesurfer (Desikan et al. 2006)□.

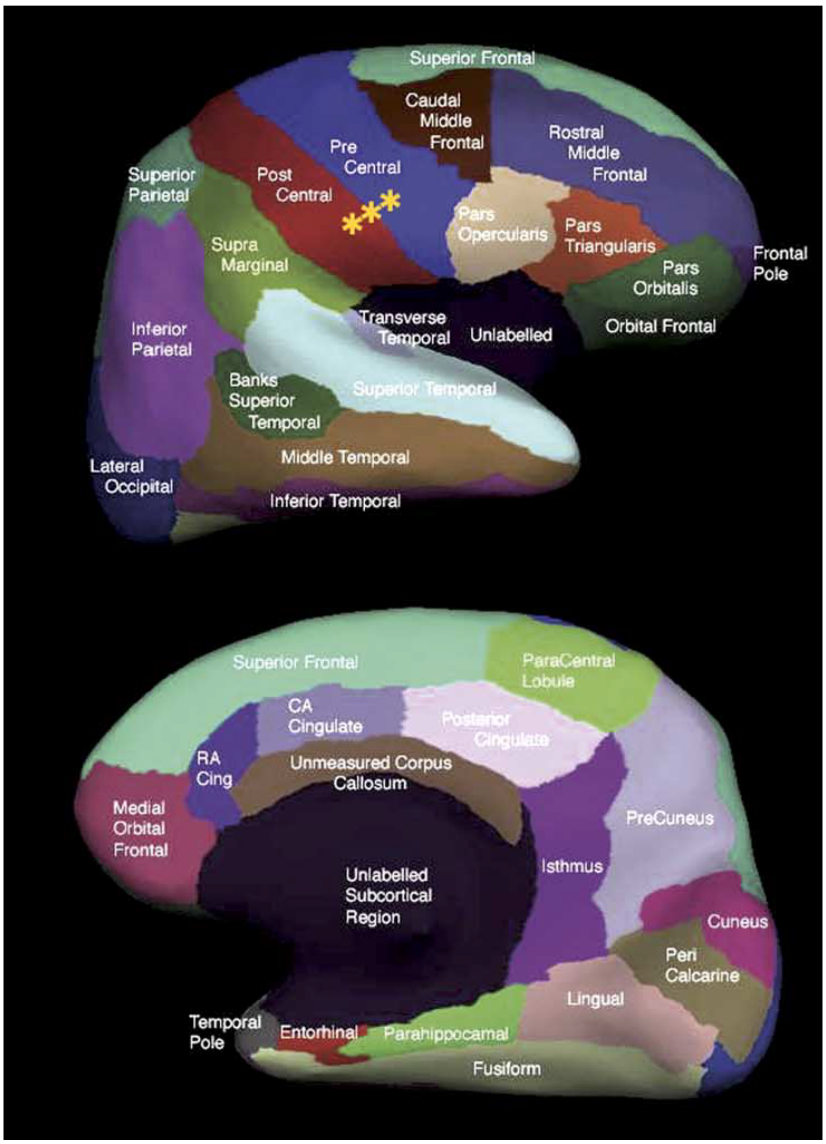

Figure 4.3: Cortical representation of different regions on an inflated brain map. The top image shows the lateral view while the bottom image shows medial view. The yellow asterisks indicate the cortex around the central sulcus which is now visible on the inflated surface.

The yellow/orange areas in the figures below show the positive activation while the blue/cyan regions show negative activation. Positive activation in this case means that the activation due to the first condition is more than the second condition at that voxel and negative activation means that activation due to second condition is more than the first condition at that voxel. Cluster information and peak coordinates are reported in Appendices III and IV.

Abstract - Nonwords

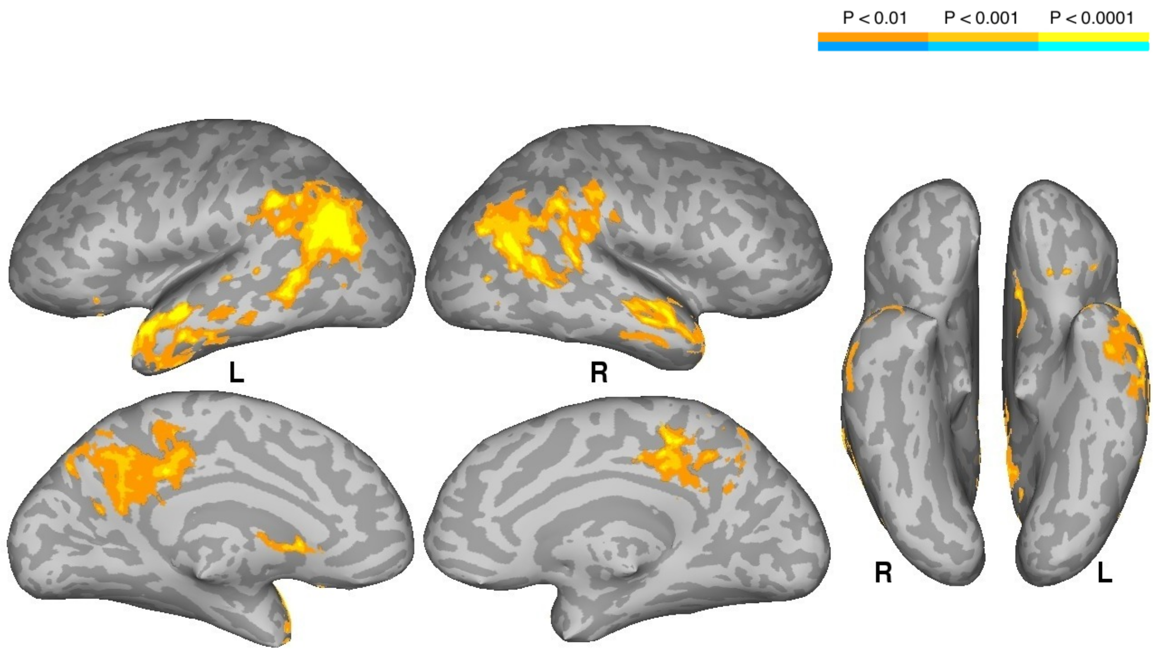

Figure 4.4: Cortical areas showing activation/deactivation for Abstract - Nonwords condition.

Bilateral activation of angular gyrus (AG), middle temporal gyrus (MTG), parahippocampal gyrus (PHG), precuneus, superior temporal sulcus (STS) and supramarginal gyrus (SMG), posterior cingulate gyrus (PCG) is observed for Abstract - Nonwords condition (Figure 4.4).

Concrete - Nonwords

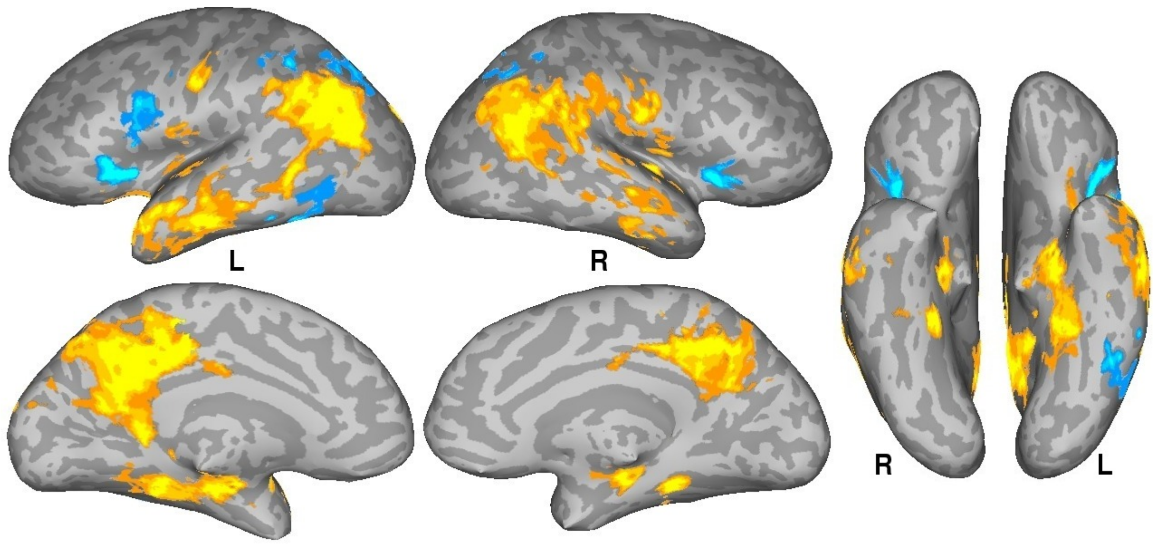

Figure 4.5: Cortical areas showing activation/deactivation for Concrete - Nonwords condition.

Left anterior ITG, bilateral Precuneus, MTG, AG, PHG, STS, SMG, PCG activated more for Concrete words as compared to Nonwords.

Bilateral activation of IPS, IFG (pars triangularis), left ITG and FG is observed for Nonwords -Concrete condition. (Figure 4.5)

Concrete - Abstract

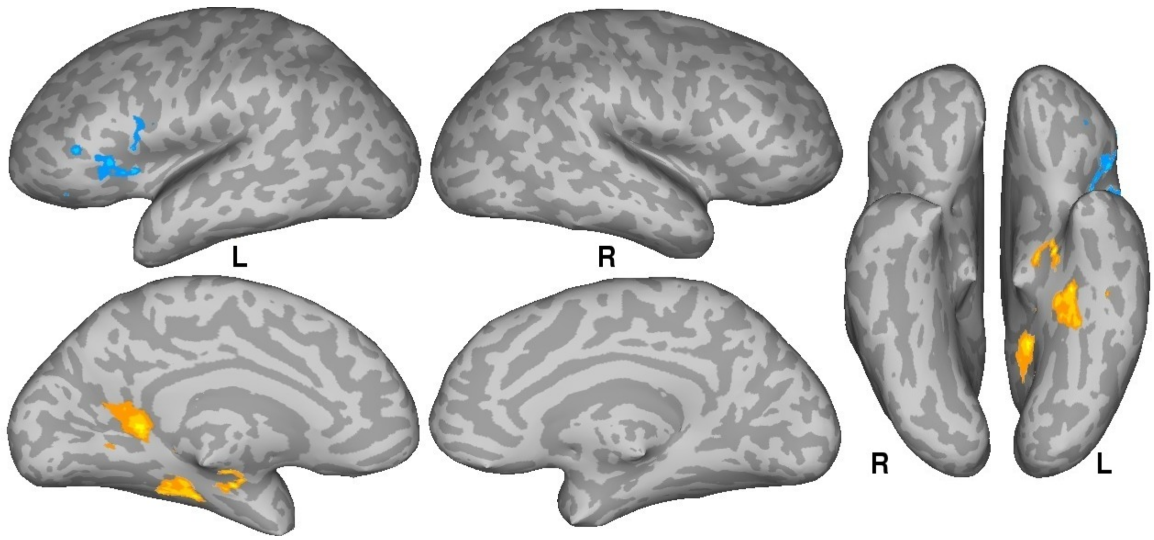

Figure 4.6: Cortical areas showing activation/deactivation for Concrete - Abstract condition.

Left parahippocampal gyrus (PHG) and posterior cingulate gyrus (PCG) are activated for Concrete - Abstract condition. Left IFG (p. triangularis) was activated for Abstract - Concrete condition. (Figure 4.6)

Words (concrete and abstract) - Nonwords

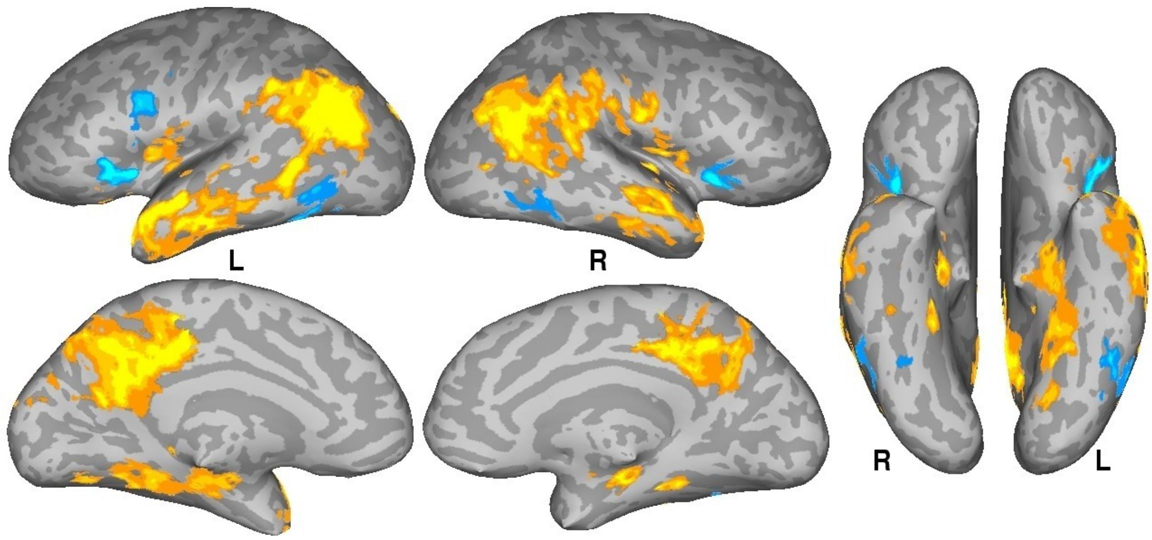

Figure 4.7: Cortical areas showing activation/deactivation for Words (concrete and abstract)-Nonwords condition.

Bilateral activation of AG, middle cingulate cortex, MTG, ITG, STS, temporal pole, FG, PCG, left STG, putamen and right hippocampus was observed for Words - Nonwords condition. Bilateral activation of insular lobe was observed for Nonwords - Words condition (Figure 4.7).

Activations with associative measures as covariates

Resonance Strength (QRSG)

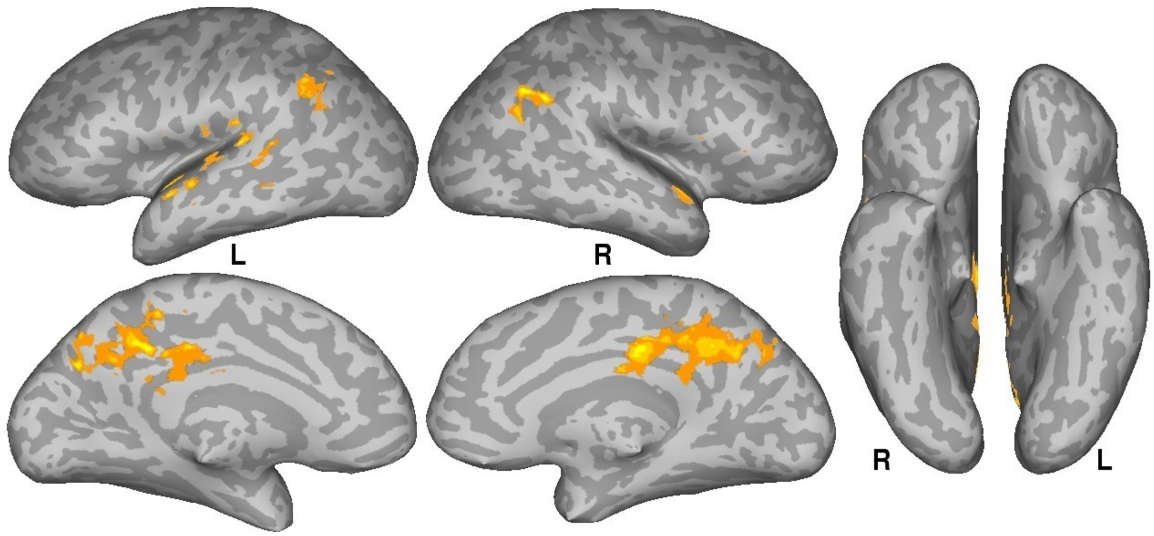

Figure 4.8: Cortical areas showing positive correlation for words with Resonance Strength (QRSG).

Bilateral AG, STG, precuneus and left transverse temporal gyrus are positively correlated with QRSG (Figure 4.8).

Set Size (QSS)

Figure 4.9: Cortical areas showing positive correlation for words with Set Size (QSS).

Left AG is positively correlated for words with QSS (Figure 4.9).

Probability (QPR)

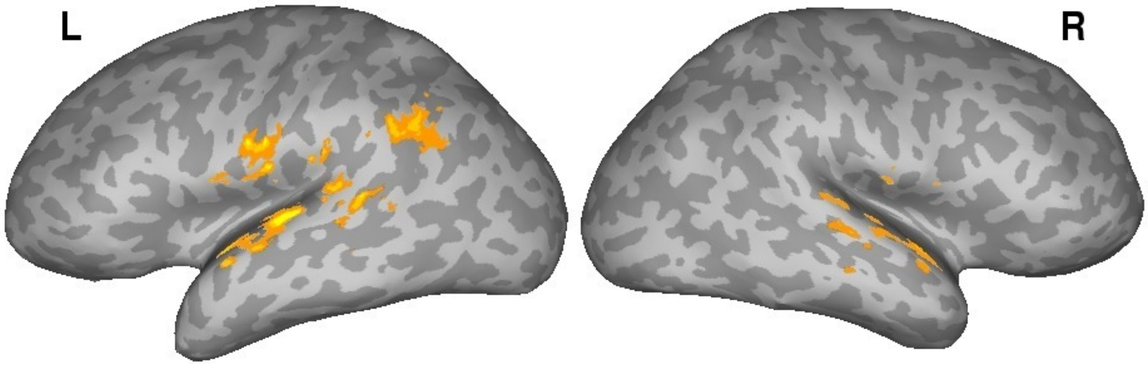

Figure 4.10: Cortical areas showing positive correlation for words with Probability (QPR).

Bilateral STG, left transverse temporal gyrus, SMG and inferior portion of post central gyrus are positively correlated for words with QPR (Figure 4.10).

Mean Connectivity (QMC)

No correlation is observed for words with QMC.

Table 4.1 below shows the correlation between different variables for Experiment I.

	#letters	Freq	MPBF	#phn	#syl	RT	QSS	QMC	QPR	QRSG	CNC	IMG	ON	semD
#letters	*													
Freq	-0.06	*												
MPBF	0.606	0.209	*											
#phn	0.779	-0.016	0.501	*										
#syl	0.671	-0.033	0.358	0.697	*									
RT	-0.123	-0.27	-0.185	-0.112	-0.101	*								
QSS	0.021	0.343	0.11	0.059	0.024	-0.177	*							
QMC	-0.025	0.091	-0.023	0.021	-0.09	0.259	0.286	*						
QPR	-0.253	0.226	-0.104	-0.206	-0.054	-0.229	-0.045	0.084	*					
QRSG	-0.179	0.165	-0.042	-0.187	-0.141	-0.162	-0.227	-0.081	0.604	*				
CNC	-0.033	0.048	-0.032	0.021	-0.034	-0.36	-0.074	0.125	0.37	0.329	*			
IMG	0.042	-0.013	0.017	0.02	0.062	-0.295	-0.104	0.168	0.468	0.397	0.913	*		
ON	-0.639	0.121	-0.163	-0.538	-0.578	0.076	-0.003	-0.066	0.186	0.116	0.019	-0.057	*	
semD	0.099	0.389	0.197	0.092	0.057	0.09	0.113	-0.111	-0.074	-0.179	-0.535	-0.558	0.056	*

Table 4.1: Correlation matrix for variables from Experiment I. The values highlighted in yellow are the ones with significant correlation.

4.2 Experiment II

4.2.1 Behavioral Results

Personally familiar people (PN) and place (PP) names had greater accuracy as compared to famous people (FN) and places (FP). Unknown people (UN) and places (UP) had greater accuracy than famous people and famous places but lesser than personally familiar people and places. There was a significant difference in accuracy between PN-FN, PP-FP, FP-UP conditions as shown in the Figure 4.11. A t-test was performed between conditions to test for significance at p<0.05.

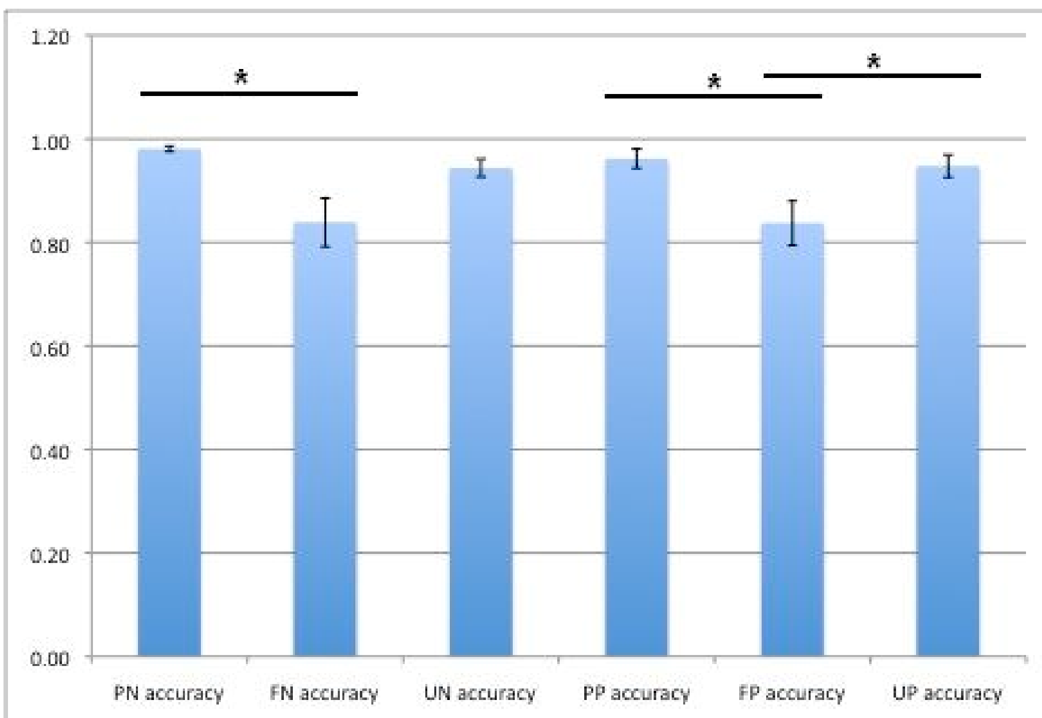

Figure 4.11: Accuracy statistics for different conditions from Experiment II. The error bars show the standard error of the mean. The asterisk (*) shows the significance value of 0.05. PN indicates Personally familiar people, FN- Famous people, UN-Unknown people. PP-Personally familiar places, FP-Famous places, UP-Unknown places.

Unknown people and place names had the greatest RTs followed by famous and personally familiar people and place names. Significant differences in RTs are observed between Personally familiar-Famous, Famous-Unknown and Personally familiar-Unknown conditions for both people and place names as shown in the Figure 4.12. A t-test was performed between conditions to test for significance at $p<0.05$.

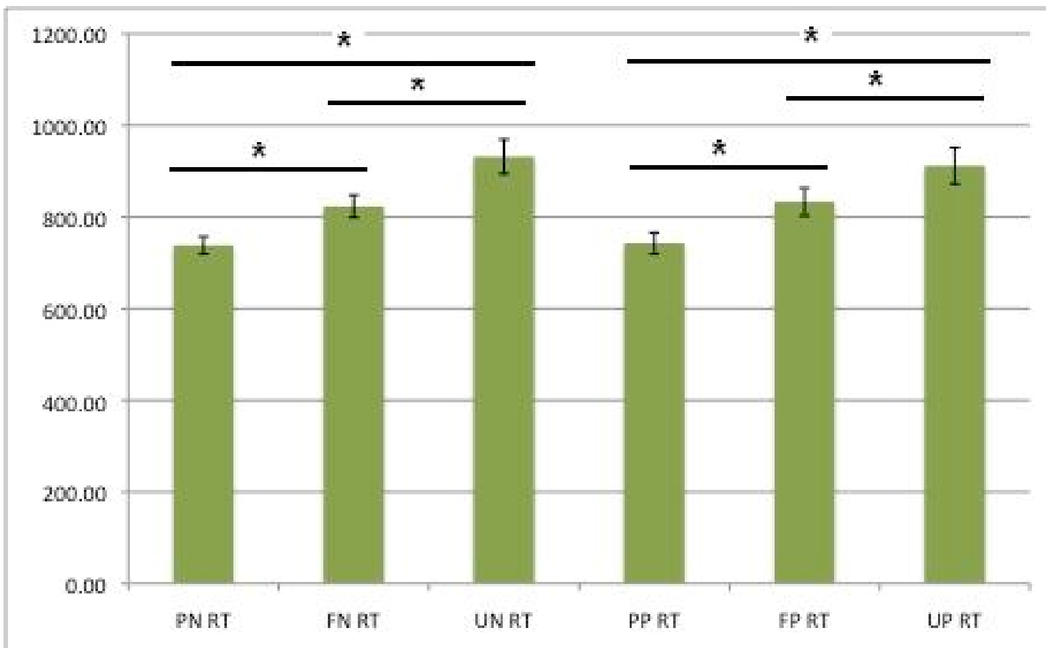

Figure 4.12: Response Time statistics for different conditions from Experiment II. The error bars show the standard error of the mean. The asterisk (*) shows the significance value of 0.05. PN indicates Personally familiar people, FN- Famous people, UN-Unknown people. PP-Personally familiar places, FP-Famous places, UP-Unknown places.

4.2.2 fMRI Results

Famous People - Unknown People

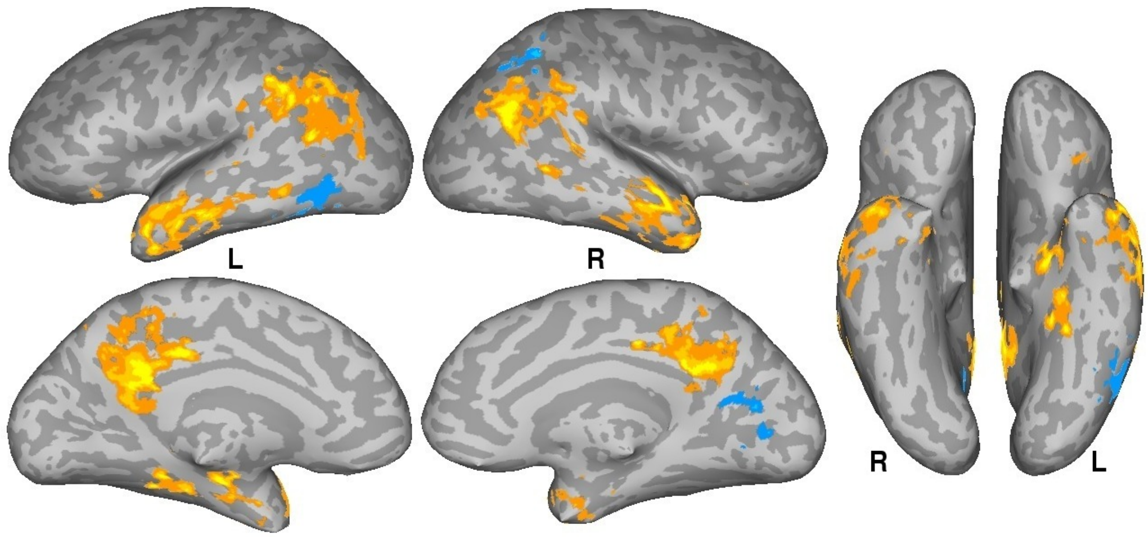

Figure 4.13: Cortical areas showing activation/deactivation for Famous - Unknown people condition.

Bilateral activation of AG, PCG, MTG, STS, STG, temporal pole and left Hippocampus is observed for Famous - Unknown people condition. Negative activation is observed in right intra-parietal sulcus (IPS), cuneus and posterior aspect of left MTG (Figure 4.13).

Famous Places - Unknown Places

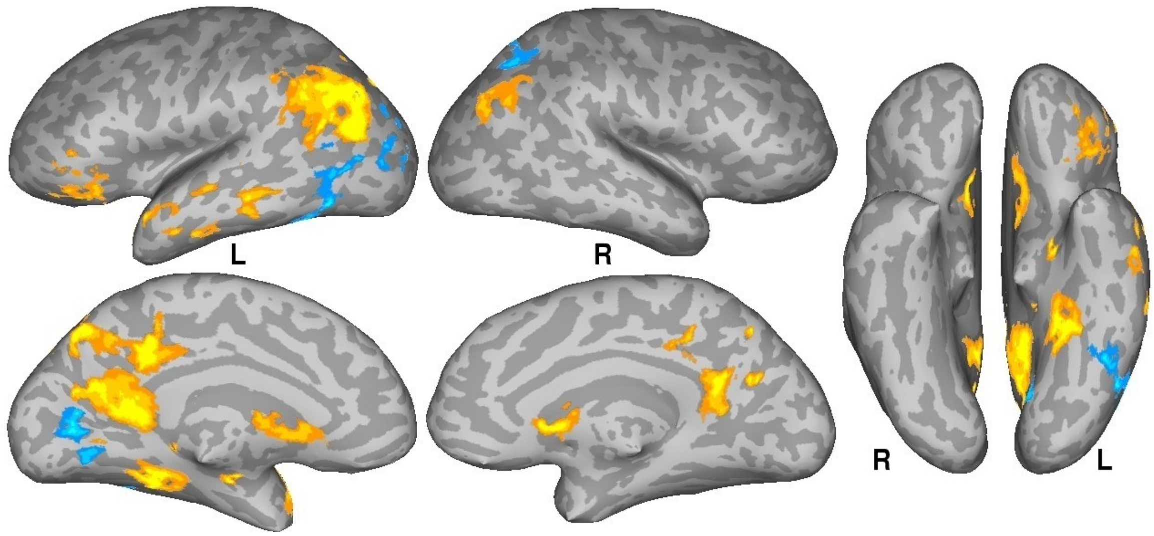

Figure 4.14: Cortical areas showing activation/deactivation for Famous - Unknown places condition.

Bilateral activation of AG, PCG, caudate, left precuneus, MTG, ITG, MCG, FG, IFG and temporal pole is observed for Famous - Unknown places. Negative activation or activation for Unknown - Famous places is observed in left cuneus, middle occipital gyrus and right superior parietal lobe (Figure 4.14).

Personally familiar people - Unknown people

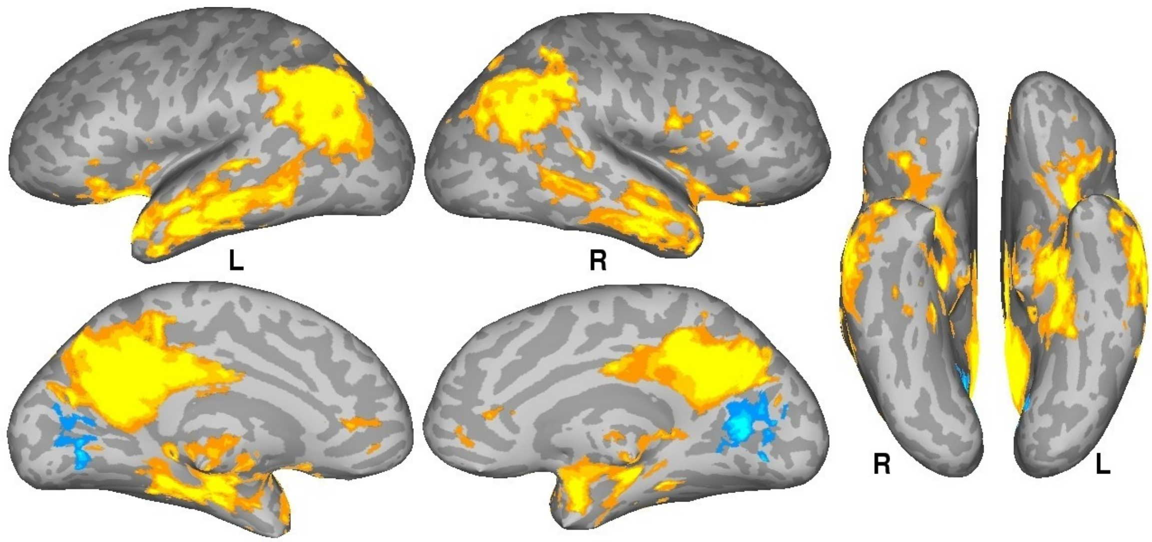

Figure 4.15: Cortical areas showing activation/deactivation for Personally familiar - Unknown people condition.

Bilateral activation of AG, PCG, precuneus, STG, MTG, ITG, PHG, IFG, temporal pole and left anterior cingulate gyrus (ACG) is observed for Personally familiar people - Unknown people condition. Lingual gyrus is activated bilaterally more for Unknown people as compared to Personally familiar people (Figure 4.15).

Personally familiar places - Unknown places

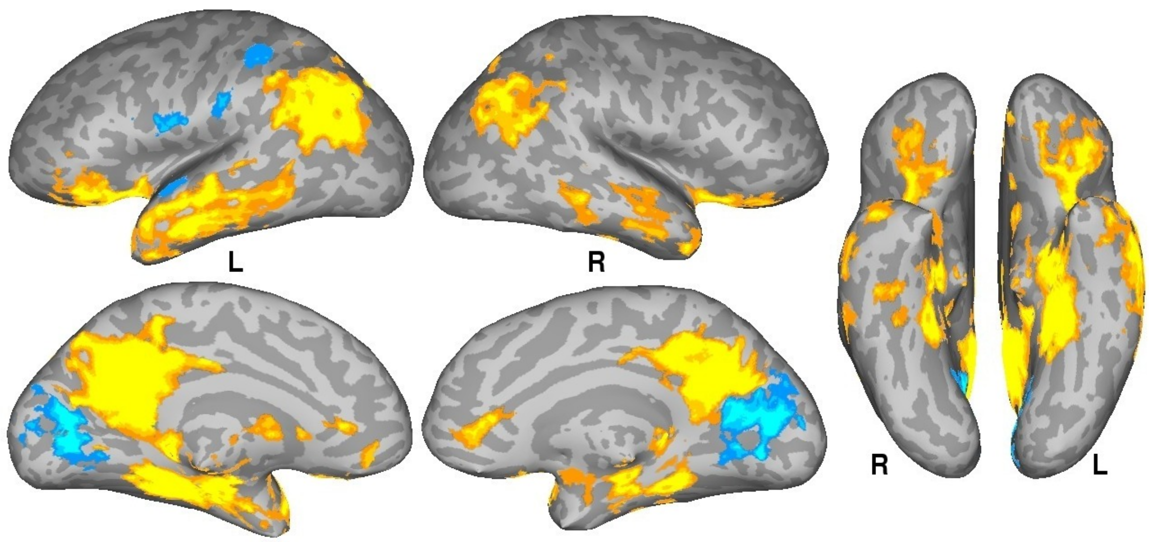

Figure 4.16: Cortical areas showing activation/deactivation for Personally familiar - Unknown places condition.

Bilateral activation of AG, PCG, precuneus, MTG (more on the left), PHG, IFG (p.orbitalis), temporal pole, anterior cingulate gyrus (ACG) and left STG is observed for Personally familiar places - Unknown places. Negative activation is observed in lingual gyrus bilaterally and portions of left pre and post central gyri (Figure 4.16).

Famous - Unknown (includes both people and places)

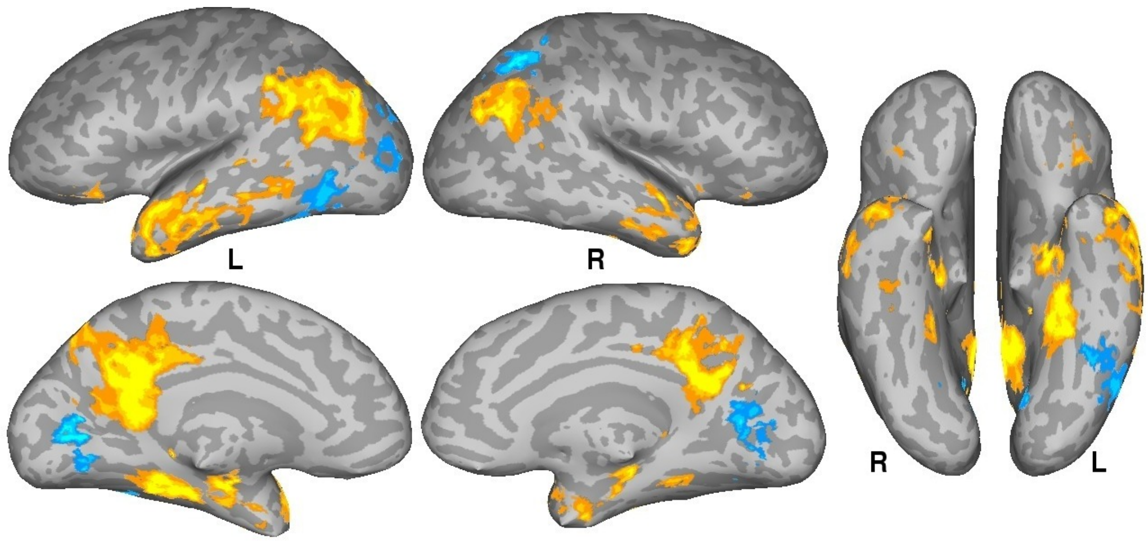

Figure 4.17: Cortical areas showing activation/deactivation for Famous-Unknown items condition.

AG, STG, MTG, PHG, precuneus, temporal pole, uncus are activated bilaterally for Famous - Unknown people and places. Negative activation is observed in right superior parietal lobule, bilateral lingual gyrus and left fusiform gyrus (Figure 4.17).

Personally familiar - Unknown (people and places)

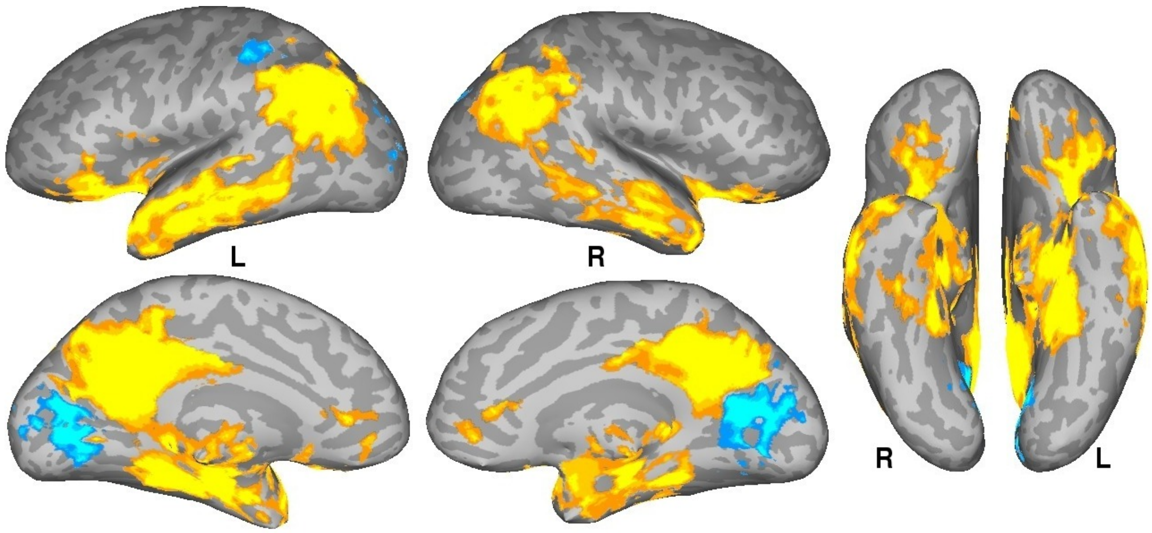

Figure 4.18: Cortical areas showing activation/deactivation for Personally familiar-Unknown items condition.

Bilateral activation of AG, PCG, precuneus, STG, MTG, ITG, temporal pole, thalamus, IFG (more on left) is observed for Personally familiar - Unknown condition. Negative activation is observed in lingual gyrus bilaterally and a small portion of left IPS (Figure 4.18).

Familiar People - Familiar Places (both famous and personally familiar)

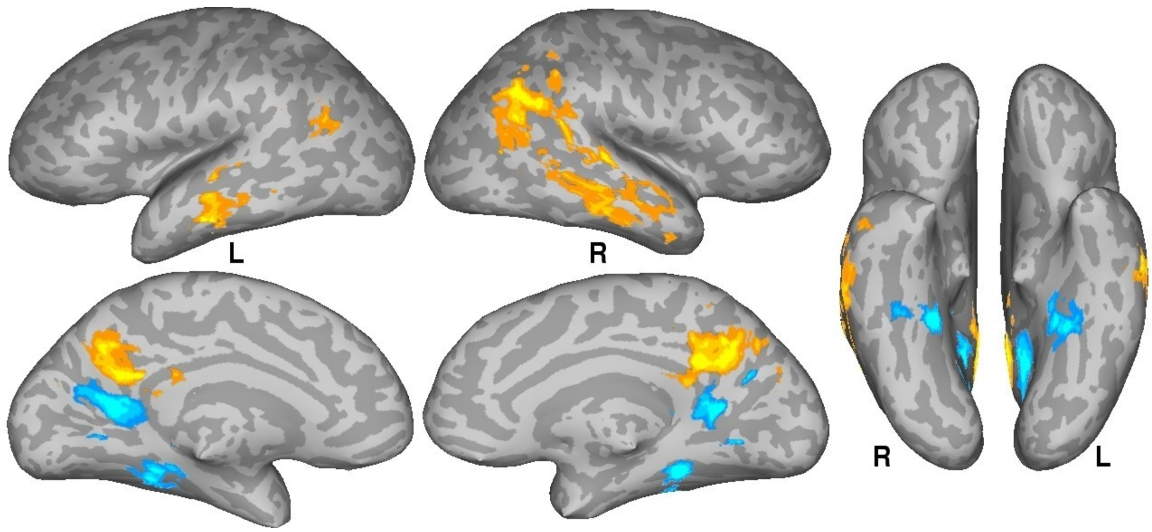

Figure 4.19: Cortical areas showing activation/deactivation for Familiar people - Familiar places (includes famous and personally familiar items) condition.

Bilateral activation of MTG (more on the right side), precuneus, right STS, SMG is observed in Familiar people - Familiar places condition. Negative activation is observed bilaterally in PCG, PHG and FG (Figure 4.19).

Personally familiar - Famous (both people and places)

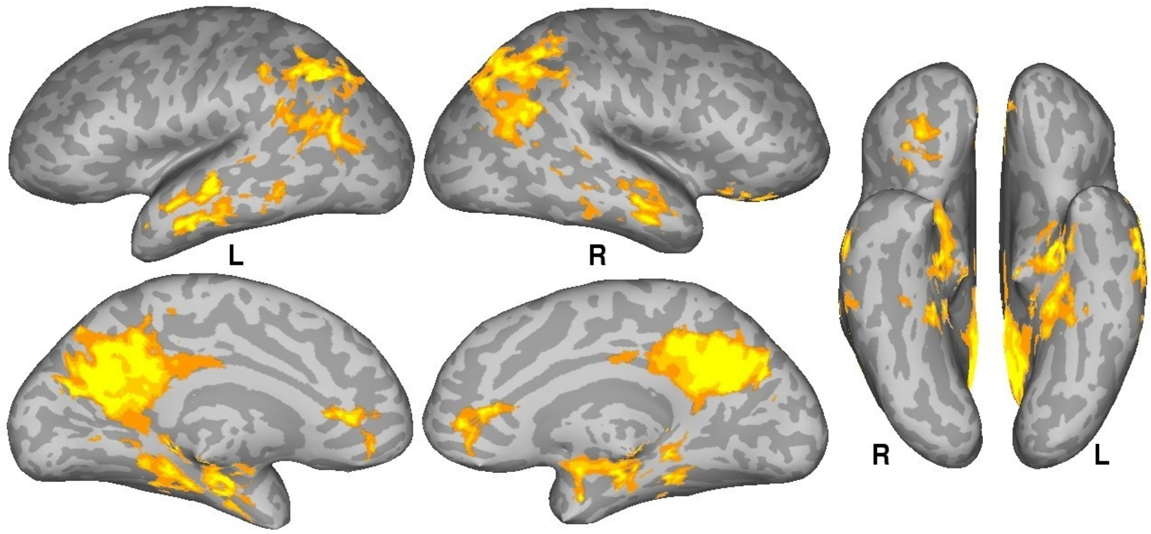

Figure 4.20: Cortical areas showing activation/deactivation for Personally familiar - Famous people and places condition.

Bilateral activation of AG, precuneus, PCG, PHG, MTG, IFG (p.orbitalis), ACG, left STS, FG is observed in Personally familiar - Famous condition. No negative activation is observed (Figure 4.20).

(Personally familiar people - Personally familiar places) - (Famous people - Famous places)

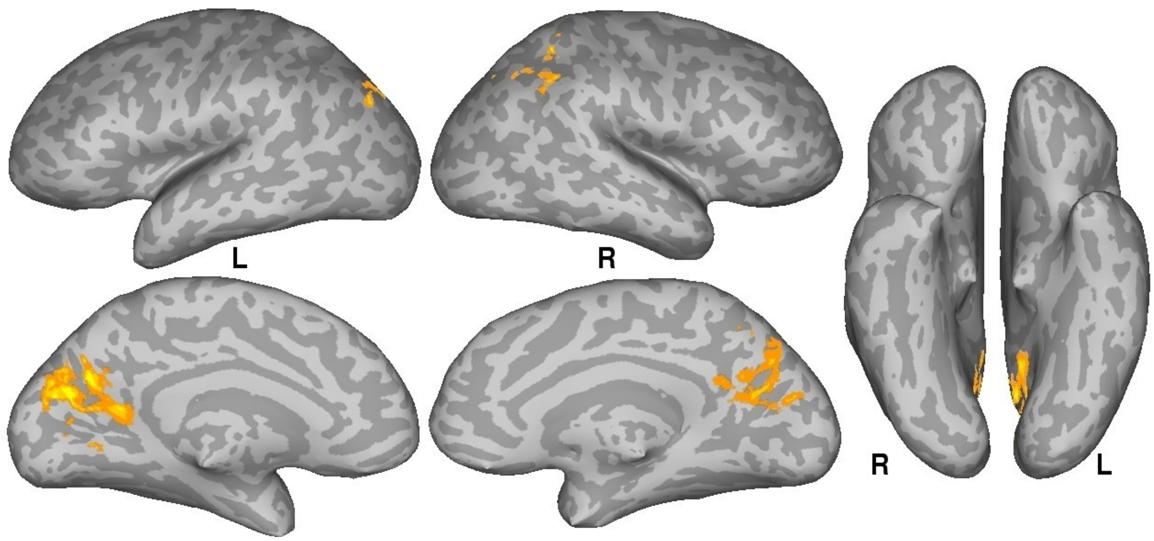

Figure 4.21: Cortical areas showing activation/deactivation for (Personally familiar people - Personally familiar places) - (Famous people - Famous places) condition

.

Bilateral activation in precuneus and right superior parietal lobule is observed (Figure 4.21)

Familiar - Unknown (personally familiar and famous vs unknown people and places)

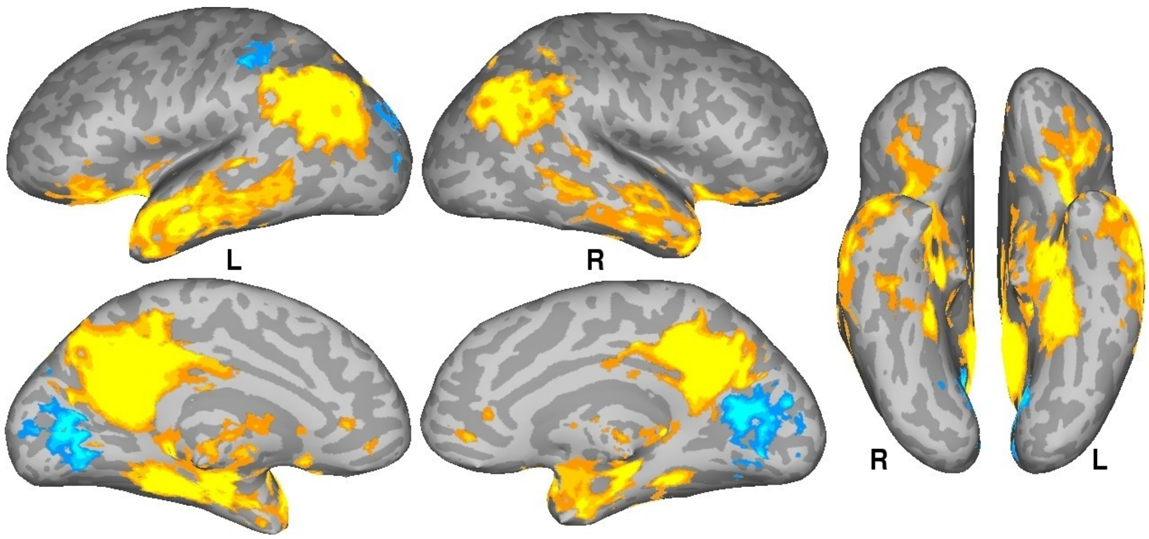

Figure 4.22: Cortical areas showing activation/deactivation for Familiar - Unknown items condition. Familiar items include Personally familiar and famous people and place names whereas unknown items include unknown people and place names.

Bilateral activation in AG, precuneus, PCG, PHG, STG, MTG, ITG, temporal pole, IFG is observed for Familiar - Unknown condition. Negative activation is observed bilaterally in cuneus, lingual gyrus and left post central gyrus (Figure 4.22).

Familiar - Unknown (including the 4 ratings as covariates)

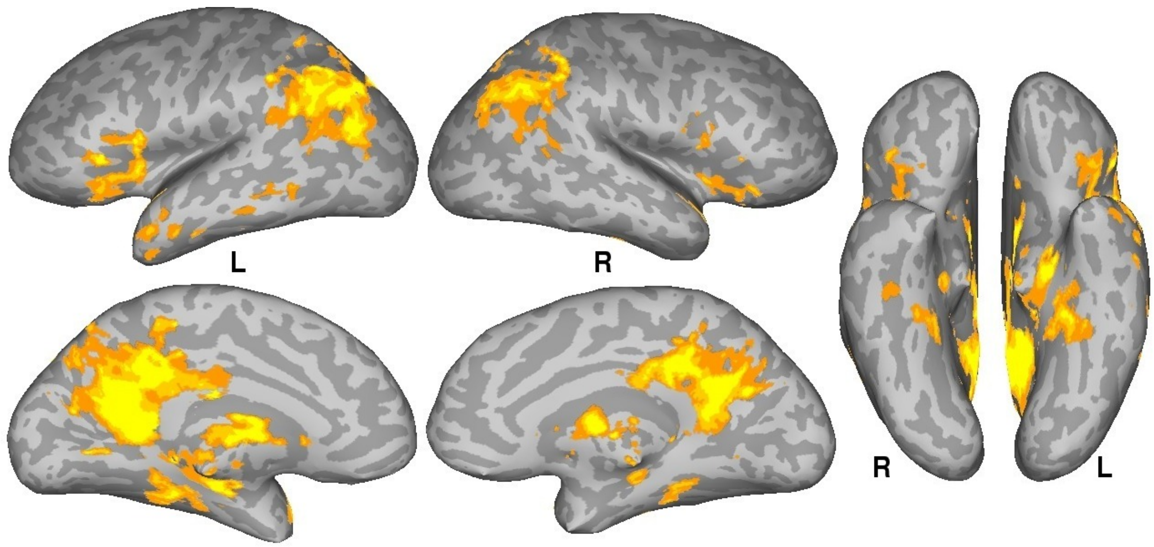

Figure 4.23: Cortical areas showing activation/deactivation for Familiar-Unknown items (all 4 ratings included).

Activation is observed in the same areas as Familiar - Unknown (without covariates) condition but there is a significant reduction in the amount of activation. Negative activation is eliminated (Figure 4.23).

<u>*Activations with ratings as covariates (famous and personally familiar people and places)*</u>

Amount of Knowledge

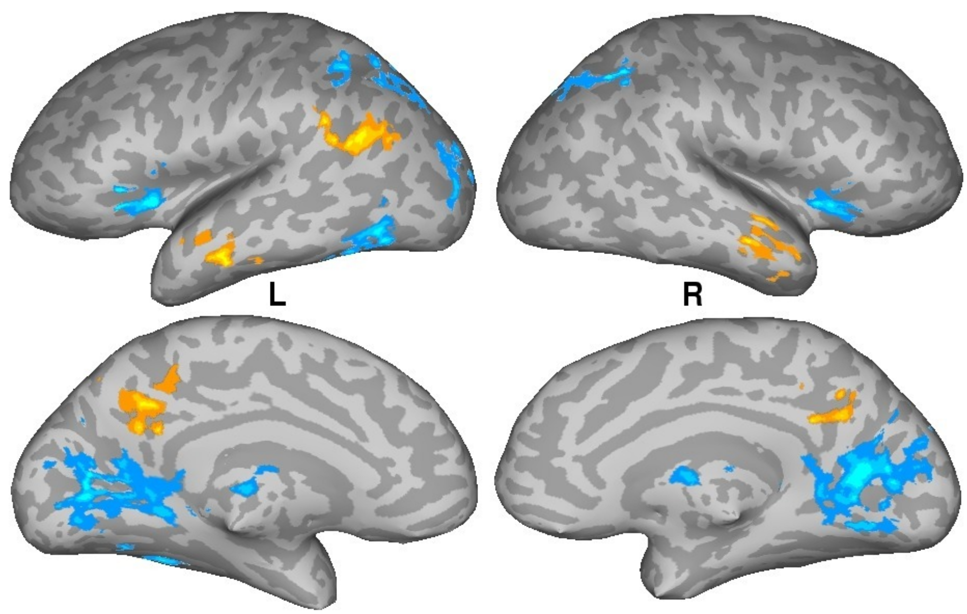

Figure 4.24: Cortical areas showing correlation of proper names with knowledge. Yellow/orange colors show positive correlation and blue/cyan colors show negative correlation.

Bilateral MTG, precuneus, left AG and right STS are positively correlated for familiar people and places with knowledge.

Negative correlation is observed in bilateral thalamus, insula and left middle occipital gyrus (Figure 4.24).

Interactive experience

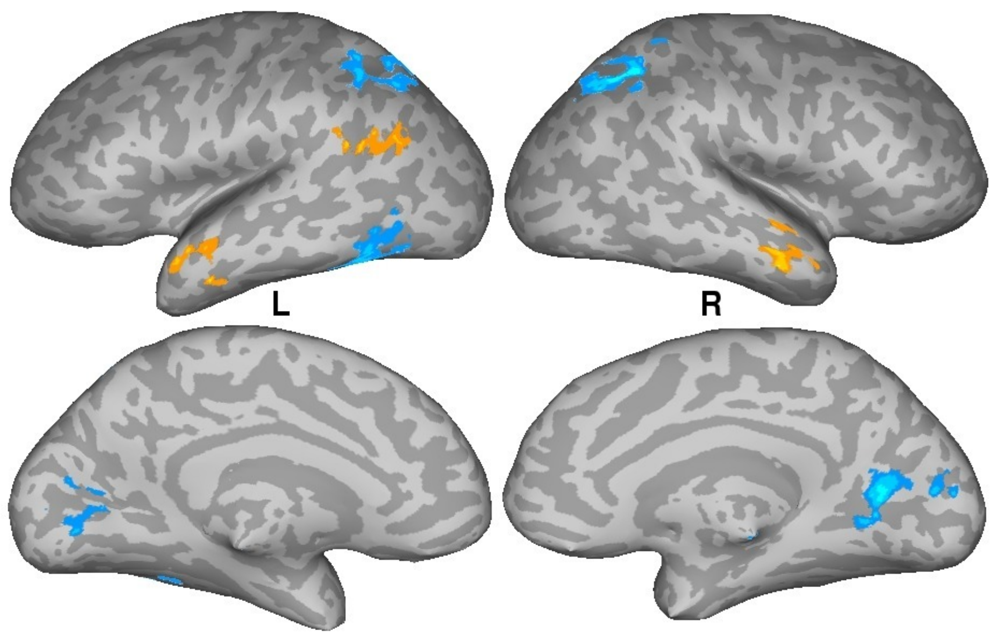

Figure 4.25: Cortical areas showing correlation of proper names with interactive experience. Yellow/orange colors show positive correlation and blue/cyan colors show negative correlation.

Bilateral MTG and left STG are positively correlated for familiar items with Interactive experience. Negative correlation is observed in left cuneus and FG (Figure 4.25).

Sensory Experience

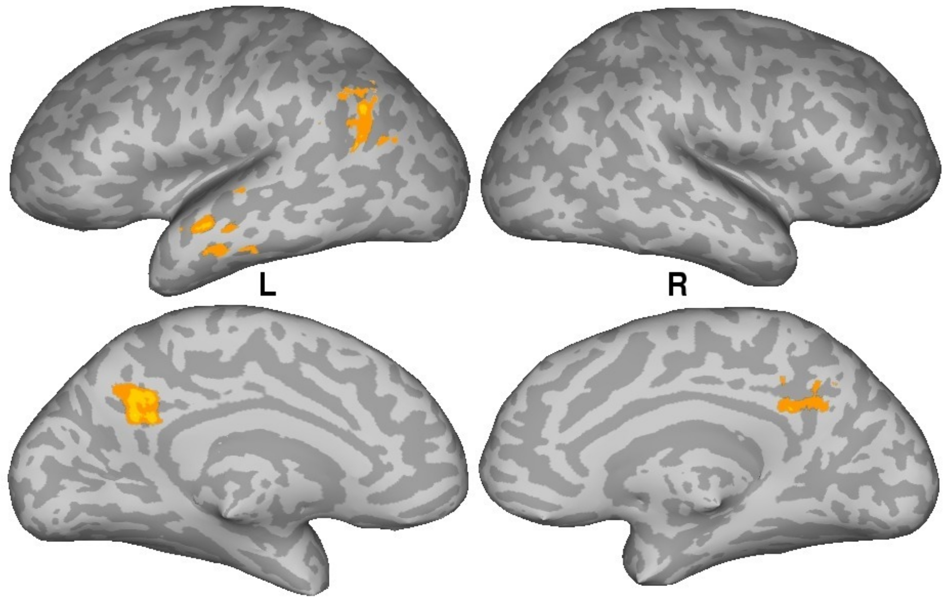

Figure 4.26: Cortical areas showing correlation of proper names with sensory experience. Yellow/orange colors show positive correlation and blue/cyan colors show negative correlation.

Left precuneus, AG, STS and right PCG are positively correlated for familiar items with Sensory experience (Figure 4.26).

Emotional Response

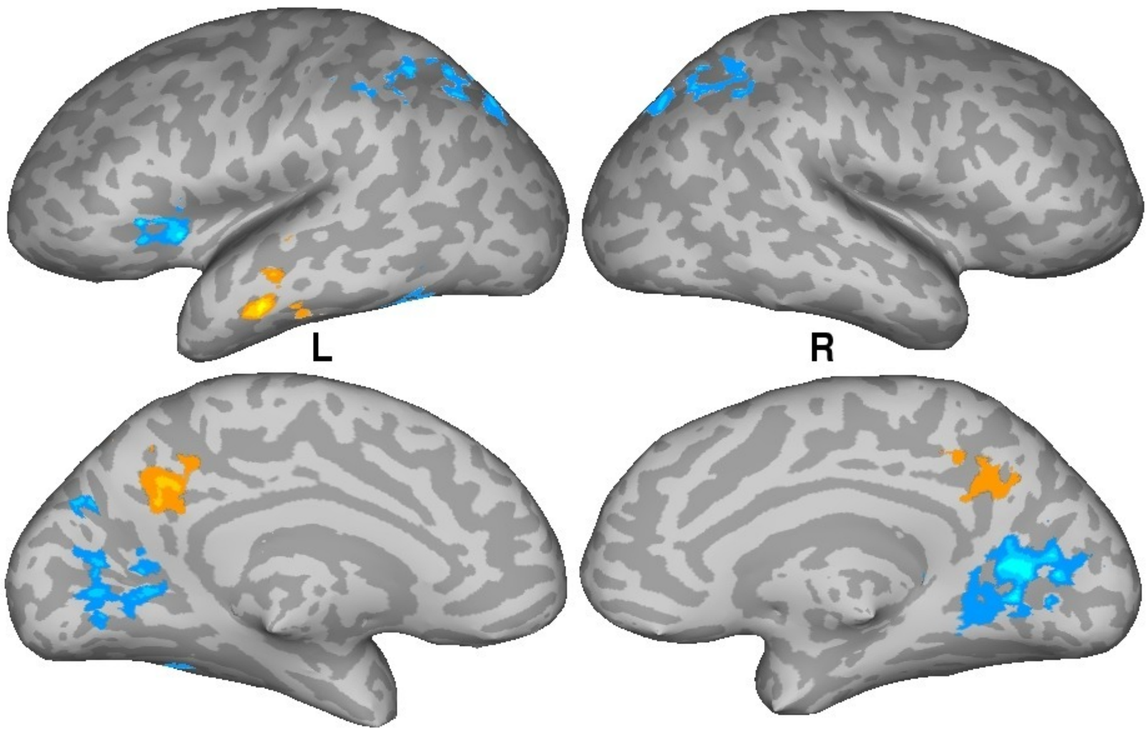

Figure 4.27: Cortical areas showing correlation of proper names with emotional response. Yellow/orange colors show positive correlation and blue/cyan colors show negative correlation.

Bilateral precuneus and left MTG are positively correlated for familiar items with Emotional response. Negative correlation is observed in bilateral IPS, cuneus, right IFG (p.traingularis) and calcarine sulcus (Figure 4.27).

Tables 4.2 and 4.3 below show the correlation between variables for Experiment II.

People	*KN*	*ER*	*IE*	*SE*	*RT*	*#Letters*
KN	-					
ER	0.755	-				
IE	0.824	0.640	-			
SE	0.602	0.460	-	-		
RT	-0.383	-0.289	-0.359	-0.194	-	
#Letters	0.039	-0.003	0.072	-0.032	0.103	-

Table 4.2: Correlation matrix for variables from Experiment II (people). The values highlighted in yellow are the ones with significant correlation.

Places	*KN*	*ER*	*IE*	*SE*	*RT*	*#Letters*
KN	-					
ER	0.607	-				
IE	0.637	0.304	-			
SE	0.558	0.512	-	-		
RT	-0.294	-0.184	-0.171	-0.233	-	
#Letters	-0.003	0.071	0.032	0.092	0.136	-

Table 4.3: Correlation matrix for variables from Experiment II (places). The values highlighted in yellow are the ones with significant correlation.

Overlap map of Words (concrete and abstract) - Nonwords and Familiar (famous and personally familiar) people - Unknown people names

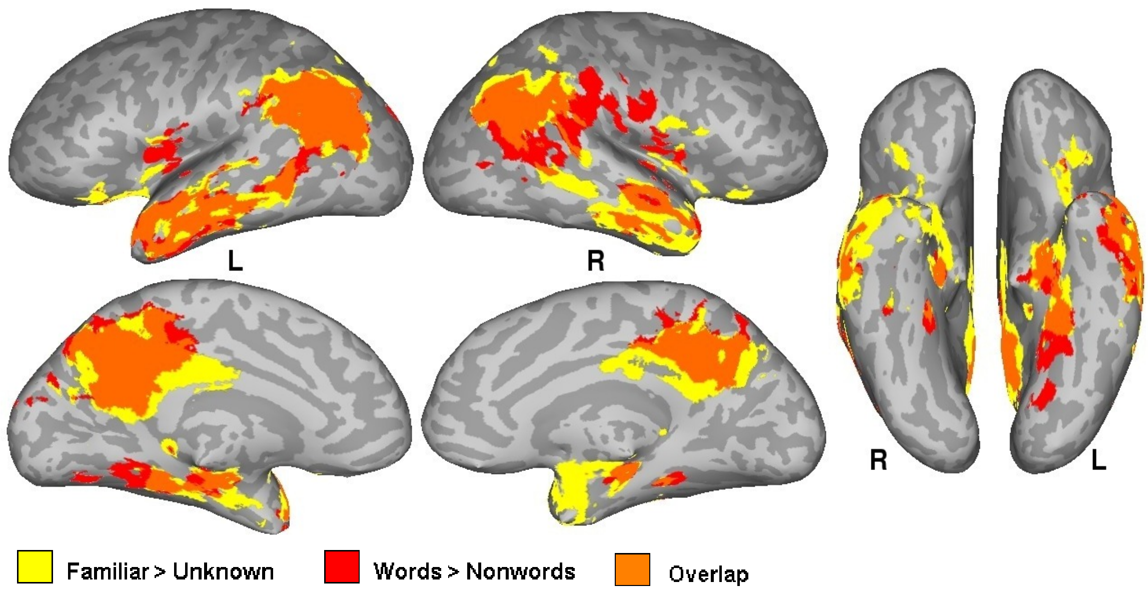

Figure 4.28: An overlap map between Words - Nonwords and Familiar - Unknown people conditions. Yellow areas are the activations for Familiar - Unknown people condition. Red areas are the activations for Words - Nonwords condition. Orange areas are the activations common for both conditions.

Regions in yellow are activations for Familiar - Unknown people condition whereas regions in red are for Words - Nonwords condition. As it is evident from the figure, AG, SMG, PCG, precuneus, and ATL are activated for both the experiments bilaterally (areas in orange). Portions of orbitofrontal cortex and right medial ATL are activated for Familiar - Unknown people and not for Words - Nonwords (Figure 4.28).

5. DISCUSSION

We presented the subjects with concrete and abstract words, pronounceable non-words, names of famous, personally familiar and unknown people and places to examine the sensitivity of ATL in semantic and social cognition.

5.1 Experiment I

The behavioral data from Experiment I confirms the previously established finding (Kiehl et al. 1999) that concrete words are recognized more quickly and accurately as compared to abstract and non-words. Abstract words are more quickly and accurately recognized relative to nonwords.

ATL and temporoparietal regions are activated bilaterally for Abstract - Nonwords, Concrete - Nonwords and Words - Nonwords conditions. While these conditions had similar patterns of activation in common areas, IFG is activated more for abstract words as compared to concrete words in the left hemisphere. Left PCG and PHG are activated more for concrete words as compared to abstract words (see Figure 4.6 for Concrete - Abstract condition).

Activation of left IFG for abstract and left PCG for concrete words is consistent with results from previous imaging studies by Binder et al. (2005).

Bilateral activation of ATL areas in semantic and language processing has also been reported in other imaging studies (Pobric, Lambon Ralph, and Jefferies 2009)□. These findings fit the theory of amodal semantic hub that is represented in left and right ATL (McClelland and Rogers 2003)□. According to this view, the ATLs extract semantic knowledge by processing information available from different modalities. Anatomically, as the sub-regions of ATL are densely connected with modality specific areas like prefrontal cortex, sensory-motor areas, amygdala (Guberman 1997)□, the ATLs are an ideal substrate for forming amodal semantic representations (Pobric, Lambon Ralph, and Jefferies 2009)□.

Other studies focusing on understanding how and where abstract concepts are processed in the brain relative to concrete concepts have reported different results. Right ATL activation has been found for abstract words relative to concrete words (Kiehl et al. 1999; Perani et al. 1999)□. This is possible due to differences in experimental paradigms or modes of stimulus input. Inconsistencies in findings can also be attributed to technical issues like imaging modalities (Visser, Jefferies, and Lambon Ralph 2010)□. ATL is located near air-bone interfaces that cause inhomogeneities in magnetic field resulting in signal loss. We took into consideration these issues and used oblique image acquisition covering the temporal and parietal areas and used a better TE value to minimize signal loss in ATL.

Previous results suggest that dorsal ATL (anterior STG) is activated more for abstract words, while ventral ATL (anterior ITG) is activated for concrete words. Here, we show more widespread activation in the ATL for both concrete and abstract words. This is likely due to lower signal loss in the ATL, and suggests that the purported division of the ATL is not so clear.

A major purpose of the study was to investigate the modulation of ATL in particular and the semantic system in general due to semantic neighborhood of words, where neighborhood is defined in terms of associations. For this purpose, we used four different measures or characteristics of neighborhoods – QSS, QRSG, QPR, and QMC. QSS is the basic measure of neighborhood size (number of associates for a given word). QRSG and QPR measure resonance (activation of the cue and the associate by each other). QRSG is total resonance while QPR is the resonance normalized with respect to associate set size. All of these measures modulated inferior parietal and/or posterior cingulate regions, but not the ATL. QMC measures the density of connections between the associates. This modulated the IFG, but not the ATL. Thus, ATL does not appear to be involved in computation of associations or in automatic propagation of activity due to associations, at least for an implicit semantic task such as lexical decision.

With respect to the design of a protocol to predict potential verbal memory and cognitive deficits in patients, these results suggest that inclusion of both concrete and abstract words and a nonword baseline is sufficient to provide a robust signal in the ATL. Weak modulation of the ATL by QSS and QRSG suggest that one could prefer words that rate high on these measures, but this need not be a deciding factor in selecting stimuli.

Pexman et al (2007) reported lower activation in the temporal lobe for increasing neighborhood size, with no regions showing greater activations. This is a counterintuitive result, and is the opposite of our results that show increasing activation in the AG with increasing neighborhood size. The difference can be explained by the task: Pexman et al (2007) used a semantic judgment task ("is this item edible?) in order to emphasize semantic processing. While the intuition behind this is to encourage deeper semantic processing, it may also be counterproductive, since all the associated information is irrelevant to and interferes with the task that requires focusing on a particular semantic feature. We used the lexical decision task, which does require focusing on any one semantic aspect, and hence is more conductive to automatic spread of activation. These results also underscore the role of AG and the inferior parietal lobe in semantic processing, consistent with Binder et al (2009).

While QRSG and QPR are similar measures, activation in the posterior cingulate was correlated with QRSG but not with QPR. QRSG measures the absolute amount of resonance (larger values for words with bigger neighborhoods), while QPR measures the probability of resonance and is hence normalized. The sensitivity of posterior cingulate to the absolute amount of connectivity suggests its role in integrating and connecting disparate pieces of information, as is consistent with its role as a functional and anatomical connectivity hub (Buckner et al. 2009)□.

5.2 Experiment II

The behavioral data from Experiment II show that Personally familiar items (people and places) are recognized more accurately and quickly as compared to famous and unknown items. Famous items are less accurately and quickly recognized as compared to Unknown items. This is possible when there is some amount of thinking involved in trying to recall information related to an unknown person or place that seems familiar. Whereas, with famous items, considering that they have lesser familiarity as compared to personally familiar items, more amount of time is spent in deciding whether the person/place is known or not.

Comparing Famous - Unknown (Figure 4.17) and Personally familiar - Unknown (Figure 4.18) items, we see a similar pattern of activation in ATL and temprorparietal areas bilaterally. However, for Personally familiar - Unknown items, the activation is more extensive and the intensity is more as compared to Famous - Unknown items. Figure 4.20 shows the comparison between Personally familiar and famous items. As it is evident, Personally familiar items produce more activation in ATL and temporoparietal regions as compared to famous items.

The bilateral activation of different subregions of ATL for personally familiar and famous names have been reported previously (Sugiura et al. 2006)□. Significant activation for famous/familiar entities rather than unfamiliar ones might indicate a role of personal memory and experience in ATL (Dolan et al. 2000)□. As there is more unique information associated with personally familiar items as compared to famous items, more activation is observed for personally familiar items.

In a comparison between familiar people and places (Figure 4.20), familiar people (both famous and personally familiar) activate MTG and precuneus bilaterally with more activation in MTG on the right side of the brain, right SMG and STS as compared to familiar places. Processing of people related information in the right ATL has been reported previously (Ellis, Young, and Critchley 1989; Gainotti, Barbier, and Marra 2003)□ and is widely accepted. Both left and right ATL are activated for person-specific information but they vary across modalities. Left ATL is activated more in retrieving person names whereas right ATL in recognizing people from visual information such as their faces (Gainotti 2007). Thus, it can be said that ATL is activated bilaterally for retrieving person specific knowledge but with a bias towards the right hemisphere.

Familiar places on the other hand activate PCG, PHG, FG bilaterally when compared to familiar people. Activation of PCG (Sugiura, Shah, Zilles, and Fink 2005b)□ and PHG (Gorno-Tempini and Price 2001; Köhler, Crane, and Milner

2002)□ is consistent with previous imaging studies. PHG and FG are activated for familiar places. This is because PHG and FG are a part of visual scene processing stream.

Comparing familiar (both famous and personally familiar people and places) and unknown items, we see that bilateral ATL and temporoparietal regions are activated for familiar items (Figure 4.22). In a similar analysis with all the covariates (knowledge, emotional response, interactive experience, sensory experience) included, comparing familiar with unknown items shows that there is a significant reduction in activation in ATL and other areas (Figure 4.23), explaining that these covariates/ratings modulate the amount of activation.

Furthermore, in individual analyses with each rating as a covariate, we observe that ATL is activated bilaterally for KN and IE but only on the left hemisphere for ER and SE. Precuneus is activated bilaterally for KN, ER and SE. AG is activated on the left side for KN, IE and SE (Figures 4.23-4.26). The activations with ratings all show a similar pattern of activation involving ATL, AG and precuneus because the ratings are significantly correlated (Tables 4.2 and 4.3).

Inferior parietal and posterior cingulate regions are positively correlated with the ratings (knowledge and experience), supporting their role in representing semantics. The de-activations or negative activation observed in visual attention areas (lingual gyrus) bilaterally for these results (Figures 4.23-4.26) might be because we did not include response times as a covariate in the analyses.

Finally, from both of these experiments, we observe that the ATL and temporoparietal areas are commonly activated bilaterally for lexical decision and familiarity judgment tasks (Figure 4.28). Figure 5.1 shows the areas activated for general semantic processes based on reported activation peaks from 120 independent functional imaging studies (Binder and Desai 2011). General semantic processes include understanding of meanings and other concept based knowledge. Our results from word and familiarity judgment tasks as seen in Figure 5.2 are consistent with the results from the meta-analysis (Figure 5.1). AG, SMG, IFG, FG, MTG and PC (Posterior Cingulate gyrus) are activated for both experiments.

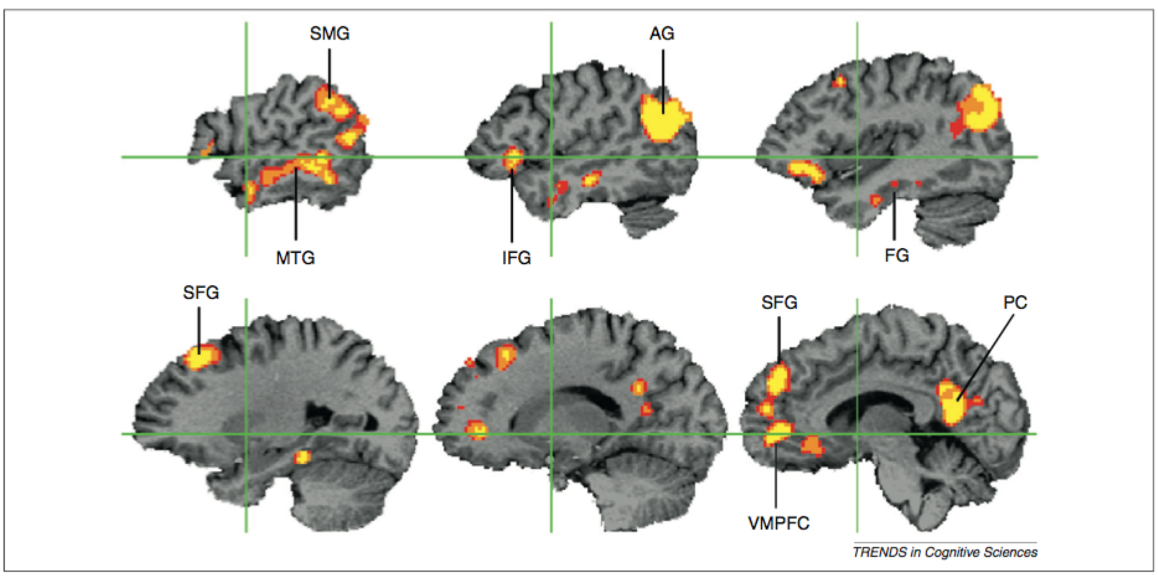

Figure 5.1: Meta-analysis of functional imaging studies of semantic processing. Brain regions reliably activated by general semantic processes from 120 imaging studies at $p<0.05$. The figure shows activation in saggital plane in left hemisphere. Right hemisphere activations occurred in similar locations but were less extensive.

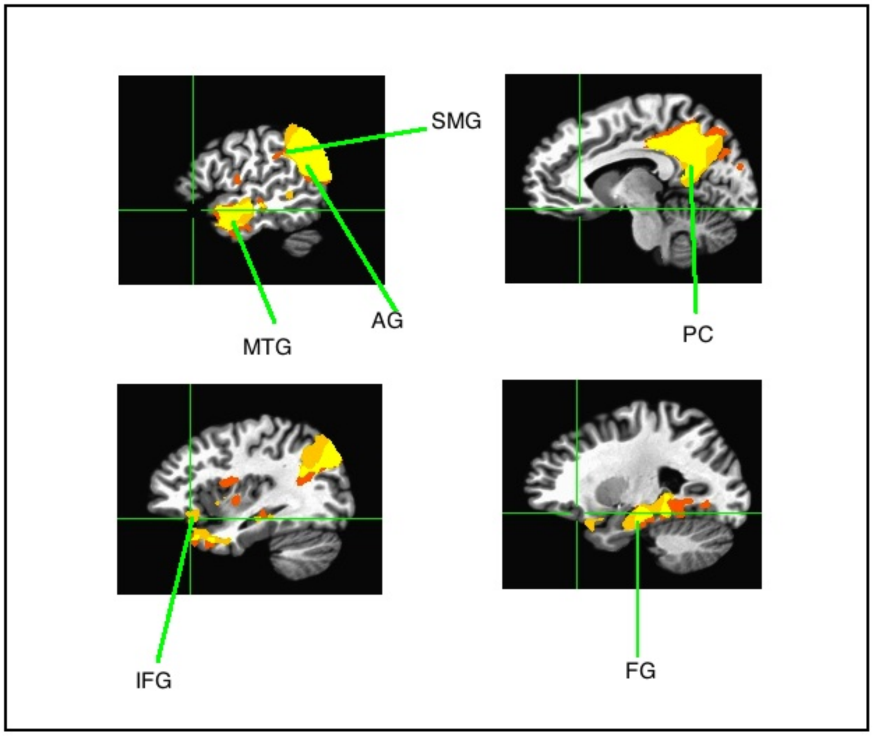

Figure 5.2: Brain regions activated for words-nonwords and familiar-unfamiliar people names at p<0.05. The figure shows activation in saggital plane in left hemisphere. Right hemisphere activations occurred in similar locations but were less extensive.

The difference in activation between the two experiments is observed in the orbitofrontal cortex (Bechara, Damasio, and Damasio 2000; Rolls 2000) bilaterally and right ATL. These areas are involved in processing emotion (reward/punishment), which is more associated with people than words.

The high degree of overlap between the proper and common names suggests that these inferior parietal and temporal regions form a semantic system that not only supports general object and event knowledge, but also person-specific knowledge. The regions activated for person and place names have more general function, and there does not appear to be a specialized or dedicated system for representing persons or social knowledge. Figure 5.3 shows a neuroanatomical model of semantic processing (Binder and Desai 2011).

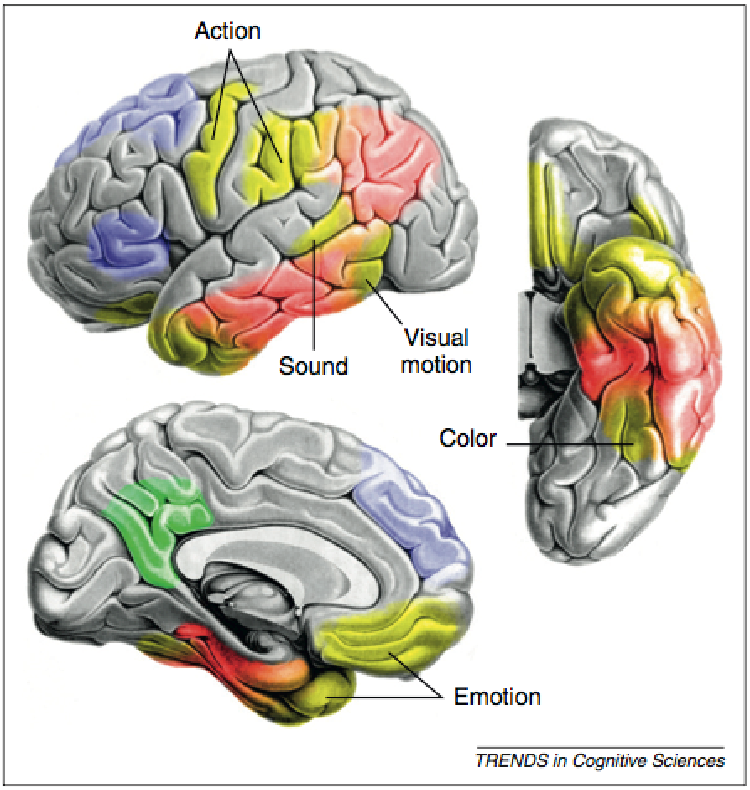

Figure 5.3: A neuroanatomical model of semantic processing. Modality specific sensory, action and emotion systems (yellow regions) provide input to temporal and inferior parietal convergence zones (red regions) that store abstract representations of entity and event knowledge. The PCG and precuneus (green regions) may serve as an interface between semantic network and hippocampal memory system to encode meaningful events into episodic memory. Inferior and dorsomedial prefrontal cortices (blue regions) control the selection of information stored in temporoparietal cortices. A similar but less extensive network exists in the right hemisphere.

Inferior parietal lobe and much of temporal lobe participate in comprehension tasks but are not modality specific. These regions lie at convergences of multiple perceptual processing streams and support a variety of functions like language, object recognition and social cognition (Binder and Desai 2011).

6. CONCLUSION AND FUTURE DIRECTIONS

ATL has been implicated in a wide variety of functions in the literature. The ITG receives input from ventral visual processing areas (Jones and Powell 1970)□ where the fusiform gyrus is located (McCarthy et al., 1997) and thus anterior ITG is associated with face, object recognition or non-lexical visual information (Wong and Gallate 2012). The MTG is believed to have a general semantic processing function as it receives input from somatosensory, olfactory, auditory processing streams (Guberman 1997)□. The anterior MTG was the site of overlap for semantic processing when combining data from multiple studies (Wong and Gallate 2012). The STG/STS is important in speech, language processing and social attention (Redcay 2008)□. The temporal pole has been associated with multiple functions including learning and memory, language processing (Binder et al. 2011)□□, social conceptual knowledge (Zahn et al. 2007)□ and processing unique stimuli (Grabowski et al. 2001)□.

The question that arises from all these findings is: what exactly is the role of ATL? The answer can conform to all the theories that ATL is associated with. It is involved in representing unique entities like abstract concepts. It is involved in language processing as it processes different kinds of words. It also acts as a semantic hub to integrate disparate pieces of information. The social cognition and processing of unique entities aspects can fit under a common semantic function of ATLs in that general semantic memory is necessary for processing information of any kind, be it emotion, personal memories or language.

With respect to the design of a protocol for ATL activation, these results suggest that names of personally familiar people and places, along with an unknown name baseline, would provide robust activation in the ATL. KN, IE, and SE activated parts of the ATL, and hence selecting names of people and places with whom the subject has high degree of experience (typically close friends and family members, as well as place visited very frequently) is likely to produce reliable activation in the ATL. Thus, a protocol that includes both word/nonword and familiar/unfamiliar names is likely to activate functionally eloquent cortex in the ATL. This activation can serve as an index for prediction of cognitive decline following ATL resection. Future studies will investigate (1) whether cognitive and verbal memory decline can be predicted from the extent and strength of activation in the ATL in presurgical patients, and (2) whether this decline can be minimized by sparing these regions from resection to the minimum possible extent.

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Appendix I: Stimulus Items for Experiment I

Concrete Words	*Abstract Words*	*Non-words*	
accident	advice	odomay	creeoe
animal	affair	dicher	ging
apple	alike	aborz	hoke
autumn	belief	floost	teevly
banana	blame	mareet	daktra
body	concept	alteed	seral
cabin	confusion	yorman	ratant
car	crisis	avinge	gareez
carrot	custom	sumbod	loober
cement	deceit	gutty	skevan
chicken	desire	sabla	kastan
circus	ego	viekle	jektry
cloud	error	jorn	shordy
coffee	esteem	kaid	viceng
curve	event	orwerl	wolvly
doctor	excuse	endimp	fram
engine	factor	pinsop	vendon
fort	fantasy	meese	arepla
friend	gain	plor	liezed
infant	guess	marate	palan
island	honor	infoon	perman
item	loyalty	rary	semize
leaf	luck	arjen	franat
lemon	magic	brarf	grak
lion	manner	nart	rompan
liquid	method	komly	vijant
meadow	norm	harlit	baktry
medicine	notion	inlite	reefan
morning	odd	kaskly	retary
pencil	offense	snate	marnch
pigeon	opinion	amteed	nort
plug	option	soun	sern
pole	pardon	gasya	fiship
potato	phase	supoid	crer
record	plan	slarst	blug
ring	pun	teernt	alally
road	regret	bleef	butly
saloon	result	dinant	gulvy
sponge	routine	mopast	feklet
spoon	rumor	fissy	gunsie
steam	scarce	pruce	ablize
summer	scheme	fandaz	fotime
sunset	sly	afle	kolist
symbol	soul	arkant	penssy
toilet	supply	reeit	lakty
truck	taboo	ennist	morty
vodka	tale	kine	rulam
walnut	theory	orkoe	fivide
window	topic	sarate	delap
yacht	virtue	parala	harz

Appendix II: Stimulus Items from Experiment II

Famous People	**Famous Places**	**Unknown People**	**Unknown places**
Al Pacino	Alcatraz	Abbey Harris	400 Alishan
Angelina Jolie	Big Ben	Adam Delgado	732 Byblos
Aretha Franklin	Central Park	Adrean Evans	Almourada Family Park
Barack Obama	Colosseum	Alfred Garcia	Antsahadinta museum
Barbara Walters	Coney Island	Alicia Sullivan	Castle Sidon
Bob Dylan	Eiffel Tower	Anthony Foster	Craigmillar Castle
Bruce Springsteen	Empire State Building	Brian Heenan	Drambuie Trail
Burt Lancaster	Grand Canyon	Brook Nomeland	Gishtlik Mosque
Chuck Norris	Great Barier Reef	Christopher Daniel	Glasgow cathedral
Clint Eastwood	Great Wall of China	David Cox	Grote Markt
Condoleezza Rice	Independence Hall	Emily Caldwell	Gudula Cathedral
David Brinkley	Jefferson Memorial	Erin Murphy	Gullfoss
Diana Ross	Kremlin	Eva Schultz	Gyeongbok gung
Dwight Eisenhower	Lake Tahoe	Gerard Kriegel	Heian Shrine
Elizabeth Taylor	Leaning tower of Pisa	Henry Newman	Holmwood House
Ellen DeGeneres	Lincoln Memorial	Inda Ugrina	Iguazu Falls
Ernest Borgnine	Miami Beach	James Hubbard	Kalta Minor Minaret
Gary Hart	Mount Everest	Joseph Thornton	Kenting National Park
Howard Cosell	Mount Rushmore	Kelly Sutton	Kravica waterfalls
Jack Palance	Notre Dame	Kristina Starkus	Lake Hredavatn
Jay Leno	Pyramids of Egypt	Lauren Lee Schakelton	Lazienki Park
Jennifer Lopez	Sears Tower	Lawrence Greene	Makgadikgadi Pans
Jimmy Carter	Smokey Mountains	Lindsey Pauley	Montevideo
Joe DiMaggio	St.Peters Basilica	Lorena Lovetinsky	Moremi game reserve
Judy Garland	Statue of Liberty	Lynn Whitten	Mount Inwang
Karl Rove	Stonehenge	Matthew Burgess	Namsan Park
Lucille Ball	Sydney Opera House	Megan O'Henry	Ocean terminal
Miley Cyrus	Taj Mahal	Mikaela Wilson	Okavango delta
Nancy Pelosi	The Alamo	Nancy Hill	Palace square
Nelson Mandela	The Arch	Nellie Jennings	Palacio Real
Peggy Flemming	The Golden Gate Bridge	Olga Brodbeck	Plaza de Torros
Ray Charles	The Rocky Mountains	Pamela Young	Ramsay Gardens
Raymond Burr	The White House	Patrick Jenkins	Rivera Recreational
Richard Burton	Victoria Falls	Peter Sanders	Salta
Robert De Niro	Wimbeldon	Rachel Peters	Skaftafell National Park
Rock Hudson	Wrigley Field	Rita Schneider	Souq El Naaga
Ronald Reagan	Yankee Stadium	Romaine Craig	Taroko Gorge
Serena Williams	Yellowstone National Park	Sharon Olson	Tsarytsino
Steven Spielberg	Yosemite National Park	Timothy Munoz	Ulica Florianska
Tiger Woods	Yucatan Peninsula	William Griffin	Valdes Peninsula

APPENDIX III: The Cluster Size (in μL), Mean and Maximum z-Scores and the Location of the Peak in the Atlas of Talairach and Tournoux for Experiment I

	Volume	Mean	Max	x	y	z	Structure
Concrete>Nonwords							
	18074	3.67	6.099	-45	-68	22	L AG
	7824	3.19	5.387	-62	-15	-12	L MTG
	6305	3.15	5.014	25	-30	-14	R PHG
	5714	3.19	5.141	-28	-18	-12	L Hippocampus
	1735	2.86	3.6	-47	-9	5	L TTG
	1183	3.12	4.241	-46	-12	31	L CS
Nonwords>Concrete							
	3980	-3.23	-5.293	-34	20	7	L Insula
	1178	-3.42	-4.835	31	20	2	R circular sulcus of Insula
	993	-2.85	-3.537	34	-58	42	R IPS
	822	-3.05	-4.004	-40	-41	41	L PCS
Abstract>Nonwords	**Volume**	**Mean**	**Max**	**x**	**y**	**z**	**Structure**
	17133	3.13	5.212	56	-63	14	R MTG
	8396	3.12	4.785	-50	6	-13	R STS
	4336	3.06	4.321	51	0	-12	R STS
	808	3.04	4.009	-8	18	5	L Caudate
	573	2.85	3.625	-65	-22	-2	L MTG
Concrete>Abstract	**Volume**	**Mean**	**Max**	**x**	**y**	**z**	**Structure**
	1824	3.04	4.159	-29	-18	-13	L Hippocampus
	933	3.05	3.979	-10	-45	6	L PCG
Abstract>Concrete							
	1610	-2.88	-3.847	-36	19	10	L IFG (p.triangularis)
Words>Nonwords	**Volume**	**Mean**	**Max**	**x**	**y**	**z**	**Structure**
	32355	3.47	6.405	-45	-68	23	L AG
	23541	3.29	5.625	56	-62	15	R AG
	22629	3.32	5.05	-3	-32	36	L MCC
	7681	3.09	4.411	28	-19	-13	R Hippocampus
	4394	3.05	4.083	-25	-47	-8	L FG
	2668	3.06	4.6	64	-11	15	R post central gyrus
	1828	2.99	4.016	-32	-5	1	L Putamen

Appendix III continued

Nonwords>Words	**Volume**	**Mean**	**Max**	**x**	**y**	**z**	**Structure**
	1373	-3.48	-4.915	-34	19	5	L Insula
	952	-3.41	-4.872	31	20	2	R Insula
QSS							
	Volume	**Mean**	**Max**	**x**	**y**	**z**	**Structure**
	499	3.01	4.032	-42	-57	29	L AG
QPR							
	Volume	**Mean**	**Max**	**x**	**y**	**z**	**Structure**
	2874	3.04	5.486	-58	-19	11	L TTG
	1357	3	4.065	-57	-34	13	L STG
	1328	2.88	3.682	-54	-49	34	L SMG
	1277	2.82	3.456	52	0	-5	R STG
QRSG							
	Volume	**Mean**	**Max**	**x**	**y**	**z**	**Structure**
	7887	3	4.734	-11	-63	34	L Precuneus
	1588	3.23	4.618	52	-58	30	R AG
	1446	2.94	4.018	-50	-30	12	L STG/TTG
	1023	2.9	3.766	-44	-55	42	L AG
	603	3.07	4.009	-54	-7	2	L STG
	569	2.92	3.491	53	12	-3	R STG

APPENDIX IV: The Cluster Size (in µL), Mean and Maximum z-Scores and the Location of the Peak in the Atlas of Talairach and Tournoux for Experiment II

Famous>Unknown people	Volume	Mean	Max	x	y	z	Structure
	10464	3.02	4.779	-58	-59	16	L AG
	9629	3.11	4.977	-4	-42	28	L PCG
	7926	3.02	5.005	52	-65	20	R AG
	5775	2.96	5	51	-1	-13	R STS
	2261	3.1	4.645	-26	-18	-13	L Hippocampus
Unknown>Famous people							
	941	-2.95	-3.823	30	-50	42	R IPS
	912	-2.79	-3.306	-41	-58	-1	L MTG

Personally familiar>Unknown people	Volume	Mean	Max	x	y	z	
	47467	3.67	5.77	-43	-69	36	L AG
	41245	3.41	5.729	56	-10	-14	R MTG
	34511	3.91	6.332	-12	-57	28	L Precuneus
	8266	3.1	4.989	28	-22	-13	R Hippocampus
	6749	3.31	5.73	-23	-19	-13	L Hippocampus
	1479	3.07	4.12	58	6	15	R IFG
	807	2.89	3.779	-2	39	5	L ACG
Unknown>Personally familiar people							
	4491	-3.08	-4.965	26	-64	2	R LG

APPENDIX IV continued

Famous>Unknown places	Volume	Mean	Max	x	y	z	
	14811	3.44	5.491	-42	-75	26	L AG
	6724	3.33	4.908	-7	-47	7	L PCG
	4152	3.26	4.662	-4	-43	33	MCG
	3788	2.96	4.206	-41	17	-17	L Tpole
	2591	2.98	3.763	47	-72	28	L AG
	2407	3.27	5.491	-30	-37	-9	L FG
	1860	3.06	3.898	-10	15	6	L Caudate
	1112	3.16	4.559	12	18	2	R Caudate
	1037	3.12	4.067	-62	-33	-5	L MTG
	564	2.91	3.948	-53	-8	-18	L MTG
Unknown>Famous places							
	1389	-2.85	-3.651	-39	-79	7	L MOG
	1286	-3.11	-4.065	-14	-72	8	L Cuneus

Personally familiar>Unknown places	Volume	Mean	Max	x	y	z	
	73264	3.67	6.649	-5	-54	25	L Precuneus
	22013	3.81	6.168	-45	-66	23	L AG
	12909	3.29	4.881	50	-56	18	R STS
	8097	3.06	4.793	28	15	-14	R IFG (p.orb)
	1936	3.21	4.378	-1	33	5	L ACG
	1144	2.93	4.112	60	-38	-9	R MTG
	1088	3.02	4.372	-8	15	8	L Caudate
Unknown>Personally familiar places							
	11389	-3.33	-5.513	2	-70	8	R Cuneus
	1579	-2.93	-3.687	-55	1	12	L Precentral gyrus
	1534	-2.89	-3.613	-53	-25	27	L SMG

APPENDIX IV continued

Personally familiar>Famous places	Volume	Mean	Max	x	y	z	
	18647	3.64	5.852	-5	-49	28	L PCG
	13245	3.21	5.384	-19	-4	-14	L Amygdala
	8240	3.15	5.337	-45	-63	19	L MTG
	2234	3.08	4.391	52	-63	18	R AG
	2077	3.1	4.473	0	39	5	L ACG
	2000	3.01	4.689	-28	15	-13	L IFG (p.orb)
	1198	3.06	4.234	29	26	-11	R IFG (p.orb)
Personally familiar (people>places)>Famous(people>places)	**Volume**	**Mean**	**Max**	**x**	**y**	**z**	
	7490	3.02	4.589	-12	-68	18	L POS
	1382	2.96	4.158	43	-57	47	R AG
Personally familiar>Unknown items	**Volume**	**Mean**	**Max**	**x**	**y**	**z**	
	172206	3.73	6.909	27	-32	-6	R Hippocampus
	1901	3.17	4.307	-3	39	4	L ACG
Unknown>Personally familiar items							
	14108	-3.43	-5.344	9	-71	9	R Cuneus
	1091	-3.04	-4.316	-38	-31	35	L Post Central Sulcus

APPENDIX IV continued

Personally familiar>Famous items	Volume	Mean	Max	x	y	z	
	32021	3.59	5.899	7	-58	28	R Precuneus
	15544	3.29	5.362	30	-71	36	R Precuneus
	4796	3.19	5.376	-26	-17	-15	L Hippocampus
	3991	3.03	4.268	-45	-65	16	L MTG
	3270	3.26	5.203	-50	-16	-6	L STS
	3091	3.11	4.509	29	-33	-7	R Hippocampus
	2300	3.15	4.607	58	-8	-16	R MTG
	2249	3.19	4.73	-5	37	5	L ACS
	1252	3.15	4.494	32	25	-9	R IFG (p.orb)
	886	2.9	3.729	-63	-43	-4	L MTG
	554	2.79	3.357	59	-40	0	R MTG

Famous>Unknown items	Volume	Mean	Max	x	y	z	
	16575	3.35	4.969	-33	-81	32	L SPG
	15868	3.37	5.917	-3	-42	28	L PCG
	10460	3.08	4.511	-49	0	-12	L STS
	6915	3.13	4.586	51	-66	23	R AG
	4723	3.38	5.644	-27	-36	-8	L OTS
	1312	2.91	4.331	51	-1	-12	R STS

Familiar people>Familiar places	Volume	Mean	Max	x	y	z	
	14314	3.04	5.116	45	-56	26	R AG
	7561	3.25	4.808	5	-49	24	R PCG
	1893	3.02	5.105	-59	-17	-14	L MTG
	518	2.83	3.434	-45	-60	20	L STS

APPENDIX IV continued

Familiar places>Familiar people	Volume	Mean	Max	x	y	z	Structure
	2235	-3.43	-5.064	11	-51	8	R Calcarine sulcus
	2162	-3.36	-4.834	-11	-54	12	L POS
	1333	-3.4	-4.774	25	-34	-10	L OTS
	1305	-3.15	-4.724	-28	-38	-8	R OTS

Familiar items>Unknown items	Volume	Mean	Max	x	y	z	
	42341	3.36	5.9	-25	-37	-9	L FG
	31199	4.06	6.726	-4	-55	27	L Precuneus
	25042	3.17	5.941	27	-32	-6	R Hippocampus
	23513	4	5.709	-43	-68	35	L AG
	19093	3.49	5.098	46	-72	28	R AG
	816	2.99	3.919	-1	38	-1	L ACG
Unknown items>Familiar items							
	1132	-2.91	-3.925	-45	-30	38	L Post central sulcus

APPENDIX IV continued

Knowledge	Volume	Mean	Max	x	y	z	
	2253	3.07	4.186	-49	-56	22	L AG
	2091	3.03	4.106	-4	-52	31	L Precuneus
	739	3.03	4.128	-60	-11	-11	L MTG
	716	3	4.067	58	-7	-13	R MTG
	497	2.86	3.6	47	3	-18	R STS
	1322	-3.06	-4.351	38	15	1	R Insula
	1275	-3.3	-5.724	-35	18	5	L Insula
	1151	-2.97	-3.847	-27	-88	14	L MOG
	930	-3.04	-3.93	-15	-12	16	L Thalamus
	794	-2.93	-4.158	16	-20	13	R Thalamus

Interactive Experience	Volume	Mean	Max	x	y	z	
	906	2.92	3.95	57	-5	-17	R MTG
	2782	-3.13	-5.376	29	-53	36	R IPS
	1938	-2.9	-3.769	-42	-46	-15	L FG/ITG
	831	-2.85	-3.532	-1	-77	8	L Cuneus

Sensory Experience	Volume	Mean	Max	x	y	z	
	1865	3	3.898	-4	-53	29	L Precuneus
	1522	2.87	3.886	-53	-63	27	L AG
	608	2.83	3.536	-53	-5	-9	L STS

Emotional Response	Volume	Mean	Max	x	y	z	
	1928	2.85	3.498	-6	-54	32	L Precuneus
	5973	-3	-4.187	20	-59	5	R Calcarine sulcus
	1058	-3.11	-4.119	-36	19	7	L IFG (p.tri)