The Neural Basis of Involuntary Episodic Memories

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Dissertation submitted in partial fulfillment of
the requirements for the degree of Doctor
of Philosophy in the Department of
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ABSTRACT

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Abstract

Involuntary episodic memories are memories that come into consciousness without preceding retrieval effort. These memories are commonplace and are relevant to multiple mental disorders. However, they are vastly understudied. We use a novel paradigm to elicit involuntary memories in the laboratory so that we can study their neural basis. In session one, an encoding session, sounds are presented with picture pairs or alone. In session two, in the scanner, sounds-picture pairs and unpaired sounds are reencoded. Immediately following, participants are split into two groups: a voluntary and an involuntary group. Both groups perform a sound localization task in which they hear the sounds and indicate the side from which they are coming. The voluntary group additionally tries to remember the pictures that were paired with the sounds. Looking at neural activity, we find a main effect of condition (paired vs. unpaired sounds) showing similar activity in both groups for voluntary and involuntary memories in regions typically associated with retrieval. There is also a main effect of group (voluntary vs. involuntary) in the dorsolateral prefrontal cortex, a region typically associated with cognitive control. Turning to connectivity similarities and differences between groups, again there is a main effect of condition showing that paired > unpaired sounds are associated with a recollection network. In addition, three group differences are found: (1) increased connectivity between the pulvinar nucleus of the thalamus and the recollection network for the voluntary group, (2) a higher association between the voluntary group and a network that includes regions typically found in frontoparietal and cingulo-

opercular networks, and (3) shorter path length for about half of the nodes in these networks for the voluntary group. Finally, we use the same paradigm to compare involuntary memories in people with posttraumatic stress disorder (PTSD) to trauma-controls. This study also includes the addition of emotional pictures. There are two main findings. (1) A similar pattern of activity is found for paired > unpaired sounds for both groups but this activity is delayed in the PTSD group. (2) A similar pattern of activity is found for high > low emotion stimuli but it occurs early in the PTSD group compared to the control group. Our results suggest that involuntary and voluntary memories share the same neural representation but that voluntary memories are associated with additional cognitive control processes. They also suggest that disorders associated with cognitive deficits, like PTSD, can affect the processing of involuntary memories.

Dedication

To my loves, my distractors, and my daemons.

Contents

List of Tables

List of Figures

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I would like to acknowledge the people who made this dissertation possible. My advisor, David Rubin, has given invaluable guidance on everything from writing to backyard bird watching. My committee members, Alison Adcock, Roberto Cabeza, and Tobias Egner have each provided a unique lens through which to view my work. Dorthe Berntsen's work has paved the way for this research and has given kind and expert feedback. Kaitlyn Brodar, Amanda Miles, Banafsheh 'Bean' Sharif-Askary, Minkyung 'Clair' Hong, Katherine Zhu are the colleagues who not only made data collection possible but provided indispensable intellectual input to this body of work. And finally, my co-authors, Simon Davis, Erik Wing, Phillip Kragel, and Dawei Li each brought knowledge from diverse backgrounds and generously gave their time to make this work better.

1. Introduction

Involuntary episodic memories are memories that come to mind spontaneously, without any effort to retrieve the whole or detailed components of their trace (Berntsen, 1996). Though involuntary memories are often considered in relation to flashbacks in post-traumatic stress disorder (PTSD, Halligan, Clark, & Ehlers, 2002; van der Kolk & Fisler, 1995), they can also be, and usually are, memories of mundane, everyday life experiences. For example:

> "I was running in the Botanical Garden, while thinking of something I had just read for my psychology class. It was a beautiful spring day with singing of birds, and not many other people out. I ran per routine-and suddenly got a side stitch (which is unusual for me). I then suddenly remembered a day in Hungary, where I was running with my friend from England. I got a severe side stitch, and, through his years in the military, he had learnt some breathing techniques against side stitches, which he then taught me." (Berntsen, Staugaard, & Sorensen, 2012, p. 426)

Not only does this example illustrate the everyday experience of involuntary memories, it also demonstrates a number of features common to many involuntary memories: the resurgence of complex and unique sensorial details, the rich autobiographical content and close relationship to an emotional experience, and the unexpected—though perhaps cued—nature of their retrieval.

These everyday involuntary memories occur often; they have been shown to occur at least as often if not more often than their voluntary counterparts (A. S. Rasmussen, Ramsgaard, S. B., Berntsen, D., 2015) and to our knowledge, they are universal in people who have a functioning memory system (Berntsen, 2010a). Given that much of our time is spent in undirected thought—during the drive to work, doing

mindless tasks at work, going to the bathroom, cooking, cleaning—there are many chances for involuntary thoughts and memories to occur. Even during conversation, ideas and memories occur spontaneously in response to something another person says. Conversational or linguistically based cues have been shown to elicit from 6% to 31% of involuntary memories, with other cues including activities, people, objects, or life/general themes (Berntsen, 1996; Mace, 2004). There is a large variety of everyday situations that can bring about involuntary memories, making them a large part of our memorial lives.

Involuntary memories also serve an important function (Berntsen, 2009). Related to our sense of self, they can help provide a sense of temporal self-continuity. They can also help to update goals and behaviors because these are memories that may not be directly related to current goals but rather, may be related to the general life situation. They can also serve a directive function, which helps guide problem-solving and planning (A. S. Rasmussen, Berntsen, D., 2009). Their usefulness with such functions is enhanced over that of voluntary memories due to the rapid access to specific events. This is useful in emergency situations that require fast retrieval of information that could be life-saving, like remembering to 'duck and cover' during an earthquake, or remembering where to hide when running from a predator.

A general understanding of involuntary memories also has implications for mental disorders: high levels of distress surrounding involuntary memory make these memories an important symptom of several mental disorders including posttraumatic stress disorder (PTSD), depression, and anxiety disorders (American Psychiatric Association, 2013; Brewin, Gregory, Lipton, & Burgess, 2010). Almost 90% of people with PTSD have

intrusive memories (Roszell, Mcfall, & Malas, 1991), demonstrating the great need to understand the mechanisms driving these memories and to understand how they become so disrupted.

Despite their importance and their frequency, and despite having been classified as a distinct type of memory over 100 years ago (Ebbinghaus, 1885/1964) involuntary memories have been shockingly understudied. The neuroimaging studies that will be presented in the following chapters represent 3 of only 5 neuroimaging studies to be done on explicit involuntary memories to our knowledge. They are the only to use a paradigm in which the occurrence of involuntary memories is not measured until after the neuroimaging scan. This eliminates thought monitoring processes that could be similar to other cognitive control processes that occur during voluntary remembering and allows for a more pure investigation of involuntary memory processes. Though there is a larger literature of behavioral work done on involuntary memories, the field is still in its infancy. A PubMed search reveals about 100 total studies done on involuntary memories out of the 20,000 found for episodic memory generally. The reasons for this scarcity of work on this topic are likely varied, and may include a lack of interest in the topic or not having a paradigm to reliably elicit these memories. "Few things that we perceive make us think of previous happenings in our own lives…many stimuli that could potentially serve as reminders or cues, even if prominently displayed to person, will have no such effect" (Tulving, 1983, p. 169). Even though eliciting them may be a challenge, we must not ignore these memories in the lab simply because they are hard to study.

It is important to note, that by our definition, involuntary memories occur to the knowledge of the rememberer, making them explicit memories (Berntsen, 1998). In the paradigm used here, described in chapter 2, participants write descriptions of their memories after they are retrieved so we know that they are explicit. It follows that voluntary memories are memories that occur with both effort and awareness, involuntary memories are memories that occur without effort but with awareness, and implicit memories occur with neither effort nor awareness. This is not to say that implicit memory processes have no impact on involuntary memories but we have no reason at present to believe that the interaction between implicit memories and involuntary memories would differ from that with voluntary memories. This would be an interesting line of future research.

1.1 Dual- versus Single-System Models

There are two models that address the relationship between voluntary and involuntary memory: a dual-system model in which the encoding and storage mechanisms differ between the two types of memories, and a single-system model in which voluntary and involuntary memories share the same encoding and storage mechanisms and differ in how they are retrieved. The dual-system model is adhered to primarily by clinicians who, in speaking to patients, noticed that the descriptions of trauma memories seemed different than other memories (McNally, 2003). It was also noted that people with PTSD had general memory deficits and over time, the interpretation of this general difficulty remembering grew more specific and became interpreted as a difficulty remembering the trauma. This led clinicians to conclude that

involuntary trauma memories must be encoded and stored in a separate memory system from other memories. Supporting this idea was evidence showing that when people with PTSD were asked to compare trauma flashbacks with other episodic memories they reported that environmental triggers did not bring non-trauma memories to mind spontaneously, that spontaneously remembered trauma memories had higher degrees of re-experiencing than voluntarily remembered non-trauma memories, and that they were fragmented, lacking in contextual details (Ehlers, Hackmann, & Michael, 2004; van der Kolk & Fisler, 1995).

Further work has revealed that these differences between voluntary and involuntary memories do not endure. Unlike the clinical observations, studies carefully designed to test the similarities and differences between involuntary and voluntary memories have shown that non-trauma memories can, and often are, recalled involuntarily (Brewin et al., 2010; A. S. Rasmussen, Ramsgaard, S. B., Berntsen, D., 2015), trauma memories are recalled voluntarily (D. C. Rubin, Boals, & Berntsen, 2008), and involuntary and voluntary trauma memories have no difference in the degree to which they are fragmented (D. C. Rubin et al., 2008). There is a greater sense of reliving for involuntary memories but this seems to be related to the fact that involuntary memories are more often of specific events rather than of general events that are more central to the life story (Berntsen & Hall, 2004; D. C. Rubin et al., 2008). Indeed, when memory specificity is controlled, there is no difference in reliving between the two types of memories (D. C. Rubin et al., 2008).

Further, if voluntary and involuntary memories are indeed part of two different memory systems, the factors that affect voluntary memory qualities would differ from those that affect involuntary memory qualities. This is not the case. Voluntary and involuntary memories have the same forgetting curve across the lifespan (Berntsen, 1998; David C. Rubin & Berntsen, 2009), they are both more often positive than negative, they are rehearsed with similar frequencies, and they are both predicted by the same memory characteristics, like emotional intensity and relevance to life story (David C. Rubin & Berntsen, 2009). There are differences between them but they can be explained by differences in the way they are retrieved. Involuntary memories occur more quickly after a cue than voluntary memories (Schlagman & Kvavilashvili, 2008) because they are directly retrieved rather than being mediated by a search process. Therefore, they are often accompanied by greater emotional impact (D. C. Rubin et al., 2008) as the rememberer does not have time to prepare for the accompanying emotion. While highly emotional involuntary memories, like flashbacks, may feel different than most memories, the single-system model posits that this is not because they are part of a different memory system but rather because differences in retrieval lead to differences in the experience of the memories.

The neural data presented here can provide support for one of these models. If the single-system model is correct and encoding and maintenance systems are the same for both memories, the neural representation in regions typically associated with memory retrieval should be the same. The only difference between voluntary and involuntary memories should be seen in regions typically associated with controlled retrieval. On the

contrary, if the dual-system model is correct and encoding and storage is different between the two types of memories, the set of regions typically involved in memory retrieval would show differences in activity.

1.2 Theoretical Relevance

Not only is the study of involuntary memories important because of the role they play in our everyday lives and their relevance to mental disorders but understanding them can also lead to a deeper understanding of other cognitive processes. Within the already thin field of involuntary memory research, many involuntary memory researchers study involuntary memories compared to other autobiographical memories rather than compared to laboratory-based voluntary episodic memories. This approach has a strong justification: since involuntary memories make up a large part of our autonoetic lives, autobiographical memory research is often charged with the task of explaining how and why these common cognitive events come about. Involuntary memories therefore represent an important and understudied branch of our knowledge of basic memory processes. But what impact would a more thorough understanding of involuntary memory have on other domains of memory research more generally? Consider the following research questions:

- How do recognition and familiarity processes differ?
- How does cognitive control impact memory performance?

Involuntary memory research can contribute to both of these complex research questions. Below, I discuss both research questions in turn.

1.2.1 Recollection versus Familiarity

According to dual-process models of recognition memory, recollection, or source memory, is a memory of the scene in which an item was encoded, whereas familiarity, or item memory, is a memory of an item without a memory of the context in which it was encoded. Familiarity is accompanied by a feeling of knowing that the stimuli has been previously encoded without an accompanying memory of the complete episode. The differences between recollection and familiarity are reflected in differences in neural activity. Proponents of the dual-process model generally propose that recollection is associated with hippocampal activity and familiarity is associated with perirhinal cortex activity (R. A. Diana, Yonelinas, & Ranganath, 2010; Yonelinas, 2002; though see Mandler, 2008). As they relate to voluntary and involuntary memory, recollection has been associated with controlled retrieval as more effort is used to recall contextual details, while familiarity has been associated with automatic retrieval (Buckner & Wheeler, 2001). Studies on recognition memory in aging and Alzheimer's disease, in which control processes are diminished, have supported this initial view as they have shown deficits in recollection but not familiarity (Yonelinas, 2002). However, if the difference between recollection and familiarity is consistent with dual-process models, with the type of information that is remembered driving the difference between recollection and familiarity, both could be remembered voluntarily or involuntarily. Deeper investigations into the relationship between aging and recollection/familiarity processes, as well as the relationship between these processes and the frontal lobes have shown that these relationships are not clear cut. Aging is sometimes, but not always

related to deficits in both processes and there is sometimes but not always a relationship between both processes and the frontal lobes (Prull, Dawes, Martin, Rosenberg, & Light, 2006; Yonelinas, 2002). One possible explanation for this diversity of results is that retrieval effort varies based on task demands and due to individual differences. If effort were controlled, some of the variation may disappear. To our knowledge, an involuntary memory study designed to explicitly probe the dynamics of recollection and familiarity has not yet been performed but the methods described here could be used in such future work.

1.2.2 Cognitive Control and Memory

In regards to the relationship between cognitive control and memory, it is useful to observe that involuntary memory paradigms are typically focused on eliminating both retrieval demands and retrieval orientation from the retrieval process. This experimental manipulation can help us separate the effects of cognitive control from before and after retrieval. In our research, reported below, we will show neural differences associated with voluntary memory, but not with involuntary memory, that are commonly correlated with cognitive control processes. However, there are many other cognitive control processes that could be involved in memory: top-down attention, decision-making, memory manipulation, and thought suppression are a few examples. Since involuntary memories occur without pre-retrieval effort, they serve as a natural way of controlling one or more of these processes in order to better hone in on ecphoric processes and extra-ecphoric processing like post-retrieval control processes.

These examples represent only two of the ways in which the study of involuntary memories could have a direct impact on the work of many basic science memory researchers. Others could include post-retrieval decision-making, reward-based modulations of involuntary retrieval, the influences of implicit memory on involuntary remembering, and many others.

1.3 Emotional Involuntary Memories in Posttraumatic Stress Disorder

Understanding involuntary memories has clear implications for mental disorders associated with high emotional reactions to these memories. PTSD is a disorder characterized by a highly distressing event followed by symptoms like flashbacks, avoidance of trauma-related stimuli, negative alterations in cognitions and mood, and alterations in arousal and reactivity (American Psychiatric Association, 2013). To understand how extreme emotion can affect involuntary memories in PTSD we must first understand the relationship between emotions and involuntary memory.

It has been established that involuntary memories are generally more emotional than voluntary memories (Staugaard & Berntsen, 2014). It is therefore not surprising that there is an intense emotional response (both physiologically and cognitively) when people have involuntary memories related to emotional events. However, behavioral similarities between emotionally voluntary and involuntary memories suggest that high emotion involuntary memories do not differ from high emotion voluntary memories. Positive memories are more frequent than negative or neutral memories for both types of memory, the frequency distribution of emotional intensity is the same (Berntsen, 2010b),

and higher emotion during encoding predicts later recall for both voluntary and involuntary memories (N. M. Hall & Berntsen, 2008). Further, there is also evidence to support the idea that the subjective qualities of high emotion voluntary and involuntary memories are similar. Higher emotion during retrieval of involuntary memories compared to voluntary memories does not change the cohesiveness of the memory, with trauma memories being no more fragmented than any other memory (D. C. Rubin et al., 2008; Talarico & Rubin, 2003).

In fact, comparing high emotion involuntary memories between people with PTSD and controls, trauma memories in people with PTSD remain more intact than memories of trauma in people without PTSD when they are recounted during a long-form free recall (Dekel & Bonanno, 2013), a process that likely includes some involuntary memory retrieval (Mace, 2006). Involuntary trauma memories in people with PTSD compared to controls have the same number of details and the same vividness (Megias, Ryan, Vaquero, & Frese, 2007). This suggests that high emotion involuntary memories share many characteristics with high emotion voluntary memories, in general and in PTSD, high emotion involuntary memories are similar to high emotion involuntary memories in people without PTSD.

There are some important differences between involuntary memories in people with and without PTSD. People with PTSD have a stronger reaction to their memories, have a greater mood change, and the memories are more central to their life story (D. C. Rubin et al., 2008). People with PTSD also have less control over their trauma memories (Megias et al., 2007). They experience these memories as a rapid succession of images,

they experience them as if the trauma were happening again, they have difficulty putting the memory into words, and they are often seen from an observer perspective rather than from the perspective of the self (Berntsen, Willert, & Rubin, 2003). The difficulty that people with PTSD have controlling their memories and controlling their reactions to them is consistent with the idea that people with PTSD have lower levels of cognitive control, like interference control (Kertzman, Avital, Weizman, & Segal, 2014). This can mean that involuntary memories can feel highly invasive due to deficits in post-retrieval processing.

1.4 General Predictions

In the following chapters, I will present three novel functional magnetic resonance imaging (fMRI) studies of involuntary memory using both neutral and emotional stimuli in people with and without PTSD. The findings above have led to three general observations on the basic qualities of involuntary memories: 1) voluntary and involuntary memories are encoded and stored in the same basic memory system, 2) voluntary and involuntary memories differ in the reliance upon controlled retrieval processes and 3) involuntary memories are more emotional in people with PTSD compared to people without PTSD and are accompanied by lower levels of cognitive control, but remain intact. In order to further elucidate the behavioral and neural mechanisms underlying involuntary memories, I therefore propose the following hypotheses:

1. If voluntary and involuntary memories are part of the same memory system, they will overlap in brain regions associated with memory retrieval.

2. Voluntary memories, but not involuntary memories, will elicit activity in and connectivity between regions associated with strategic retrieval
3. Involuntary memories in people with PTSD and controls will elicit similar activity in regions associated with memory retrieval.
4. There will be differences in involuntary memories in PTSD in regions associated with emotion, and differences due to deficiencies in cognitive control processes. Though this will not affect controlled retrieval (as there is none in involuntary remembering), it could affect attention orientation such that a cue will longer to elicit a memory in people with PTSD than controls.

The studies presented in chapters 2 and 3 will address the first two hypotheses and the study presented in chapter 4 will address the second two hypotheses.

We use behavioral information about how involuntary memories are naturally cued to bring them into the lab. Involuntary memories are most frequently brought to mind via external, environment cues, like activities, objects, people, or places, but can also be brought to mind via an internal cue, like a sensory experience or a feeling (Berntsen, 1996). Evidence suggests that the key to evoking an involuntary memories is by pairing a highly discriminable, or unique cue with a unique stimulus (Berntsen, Staugaard, & Sorensen, 2013). For example, after hearing many bird sounds, the sound of a car backfiring would be a unique cue. A unique stimulus might be seeing a car presented in the middle of many trees. If the sound of the car backfiring is presented simultaneously with the image of a car, then later hearing the sound of a car backfiring would likely elicit a memory of the car. These sensory cues, though they do not place an

explicit retrieval demand on the subject, have been shown to reliably induce involuntary memories (Berntsen et al., 2012). We will use this finding to induce involuntary memories in the studies presented below.

2. Neural Activity Associated with Involuntary versus Voluntary Memory Retrieval

The work presented in the following chapter has been previously published (S. A. Hall et al., 2014).

2.1 Introduction

The goal of this chapter is to investigate the neural correlates of involuntary memory, a basic form of memory retrieval, which in its maladaptive forms is related to a variety of clinical syndromes. The most efficient way to accomplish this goal is to compare involuntary memories to the more thoroughly studied voluntary memories, thereby making use of and situating our findings in the general memory literature.

Although laboratory investigations of the neural basis of involuntary memories have been limited, recent advances in neuroimaging allow for the possibility of assessing the neural processes supporting involuntary memories, independent of any overt response demands. Here, we present a neuroimaging study specifically designed to aid in understanding the neural basis of involuntary episodic memories. In our view, three types of measurements are needed. The first is simultaneous event-related functional imaging data to examine the neural basis of this behavior, which may indicate that mnemonic details were retrieved, despite the lack of an overt response. The second is a post-scan behavioral measure to confirm that an accurate involuntary memory was recalled. The third is a post-scan report that voluntary effort did not occur or was minimal. By its nature, this report must be a private phenomenological report, but one that should be confirmed by observable phenomena. Studies in which participants report involuntary

memories as they occur have been successful in producing replicable and theoretically informative results. However, reporting on involuntary memories as they occur necessarily involves a voluntary search after the involuntary memory comes to mind to judge whether the involuntary memory is accurate and should be reported. This makes it difficult to dissociate neural activity due to involuntary memory retrieval from neural activity due to voluntary postretrieval processes.

In addition, if involuntary memories are to be compared with voluntary memories, the study should be a between-subjects design. If participants were instructed to do both voluntary and involuntary retrieval, it is unclear whether participants would be able to switch strategies across trials and refrain from using voluntary retrieval strategies during involuntary memory trials. Again, this has the potential to confound neural activity due to involuntary retrieval with neural activity due to voluntary retrieval strategies. Thus, we intend not only to report theoretically interesting results but also to propose a basic design that can be modified to study the neural basis of many aspects of involuntary memories in healthy and clinical populations while avoiding the most obvious experimental confounds.

We predict that the primary neural difference between voluntary and involuntary memories will be in the prefrontal cortex (PFC). Although episodic memory researchers originally interpreted PFC contributions in terms of processes specific to episodic memory, it is now generally accepted that the processes contributed by PFC to episodic retrieval are control processes shared with other cognitive tasks, such as working memory (Roberto Cabeza, Dolcos, Graham, & Nyberg, 2002) and decision-making (Fleck,

Daselaar, Dobbins, & Cabeza, 2006).

Whereas the left PFC has long been associated with both verbal working memory operations (D'Esposito, Postle, & Rypma, 2000) and controlled semantic retrieval (Thompson-Schill, D'Esposito, Aguirre, & Farah, 1997), there are regions in the lateral PFC that are associated with controlling strategic retrieval operations in episodic retrieval (Buckner & Wheeler, 2001; K. J. Mitchell & Johnson, 2009). For example, compared with item recognition tasks, source memory tasks elicit greater activity in left dorsolateral PFC (DLPFC; Dobbins, 2005; Dobbins & Han, 2006). Importantly, in contrast to neighboring ventrolateral PFC (VLPFC, O'Connor, Han, & Dobbins, 2010; Kaia L. Vilberg & Rugg, 2008), studies that report left DLPFC activity for contextual retrieval find that activations in this region do not differ for successful and unsuccessful retrieval trials (Dobbins, 2001; Dobbins, Rice, Wagner, & Schacter, 2003; Meltzer & Constable, 2005), suggesting that DLPFC is associated with strategic retrieval, not with retrieval success. Conversely, a constellation of more posterior and ventral cortical regions, including the medial temporal lobe (MTL), the posterior midline cortex (retrosplenial cortex, posterior cingulate), ventral parietal cortex (VPC), and sensory reactivation areas, is reliably more active for successful than unsuccessful retrieval independent of how a particular memory trace is activated (Habib & Nyberg, 2007). These regions likely form the neural correlates for involuntary as well as voluntary memory retrieval, with voluntary memories activating additional regions associated with strategic retrieval.

Only two functional imaging studies have examined involuntary memories in this context. The first study paired a picture with a word describing the main contents of the

picture during encoding (N. Hall, Gjedde, & Kupers, 2008). During recall, participants saw the words and made a judgment about whether the item could be worn. The blocks alternated between involuntary retrieval, in which participants were not told to try to recall the picture that had been paired with the word, and voluntary retrieval, in which they were told to recall the picture. Among other findings, the results showed that both voluntary and involuntary memories activated PFC regions. One limitation of this study is the use of a within-subjects design with alternative involuntary and voluntary blocks. PFC activations during involuntary memory could reflect a contamination by voluntary retrieval strategies as discussed above.

In the other study of involuntary memory, a combined event-related fMRI and EEG study by Kompus, Eichele, Hugdahl, and Nyberg (2011), participants were presented with sounds and pictures of objects during encoding. In the voluntary memory condition, participants were shown a word and were asked to try to recall whether the word described an object presented during encoding and whether the word was concrete or abstract. During the involuntary memory condition, participants were asked to decide whether the word was concrete or abstract. They also were asked, however, to press a button if they had a spontaneous memory of the object when they saw the word. Imaging results in this study suggested that voluntary memories rely on DLPFC to a greater extent than involuntary memories. In contrast, successful memories in both conditions showed a general overlap in neural recruitment. Although this study provides strong event-related evidence that involuntary and voluntary memories share a distinct, but overlapping, neural signature, it also has the limitation of a within-subject design. Moreover, because

participants had to press a key when they had an involuntary memory, having episodic memories became in practice a secondary goal of the task. Because there was a dedicated response for having associated memories, it is likely that participants checked the accuracy of these memories before responding, thereby introducing a voluntary memory component in the task. Thus, the differences in activity found could be explained in quantitative terms by greater strategic retrieval in the voluntary condition rather than in qualitative terms.

In the current study, we sought to address the issues in the previous studies by having a between-subjects design in which participants in the involuntary group were not told that they were in a memory experiment, and there was no online reporting of involuntary memories so there was no expectation that they may have felt compelled to fulfill. We adapted to fMRI a behavioral paradigm that successfully elicits involuntary memories (Berntsen et al., 2013). During an encoding session (see Figure 1), participants heard a series of environmental sounds (e.g., doorbell ringing). Half of the sounds were presented alone (unpaired sounds), whereas the other half were paired with pictures of complex scenes (paired sounds), which participants tried to associate with the sounds. During both voluntary and involuntary retrieval in the fMRI scanner, paired and unpaired sounds were presented, panned to either the left or right. Participants in the involuntary condition were asked to decide from which side the sound originated, whereas participants in the voluntary condition did the same task and were also asked to recall the corresponding picture from encoding if there had been one. After the scan, participants heard all of the sounds and identified those for which they experienced a memory in the

scanner and tried to describe the associated picture in detail, allowing us to analyze only the trials in which a memory was recalled.

We made two predictions. First, we predicted that brain regions associated with successful retrieval would be similar for voluntary and involuntary memories. Specifically, in both the voluntary and involuntary conditions, we expected that paired sounds compared with unpaired sounds would elicit greater activity in a network of regions associated with successful memory retrieval, including the MTL, retrosplenial cortex, and posterior cingulate (K. J. Mitchell & Johnson, 2009), VPC (R. Cabeza, Ciaramelli, Olson, & Moscovitch, 2008; Ciaramelli, Grady, & Moscovitch, 2008; Kaia L. Vilberg & Rugg, 2008; Wagner, Shannon, Kahn, & Buckner, 2005), and sensory reactivation areas (Danker & Anderson, 2010). Given that the sensory information retrieved for paired compared with unpaired sounds was visual (memory for the pictures), we predicted reactivation activity in visual cortex. Second, we predicted that brain regions generally associated with cognitive control (Miller, 2000) and more specifically with strategic retrieval, such as lateral PFC (Dobbins, Foley, Schacter, & Wagner, 2002; Dobbins et al., 2003; K. J. Mitchell & Johnson, 2009), would show greater activity in the voluntary memory group than the involuntary memory group. In summary, we expected a dissociation between regions often associated with retrieval success, namely MTL, retrosplenial cortex, posterior cingulate regions, VPC, and sensory reactivation areas, which would be shared for voluntary and involuntary memory, and lateral PFC, which would be active for both paired and unpaired sounds in the voluntary memory group but not the involuntary memory group.

2.2 Methods

2.2.1 Participants

Twenty-nine participants (18 women, mean age = 26 years, range = 18–40 years) were recruited through e-mail and through the Brain Imaging and Analysis Center at Duke University. All participants were right-handed, native English speakers with normal or corrected-to-normal vision. Three participants were excluded because of excessive movement during the fMRI session (any scans with >5 mm or more than 6% of their total scans with between 3 and 5 mm). Participants had no past or current neurological or psychiatric disorders. The between-subjects design had 14 participants in the involuntary group (eight women, six men, mean age = 25 years, range = 19–35 years) and 12 in the voluntary group (eight women, four men, mean age = 28 years, range = 21–35 years). Participants gave written informed consent for a protocol approved by the Duke University Institutional Review Board.

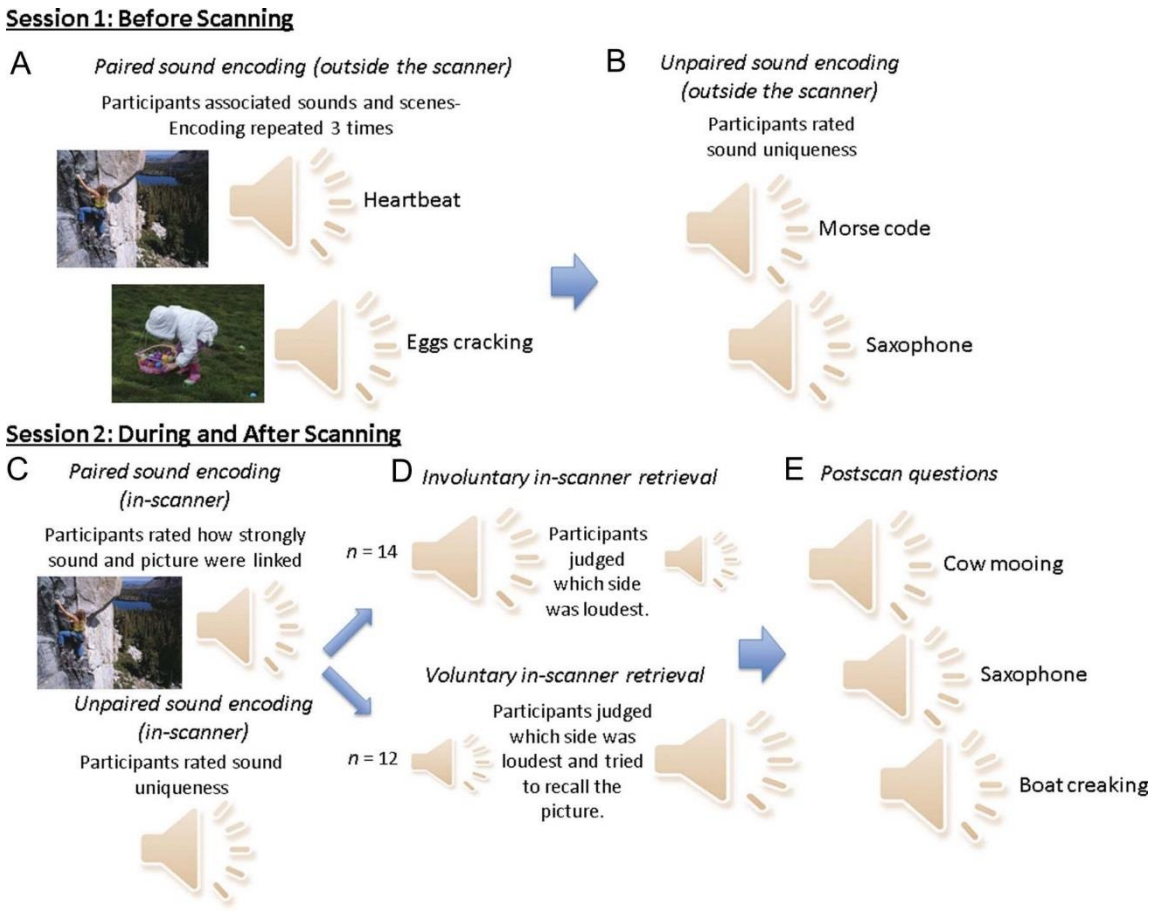

Figure 1: Experimental design.During prescan encoding, participants heard a sound paired with a picture and were asked to type a sentence linking the sound and picture. (B) During another prescan encoding session, participants heard unpaired sounds and rated the uniqueness of the sound. (C) On Day 2, participants performed a "re-encoding" session in the scanner, whereupon they were presented with previous sound–picture pairs and asked to rate on an 8-point scale how well the sound and picture went together based on the story they had formulated previously; with the unpaired sounds, they were asked how distinguishable the sounds were from the other sounds. (D) Participants were subsequently divided into either involuntary or voluntary memory groups. The involuntary group heard both paired and unpaired sounds and was asked to judge on which side the sound was located, whereas the voluntary group was additionally told to also try to remember the picture that had been paired with the sound during encoding, if there had been one. (E) After the scan, all participants heard all sounds and were asked questions about their experiences in the scanner (see text for postscan questionnaire details).

2.2.2 Materials We used 50 scenes and 100 environmental sounds (e.g., dog panting, doorbell ringing). The images and sounds were obtained from multiple sources including the International Affective Picture System (Lang, Bradley, & Cuthbert, 2005) for the pictures and the SUN database (groups.csail.mit.edu/vision/SUN/) for the sounds. All sounds were calibrated to be of equal volume and equal duration (4 sec). As part of the retrieval manipulation, versions of the sounds were produced, in which the sounds were panned 15% to the left or to the right.

2.2.3 Experimental Design and Procedure

2.2.3.1 Session 1: Two Days before Scanning

Two days before scanning, participants encoded paired and unpaired sounds outside the scanner (see Figure 1). To disguise the later involuntary memory task, participants were given the cover story that the study was investigating the effects of pairing sounds with pictures on a later sound laterality task (in the scanner). All encoding trials were self-paced. First, participants encoded 50 paired sounds. Each sound was presented with a picture (4 sec) and, to ensure strong memory associations, the entire 50 pair list was encoded three times: (i) each sound was presented simultaneously with a picture and participants typed a sentence integrating the pair into a plausible story, (ii) each sound–picture pair was presented with the subject-generated sentence and participants edited the sentence if they could improve it, and (iii) each sound was presented alone immediately preceding the sound– picture pair, and participants were to recall the associated sentence and imagine the corresponding picture. An attempt was made to show pictures with some semantic relevance to the sound, but that could not be

described by simply describing the sound. This was done so that when participants were later asked to describe the pictures from memory, it would not be possible for a description of the sound to be confused with a description of the picture. We piloted to make sure the sound–picture associations could be made and that recall would include information that was clearly not in the sound alone. After encoding the sound–picture pairs, participants encoded 50 unpaired sounds. We blocked the paired and unpaired sounds to separate them and thereby improve source monitoring of which sounds had and did not have associated pictures. We used the paired–unpaired sound order because it allowed us to have participants rate each unpaired sound on an 8-point scale how distinguishable the sound was compared with other sounds encountered in the study, thereby further decreasing the likelihood of the participant confusing paired and unpaired sounds and later erroneously recalling pictures to the unpaired sounds. This rating scale required the unpaired sounds to be presented after all paired sounds. We accepted this lack of randomization because it was unlikely to interact with our hypotheses.

2.2.3.2 Session 2: During and After Scanning

The fMRI session consisted of the re-encoding of paired and unpaired sounds (two runs) followed by the critical memory recall task (two runs). Before the re-encoding runs, participants briefly practiced the recall task described below to ensure that participants were comfortable with the responses and the pace. During the re-encoding runs, each stimulus was presented for 4 sec and followed by a 4-sec response window and then by a fixation period (jittered with a mean of 4 sec). The fixation period served as the implicit baseline against which task-related BOLD activity was measured. In the re-

encoding of paired sounds, the 50 sound–picture pairs were presented, and participants rated on an 8-point scale how well the sound and picture went together based on the story they had formulated previously. In the re-encoding of unpaired sounds, the 50 sounds were presented, and participants made the same distinguishability judgment they had made previously.

During the recall runs, the 50 paired and 50 unpaired sounds (randomly intermixed) were presented, panned 15% to either the left or the right using specialized audio software (Audacity, audacity.sourceforge.net/). Participants were instructed to use their index finger to press the button corresponding to the side on which the sound was louder (i.e., the direction from which the sound seemed to originate). Each sound was presented for 4 sec, followed by a 2-sec response window and a jittered fixation period with a mean of 4 sec. Participants were instructed at the beginning of the run that they must wait until after the sound had ended to make their response. The sound lateralization task was thus matched across voluntary and involuntary groups. In addition to performing the spatial discrimination task, participants in the voluntary group were asked to recall the pictures that had been paired with the sound with as many of the details as possible. Participants in the involuntary group were told that having an image come to mind spontaneously was fine but they should not try to recall the images intentionally. This instruction was necessary because pilot evidence suggested that some participants in the involuntary group might try to recall pictures even though the instructions did not require it. After the instruction was added, effort ratings decreased in the involuntary group.

2.2.3.3 Post Scanning Phase

Immediately following the scanning session, participants completed a postscanning questionnaire to assess their memory for the pictures. At a computer terminal outside the scanning room, participants were presented with all 100 sounds (50 paired and 50 unpaired, randomly intermixed) on stereophonic headphones. After the presentation of each sound, participants were asked whether they recalled an image during the scan (yes, no), how vivid the image was during the scan (1 = not at all vivid, 8 = very vivid), and how hard they tried to recall an image during the scan (0 = did not try at all, 7 = tried very hard).

Next, the 50 paired sounds were presented, and participants were asked to provide a description of the picture originally presented with the sound. This was to provide a final check that the image that participants recalled as being originally paired with a sound was indeed of the original picture. Three independent raters scored the similarity between the original picture and the description based on information than what could not be guessed on the basis of the sound alone (1 = no similarity to picture, 10 = exact/highly detailed description). The scores of all three raters were then averaged for each sound for each participant. The only scores that were analyzed were scores for pictures in which participants reported having a memory in the scanner.

2.2.4 Image Acquisition and Preprocessing

Imaging was conducted on a 3T GE Signa Excite MRI scanner (GE Healthcare, Waukesha, WI) with an eight-channel head coil. Head motion was minimized with foam pads and a headband, and participants wore earplugs to reduce scanner noise. The

imaging sequence included a 3-D plane localizer, followed by T1-weighted structural image and four runs of T2*-weighted (functional). The two encoding runs were followed by two retrieval runs; a resting state scan (360 sec) was acquired before the first encoding run and after the final retrieval run. Slice orientation was near-axial, parallel to the anterior–posterior commissure plane. The T1-weighted anatomical images were 60 contiguous slices acquired with a high-resolution, 3-D fast inverse recovery-prepared spoiled gradient recalled sequence, with repetition time (TR) = 7.3 msec, echo time = 2.97 msec, inversion recovery time = 450 msec, field of view = 256 mm, 2 mm slice thickness, flip angle = 12°, voxel size=2×2×2mm, 256×256 matrix, and a parallel imaging with a selection factor of 2. The T2*- weighted echo-planar, functional images were sensitive to the BOLD signal. These were 30 contiguous slices acquired using an inverse spiral sequence, with TR = 2000 msec, echo time = 30 msec, field of view = 256 mm, 4 mm slice thickness, flip angle = 60°, voxel size = 4 × 4 × 4 mm, and 64 × 64 matrix.

Preprocessing and analyses of functional imaging data were conducted with Statistical Parametric Mapping software (SPM5; Wellcome Department of Cognitive Neurology, London, UK), along with locally developed Matlab (Mathworks, Natick, MA) scripts. The first three volumes of each run were discarded. Images were corrected for slice-timing and head motion, spatially normalized to the Montreal Neurological Institute template, and then spatially smoothed with an 8-mm Gaussian kernel. A high-pass filter was included in every model to correct for scanner drift. Participants with between 3 and 5 mm of movement in 6% or fewer of their scans were corrected with

Artrepair (cibsr.stanford.edu/tools/ArtRepair/ArtRepair.htm).

2.2.5 fMRI Data Analysis

fMRI results were analyzed using SPM5. The first level model included regressors for paired sound trials (excluding those for which no picture memory was reported after scanning) and unpaired sound trials (excluding those for which a picture memory was reported after scanning). These trials were split according to sound lateralization (paired left, paired right, unpaired left, and unpaired right) to account for the additional variance due to the difference in sound laterality, but this factor was collapsed at the second level. As nuisance regressors, the model also included paired sound trials with no picture memories and unpaired sound trials with picture memories, as well as motion and run regressors.

Activations were identified using a finite impulse response (FIR) model, which was preferred over a standard canonical hemodynamic response (HDR) model to better understand group effects. An examination of the main effects of group or condition should reveal activity that is sustained over the entire trial. An examination of the interaction between group or condition and time should reveal activity that changes with time. Voluntary and involuntary memory groups performed different tasks; hence, they could differ not only in transient (event-related) but also in more sustained (task-related) activations. Because we could not formulate clear and theoretically defensible hypotheses of the time courses of activation, we used FIR analyses throughout our main analyses. Other studies have used FIR to differentiate between sustained and transient activity (Corbetta, Kincade, Ollinger, McAvoy, & Shulman, 2000; Preuschhof, Heekeren, Taskin,

Schubert, & Villringer, 2006) and have found sustained activity in a variety of regions in response to sustained stimuli or cognitive responses (Courtney, Ungerleider, Keil, & Haxby, 1997). In contrast to the group effects, condition effects (paired vs. unpaired) can only occur after the sound cue is presented; hence, they should show a canonical HDR. Because we investigate both types of effects within the same model, for condition effects we focus exclusively on effects that showed a significant interaction with time (TRs), whereas for group effects we also considered main effects of group. In all cases, the significance threshold was $p < 0.001$ (uncorrected) with a minimum cluster size of 10 contiguous voxels.

2.3 Results

2.3.1 Behavioral Results

During the scan, both groups performed equally well on the laterality task (voluntary correct: 67.50%, SD = 11.00%; involuntary correct: 69.86%, SD = 8.04%, $t(24) = -0.63$, $p > 0.50$), indicating that the level of attentiveness was similar between the groups during the recall block. Postscan questionnaires were administered to fully characterize and verify that participants did in fact undergo the expected mnemonic experience. Critically, participants were first asked whether they recalled mnemonic details (voluntarily or involuntarily) for each sound played during the recall phase. There was a main effect of Group, $F(1, 24) = 7.75$, $p < 0.05$, and Condition, $F(1, 24) = 268.68$, $p < 0.001$, on self-reported recall, and an interaction, $F(1, 24) = 7.59$, $p < 0.05$, such that voluntary participants recalled a greater proportion of memories of the pictures from paired sound trials (94.50%, SD = 5.92%) than did involuntary participants (68.71%, SD

= 31.11%, $t(14.10) = 3.04$, $p < 0.001$), but there was no difference in the pictures that were incorrectly recalled to unpaired sound trials (3.83%, SD = 4.22% vs. 4.14%, SD = 4.74%, respectively). Participants were also asked to report how effortful they found retrieving each associated picture for each sound. There was a main effect of Group, $F(1, 24) = 60.12$, $p < 0.001$, and a main effect of Condition, $F(1, 24) = 5.59$, $p < 0.05$, and no significant Group × Condition interaction on these effort ratings, $F(1, 24) = 3.40$, $p > 0.05$. On a 0–7 retrieval effort scale, voluntary memory participants reported an average retrieval effort of 4.20 (SD = 2.13) for the paired sounds and 2.33 (SD = 2.02) for the unpaired sounds. Involuntary memory participants reported an average retrieval effort of 0.49 (SD = 0.74) for the paired sounds and 0.26 (SD = 0.45) for the unpaired sounds. The participants had considerable training on the paired and unpaired sounds, so the increased effort for paired sounds compared with unpaired sounds in the voluntary condition most likely reflects their knowledge of whether retrieving a picture was possible. The large difference in retrieval effort between voluntary and involuntary groups combined with the differences in their reports of the number of sounds that led to recall of mnemonic details lends support to the effectiveness of the retrieval manipulation.

Ratings of vividness were made for each recalled picture on a scale from 1 to 8. There was no Group × Condition interaction for vividness, $F(1, 24) = 2.50$, $p > 0.10$, but there was a main effect of Group, $F(1, 24) = 12.06$, $p < 0.005$, and a main effect of Condition, $F(1, 24) = 115.70$, $p < 0.001$. Consistent with their instructions to recall the image with as many details as possible, the voluntary group reported higher vividness ratings (M = 4.19, SD = 0.41) than the involuntary group (M = 3.00, SD = 1.15). The

recalled pictures from the paired sounds elicited higher vividness ratings (M = 5.66, SD = 1.96) than the pictures that were incorrectly recalled to the unpaired sounds (M = 1.42, SD = 0.79) for all trials in which an image was recalled.

Finally, participants wrote descriptions of the pictures, which were rated by three independent raters for similarity to the picture presented during encoding. Descriptions typically ranged from one to two sentences with two to three descriptive elements. There was no significant difference between similarity ratings of the descriptions of the pictures between the groups, $t(24) = 1.12$, $p = 0.27$. Interrater reliability was high ($\alpha = 0.95$). The average rating for the voluntary participants was 9.31 (±0.72), and the average rating for the involuntary participants was 9.54 (±0.27). This suggests that the sound–picture pairings were learned well and that the difference in the number of sounds that evoked a memory was not because of a difference in the participants' ability to recall the pictures.

2.3.2 fMRI Results

Table 1 lists regions showing differences of Condition (paired vs. unpaired sounds) × Time, main effects of Group, and Group (voluntary vs. involuntary memory) × Time. All interactions with time were conducted with all seven time points. Consistent with our first prediction, there were significant differences across the voluntary and involuntary groups between paired and unpaired sounds. In Figure 2A, activity from the Condition × Time interaction is shown, in part to make clearer the extent of the large 776-voxel cluster shown in Table 1.

Table 1: Brain Regions Showing Differences as a Function of Condition or Group (p < 0.001, Cluster Size = 10)

Region	*BA*	*Lat*	*Voxel Count*	*x*	*y*	*z*	*F*
Condition (Paired > Unpaired) x Time							
Hippocampus		L	776	-26	-34	-4	6.39
Parahippocampal cortex	36	L		-26	-30	-19	6.98
	30	R		11	-41	4	10.52
Retrospleinal cortex	30	R		8	-53	15	8.95
Posterior cingulate gyrus	31	L		-8	-34	30	7.63
Precuneus	31	L		-4	-60	34	7.50
	31	R		4	-64	34	7.80
Angular gyrus	39	L		-49	-71	30	7.27
	39	L		-49	-68	23	7.38
Superior parietal lobule	7	L		-30	-71	49	6.24
Thalamus		L		-15	-34	0	7.37
Visual cortex	19	L		-38	-79	34	8.00
Superior temporal gyrus	22	L	44	-53	-15	4	6.85
	22	R	144	60	-8	4	7.22
Auditory cortex	41/42	R		49	-23	11	5.36
Middle temporal gyrus	20	R		53	-4	-23	4.42
Cerebellum		R	17	11	-68	-19	4.93
Group (Voluntary > Involuntary)							
DLPFC (middle frontal gyrus)	9	L	11	-38	11	38	3.68
(Voluntary > Involuntary) x Time							
Auditory cortex	41/42	L	13	-45	-26	19	6.21

This large ROI was masked with MTL, posterior midline, ventral parietal, and visual regions, respectively, using ROIs from the Wake Forest University PickAtlas toolbox (www.fmri.wfubmc.edu/download.htm), and significant voxels within those masks are shown in Figure 2B. The time courses in Figure 2C represent the difference in activity for paired– unpaired sounds for four sub-ROIs over seven time points. The time courses in Figure 2D represent activity for all four conditions (voluntary paired sounds,

voluntary unpaired sounds, involuntary paired sounds, and involuntary unpaired sounds) separately. Parahippocampal gyrus, posterior cingulate, and precuneus were also active in a conjunction analysis between voluntary paired > unpaired sounds and involuntary paired > unpaired sounds (see Table 2). The joint probability of the conjunction map was $p < 0.001$. None of these regions showed significant interactions with group, indicating that they were common for voluntary and involuntary memory. As illustrated by Figure 2C, paired > unpaired differences largely overlapped and had a very similar time course for the voluntary and involuntary conditions. No region showed greater activity for unpaired than paired sounds.

Consistent with our second prediction, left DLPFC (middle frontal gyrus) showed greater activity for voluntary than involuntary memory groups with no difference between paired and unpaired sounds. As illustrated by Figure 3B, the voluntary–involuntary difference can be observed at all TRs including 1 and 7, indicating a sustained effect that persisted during the intertrial interval. This pattern suggests that participants in the voluntary group maintained a controlled strategic retrieval throughout the task. The only other region that showed a significant group effect was the left auditory cortex, which suggests greater top–down attention to the sound in the voluntary than the involuntary group. This effect showed an interaction with time at $p < 0.001$, because it was time-locked to the sound presentation and disappeared by the end of the trial. No region showed greater activity for the involuntary than the voluntary memory group, nor were there other regions showing differences in either the main effect of Group or the Group × Time interaction, as can be seen in Table 1.

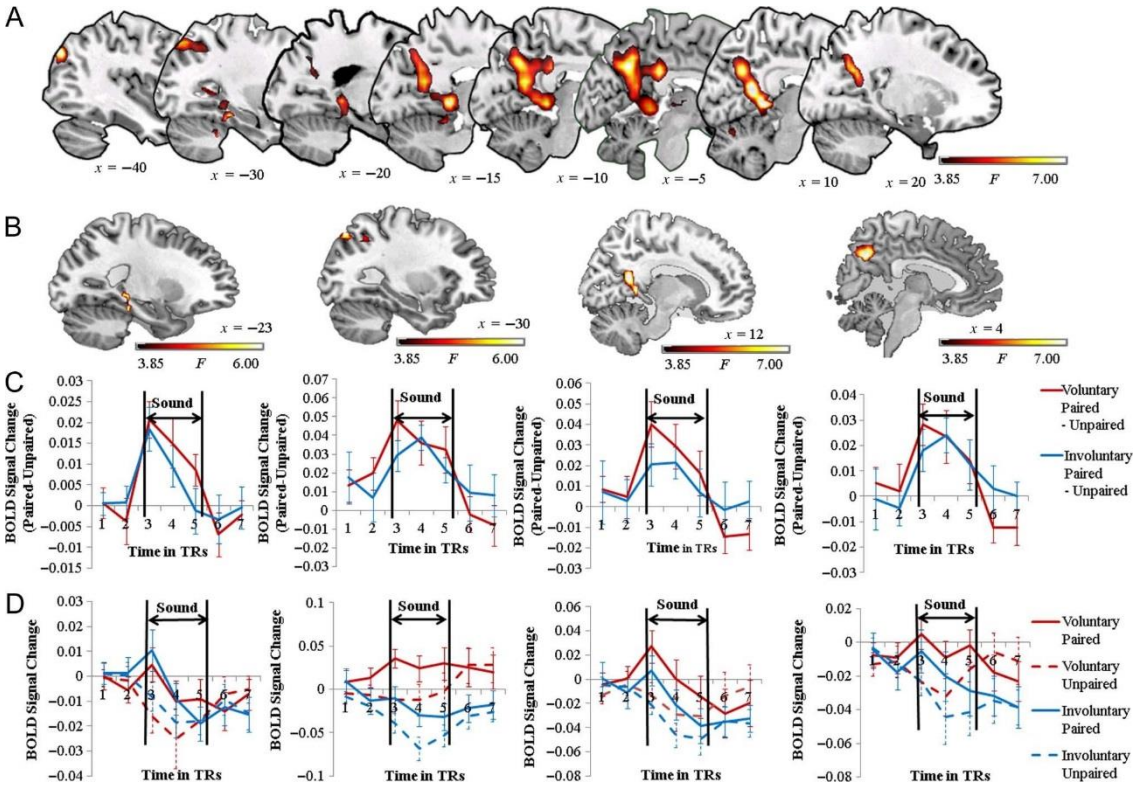

Figure 2: Effects of condition on voluntary and involuntary memory recall.Brain images display significant activations at p < 0.001, 10 voxels. (A) Sagittal views of brain activity from the Condition × Time interaction. This broad posterior activation pattern demonstrates a pattern of activation typical of voluntary memory retrieval, suggesting that voluntary and involuntary memory retrieval recruit the same regions. (B) From left to right, selective clusters in the hippocampus and parahippocampal cortex, left angular gyrus, posterior midline (including posterior cingulate gyrus and retrosplenial cortex), and visual cortex. Clusters were produced by masking the large 776 voxel cluster above with the ROIs of MTL, inferior parietal cortex, posterior midline regions, and visual regions, respectively, derived from the Wake Forest University PickAtlas. (C) Graphs plot the estimated FIR response difference between paired and unpaired sounds for the voluntary (red) and the involuntary (blue) groups within each cluster of activity shown above (B). The activity between the bold vertical lines indicates activity correlating with the peak of activity expected for the sound assuming a normal HDR. Significant differences between paired and unpaired trial activity in these regions demonstrate that these are regions that are active more during trials in which there is a memory. Similarity between the voluntary and involuntary groups demonstrates that this activity is similar between groups. (D) Same data as above, divided to show the estimated FIR response for the voluntary paired sounds, voluntary unpaired sounds, involuntary paired sounds, and involuntary unpaired sounds separately.

Table 2: Brain Regions Showing Similarities in a Voluntary Paired > Unpaired x Time and Involuntary Paired > Unpaired x Time Conjunction Analysis (p < 0.001, Cluster Size = 10)

Region	*BA*	*Lat*	*Voxel count*	*x*	*y*	*z*	*F*
Posterior cingulate	30	R	25	8	-53	15	6.94
Posterior cingulate	30	L		-11	-56	15	5.14
Precuneus	7	R	43	4	-64	34	6.76
Precuneus	7	L		-11	-64	34	3.85
Parahippocampal gyrus	27	L	20	-15	-38	0	5.94
Superior temporal gyrus	22	R	10	56	-11	0	5.40
Superior temporal gyrus	22	L	10	-53	-15	4	4.32
Middle temporal gyrus	21	L		-56	-11	-4	4.14
Superior parietal lobule	7	L	10	-30	-71	49	5.33
Posterior cingulate	23	L	16	-8	-34	34	4.28
Posterior cingulate	31	L		-8	-45	30	3.85

The design in this study could not ensure that the between-group difference in DLPFC during retrieval was not because of spontaneously occurring group differences. To address this, we compared activity during encoding. During encoding, participants did not know to which group they had been assigned, and there had not yet been any differences in the instructions. Analyses within the DLPFC cluster from the between-group analysis revealed no difference between groups at $p < 0.05$ with a cluster size of 1. Looking bilaterally within middle frontal gyrus, superior frontal gyrus, superior orbitofrontal cortex (OFC), and middle OFC as defined by the PickAtlas toolbox (www.fmri.wfubmc.edu/ download.htm) at $p < 0.01$ with a cluster size of 10, there was also no difference between groups. Finally, at $p < 0.01$ with a cluster size of 1 in these same frontal regions, there were only 17 total voxels active out of a total of 2178 voxels, whereas 22 would be expected by chance. Thus, the differences in the DLPFC during

retrieval could not have been a carryover of encoding differences.

2.3.2.1 Post hoc Analysis: Mnemonic Success

Our initial analysis of the Paired Status × Time interaction provided a clear set of posterior temporal and midline parietal cortices demonstrating activation greater in the paired than unpaired conditions. However, because memory retrieval analyses were conducted only on recalled pictures for paired stimuli, we performed a post hoc FIR analysis of trials for which participants reported experiencing a memory during retrieval versus trials in which they did not. This analysis was done at the group level. The only trials analyzed were those in which the post-retrieval description of the picture provided by the participants was judged to be accurate. We created a mask from the Paired Status × Time analysis (to investigate whether there was an overlap with regions associated with retrieval success) and from the main effect of Group analysis (to investigate whether there was an overlap with regions associated with strategic retrieval) within which we examined activity at the group level. The analysis was only performed within the involuntary group because there were not enough trials in which voluntary participants failed to recall an event (<9 trials for each participant). Furthermore, only eight participants from the involuntary condition could be included in the analysis to ensure high statistical power; the remaining six had fewer than nine not recalled trials. The threshold for these initial analyses was lowered to $p < 0.05$ to reflect the small group size and the post hoc nature of the analysis. All activity is reported at a cluster size of 5. The results from this analysis are shown in Table 3.

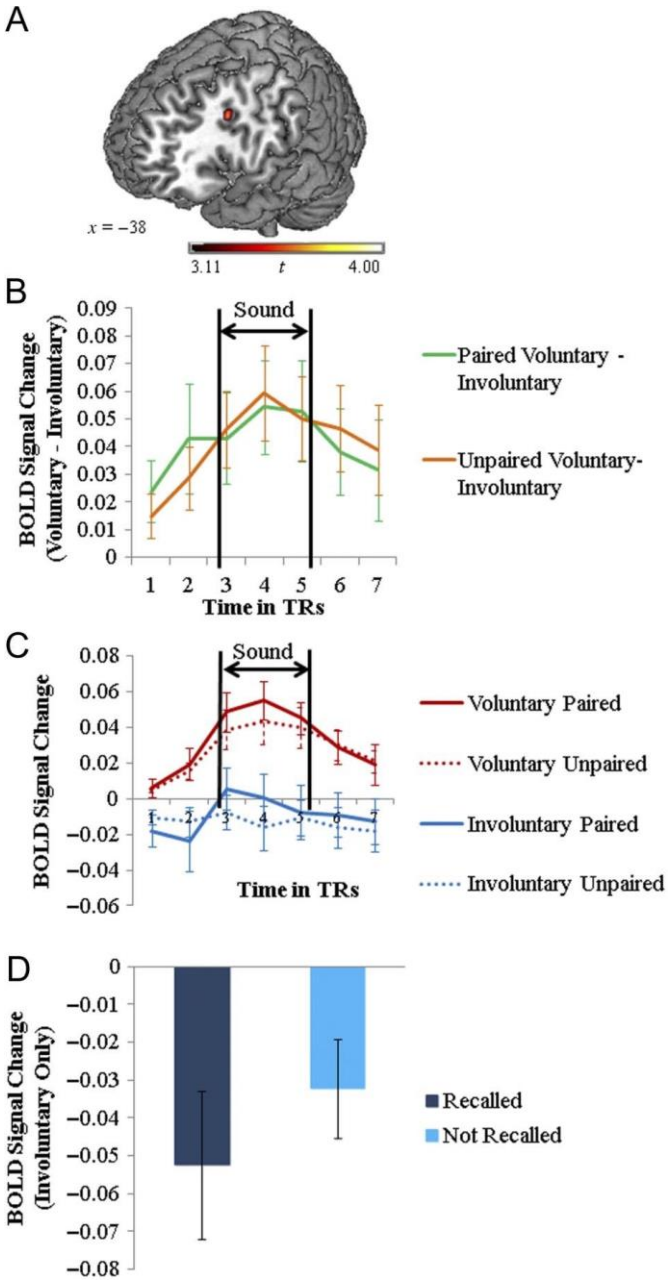

Figure 3: Effects of group on voluntary or involuntary memory recall.(A) Clusters showing differences between the voluntary and involuntary groups. The region shown is the left DLPFC. Brain images display significance at $p < 0.001$, 10 voxels. (B) Graphs plot the estimated FIR response difference between voluntary and involuntary groups for the paired and the unpaired sounds within the DLPFC. The activity in the area between the two vertical lines indicates activity correlating with the peak of activity expected for the sound assuming a normal HDR. There is a

significant difference between group (voluntary and involuntary groups) in this region but not condition (paired and unpaired sounds). (C) A graph plots the estimated FIR response for paired and unpaired sounds in the voluntary and the involuntary groups. (D) Activity within the DLPFC for the involuntary group for recalled trials compared with not recalled trials. There is no difference in activity within this region. This post hoc analysis was conducted at $p < 0.05$.

When we conducted an analysis using the clusters of activity from the Paired Status × Time interaction as a mask, we found right posterior cingulate, left parahippocampal gyrus, right precuneus, and a left lateralized cluster in superior parietal cortex, extending to inferior parietal cortex, to be active for recalled > not recalled trials (Table 3, Figure 4). When we conducted an analysis using the frontal activity found in the main effect of Group analysis as a mask, we found no activity for recalled > not recalled within the mask (Table 3; Figure 3D), supporting the earlier claim that DLPFC does not contribute to the nonstrategic retrieval of mnemonic details or the retrieval of mnemonic details outside of a state of strategic retrieval. To further probe this result, we raised the threshold to $p < 0.01$ while retaining our initial cluster size of 10.

Table 3: Maxima of Regions for Recalled and Not Recalled within Involuntary Paired Sounds, Masked as Noted (p < 0.05, Cluster Size = 5)

Region	*BA*	*Lat*	*Voxel count*	*x*	*y*	*z*	*t*	*p (Uncorrected)*
Recalled > Not Recalled								
Masked with Paried Status x Time activity								
Posterior cingulate	30	R	100	8	-53	11	2.92	0.002
Parahippocampal gyrus	30	L		-8	-41	4	2.72	0.004
Precuneus	32	R		11	-60	23	2.04	0.022
Superior parietal lobule	7	L	12	-26	-68	46	2.42	0.009
Recalled > Not Recalled								
Masked with left frontal cortex main effect of group								
No significant clusters								

The results from this analysis with a raised threshold are reported in Table 4. First, we looked within a mask comprising all frontal regions in the PickAtlas toolbox (www.fmri.wfubmc.edu/download.htm) to examine whether there was activity anywhere in the frontal lobes. None was present. We then looked elsewhere in the brain and found activity overlapping with two of the four regions that are relevant to successful voluntary and involuntary retrieval, specifically visual regions, and posterior midline regions. These three regions are represented in bold in Table 4. In addition to these regions, we found activity in the cuneus and the parahippocampal gyrus (Table 4). Although a sample with enough power to use a more stringent threshold would be needed to confirm these results, they suggest that regardless of the control condition, involuntary memories do not elicit activity in frontal regions and they do elicit activity in regions typically associated with successful voluntary memory retrieval.

Table 4: Maxima of Regions for Recalled and Not Recalled within Involuntary Paired Sounds, Unmasked (p < 0.01, Cluster Size = 10)

Region	*BA*	*Lat*	*Voxel count*	*x*	*y*	*z*	*t*	*p (Uncorrected)*
Recalled > Not Recalled								
Precuneus	7	R	25	4	-79	46	3.30	0.001
Cuneus	19	R	99	11	-98	23	2.99	0.002
Precuneus	31	L		-8	-71	15	2.94	0.002
Cuneus	17	L		-8	-83	11	2.91	0.002
Cuneus	18	R		15	-83	19	2.91	0.002
Middle occipital gyrus	18	R		11	-98	11	2.86	0.003
Cuneus	17	R		8	-94	4	2.81	0.003
Posterior cingulate	30	R	15	8	-53	11	2.92	0.002
Parahippocampal gyrus	30	L		-8	-41	4	2.72	0.004
Not Recalled > Recalled								
Fusiform gyrus	20	R	16	45	-23	- 	3.46	0.000
Anterior cingulate	32	L	20	-4	26	-8	3.37	0.001
Anterior cingulate	32	R		4	23	-8	2.71	0.004
Anterior cingulate	24	R		4	30	-4	2.51	0.007

2.4 Discussion

Our study yielded two main findings. First, voluntary and involuntary memories share considerable overlap in a network of regions strongly associated with successful episodic retrieval, including MTL (hippocampus, parahippocampal gyrus), posterior midline (retrosplenial and posterior cingulate cortices), VPC (angular gyrus), and sensory reactivation regions (visual cortex). Second, in contrast, voluntary memory was uniquely associated with activity in the left DLPFC, a region generally associated with cognitive control, and more specifically often found to be associated with controlled episodic retrieval. These findings represent strong evidence that voluntary and involuntary

memories share the same basic neural structures with the primary difference being the difference in DLPFC activity. These findings are discussed in greater detail below.

2.4.1 Paired versus Unpaired Sounds: Retrieval Success Network

Voluntary and involuntary memories have many similarities. They have a similar distribution of emotional valence and intensity, they follow the same forgetting curve, and they occur with similar frequencies to each other at each stage of the life span (Berntsen, 2009; Berntsen & Hall, 2004; Berntsen & Rubin, 2013; A. S. Rasmussen & Berntsen, 2009; David C. Rubin & Berntsen, 2009). Because of these behavioral findings, we predicted that there would also be overlapping regions of activity for voluntary and involuntary memories in regions typically associated with successful recall in voluntary memory studies.

Consistent with this first prediction, we found that both voluntary and involuntary groups showed paired–unpaired differences in regions strongly associated with successful episodic retrieval, including MTL (hippocampus, parahippocampal cortex), posterior midline (retrosplenial and posterior cingulate cortices), ventral parietal (angular gyrus), and sensory reactivation (visual cortex) regions (see Figure 2). These regions are commonly found in fMRI studies of recognition memory that compare activity for hits versus correct rejections or misses (for meta-analyses, see H. Kim, 2013; Spaniol et al., 2009).

Activations in the hippocampus and parahippocampal cortex have been linked to successful retrieval of contextual information or recollection, rather than to retrieval in the absence of contextual recollection or familiarity (for a review, see Rachel A. Diana,

Yonelinas, & Ranganath, 2007). Retrosplenial and posterior cingulate regions also tend to show greater activity for recollection than familiarity, consistent with their strong anatomical connections to the MTL (Daselaar, 2006; Yonelinas, 2005). The current results are important because they indicate that the recruitment of these recollection-related MTL and posterior midline regions does not require the conscious intention to retrieve past events but also occur when retrieval is involuntary and spontaneous. The finding that the hippocampus had similar activity for voluntary and involuntary memories fits very well with the hypothesis that the hippocampus is a module that automatically retrieves information in response to retrieval cues (Moscovitch, 1992, 1995).

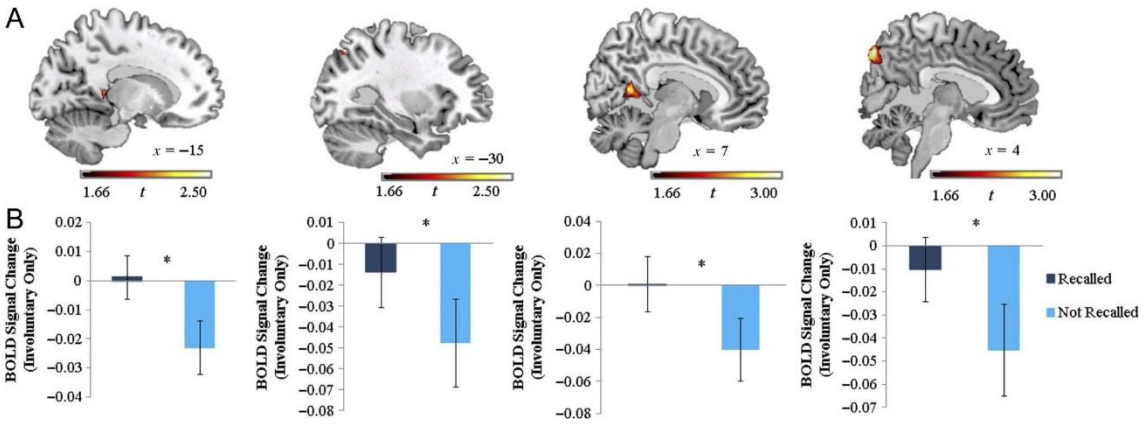

Figure 4: Regions showing activity within the involuntary group for trials in which participants recalled a picture compared with trials in which participants did not recall a picture for paired sounds. This post hoc analysis revealed a difference between these conditions at $p < 0.05$. (A) All regions overlap with regions in corresponding columns found in the Condition × Time interaction displayed in Figure 2. From left to right, the regions are MTL, inferior parietal cortex, posterior midline regions, and visual regions. (B) Graphs showing the difference between recalled and not recalled trials. In all cases, there is greater activity in the recalled condition than the not recalled condition.

The current finding that involuntary memory activates the MTL and posterior midline regions as much as voluntary memory is consistent with the results by Kompus et

al. (2011) and Hall et al. (2008). As noted before, however, these previous studies used within-subject designs where the same participants performed both involuntary and voluntary memory tasks; hence, they could not control for the use of voluntary retrieval strategies during involuntary memory tasks. In the current study however, involuntary memory participants never performed an intentional retrieval task until the postscan questionnaire. Thus, our study provides the first clear evidence that the recruitment of the MTL and posterior midline regions is independent of the intention to retrieve episodic memory.

The VPC, particularly the angular gyrus, is another region that consistently shows greater activity for recollection than familiarity across fMRI studies (Ciaramelli et al., 2008; Kaia L. Vilberg & Rugg, 2008). According to an episodic buffer hypothesis (Kaia L. Vilberg & Rugg, 2008), this region mediates the maintenance of multimodal information within working memory, where it is held available to access given the appropriate retrieval cue. Conversely, according to the attention to memory (AtoM) model (R. Cabeza, 2008), activity in VPC is driven by bottom–up attention processes, which are captured by recovered memories. Given that the voluntary retrieval of multimodal information and the maintenance of this information were requirements in the voluntary but not in the involuntary memory condition, the episodic buffer hypothesis would predict greater ventral parietal activity for voluntary memories, which were explicitly maintained, than involuntary memories, which were not (K. L. Vilberg & Rugg, 2012). Thus, participants in the involuntary condition may have held such information in the episodic buffer, but such maintenance processes were not necessary in

these individuals. In contrast, the AtoM model predicts similar ventral parietal activity for voluntary and involuntary memory because both capture attention bottom–up. Thus, although we cannot discount the possibility that participants in the involuntary condition engaged in covert elaborative voluntary retrieval, the current finding seems to be more consistent with the AtoM model than the episodic buffer hypothesis.

Finally, the finding of greater visual cortex activity for paired than unpaired sounds fits with previous fMRI evidence that sensory regions activated during encoding are reactivated during voluntary and involuntary retrieval (for a reviw, see Danker & Anderson, 2010). In the current study, participants encoded sound–picture pairs (paired sounds) or sound alone (unpaired sounds), and during retrieval, only sounds were presented. Thus, as in previous studies of visual reactivation (Fletcher et al., 1995; Ishai, Ungerleider, & Haxby, 2000; Vaidya, Zhao, Desmond, & Gabrieli, 2002; M. E. Wheeler & Buckner, 2003; Mark E. Wheeler & Buckner, 2004; M. E. Wheeler, Petersen, & Buckner, 2000; M. E. Wheeler et al., 2006), our findings of activity in visual processing regions (e.g., superior occipital gyrus and precuneus) likely reflect the recovery of visual information. The new contribution of this study is that visual reactivation was similar for voluntary and involuntary memories, providing strong evidence that the reactivation can be bottom–up and does not require the intention to retrieve.

2.4.2 Voluntary versus Involuntary Memory: Left DLPFC

In addition to commonalities in retrieval success, there is also robust behavioral support for specific differences between voluntary and involuntary memories because of differences in retrieval (Berntsen, 2009). Consistent with our second prediction derived

from these behavioral findings, we found that compared with involuntary memory, voluntary memory was associated with greater activity in lateral PFC. As illustrated by Figure 3, left DLPFC showed greater sustained activity in the voluntary than involuntary memory group for paired and unpaired sounds, suggesting a general state of strategic retrieval. The frequent association of this region with verbal working memory tasks and contextual reinstatement suggests that, in our task, the requirement for voluntary participants to maintain task goals and plan the associative retrieval put more demands on this region.

In fMRI studies of episodic retrieval, left DLPFC activity tends to increase as a function of the demands placed on controlled retrieval processes (K. J. Mitchell & Johnson, 2009). The lateral PFC is also implicated in controlled and strategic cognitive processing (Koechlin, Ody, & Kouneiher, 2003; Miller, 2000). Dobbins and collaborators (Dobbins et al., 2002; Dobbins et al., 2003) found that left DLPFC (middle frontal gyrus) shows greater activity for source than item memory tasks and that this activity was similar for correct and incorrect source memory trials. According to these authors, this pattern suggests that left DLPFC mediates the attempt to retrieve episodic memory details (recollective attempt) rather than a process conditional on successful retrieval. This account fits well with the current finding that left DLPFC showed greater activity for voluntary than involuntary memory but did not differ between the condition in which retrieval success was extremely high (paired sounds: 94.50% picture recall) and the condition in which it was extremely low (unpaired sounds: 3.83% picture recall). The fact that this region was partly active during intertrial intervals (see activation time course in

Figure 3) further suggests that this region may mediate not only trial-specific retrieval attempt processes but also more sustained strategic retrieval (Dobbins & Han, 2006).

2.5 Conclusion

To summarize, we found that both voluntary and involuntary memories engaged the retrieval success network of MTL, posterior midline, ventral parietal, and sensory re-activation regions, whereas only voluntary memories recruited PFC. These findings clarify the functions of these regions and have implications for the understanding of the neural mechanisms of both involuntary and voluntary memory retrieval. They also have clinical implications because involuntary memories are a symptom in many clinical disorders, including bipolar disorder, depression, social phobia, and posttraumatic stress disorder. Future studies may wish to further probe differences between voluntary and involuntary memories in people with clinical disorders as well as in populations with limited PFC resources, including children and older adults

3. Neural Networks Involved in Involuntary Memories

3.1 Introduction

Involuntary memories are explicit memories that occur without retrieval effort (Berntsen, 2009). Our previous work suggests that a key difference between voluntary and involuntary memories is that voluntary memories require additional cognitive control processes for their retrieval but that the memory representation is the same. Because differences in cognitive processes, like those related to the level of item recovery or learning demands, can be revealed by differences in connectivity in the absence of differences in activity (Nyberg et al., 2000) (Sauseng, Hoppe, Klimesch, Gerloff, & Hummel, 2007), we choose to follow-up our previous work with an investigation into connectivity differences in voluntary versus involuntary memories.

Voluntary and involuntary memories both recruit regions that are commonly found to be active during recollection, like the parahippocampal gyrus, posterior midline regions, precuneus, and inferior parietal cortex (S. A. Hall et al., 2014). Previous work has shown that these regions, plus the medial prefrontal cortex (mPFC), are frequently connected during voluntary remembering (Benoit & Schacter, 2015; Sadeh, Maril, & Goshen-Gottstein, 2012; Vincent et al., 2006), at rest (Vincent, Kahn, Snyder, Raichle, & Buckner, 2008), and even during retrieval requiring varying levels of effort (Skinner, Fernandes, & Grady, 2009). Whether this same network coheres during retrieval that requires no controlled processing is unknown.

If the recollection network does cohere for both voluntary and involuntary memories, it could still differ between memory types, with differences in internal

integrity. Connectivity within the recollection network has been shown to change depending on task demands and retrieval outcomes. Stronger within-recollection network connectivity occurs with increased retrieval success, (King, de Chastelaine, Elward, Wang, & Rugg, 2015; Schedlbauer, Copara, Watrous, & Ekstrom, 2014), increased retrieval accuracy (Skinner et al., 2009), and the retrieval of more detailed information (Hayama, Vilberg, & Rugg, 2012). Conversely, the recollection network has lower internal integrity during the retrieval of weaker memories, encoded in the presence of distractors compared to those encoded without distractors (Wais, Rubens, Boccanfuso, & Gazzaley, 2010). To our knowledge, there has not been a study addressing differences in recollection network coherence relating to controlled versus automatic retrieval. We predict that for voluntary memories, there will be increased integrity during voluntary remembering compared to involuntary remembering.

In addition to affecting network coherence, cognitive control in voluntary remembering could also correlate with networks that have been previously associated with cognitive control processes. It has been shown that voluntary memories elicit additional activity in the DLPFC, a region thought to be associated with controlled retrieval processes (N. Hall et al., 2008; S. A. Hall et al., 2014; Kompus et al., 2011). However, cognitive control is a broad term, likely is referring to multiple control processes, such as initiating task-related action, goal maintenance and orienting attention to goal-relevant stimuli (Dosenbach, Fair, Cohen, Schlaggar, & Petersen, 2008). These processes have been shown to be related to the frontoparietal and cingulo-opercular networks, (Menon & Uddin, 2010; Seeley et al., 2007). To retrieve a memory voluntarily,

there must first be an intention to retrieve, or a retrieval goal, and then there must be effort act upon that goal, or effort to retrieve. Involuntary remembering, on the contrary, requires neither a retrieval goal nor any effort to achieve that goal. Therefore, both the cingulo-opercular network, which consists of dorsal anterior cingulate cortex, insular cortex, thalamus, and OFC (Dosenbach et al., 2007; Seeley et al., 2007) and the frontoparietal network, which consists of the anterior PFC, DLPFC, mPFC, inferior parietal lobule, and anterior insular cortex (Vincent et al., 2008) are likely associated with voluntary remembering but not involuntary remembering.

Based on the evidence above, we have two sets of predictions. The first prediction pertains to the similarities between voluntary and involuntary memories: (1.1) the recollection network will be cohesive for both involuntary and voluntary memories. The second set pertains to the differences between voluntary and involuntary memories: (2.1) the recollection network will be more internally coherent during voluntary memories, and (2.2) networks associated with cognitive control processes, like the frontoparietal and cingulo-opercular networks, will be related to voluntary memories.

To test these predictions, we use independent components analysis (ICA) a data-driven method that derives large-scale networks which can then be related to the task (V. D. Calhoun, Adali, Pearlson, & Pekar, 2001b) and a graph theory measure of path length, which is a measure of network integration (Rubinov & Sporns, 2010).

3.2 Methods

As the task paradigm is the same as that from a previously published paper (S. A. Hall et al., 2014), and is described above, it will not be replicated here. This design was

adapted from extensive behavioral work in involuntary memory (Berntsen et al., 2013) for use in fMRI.

3.2.1 MRI Preprocessing

Preprocessing functional imaging data was conducted with the Statistical Parametric Mapping software (SPM12; Wellcome Department of Cognitive Neurology, London, UK), in Matlab (Mathworks, Natick, MA). The first 3 volumes of each run were discarded. Images were corrected for slice-timing and head motion, co-registered to the first scan of each run, spatially normalized to the Montreal Neurological Institute (MNI) template, and then spatially smoothed with a full-width at half maximum 8 mm Gaussian kernel. A high-pass filter was included in every model to correct for scanner drift.

3.2.2 Independent Components Analysis

Functional imaging data were analyzed with ICA using the GIFT toolbox (V. D. Calhoun, 2004) implemented in MATLAB. Components were derived without assumptions of the temporal model of the hemodymanic activity. Prior to the ICA, dimensionality of the data was reduced using a subject-specific principal component analysis (PCA). Next, the timeseries were concatenated across participants and an ICA was conducted using the Infomax algorithm. The GIFT dimensionality estimation tool was used to determine the number of spatially independent components. The number of components was determined to be 47 using the Minimum Description Length (MDL) criteria (Y. O. Li, Adali, & Calhoun, 2007). The time courses and spatial maps were then back-reconstructed for each participant (V. Calhoun, Adali, Pearlson, & Pekar, 2001a). The components then underwent a one-sample t-test to determine their associated

regions. The t-scores were converted to Z-scores, which represent individual voxel's contribution to the component timecourse. Tables 5-9, below, show the peak voxels for five components of interest (determined using temporal sorting, described in the next section), at a p-threshold of $p < 0.001$ with a cluster size of 100, Monte Carlo corrected using AlphaSim implemented in the REST toolbox. A simulation of 1000 iterations for each regression model produced a threshold of cluster size = 100 to fulfill a corrected false positive rate of $\alpha < 0.05$. Regions that survive FDR correction at $p < 0.05$ are annotated with an asterisk.

3.2.2.1 Temporal Sorting

To identify components related to the experimental task, the time course of each component was used as the dependent variable in a regression, with regressors from task conditions serving as independent variables. Task regressors were modeled as four-second duration delta functions beginning at the onset of each trial convolved with the canonical HRF function implemented in SPM12. A four-second duration was chosen to capture activity occurring during the duration of the four-second sound. Since the timing of memory retrieval was unmeasured this allowed for variation in the memory onset time. The model comprised four task condition regressors (paired and unpaired sounds presented on the left and right). Regressors were split by direction to account for additional variance. Six head motion regressors plus run regressors were also included in the regression as nuisance regressors. Beta weights were assigned to each regressor of interest, which could then be used for further statistical analyses.

One-sample t-tests were performed on beta weights associated with paired sound regressors in each component to first determine which components were task related for this condition of interest. Components for which paired sounds accounted for a significant amount of variance at $p < 0.05$ in at least one of the groups were considered task-related and were carried on to the next step. Then, for these components, beta values were compared across condition (paired versus unpaired sounds) or across group (voluntary versus involuntary). The components for which paired sounds accounted for a significantly greater amount of variance than the unpaired sounds collapsed across group in a t-test ($p < 0.05$), as well as components that showed a group difference, collapsed across condition in a t-test ($p < 0.05$) were considered to show main effects of Condition or Group and will be reported below. A Group x Condition interaction was also conducted in an ANOVA but no components showed a significant interaction effect.

Finally, because we hypothesized that there would be differences in internal coherence in networks that showed a paired > unpaired sound difference for both groups, we used back-reconstructed maps for each subject in a two-sample t-test for these components of interest. This is a method that has been used to determine group differences within components of interest for clinical populations (Assaf et al., 2010; V. D. Calhoun, Maciejewski, Pearlson, & Kiehl, 2008), and for different cognitive states (Otti et al., 2010). Regions that show differences between groups contribute more to the component timecourse, and have greater connectivity with the rest of the component for one group. Differences are shown at $p < 0.001$, with a cluster size of 100, Monte Carlo corrected for multiple comparisons.

3.2.3 Graph Theory

As a secondary test of network integrity, we used graph theory measures of path length. This was chosen because it is widely used to measure network efficiency (Salvador et al., 2005). To measure path length, nodes were first defined by the automated anatomical labeling (AAL) atlas (Tzourio-Mazoyer et al., 2002) corresponding to the peak voxels in the networks of interest, defined by the ICA. Connectivity matrices were formed reflecting the connectivity between each node and every other node in the network. Connectivity values were derived by correlating single-trial beta estimates of the model fit for each node with those beta estimates for every other node. Like the model used in the ICA, four seconds were modeled for each trial to capture activity associated with varying memory onset times.

Path length is the number of edges between any two nodes. Lower path length indicates more efficient communication between nodes. Path length was derived from Dijkstra's algorithm (Dijkstra, 1959) implemented in the Brain Connectivity Toolbox (BCT) in Matlab (Rubinov & Sporns, 2010). Path length (B) was calculated as

$$B = \frac{N\ (N-1)}{\sum_{i \neq j} \frac{1}{d_{ij}}}$$

where d_{ij} is the geodesic distance between nodes i and j, and N is the number of nodes. The average number of edges between each node and every other node was calculated for each participant and then averaged across groups. To test for differences between groups, the path length between each pair of nodes was calculated for each participant. These values were then entered into a MANOVA with path length at each node as dependent

variables and group (voluntary versus involuntary) and node as independent variables. This allowed us to test for main effects of Group, which would show differences between groups in the average path length from each individual node all other nodes in the network, and Group x Node interactions, which would show differences between groups in the path length for each node to any other single node in the network.

3.3 Results

Refer to Chapter 2 for behavioral results as the analyses presented in this chapter were done on the same data.

The ICA run with all participants from both the voluntary and the involuntary groups resulted in 47 components. Of those 47 components, 14 had a significant positive relationship with the paired sound trials at $p < 0.05$. Of those 14 paired sound components, three showed a significant paired > unpaired sounds difference (components will be named based on notable peak clusters): component A (henceforth referred to as the medial temporal lobe component, or MTL component), $t(80) = 2.02$, $p < 0.05$ (Figure 5), component B (henceforth referred to as the posterior midline component), $t(80) = 3.74$, $p < 0.001$, and component C (henceforth referred to as the auditory #1 component), $t(80) = 4.58$, $p < 0.0001$. The MTL and the auditory #1 component were task-related for paired sounds for both groups (MTL: voluntary left: $t(11) = 3.25$, $p < 0.01$, right: $t(11) = 4.69$, $p < 0.001$, involuntary right: $t(13) = 2.96$, $p < 0.05$, auditory #1: voluntary left: $t(11) = 6.47$, $p < 0.0001$, right: $t(11) = 8.19$, $p < 0.00001$, involuntary left: $t(13) = 4.78$, $p < 0.001$, right: $t(13) = 6.62$, $p < 0.0001$). The posterior midline component was only task-

related for the voluntary group (voluntary right: $t(11) = 2.74$, $p < 0.05$). See Tables 5-7 for component peaks.

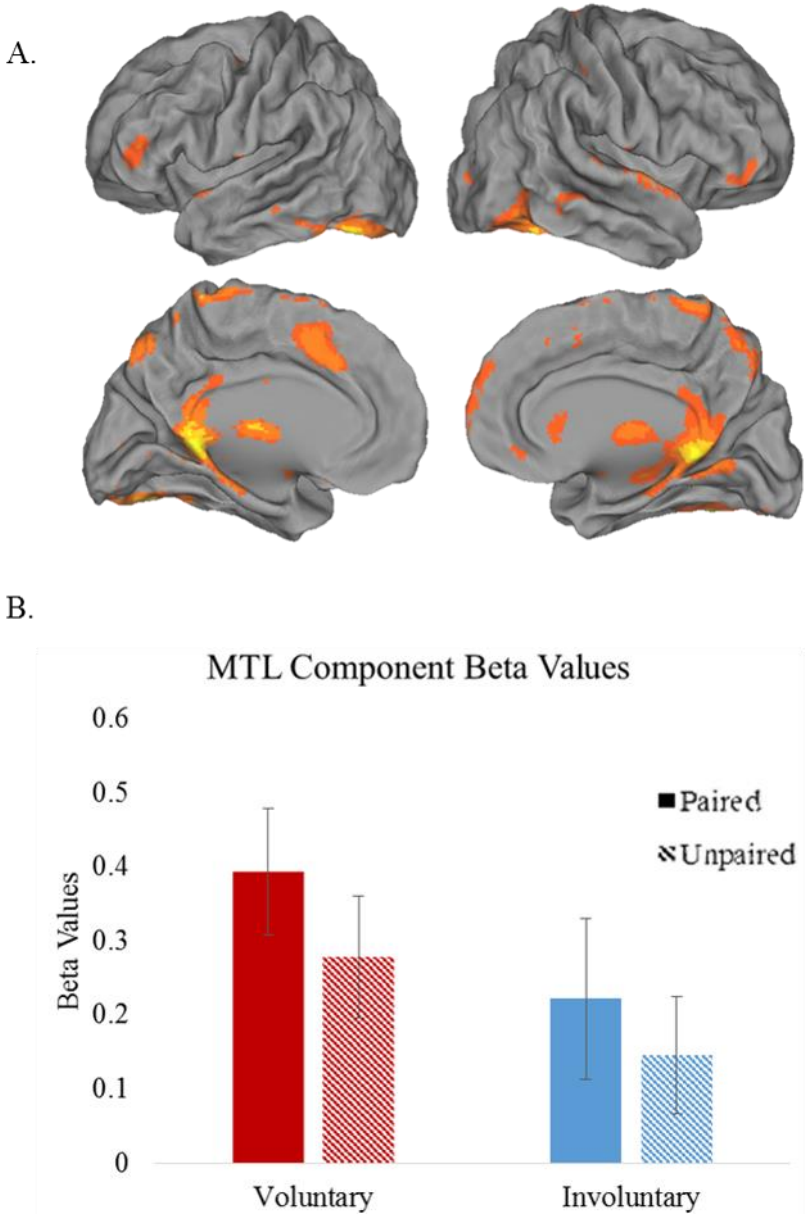

Figure 5: MTL Component. A. The MTL component map is shown at a threshold of $p < 0.001$ with a cluster size of 100, Monte Carlo corrected for multiple comparisons. This component contains regions typically associated with memory retrieval, including the hippocampus, parahippocampal gyrus, precuneus, retrosplenial cortex, and medial PFC. B. Beta values showing the relationship between paired and unpaired sounds for both groups

and the component timecourse. There is a paired > unpaired sound difference, collapsed across group at a significance level of $p < 0.05$.

The MTL component included regions consistent with our hypothesis that a 'recollection' network would be task-related for both groups. Those regions included the hippocampus, parahippocampal gyrus, precuneus, posterior midline regions like the posterior cingulate cortex and retrosplenial cortex, and the mPFC (Figure 5).

In addition, two components showed a significant main effect of group (voluntary versus involuntary): component D (henceforth referred to as the frontoparietal/cingulo-opercular component, or FP/CO component), $t(80) = 2.39$, $p < 0.05$, (Figure 6), and component E (henceforth referred to as the auditory #2 component), $t(80) = 2.78$, $p < 0.01$. Both of these components were task-related for paired sounds for both groups (FP/CO: voluntary left: $t(11) = 3.82$, $p < 0.01$, right: $t(11) = 5.60$, $p < 0.001$, involuntary right: $t(13) = 2.57$, $p < 0.05$, auditory #2: voluntary left: $t(11) = 10.44$, $p < 0.000001$, right: $t(11) = 14.89$, $p < 0.0000001$, involuntary left: $t(13) = 5.50$, $p < 0.001$, right: $t(13) = 6.87$, $p < 0.0001$). See Tables 8-9 for component peaks.

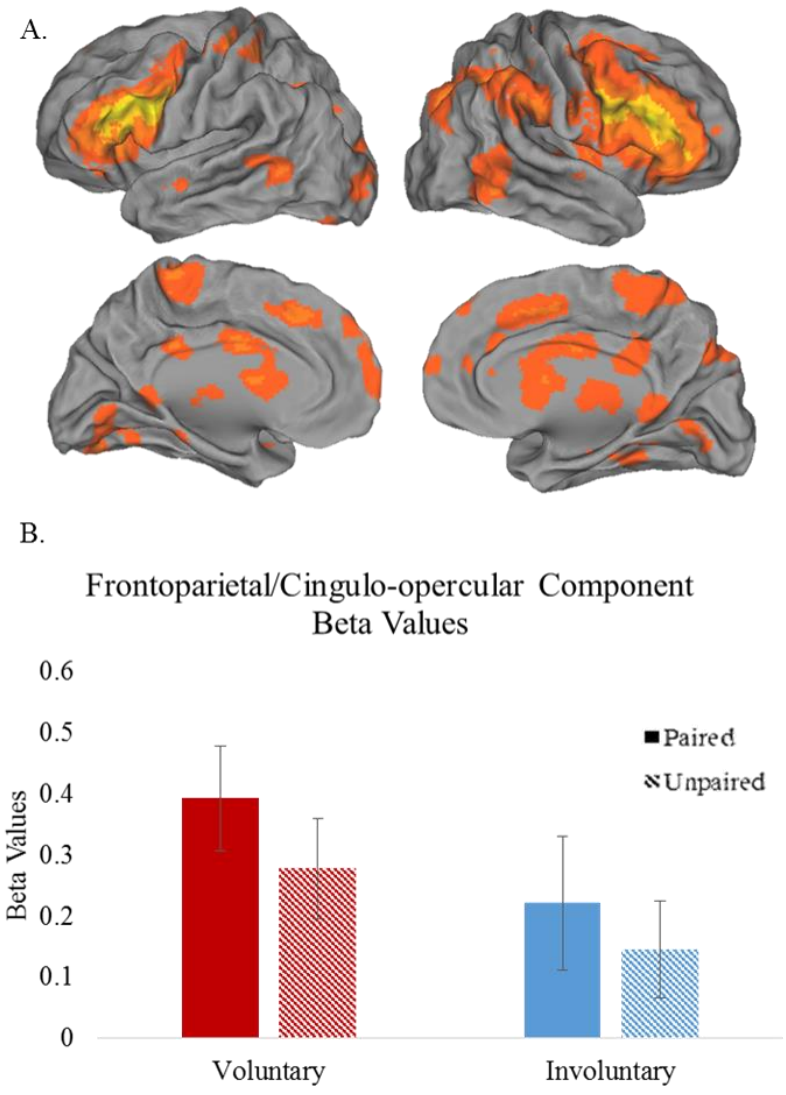

Figure 6: Frontoparietal/Cingulo-opercular Component. A. The frontoparietal/cintulo-opercular component map is shown at a threshold of $p < 0.001$ with a cluster size of 100, Monte Carlo corrected for multiple comparisons. This component contains regions typically associated with the frontoparietal network and the cingulo-opercular networks. These regions include DLPFC, mPFC, inferior parietal cortex, insula, and anterior cingulate cortex. B. Beta values showing the relationship between paired and unpaired sounds for both groups and the component timecourse. There is a voluntary > involuntary difference, collapsed across condition at a significance level of $p < 0.05$.

The FP/CO component included peaks consistent with both networks, including peaks in the DLPFC, mPFC, and inferior parietal cortex, consistent with regions typically found in

the frontoparietal network, and the insula and anterior cingulate cortex, consistent with regions typically found in the cingulo-opercular network.

Table 5: Peaks for MTL component. Peaks are shown at p < 0.001, with a cluster size of 100, Monte Carlo corrected for multiple comparisons. Regions that survive FDR correction at p < 0.05 are indicated with an asterisk.

Region	*Lat*	*Voxel Count*	*x*	*y*	*z*	*t*
Retrosplenial Cortex*	R	13111	6	-44	4	27.55
Retrosplenial Cortex*	L		-4	-40	2	24.23
Fusiform Gyrus*	R		40	-60	-22	17.09
Lingual Gyrus*	R		2	-80	-16	16.15
Cerebellum*	R		44	-68	-22	16.09
Fusiform Gyrus*	L		-28	-76	-22	15.05
Cerebellum*	L		-36	-70	-20	14.82
Inferior Temporal Gyrus*	L		-50	-60	-20	9.64
Parahippocampal Gyrus*	R		22	-24	-14	9.47
Thalamus*	R		14	-10	12	9.45
Parahippocampal Gyrus*	L		-16	-24	-14	9.09
Hippocampus*	R		34	-32	0	7.72
Insula*	L		-34	-16	28	6.65
Middle Temporal Gyrus*	R		64	-38	-10	6.24
Postcentral Gyrus*	R	1410	4	-50	70	14.98
Precuneus*	R		2	-62	60	14.49
Cuneus*	R		6	-90	30	7.07
Cuneus	L		-4	-94	24	4.45
Superior Temporal Gyrus*	R	450	54	16	-8	9.23
Dorsal Medial Frontal Gyrus*	Mid	1131	0	20	46	8.08
Anterior Cingulate Gyrus*	L		-4	24	36	6.7
Dorsal Medial Prefrontal Gyrus*	R		2	24	62	5.83
Dorsal Medial Prefrontal Gyrus	L		-4	6	68	3.77
Ventral Medial Prefrontal Gyrus*	R	266	2	70	8	7.16
Superior Temporal Gyrus*	L	437	-56	12	-6	7.03
Inferior Frontal Gyrus	L	169	-44	44	10	4.86

Table 6: Posterior midline component. Peaks are shown at p < 0.001, with a cluster size of 100, Monte Carlo corrected for multiple comparisons. Regions that survive FDR correction at p < 0.05 are indicated with an asterisk.

Region	*Lat*	*Voxel Count*	*x*	*y*	*z*	*t*
Posterior Cingulate Cortex*	R	19468	4	-42	26	32.64
Posterior Cingulate Corte*	Mid		0	-44	22	31.46
Precuneus*	R		10	-68	30	29.68
Posterior Cingulate Cortex*	L		-2	-28	32	28.5
Precuneus*	L		-4	-66	34	24.88
Inferior Parietal Cortex*	R		36	-58	44	16.75
Thalamus*	R		14	-26	10	13.66
Inferior Parietal Cortex*	L		-34	-66	40	12.63
Postcentral Gyrus*	R		46	-24	30	7.85
Cerebellum	R		16	-38	-26	5.32
Paracentral Lobule	R		6	-46	66	5.2
Postcentral Gyrus*	L	701	-58	-20	20	9.05
Inferior Parietal Cortex	L		-44	-32	32	4.79
Anterior Insula*	L	1075	-40	4	-14	7.07
Middle Frontal Gyrus*	L		-38	14	44	6.5
Inferior Frontal Gyrus	L		-44	20	4	4.98
Middle Temporal Gyrus	L		-48	4	-28	4.79
Superior Temporal Gyrus	L		-42	18	-32	3.56
Cuneus*	L	212	-22	-92	10	6.62
Dorsal Medial Prefrontal Cortex*	L	521	-2	4	56	6.16
Dorsal Medial Prefrontal Cortex	Mid		0	-2	66	4.81
Inferior Frontal Gyrus*	L	115	-24	34	-18	6.09
Cuneus*	R	124	24	-86	12	5.53
Middle Frontal Gyrus	R	284	38	16	46	5.48
Inferior Frontal Gyrus	R		44	16	32	4.5
Orbitofrontal Gyrus	L	248	-16	54	-4	5.27
Ventral Medial Frontal Gyrus	L	198	-2	46	-16	5.04
Ventral Medial Frontal Gyrus	Mid		0	68	-6	3.87
Anterior Cingulate Gyrus	R	247	2	42	12	5
Anterior Cingulate Gyrus	Mid		0	32	24	4.32
Middle Temporal Gyrus	R	104	62	-24	-8	4.38
Superior Temporal Gyrus	R		48	-20	-8	3.84

Table 7: Auditory #1 Component. Peaks are shown at p < 0.001, with a cluster size of 100, Monte Carlo corrected for multiple comparisons. Regions that survive FDR correction at p < 0.05 are indicated with an asterisk.

Region	*Lat*	*Voxel Count*	*x*	*y*	*z*	*t*
Superior Temporal Gyrus*	L	5487	-56	-26	2	25.65
Middle Temporal Gyrus*	L		-58	-16	-10	17.17
Parahippocampal Gyrus	L		-20	-12	-18	5.46
Fusiform Gyrus	L		-24	-32	-20	5.05
Putamen	L		-12	12	-12	4.3
Inferior Frontal Gyrus	L		-40	22	-22	3.89
Superior Temporal Gyrus*	R	4643	52	-14	6	22.21
Inferior Parietal Cortex*	R	267	42	-58	44	6.93
Inferior Frontal Gyrus*	R	166	42	32	-4	6.53
Precentral Gyrus*	L	471	-44	0	56	6.37
Cerebellum*	L	137	-34	-56	-22	5.8
Fusiform Gyrus	L		-32	-48	-24	4.52
Retrosplenial Cortex*	R	156	10	-44	2	5.66
Superior Parietal Cortex*	R	153	24	-50	64	5.56
Amygdala	R	372	22	-4	-14	5.52
Putamen	R		22	12	0	5.18
Middle Frontal Gyrus	L	521	-28	42	26	5.36
Superior Frontal Gyrus	L		-14	50	32	4.93
Medial Frontal Gyrus	L	642	-2	68	8	5.31
Medial Frontal Gyrus	R		10	66	4	5.02
Middle Frontal Gyrus	R		36	44	20	4.29
Inferior Frontal Gyrus	R		38	48	6	4.24
Precentral Gyrus	R	215	48	-6	48	5.31
Postcentral Gyrus	L	106	-40	-32	42	4.97
Postcentral Gyrus	Mid	124	0	2	62	4.82
Posterior Cingulate	R	118	8	-46	38	4.59

Table 8: Frontoparietal/Incgulo-opercular component. Peaks are shown at p < 0.001, with a cluster size of 100, Monte Carlo corrected for multiple comparisons. Regions that survive FDR correction at p < 0.05 are indicated with an asterisk.

Region	*Lat*	*Voxel Count*	*x*	*y*	*z*	*t*
Inferior Frontal Gyrus*	R	24023	48	34	14	34.72
Inferior Parietal Cortex*	R		36	-48	42	19.07
Middle Frontal Gyrus*	R		44	50	-6	18.52
Middle Temporal Gyrus*	R		58	-46	-6	12.95
Mid Cingulate Cortex*	R		4	2	30	12.82
Anterior Insula*	R		38	20	6	11.91
Precuneus*	R		34	-72	38	11.62
Postcentral Gyrus*	R		62	-20	28	11.14
Superior Frontal Gyrus*	R		26	8	56	10.96
Dorsal Anterior Cingulate Gyrus*	R		8	12	48	10.11
Caudate*	R		12	12	8	9.41
Inferior Frontal Gyrus*	L	6683	-46	28	18	24.41
Middle Frontal Gyrus*	L		-48	20	28	21.93
Postcentral Gyrus*	L		-38	-30	60	10.06
Inferior Parietal Cortex*	L	793	-32	-60	44	8.65
Precuneus*	L		-30	-70	38	8.45
Posterior Cingulate Cortex*	R	2909	8	-52	12	8.64
Lingual Gyrus*	L		-10	-72	-12	7.39
Fusiform Gyrus*	R		24	-42	-14	7.01
Cerebellum*	L		-8	-72	-28	6.58
Cerebellum*	R		14	-52	-20	6.5
Lingual Gyrus*	R		6	-68	-2	6.3
Parahippocampal Gyrus*	R		32	-30	-18	6.26
Posterior Cingulate Cortex*	L		-10	-50	6	5.4
Cuneus	L		-8	-78	-2	5.27
Paracentral Lobule*	R	1309	8	-38	72	8.49
Paracentral Lobule*	L		-2	-32	70	6.54
Precentral Gyrus	R		6	-16	70	5.33
Precentral Gyrus	L		-12	-28	74	3.63
Posterior Cingulate Cortex*	R	607	4	-32	34	7.36
Thalamus*	R	775	10	-16	10	7.25
Thalamus	L		-8	-16	6	5.24
Cuneus*	L	649	-16	-90	10	6.83
Medial Frontal Gyrus*	L	608	-2	68	2	6.78

Medial Frontal Gyrus*	R		10	66	4	6.01
Superior Frontal Gyrus	R		18	62	6	5.25
Superior Frontal Gyrus	L		-16	58	6	3.98
Middle Temporal Gyrus*	L	354	-56	-54	4	6.61
Superior Temporal Gyrus	L		-52	-44	8	4.87
Superior Frontal Gyrus*	L	174	-2	60	34	6.55
Superior Frontal Gyrus	R		10	52	44	3.39
Medial Frontal Gyrus	L		-8	52	28	3.37
Insula*	L	308	-36	-6	-8	5.92
Parahippocampal Gyrus*	L	206	-20	-38	-16	5.78
Fusiform Gyrus	L		-26	-34	-20	4.89
Cerebellum	L		-8	-36	-16	3.77
Superior Temporal Gyrus*	L	147	-52	-6	-10	5.53

Table 9: Auditory #2 Component. Peaks are shown at p < 0.001, with a cluster size of 100, Monte Carlo corrected for multiple comparisons. Regions that survive FDR correction at p < 0.05 are indicated with an asterisk.

Region	*Lat*	*Cluster size*	*x*	*y*	*z*	*t*
Superior temporal gyrus*	L	8201	-46	-22	8	47.21
Insula*	L		-34	-42	20	11.91
Thalamus*	L		-14	-26	-4	7.34
Thalamus*	R		12	-18	10	7.16
Retrosplenial Cortex*	R		18	-34	-14	5.68
Insula*	R	5809	40	-22	14	39.06
Superior temporal gyrus*	R		48	-16	6	34.33
Angular gyrus	R		52	-50	22	5.22
Supramarginal gyrus	R		52	-56	24	4.98
Insula*	R	283	30	26	0	8.51
Insula*	L	201	-30	22	-2	7.61
Anterior cingulate cortex*	Mid	1070	0	44	10	7.53
Dorsal medial prefrontal cortex*	R		4	30	36	6.14
Anterior cingulate cortex	L		-4	34	30	5.47
Ventral medial prefrontal cortex	L		-2	54	0	5.2
Posterior cingulate cortex*	R	283	16	-62	24	6.85
Inferior parietal lobule*	R	166	50	-52	52	6.31
Cerebellum*	R	128	22	-66	-22	6.16
Dorsal medial prefrontal cortex*	R	210	6	8	50	6.1
Dorsal medial prefrontal cortex	L		-2	16	44	4.26
Precuneus*	Mid	333	0	-70	52	5.87
Precuneus	L		-14	-76	52	5.37
Precuneus	R		2	-54	54	4.6
Precentral gyrus*	L	120	-38	-28	60	5.65
Precentral gyrus	R		-28	-36	66	3.35
Orbitofrontal cortex	R	155	28	58	-6	5.37
Superior frontal gyrus	R	317	16	30	56	5.29
Superior frontal gyrus	L		-2	32	56	4.8
Cuneus	R	144	28	-82	22	5.29
Precentral gyrus	R	181	50	-4	52	5.25
Cerebellum	L	130	-28	-64	-28	5.23
Precuneus	L	178	-14	-62	20	4.96
Posterior cingulate cortex	L		-8	-54	16	3.91

Turning to the differences between groups within components, only one component showed a significant difference between groups: the MTL component had greater connectivity with the pulvinar nucleus of the thalamus for the voluntary group than the involuntary group (see Figure 7, Table 10). Since the pulvinar is a region that has been associated with the orienting of visual attention (Robinson & Petersen, 1992), this suggests that additional attention during voluntary remembering affects connectivity within the MTL network.

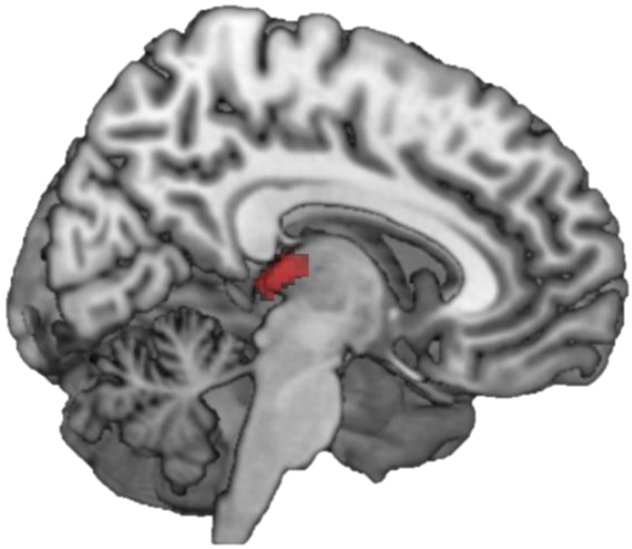

Figure 7: Differences within MTL network. Within the MTL network, there was greater connectivity between the pulvinar and the rest of the network for the voluntary group compared to the involuntary group. Results are shown at $p < 0.001$ with a cluster size of 100, Monte Carlo corrected.

Table 10: Differences in MTL network. Peaks are shown at p < 0.001, with a cluster size of 100, Monte Carlo corrected for multiple comparisons.

Region	*Lat*	*Cluster size*	*x*	*y*	*z*	*t*
Thalamus-Pulvinar Nucleus	R	119	4	-24	10	4.33

Finally, we tested for difference in efficient network processing by measuring path length within the component networks. Using anatomically defined nodes corresponding to the peak voxels within the MTL component and the FP/CO component, our two components of interest, a MANOVA revealed a main effect of Group for the MTL component, $F(22, 507) = 4.92$, $p < 0.001$, Wilks' $\Lambda = .82$, and a main effect of Group for the FP/CO component, $F(36, 829) = 7.90$, $p < 0.001$, Wilks' $\Lambda = .75$. There was no Group x Node interaction for either component (MTL component: $F(462, 7797.03) = 1.05$, $p < 0.05$, Wilks' $\Lambda = .40$, FP/CO component: $F(1260, 21049.31) = .89$, $p < 0.05$, Wilks' $\Lambda = .27$). Post-hoc tests revealed that about half of the nodes in the MTL component and FP/CO components showed decreased path length for the voluntary group (see Figure 8).

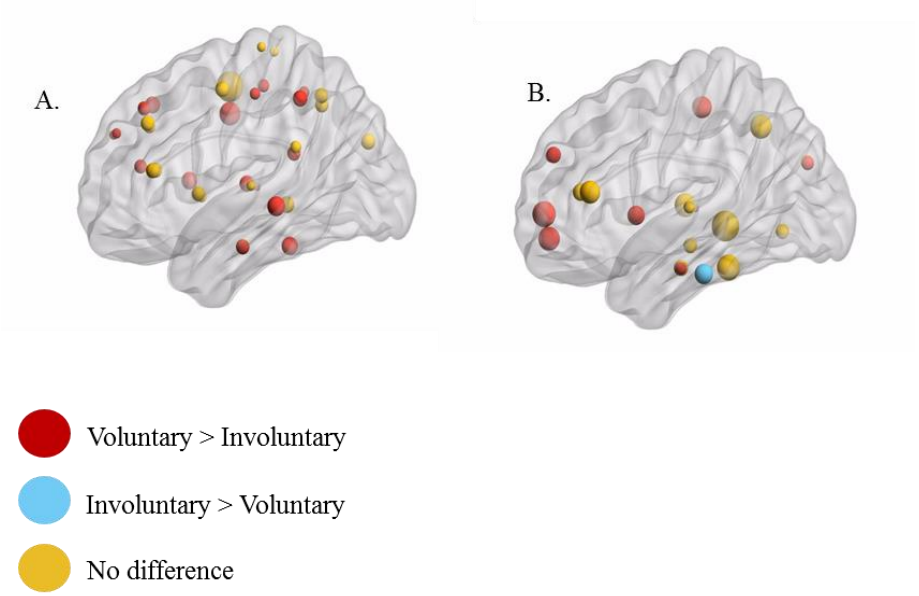

Figure 8: Path length differences. Node colors indicate group differences revealed by a main effect of Group. Node size corresponds to the voluntary-involuntary average path length (the average path length from that node to the rest of the network) difference. Larger nodes indicate a shorter average path length, and therefore greater connectivity, for the voluntary group. Red nodes are significantly greater for the voluntary group, blue nodes are significantly greater for the involuntary group and yellow nodes show no significant group difference. A. Nodes in the frontoparietal/cingulo-opercular component. B. Nodes in the MTL component.

Only one node, in the inferior temporal gyrus in the MTL component, showed decreased path length for the involuntary group. The MTL network had decreased path lengths in the voluntary group in bilateral dorsal medial prefrontal cortex, right ventral medial prefrontal cortex, left parahippocampal gyrus, right fusiform gyrus, and left cuneus, and retrosplenial cortex. In the FP/CO component, the right anterior, mid, and posterior cingulate cortex, bilateral dorsal medial prefrontal cortex, bilateral superior frontal gyrus, bilateral fusiform gyrus, left parahippocampal cortex, bilateral inferior parietal cortex, and bilateral thalamus had shorter path lengths for the voluntary group than the involuntary group. The nodes with decreased path length included key nodes

corresponding to the nodes typically found within these networks. A full list of nodes showing group differences can be found in Tables 11-12.

Table 11: Path length differences in MTL network. Shorter path lengths indicate greater connectivity with the rest of the network. Degrees of freedom for all nodes are 1, 528.

Region	*F*	*Sig*	*Voluntary group mean path length*	*Involuntary group mean path length*
Voluntary > involuntary				
Left parahippocampal gyrus	17.07	0.00	1.36	1.58
Right ventral medial PFC	16.61	0.00	1.19	1.37
Left insula	12.82	0.00	1.25	1.40
Right fusiform gyrus	11.61	0.00	1.21	1.35
Right superior temporal gyrus	9.92	0.00	1.44	1.60
Left dorsal medial PFC	9.32	0.00	1.30	1.45
Left cuneus	8.31	0.00	1.33	1.48
Right postcentral gyrus	6.25	0.01	1.22	1.32
Right dorsal medial PFC	4.34	0.04	1.38	1.48
Retrosplenial cortex	3.91	0.05	1.16	1.24
Involuntary > voluntary				
Left inferior temporal gyrus	6.06	0.01	1.24	1.16
No difference				
Left fusiform gyrus	2.98	0.09	1.17	1.23
Left inferior frontal gyrus	2.34	0.13	1.20	1.26
Right thalamus	1.91	0.17	1.19	1.24
Left anterior cingulate cortex	1.04	0.31	1.28	1.24
Left superior temporal gyrus	0.52	0.47	1.37	1.40
Right mid temporal gyrus	0.31	0.58	1.11	1.12
Right precuneus	0.26	0.61	1.19	1.20
Right cuneus	0.03	0.87	1.36	1.36
Right hippocampus	0.02	0.90	1.32	1.33
Right parahippocampal gyrus	0.01	0.90	1.31	1.31
Right lingual gyrus	0.00	0.99	1.32	1.32

Table 12: Path length differences in the frontoparietal/cingulo-opercular network. Shorter path lengths indicate greater connectivity with the rest of the network. Degrees of freedom for all nodes are 1, 864.

Region	*F*	*Sig*	*Voluntary group mean path length*	*Involuntary group mean path length*
Voluntary > involuntary				
Left parahippocampal gyrus	32.03	0.00	1.41	1.66
Left superior frontal gyrus	31.61	0.00	1.43	1.68
Left thalamus	25.23	0.00	1.43	1.66
Right fusiform gyrus	22.36	0.00	1.30	1.48
Right postcentral gyrus	21.05	0.00	1.48	1.69
Right posterior cingulate cortex	15.70	0.00	1.40	1.57
Left dorsal medial PFC	15.10	0.00	1.62	1.81
Right mid cingulate cortex	14.34	0.00	1.13	1.24
Right caudate	13.20	0.00	1.31	1.45
Left postcentral gyrus	11.85	0.00	1.53	1.68
Right anterior cingulate cortex	10.84	0.00	1.44	1.57
Right superior frontal gyrus	9.12	0.00	1.33	1.44
Right inferior parietal cortex	7.16	0.01	1.53	1.65
Right dorsal medial PFC	7.04	0.01	1.66	1.79
Left middle temporal gyrus	6.82	0.01	1.23	1.32
Right superior temporal gyrus	5.72	0.02	1.70	1.82
Left fusiform gyrus	5.54	0.02	1.28	1.36
Left inferior parietal cortex	4.61	0.03	1.36	1.43
Right thalamus	4.42	0.04	1.33	1.41
No group difference				
Left insula	2.70	0.10	1.41	1.47
Right inferior frontal gyrus	1.49	0.22	1.39	1.44
Left cuneus	1.22	0.27	1.35	1.39
Right parahippocampal gyrus	1.20	0.27	1.39	1.35
Left inferior frontal gyrus	0.81	0.37	1.40	1.43
Left posterior cingulate cortex	0.80	0.37	1.50	1.54
Left paracentral lobule	0.51	0.47	1.64	1.61
Right middle frontal gyrus	0.45	0.50	1.46	1.49
Right precuneus	0.34	0.56	1.40	1.38

Right paracentral lobule	0.20	0.65	1.62	1.64
Left precentral gyrus	0.19	0.66	1.38	1.37
Right insula	0.05	0.82	1.58	1.59
Left middle frontal gyrus	0.02	0.88	1.39	1.38
Right middle temporal gyrus	0.01	0.92	1.33	1.33
Left superior temporal gyrus	0.00	0.97	1.63	1.63
Left precuneus	0.00	0.98	1.40	1.39
Right precentral gyrus	0.00	1.00	0.97	0.97

3.4 Discussion

We used a novel paradigm, in which involuntary memories of pictures were elicited to a sound cue, to investigate differences in connectivity between voluntary and involuntary memories. A voluntary group was instructed to try to remember the pictures paired with the sound cue while an involuntary group was give no such instruction. We have two major findings: (1) the MTL network is related to both voluntary and involuntary memories and (2) voluntary memories are associated with enhanced connectivity compared to involuntary memories within multiple networks and regions that have not been shown in studies investigating difference in activity. Specifically, the MTL network has enhanced connectivity with the pulvinar nucleus of the thalamus for voluntary memories, a FP/CO network is more related to voluntary than involuntary memories, and about half of the nodes for both the MTL network and the FP/CO networks have decreased path length for voluntary memories. Details of these findings are discussed below.

3.4.1 Similarities between Voluntary and Involuntary Memories

The MTL network was associated with both voluntary and involuntary memories. This network included many of the same regions as the recollection network that is commonly found for memory retrieval (Vincent et al., 2006). These regions included the hippocampus, parahippocampal gyrus, precuneus, posterior cingulate cortex, and mPFC. Though activity in most of these regions has been previously associated with involuntary remembering (S. A. Hall et al., 2014), connectivity between them suggests for the first time that information is being communicated between them. Coactivation in the hippocampus, parahippocampal gyrus, and precuneus is consistent with the idea that for item memory and context memory, projections from “what” and “where” pathways in medial temporal lobe, converge in the hippocampus and then communicate with cortical regions implicated in processing the sensory information (Eichenbaum, 2006; Eichenbaum, Yonelinas, & Ranganath, 2007), in this case the precuneus (Cavanna & Trimble, 2006; Fletcher et al., 1995; Hofstetter, Achaibou, & Vuilleumier, 2012), to reinstate the memory. Within this framework, the hippocampal connectivity in this network would be expected given that whole scenes, including item and context information, were being recalled (and would likely be recalled during 'real world' involuntary remembering; D. C. Rubin & Umanath, 2015).

Connectivity between these regions is also consistent with the idea that they are involved with bottom-up retrieval. Lesions to the parietal cortex, including the precuneus, have been associated with detriments in spontaneously recovering memory details in a free recall task (Berryhill, Phuong, Picasso, Cabeza, & Olson, 2007). The involvement of

the parietal cortex in voluntary memory retrieval has been well-established (Wagner et al., 2005). It is thought to play a role in the reinstantiation of visual details during visual memory (Fletcher et al., 1995). Therefore, this suggests that not only do these parietal regions share information with other regions in a bottom-up memory network but their involvement in this network is vital to the full retrieval of a memory, regardless of retrieval intentionality.

The association of the mPFC with the MTL network during involuntary memories is also a novel finding as our previous work has not shown activity in this region to be associated with involuntary memory retrieval (S. A. Hall et al., 2014). In the context of episodic memory retrieval, the mPFC is thought to be involved in the processing of contextual details (Kveraga et al., 2011) and to be part of a 'context network' along with the parahippocampal gyrus and retrosplenial cortex, that is coherent during the retrieval of items that have a strongly associated context (Panichello, Cheung, & Bar, 2012). One model posits that it is likely that the mPFC receives input about contextual information from the hippocampus and uses that information to guide post-retrieval behavior (Alexander & Brown, 2011; Euston, Gruber, & McNaughton, 2012). This is supported by evidence that shows delayed activity in the mPFC compared to other regions associated with recollection (Kveraga et al., 2011) and that activity in this region increases over time (Nieuwenhuis et al., 2012). The integration of the mPFC with other recollection network regions during involuntary remembering suggests that this contextual processing can happen outside of explicit memorial goals.

Though the MTL network is common to both voluntary and involuntary memories, there is evidence to suggest that the origin of the memory signal differs depending on retrieval intentionality. Studies done in monkeys have shown that the automatic retrieval of a paired associate begins in the monkey area 36, which corresponds to the medial temporal lobe in the human brain, and then propagates forward to the visual association cortex, area TE. Controlled retrieval, in contrast, starts with broad categorical information about the to-be-retrieved stimulus, thought to originate in the frontal cortex, which then propagates down to temporal cortex (Miyashita, 2004; Osada, Adachi, Kimura, & Miyashita, 2008). Critically, though frontal cortex is often involved in memory retrieval, frontal lesion patients and older adults, who have deterioration in cognitive control functions, appear to have spared automatic retrieval. When retrieval cues are supplied or during cued recall (Incisa della Rocchetta & Milner, 1993; Kopelman, Stanhope, & Kingsley, 1999), frontal lesion patients see spared memory but they have impaired memory for details, like temporal order or detailed autobiographical remembering (Kopelman, Stanhope, & Kingsley, 1997; Kopelman et al., 1999; Milner, Corsi, & Leonard, 1991; Shimamura, Janowsky, & Squire, 1990). Additionally, older adults report having as many involuntary memories as younger adults but show decreases in thought suppression, a measure of cop-down control (Berntsen, Rubin, & Salgado, 2015). Given that our previous results suggest that the DLPFC is involved in controlled retrieval processes, the current results suggest that the MTL network and control networks involving the DLPFC, though related, are separable. Further, though future work will be necessary to investigate the causal mechanisms, there is some evidence to

suggest that networks involved in cognitive control processes may be driving MTL network activity during voluntary remembering but that without such input, cortical-MTL connectivity drives involuntary memory retrieval.

3.4.2 Differences between Voluntary and Involuntary Memories

Though the MTL network is related to both voluntary and involuntary memories, there are differences in connectivity within this network between the two types of memories. Specifically, the pulvinar nucleus of the thalamus was more highly connected to the MTL network for voluntary memories than for involuntary memories. The pulvinar has a role in the control of attention. It has been associated with the orienting of attention to visual stimuli (Posner & Petersen, 1990; Purushothaman, Marion, Li, & Casagrande, 2012) and has been shown to be connected to the cingulo-opercular network (Barron, Eickhoff, Clos, & Fox, 2015), a network associated with attention to salient stimuli (Dosenbach et al., 2007). Degeneration or lesions in the pulvinar have been correlated with deficits in attention switching (Danziger, Ward, Owen, & Rafal, 2004; G. A. Michael & Buron, 2005; Rafal & Posner, 1987) and decreased connectivity amongst cingulo-opercular network regions (Lee et al., 2014). Not only is it involved in orienting attention to external stimuli, it has also been shown to be part of the dorsal parietal network, which is associated with top-down attention to memory (Burianova, Ciaramelli, Grady, & Moscovitch, 2012). Models of the role of the pulvinar posit that it has a causal role in synchronizing activity across cortical regions according to attentional allocation (Saalmann, Pinsk, Wang, Li, & Kastner, 2012) and it may do this by channeling information from the parietal cortices to visual cortex (Burianova et al., 2012). This

suggests that during voluntary remembering, increased top-down attention to memory prompts the pulvinar to coordinate synchronized activity within regions associated with that memory.

In addition to increased connectivity between the pulvinar and the MTL network, the FP/CO network was more related to the voluntary memories than involuntary memories. The cingulo-opercular network has been associated with maintaining goals and orienting attention to goal-relevant stimuli, and the frontoparietal network has been associated with acting on those goals (Dosenbach et al., 2008). With regards to memory retrieval, the frontoparietal network has been shown to correspond to memory search (Reas & Brewer, 2013), suggesting it is involved in retrieval effort. There is also evidence showing that frontoparietal regions are more active for increasing demand during working memory, suggesting that frontoparietal regions may be involved in both bringing memories to mind and holding them there (Klingberg, OSullivan, & Roland, 1997). The cingulo-opercular network has demonstrated increasing activity with increasing familiarity strength, suggesting it responds to salient stimuli (H. Kim, 2010). The relationship between voluntary remembering and nodes in these two networks suggests that there may be at least two control processes that are more related to voluntary memory retrieval than involuntary memory retrieval: the maintenance of the goal to retrieve a memory and effort to retrieve the memory.

Typically, the frontoparietal and cingulo-opercular networks are separable but there can be connectivity between regions in these networks. For example, increasing working memory demands has been associated with increased cooperation between these

two networks (Cohen, Gallen, Jacobs, Lee, & D'Esposito, 2014), suggesting that the integration of task-relevant networks facilitates task performance under increasing cognitive demands. In the current task, this suggests that goal maintenance and goal-driven behaviors are operating together during voluntary memory. When presented with a cue, participants may remind themselves of their retrieval goal, orient their attention to the sound, attempt to retrieve the memory of the picture paired with the sound, orient attention to the memory after it is retrieved, and attempt to hold the memory in working memory. Attention orientation and action based on that attention work closely together during complex memory retrieval.

Finally, there was decreased path length for voluntary memories in about half of the nodes in both the MTL network and the FP/CO networks. Amongst these nodes were key nodes for both networks: left parahippocampal gyrus, mPFC, and retrosplenial cortex for the MTL network and DLPFC, mPFC, inferior parietal cortex, and thalamus for the FP/CO network. A shorter path length is associated with more efficient information transfer between regions, or greater integration of the network (Bullmore & Sporns, 2009; Rubinov & Sporns, 2010). Decreased path length has also been seen in other tasks that require controlled processing. Increased global efficiency throughout the whole brain, measured by path length, is associated with greater working memory performance (Stanley et al., 2015). Conversely, groups that have deficits in cognitive control processes show decreased network efficiency throughout the whole brain and in networks like the default mode network. Older adults have longer average path lengths during working memory (Toussaint et al., 2014; Wang, Li, Metzak, He, & Woodward, 2010), people with

Parkinson's disease have greater path length in resting state networks (Baggio et al., 2014), and cognitively impaired children with epilepsy have increased path length during visual search. Though most of the studies using graph metrics to date have investigated changes in connectivity throughout the whole brain rather than in theoretically relevant regions, one study has shown decreased path length between the hippocampus and the rest of the brain for increasingly vivid memories (Geib, Stanley, Wing, Laurienti, & Cabeza, 2015), demonstrating that changes in path length can be seen in the whole brain, in individual networks, and in individual nodes. Our findings that about half of the nodes in the MTL and FP/CO networks had a difference in path length between the groups, that all but one of these nodes had a shorter path length for the voluntary group, and that these nodes included functionally relevant nodes is consistent with prior work that has shown decreases in path length with increased cognitive demand. This suggests that this demand increases communication efficiency within networks typically associated with cognitive control, and within networks that are targets of that control.

3.5 Conclusion

We have shown that voluntary and involuntary memories recruit an overlapping network containing regions typically found in the recollection network. However, internal network coherence increases for voluntary remembering compared to involuntary remembering in the form of decreased path length and increased connectivity with the pulvinar. In addition, voluntary memories are more strongly associated with a network that contains regions typically found in frontoparietal and cingulo-opercular networks than involuntary memories. Though our results do not provide any information about

causality, we can make preliminary inferences about causal processes. These data support the idea that voluntary and involuntary memories have the same neural representation but that cognitive control processes, like goal-related attention and retrieval effort, drive more efficient information transfer between networks associated with memory retrieval and networks and regions associated with cognitive control processes.

4. Involuntary Memories in PTSD

4.1 Introduction

Involuntary memories of a traumatic event are a hallmark symptom of posttraumatic stress disorder (PTSD, American Psychiatric Association, 2013), with intrusive memories being present in almost 90% of PTSD cases (Roszell et al., 1991). The frequency of these intrusive memories—and associated behaviors such as negative reinterpretations and maladaptive responses to the memories—explains over 50% of the variance in PTSD severity (T. Michael, Ehlers, Halligan, & Clark, 2005). They are also amongst the most distressing of the symptoms of PTSD (Steil & Ehlers, 2000). Despite their centrality to the disorder, the basic cognitive and neural mechanisms underlying both emotional and non-emotional involuntary memories in PTSD are not well understood. As some of the more effective treatments of PTSD, like propranalol, target memory processes (Giustino, Fitzgerald, & Maren, 2016), a better understanding of the memories that are so central to the disorder is necessary to tailor treatment for this disorder. However, empirical studies have not measured the neural underpinnings of either aversive or neutral involuntary memories in PTSD in a controlled setting.

Given that involuntary memories are universal and are not restricted to memories of negative events, how do they become so problematic in PTSD? Are the memories themselves distorted or is there a difference in the emotional response to the memories? Or perhaps a third moderating factor impacts both the memory and emotional experience of the memory. Models of PTSD posit that people with PTSD have deficits in the memory system, the emotion system, and the dorsal attention system. These deficits are

characterized by deficits in hippocampal function, by an exaggerated amygdala response, and an attenuated ventral medial prefrontal cortex (VMPFC)/rostral anterior cingulate cortex (rACC) response (Rauch, Shin, & Phelps, 2006), and by deficits in the dorsal lateral prefrontal cortex (DLPFC, specifically the middle frontal gyrus) and the superior parietal cortex (Hayes, Labar, Petty, McCarthy, & Morey, 2009), respectively. What is not understood is how these deficits affect involuntary memories in PTSD.

Models of PTSD claiming that there is hypoactivity in the hippocampus are based on evidence that either voluntary memories or memories induced via symptom provocation, in which participants are given trauma-related cues that provoke PTSD symptoms, evoke hypoactivation in the hippocampus (Lanius, Bluhm, Lanius, & Pain, 2006). However, it is unclear whether the involuntary memory system itself is impacted by memory system dysfunction or whether this hippocampal hypoactivity is due to processes unique to voluntary memories or emotional recollections. Previous work has suggested that dysfunction in memory processes may be due to encoding deficits, in which case memories would be weaker in PTSD and disrupted hippocampal activity would be expected (Samuelson, 2011). However, even when memory performance is matched on a memory task, implying that encoding processes remained intact, there are still deficits in hippocampal function, suggesting that controlled retrieval is also impacted by these cognitive deficits (Carrion, Haas, Garrett, Song, & Reiss, 2010; Werner et al., 2009). Therefore, if people with PTSD have fewer involuntary memories during an involuntary memory task, suggesting degraded learning, we predict that there will be deficits in the memory system as evidenced by hypoactivation in the hippocampus, and

potentially in other regions associated with involuntary memory retrieval, like the parahippocampal gyrus, the inferior parietal cortex, the posterior cingulate cortex (PCC), and the precuneus (S. A. Hall, Li, Kragel, Rubin, & Berntsen, In prep; S. A. Hall et al., 2014). If people with PTSD and people without PTSD have an equal number of memories, we predict that the memory system will remain intact.

A second pathway through which involuntary memories in PTSD may be disrupted is the emotional response and regulation system, which includes the amygdala and the ventral medial prefrontal cortex (VMPFC). Evidence for disruptions in the emotion system in PTSD come from differential behavioral responses to emotional stimuli. People with PTSD rate negative stimuli as more arousing (Wolf, Miller, & McKinney, 2009) and they have more intense emotional reactions to negative autobiographical memories (D. C. Rubin et al., 2008). Fear conditioning models of PTSD posit that this hyper-responsiveness to emotional stimuli is because people with PTSD have a diminished ability to regulate their fear response to items that once predicted danger and therefore this fear response does not get extinguished even after the threat is gone (Milad et al., 2009). This process of emotion regulation/fear extinction is mediated by increased activity in the VMPFC, which downregulates amygdala activity (Myers & Davis, 2007; Quirk & Mueller, 2008). In PTSD, this circuit is disrupted; there is hypoactivation in the VMPFC along with hyperactivation in the amygdala in response to emotional stimuli. Though this response is well studied in models of conditioning, it is unknown how these emotion responses will affect involuntary memory retrieval. If

disturbances in the emotion system also apply to involuntary memories, there would likely be decreased VMPFC and increased amygdala activity.

Finally, both the memory system and the emotion system could be affected by deficits in the internally-focused attentional system. Attention has been shown to be degraded in PTSD for neutral stimuli and enhanced for emotional stimuli (Cisler et al., 2011; McNally, 1995). For non-emotional stimuli, this results in deficits in sustained attention and mental manipulation (Brandes et al., 2002; Vasterling et al., 2002), as well as slowed responses to voluntary memory tasks (Chen, Li, Xu, & Liu, 2009) and automatic tasks (Kanagaratnam & Asbjornsen, 2007). On the contrary, people with PTSD have increased memory for negative stimuli (Paunovic, Lundh, & Ost, 2002), they respond more quickly to negative stimuli (Bryant & Harvey, 1997) and are more distracted by negative stimuli (Cisler et al., 2011). If these alterations in attentional resources affect both bottom-up and top-down attention it could explain why people with PTSD report more negative, emotionally intrusive involuntary memories cued either by their internal thoughts or by environmental stimuli that lead to involuntary memories (Berntsen et al., 2003). We have two attention-related predictions: (1) that the attention network, which includes superior parietal cortex and DLPFC, will show decreased activity in PTSD (Hayes et al., 2009) in response to non-emotional memories, including voluntary memories and will show increased activity in response to emotional memories, and (2) there will be slowed activity in the involuntary memory network, reflecting a delayed retrieval time for all memories, including involuntary memories, but there will be an earlier peak of activity for regions associated with emotion, like the amygdala.

To test these hypotheses, we induce involuntary memories of negative and neutral scenes in people with PTSD and controls. We use a similar paradigm as that described in Chapter 2, with slight modifications. Here, there is no voluntary memory condition and scene images are from the International Affective Picture Set (IAPS) and have normed emotional valence ratings. Neural activity from two time periods are analyzed: that associated with the time period during which the sound is playing (early) and that associated with the time period after the sound has stopped playing (late). This design will allow us to test disturbances in involuntary memory in PTSD, and in particular allow us to arbitrate between deficits in memory, emotion regulation, and internally-oriented attention systems.

4.2 Methods

4.2.1 Participants

57 participants (35 women, mean age = 21.9 years, range = 18–37 years) completed the scan session. They were recruited through the Duke subject pool, through flyers, and through DukeList, a website used to advertise goods and services available to the Duke community. All participants included in the final analysis were right-handed, fluent English speakers with normal or corrected-to-normal vision. Six participants were excluded because of excessive head motion during the fMRI session (20% or more of their total scans with > 3 mm of movement), three were removed because they had ten or fewer memories, four were removed because they had no more than three trials with low effort ratings (1 or 2 out of 8), one was removed because he was left-handed, and one was removed because she did not follow task instructions. This resulted in a between-subjects

design consisting of 21 participants in the PTSD group (15 women, mean age = 21.5 years, range = 18-31 years) and 21 in the control group (14 women, mean age = 22.1 years, range = 18–37 years). Participants gave written informed consent for a protocol approved by the Duke University Institutional Review Board. Participants were paid $25/hour or were given the option of receiving course credit for the non-fMRI sessions if they were students.

Participants were all screened for PTSD by a staff member trained at the Veteran's Administration Hospital to administer the Clinician Administered PTSD Scale (CAPS). All participants in the PTSD group met criteria for a PTSD diagnosis. All participants in both groups had an A1 trauma.

4.2.2 Materials

We used 55 scenes and 95 environmental sounds (e.g., woman sneezing, lawn mower starting) were used. The images were obtained the International Affective Picture System (Lang et al., 2005). The sounds were obtained from multiple sources, including the SUN database (groups.csail.mit.edu/vision/SUN/) and the internet. All sounds were calibrated to be of equal volume and equal duration (4 sec). As part of the retrieval manipulation, versions of the sounds were produced in which the sounds were panned 15 degrees to the left or to the right.

4.2.3 Experimental Design and Procedure

As the experimental design and procedure is nearly identical to that described in Chapter 2 (S. A. Hall et al., 2014), here we reproduce the experimental design and

procedure with modifications to fit the current study. Differences from the previous design are indicated in **bold.**

4.2.3.1 Session 1: Two days before scan

Two days before scanning, participants encoded the **55** paired and **40** unpaired sounds outside the scanner (see Figure 9). To disguise the later involuntary memory task, participants were told that they were participating in a study investigating how pairing sounds with pictures affects performance on a later sound localization task. To ensure strong memory associations, there were **four** encoding runs, all of which were self-paced. Each encoding run was intended to increase in difficulty to enhance the deepness of encoding. The order was as follows: (i) each sound was presented simultaneously with a picture and participants typed a sentence integrating the pair into a plausible story, (ii) each sound–picture pair was presented with the subject-generated sentence and participants edited the sentence if they wished, (iii) each sound was presented alone, during which participants were instructed to recall the associated sentence and imagine the corresponding picture while the sound played, immediately followed by a presentation of the sound–picture pair and **(iv) each sound was presented alone, during which participants were again instructed to recall the associated sentence and imagine the corresponding picture, followed by an 2 second pause, followed by a presentation of the sound–picture pair**. After encoding the sound–picture pairs, participants encoded 40 unpaired sounds and rated how distinguishable each sound was from the previous sounds they had heard on a 7-point scale.

An attempt was made to pair pictures with some semantic relevance to the sound, but that could not be described by simply describing the sound. This was done so that when participants were later asked to recall the pictures, it would not be possible for a description of the sound to be confused with a description of the picture. We blocked the paired and unpaired sounds during the initial encoding session to separate them and thereby improve memory of whether the sounds had an associated picture. The unpaired sounds followed the paired sounds so that when participants did the distinguishability judgment on the unpaired sounds, they would have heard all of the paired sounds. This task was intended to decrease the likelihood of the participant confusing paired and unpaired sounds and later erroneously recalling pictures to the unpaired sounds. We accepted this lack of randomization because it was unlikely to interact with the questions of interest.

4.2.3.2 Session 2a: During scan

Two days after encoding, participants were run in an fMRI session. The fMRI session consisted of a resting state run, a re-encoding of paired and unpaired sounds (two runs) followed by the critical sound localization/memory recall runs (two runs), and ending with a final resting state run. Before the scan, participants briefly practiced the re-encoding and sound localization tasks, described below, to ensure that participants were comfortable with the response choices and the pace.

During the re-encoding runs, each sound-picture pair and unpaired sound was presented and **participants rated on a 7-point scale how emotional the stimuli were**. The pairs were presented for 4 sec and followed by a **2.5**-sec response period during

which the stimuli disappeared and a response scale appeared, and then followed by a fixation period (jittered with a mean of 4 sec). The stimuli were randomly intermixed. **The stimuli were presented in two different orders, one of which was the reverse of the other.**

During the recall runs, the **55 paired and 40 unpaired sounds** (randomly intermixed) were presented, panned 15 degrees to either the left or the right using specialized audio software (Audacity, audacity.sourceforge.net/). **The stimuli were presented in two random orders, one of which was the reverse of the other**. The order was different from that used during encoding. Participants were instructed to use their index finger to press the button corresponding to the side on which the sound was louder (i.e., the direction from which the sound seemed to originate). Each sound was presented for 4 sec, followed by a **1.5**-sec response period, during which the screen was blank and participants did the sound localization judgment, and then followed by a fixation period (jittered with a mean of 4 sec). Participants were instructed at the beginning of the run to wait until after the sound had ended to make their response. Participants were told that having an image come to mind spontaneously was fine but they should not try to recall the images intentionally. This instruction was necessary because pilot evidence suggested that participants might try to recall pictures even though the instructions did not require it.

4.2.3.3 Session 2b: Post-scan

Immediately following the scanning session, participants completed a post-scanning questionnaire to assess their memory for the pictures. At a computer terminal

outside the scanning room, participants were presented with all 95 sounds (55 paired and 40 unpaired, randomly intermixed) on stereophonic headphones. After the presentation of each sound, participants were asked whether they had remembered a picture when the sound was played during the sound localization task (yes/no), **how hard they tried to perform the sound localization task (1 = did not try at all, 7 = tried very hard)**, how hard they tried to recall a picture during the scan (1 = did not try at all, 7 = tried very hard), and how vivid the memory of the picture was during the scan (1 = not at all vivid, 7 = very vivid).

Next, the 55 paired sounds were presented a final time and participants were asked to provide a description of the picture originally presented with the sound. This was to provide a final check that the picture that participants recalled was the original picture that had been paired with the sound.

A week later, participants returned to answer follow-up questions. They were asked to again write a description of the picture and were asked whether a memory of the picture had come to them spontaneously during the last week, how intense their emotions were when the picture was remembered, what the valence of their emotions was, whether they had a physical reaction to the memory, what cued the memory, and whether the picture was similar to a trauma or negative event they had experienced. These follow-up data are not included in these analyses and will not be discussed further.

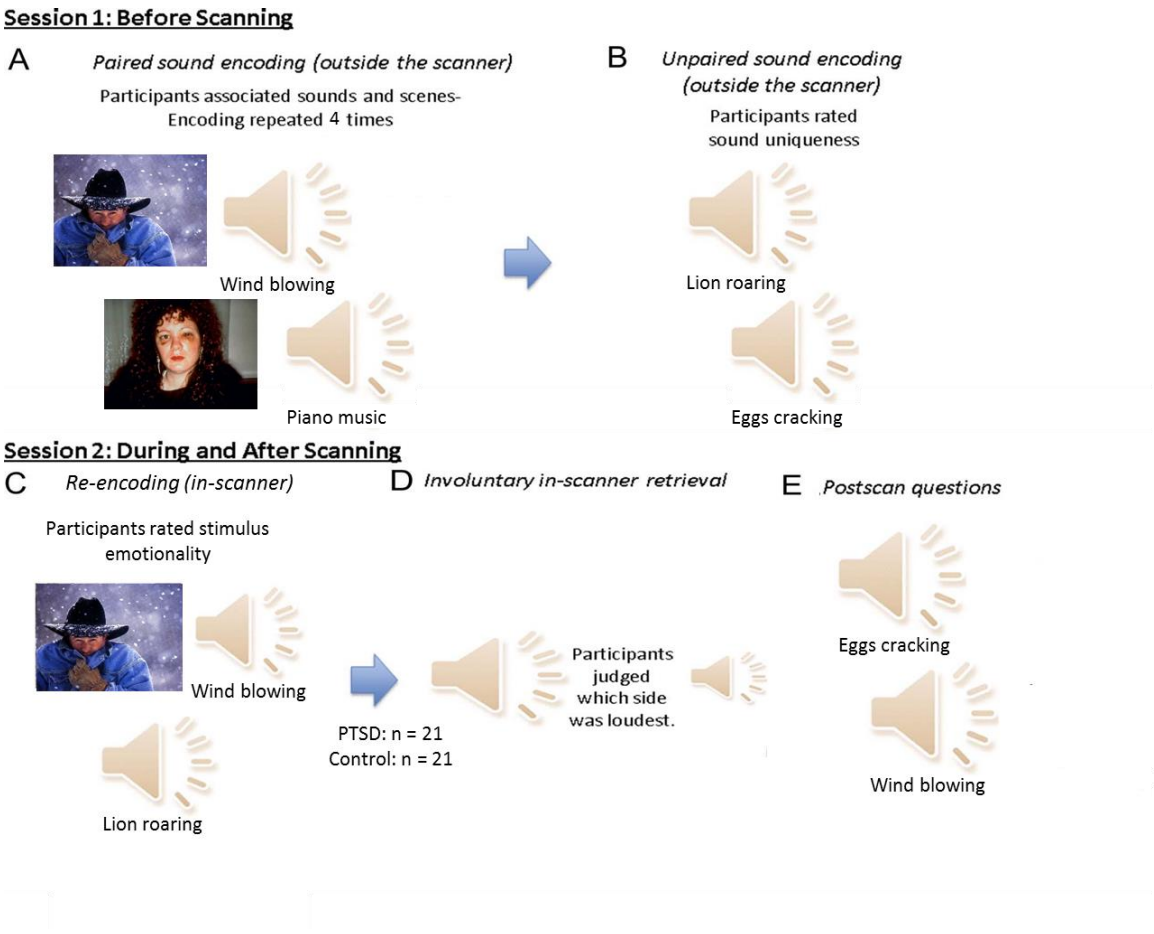

Figure 9: Behavioral paradigm. During prescan encoding, participants heard a sound paired with a picture and were asked to type a sentence linking the sound and picture. (B) During another prescan encoding session, participants heard unpaired sounds and rated the uniqueness of the sound. (C) On Day 2, participants performed a "re-encoding" session in the scanner, whereupon they were presented with previous sound–picture pairs and asked to rate on a 7-point scale emotional the stimuli were. (D) Participants subsequently heard both paired and unpaired sounds and were asked to judge where the sound was located (left or right). (E) After the scan, all participants heard all sounds and were asked questions about their experiences in the scanner (see text for postscan questions details).

4.2.4 Image Acquisition and Preprocessing

Imaging was conducted on a 3T GE Signa Excite MRI scanner (GE Healthcare, Waukesha, WI) with an eight channel head coil. Head motion was minimized with foam

pads and a headband, and participants wore earplugs to reduce scanner noise. The imaging sequence included a 3D plane localizer, followed by T1-weighted structural image and four runs of T2*-weighted (functional). The two encoding runs were followed by two retrieval runs; a resting state scan (360 sec) was acquired before the first encoding run and after the final retrieval run. The resting state and encoding runs were analyzed separately and will not be discussed further. Slice orientation was near-axial, parallel to the anterior–posterior commissure (AC-PC) plane. The T1-weighted anatomical images were 96 contiguous slices acquired with a high-resolution, 3D fast inverse recovery-prepared spoiled gradient recalled (SPGR) sequence, with repetition time (TR) = 3.22 msec, echo time (TE) = 8.2 msec, inversion recovery time (TI) = 450 msec, field of view (FOV) = 240 mm, 1 mm slice thickness, flip angle = 12°, voxel size = 0.9375 x 0.9375 x 1.9 mm, 256 × 256 matrix, and a parallel imaging with a selection factor of 2. The T2*-weighted echo-planar, functional images were sensitive to the BOLD signal. These were 34 contiguous slices acquired using a spiral-in sequence using sense imaging with a sense of 2, with TR = 2000 msec, TE = 30 msec, FOV = 240 mm, 3.8 mm slice thickness, flip angle = 70°, voxel size = 3.75 x 3.75 x 3.8 mm, and 64 × 64 matrix.

Preprocessing and analyses of functional imaging data were conducted with Statistical Parametric Mapping software (SPM12; Wellcome Department of Cognitive Neurology, London, UK), along with locally developed Matlab (Mathworks, Natick, MA) scripts. The first three volumes of each run, which includes the first trial of each run, were discarded for scanner stability. The discarded trials for each run will also be excluded from behavioral analyses. Images were corrected for slice-timing and head

motion, spatially normalized to the Montreal Neurological Institute template using a 12-parameter affine model, and then spatially smoothed with an 8-mm Gaussian kernel. A high-pass filter was included in every model to correct for scanner drift.

4.2.5 fMRI Data Analysis

Two GLM models were performed: a Memory model comparing paired and unpaired sound trials and an Emotion model comparing high and low emotional valence trials. In the Memory model, the first level model included regressors for paired sound trials in which there was a reported memory and a low effort rating (1 or 2 out of 7), and unpaired sound trials for which there was no reported memory and a low effort rating. These trials were split according to sound lateralization (paired left, paired right, unpaired left, and unpaired right) to account for this additional variance. The sound lateralization factor was collapsed at the second level. In both models all high effort trials, paired sound trials that did not elicit a memory, and unpaired sound trials that did elicit a memory trials were included as trials of no interest, as well as regressors accounting for motion and run-level effects.

In the Emotion model, IAPS ratings of valence were used. We considered ratings from 1.0-3.5 to be negative, 3.6-5.5 to be neutral, and 5.6-9.0 to be positive. Only negative and neutral pictures were included in this study. At the first level, regressors were included for high emotion, low effort paired sounds that elicited a memory and low emotion, low effort paired sounds that elicited a memory. Only paired sounds were used in this model because unpaired sounds did not have a paired picture from which IAPS

ratings could be used to classify it as high or low emotion, and therefore were included as trials of no interest.

Activations were initially identified using a finite impulse response (FIR) model (Goutte, Nielsen, & Hansen, 2000; R. Henson, Rugg, & Friston, 2001), which was preferred over a standard canonical hemodynamic response (HDR) model to better understand the temporal dynamics of involuntary memory retrieval. Seven TRs, or 14 seconds, starting at the beginning of the trial, not adjusted for the hemodynamic lag, were initially modeled. The FIR model revealed that activity was usually similar in the in the 3rd and 4th time points, which corresponded to the time that the sound was playing, accounting for hemodynamic lag, and similar in the 5th and the 6th time points, which corresponded to the four seconds after the offset of the sound, accounting for hemodynamic lag. We therefore created a model in which the 3rd and 4th time points were combined to create an early time point, and the 5th and the 6th time points were combined to create a late time point. The 1st, 2nd, and 7th time points were not analyzed. In all cases, the significance threshold is $p < 0.001$ (uncorrected) with a minimum cluster size of 10 contiguous voxels. Regions that survive FDR correction are indicated with an asterisk in the tables.

4.3 Results

4.3.1 Behavioral Results

Scores on the CAPS, an assessment of PTSD symptomology, significantly differed between groups ($t(40) = -10.3$, $p < 0.001$). The mean CAPS score for the PTSD group was 54.3 (SD = 15.9) and for the control group was 11.3 (SD = 10.8).

4.3.1.1 Memory model: Paired > unpaired

All behavioral results for paired > unpaired sounds are reported in Table 13. As the localization task was intended to draw attention to the sound, all trials in which there was a response to the localization task are included in this analysis, regardless of effort or whether the trials elicited memories. Collapsing across both group and pairing, performance was better than chance ($t(83) = 3.1$, $p < 0.01$). An ANOVA revealed no main effect of pairing or group and no interaction (p's > 0.05). Next, we checked effort ratings on this task. If participants were trying to do the localization task, they would necessarily have been paying attention to the sounds. All average effort ratings were between 4 and 5. An ANOVA revealed no main effects of group or pairing, and no interaction (p's > 0.05). As the highest effort rating possible was 7, this indicates that participants were trying to do the localization task, and therefore listening to the sounds.

Since only low effort trials were analyzed in the fMRI data, the rest of the behavioral results will only be reported on those trials. Participants in the control group remembered an average of 30.0 memories for the paired sounds (SD=12.9, average % recalled = 64.9%, SD = 25.3%) and 1.6 memories for the unpaired sounds (SD=2.1, average % recalled = 5.6%, SD = 7.3%). Participants in the PTSD group remembered and average of 37.0 memories for the paired sounds (SD = 12.1, average % recalled = 80.7%, SD = 22.4%) and 2.6 memories for the unpaired sounds (SD = 2.1, average % recalled = 9.5%, SD = 11.3%). An ANOVA revealed a main effect of pairing ($p < 0.001$), a main effect of group ($p < 0.05$), but no interaction ($p > 0.05$), indicating that PTSD participants had more involuntary memories than controls.

For the rest of the behavioral analyses, since only paired sounds that elicited a memory and unpaired sounds that did not elicit a memory were included in neural analyses, only those trials will be included in behavioral analyses. An ANOVA revealed higher emotion ratings and vividness for paired sounds ($p < 0.001$) but no main effect of group or interaction (p's > 0.05). Further, there was no difference in reaction time between groups, pairing, and no interaction (p's > 0.05). Notably, participants were told to wait to respond to the localization task after the sound had stopped playing. Reaction times are measured from the beginning of the response period, not the beginning of the sound, indicating that reaction times may provide inaccurate measures of processing speed.

Table 13: Memory model behavioral results.

	Localization Accuracy		Localization Effort		% Recalled		Emotion		Vividness		Reaction Time	
	Average	SD	Average	SD	Average	SD	Average	SD	Average	SD	Average	SD
Control												
Paired sounds	53.3%	13.5%	4.3	1.9	64.9%	25.3%	4.1	1.2	4.5	1.4	690.1	231.5
Unpaired sounds	54.2%	17.1%	4.3	1.9	5.6%	7.3%	2.5	1.2	1.1	0.4	745.4	223.2
PTSD												
Paired sounds	56.5%	9.7%	4.6	1.6	80.7%	22.4%	4.2	0.7	5.3	1.3	734.5	138.6
Unpaired sounds	54.3%	14.0%	4.7	1.9	9.5%	11.3%	2.4	0.8	1.1	0.2	748.2	157.0
ANOVA	F-score	p	F-score	p	F-score	p	F-score	p	F-score	p	F-score	p
Main effect of group	0.1	>0.05	0.8	>0.05	6.2	<0.05*	0.1	>0.05	2.8	>0.05	0.3	>0.05
Main effect of pairing	0.3	>0.05	0	>0.05	270.0	<0.001**	58.7	<0.001**	309.5	<0.001**	0.7	>0.05
Interaction	0.2	>0.05	0	>0.05	2.3	>0.05	0.2	>0.05	3.4	>0.05	0.2	>0.05

4.3.1.2 Emotion model: High > low emotion

Next, behavioral results for high emotion compared to low emotion paired sounds are presented. All behavioral analyses for high > low emotion sounds are reported in Table 14. Pictures with IAPS valence scores of 1.0-3.5 are negative, or high emotion, and those with IAPS valence scores of 3.6-5.5 are neutral, or low emotion. Performance on the localization task is significantly better than chance ($t(83) = 3.4$, $p = 0.001$) collapsed across high and low emotion paired sounds. An ANOVA revealed no main effect of emotion or group and no interaction (p's > 0.05). Effort on the localization task and effort was between 4 and 5 for all conditions and there was also no main effect of emotion or group and no interaction (p's > 0.05).

The average number of memories retrieved for high emotion trials for the control group was 19.0 (SD = 8.5, average percent: 55.4%, SD = 24.8%), and for low emotion trials was 11.0 (SD = 5.0, average percent: 57.6%, SD = 26.0%). For the PTSD group, the average number of memories retrieved for high emotion trials was 24.3 (SD = 8.2, average percent: 70.1%, SD = 23.5%) and for low emotion trials was 12.7 (SD = 4.3, average percent: 66.5%, SD = 22.5%). An ANOVA based on average percent revealed a main effect of group ($p < 0.05$), but no main effect of emotion ($p > 0.05$), and no interaction ($p > 0.05$). This indicates that people with PTSD had more memories to both paired and unpaired sounds than controls did and that both groups had more memories for high emotion trials than low emotion trials.

For vividness ratings an ANOVA revealed a main effect of group $p < 0.05$), but no main effect of emotion or interaction (p's > 0.05). This indicates that people with PTSD experience involuntary memories as more vivid, regardless of emotion. Reaction times were not different for group or emotion, nor was there an interaction (p's > 0.05).

Table 14: Emotion model behavioral results.

	Localization Accuracy		Localization Effort		% Recalled		Vividness		Reaction Time	
	Average	SD	Average	SD	Average	SD	Average	SD	Average	SD
Control										
High emotion	54.0%	15.0%	4.2	2.0	55.4%	24.8%	4.6	1.4	694.8	235.1
Low emotion	52.8%	16.1%	4.3	1.9	57.6%	26.0%	4.4	1.5	693.4	289.5
PTSD										
High emotion	56.7%	10.1%	4.6	1.7	70.1%	23.5%	5.4	1.3	737.6	151.5
Low emotion	56.3%	12.0%	4.6	1.6	66.5%	22.5%	5.1	1.5	732.4	150.8
ANOVA	F-score	p	F-score	p	F-score	p	F-score	p	F-score	p
Main effect of group	1.1	>0.05	0.8	>0.05	5.0	<0.05*	5.6	<0.05*	0.8	>0.05
Main effect of emotion	0.1	>0.05	0	>0.05	0.02	>0.05	0.7	>0.05	0.005	>0.05
Interaction	0.02	>0.05	0	>0.05	0.02	>0.05	0.1	>0.05	0.002	>0.05

4.3.2 Neuroimaging Results

Activity during two time periods was analyzed: the time period corresponding with the four seconds while the sound was playing (early) and the time period corresponding with the four seconds following the offset of the sound (late). All paired sounds analyzed are paired sounds in which a memory occurred with low effort. All unpaired sounds analyzed are unpaired sounds in which a memory did not occur with low effort.

4.3.2.1 Memory model: Paired versus unpaired sounds

First described are results from the memory model comparing paired sounds > unpaired sounds, characterizing activity associated with involuntary memory retrieval.

4.3.2.1.1 Group effects

The main effect of Group will reveal differences between groups within the memory network, allowing us to test our memory hypotheses. Since the number of memories retrieved was not diminished for PTSD, we predict that the involuntary memory network will remain intact in the PTSD group. Using the activity that was significant for the main effects of Group F-test as a mask, the PTSD group showed no activity greater than the control group. For control > PTSD, there was activity in the superior parietal cortex and postcentral gyrus (Figure 10, Table 15). This suggests that not only is there no difference in the hippocampus, there is no difference in regions

typically involved in the involuntary memory network, including parahippocampal gyrus, inferior parietal cortex, PCC, and precuneus (S. A. Hall et al., 2014).

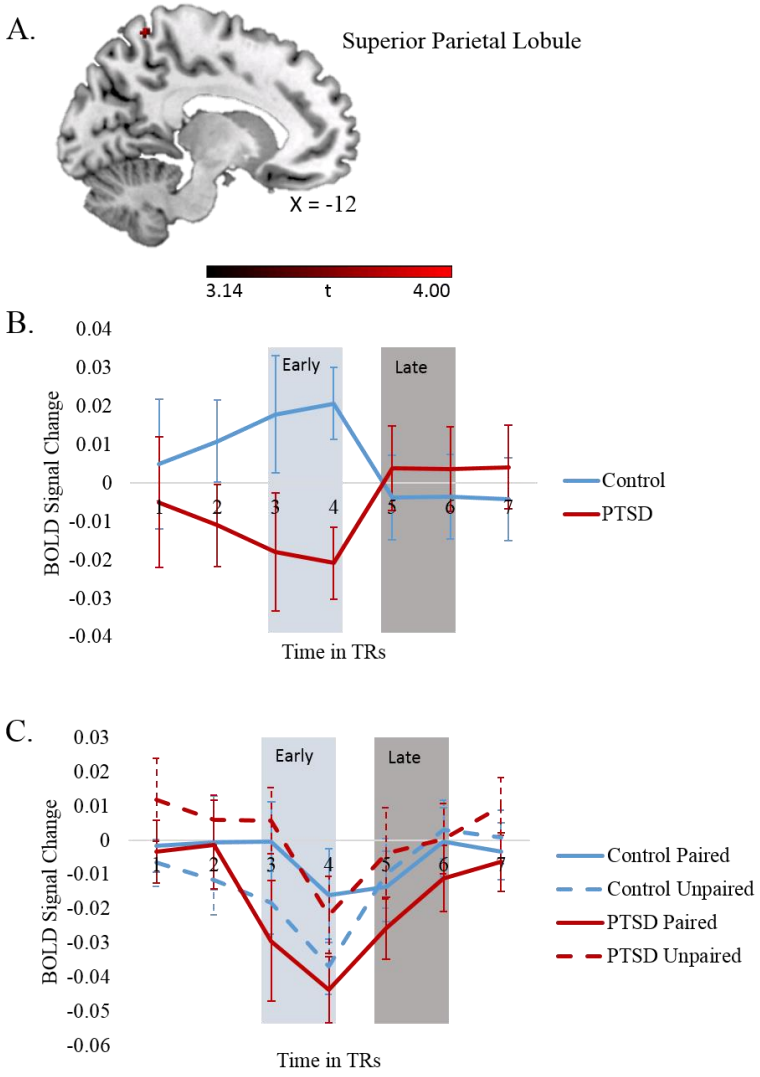

Figure 10: Memory model. Main effect of Group (PTSD versus Control). All activity is significant at p < 0.001 with a cluster size of 10. A. Significant activity in the superior parietal lobule. B. Time courses plotting paired > unpaired differences at each TR for regions of interest shown above. Each TR is 2 seconds. The first, second, and seventh TRs were not included in any analyses and are included for illustrative purposes only. Activity relating to the early and late time points are indicated with

light and dark gray boxes over the respective time points. These graphs indicate that the paired > unpaired sound difference in this region is greater for the control group than the PTSD collapsed across both timepoints. C. The timecourses for each region of interest are plotted for paired and unpaired sounds separately for both groups.

Table 15: Memory model. Main effect of Group (PTSD versus Control). All results are significant at p < 0.001 with a cluster size of 10. Regions that survive FDR correction are indicated with an asterisk.

Region	*Cluster Size*	*Lat*	*x*	*y*	*z*	*t-score*
Control > PTSD						
Postcentral gyrus	66	Right	16	-44	72	4.62
Superior parietal lobule	10	Left	-12	-54	68	3.74
PTSD > Control						
None						

4.3.2.1.2. Group x Time interaction

Results from the Group x Time interaction address our hypothesis that a lack of attentional resources slows the retrieval of involuntary memories in PTSD. Using the activity in the interaction F-test as a mask, we looked at the Group x Time interaction with control early > late and PTSD late > early. Right parahippocampal gyrus, hippocampus, PCC, precuneus, inferior parietal cortex, right DLPFC, VLPFC, ACC, and midcingulate were active in this contrast (Figure 11, Table 16). The reverse revealed no significant activity. As parahippocampal gyrus, inferior parietal cortex, PCC, and precuneus make up the important nodes of the involuntary memory network (S. A. Hall et al., 2014), this is consistent with our hypothesis that the PTSD group would have delayed activity in involuntary memory network regions.

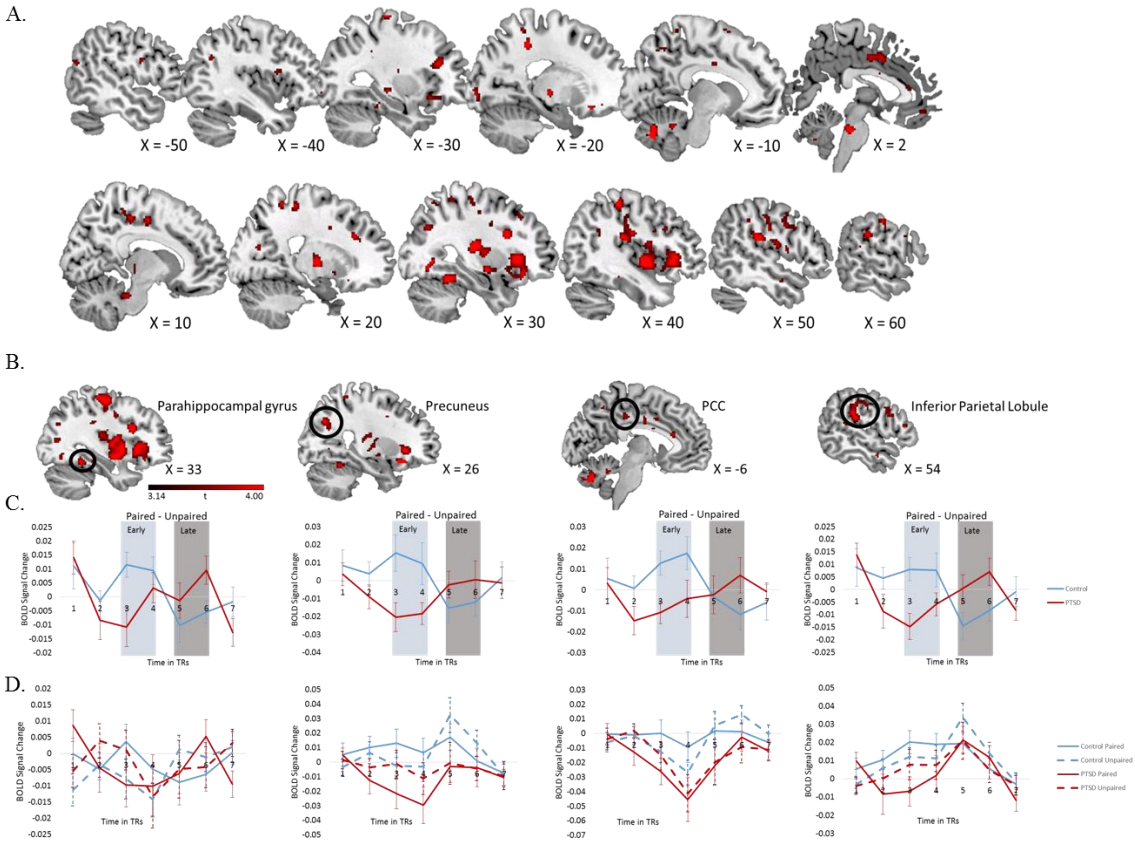

Figure 11: Memory model. Group (PTSD, Control) x Time (Early, Late) interaction. All activity is significant at $p < 0.001$ with a cluster size of 10. A. Significant activity across the whole brain. B. Regions of theoretical interest are highlighted: the parahippocampal gyrus, the precuneus, the posterior cingulate cortex, and the inferior parietal lobule. These regions are active in both groups at different times. C. Timecourses plotting paired > unpaired differences at each TR for regions of interest shown above. Each TR is 2 seconds. The first, second, and seventh TRs were not included in any analyses and are included for illustrative purposes only. Activity relating to the early and late time points are indicated with light and dark gray boxes over the respective time points. These graphs indicate that the paired > unpaired sound difference is greater for the control group than the PTSD group during the early time point but that this difference is greater for the PTSD group than the control group in the late time point. D. The timecourses for each region of interest are plotted for paired and unpaired sounds separately for both groups.

Table 16: Memory model. Group (PTSD, Control) x Time (Early, Late) interaction.All results are significant at p < 0.001 with a cluster size of 10. Regions that survive FDR correction are indicated with an asterisk.

Region	*Cluster Size*	*Lat*	*x*	*y*	*z*	*t-score*
Control Early > Late and PTSD Late > Early						
Claustrum*	688	Right	26	22	-16	5.04
Insula*		Right	38	24	-2	4.16
VLPFC (Inferior frontal gyrus)*		Right	32	30	-12	3.97
Putamen*		Right	30	14	-8	3.50
Cerebellum*	221	Left	-10	-72	-36	5.01
Claustrum*	2189	Right	38	-2	-2	4.67
Insula*		Right	50	-26	22	4.48
Thalamus*		Right	20	-12	4	4.35
Postcentral gyrus*		Right	40	-30	54	4.27
Precentral gyrus*		Right	34	-16	56	4.21
Putamen*		Right	34	-4	-10	4.20
Supramarginal gyrus*		Right	58	-30	28	4.14
Superior temporal gyrus*		Right	56	-38	16	3.75
Cerebellum*	148	Right	14	-38	-26	3.74
VLPFC (Inferior frontal gyrus)*	131	Right	40	18	30	3.63
Fusiform gyrus*	126	Right	30	-48	-18	4.49
Lateral globus pallidus*	100	Left	-22	-16	-2	4.45
Putamen*		Left	-30	-22	-4	3.77
Orbitofrontal cortex*	141	Left	-20	26	-16	4.24
VLPFC (Inferior frontal gyrus)*		Left	-32	22	-12	4.11
Lingual gyrus*	100	Left	-16	-94	0	4.19
Mid cingulate cortex*	293	Right	6	-8	44	4.17
Anterior cingulate cortex*	46	Right	18	28	30	4.15
Lateral globus pallidus*	57	Right	16	10	-8	4.13
Middle temporal gyrus*	35	Right	44	-58	-6	4.08
Precuneus*	171	Right	26	-68	32	4.06
Cuneus*		Right	18	-72	18	3.88
DLPFC (Middle frontal gyrus)*	114	Left	-32	28	22	4.03
Fusiform gyrus*	57	Right	30	-68	-6	4.01
Precentral gyrus*	15	Left	-30	-24	68	4.01
Paracentral lobule*	177	Right	14	-36	58	3.99

VLPFC (Inferior frontal gyrus)*	21	Left	-48	-2	24	3.96
Mid cingulate gyrus*	30	Right	22	4	38	3.93
Supramarginal gyrus*	34	Left	-44	-38	28	3.93
VLPFC (Inferior frontal gyrus)*	16	Right	56	28	14	3.91
Precuneus*	63	Right	18	-48	60	3.90
Postcentral gyrus*		Right	28	-44	60	3.73
Postcentral gyrus*	56	Left	-18	-46	62	3.86
Hippocampus*	17	Right	36	-30	-16	3.86
Anterior cingulate cortex*	70	Left	-4	26	18	3.85
Cerebellum*	41	Left	-10	-48	-26	3.83
Thalamus*	28	Right	12	-24	4	3.78
Lingual gyrus*	22	Left	-14	-70	2	3.77
VLPFC (Inferior frontal gyrus)*	158	Right	48	2	34	3.76
Middle temporal gyrus*	14	Right	52	-2	-22	3.75
Cuneus*	24	Right	34	-74	10	3.74
DLPFC (Middle frontal gyrus)*	28	Right	32	-4	38	3.72
Precuneus*	40	Left	-14	-62	50	3.72
Posterior cingulate cortex*	21	Left	-6	-30	40	3.69
Claustrum*	35	Left	-36	-2	8	3.69
VLPFC (Inferior frontal gyrus)*	14	Right	48	36	20	3.69
Parahippocampal gyrus*	20	Left	-28	-34	-22	3.64
Hippocampus*		Left	-32	-32	-14	3.55
Supramarginal gyrus*	15	Left	-40	-60	30	3.64
Parieto-occipital cortex*	15	Left	-50	-68	22	3.64
DLPFC (Middle frontal gyrus)*	19	Right	30	26	44	3.58
Caudate*	23	Left	-24	-18	14	3.57
DLPFC (Superior frontal gyrus)*	11	Left	-12	2	68	3.57
Insula*	19	Left	-40	10	16	3.57
Anterior cingulate cortex*	19	Right	2	46	-12	3.50
Superior parietal lobule*	10	Right	30	-62	56	3.50
VLPFC (Inferior frontal gyrus)*	10	Right	48	18	16	3.50
Supramarginal gyrus*	10	Right	38	-52	30	3.47

Control Late > Early and PTSD Early > Late

None

4.3.2.1.3 Time effects

An analysis of the main effects of Time will reveal activity common to both groups that differs across timepoints. This will allows us to address the attention hypothesis that activity in memory network regions will peak at different times. Using the regions that were active in the F-test for the main effect of Time as a mask, early > late across both groups elicited activity in the retrosplenial cortex, and PCC. Late > early elicited activity in the cerebellum (Table 17). Although the majority of the involuntary memory network is delayed in PTSD, PCC and retrosplenial activity is not. This finding may represent intact search processes beginning early in both groups (Daselaar et al., 2008).

Table 17: Memory model. Main effect of Time (Early versus Late). All results are significant at p < 0.001 with a cluster size of 10. Regions that survive FDR correction are indicated with an asterisk.

Region	*Cluster Size*	*Lat*	*x*	*y*	*z*	*t-score*
Early > Late						
Cerebellum	132	Left	-10	-30	-10	4.79
Superior temporal gyrus	134	Left	-50	-20	6	4.49
Superior temporal gyrus	147	Right	52	-16	4	4.32
Retrosplenial cortex	67	Left	-10	-42	4	4.49
Posterior cingulate cortex	23	Left	-18	-56	22	3.84
Insula	12	Right	40	-24	8	3.63
Late > Early						
Cerebellum	23	Right	40	-68	-34	4.48

4.3.2.2 Emotion model: High versus low emotion

Next we turn to comparisons between high and low emotion, characterizing activity associated with emotional responses to involuntary memories while controlling for general involuntary memory retrieval. These analyses test hypotheses about the emotion network and the effects of attention on emotional processing.

4.3.2.2.1 Group effects

Comparing groups, using the regions that were active in the main effects of group F-test as a mask, PTSD > control across both time points elicited activity in VMPFC, ACC, superior parietal cortex, DLPFC, superior temporal cortex, and lentiform gyrus. For control > PTSD across both time points there was no activity (Figure 12, Table 18). These results are inconsistent with an interpretation of reduced emotional regulation in PTSD (see discussion).

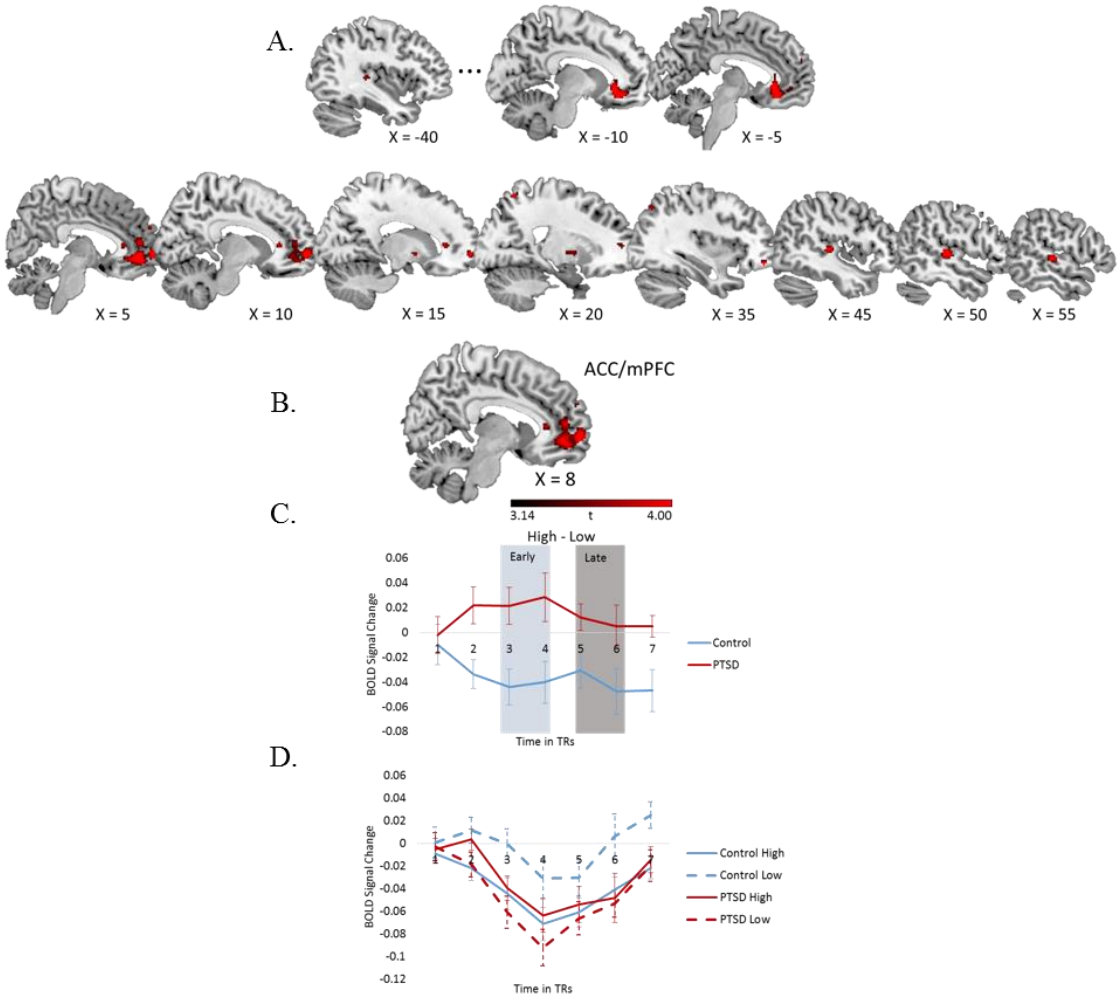

Figure 12: Emotion model. Main effect of Group (PTSD versus Control). All activity is significant at $p < 0.001$ with a cluster size of 10. A. Significant activity across the whole brain. B. A region of theoretical interest are highlighted: mPFC/ACC. This region is greater for both high and low emotion stimuli in the PTSD group compared to the control group. C. Time courses plotting high > low emotion differences at each TR for the mPFC. Each TR is 2 seconds. The first, second, and seventh TRs were not included in any analyses and are included for illustrative purposes only. Activity relating to the early and late time points are indicated with light and dark gray boxes over the respective time points. This graph indicates that the high > low emotion difference is greater for the control group than the PTSD group across both timepoints. D. The timecourses for the mPFC are plotted for high and low emotion stimuli separately for both groups.

Table 18: Emotion model. Main effect of Group (PTSD versus Control). All results are significant at p < 0.001 with a cluster size of 10. Regions that survive FDR correction are indicated with an asterisk.

Region	*Cluster Size*	*Lat*	*x*	*y*	*z*	*t-score*
Control > PTSD						
None						
PTSD > Control						
Anterior cingulate cortex*	901	Left	-8	30	-4	4.80
Anterior cingulate cortex*		Right	2	34	-6	4.19
Ventral medial prefrontal cortex*		Right	8	62	-2	4.58
Superior temporal gyrus*	119	Right	50	-24	4	4.70
Superior parietal lobule*	26	Right	22	-62	62	4.28
DLPFC (Middle frontal gyrus)*	21	Right	34	48	-14	4.21
Lentiform nucleus*	42	Right	16	2	-2	3.99
Corpus callosum*	53	Right	10	32	8	3.87
Ventral medial prefrontal cortex*	76	Left	0	60	22	3.85
Superior parietal lobule*	24	Right	34	-70	46	3.75
Superior temporal gyrus*	31	Left	-42	-28	6	3.70

4.3.2.2.2 Group x Time interaction

Using the regions that were active in the F-test for the interaction as a mask, the control group late > early and the PTSD group early > late revealed activity in amygdala, left VLPFC, precuneus, fusiform gyrus, insula, precentral gyrus, cuneus, lingual gyrus, uncus, claustrum, and striatum. The reverse interaction, with the control group early > late and PTSD group late > early revealed no activity (Figure 13, Table 19). The early activity in the amygdala in the PTSD group compared to the control group suggests that attentional processes in PTSD are hyperresponsive to emotional stimuli.

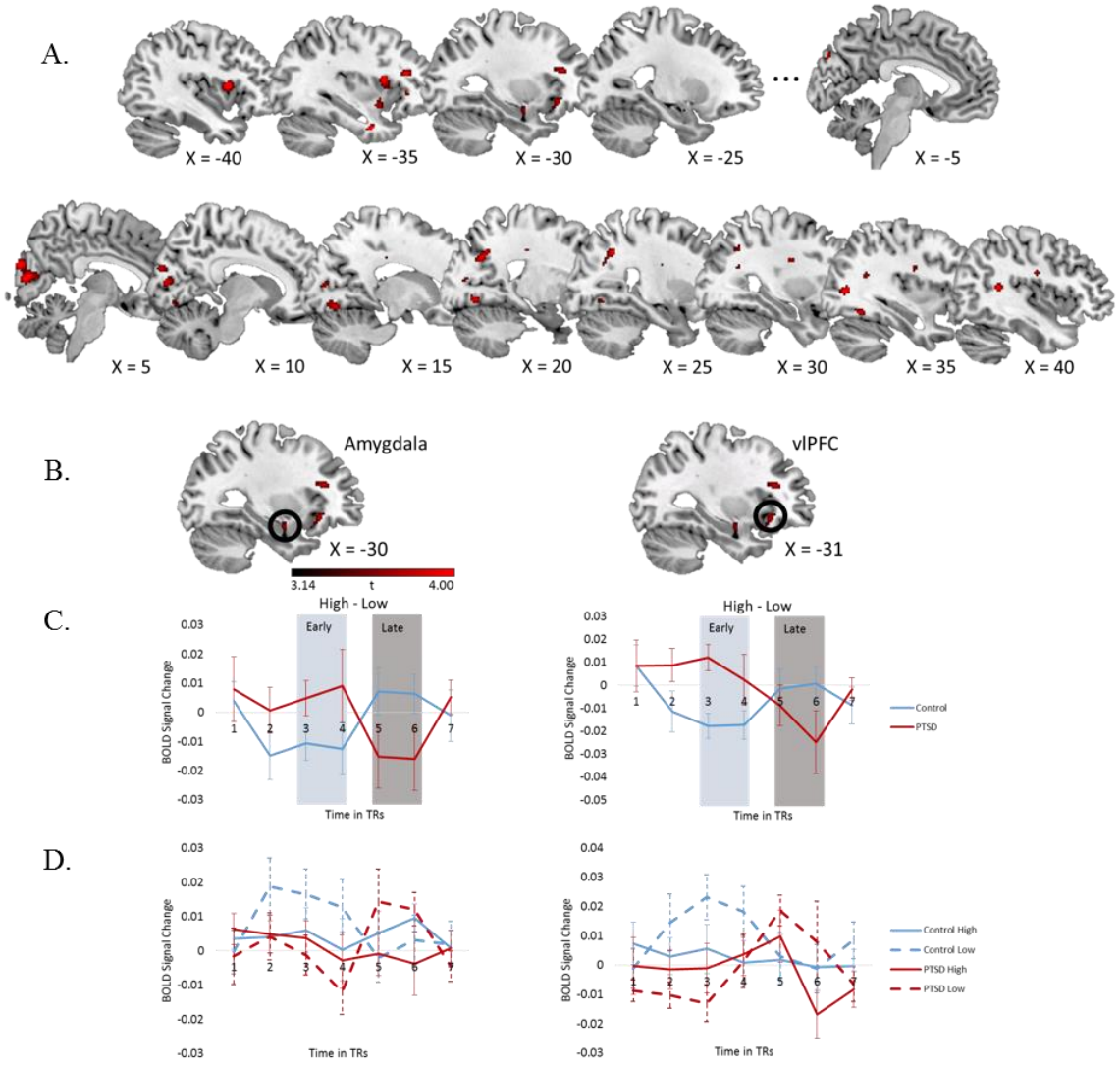

Figure 13: Emotion model. Group (PTSD, Control) x Time (Early, Late) interaction. All activity is significant at $p < 0.001$ with a cluster size of 10. A. Significant activity across the whole brain. B. Regions of theoretical interest are highlighted: the amygdala and the VLPFC. These regions are active in both groups at different times. C. Time courses plotting high > low emotion differences at each TR for the mPFC. Each TR is 2 seconds. The first, second, and seventh TRs were not included in any analyses and are included for illustrative purposes only. Activity relating to the early and late time points are indicated with light and dark gray boxes over the respective time points. These graphs indicate that the high > low emotion difference is greater for the PTSD group than the control group in the early timepoint

but greater for the control group than the PTSD group in the late timepoint. D. The timecourses for the amygdala and VLPFC are plotted for high and low emotion sounds separately for both groups.

Table 19: Emotion model. Group (PTSD, Control) x Time (Early, Late) interaction. All results are significant at p < 0.001 with a cluster size of 10. Regions that survive FDR correction are indicated with an asterisk.

Region	*Cluster Size*	*Lat*	*x*	*y*	*z*	*t-score*
PTSD Early > Late and Control Late > Early						
Insula	147	Left	-36	12	14	4.60
Precentral gyrus		Left	-44	2	8	3.84
Cuneus	352	Left	2	-80	12	4.35
Cuneus		Right	6	-86	24	4.27
Lingual gyrus		Right	18	-80	10	3.65
Uncus	25	Left	-34	0	-32	4.34
Lingual gyrus	37	Right	34	-72	6	4.15
Precuneus	149	Right	22	-64	30	4.04
Lingual gyrus	112	Right	18	-70	-8	4.03
Cuneus	13	Left	-6	-86	36	3.97
Fusiform gyrus	33	Right	36	-58	-14	3.95
Claustrum	39	Left	-36	6	-10	3.86
VLPFC (Inferior frontal gyrus)	27	Left	-28	26	-10	3.76
VLPFC (Inferior frontal gyrus)	10	Left	-32	32	0	3.64
Amygdala	16	Left	-30	-4	-18	3.60
PTSD Late > Early and Control Early > Late						
None						

4.3.2.2.3 Time effects

For both groups using the regions that were active in the main effect of Time F-test as a mask, early > late elicited activity in right VLPFC, and caudate, and late > early elicited activity in dorsomedial PFC, precuneus, inferior parietal cortex, and cerebellum (Table 20).

Table 20: Emotion model. Main effect of Time (Early, Late). All results are significant at p < 0.001 with a cluster size of 10. Regions that survive FDR correction are indicated with an asterisk.

Region	*Cluster Size*	*Lat*	*x*	*y*	*z*	*t-score*
Early > Late						
VLPFC (Inferior frontal gyrus)	10	Right	52	34	-4	3.77
Caudate	25	Left	-20	-6	26	3.75
Caudate	13	Left	-18	32	8	3.71
Late > Early						
Precuneus	90	Left	-12	-68	50	4.59
Dorsal medial prefrontal gyrus	87	Left	-8	-4	62	4.05
Cerebellum	54	Left	-32	-62	-38	3.97
Supramarginal gyrus	20	Right	38	-42	40	3.61

4.4 Discussion

Our study tested whether deficits in any of three systems—the memory system, the emotion system, and the attention system—could account for the differences in the way some involuntary memories are experienced in PTSD compared to controls. Our study yielded four main findings. First, the involuntary memory network remains intact in PTSD. Second, differences in activity during memory retrieval and the timing of this activity suggest that fewer attentional resources are devoted to involuntary memory retrieval during retrieval. Third, there was increased rather than decreased VMPFC activity in the PTSD group compared to the control group for high > low emotion stimuli. Fourth, there was hyperactivity in the superior parietal cortex and the DLPFC along with early activity in the emotion network for high > low emotion stimuli, suggesting

additional attentional resources are devoted to emotion processing in PTSD. These findings are discussed in more detail below.

4.4.1 Finding 1: Similarities in the memory network between PTSD and controls

Although there were increased involuntary memories in PTSD, involuntary memory systems, including hippocampus, parahippocampal gyrus, inferior parietal cortex, PCC, and precuneus, remained intact in PTSD. Though behavioral work has suggested that degraded encoding processes can explain some of the degradation in voluntary memory performance (Dickie, Brunet, Akerib, & Armony, 2008), this is unlikely to be the case here. Due to idiosyncrasies of our task, specifically the over-training of the sound-picture pairs that was necessary to ensure that participants would have enough involuntary memories to make an fMRI analysis feasible, learning/encoding was matched between the groups. Because of this match, our interpretations can be targeted at retrieval processes. The similarity in activity implies that automatic retrieval is not impaired in PTSD and therefore does not account for the difficulties that people with PTSD experience with involuntary memories. Since PTSD is associated with hypoactivity in memory network during voluntary retrieval (Carrion et al., 2010; Werner et al., 2009), but there is no such hypoactivity in involuntary memories, network integrity likely depends on whether or not retrieval is effortful.

4.4.2 Finding 2: Decreased attentional resources devoted to general memories

Though there was similar activity in the involuntary memory network between people with PTSD and controls, there was hypoactivity in the superior parietal cortex in the PTSD group compared to the control group. Emerging models of memory suggest that superior parietal cortex is involved in top-down attention to memory guided by retrieval goals, particularly by maintaining sustained, purposeful attention (R. Cabeza et al., 2008; R. Cabeza et al., 2011). Hypoactivty here suggests that people with PTSD devote fewer attentional resources to general memories collapsed across emotion rating. This is consistent with the idea that there are deficits in the attention system in PTSD and that these deficits are associated with declines in activity in the superior parietal cortex (Hayes et al., 2009). Our work extends these findings by showing activity in this region in response to a memory recalled involuntarily, and suggests that top-down post-retrieval attention to memories can happen even in response to unexpected retrieval.

Analyses also indicated a delay in activity in the involuntary memory network in the PTSD group compared to the control group. These findings are consistent with behavioral work that has found delayed response times during voluntary memory tasks (Werner et al., 2009). Further, voluntary memories also show delayed activity in the hippocampus in PTSD (St Jacques, Botzung, Miles, & Rubin, 2011). In an autobiographical memory study, participants were asked to remember positive and negative autobiographical memories. For positive autobiographical memory retrieval in

PTSD there was greater hippocampal activity during late phases of memory retrieval (i.e., elaboration) versus early memory retrieval, a pattern that was reversed in healthy controls. Our findings extend this current work by demonstrating that this processing delay can also occur cognitive tasks that do not require cognitive control, like involuntary memory retrieval.

Moores (2008) puts forth a model of PTSD positing that when the attentional load is low, neural activity associated with cognitive control, including top-down attention, is increased in PTSD compared to controls but when the attentional load is high, cognitive control activity is decreased. This could be because people with PTSD overcompensate when the cognitive load is low but there is a breaking point after which they can no longer sustain attention. This is supported by evidence showing that during a working memory task with emotional distracters, there is decreased DLPFC and parietal cortex activity in the PTSD group compared to the control group during the working memory task (Hayes et al., 2009; Morey et al., 2009; Morey, Petty, Cooper, Labar, & McCarthy, 2008). Other models posit that people with PTSD have decreased attentional control because they use their attentional resources to cope with internal psychological distress (DePrince & Freyd, 2004) or to monitor the environment for threats (Jennings, 1986). This draws attention away from non-threatening environmental stimuli. Our data are consistent with both of these models. Decreased activity in the superior parietal cortex could reflect decreased attentional resources available to people with PTSD to both

perform the localization task and simultaneously process the memory while the delay in memory network activity could reflect split attention.

4.4.3 Finding 3: Disrupted emotion regulation

The most surprising finding was that the PTSD group showed greater VMPFC activity for the high emotion stimuli versus the low emotion stimuli compared to the control group. One possible explanation for this hyperactivity is that the VMPFC is part of a rapidly responding emotional system that is active for nonconscious signals of fear responsible for reorienting attention to a threatening stimulus quickly (Bryant, Kemp, et al., 2008; Liddell et al., 2005). Evidence for this hypothesis is found in studies in which emotional stimuli presented sub-threshold elicit heightened VMPFC activity in people with PTSD compared to controls (Bryant, Felmingham, et al., 2008; Bryant et al., 2010; Bryant, Kemp, et al., 2008). Our data suggest that this alarm system is not only active for nonconscious fear but that it can also be active for unexpected fear signals. Like the current study, other studies in which emotional stimuli are presented unexpectedly, specifically during attention tasks with emotional and neutral distractors, found increased VMPFC in PTSD (Bruce et al., 2013; Fani et al., 2012; Shin et al., 2007; but see M. J. Kim et al., 2008). This suggests that the VMPFC quickly overcompensates for unexpected fear in the environment when it first occurs and then is unable to regulate that fear in the long-term.

This finding may seem contradictory to previous models of PTSD and fear regulation have posited that the VMPFC modulates fear extinction and emotion

regulation (Koenigs & Grafman, 2009). The VMPFC has been shown to downregulate activity in the amygdala; in PTSD, hypoactivity in the VMPFC leads to a hyperactive amygdala response to emotional stimuli (Shin, Rauch, & Pitman, 2006). However, many of the studies that find hypoactivation in the VMPFC use paradigms in which the emotional stimuli are expected and are the main focus of the task, like script-driven imagery studies (Bremner, Narayan, et al., 1999; Britton, Phan, Taylor, Fig, & Liberzon, 2005; Lanius et al., 2001; Lanius et al., 2003; Shin et al., 1999; Shin et al., 2004) and passive viewing of emotional pictures (Bremner, Staib, et al., 1999; Hou et al., 2007; Mazza et al., 2013; Phan, Britton, Taylor, Fig, & Liberzon, 2006; Shin et al., 2005; L. M. Williams et al., 2006). A different interpretation of the role of the VMPFC is that though the VMPFC is involved in emotion regulation and extinction processes, decreased VMPFC activity does not cause increased amygdala activity (Motzkin, Philippi, Wolf, Baskaya, & Koenigs, 2015). Consistent with this interpretation, a lesion study has shown that not only do VMPFC lesions not increase the likelihood of having PTSD symptoms, as would be predicted if hypoactivation in VMPFC caused hyperactivation in the amygdala, but they actually decrease the likelihood of developing PTSD (Koenigs & Grafman, 2009). The role of the VMPFC is multifaceted. It has been shown to be involved in self-referential thought (Motzkin et al., 2015; St Jacques, Conway, Lowder, & Cabeza, 2011), and the retrieval of contextual details and initiating subsequent action based on those details (Kveraga et al., 2011; Panichello et al., 2012). It is possible that hyperactivation in VMPFC that occurs in response to unexpected memories reflects the

initial recovery of contextual and self-referential information, a bottom-up process, but subsequent actions based on the recovery of these details, like emotion regulation, a process requiring cognitive control, is impaired.

4.4.4 Finding 4: Increased attentional resources devoted to emotional stimuli

Consistent with our hypothesis that attention processes would elicit increased activity in the attention network in response to emotional stimuli for PTSD, there is increased activity for high > low emotion stimuli in the DLPFC and superior parietal cortex in PTSD compared with controls, regions associated with the dorsal attention stream (Hayes et al., 2009). As some models of PTSD posit that attention is pulled away from external stimuli when it is not threatening, the converse is that threatening stimuli utilize additional attentional resources and that this results in hyperactivation of the dorsal attention stream (Aupperle, Melrose, Stein, & Paulus, 2012). The results shown here suggest that those threatening stimuli can come in the form of involuntary memories. The hyperactivation of regions associated with top-down attention in PTSD could partially explain why emotional memories feel so disturbing for people with PTSD.

Also consistent with our hypothesis that the increase in attentional resources that are devoted to processing emotional stimuli would lead to earlier processing of emotional stimuli, there was early activity in the amygdala in the PTSD group compared to the control group. A model of anxiety proposes just that (Bishop, Duncan, & Lawrence, 2004): that an oversensitivity of the fast thalamo-amygdala pathway leads to increased

bottom-up attention to emotional stimuli. One possible explanation for this early activity is that the amygdala has two afferent pathways. The first is a direct thalamo-amygdala pathway in which coarse input is quickly sent to the amygdala so if there is a threat, an automatic response can be made before too much time is spent processing the threat. The second is a thalamo-cortical-amygdala pathway that provides more detailed input but is slower (X. F. Li, Stutzmann, & LeDoux, 1996). Ours is not the only study to show early amygdala activity in PTSD in response to emotional stimuli. In a study investigating responses to emotional faces in youth with PTSD, the PTSD group had greater activity in the amygdala early in the trial compared to the control group but not late in the trial (Garrett et al., 2012). These results suggest that an overreliance on this faster pathway is not limited to interactions with external stimuli but extends to interactions with internal stimuli, like memories, as well.

While this amygdala activity peaked early in the PTSD group, it was not sustained. Though we did not have hypotheses about the time course of activity in the amygdala after its initial early peak, one possible explanation for the decrease in emotion-related activity is that the PTSD group was trying to avoid having emotional memories. People with PTSD avoid thinking about reminders of their trauma (Berntsen et al., 2003), they avoid engaging in active problem solving with regards to emotional thoughts (Moulds, Kandris, Starr, & Wong, 2007) and avoid emotionally processing memories (A. D. Williams & Moulds, 2007). Negative reinterpretations of intrusive memories, as well as rumination, suppression, and dissociation associated with these memories predict

worse symptoms of PTSD (Clohessy & Ehlers, 1999). In contrast, people who have recovered from PTSD or depression are more likely to use reappraisal and distraction rather than worry and self-punishment (Reynolds & Wells, 1999) in response to intrusive memories. People without PTSD are less likely to suppress or distract themselves after an involuntary memory (Reynolds & Brewin, 1998). Activity in the VLPFC, which peaked early in the PTSD group and late in the control group for high > low emotion stimuli, is consistent with the idea that people with PTSD were trying to avoid thinking about these negative memories. VLPFC is commonly active during emotion suppression (Beauregard, Levesque, & Bourgouin, 2001; Goldin, McRae, Ramel, & Gross, 2008; Wager, Davidson, Hughes, Lindquist, & Ochsner, 2008; for a review, see Ochsner, Silvers, & Buhle, 2012). It also is involved in memory suppression. In studies in which participants are instructed to try to not think about items they have previous encoded, no-think trials elicit activity in VLPFC, even when memories continue to come to mind (Anderson et al., 2004; Bastin et al., 2012; Butler & James, 2010; Depue, Curran, & Banich, 2007; J. P. Mitchell et al., 2007). Lesion studies have shown that patients with frontal lobe lesions have an impaired ability to suppress unwanted memories (Conway & Fthenaki, 2003). Emotion suppression and memory suppression are methods that could have been used to try to avoid thinking about these negative memories.

4.5 Conclusion

In summary, the neural representation of involuntary memories remained largely intact in PTSD compared to controls. This suggests that involuntary memories

themselves may not be distorted in PTSD, and that bottom-up retrieval is spared. However, there was a late peak in activity for many of the regions involved in memory retrieval in the PTSD group compared to the control group. In contrast, regions that are important for emotional experience and processing were similarly active for both groups but activity in these regions peaked earlier in the PTSD group. In addition to the differences in timing, there was increased activity in regions associated with the dorsal attention network for involuntary memories but decreased activity in these regions for high compared to low emotion memories. These differences in timing and activity within the dorsal attention network suggest that attention processes during involuntary memory retrieval are distorted in PTSD, with hyperactivity in attention to emotional memories but hypoactivity in attention to general memories. Finally, people with PTSD have hyperactivity in the VMPFC in response to emotional memories. The VMPFC is a region associated with emotion regulation and though its precise role in this process is not fully understood, this hyperactivity suggests that the emotion regulation system is impaired in PTSD. These differences in the response to involuntary memories in PTSD could help to explain why they become a highly distressing symptom of PTSD.

5. General Discussion

5.1 Summary of Results

The body of work put forth in this dissertation has supported two main ideas: (1) voluntary and involuntary memories share the same underlying neural representation of mnemonic information, and (2) a key difference between voluntary and involuntary memory concerns the additional cognitive control processes necessary for voluntary remembering. Through the use of a paradigm designed to induce a high frequency of involuntary memories, making the study of this form of memory amenable to the scanner, I have presented evidence showing the similarities and differences between neural activity in voluntary and involuntary memories (Chapter 2, S. A. Hall et al., 2014). A reliable set of regions found to support voluntary memory retrieval is common to both voluntary and involuntary memory retrieval, namely the parahippocampal gyrus, precuneus, posterior midline regions, and inferior parietal cortex. This common activity suggests that these regions are not selective to voluntary memory, which has been studied more thoroughly, but rather that they support memory retrieval regardless of retrieval orientation. The only difference in neural activity between memory types was increased activity in the DLPFC for voluntary memories, a region typically associated with controlled retrieval. This supports the idea that the difference between voluntary and involuntary memory is at least partially explained by the additional control processes required to retrieve memories voluntarily, even if the neural representation of those memories are retrieved without conscious effort.

Differences in univariate activity between voluntary and involuntary memory were relatively subtle and confined to lateral frontal cortex. In comparison, patterns of functional connectivity showed some similarities but also more pronounced differences that also provided converging evidence for the hypothesis that differences between voluntary and involuntary memories are explained by differences in cognitive control (Chapter 3, S. A. Hall, Li, et al., In prep). Both types of memories were found to be supported by a distributed network of regions that has been described in several other studies of episodic retrieval, referred to here as the MTL network. In addition to regions like the parahippocampal gyrus, posterior midline regions, and precuneus, the medial PFC was also found to be important for retrieval for both voluntary and involuntary memories. The mPFC is a region typically associated with on contextual memory and executing behavior based on that memory. This suggests that for both voluntary and involuntary memories, similar brain regions within this recollection network are exchanging information, and that there may be similar post-retrieval behavior based on these memories regardless of how they are retrieved.

There are also several connectivity differences between voluntary and involuntary memories of the visual scenes paired with the sounds, all of which are in regions typically associated with top-down control processes. First, voluntary retrieval was characterized by enhanced connectivity between the MTL network and the pulvinar nucleus of the thalamus during voluntary retrieval, a region associated with visual attention (Robinson & Petersen, 1992). Second, voluntary memories are associated with increased

connectivity between regions that typically make up a cingulo-opercular network and a frontoparietal network. These networks have been associated with holding a goal in mind and acting on that goal, respectively, suggesting that voluntary remembering may be associated with the convergence of multiple cognitive control processes. Third, within the MTL and frontoparietal/cingulo-opercular networks, a higher degree of communication efficiency was found during voluntary retrieval, as evidenced by shorter average path length compared to that for involuntary retrieval. This finding suggests that the cognitive processes involved in voluntary remembering enhance communication efficiency in multiple networks associated with memory retrieval. Together, these results suggest that voluntary memories elicit enhanced connectivity both within and between networks associated with recollection and with cognitive control.

Finally, I discuss the differences between emotional and non-emotional involuntary memories in a PTSD group and a trauma-control group (Chapter 4, S. A. Hall, Brodar, LaBar, Berntsen, & Rubin, In prep). PTSD is a particularly informative disorder in which to examine involuntary memories because of the highly distressing nature of trauma-related involuntary memories in PTSD. We found evidence that both attention and emotion processing were disrupted in PTSD. Examining the timecourse of involuntary memory activity showed that activity in regions associated with involuntary retrieval was similar between groups but peaked later in the PTSD group. A contrasting finding appeared when looking at activity associated with the spontaneous retrieval of memories of pictures with high emotional valence compared to low emotion valence.

This yielded similar activity in regions typically associated with experiencing and processing emotions, like the amygdala and the VLPFC, but neural responses occurred earlier in the PTSD relative to the control group. There was also increased activity in regions associated with the dorsal attention network for PTSD for high > low emotion memories but decreased activity in these regions across all memories. The latency differences and dorsal attention network activity differences suggest that there is hyperactive attention to emotional involuntary memories but hypoactive attention to non-emotional involuntary memories. In addition, the PTSD group showed increased activity in the VMPFC during emotional processing, a region associated with emotion regulation. Taken together, these results suggest that involuntary memories have a similar representation in people with PTSD compared to controls, but there are deficits in other systems, like the emotion system and the attention system. Though there is no evidence to suggest that the memories themselves are distorted in PTSD, attention and affective responses to those memories may be.

5.2 Relationship to the Dual-System Model

The dual-system model of intrusive memories in PTSD posits that intrusive (i.e., negative involuntary) memories are part of a different memory system than voluntary memories, and are encoded without contextual details of the episode (Brewin et al., 2010). They would therefore have decreased activity in ventral stream regions associated with the retrieval of contextual information, like inferior and middle temporal regions (Whalley et al., 2013). We find no neural evidence to support idea that these memories

are part of two different memory systems. Regions associated with voluntary and involuntary memories were commonly activated and there was simlar activity in regions associated with emotional involuntary memories in people with PTSD compared to controls. These brain-related results are consistent with behavioral work that shows broad similarities in encoding and storage for voluntary and involuntary memories. Specifically, they are consistent with Rubin and Berntsen's model of involuntary memories (2009) in which they propose, based on behavioral evidence, that voluntary and involuntary memories are part of the same memory system and that the differences between them can be explained by differences in controlled retrieval. Our results are also inconsistent with other distinctions in the memory literature that have identified dissociable neural correlates for memories thought to be supported by different overarching systems. For example, consider implicit versus explicit memories (Schacter, Wagner, & Buckner, 2000; Squire, 2004; but see Dew & Cabeza, 2011). Neuroimaging studies have found differences in regions typically assocaited with memory retrieval between the two types of memories, with the medial temporal lobes mediating explicit memory but not implicit memory (R. N. A. Henson, 2003). The studies presented here do not show differences in any of the regions that have been predicted to show or have shown differences between different memory systems. This provides the groundwork for future investigations of involuntary memories of trauma-relevant emotional stimuli in PTSD to further investigate the dual-system versus single-system models.

5.3 Open Questions and Future Directions

5.3.1 Encoding-Retrieval Match

If it is the case that voluntary memories are associated with additional cognitive control, the above results prompt the following question: how are involuntary memories retrieved? One possibility to be tested is that the encoding/retrieval match must be high for involuntary memories to occur. The viewpoint that similarity between encoding and retrieval drives memory retrieval is a widely held one (Eysenck & Keane, 2010). Though most studies have investigated the encoding-retrieval match in the context of voluntary memories, it is also thought to drive involuntary memories. Involuntary memory theorists propose several models of involuntary retrieval that support this view. Though each model may have difference mechanisms through which involuntary memories come to mind, all models of involuntary memory function share the idea that a cue that matches the encoding episode engenders the retrieval (Ball & Little, 2006; Conway, 2005; Conway & Pleydell-Pearce, 2000; Kvavilashvili & Mandler, 2004). Berntsen (Berntsen et al., 2013; Staugaard & Berntsen, 2014) proposes that the more discriminable the cue, the higher the likelihood that an involuntary memory will be retrieved, suggesting that cues that have a unique overlap with target memory features will more likely reactivate that memory automatically.

The neural consequence of this encoding-retrieval match phenomenon is that when the encoding episode matches the retrieval episode closely enough, there is cortical reinstatement of the memory (for a review, see Danker & Anderson, 2010). This process

is mediated by pattern completion circuits in the hippocampus in which a cue reactivates a fragment of the same neurons that were responsive during encoding, which then reinstates the remainder of the memory (Rolls, 2013). Though our data have provided evidence that activity in frontal regions is associated with voluntary memories alone, it is not clear if these regions are primarily involved in higher-order cue processing. Models of automatic retrieval posit that cortical-MTL connectivity modulates automatic retrieval while PFC-MTL-cortical connectivity modulates voluntary retrieval (Miyashita, 2004; Osada et al., 2008). For involuntary memories, cortical regions that are activated in response to a cue, for example, early visual regions for visual cues, have hippocampal targets, which can then spur pattern completion (Yassa & Stark, 2011). For voluntary memories, pattern completion processes may be mediated by PFC inputs, which communicate information about the to-be-remembered stimulus and modify hippocampal activity accordingly. An investigation into the encoding-retrieval match within the hippocampus and within cortical regions associated with reinstatement over time, as well as an investigation into hippocampal connectivity with PFC regions over time would test this hypothesis. For involuntary memories, there would be a high encoding-retrieval match quickly after the cue and immediately preceding an involuntary memory. It would be immediately followed by cortical reinstatement. In contrast, for voluntary memories, this encoding-retrieval match would grow over time, with increasing hippocampal similarity between encoding and retrieval modulated by connectivity with the PFC. It also may happen simultaneously with cortical reinstatement as pieces of the memory are

retrieved and reinstated. This line of questioning also opens the door to questions about the encoding-retrieval match threshold that must be met and whether this threshold differs between involuntary and voluntary memories.

Though there have been few studies that have investigated changes in cortical reinstatement over time or dynamic connectivity between PFC and MTL during memory retrieval, there is some evidence that supports the hypothesis that there is fast reactivation for automatic retrieval. In a study of people with epilepsy who had depth electrodes implanted in the medial PFC and the hippocampus, participants watched television clips 5-10 times and were asked to report when they had spontaneous memories of the clips over the next 1-5 minutes (Gelbard-Sagiv, Mukamel, Harel, Malach, & Fried, 2008). They showed that the same ensemble of neurons that had fired during clip viewing showed an increased firing rate immediately preceding the memory report in the hippocampus but not the mPFC. In an EEG study of reactivation during a recognition memory task, there were more reactivation spikes for 'sure old' than for 'unsure' or 'new' judgments (Johnson, Price, & Leiker, 2015). Though 'sure old' responses may not always correspond to involuntary memories, in this case they were associated with faster response times than 'unsure/new' judgments, suggesting that they arise more automatically. There were also a greater number of early reactivations for 'sure old', suggesting that involuntary memories may be associated with a greater and earlier encoding-retrieval match. Further work targeting involuntary memories specifically will need to be done in order to resolve the precise timing of these cognitive processes.

In a preliminary effort to provide support for the idea that the encoding-retrieval match is greater for involuntary memories, we have investigated the informational content shared between voluntary and involuntary memory using a multilinear approach. We performed a representational similarity analysis in which the pattern of activity within regions-of-interest, specifically the hippocampus and the precuneus, during the encoding of each sound-picture pair was compared to the pattern of activity during the retrieval of the corresponding stimulus. Four seconds were modeled for each trial and only paired-sound trials in which a memory occurred were analyzed. There was a smaller dissimilarity in the left hippocampus for involuntary memories than voluntary memories ($t(13.17) = -2.33$, $p<0.05$) but not in the other regions we tested (right hippocampus: $t(14.50) = 1.28$, $p > 0.2$, left precuneus: $t(23) = .67$, $p > 0.5$, right precuneus: $t(16.94) = 1.10$, $p > 0.2$). The hippocampus has previously been implicated in the reinstantiation of episodic memory and has been shown to have distinguishable neural patterns for different episodic memories (Chadwick, Hassabis, Weiskopf, & Maguire, 2010). Critically, there is no difference in dissimilarity in the precuneus between the two groups, suggesting that though cortical reinstatement is similar, hippocampal signals may be less similar, or less accurate, for voluntary memories. Hippocampally-driven cortical reinstatement may be similar for voluntary and involuntary memories, but the signal within the hippocampus may be less similar for voluntary memories, with frontal inputs helping to fill in the missing pieces of the memory. Though these are preliminary analyses and the paradigm was not designed to test this question, this provides a hint that a strong encoding-retrieval

match may be driving involuntary memory retrieval but that voluntary memories may be reinstantiated via a generative search process.

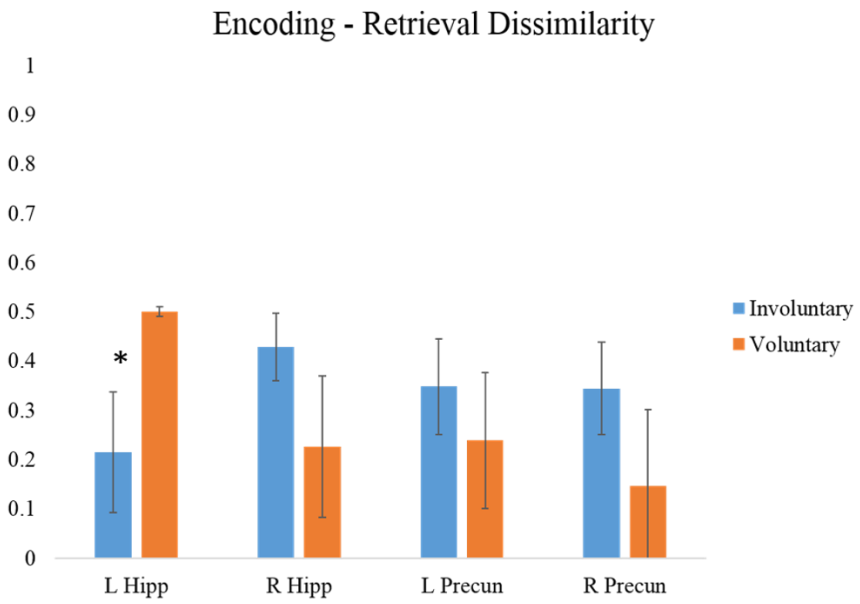

Figure 14: RSA encoding-retrieval similarity in the bilateral hippocampus and precuneus. There is a significant group difference in the left hippocampus at $p < 0.05$.

This result may be driven in party because of the way the memory is cued. Externally cued memories that do not occur automatically may require relatively intense search processes, which therefore could affect the timing of the encoding-retrieval similarity. When a memory occurs after an external cue, like seeing an acquaintance and remembering their name, involuntary memories may have a stronger encoding-retrieval match than their voluntary counterparts. An involuntary memory of their name may come to mind if the cue-stimulus link is strong enough, but if not, search will be required. Over time, as these control processes bring more details of the person to mind, the encoding-retrieval similarity may grow until the name is remembered. Since the cues in this

paradigm are external, the result presented here may be reflecting this initial heightened cue-stimulus match for involuntary memories, which could grow over time for voluntary memories. However, when memories occur after an internal cue, even though goal-driven search is required, the cue-stimulus match could be strong and the search would be light. This could happen, for example, if you decide to do research on a rising political candidate and you have to search your memory for his or her name. The cue 'rising political candidate' may have a strong stimulus match that comes to mind quickly, but is driven by an initial search process. Of course, the cue-stimulus strength could be modulated by many factors. Future work will be necessary to determine how different cues and other factors affect these retrieval processes.

5.3.2 Retrieval Effort and Involuntary Remembering

Another open question is: what is the relationship between continuous retrieval effort and involuntary memory? The simple answer is that involuntary memories are elicited in the absence of retrieval effort but this relationship may be more complex than it appears. There is a subjective difference in the experience of trying to remember and slowly piecing the memory together and trying to remember when suddenly a memory pops into mind. Retrieval cue specificity asserts that during retrieval effort, the PFC is comparing the features of a retrieval cue to possible sources (Dobbins, 2001). There could be memories that occur slowly, perhaps due to partial pattern completion, with memory strength building as sources that elicit weak pattern completion accumulate until the narrowing in upon the correct source. These would be voluntary memories. There

could be memories that occur suddenly, which could occur as a result of a sudden match between the cue and a 'found' memory. This would also be voluntary memories, guided by effortful memory search. But, critically, there could be memories that suddenly pop into mind during memory search but before search processes check the correct cue. These could be counted as involuntary memories because their retrieval was not driven by the search process, even though they occur during effortful search.

Though there would likely be PFC-hippocampal connectivity during these memories, which would make them appear to be voluntary, there is evidence to suggest that PFC-hippocampal connectivity is strengthened by successful memory retrieval rather than retrieval effort. A study investigating connectivity between hippocampus and PFC during the retrieval of memories whose strength was modulated by having been encoded with or without a distractor present (Wais et al., 2010). The authors found decreased connectivity between hippocampus and inferior frontal gyrus for the retrieval of weaker memories that were encoded when there was a visual distractor. Though retrieval effort was not measured, memory strength has been found to be dissociable from retrieval effort (Reas & Brewer, 2013), suggesting that retrieval effort could be the same for both strong and weak memories. If this were the case, then the decreased hippocampus-PFC connectivity would be due to increased memory strength rather than retrieval effort. Though this study was not designed to test questions about retrieval effort and therefore conclusions about retrieval effort versus success driving PFC-hippocampal connectivity based on this work would be tenuous at best, we can start to form hypotheses about

involuntary memory retrieval that can be tested. One hypothesis is that involuntary memories that are retrieved in the context of retrieval effort would not be preceded by PFC-hippocampal connectivity, but that it would precede voluntary memory retrieval. Neuroimaging methods with high temporal resolution, like EEG or MEG, would be necessary to help answer this question.

5.3.3 Remaining Open Questions

Finally, there are a number of novel questions that this line of work engenders, which suggest fruitful avenues for future research:

- Retrieval mechanisms:
    - What bottom-up processes facilitate involuntary memory retrieval? Specifically, what are the processes that modulate neural reinstantiation during involuntary retrieval and how do these processes differ between voluntary and involuntary memories?
    - How do explicitly and implicitly cued, and no-cue involuntary memories differ from each other and from their voluntary counterparts?
- Differences between voluntary and involuntary memory:
    - How are post-retrieval processes different and similar between voluntary and involuntary memories?
    - How do involuntary recollection and familiarity differ from voluntary recollection and familiarity?

- Disorders:
    - How do involuntary memories in PTSD differ from those in other disorders in which involuntary remembering is considered troublesome?
    - How do disorders affecting bottom-up processes, like attention deficit-hyperactivity disorder, affect involuntary memories?
- Relationships with other cognitive processes:
    - How does implicit memory interact with involuntary memory? How much do they share informational content?
    - Do promises of reward and threats of punishment affect involuntary remembering?

5.4 General Conclusion

The results presented in this body of work have shown that voluntary and involuntary memories have overlapping neural representations. Neural differences between the two are in regions typically associated with cognitive control processes. This suggests that voluntary and involuntary memories are part of the same memory system and that differences between them are driven by differences in the way in which they are retrieved. I have also shown that there are differences in the timing of activity associated with involuntary remembering and the emotional processing of involuntary memories in PTSD, a disorder associated with deficits in cognitive control. This suggests that even

though involuntary memory is not associated with cognitive control, post-retrieval processing may yet require these control processes. The disturbing nature of involuntary memories in disorders like PTSD may be due to the processing of the memory rather than qualities of the memory itself. This foray into the neural underpinnings of involuntary memories provides evidence to support existing theories about involuntary memory, gives hints about the mechanisms underlying voluntary and involuntary memory retrieval, and paves the way for the exploration of new questions about these memories.

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Biography

Shana Hall was born in Fullerton, California on March 17, 1983. She received her Bachelor of Arts degree from the University of California, San Diego in International Studies, with a minor in psychology in 2001. She then worked as a research assistant in a laboratory investigating levels of response to alcohol. From her time working in that lab, she has five publications: *High versus low level of response to alcohol: evidence of differential reactivity to emotional stimuli* (Paulus et al., 2012), *fMRI differences between subjects with low and high responses to alcohol during a stop signal task* (Schuckit et al., 2012), *Alcohol effects on cerebral blood flow in subjects with low and high responses to alcohol* (Tolentino et al., 2011), *Comparing structural equation models that use different measures of the level of response to alcohol* (Schuckit, Smith, Trim, Tolentino, & Hall, 2010), and *Acute ethanol effects on the brain activation in low- and high-level responders to alcohol* (Trim et al., 2010). She then began her graduate work at Duke University where she has published a paper entitled *The neural basis of involuntary episodic memories* (S. A. Hall et al., 2014). She has been a Program for Advanced Research in the Social Sciences Fellow, a Preparing Future Faculty Fellow, and a Summer Research Fellow. She is the recipient of the Duke Graduate School Conference Travel award and the Claire Hamilton Travel Award and she has had memberships in the Cognitive Neuroscience Society, the Society for Neuroscience, and the Association for Psychological Science.