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Investigating the Neural Correlates of Autobiographical Memory

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Abstract

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Autobiographical memory is a form of episodic memory comprised of an individual's personal experiences. We examined whether autobiographical memory retrieval dynamically recruits content specific brain regions at a second to second time scale. Participants were asked to retrieve unrehearsed autobiographical memories during specified retrieval periods and then to narrate their memories within the scanner. Autobiographical memories were coded for words related to four content categories: spatial-relationship (e.g., on, over), time-referential (e.g., yesterday, 2 days ago), self-referential (e.g., I, me), and other-referential (e.g., Kate, dad). Each content category was contrasted individually against a baseline of all other speech during autobiographical memory retrieval. We observed that content related cortex activated for specific content categories during autobiographical memory retrieval at a second to second time scale. Spatial-relationship words were associated with observed activation of the left basal ganglia, the left supramarginal gyrus, and the left dorsolateral prefrontal cortex. Time-referential words were associated with observed activation of the left ventrolateral prefrontal cortex. Self-referential words were associated with observed activation of the left insula, the medial prefrontal cortex, and the orbitofrontal cortex. Other-referential words were associated with observed activation of the left temporoparietal junction. These results suggest that autobiographical memory retrieval dynamically recruits cortex associated with specific content processing as corresponding content is reported during autobiographical memory retrieval.

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Introduction

Episodic memory is a memory system that allows humans to remember their past experiences (Tulving, 2002). There are three processes involved in episodic memory which are known as encoding, consolidation, and retrieval (Eldridge, Engel, Zeineh, Bookheimer, & Knowlton, 2005). The hippocampus is a brain structure important for all three processes and is involved in learning and remembering information. The first stage of creating a memory is the process of encoding; the second stage of storing a memory is the process of consolidation; the final stage of remembering a memory at a later point is the process of retrieval (Eldridge et al., 2005). This paper will focus on episodic memory retrieval.

Episodic memory retrieval is the process through which an individual recalls a past event and subjectively re-experiences it (Tulving, 2002). Autobiographical memories are a subset of episodic memories that are characterized by being long-lasting and possessing self-referential content (Nelson, 1993). Autobiographical memories are also richer, more complex, and take longer to retrieve relative to other episodic memories (Cabeza & St Jacques, 2007). Autobiographical memories are critical to an individual's sense of self and to their daily life, and an impairment to the ability to form or retrieve these memories is devastating to an individual (Corkin, 1984). For example, individuals with episodic memory impairment caused by Alzheimer's disease experience confusion, irritation, and a reduction in their quality of life (Gold, 2009).

The process of retrieving an autobiographical memory has been theorized to have two distinct periods: search and elaboration (Daselaar et al., 2008; Inman, James, Vytal, & Hamann, 2018). The search period begins when a memory is cued by a stimulus which triggers memory retrieval by causing an individual to (either intentionally, or unintentionally) explore and then select a memory from their past experiences. Following memory search, the individual enters an elaboration period, where one relives the memory and recollects additional sensory detail (Daselaar et al., 2008). During this elaboration period, an individual can also in turn retrieve cues which cause additional search and further elaboration. The elaboration period has been observed to engage a network of brain regions including the visual cortex, the precuneus, and sub-regions of the left prefrontal cortex (Daselaar et al., 2008). Though search and elaboration are each important aspects of autobiographical memory retrieval, this paper focuses primarily on a set of novel analyses of memory content which is retrieved during the elaboration period.

Though significant progress has been made in identifying key regions associated with autobiographical memory retrieval including the hippocampus, medial temporal lobe structures, and medial prefrontal cortex (Nadel, Campbell, & Ryan, 2007), less work has focused on why sensory cortex is commonly observed to activate during autobiographical memory retrieval. One possibility is that sensory specific cortex supports recapitulation, or reactivation of cortical patterns that occurred at the time of encoding during memory retrieval (Bowen & Kensinger, 2017).

Some neuroimaging studies have helped shed light on the role of the sensory cortex during autobiographical memory retrieval through the use of imagination paradigms. Imagination paradigms in neuroimaging instruct individuals to think of a specific item or a category of items and examine the resulting neural correlates. Similarities between imagination and memory give reason to investigate whether specific cortex is recruited dynamically for content specific categories during memory retrieval (Maguire, Intraub, & Mullally, 2015). One key similarity is that both imagination and memory retrieval are understood to be constructive. Imagination is the construction of a scene or an event using prior experiences and previous memories (Maguire et al., 2015). One study showed that participants who were asked to imagine a future event recruited similar brain regions as when they were asked to remember a past event (Addis, Wong, & Schacter, 2007). In this study, the left hippocampus as well as the posterior visuospatial regions activated during past reconstruction and future construction (imagination) of events (Addis et al., 2007). Another study indicated that in addition to these brain regions, content specific activation of cortices occurs during imagination paradigms (Hassabis, Kumaran, & Maguire, 2007). These similarities between imagination and memory raise the question of whether specific cortical activation also occurs as individuals retrieve memory content from corresponding content categories in the same way that imagination does.

Past studies of memory retrieval have had difficulty subdividing retrieval periods due to the limitations of neuroimaging. For example, it is difficult to know at what point individuals are retrieving specific content during the memory retrieval period without a participant actively indicating (by button pressing) when they subjectively experience the retrieval of a specific type of memory content. While this type of explicitly marking the retrieval of information can be fruitful, it is limited to the number or type of instructions a participant can remember and follow using a button box. Additionally, a participant explicitly indicating when specific types of memory content is remembered during retrieval inherently involves atypical non-memory processes including decision making, monitoring, and button pressing processes. One-way studies have attempted to overcome these problems is by intentionally eliciting specific memories corresponding to a content category of interest, or by approximating this process. One study aimed at approximating episodic memory processes using an imagination paradigm showed activation of content specific functionally specialized sensory cortex corresponding to the categories being imagined (Hassabis, et al., 2007). Similar functionally localized content category specific regions of the brain have been shown to activate when viewing stimuli corresponding to their preferred categories which are faces, scenes, and objects (Kanwisher, 2010). Another way of approximating episodic memory processes is by measuring the vividness of retrieved memories. One study of episodic memory retrieval suggests that vivid recall is associated with greater activation of sensory specific cortex during elaboration (Hassabis, et al., 2007). Though activation of sensory cortex has been observed throughout memory retrieval, it is not yet known whether this activation typically persists throughout elaboration, or if activation is occurring at a more dynamic second to second time scale recruitment of specific cortex corresponding to the retrieval of specific memory details.

One way to investigate what type of dynamic second to second neural activation is occurring during autobiographical memory retrieval is by using functional magnetic resonance imaging (fMRI) in conjunction with participants narrating their memories in real time as they are retrieved. The collection of narrated memories would allow for coding of memory content as it is being narrated and examination of the correlated neural activation associated with the content of interest. However, this has not been done in the past in part due to head movement creating degradation of fMRI data. This study controls for this problem by using new microphone technology (FOMRI-III, Optoacoustics) in conjunction with an advanced independent components analysis(ICA) method of preprocessing fMRI data (Pruim, Mennes, van Rooij, Llera, Buitelaar, & Beckmann, 2015). Together, these approaches allowed for the investigation of the neural correlates of specific autobiographical memory content during retrieval.

Though this method is novel, previous analyses in fMRI performed by the Hamann lab using a scanner compatible microphone and ICA preprocessing have observed that dedicated face, scene, and object processing regions are activated during memory retrieval of matching content (Ferris, Inman, & Hamann, 2018). This novel neuroimaging paradigm in which participants narrated their memories in real time during retrieval will also be used in this paper. Building off that hypothesis, we investigated whether brain regions activated by content specific tasks, that are not classically single content specific brain regions, would activate in a similar manner. In other words, in the previous experiment by the Hamann lab, one category explored was the face category and activation of the fusiform face area was observed (Ferris, Inman, & Hamann, 2018). The fusiform face area is a brain region commonly known to be involved in processing faces (Ferris, Inman, & Hamann, 2018). Therefore, individuals retrieving autobiographical memories dynamically activated the fusiform face area when retrieving face content at a second to second time scale. These results indicate that there is a second to second dynamic activation of one specific cortex associated with one category during autobiographical memory retrieval. This leads to our main question: do we observe similar second to second dynamic activation of more than one brain region associated with a single category during autobiographical memory retrieval? To address this question, we selected a set of categories (spatial-relationship, time-referential, self-reference, and other-referential) which are integral to autobiographical memories (Fivush, 2011) and have been shown to activate multiple brain regions across studies.

Spatial-Relationship

Spatial relationships between objects, beings, and components of the environment are a core factor of autobiographical memory. Autobiographical memories definitionally involve spatial components as individuals retrieve the specific place in which the memory occurred (Robin, Wynn, & Moscovitch, 2016). Spatial perception and memory are defined by a reference frame which determines the type of spatial location represented in the brain and how spatial locations are specified within a representation (Galati, Pelle, Berthoz, &Committeri, 2010). Within that memory, individuals, objects, and items all have spatial relationships with one another. In our research, the spatial-relationship category refers to the position of an item in space or the relationship between two items in space.

Spatial-relationship words are commonly used in our every-day lives and they are important to remembering episodic details (Sheldon & Chu, 2017). How the brain processes and represents spatial relationships has been a significant area of interest in psychology (Galati et al., 2010). However, naturalistic online retrieval of spatial content in memories has been difficult to study using neuroimaging, and as a result the temporal dynamics of when and how spatial content is accessed during autobiographical memory retrieval is not well understood.

Though the temporal dynamics of spatial processing during retrieval are not well characterized, there have been numerous studies examining the neural processes of spatial content. Studies have shown that spatial word processing selectively activates the right posterior parietal cortex and right dorsolateral prefrontal cortex (van Asselen et al., 2006), as well as the parahippocampal cortex, supramarginal gyrus, and precuneus (Hirshhorn, Grady, Rosenbaum, Winocur, & Moscovitch, 2012). Other areas that also activate for the spatial-relationship category are the basal ganglia (Menon, Anagnoson, Glover, & Pfefferbaun, 2000; Kim &Hikosaka, 2015) and retrosplenial cortex (Galati et al., 2010).

The retrosplenial cortex has been associated with a large network of brain regions involved in processing and storing spatial information (Czajkowski et al., 2014). A review of neuroimaging studies suggests that the retrosplenial cortex is involved in encoding object locations (Galati et al., 2010). One study used fMRI to investigate which brain regions activated during encoding and retrieval of locations with different spatial frames of reference while participants detected target displacements across many views of a familiar room (Sulpizio, Committeri, Lambrey, Berthoz, & Galati, 2013). The retrosplenial cortex was observed to activate during encoding and retrieval of spatial locations in a stable environmental frame, a new environmental frame, and an individual's perspective of an environmental frame (Sulpizio et al., 2013). The researchers concluded that the retrosplenial cortex is important for updating location viewpoint changes within stable environments, coding for one's own position in familiar environments, and translating between the varying viewpoints of the world (Sulpizio et al., 2013). Additionally, a review paper indicates that disruption to the retrosplenial cortex results in impairments to the spatial representations of the environment as well as impairments to obtaining navigational information from the environment (Miller, Vedder, Law, & Smith, 2014). Evidence from both human and rodent navigation highlights the importance of the retrosplenial cortex in processing components of an area along with the spatial relationships between those components (Miller et al., 2014).

The basal ganglia have been suggested to have a role in memory guided movements and gaze orienting (Menon, et al., 2000; Kim & Hikosaka, 2015; Neggers, Zandbelt, Schall, & Schall, 2015). A review shows that the basal ganglia are also involved in the automatic process of orienting towards an object in space (Kim & Hikosaka, 2015). In one fMRI study participants who performed a motor sequence task were observed to activate the basal ganglia for long term memory-guided movements as well as working-memory guided movement sequencing (Menon et al., 2000). Another study compared the performance of healthy participants to participants with spatial neglect, both of whom had lesions to the basal ganglia and thalamus, as they completed four separate tasks 1) finding a target letter among distractors, 2) finding a target letter among distractors on different sides of the paper, 3) placing identical items evenly on a sheet of paper, and 4) copying a complex object on a paper (Karnath, Himmelbach, & Rorden, 2002). The results indicated that the putamen, and the caudate nucleus (which are two of many structures that make up the basal ganglia) are associated with spatial neglect in these individuals with lesions (Karnath et al., 2002). As such, the basal ganglia have been implicated in spatial processing.

The right posterior parietal cortex has been suggested to have a role in sustaining attention to spatial locations (Malhotra, Coulthard, & Husain, 2009; van Asselen et al., 2006). One study compared right hemisphere patients with spatial neglect to stroke patients and to healthy individuals in a simple detection task; an overall deficit in maintaining spatial attention was observed in individuals with lesions in the posterior parietal cortex (Malhotra et al., 2009). The researchers also performed another task in which participants were asked to focus their attention on spatial location rather than verbal material, and individuals with lesions to the right posterior parietal cortex demonstrated a performance deficit. Finally, the same participants were instructed to maintain attention to visual patterns as well as to spatial locations, and the researchers observed deficits only in the spatial attentional task performance of individuals with right posterior parietal cortex lesions (Malhotra et al., 2009). The researchers concluded that the right posterior parietal cortex was causally involved in maintaining attention to spatial locations. In another study, stroke patients performed a spatial search task, where they were asked to search through various boxes in different locations to find an object; patients who had damage in both their right posterior parietal cortex and right dorsolateral prefrontal cortex had problems performing these spatial tasks and demonstrated difficulty sustaining spatial information in working memory (van Asselen et al., 2006). The researchers concluded that the right posterior parietal cortex is important for spatial task performance and maintenance of spatial information in working memory (van Asselen et al., 2006).

The right dorsolateral prefrontal cortex has also been theorized to play a role in spatial information processing, spatial search task performance, and maintaining spatial working memory (van Asselen et al., 2006; Malhotra et al., 2009). Another study suggested that the dorsolateral prefrontal cortex is associated with spatial working memory as well as manipulating spatial information to facilitate learning of a predictable action sequence (Robertson, Tormos, Maeda, & Pascual-Leone, 2001). In this study participants received inhibitory transcranial magnetic stimulation (TMS) to the dorsolateral prefrontal cortex which impaired performance on a spatial positioning task, leading the researches to conclude that the dorsolateral prefrontal cortex is important in spatial cue learning (Robertson et al., 2001).

The parahippocampal cortex has been proposed to play a role in spatial memory function (Hirshhorn, Grady, Rosenbaum, Winocur, & Moscovitch, 2012). In a review of neuropsychological, behavioral, and neuroimaging studies, the parahippocampal cortex has been observed to be involved in the processing of spatial scenes (Burgess, Maguire, & O'Keefe, 2002). One study examined the role of parahippocampal cortical function in spatial memory by having patients with parahippocampal and perirhinal lesions perform a response task related to memory guided eye movements (Ploner et al., 2000). The results showed that patients with both parahippocampal and perirhinal lesions had a delay dependent reduction in accuracy of memory-guided eye movements. However, patients with only perirhinal lesions did not have a delay performing the memory guided eye movement task; the researchers thereby concluded that spatial memory processing in this task relied on the parahippocampal cortex (Ploner et al., 2000). Another study utilized fMRI to investigate the activity of the brain as individuals retrieved three types of details: 1) coarse-grained spatial details related to a geographic location, 2) fine-grained spatial details related to a geographic location, or 3) episodic details related to a previously visited location (Hirshhorn et al., 2012). Participants making fine-grained spatial judgements were observed to activate the parahippocampal cortex, suggesting its specific function in spatial memory (Hirshhorn et al.,2012).

The supramarginal gyrus is a region that has been suggested to be important for processing and integrating spatial information (Assmus et al., 2003; Hirshhorn et al., 2012). An fMRI study investigating fine-grained spatial judgements and coarse-grained spatial judgements concluded activation of the supramarginal gyrus as well, suggesting its role in making spatial judgements (Hirshhorn et al., 2012). Another study in which participants performed a perceptual judgement task inside the fMRI about whether two moving objects of various sizes would collide, suggested that the supramarginal gyrus is important for detecting spatial relationships between two different objects of various sizes (Assmus et al., 2003). In another study, individuals with lesions were asked to make categorical spatial judgements between objects (left or right) along with coordinate spatial judgements (10 meters away), and the researchers observed that individuals with lesions to the supramarginal gyrus were unable to perform categorical spatial judgements between objects (Amorapanth, Widick, & Chatterjee, 2010). As such, the researchers concluded the importance of the supramarginal gyrus in making spatial judgements between objects (Amorapanth, et al., 2010).

The precuneus has been associated with processing spatial information (Galati et al., 2010; Hirshhorn et al., 2012). A review of functional imaging studies concluded that the precuneus supports processing of visuo-spatial imagery (Cavanna & Trimble, 2006). One study investigating fine grained and coarse-grained spatial judgements observed that participants making fine-grained spatial judgements activated the precuneus (Hirshhorn et al., 2012). In another study, participants were asked to identify the age or the position of people or objects, and the researchers observed activation of the precuneus for both conditions; this activation was stronger for individuals who performed well on the task, which indicated that the precuneus supports spatial working memory (Wallentin, Roepstorff, Glover, & Burgess, 2006).

Taken together these studies offer a wealth of hypotheses as to what areas of the brain might be activated during the retrieval of specific spatial-relationship content as represented by narrative reporting of corresponding words. We therefore hypothesize that if retrieving memories associated with spatial processing utilizes the same neural substrates as performing various spatial relationship tasks then we will observe activation in the retrosplenial cortex, basal ganglia, right posterior parietal cortex, right dorsolateral prefrontal cortex, parahippocampal cortex, supramarginal gyrus, and precuneus at a second to second time scale during autobiographical memory retrieval.

Time-Referential

Autobiographical memories definitionally involve a combination of processes that give us a sense of a past and a chronological order to events of a specific memory that occurred at a specific time (Friedman, 2004); as such, time referential content is a crucial component of autobiographical memory. Time referential content, often also discussed as temporal distance, is defined as the amount of time that passed between a memory and the present (Friedman, 2004). Time referential content can also be discussed in terms of temporal location which refers to personal time patterns, such as “during the summer” (Friedman, 2004). Further, time can also be discussed as temporal order which refers to the chronological order of events (Friedman, 2004). In this study we combine these three concepts into a general framework of time-referential content, which we define as words or short phrases that refer to a certain moment or specific period such as an hour, a day, a week, or a month. How the brain process and represents time has been a significant area of interest in psychology (Rubia & Smith, 2004) as the conceptualization of time is omnipresent in our daily lives and allows us to differentiate between what happened, what is happening, and what will happen (Block & Gruber, 2014). Despite this interest having led to fruitful investigation into which brain regions support time processing more generally, the temporal dynamics of online autobiographical memory retrieval of time content remain largely unknown.

Numerous studies examine the neural underpinnings of time-referential representations and processing. Studies associated with time-referential processes have been shown to activate the anterior cingulate, right inferior frontal gyrus, and right caudate nucleus (Pouthas et al., 2005; Pouthas, Garnero, Ferrandez, & Renault, 2000). Other studies have indicated regions that activate for time references are the right posterior parietal cortex (Bueti, Bahrami, & Walsh, 2008), and right prefrontal cortex (Pouthas et al., 2000). Further, other studies have also shown activation in the right lateral prefrontal cortex (Rubia & Smith, 2004), and inferior parietal lobule (Rubia & Smith, 2004; Rao, Mayer, & Harrington, 2001) to references of time.

The anterior cingulate has been theorized to have a role in processing time references (Pouthas et al., 2005; Pouthas et al., 2000). In one fMRI study, participants estimating long time and short time durations were observed to activate the anterior cingulate, highlighting the role it plays in time estimation (Pouthas et al., 2005). In another study using positron-emission tomography (PET) and event-related potentials (ERP) participants performed duration estimations for LED light stimulus during which observed activation of the anterior cingulate indicated its role in making temporal judgements (Pouthas et al., 2000). Another study using PET followed a similar estimation paradigm that involved assessing the duration of an LED light stimulus which showed observed activation of the anterior cingulate, suggesting that this region is involved in prospective time judgements (Maquet et al., 1996).

The right inferior frontal gyrus has been suggested to have a role in duration judgments of time. In one fMRI study, participants estimating long and short time durations activated the right inferior frontal gyrus, indicating its role in time estimation (Pouthas et al., 2005). Another study utilized fMRI to investigate neural activity as participants performed a time task and a color task; the inferior frontal gyrus was observed to activate, suggesting that it is directly involved with judging durations (Livesey, Wall, & Smith, 2007).

The right caudate nucleus has been proposed to have a role in time estimations (Pouthas et al., 2005). In one fMRI study, participants estimating long and short time durations also activated the right caudate nucleus, indicating that it may play a role in time estimation (Pouthas et al., 2005). Another fMRI study in which participants decided between an immediate and a delayed hypothetical reward using a delayed discounting task, indicated increased observed activity in the caudate nucleus for shorter delays relative to longer delays, suggesting that it is involved in reward prediction and time estimation (Wittmann, Leland & Paulus, 2007).

The right posterior parietal cortex has been theorized to have a role in time perception (Bueti et al., 2008). The PET and ERP study in which participants performed visual and auditory temporal interval discrimination tasks and a visual shape identification tasks showed activation in the right posterior parietal cortex for the temporal discrimination tasks, suggesting that it is involved in the timing of visual events (Pouthas et al., 2000). Another study utilized transcranial magnetic stimulation (TMS) to disrupt the left or right parietal cortex as participants performed a similar visual and auditory temporal interval discrimination tasks and a visual shape identification task (Bueti et al., 2008). Results showed that disruption to the right posterior parietal cortex lead to abnormal time perception, which indicates that it is important for the timing of auditory and visual stimuli (Bueti et al., 2008). Additionally, a study also disrupting the function of the posterior parietal cortex using TMS as participants judged different time intervals or pitches indicated that the disruption slowed the reaction times only for time judgements, suggesting the function of the posterior parietal cortex in processing temporal judgements (Alexander, Cowey, & Walsh, 2007).

The right prefrontal cortex is associated with processing temporal information and time estimations (Pouthas et al., 2000). A PET and ERP study in which participants performed visual and auditory temporal interval discrimination tasks and a visual shape identification task showed activation in the right prefrontal cortex for the temporal discrimination tasks (Pouthas et al., 2000). A review of fMRI studies suggested that the right lateral portion of the prefrontal cortex is associated with time estimations and motor timing processes (Rubia & Smith, 2004). Another study examined patients with prefrontal cortex lesions performing three tasks: 1) a temporal discrimination task of 400-ms and 4-s intervals, 2) a working memory non-temporal task, and 3) a long duration discrimination task (Mangels, Ivry, & Shimizu, 1998). Results showed that patients with lesions to the prefrontal cortex had deficits in only the long duration discrimination task, and they were disproportionately sensitive to strategic manipulations in long duration discrimination tasks (Mangels et al., 1998). The researchers concluded that the prefrontal cortex is associated with acquiring, maintaining, monitoring, and organizing the temporal representations in working memory (Mangels et al., 1998).

The inferior parietal lobule is important for time estimations and temporal attention processes in working memory (Rubia & Smith, 2004). A review of fMRI studies indicated that the inferior parietal lobule is involved in motor timing tasks (Rubia & Smith, 2004). In another fMRI study participants were asked to perform a long duration estimation task, which showed increased activity for the time estimation task compared to the working memory and to the motor tasks, indicating that the inferior parietal lobule is involved in durations of visual stimuli (Basso, Nichelli, Wharton, Peterson, & Grafman, 2003).

Taken together these studies offer a wealth of hypotheses as to what areas of the brain might be activated during the retrieval of specific time-referential content as represented by narrative reporting of corresponding words. We therefore hypothesize that if retrieving memories associated with time-referential processing utilizes the same neural substrates as performing various temporal(time-referential) tasks then we will observe activation in the anterior cingulate, right inferior frontal gyrus, right caudate nucleus, right posterior parietal cortex, right prefrontal cortex, right lateral prefrontal cortex, and inferior parietal lobule at a second to second time scale during autobiographical memory retrieval.

Self-Referential

Self-referential processes including self-reflection, self-judgement, self-regulation, and self-efficacy are core components of autobiographical memories. Autobiographical memories definitionally involve reference to the individual who is retrieving a memory from their own past experience (Cabeza & Jacques, 2007). Self-referential processing is the center of our self-identity and is essential for expanding on experiential feelings of the self (Northoff, Heinzel, Greck, Bermpohl, Dobrowolny, & Panksepp, 2006). In our research, self-referential content reflects direct references to oneself, specifically, the self-referential category describes any first-person singular reference.

Self-referential processing is essential in our daily lives as individuals form relationships and interact with stimuli in the world (James, 1892; Northoff et al., 2006). As such, self-reference is mediated by subjective experience and ownership of these experiences (Zahavi, 2003; Gallagher & Zahavi, 2005; Legrand, 2005; Northoff et al., 2006). How the brain processes and represents self-referential information has been a significant area of interest in psychology (Levine, 2004; Heatherton, 2011). A review paper that investigated lesion, aging, and functional neuroimaging studies suggests that the fronto-temporo-parietal system including the anteromedial prefrontal cortex mediate retrieval of autobiographical memory with self-specific information (Levine, 2004).

Though the temporal dynamics of self-referential processing during retrieval are not well characterized, there have been numerous studies examining the brain processes and representations of self-referential information. Self-referential processes have shown to activate the posterior cingulate cortex, precuneus, ventral anterior cingulate cortex (Heatherton, 2011) as well as the right dorsomedial prefrontal cortex, left inferior parietal lobe (Herwig, Kaffenberger, Schell, Jäncke, & Brühl, 2012), and insula (Vogelet & Fink, 2003).

The posterior cingulate cortex has been associated with processing self-referential judgements (Heatherton, 2011). A review paper that examined fMRI and PET studies discussed how the posterior cingulate cortex has been shown to activate during self-reflection and processing of self-referential information (Heatherton, 2011). In one study utilizing fMRI participants selected whether or not a trait adjective represented them in the 1) self-reference condition, 2) non-self-reference condition, or 3) rest condition (Davey, Pujol,& Harrison, 2016). Results showed increased activation of the posterior cingulate cortex during self-referential activity, indicating that this region is involved in processing self-related information (Davey et al., 2016). Another study also using fMRI had participants make judgements about positive and negative trait words in the 1) self-reference condition, 2) other-reference condition, 3) semantic processing condition, and 4) letter processing condition (Yoshimura et al., 2009). The researchers observed more activation in the posterior cingulate gyrus during the self-referential condition, suggesting that it is involved in processing self-referential emotional judgements (Yoshimura et al., 2009).

The precuneus has been proposed to process information about self-reference and self-consciousness (Heatherton, 2011; Cavanna & Trimble, 2006). A review of fMRI and PET studies identified the precuneus as a region that activates for processing self-related information (Heatherton, 2011). One fMRI study in which participants made judgements about positive and negative trait words (four conditions stated above), observed activation in the precuneus during the self-referential condition suggesting that this region is involved in processing self-referential emotional judgements (Yoshimura et al., 2009) Another fMRI study had participants retrieve an autobiographical memory in the scanner, and at the end they were asked to rate the perspective from a range of exclusively third-person to exclusively first-person reference (Freton, Lemogne, Begouignan, Delaveau, Lehericy, & Fossati, 2013). Results indicated a positive correlation between the spontaneous tendency to recall memories from a first-person perspective and the volume of the right precuneus (Freton et al., 2013). In other words, the larger the volume of the precuneus the more likely a participant will remember a memory in first person perspective, suggesting that the precuneus regulates emotions and self-related processes (Freton et al., 2013).

The ventral anterior cingulate cortex is associated with self-referential processing (Heatherton, 2011). A review of fMRI and PET studies suggested that the ventral anterior cingulate cortex is involved in processing self-descriptive traits (Heatherton, 2011). In one fMRI study, participants made judgements about positive and negative trait words in four conditions; the self-reference condition showed increased activation of the right ventral anterior cingulate gyrus to negative emotional stimuli, portraying that this region is involved in processing self-referential information related to negatively emotional stimuli (Yoshimura et al., 2009). Further, another fMRI study examined the role of neural correlates in processing positive, negative, and neutral words in the 1) self, 2) other, and 3)no reference conditions; researchers observed increased activation of the anterior cingulate cortex only in the self-condition when processing emotional words, suggesting that this region is involved in the subjective experience of one's own emotions (Herbert, Herbert, & Pauli, 2011).

The right dorsomedial prefrontal cortex has been theorized to process information related to self-awareness and self-knowledge (Modinos, Ormel, & Aleman, 2009; Heatherton, 2011). A review of fMRI and PET studies indicated that the medial prefrontal cortex has been observed to activate for self-reflection, self-awareness, self-regulation, and self-knowledge processes (Heatherton, 2011). Another review of neuroimaging studies suggested that the dorsomedial prefrontal cortex activates for self-referential processing (Northoff & Bermpohl, 2004). In one fMRI study participants asked to self-reflect on themselves, or a personally known or unknown person were observed to activate the right dorsomedial prefrontal cortex (Herwig et al., 2012). Further, another fMRI study in which participants made judgements about positive and negative trait words in the self-reference condition compared to the other three conditions showed observed activation of the medial prefrontal cortex, suggesting that this region is involved in processing self-referential emotional judgements (Yoshimura et al., 2009).

The left inferior parietal lobe has been proposed to process self-referential information (Northoff & Bermpohl, 2004; Herwig et al., 2012). An an fMRI study in which participants were asked to self-reflect resulted with an observed activation in the left inferior parietal lobe (Herwig et al., 2012). In another fMRI study examining brain activity during self-referential processing compared to resting state, the inferior parietal lobule was observed to increase its activation, suggesting that it is involved in processing self-related information (Davey et al., 2016). Further, in a PET study, participants retrieved previous judgements about themselves, their best friend, and the Danish Queen; results showed a decrease in the activation of the right inferior parietal lobe with decreasing self-reference, indicating that the right inferior parietal lobe is a nodal structure in the network of self-awareness and self-referential processing (Lou et al., 2004).

The insula has a been proposed to have a role in processing self-reflection, self-awareness, and internal body states (D'Argembeau, Jedidi, Balteau, Bahri, Phillips, & Salmon, 2011; Vogelet & Fink, 2003; Modinos et al., 2009). A review of fMRI studies suggests that the insula is associated with thinking about oneself performing an action (Vogelet & Fink, 2003). In one fMRI study, participants judged self-descriptions of traits and evaluated the importance and certainty of their self-view (D'Argembeau et al., 2011). Results showed that observed activation in the right insula was positively associated with self-descriptiveness (D'Argembeau et al., 2011). The personal importance ratings of participants were positively correlated with neural activity in the right insula, suggesting that the insula is involved in processing self-judgements, self-views, and self-agency (D'Argembeau et al., 2011). Another fMRI study compared participants self-reflecting on their qualities to reflecting on the qualities of their acquaintances, and observed activation of the left insula during self-reflection emphasizes that this region plays an important role in self-reflection (Modinos et al., 2009). Further, in another fMRI study, participants made choices, expressed believes, and expressed what they think others believe they would do (Bhatt & Camerer, 2005). Strategic IQ, and earnings from choices and beliefs showed a negative correlation with insula activation, suggesting that individuals with lower strategic IQ and earnings from their own choices have greater insula activation and as such are too focused on themselves (Bhatt & Camerer, 2005).

Taken together these studies offer a wealth of hypotheses as to what areas of the brain may be supporting retrieval of specific self-referential content as represented by narrative reporting of corresponding words. We therefore hypothesize that if retrieving memories associated with self-referential processing utilizes the same neural substrates as performing various self-related tasks then we will observe activation in the posterior cingulate cortex, precuneus, ventral anterior cingulate cortex, right dorsomedial prefrontal cortex, left inferior parietal lobe and insula at a second to second time scale during autobiographical memory retrieval.

Other-Referential

In contrast to self-referential processing we are interested in what brain regions activate when a person retrieves memories about other people. Other-referential processes including thinking of other people, their opinion, or their feelings are important to social autobiographical memories. As social beings, we constantly interact with other people in our daily life (Gallagher & Frith 2003). We are able to deceive, cooperate, empathize, read others' body language, and anticipate others' behaviors (Gallagher & Frith 2003). This social cognitive capacity is known as having theory of mind (Gallagher & Frith 2003; Saxe & Powell, 2006).

Theory of mind refers to thinking of others and understanding another person's beliefs, perspectives, intentions, and desires (Saxe & Wexler, 2005). As such, we are able to explain, understand, and predict other's behaviors (Gallagher & Frith 2003). Part of understanding others is taking their perspective, which at times involves simulating another individual's experience (Spreng, Mar, & Kim 2008). Social cognition, which we include in "other-referential" content, includes theory of mind and processes supporting thinking of others (Flavell & Miller, 1998). In our research, other-referential content is characterized by direct references to other individuals, specifically, the other-referential category describes any name or a third-person pronoun reference to another human individual or a group of humans.

The other-referential category is crucial in our daily lives because we are constantly trying to make sense of other people and construct representations of other people around us (Macrae & Bodenhausen, 2000). How the brain processes and represents other-referential content has been a significant area of interest in psychology (Heatherton, 2011). A review of functional imaging studies investigated brain regions specific to the ability of having theory of mind and the functional significance of these regions in the social cognitive network (Gallagher & Frith, 2003).

Though the temporal dynamics of other-referential processing during memory retrieval are not well characterized, there have been numerous studies examining the brain processes and representations of other-referential content. Thinking or talking about others has been shown to activate the temporoparietal junction, medial prefrontal cortex, temporal poles, medial parietal cortex (Heatherton, 2011), and superior temporal sulcus (Zilbovicius et al., 2006).

The temporoparietal junction is crucial for thinking of other people and understanding how others feel (Saxe & Kanwisher, 2003; Heatherton, 2011). A review of fMRI and PET studies showed that the temporoparietal junction activates for other-information processes, such as when one thinks of other people (Heatherton, 2011). In one fMRI study, participants completed a false belief story task that involved either another person's mental state, another person's physical state, or a nonhuman (Saxe & Kanwisher, 2003). Results indicated greater observed activation of the temporoparietal junction when participants were asked to read stories about the mental state of others rather than reading about the physical characteristics of others, suggesting that it is involved in understanding another individual's mind (Saxe & Kanwisher, 2003). More specifically, the right temporoparietal junction activates for the mental states of others rather than the social facts about a person (Saxe & Wexler, 2005). Another fMRI study in which participants remembered their own experiences from personal photos and imagined others' experiences from strangers' photos found observed activation of the right temporoparietal junction during imagination of other individual's experiences, indicating that this region is needed for theory of mind (Rabin, Gilboa, Stuss, Mar, & Rosenbaum, 2010).

The medial prefrontal cortex plays a broad role in general social cognition (Saxe & Powell, 2006). Studies associated the activation of the medial prefrontal cortex with thinking of others (Benoit, Gilbert, Volle, & Burgess, 2010). A review investigating fMRI and PET studies examined the neural correlates of other-referential processing as well as self-referential processing and suggested that the medial prefrontal cortex is activated when one thinks of another (Heatherton, 2011). Further, an fMRI study asking participants to judge personality trait words that either describe them or describe their best friend found observed activation of the medial prefrontal cortex during both conditions, signifying that the medial prefrontal cortex is not only involved in processing judgements about oneself but also in appraising other's personality traits and judging them (Benoit et al., 2010). In another fMRI study, participants read about a protagonist's thoughts, about other subjective and internal states, and other socially relevant information about individuals (Saxe & Powell, 2006). Activity in the medial prefrontal cortex was observed for all three tasks, which indicates that the medial prefrontal cortex is important for processing not only self-referential information, but also other-referential information (Saxe & Powell, 2006).

The temporal poles have been proposed to play a role in empathizing with others and connecting with other individuals (Schulter-Ruther, Markowitsch, Fink, & Piefke, 2007;Heatherton, 2011). A review of fMRI and PET studies suggests that the temporal poles are involved with processing other-referential information, such as thinking intimately of others (Heatherton, 2011). Another review that examined functional imaging studies indicated that the temporal poles are consistently activated in association with theory of mind (Gallagher & Frith, 2003). An fMRI study examined participants performing a visual activation paradigm that had a series of comic strips each representing a short story with different categories including theory of mind and empathy (Vollm et al., 2006). Results showed that the temporal poles were common areas of activation between the two categories, suggesting that theory of mind and empathy both rely on networks that are involved with predicting other individual's mental states (Vollm et al., 2006). In another fMRI study, participants looked at faces expressing emotions with either a 1) direct, or 2)averted gaze and were asked to either focus on 1) their own emotional response to the face or 2) the emotional state expressed by the face; observed activation of the temporal poles was evident for both the self and the other task, suggesting that the temporal poles are involved in empathetic states and empathizing with others (Schulter-Ruther et al., 2007).

The medial parietal cortex has been associated with processing information related to social interactions (Heatherton, 2011). In one fMRI study, participants viewed food names and made three judgements based on whether 1) they liked the food, 2) their friend liked the food, or 3) there were more than two vowels in the name (Seger, Stone, Keenan, 2004). Results showed greater activation in the medial parietal cortex when participants judged whether their friend liked the food, suggesting that this region is involved in processing information related to other individuals (Seger, Stone, Keenan, 2004). Another fMRI study examined participants watching social interactions in cartoons and reflecting on the intentions of the protagonist; the researchers observed activation of the medial parietal cortex during both the cooperation and deception conditions, indicating that this region is involved in processing information about other people as well as processing social interactions (Lissek et al., 2008).

The superior temporal sulcus has been theorized to process social interactions (Zilbovicius et al., 2006). A review of the neural basis of social perception, action observation, and theory of mind indicates that the superior temporal sulcus plays a central role in all three of these processes (Yang, Rosenblau, Keifer, & Pelphrey, 2015). Another review of brain imaging studies suggested that children with autism have shown a highly abnormal superior temporal sulcus function and as such, children with autism have impaired social interactions and deficits in communication (Zilbovicius et al., 2006). In one study, participants watched an animated character making reaching to grasp movements either in the correct way or the incorrect way towards a stimulus and results showed that in both cases the right superior temporal sulcus was observed to activate (Pelphrey, Morris, & McCarthy, 2006). However, there was greater activation in the right superior temporal sulcus when the animated character reached and grasped in the incorrect way, indicating that this region has a role in analyzing individual's intentions and interactions (Pelphrey, Morris, & McCarthy, 2006).

Taken together these studies offer a wealth of hypotheses as to what areas of the brain might be activated during the retrieval of specific other-referential content as represented by narrative reporting of corresponding words. We therefore hypothesize that if retrieving memories associated with other-referential processing utilizes the same neural substrates as performing various tasks related to thinking of others then we will observe activation the temporoparietal junction, medial prefrontal cortex, temporal poles, medial parietal cortex, and superior temporal sulcus at a second to second time scale during autobiographical memory retrieval.

Hypotheses

We hypothesize that a subset of the regions associated with general content processing will activate during memory retrieval of corresponding content. This study extends current knowledge of the roles of these brain regions using a novel method—examining activation of these brain regions during narrated memory retrieval, and the degree to which cortex associated with specific content is recruited into this network. We did this by examining brain activation associated with memories which were narrated as they were retrieved. We predict that during autobiographical memory retrieval, as participants remember content specific detail, corresponding content specific cortex will activate as participants narrate memories in real time. This study will be testing the hypothesis that content specific cortex will activate during memory retrieval of matching content, and that activation will occur dynamically at a second-to-second time scale.

Methods

Participants

Eighteen of an initial twenty-one participants from the greater Atlanta community were recruited for this study. Two participants were excluded from the study because they failed to retrieve memories over 20% of the time. One participant was excluded due to a neuroanatomical variation that prevented their inclusion in group level models. Participants were briefly trained outside the scanner to talk with minimal movements of the head.

Design

Participants were scanned using functional magnetic resonance imaging while they retrieved unrehearsed autobiographical episodic memories in response to a neutral cue word (e.g., river, party). Each participant was scanned during 4 runs in which they retrieved 12 memories per run. During half of the runs participants narrated their memories in real time as they retrieved them. During the other half of the runs, participants were instructed to silently narrate their memories in their heads to themselves. Participants retrieved a total of 48 autobiographical memories. This study only examines narrated trials. All narrated retrievals were recorded during scanning using an opto-acoustic microphone (FOMRI-III, Optoacoustics).

Prior to memory retrieval, participants completed a 7 second attentional baseline in which they indicated the direction of arrows projected on a screen using button presses to indicate left or right. Following the baseline participants were presented with a cue word and they were given 24 seconds to search for a memory. Once they had a memory firmly in mind, they used a button press to indicate that the memory had been selected. Following the button press, participants narrated the memory between 12 and 24 seconds, depending on how quickly they retrieved the memory. Three seconds before the end of the narrated memory, a fixation cross appeared on the screen indicating that they should come to the end of their memory. They were then asked to rate their memory based on “reliving” (how vivid the memory was) (Low-1-2-3-4- High) prompted with the cue word on the screen for 3 seconds. They were also asked to rate the memory based on “valence” (how positive or negative the memory was) (Low-1-2-3-4-High), where “low” represents a “more negative” valence and “high” represents “more positive” valence.

fMRI Acquisition

Data were acquired on a 3.0-T Siemens Trio fMRI scanner. BOLD sensitive T2* weighted functional images were acquired in a multiband sequence with 2mm isotropic voxels with a repetition time TR of 1.

fMRI Analysis

Recordings of the memories narrated inside the scanner were transcribed by two independent coders. The two transcriptions of the memories were then joined together into a canonical transcription by a third person who compared the previous transcriptions for any discrepancies. A content analysis of each transcribed memory was performed based on four main categories: spatial-relation words, time-referential words, self-referential words, and other-referential words (people who were not the participant).

Content words (or short phrases) were identified from the transcriptions of memories. For each category, content specific words were selected based on customized operational definitions. Ambiguous words were adjudicated by an external rater. Spatial words were selected to refer to the position of an item in space or the relationship between two items in space. Examples of spatial words include “down the road,” “in New York,” and “on a towel.” By contrast, size words were not included (e.g., “big sofa,” “small desk,” “big room”). Time-referential words were selected to identify descriptions of specific memories occurring in a certain time period (e.g., seasons, years, months, weeks, days) or for specific points in time (e.g., time of the day), but excluded frequency words. Examples of time words include “two years ago,” “yesterday,” but exclude “often” or “every other week.” Self-referential words that referred to oneself and mainly included first person self-referential terms were selected. Examples of self-referential words include” I” and “me,” but exclude possessive descriptors (e.g., my). By contrast “other-referential” words refer to other human beings in the memory (e.g., mother, friend, Jeff), but exclude possessive terms (e.g., his, her, hers).

Neural activity was contrasted for each category against a baseline of spoken memory retrieval using a standard general linear model approach in SPM12 (Friston, Ashburner, & Heather, 2003). The baseline for each category was slightly different. The baseline consisted of all the words that the participant said during memory retrieval except the words that pertained to a specific content category of interest that it was being contrasted against. For instance, if someone said, “I put my book on the table,” the preposition “on” would be considered a spatial-relation word and neural activity during the period in which a participant narrated “I put my book… the table” would be the baseline activation (see Figure 1). These words were used as a contrast baseline to isolate and remove neural activity associated with brain areas that are active due to movement of the tongue, other speech related activity, and other memory related activity that is not necessarily associated with the specific memory content category being investigated.

fMRI data was preprocessed using a traditional pipeline (realignment, normalization, and smoothed using a 6mm kernel). Further, fMRI data was preprocessed with a program called ICA-AROMA using FSL environment to perform independent component analysis to reduce the effect of motion due to speech as participants retrieved autobiographical memories.

fMRI data was analyzed using SPM12 following a typical GLM approach fMRI software (Friston, Ashburner, & Heather, 2003). Correction for multiple comparisons was performed using SNPM to a threshold of $p < .05$ family-wise error corrected (Nichols & Holmes, 2002).

Results

All results show observed activation for each content category and represent a contrast of the content category of interest versus the baseline of other spoken phrases during autobiographical memory retrieval.

Spatial-Relationships

We found that retrieval of spatial words activated three regions that we hypothesized to be associated with spatial words: the left dorsolateral prefrontal cortex (-24, 16, 52), the left supramarginal gyrus (-56, -42, 10), and the left basal ganglia (-20,4, 4). The activation of these regions can be seen in Figure 2. We hypothesized that there would be activation in the right dorsolateral prefrontal cortex, but we found activation in the left.

Other regions (see Table 1) which we had not hypothesized would activate showed activation. Those regions are precentral gyrus, superior temporal gyrus, central opercular cortex, heschl's gyrus, planum temporale, middle frontal gyrus, middle temporal gyrus, superior frontal gyrus, insular cortex, lateral occipital cortex, supplementary motor cortex, and cingulate cortex.

Time-Referential

We found activity in one region that we hypothesized to be associated with time words: the left ventrolateral prefrontal cortex (-38,44,4). The activation of this region can be seen in Figure 3.

Other regions (see Table 2) which we had not hypothesized would activate showed activation. Those regions are the precentral gyrus, heschl's gyrus, planum temporale, superior temporale gyrus, inferior temporal gyrus, postcentral gyrus, superior parietal lobule, supplementary motor area, lateral occipital cortex, intracalcarine cortex, cingulate cortex, cuneus, and primary motor cortex.

Self-Referential

We found activity in two regions we hypothesized would activate to self-referential words: the medial prefrontal cortex (-12, 54, 24), and the left insula (-30, 14, 4). The activation of these regions can be seen in Figure 4.

Other regions (see Table 3) activated which we had not hypothesized would activate. Those regions are the precentral gyrus, heschl's gryrus, superior temporal gyrus, planum temporale, middle temporal gyrus, inferior temporal gyrus, planum polare, middle frontal gyrus, frontal orbital cortex, superior frontal gyrus, frontal pole, left putamen, and supplementary motor cortex.

Other-Referential

We found activity in one region we hypothesized would activate to other-referential words: the temporoparietal junction (-48, -60, 22; -42, -56, 22). This activation can be seen in Figure 5. We hypothesized that there would be activation in the right temporoparietal junction. However, we found activation in the left.

Other regions (see Table 4) activated which we had not hypothesized would activate. Those regions are the precentral gyrus, postcentral gyrus, planum temporale, supramarginal gyrus, and superior temporal gyrus.

Discussion

Our findings support the hypothesis that memory retrieval of specific content activates corresponding regions which support cognitive processing of that content in different contexts on a second-to-second time scale. This finding reflects similar observations in studies using imagination paradigms where researchers have observed that there is content specific cortex that selectively activates when people imagine that content. However, this is the first time this finding has been demonstrated across multiple categories in one study using naturalistically narrated memories (Hassabis, Kumaran, & Maguire, 2007; Kanwisher, 2010; Addis, Wong, & Schacter, 2007).

Spatial-Relationship

We observed activation that is consistent with our hypothesis for the spatial-relationship category in the left basal ganglia, and the left supramarginal gyrus. We hypothesized that the right dorsolateral prefrontal cortex would also activate, but we found activation in the left prefrontal cortex. We further hypothesized activity in the retrosplenial cortex, basal ganglia, right posterior parietal cortex, right dorsolateral prefrontal cortex, parahippocampal cortex, and supramarginal gyrus, but we did not observe activity in these regions.

The basal ganglia which activated in our spatial-relationship category have an important role in gaze orienting in space. The first gaze-orienting processes occur for humans in the basal ganglia (Neggers et al., 2015). Recent findings have identified these gaze-orienting processes as movements of the eyes in saccades; usually the basal ganglia are involved in this automatic process of orientation of the eyes and body towards a reward or an object in space (Kim & Hikosaka, 2015). Further, the basal ganglia are also important in processing motor-guided movements. In a study were participants performed a motor sequence task, the basal ganglia were recruited for memory guided movements and working memory guided movement sequencing (Menon et al., 2000). Another study examining patients with spatial neglect performing motor guided movement tasks such as redrawing objects or arranging identical items evenly on a paper, indicated that the basal ganglia are associated with the pathological asymmetrical spatial behaviors exhibited by spatial neglect patients (Karnath et al., 2002). Taken together, these results suggest that as participants are retrieving an autobiographical memory, the basal ganglia may be activating as participants are imagining the space they were in, gaze orienting in the constructed space, and moving throughout the space as they narrate their memories; this activity is most intense during the retrieval of spatial content and the narration of that content.

The left supramarginal gyrus has been associated with integrating spatiotemporal information. fMRI studies have indicated that the supramarginal gyrus is involved in making fine-grained spatial judgements (Hirshhorn et al., 2012) and making spatial judgements of various distances and sizes (Assmus et al., 2003). Another study of patients with lesions to the supramarginal gyrus found that the patients had impaired performance on spatial judgement tasks (Amorapanth et al., 2010). Together, the observed pattern of results suggests that when participants are retrieving autobiographical memories with spatial-relationship content, the left supramarginal gyrus is activating to support reconstruction of spatial locations as well as the location of objects from their memory.

The right dorsolateral prefrontal cortex which activated in our spatial-relationship category is important for spatial perception and maintaining spatial information within working memory. Studies have observed that stroke patients with right dorsolateral prefrontal cortex lesions were impaired on spatial search tasks (van Asselen et al., 2006) and that TMS to the dorsolateral prefrontal cortex impaired participants' ability to perform spatial pattern learning (Robertson et al., 2001).

In our experiment we found activation only in the left dorsolateral prefrontal cortex and not in the right. Results from other studies as well as our findings give us reason to believe that the left dorsolateral prefrontal cortex also has a role in spatial processing. Therefore, we believe that as participants are retrieving an autobiographical memory, the left dorsolateral prefrontal cortex is activating as participants are remembering the spatial features of the location they were in and maintaining it in spatial working memory as they verbalize their memory.

We additionally observed activation during retrieval of spatial autobiographical memory content in other regions associated with speech related processing (see below).

Time-Referential

We observed activation for the time-referential category in the left ventrolateral prefrontal cortex, but we hypothesized activation in the right lateral prefrontal cortex. We also hypothesized activity in the anterior cingulate, right inferior frontal gyrus, right caudate nucleus, right posterior parietal cortex, and inferior parietal lobule, but we did not observe activity in these regions.

The right lateral prefrontal cortex has been associated with time estimations (Rubia & Smith, 2004; Pouthas et al., 2000), and temporal interval discrimination tasks (Mangels et al., 1998; Pouthas et al., 2000). These results indicate that the prefrontal cortex has an important role in acquiring, maintaining, monitoring, and organizing temporal representations in working memory. Studies found activation in the prefrontal cortex or in the right lateral portion of the prefrontal cortex. However, in our study we found activation in the left ventrolateral portion of the prefrontal cortex. This gives us reason to believe that the left ventrolateral portion of prefrontal cortex may also be involved in time estimation and motor timing processes. As such, when participants are retrieving autobiographical memories with time-referential content, we suggest that the left ventrolateral prefrontal cortex is activating to support reconstruction of their past and estimating time durations and maintaining temporal detail in working memory.

We additionally observed activation during retrieval of time-referential autobiographical memory content in other regions associated with speech related processing (see below).

Self-Referential

We observed activation that is consistent with our hypothesis for the self-referential category in the left insula. We also hypothesized activation of the medial prefrontal cortex, but we found activity in the left dorsomedial prefrontal cortex. Further, we hypothesized activity in the posterior cingulate cortex, precuneus, ventral anterior cingulate cortex, and left inferior parietal lobe. However, we did not observe activity in those regions. We did not hypothesize activation of the orbiotofrontal cortex, but we observed activity in that region.

The insula was observed to activate when participants retrieved self-referential content which is consistent with accounts of its role in self-reflection processes, internal body states, and awareness of oneself. A review of fMRI studies indicates that the insula is involved in thinking about oneself in action (Vogelet & Fink, 2003). In one study, participants judging self-descriptiveness of traits as well as high personal importance ratings of those traits showed increased activation in the right insula (D’Argembeau et al., 2011). Additionally, during fMRI participants who self-reflected on their personal qualities were observed to activate the left insula compared to reflecting on the personal qualities of an acquaintance (Modinos et al., 2009). Further, in another fMRI study, participants made choices, expressed beliefs, and expressed what they think others believe they would do, further demonstrating the role of the insula in self-reflective processing (Bhatt & Camerer, 2005). Taken together, these studies and our results suggest that the insula is being activated as participants retrieve autobiographical memory content specific to the self and narrate that content, as the insula supports self-reflective processes and self-judgement.

The left dorsomedial prefrontal cortex which activated for our self-referential category has been associated with processing information related to self-awareness and self-knowledge. Unlike our findings most studies of self-referential processes observe activation in the medial prefrontal cortex more generally, or in the right dorsomedial prefrontal cortex, making our findings somewhat novel. Previous work has associated the medial prefrontal cortex with judgements of positive and negative self-referential trait words (Yoshimura et al., 2009). The right dorsomedial prefrontal cortex has been associated with self-reflection (Herwig et al., 2012) as well as self-referential processing (Northoff & Bermpohl, 2004). Similarly, the medial prefrontal cortex has been associated with self-reflection, self-awareness, self-regulation, and self-knowledge processes (Heatherton, 2011). Taken together, these studies and our findings give us reason to believe that the left dorsolateral prefrontal cortex is activating to support self-reflection, self-awareness, self-regulation, as well as self-knowledge processes as participants are retrieving autobiographical memories with self-referential content. We suggest that the dorsolateral prefrontal cortex is supporting autobiographical memory as participants reconstruct their past and imagine themselves, their thoughts, and their emotional states.

We also observed activation in the orbitofrontal cortex, which we believe may be involved in self-referential processing. The orbitofrontal cortex is associated with a diverse array of emotional and cognitive functions (Paulmann, Seifert, & Kotz, 2009). The orbitofrontal cortex has been observed to activate when participants are viewing emotional words and reflecting on what the words mean to them on a personal level (Ethofer et al., 2006).

Additionally, the orbitofrontal cortex has been implicated in the accuracy of self judgements. One study observed that patients with orbitofrontal cortex lesions had unrealistically positive or negative views of their social skills compared to controls (Beer, 2007). Another study using fMRI observed activation of the orbitofrontal cortex when participants were performing the overconfident tasks (Beer, Lombardo, & Bhanji, 2010). Together with our results, this pattern of findings suggests that the orbitofrontal cortex may be supporting self-referential processes and accurate self-evaluation during autobiographical memory retrieval.

We additionally observed activation during retrieval of self-referential autobiographical memory content in other regions associated with speech related processing (see below).

Other-Referential

We observed activation for the other-referential category in the left temporoparietal junction. However, we hypothesized activation in the right temporoparietal junction. Further, we hypothesized activity in the medial prefrontal cortex, temporal poles, medial parietal cortex and superior temporal sulcus, but we did not observe activity in these regions.

The temporoparietal junction which was observed to activate when people retrieved autobiographical other-referential memory content has been associated with the ability to think about the thoughts of other people (Saxe & Wexler, 2005). Though we predicted activation of the right temporoparietal junction, we instead observed activation of the left temporoparietal junction. We predicted activation of the right temporoparietal junction as it has been shown to activate when participants try to understand another individual's mind (Saxe & Kanwisher, 2003), imagine mental states of another (Saxe & Wexler, 2005), or imagine others' experiences from strangers' photos (Rabin et al., 2010). However, studies have also observed similar patterns of activation in the left temporoparietal junction (Heatherton, 2011; Saxe & Kanwisher, 2003; Saxe & Powell, 2006). A study in which patients with temporoparietal lesions performed a false belief reasoning task, indicated that the left temporoparietal junction is necessary for understanding the beliefs of others (Samson, Apperly, Chiavarino, & Humphreys, 2004). Overall, though we predicted stronger activation in the right temporoparietal junction, we still observed activation of the left temporoparietal junction which we suggest is associated with thinking about the beliefs and mental states of others. Our results support the suggestion that during autobiographical memory retrieval of other-referential content, the temporoparietal junction is activating to support processing of the perspectives, thoughts, feelings, and mental states of other individuals.

We additionally observed activation during retrieval of other-referential autobiographical memory content in other regions associated with speech related processing (see below).

Speech-Related Processes

We had not previously hypothesized activation of the following brain regions which have been implicated in speech-related processes. However, we observed activation of the precentral gyrus, postcentral gyrus, planum temporale, heschl's gyrus, middle temporal gyrus, and supplementary motor area. Even though our experiment attempted to control for speech by contrasting against a baseline composed mainly of speech, there is more speech that occurs during each content category because each content category definitionally only includes words, whereas the baseline includes brief pauses.

Speech is one of the most complex mechanisms that is important for the human species (Behroozmand et al., 2015). Speech requires highly technical sensory-motor interactions for sound production which must be regulated, monitored, and controlled by auditory and semantic feedback information (Behroozmand et al., 2015). We observed activation in the precentral gyrus, postcentral gyrus, heschl’s gyrus, and supplementary motor area, which have been suggested to play a role in speech processes. A review of fMRI and PET studies observed activation of the precentral gyrus, postcentral gyrus, planum temporale, supplementary motor area, putamen, and supramarginal gyrus during auditory speech comprehension and speech production tasks (Price, 2012). Additionally, an fMRI study, in which participants produced a steady vowel sound or listened to a playback of themselves producing that vowel sound, suggested that the hechl’s gyrus, precentral gyrus, supplementary motor area, and postcentral gyrus play an important role in speech production and motor control (Behroozmand et al., 2015).

We also observed robust activation of the inferior temporal cortex which has been associated with auditory comprehension (Hickock & Poeppel, 2016), semantic word retrieval as well as letter fluency (Baldo, Schwartz, Wilkins, & Dronkers, 2006). The postcentral gyrus, associated with speech production (Gracco, Tremblay, & Pike, 2005), and the operculum cortex, associated with auditory analysis and speech articulation (Friederici, Ruschemeyer, Hahne, & Fiebach, 2003), were also observed to activate. Other regions that have also been observed to activate are the planum temporale which translates acoustic representations of speech into articulatory representations of speech was observed to activate (Hickock & Poeppel, 2016) and the supramarginal gyrus which processes phonological speech for both language and verbal working memory (Deschamps, Baum, & Gracco, 2014). Additionally, we observed activation in the putamen which has been associated with speech articulation, motor control, and bilingual language production and comprehension (Vinas-Guasch & Wu, 2017).

Taken together, we have reason to believe that the precentral gyrus, planum temporale, heschl's gyrus, supplementary motor area, inferior temporal cortex, postcentral gyrus, opercular cortex, putamen, and supramarginal gyrus are recruited for speech-related processes during autobiographical memory retrieval.

Future Directions

Understanding the causal role that the content specific regions play in the retrieval of memories is key to identifying the processes and regions supporting autobiographical memory retrieval. Our study is correlational and as a result our findings do not address the question of the role in causality that these content specific regions have in the retrieval of autobiographical memories. However, we suggest that the observed pattern of activation is consistent with the assertion that content specific cortex is being recruited to reconstruct memories and is supporting the subjective re-experience of these memories. Future research should address the causal roles of each of the brain regions identified herein during the retrieval of their corresponding categories of memory content.

Future research should also utilize longer retrieval periods which will lead to a larger number of content words and a more robust ability to investigate the neural underpinnings of memory content retrieval. Further, longer memories would allow for new content categories to be proposed and investigated. Possible categories to be investigated that were discarded due to insufficient events of interest include: positive and negative valence words, highly abstract words, and words corresponding to emotional subcategories.

Limitations

One limitation of this study is that it is a rough estimate of when the neural activity is peaking in a content specific region in relation to the utterance of the word. Our analysis does not help us understand whether the activation peak for a brain region is happening prior to the participant saying the word or immediately when they say the word. Unfortunately, this analysis is not able to ascertain the moment (seconds) that the peak of activity in each brain region is occurring. It could be occurring at any point prior to or during the utterance of the word, and that relationship between peak activation and utterance may be stable or variable.

Conclusion

In conclusion, this method of interrogating the content of memories as they are being retrieved has provided a rich opportunity to better understand what brain regions are supporting different aspects of memory retrieval. This paper addresses a gap in the literature involving understanding dynamic second to second activation of content specific cortex during autobiographical memory retrieval of content specific categories. This finding expands our understanding of how the brain supports the online retrieval of memories, and potentially sheds light on how memories are reconstructed from disparate content into a coherent experience.

Figures and Tables

Figure 1

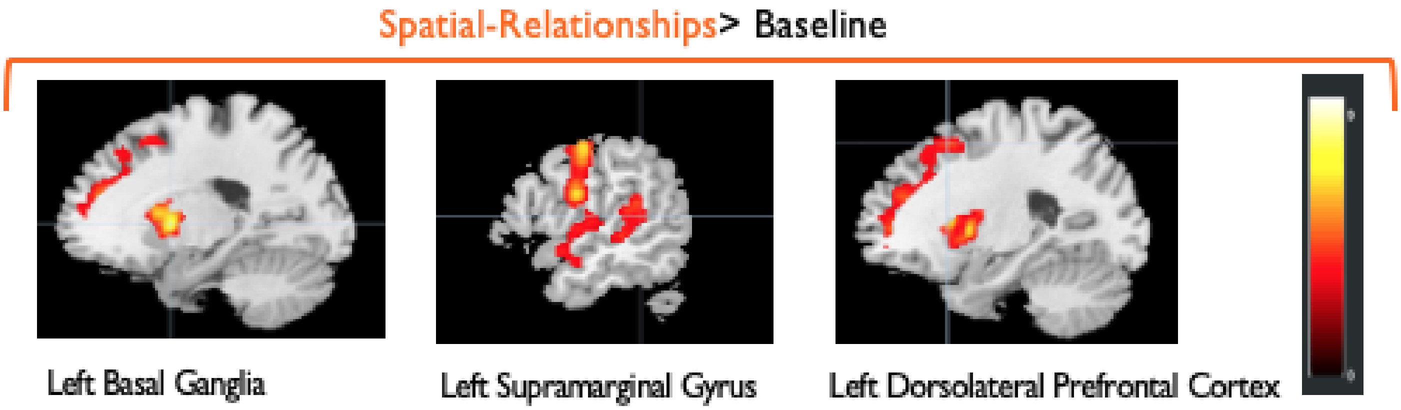
Example of word selection for all four of the content categories (spatial-relationship, temporal referential, self-referential, and other-referential).

Yesterday, **I** went to the beach and sat **on** my towel. **I** read a book as **I** waited for **Karla** to arrive and **Karla** and **I** spent an **hour** or so walking **around** the pier.

Spatial-Relationship
Temporal-Referential
Self-Referential
Other-Referential

Figure 2

Activation in the left basal ganglia, the left supramarginal gyrus, and the left dorsolateral prefrontal cortex for spatial-relationship content.



*All activation reported at $p < .05$ (FWE corrected).

Table 1

Coordinates of brain regions active for spatial-relationship content

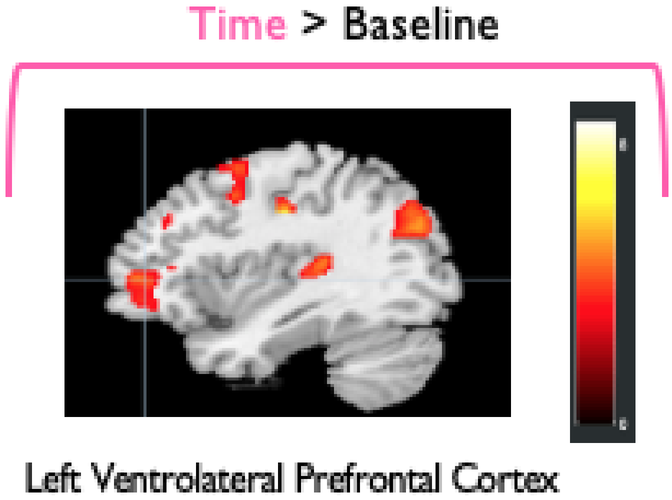
Region	Cluster-Extent	Peak t-value	X MNI	Y MNI	Z MNI
Precentral Gyrus	2189	9.5591	44	-12	36
Precentral Gyrus	2189	6.4397	56	-6	46
Superior Temporal Gyrus, anterior division	2189	6.3495	64	2	0
Superior Temporal Gyrus, anterior division	2189	6.178	66	-6	2
Precentral Gyrus	2189	5.8349	64	2	18
Superior Temporal Gyrus, posterior division	2189	5.729	68	-26	4
Central Opercular Cortex	2189	5.5492	64	-2	8
Superior Temporal Gyrus, posterior division	2189	5.2373	66	-18	6
Heschl's Gyrus (includes H1 and H2)	2189	5.0753	54	-16	6
Precentral Gyrus	2189	4.8163	62	-2	32
Heschl's Gyrus (includes H1 and H2)	2189	4.571	50	-20	10
Precentral Gyrus	4206	9.2589	-52	-8	50
Precentral Gyrus	4206	8.7465	-44	-14	36
Postcentral Gyrus	4206	6.866	-58	-6	22
Superior Temporal Gyrus, anterior division	4206	6.0337	-64	-12	2
Left Cerebral White Matter	4206	6.0189	-12	42	26
Left Cerebral White Matter	4206	5.9266	-14	44	20
Planum Temporale	4206	5.6819	-52	-40	18
Superior Temporal Gyrus, posterior division	4206	5.6494	-66	-24	2

Middle Frontal Gyrus	4206	5.5703	-38	2	60
Superior Temporal Gyrus, posterior division	4206	5.4847	-62	-30	2
Left Cerebral White Matter	4206	5.2033	-20	46	22
Heschl's Gyrus (includes H1 and H2)	4206	5.1862	-46	-24	8
Planum Temporale	4206	5.0732	-42	-30	10
Left Cerebral White Matter	4206	4.8605	-24	50	4
Middle Temporal Gyrus, posterior division	4206	4.5656	-64	-12	-10
Superior Frontal Gyrus	4206	4.4402	-24	16	54
Left Cerebral White Matter	4206	4.4335	-24	48	10
Left Cerebral White Matter	4206	4.1562	-28	50	-8
Left Cerebral White Matter	4206	4.1154	-20	38	28
Supramarginal Gyrus, posterior division	4206	3.9891	-56	-42	10
Left Putamen	693	8.3743	-20	4	4
Left Cerebral White Matter	693	6.7729	-18	8	10
Left Cerebral White Matter	693	6.4143	-22	14	8
Left Cerebral White Matter	693	4.9738	-28	14	-4
Left Cerebral White Matter	693	4.8733	-32	28	10
Insular Cortex	693	3.9544	-28	24	4
Lateral Occipital Cortex, superior division	334	6.186	-40	-76	30
Juxtapositional Lobule Cortex (Supplementary Motor Cortex)	649	5.8672	-2	8	66

All activation reported at p < .05 (FWE corrected). Peaks within the same cluster separated by a minimum of 10 mm. Regions labeled using the Harvard-Oxford Atlas.

Figure 3

Activation in the left insula, and the medial prefrontal cortex for time content.



* All activation reported at $p < .05$ (FWE corrected).

Table 2

Coordinates of brain regions active for time-referential content

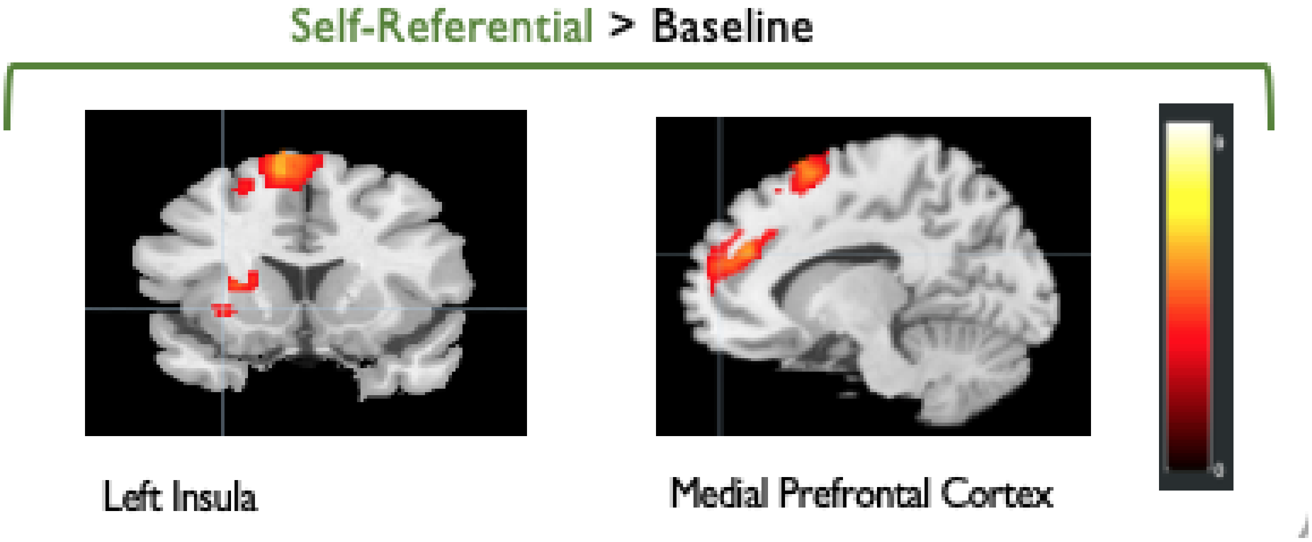
Region	Cluster-Extent	Peak t-value	X MNI	Y MNI	Z MNI
Precentral Gyrus	5684	8.6078	-44	-14	36
Left Cerebral White Matter	5684	7.6591	-26	48	4
Precentral Gyrus	5684	7.4605	-50	-8	28
Precentral Gyrus	5684	7.0111	-54	-10	48
Heschl's Gyrus (includes H1 and H2)	5684	6.8541	-46	-24	8
Left Cerebral White Matter	5684	6.6808	-26	46	12
Left Cerebral White Matter	5684	6.1036	-28	40	20
Planum Temporale	5684	5.8926	-64	-16	8
Superior Temporal Gyrus, posterior division	5684	5.766	-66	-28	8
Left Cerebral White Matter	5684	5.5274	-14	38	24
Superior Temporal Gyrus, posterior division	5684	5.4898	-66	-22	2
Superior Temporal Gyrus, anterior division	5684	5.3758	-62	-4	4
Planum Temporale	5684	5.3019	-48	-38	16
Left Cerebral White Matter	5684	5.2082	-26	52	-6
Left Cerebral White Matter	5684	5.0845	-14	44	20
Inferior Temporal Gyrus, posterior division	5684	4.6914	-52	-12	-36
Superior Temporal Gyrus, posterior division	5684	4.6909	-58	-30	0
Left Cerebral White Matter	5684	4.6661	-18	48	24
Left Cerebral White Matter	5684	4.6521	-18	44	28
Planum Temporale	5684	4.6373	-54	-34	14
Precentral Gyrus	2732	8.3704	46	-10	36
Precentral Gyrus	2732	6.3361	54	-6	28
Planum Temporale	2732	5.9505	66	-16	8
Superior Temporal Gyrus, posterior division	2732	5.8314	68	-28	4
Superior Temporal Gyrus, posterior division	2732	5.6469	68	-20	0

Heschl's Gyrus (includes H1 and H2)	2732	5.4619	52	-18	6
Superior Temporal Gyrus, anterior division	2732	5.4114	64	2	0
Superior Temporal Gyrus, posterior division	2732	5.307	58	-26	0
Precentral Gyrus	2732	5.243	64	-2	10
Precentral Gyrus	2732	5.2182	20	-26	62
Precentral Gyrus	2732	4.7697	64	2	16
Precentral Gyrus	2732	4.3629	24	-14	60
Postcentral Gyrus	2732	4.1561	28	-32	60
Superior Parietal Lobule	2732	3.8611	22	-46	64
Precentral Gyrus	2732	3.4596	38	-18	48
Right Cerebral White Matter	2732	3.2761	16	-10	64
Postcentral Gyrus	2732	3.1359	30	-32	70
Right Cerebral White Matter	2732	3.0345	18	-6	58
Juxtapositional Lobule Cortex (Supplementary Motor Cortex)	701	5.9031	-2	4	64
Superior Frontal Gyrus	701	5.1056	-8	12	72
Lateral Occipital Cortex, superior division	938	5.5914	-40	-74	30
Left Cerebral White Matter	938	5.5353	-18	-80	24
Intracalcarine Cortex	938	4.092	-10	-78	14
Lateral Occipital Cortex, superior division	938	3.8355	-22	-82	44

All activation reported at p < .05 (FWE corrected). Peaks within the same cluster separated by a minimum of 10 mm. Regions labeled using the Harvard-Oxford Atlas.

Figure 4

Activation in the left insula, and the medial prefrontal cortex for self-referential content.



* All activation reported at p < .05 (FWE corrected).

Table 3

Coordinates of brain regions active for self-referential content

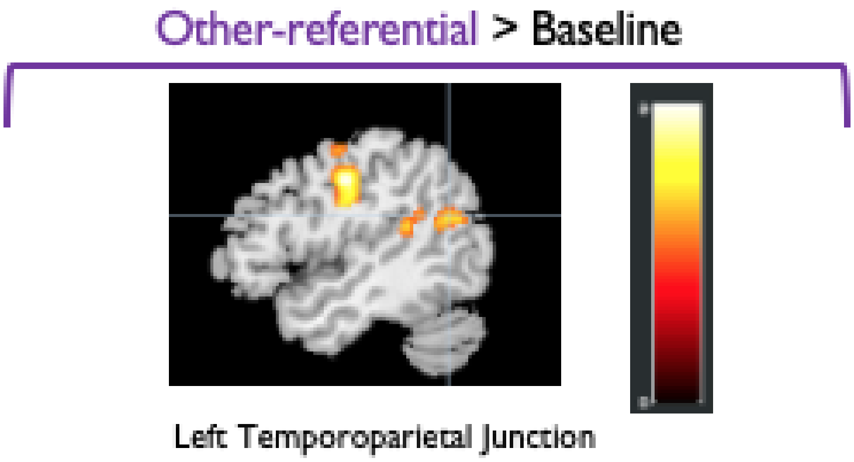
Region	Cluster-Extent	Peak t-value	X MNI	Y MNI	Z MNI
Precentral Gyrus	2475	9.4986	46	-10	36
Precentral Gyrus	2475	7.8543	54	-6	28
Heschl's Gyrus (includes H1 and H2)	2475	6.4419	52	-16	6
Superior Temporal Gyrus, anterior division	2475	5.7228	64	-2	2
Superior Temporal Gyrus, posterior division	2475	5.7057	68	-26	2
Superior Temporal Gyrus, posterior division	2475	5.3756	58	-24	0
Planum Temporale	2475	4.5587	66	-18	8
Superior Temporal Gyrus, posterior division	2475	4.0098	48	-30	0
Precentral Gyrus	2475	3.7467	44	-16	64
Precentral Gyrus	3340	8.9698	-46	-12	34
Precentral Gyrus	3340	8.2432	-50	-8	28
Precentral Gyrus	3340	7.8716	-60	-6	20
Precentral Gyrus	3340	7.325	-52	-8	50
Planum Temporale	3340	6.4478	-64	-12	4
Planum Temporale	3340	6.012	-50	-38	16
Superior Temporal Gyrus, posterior division	3340	5.5745	-66	-26	6
Heschl's Gyrus (includes H1 and H2)	3340	5.4277	-46	-24	10
Planum Temporale	3340	5.4155	-40	-32	12
Middle Temporal Gyrus, anterior division	3340	4.9193	-56	-8	-18
Superior Temporal Gyrus, anterior division	3340	4.2428	-58	-2	-10
Inferior Temporal Gyrus, anterior division	3340	4.2121	-52	-10	-34
Planum Polare	3340	4.1549	-52	-4	0
Middle Frontal Gyrus	3340	3.8855	-38	4	60
Middle Temporal Gyrus, posterior division	3340	3.8329	-56	-10	-28
Middle Temporal Gyrus, posterior division	3340	3.5461	-54	-26	-6

Superior Temporal Gyrus, posterior division	3340	3.3144	-54	-38	6
Left Cerebral White Matter	1687	7.5279	-26	48	4
Left Cerebral White Matter	1687	6.7089	-26	44	16
Left Cerebral White Matter	1687	6.6815	-22	48	16
Left Cerebral White Matter	1687	6.3057	-18	54	16
Left Cerebral White Matter	1687	6.0589	-24	52	-6
Left Cerebral White Matter	1687	5.6764	-18	44	28
Left Cerebral White Matter	1687	5.6286	-12	40	28
Left Cerebral White Matter	1687	5.059	-14	46	18
Frontal Orbital Cortex	1687	4.6699	-40	34	-14
Superior Frontal Gyrus	1687	4.0162	-24	28	44
Left Cerebral White Matter	1687	3.8653	-12	32	34
Superior Frontal Gyrus	1687	3.7892	-22	14	56
Left Cerebral White Matter	1687	3.658	-36	32	14
Frontal Pole	1687	3.5027	-38	40	-10
Superior Frontal Gyrus	1687	3.1896	-26	20	48
Left Cerebral White Matter	1687	3.1555	-12	58	8
Left Putamen	456	6.4091	-22	4	4
Left Cerebral White Matter	456	5.0835	-32	28	10
Left Cerebral White Matter	456	4.7055	-26	16	8
Left Cerebral White Matter	456	4.096	-30	14	-4
Left Cerebral White Matter	456	4.0432	-30	20	14
Left Cerebral White Matter	456	3.2848	-26	4	8
Superior Frontal Gyrus	729	6.3136	-10	12	64
Supplementary Motor Cortex	729	6.1226	-2	4	64
Superior Frontal Gyrus	729	6.0724	-8	16	70
Superior Frontal Gyrus	729	3.092	-12	28	56

All activation reported at $p < .05$ (FWE corrected). Peaks within the same cluster separated by a minimum of 10mm. Regions labeled using the Harvard-Oxford Atlas.

Figure 5

Activation in the left temporoparietal junction for other-referential content.



**All activation reported at p < .05 (FWE corrected).*

Table 4

Coordinates of brain regions active for other-referential content

Region	Cluster-Extent	Peak t-value	X MNI	Y MNI	Z MNI
Precentral Gyrus	657	6.087	-48	-10	40
Postcentral Gyrus	657	4.6489	-62	-6	18
Postcentral Gyrus	657	4.4374	-56	-8	22
Precentral Gyrus	559	5.3536	50	-8	42
Precentral Gyrus	559	5.2334	46	-10	38
Precentral Gyrus	559	5.1716	56	-6	46
Precentral Gyrus	559	4.4989	56	-4	26
Precentral Gyrus	559	4.3684	52	-6	32
Precentral Gyrus	559	4.1817	62	0	24
Precentral Gyrus	559	3.4399	64	4	16
Precentral Gyrus	559	3.3975	64	0	12
Angular Gyrus	342	5.0398	-42	-56	22
Angular Gyrus	342	4.3015	-48	-60	22
Planum Temporale	342	4.0435	-48	-40	18
Left Cerebral White Matter	342	3.6194	-46	-46	24
Supramarginal Gyrus, posterior division	342	3.5357	-52	-48	22
Superior Temporal Gyrus, anterior division	306	4.8363	-64	-10	2
Superior Temporal Gyrus, posterior division	306	4.2972	-66	-26	4

All activation reported at p < .05 (FWE corrected). Peaks within the same cluster separated by a minimum of 10mm. Regions labeled using the Harvard-Oxford Atlas.

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