An fMRI Investigation of Source Memory in Obsessive-Compulsive Disorder

By

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Abstract

Obsessive-compulsive disorder (OCD) is a serious and debilitating psychiatric disorder that affects 2.2 million Americans (Kessler, Chiu, Demler, & Walters, 2005). Individuals with OCD often complain about poor memory and evidence suggests that individuals with OCD exhibit deficits on a variety of tasks, including those that are unrelated to obsessional concerns. As individuals with OCD tend to focus on details and miss the larger context, the construct of source (contextual) memory may be particularly relevant to memory complaints in OCD. Memory for different types of information (object versus contextual information) may rely on distinct regions within the prefrontal cortex and medial temporal lobe, and may be differentially impacted by obsessive-compulsive symptoms. Using a novel task, 16 individuals with OCD and 17 age, education, and gender matched healthy control group participants (age 18 to 50) studied objects in the context of four rooms. While undergoing functional Magnetic Resonance Imaging (fMRI), participants completed source and object recognition testing. While no significant differences were found between the two groups in terms of behavioral performance, individuals with OCD exhibited greater task related activation in the left medial prefrontal cortex, premotor cortex/ dorsolateral prefrontal cortex, right parietal region, and posterior cingulate cortical areas relative to healthy controls during correct source verses object recognition trials. Results are discussed in terms of compensatory activation and altered activation patterns in individuals with OCD.

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Background and Significance

Obsessive-compulsive disorder (OCD) is a serious and debilitating psychiatric condition that affects 2.2 million Americans (Kessler, et al., 2005). OCD is characterized by recurrent thoughts or images that are experienced as intrusive and inappropriate (obsessions), and/or repetitive behaviors or mental acts meant to prevent an imagined feared outcome or avoid anxiety (compulsions). The content of obsessions can vary widely. Common obsessional concerns include fear of contamination, doubting, sexual or aggressive thoughts or images, and need for symmetry. OCD has a significant impact on quality of life and places tenth in overall global disease burden (combined measure of deaths and disability) as reported by the World Health Organization (Murray & Lopez, 1996).

Individuals with obsessive-compulsive disorder often complain of poor memory and neuropsychological research has demonstrated impairments, particularly in the "meta-cognitive" aspects of memory, such as strategic processing (organization and selecting a strategy in an unstructured task). Past research has revealed subtle differences in how information is acquired, with OCD patients underutilizing organizational strategies during encoding (Deckersbach, Otto, Savage, Baer, & Jenike, 2000; Savage et al., 1999; Savage et al., 2000). Meaningful organization of information is known to enhance encoding and retrieval of new memories, and previous research has shown that individuals with OCD tend to focus on details and miss the larger context. "Source memory" – the ability to identify the specific origin of a learning episode – is another meta-cognitive process that may be particularly relevant to OCD. Individuals with OCD may focus on the details and fail to attend to the larger picture, thus neglecting the context of the learning episode. Poor source memory may contribute to doubt, which is pervasive in OCD. For

example, OCD sufferers may have difficulty distinguishing one checking episode from another, thereby contributing to doubting (e.g., "How do I know I am remembering the most recent time I turned off the stove and not some other time?"). Although many studies have examined memory deficits in OCD, few studies have examined source memory deficits. In the following sections, I will first review past research related to memory and OCD and then discuss the present study which used fMRI to examine source and item memory performance in OCD.

OCD and Verbal Memory

In general, studies have not found deficits on verbal tasks in individuals with OCD. Results from studies examining verbal working memory as well as declarative verbal memory fail to show impairments in individuals with OCD (Boone, Annanth, Philpott, Kaur, & Djenderedijian, 1991; Christensen, Kim, Dysken, & Hoover, 1992; Jurado, Junque, Vallejo, & Salgado, 2001; Martin, Wiggs, Altemus, Rubenstein, & Murphy, 1995; Zielinski, Taylor, & Juzwin, 1991). However, deficits have been found on tasks that require use of strategic clustering, such as the California Verbal Learning Test (Savage & Rauch, 2000). Meaningful organization of information aids in subsequent recall. For example, organization by semantic category during encoding aids in the recall of verbal information. A study by Savage and colleagues (2000) found that individuals with OCD failed to spontaneously utilize semantic clustering strategies. However, individuals with OCD do not appear to be deficient in their ability to implement such strategies when instructed to do so. Deckersbach et al (2005) found that when individuals with OCD were prompted to use semantic clustering they were able to do so and performed as well as control group participants. In contrast, individuals with bipolar disorder did not show a similar improvement with prompting. This suggests that recall deficits in individuals with OCD do not result from impairment in the capacity to use such strategies, but

rather the impaired ability to *spontaneously* initiate efficient strategies. The fact that individuals with OCD are able to use effective strategies, but fail to do so spontaneously suggests that they may not attend to the organizational demands of a task. This suggests a primary failure of strategic processing.

OCD and Nonverbal Memory

In contrast with verbal memory, OCD is more consistently associated with impairments on visuospatial memory tasks. When compared to healthy age and gender-matched adults, individuals with OCD show evidence of impaired visuospatial performance and nonverbal memory on tasks such as the Corsi's Blocks (Zielinski, et al., 1991), the Hooper Visual Organization Test (Boone, et al., 1991), and the Rey-Osterrieth Complex Figure Test (Deckersbach, et al., 2000; Savage et al., 1996). While many studies have reported impairments in nonverbal memory and organization, not all studies have found impairments in individuals with OCD (Basso, Bornstein, Carona, & Morton, 2001; Cohen et al., 1996). Impairments may be more evident on tasks with greater organizational demands, such as the Rey-Osterrieth Complex Figure Test (RCFT). The RCFT requires the participant to copy a complex geometrical figure and then reproduce it immediately after the copy (immediate recall) and then again after 30 minutes (delayed recall). Several studies examining the immediate visual recall rate on this task have found impairments in the performance of individuals with OCD compared to healthy control participants (Boldrini et al., 2005; Deckersbach, et al., 2000; Savage, et al., 1996). The reason for this impairment was suggested by Savage et al. (1999) who found that individuals with OCD showed impairments in the use of organizational strategies when asked to copy the Rey-Osterrieth Figure. For example, individuals with OCD focused on irrelevant details of the figure instead of constructing larger structural elements. Similarly, Deckersbach et al. (2000)

reported that individuals with OCD used a fragmented approach to the reproduction of the figure. Impaired use of organizational strategies were correlated with both impaired immediate and delayed recall of the figure (Deckersbach, et al., 2000; Savage, et al., 1999; Savage & Rauch, 2000) and were found to mediate memory performance deficits in statistical mediation modeling. The failure to spontaneously use strategies efficiently may explain the impaired performance of individuals with OCD on such tasks (Savage, 1997). Individuals with OCD have been found to under-utilize organizational strategies during encoding. Impairments in verbal and nonverbal memory tasks may be mediated by difficulties in spontaneous implementation of organizational strategies (Deckersbach, et al., 2000; Savage, et al., 1999; Savage, et al., 2000).

Research suggests that memory deficits in OCD may reflect a failure to recognize and exploit important organizational elements of the task. Specifically, individuals with OCD fail to recognize that the comprehensive picture (gestalt) is more important than the details (Savage, et al., 1999; Savage, et al., 2000). While individuals with OCD may focus on small details in an attempt to gain "perfect" memory, this approach paradoxically lends itself to neglect of the larger context and, thus, leads to poor recall.

Implementation of strategies may be considered a higher order process. Failure to use effective organizational strategies places a greater load on cognitive resources. Attention to irrelevant material may also burden the ability to successfully encode stimuli into memory. For example, age related changes in memory suggest that inclusion of irrelevant details in a mental image is associated with poor subsequent memory recall. In a study of age related changes in memory, older participants were found to include a greater number of irrelevant details when asked to create a mental image of a word. In contrast, younger adults spontaneously produced more specific and contextual images. Inclusion of irrelevant details predicted poor subsequent

memory recall (Palladino & De Beni, 2003). Individuals with OCD may focus on the details and fail to attend to the larger picture, thus neglecting the context of the learning episode. A study by Sher et al. (1989) found that individuals with OCD use less imagery, especially visual imagery, when recalling biographical information. Results of experimental studies suggest that contextualized images are more memorable compared to non-contextualized images (De Beni & Pazzaglia, 1995). Therefore, failure to connect learning episodes with a larger context, may lead to impairments in memory recall.

Functional neuroimaging studies of individuals with OCD have found evidence of prefrontal dysfunction, especially in orbitofrontal cortex, caudate nucleus, and anterior cingulate cortex (Schwartz, Stoessel, Baxter, Martin, & Phelps, 1996). A study by Savage et al. (2001) of normal memory found that blood flow to orbitofrontal cortex during encoding of word lists predicted spontaneous implementation of semantic clustering during immediate recall. The orbitofrontal cortex is thought to play a role in decision making, motivation, and selecting a strategy in an unstructured setting; this region is likely linked to memory problems in OCD.

Memory deficits in OCD may, therefore, reflect impairments in planning, organization, and the ability to flexibly adapt to stimuli. In addition to the failure to spontaneously implement strategies, individuals with OCD may have difficulty generating alternative strategies following an error. On a computerized version of the Tower of London test of planning, Veale et al. (1996) found that individuals with OCD were no different from healthy control participants in terms of their solutions. However, following a mistake the OCD group participants spent more time than the healthy control group in generating alternative solutions or checking the accuracy of the next move. These results suggest that individuals with OCD have difficulty in selecting alternative strategies, especially following an error.

Past research suggests that individuals with OCD may be able to compensate for less efficient strategies and deficits may only be apparent on more difficult tasks. At least a portion of individuals with OCD use effortful strategies to compensate for tendencies towards less efficient processing. For example, even when no differences are observed in performance accuracy, greater neural activation has been observed in individuals with OCD (Ciesielski, 2005).

In individuals with OCD, deficits in performance may only be apparent on difficult tasks. For example, Purcell et al. (1998) examined spatial working memory in individuals with OCD and matched healthy control group participants using a paradigm with an increasing working memory load. Individuals with OCD performed as well as control group participants at lower levels of task difficulty, however performance dropped significantly at the highest levels of difficulty, compared to the control group participants. Individuals with OCD also failed to use organizational strategies during the more difficult levels of the task compared to the healthy control group. Using functional magnetic resonance imaging, Henseler et al. (2008) examined neural activation underlying working memory performance in individuals with OCD and healthy control group participants. OCD and healthy control group participants who performed normally on a working memory task one month prior to scanning were selected for the study. As expected OCD and healthy control group participants did not differ in terms of memory performance. Individuals with OCD and healthy control participants engaged the same brain regions during the recognition task. However, individuals with OCD exhibited greater task related activity in the frontal and parietal areas suggesting that they may be working harder to perform at the same level as the healthy control group participants. Other studies show similar results. A study by Ciesielski (2005) examined magnetoencephalographic signals (MEG) in individuals with OCD

during the encoding, retention and retrieval phases of a delayed matching to sample working memory task (DMST). No differences were found in terms of performance between the OCD and healthy control group. However, the OCD group exhibited increased activation during encoding in an anterior insular region and reduced activation in the posterior-inferior parietal cortex. During retrieval, increased activation was found in the right anterior insula and right superior sulcus. These results suggest that although performance was maintained, individuals with OCD may differ in terms of the neural activation underlying memory performance.

Source Memory

As reviewed previously, research suggests that deficits in implementation of organization strategies mediate memory deficits in OCD (Savage, et al., 1999). However, further investigation is needed to better characterize how individuals with OCD encode and remember information and how differences in memory may contribute to clinical phenomena such as compulsive checking. It may be that individuals with OCD suffer from decreased richness of memory, or a lack of attention to the context of a learning episode (Savage, 2002). In some situations, individuals with OCD lack confidence in their memory, even when accuracy is normal (Hermans et al., 2008). Individuals with OCD may fail to attend to the context of the learning episode and this lack of richness may affect their memory confidence. However, objective deficits in performance may only be apparent on more difficult tasks. Results of experimental studies suggest that contextualized images are more memorable compared to non-contextualized images (De Beni & Pazzaglia, 1995). Therefore, failure to connect learning episodes with a larger context, may lead to impairments in memory recall.

Given findings that individuals with OCD tend to miss the "big picture," source memory may be particularly relevant to OCD. "Source memory" refers to the ability to remember the

specific context of the learning episode. Source memory involves the binding of content with the context, while item memory simply refers to the content. One real world example of source memory is the need to remember where objects are located. The ability to recall where the object was seen involves linking item (object) with source (location). Individuals with OCD may fail to attend to the context and therefore have difficulty integrating information from the learning episode into a coherent whole and in differentiating one learning episode from another. Support for a distinction between source and item memory comes from results of behavioral and neuroimaging studies in healthy and neurologically impaired groups. A study by Koriat, Ben-Zur, and Druch (1991) found that performing an action increases memory for that action (item specific memory) while decreasing memory for the context of the action (source memory). Therefore, it is possible that the act of compulsive checking may increase item specific memory while decreasing source memory. While memory for the action may be intact, low memory confidence may reflect poor memory for the context of the action (i.e., when or where the action occurred). This may partially explain the paradoxical observation that repeated checking diminishes memory confidence in OCD (Radomsky, Gilchrist, & Dussault, 2006; van den Hout & Kindt, 2003).

Support for a distinction between source and item memory also comes from studies of individuals with frontal lobe dysfunction (Glisky, Polster, & Routhuieaux, 1995; Janowsky, Shimamura, & Squire, 1989). For example, a study by Glisky (1995) classified a group of healthy older adults as either high or low functioning based on tests of frontal lobe and temporal lobe functioning. She found that low frontal function was associated with poorer performance on a source memory task, while item memory remained unaffected. The opposite results were found for the group based on classification of high and low temporal functioning. Finally, in an

event-related fMRI study, prefrontal activity was related more to source than item retrieval (Curran, DeBuse, Woroch, & Hirshman, 2006). These studies suggest dissociation between item and source memory. Memory for different types of information (object versus contextual information) may rely on various regions within the prefrontal cortex and medial temporal lobe, and may be differentially impacted by obsessive-compulsive symptoms. Source memory may be impacted to a greater degree compared to item memory. Impairments in source memory may contribute to doubt and low confidence in the accuracy of the memory episode.

The type of source information may also be important. A distinction has been proposed between associative or intrinsic source information and organizational or extrinsic source information. (Baddeley, 1982; Moscovitch, 1992) Associative source information is more closely tied to the stimulus itself (e.g., color of the word or mode of presentation), while extrinsic or organizational source information is independent of the stimulus (e.g., where an object appeared or in what order). Because associative source information is more closely tied to the stimulus it may be less dependent on strategic processing. For example, age related memory deficits are more pronounced on organizational source memory tasks compared to associative source memory tasks (Spencer & Raz, 1995).

A small number of studies have examined associative source memory in OCD, with inconsistent findings. A study by Rubenstein et al. (1993) investigated memory for actions in a group of college students with subclinical checking symptoms and those with no OC symptoms. Participants read statements that described actions that they were instructed to either write down, perform, or observe. Following the first phase of the study participants were asked to write down all the actions they could remember and whether they had performed, observed, or written down the action. Individuals with subclinical checking symptoms had significantly more

difficulty identifying the actions as well as identifying in what form the action took (observed, written, or performed).

A study by Ecker and Engelkamp (1995) found similar results; namely, that individuals with OC checking rituals had greater difficulty distinguishing between performed and imagined actions. Using an event-related potential (ERP) word recognition test, Kim, Roh, Yoo, Kang, and Kwon (2009) also investigated source memory and item memory in individuals with OCD. Fourteen individuals with OCD and fourteen age, gender, and education matched control group participants listened to words spoken by either a male or female voice. Both groups were then presented with a set of words and were asked to identify whether the word was old or new. In addition, participants were asked to identify the source of previously presented words (male or female speaker). No differences were found on item memory; however individuals with OCD performed more poorly compared to the healthy control group on the source memory task. There were no differences between the OCD and control groups with regard to the locations of the event-related brain potential generators elicited by source correct and correct rejection conditions. However, during the source memory task, the control group showed ERP old/new effects at 400-700 ms post stimulus, while the OCD group did not. That is, for the control group, correct recognition of the source of old words elicited higher amplitude at most electrode sites compared to correct rejection of novel words. This effect was not observed in the OCD group. Source localization analysis revealed that both groups engaged the frontal regions during the source memory task. However, individuals with OCD showed significantly altered hemispheric asymmetry of equivalent current dipole power in the frontal lobe during source memory retrieval, compared with the control group participants. The OCD group showed rightward frontal asymmetry in the equivalent current dipole of ERP generators, whereas the healthy

control group participants exhibited leftward frontal asymmetry. The left frontal cortex is known to play a greater role in successful retrieval of contextual information compared to the right frontal cortex. Therefore, this finding may reflect successful retrieval of source information in the healthy control group participants and impaired retrial of source information in individuals with OCD. Results of this study support the hypothesis that individuals with OCD have impairment in source memory, while item memory may be unaffected on some tasks.

However, several other studies have not found significant differences between individuals with OCD and healthy controls on source memory performance (Constans, Foa, Franklin, & Mathews, 1995; McNally & Kohlbeck, 1993; Moritz, Jacobsen, Willenborg, Jelinek, & Fricke, 2006). For example, Constans et al. (1995) examined item (action) and associative source memory (whether the action was performed or imagined) in twelve individuals with OCD and seven age and gender matched controls. Participants were asked to perform a sequence of actions that involved the manipulation of objects. Each action was either real (e.g.,"turn off the curling iron") or imagined ("image turning off the curling iron"). Participants were instructed that their memory would be tested following completion of all the actions. Following completion of twenty sequences, participants were asked to indicate whether the last action was imagined or performed. No differences were found in terms of memory for what form the last action took (real or imagined) between the OCD and healthy control group. However, memory for actions prior to the last action was not tested. Furthermore, the task may have not been difficult enough to detect subtle differences in performance. In addition, the small sample size makes interpretation of the null findings difficult. A study by Moritz et al. (2006) also examined source and item memory using an associative source memory task. Twenty-seven individuals with OCD and fifty-one age and education matched healthy control group participants viewed simple word

riddles on the computer. Participants either provided the answer or listened to a computer generated answer (response type was indicated prior to each riddle). Participants then completed an item and source recognition task, during which they indicated whether the word was computer generated, self-generated or new. Individuals with OCD performed more poorly on source memory for words that were self-generated. However, severity of depressive symptoms, but not OCD symptoms, negatively correlated with impaired recognition for self-generated items, suggesting that depressive symptoms may have accounted for differences between the OCD and healthy control group.

While some studies support source memory deficits in OCD, others have not found impairments. Inconsistent findings on source memory tasks might be due to differences in sample size and statistical power, study instructions or task difficulty. Past research has also focused exclusively on associative source memory (i.e., mode of presentation), which may be less sensitive to deficits in strategic processing. Given findings that individuals with OCD neglect the context of the learning episode and use a fragmented approach, impairments are likely to be greater on organizational source memory tasks. This finding would support the theory that impairments are greater for tasks that make greater organizational demands. Based on this logic, the present study focused on organizational source memory.

The Present Study

Although no neuroimaging studies have examined source memory in individuals with OCD, past research concerning source memory in healthy individuals suggests that greater activation in bilateral medial temporal cortex, anterior hippocampus, parahippocampal gyrus, and left prefrontal cortex is associated with correct recall of source information (Glisky, et al., 1995; Johnson, Kounios, & Nolde, 1997). Considering evidence of prefrontal dysfunction in

OCD, it hypothesized that individuals with OCD will exhibit source memory impairments and such impairments would be associated with decreased activation of the left prefrontal cortex.

Past research has relied heavily on highly structured tasks with explicit instructions. However, memory deficits may be more apparent for unstructured tasks. Past research has also suffered from a lack of ecological validity. Although subtle memory deficits have been reported on tests like the RCFT, it is not clear how deficits in performance observed using abstract neuropsychological tests translate to real life settings. The present study examined performance in the context of a memory test with high ecological validity. The task involved items presented in the context of four different household rooms. This allowed us to test memory for objects as well as memory for source (which room the object was viewed in). Items either matched the context of the room or were out of place. Functional magnetic resonance imaging (fMRI) was used to identify brain networks underlying differences in performance between individuals with OCD and healthy controls during an item and source recognition test.

Specific Aims

The present study's specific aims were:

Aim 1: Examine whether individuals with OCD differ in their memory for multi-contextual information, including item and source memory.

1.1: It was hypothesized that individuals with OCD would exhibit impairments in performance compared to healthy control group participants on both item and source memory during recognition testing.

Aim 2: Use fMRI to identify brain systems underlying item and source memory in individuals with OCD and healthy control group participants. *A priori* regions of interest include areas believed to be important for item and source memory based on previous research.

2.1: It was hypothesize that the OCD group would show greater activation during correct item responses than the HC group, suggesting that individuals with OCD compensate for tendencies toward less efficient encoding strategies. We predicted increased activation in areas previously implicated in item memory (right prefrontal cortex, and anterior medial temporal lobe).

2.2: Prior memory research suggests that greater activation in the bilateral medial temporal cortex, anterior hippocampus, parahippocampal gyrus, and left prefrontal cortex is associated with correct recall of source information. It was hypothesized that the OCD group would show decreased activation in regions previously implicated in source memory judgments.

Approach to Alternative Outcomes

The hypotheses proposed study were based on past research. However, possible alternative outcomes were also considered, and included:

Behavioral Data:

1) Groups may differ on item (object) memory, but not source memory. This would suggest some memory impairment, but would not support the theory that memory for the context of the learning episode is affected. 2) Groups may differ on source, but not object memory. This would support the theory that memory may be impaired for the context of the learning episode, but that item memory is unaffected. 3) No differences may be found between the two groups on either item or source memory. This would not support the theory that individuals with OCD show impaired behavioral memory performance for objects or the context of the learning episode in an ecologically valid task.

fMRI and Behavioral Data:

1) There may be no behavioral difference, but greater brain activation in regions know to be related to object memory in the OCD group compared to the healthy control group. This would

suggest less efficient activation or that the OCD group is working harder to perform at the same level as the control group. 2) Groups may differ behaviorally, but no differences in brain activation may be found. Superior performance would be interpreted in this context as evidence of more efficient neural activation.

Approach to Interpretation of fMRI Data

Differences in neural activation were interpreted within the context of behavioral performance. It is often difficult to determine whether observed brain activation is the cause or the outcome of the behavior. One way to disentangle these is to examine brain activation differences where no behavioral differences are found. For example, differences in neural activation underlying only correct responses between the OCD and control group were examined in this study.

Method

Participants

Participants were sixteen females with OCD and seventeen healthy control females. Participants were recruited from the Kansas City Center for Anxiety Treatment (KCCAT) and its community contacts, community advertisements, University of Kansas Medical Center advertisements, University of Kansas Lawrence campus advertisements, and the University of Kansas undergraduate research subject pool. Participants were offered $75 remuneration for their participation in the study. All participants were between 18 and 50 years of age. Groups were matched for age, gender (all female), handedness (all R), education, and general cognitive ability (estimated IQ). Each participant was administered the Mini International Neuropsychiatric Interview (MINI; Sheehan et al., 1998) and the Wechsler Abbreviated Scale of

Intelligence Vocabulary and Matrix Reasoning subtests (WASI;Corporation, 1999) by a trained clinician. Participants in the OCD group met criteria for OCD as assessed by the MINI.

Study exclusion criteria included the presence of any other Axis I disorder, neurological illness or injury, current use of antipsychotic or anxiolytic (i.e., benzodiazepam) medication, and history of drug dependence/abuse. Because research suggests that compulsive hoarding may be distinct from OCD in terms of neurobiology and clinical course (Saxena, 2007), individuals with clinically significant compulsive hoarding symptoms, defined according to criteria proposed by Steketee and Frost (Steketee & Frost, 2003), were also excluded. Individuals who were taking antidepressant medication were on a stable dose for at least two months prior to scanning. A study comparing neuropsychological performance between SSRI medicated and un-medicated individuals with OCD found no differences between the two groups on a comprehensive battery of neuropsychological tests (Mataix-Cols, Alonso, Pifarre, Menchon, & Vallejo, 2002); therefore, it was not expected that antidepressant medication would impact performance on this task. Pregnant women and participants with conditions contraindicated or unsuitable for fMRI scanning were excluded. All women of childbearing potential were tested using a urine HCG pregnancy test to rule out possible pregnancy prior to MRI. Participants reporting psychological distress were offered resources and referrals for treatment.

Recruitment and Informed Consent

Potential participants were prescreened. Eligible participants were scheduled for an initial assessment at the Kansas City Center for Anxiety Treatment (KCCAT) or the KU Health Psychology Laboratory. Study procedures were explained to potential participants verbally and in writing as part of the informed consent process. The University of Kansas Medical Center

Human Subjects Committee approved all study procedures, and informed written consent was obtained from all study participants.

Procedures

Following the consent procedure, a trained clinician administered clinical assessments. Severity of obsessive compulsive symptoms were be measured by the Obsessive- Compulsive Inventory-Revised Version (OCI-R; Foa et al., 2002), the Dimensional Obsessive Compulsive Scale (DOCS; (Abramowitz et al., 2010)) and the Yale- Brown Obsessive- Compulsive Scale (YBOCS; Goodman et al., 1989). Clinical assessments included a set of questionnaires, the WASI Vocabulary and Matrix Reasoning subtests (WASI;Corporation, 1999) and the MINI diagnostic interview (MINI; Sheehan, et al., 1998). Individuals who met study inclusion criteria were scheduled for a second session during which they completed fMRI scans and a source and object memory test at the Hoglund Brain Imaging Center. Participants received $75 remuneration for completion of the second session. During the second study session, participants were asked to walk through four different rooms (office, living room, bathroom, and kitchen). Individuals were given the following instructions: "I will be showing you a number of rooms, try to remember as much as you can about the things you see. You may walk around inside the room, but do not touch anything. You will have 30 seconds per room."

Memory Items

Objects were selected that were unique to each context and exemplifiers of each context (e.g., bathroom-toothbrush, living room-coasters, office-stapler). In each condition, 12 objects from each category served as target items and 12 served as distracters. Each room contained six objects that were context congruent and six context incongruent objects. Incongruent objects were selected from the other categories, for example the bathroom always contain six bathroom

objects, two living room objects, two kitchen objects, and two office objects. Both context congruent and incongruent items were used to make source memory judgments more difficult. Objects were rotated and counterbalanced across conditions. Objects were placed where items might reasonably appear. Digital photographs of the rooms for each condition were taken for a visual record of object placement. The order of room presentation was rotated across conditions. Participants were given 30 seconds per room.

Preliminary Studies

The object and source memory test was developed and validated with an undergraduate population. During the development phase, a group of college students were asked to name objects that they would commonly expect to see in each room. The most commonly reported objects were obtained and photographed on an all white background for use during the recognition task. This task – the Memory for Rooms Test (MFRT) – was pilot tested in a subclinical high OC group and healthy control population. The Memory for Rooms Test (MFRT) was based on previously published item and source memory paradigms (Dennis, et al., 2008; Mitchell, Raye, Johnson, & Greene, 2006). In a pilot study with a subclinical OC and healthy undergraduate population, the MFRT was found to have good internal reliability (split half reliability, r =.7) and a high level of internal consistency (Cronbach alpha=.8). The MFRT was piloted for adequate difficulty (no floor or ceiling effect). The present study used a revised version of the original MFRT.

Measures

Obsessive Compulsive Inventory-Revised (OCI-R; Foa, Huppert, Leiberg, Langer, Kichic, Hajcak and Salkovskis, 2002). The OCI-R is an 18 item self-report measure of distress associated with obsessions and compulsions. The OCI-R includes 6 subscales: washing,

checking, ordering, obsessing, neutralizing and hoarding. The OCI-R has good internal consistency and reliability (Foa et al., 2002).

Yale-Brown Obsessive Compulsive Inventory- Self Report Version (Y-BOCS; Baer, 1993). The Y-BOCS is a self-report measure of OCD symptoms. The 10-item severity scale yields a total score (0 – 40) based on individual's obsessions and compulsions. The self-report YBOCS has been shown to have good psychometric properties (Steketee, Frost, Bogart, 1996).

Dimensional Obsessive-Compulsive Scale (Abramowitz, et al., 2010). The DOCS is a 20-item measure of the severity of obsessive-compulsive symptoms. The DOCS has shown to have good psychometric properties (Abramowitz, et al., 2010).

Beck Depression Inventory-II (BDI-II; Beck et al., 1961). The BDI-II consists of 21 items that assess depressive symptoms. Each item is composed of four statements that reflect symptom severity. Individuals rate symptoms on a scale of 0 to 3. Total score ranges from 0 to 63. The BDI-II has adequate internal consistency (α = .93 among college students, α = .92 among outpatients; Beck, Steer, Ball, & Ranieri, 1996; Beck et al., 1996).

Beck Anxiety Inventory (BAI; Beck, A., Epstein, N., Brown, G., & Steer, R., 1988). The BAI consists of 21 items that assess subjective, somatic or panic symptoms of anxiety. Individuals rate symptoms on a scale of 0 to 3. The BAI has been shown to have good psychometric properties (Beck et al., 1988).

The Wechsler Abbreviated Scale of Intelligence (WASI;Corporation, 1999). The WAIS has demonstrated good psychometric properties. The vocabulary and matrix reasoning subscales have demonstrated good internal consistency and reliability, r= 0.88 to 0.98, and convergent validity with the WAIS-III.

The Mini-International Neuropsychiatric Interview (MINI; Sheehan et al, 1998). The MINI is a brief diagnostic interview used to make diagnoses according to DSM-IV criteria for Axis I disorders. The MINI is highly correlated with the SCID-IV (Sheehan et al, 1998).

fMRI Paradigm

The fMRI paradigm was based on studies previously conducted at Hoglund Brain Imaging Center as well as previously published studies from other groups (Chua, Schacter, Rand-Giovannetti, & Sperling, 2006). Following the encoding period, participants completed a recognition test in the scanner during which they made both item recognition and source memory judgments. Participants were presented with ninety-six pictures (48 target items and 48 distracters) and were asked to identify whether the object was old or new. Recognition stimuli (item and source) were presented for 4.5 second each and followed by .5 seconds of fixation, which was then be followed by a variable duration of fixation (0 to 18 seconds) in order to appropriately "jitter" the data to allow deconvolution of the hemodynamic response. During the fixation baseline, participants focused on a fixation cross (+). Fixation duration was optimized by the RFSgen program from AFNI (Cox, 1996). If an object was identified as old, a second screen appeared (following fixation) and participants were instructed to indicate the location (room) in which the item was learned. If an object was identified as new, the next object appeared on the screen. Participants indicated their choice by pressing the appropriate button on the response box. The order of response options was counterbalanced across participants. Participants were instructed to make their best guess if they were unsure. Old and new items were presented pseudo-randomly, based on design optimization by the RFSgen program from AFNI (Cox, 1996).

Scanning Parameters

fMRI scanning was performed at the University of Kansas Hoglund Brain Imaging Center (HBIC), using a 3-Tesla head-only Siemens Allegra Scanner (Siemens, Erlangen, Germany) fitted with a quadrature head coil. Structural scanning included T1-weighted anatomical images with 3D SPGR sequence (TR/TE= 23/4ms, flip angel =8°, FOV=256 mm, matrix=256x192, slice thickness=1 mm). This scan was used for slice localization for the functional scans, Talairach transformation, and coregistration with fMRI data. Gradient echo blood oxygen level dependent (BOLD) scans were acquired in 43 contiguous oblique axial 3 mm slices at a 40º angle (TR= 2500 ms, TE= 30ms, flip angle = 90°, in-plane resolution=3mm). Visual stimuli were back-projected to a screen from a shielded LCD projector. Participants viewed the stimuli via a mirror that reflected the images on a screen.

Methods to minimize susceptibility artifact: To optimize signal in ventromedial prefrontal regions by minimizing susceptibility artifact, all participants were positioned in the scanner so that the angle of the AC-PC plane is between 17° and 22° in scanner coordinate space. The angle was verified with a localization scan. This careful positioning ensured that the 40° slice acquisition angle was applied in the same way for all participants. These procedures were developed in collaboration with the HBIC MR physicist, Dr. Phil Lee.

fMRI Analysis

Data Analysis: Item and source memory performance data in the scanner were analyzed in SPSS using independent t-tests. fMRI data were analyzed using the Brain Voyager QX (version 2.4.2) statistical package and random effects (Brain Innovation, Maastricht, Netherlands, 2004). Following standard preprocessing steps, functional images were realigned to the anatomic images obtained within each session and normalized to Talairach space (Talairach, 1988).

Motion in any run of more than 3 mm along any axis (x, y, or z) resulted in the discard of that run. Out of 134 runs, two were discarded due to motion. Activation maps were generated using statistical parametric methods and random effects contained within the Brain Voyager QX software (version 2.4.2). Statistical parametric maps were overlaid on 3-D renderings of average structural scans. Statistical contrasts were conducted using multiple regression analysis within the general linear model. Contrasts between conditions of interest were assessed with *t* statistics across the whole brain. The analysis of interest included the following contrasts: 1) item hits verses correct rejections and 2) source memory hits verses item memory hits. Voxel values were considered significant if the activation survived a statistical cluster-based threshold of $p < .01$. A family-wise approach was used to correct for multiple comparisons ($a < .05$; $p < .01$; $k=7$ voxels). Computation of the minimum cluster threshold was accomplished via MonteCarlo simulation of the data using a thousand iterations. This method exploits the assumption that areas of activity tend to stimulate signal changes over spatially contiguous groups of voxels rather than over sparsely isolated voxels.

Whole Brain Analyses

The analysis of interest included the following contrasts: 1) item hits verses correct rejections and 2) source memory hits verses item memory hits. There was adequate power to test these contrasts. There were on average 30 samples to average for each subject in each of these conditions. Two sets of analysis were performed. First, an interaction analysis was performed examining group (OCD, HC) x stimulus type (Target Hit verses Correct Rejection). The regions resulting from this analysis identify brain regions in which the OCD group showed greater activation compared to healthy controls during correct recognition of target objects compared to correct rejection of distracters. Second, to determine whether there were differences between

individuals with OCD and healthy controls during source memory recall, we performed an analysis examining activation during correct source recall compared to object recognition, this time focusing on group (OCD, HC) x stimuli (Source Hit verses Target Hit). The regions resulting from this analysis identify brain regions in which the OCD showed greater activation compared to healthy controls during correct recall of source (the room where the object was encoded) compared to correct recognition of the object.

Region of Interest (ROI) Data Analyses

Follow-up analyses of ROIs were conducted in regions that achieved statistical significance in the group analyses. Mean percent signal change from baseline for each condition (Target Hits, Correct Rejection, and Source Hits) in the maximum voxel within each region for each individual was exported to Microsoft Excel for Mac 2008 (Microsoft Corporation).

Results

Demographic Data

Demographic data for the OCD and healthy control group are shown in Table 1. There were no significant differences between the OCD and healthy control group in terms of age, education, or general cognitive ability (all p's $> .05$). In terms of racial or ethnic background, the study sample was 87.9% Caucasian, 3% African American, and 9.1% Hispanic. Regarding medication use, 27% ($n = 9$) of participants (in the OCD group) reported taking anti-depressant medication, specifically a selective serotonin reuptake inhibitor (SSRI). No other psychoactive medications were allowed. Participants with OCD reported a moderate level of OC symptoms (*Mean YBOCS* = 18.9, *SD* = 3.6), compared to the healthy participants, who reported minimal symptoms, (Mean YBOCS= .89, SD= 1.4). Compared to the control group, participants with

OCD reported significantly higher levels of OC symptoms, $F(1,56)= 49.45$, $p < .01$, anxiety, $F(1,56) = 44.50$, $p < .01$, and depressive symptoms $F(1,56) = 48.45$, $p < .01$.

Behavioral Performance

Accuracy and reaction time results are shown in table 2. For each subject, all runs for the task were combined for analysis of behavioral responses. Each target response was classified as either a target hit or a target miss. Each distracter recognition response was classified as either a correct rejection or a false alarm. Overall memory descriminabilty index was calculated as: (Target-Hits – False Alarms)/ Total Number of Items. Each source response was classified as either source correct or source incorrect, and source accuracy was calculated based on the proportion of objects correctly recognized as old that were attributed to the correct source. There were no significant differences in behavioral performance between the OCD and healthy control groups on target (t= 1.2, p=.26), distracter (t= -2.39, p = .81), or source memory accuracy (t= -72, p= .43). In addition, no significant differences were observed in terms of reaction time (all p's > .05), respectively.

fMRI Results

Contrast 1: Target-Hits verses Correct Rejections

First, we sought to determine whether there were between group differences in terms of neural activation related to object memory performance. An interaction analysis was performed examining group (OCD, HC) x stimulus type (Target Hit verses Correct Rejection). The regions resulting from this analysis identify brain regions in which the OCD group showed greater activation compared to healthy controls during correct recognition of target objects compared to correct rejection of distracters. Comparison between the OCD and healthy control group revealed no regions of significant difference. When each group was examined separately,

significant activation was observed in regions previously implicated in object memory in both groups, including the left prefrontal cortex, medial temporal lobe, and parietal cortex. Additionally, examining these maps indicated a large degree of overlap between the OCD and HC group.

Contrast 2: Source Correct verses Target Hits

Second, to determine whether there were differences between individuals with OCD and healthy controls during source memory recall, we performed an analysis examining activation during correct source recall compared to object recognition, this time focusing on group (OCD, HC) x stimuli (Source Hit verses Target Hit). The regions resulting from this analysis identify brain regions in which the OCD showed greater activation compared to the healthy controls during correct recall of source verses correct recognition of the object. Statistically significant differences were observed between the OCD and HC groups (see Table 3). Specifically, the OCD group exhibited greater source memory verses item memory effects in the left medial PFC, right premotor cortex/dorsolateral PFC, posterior bilateral cingulate cortices, and right parietal cortex, when compared to the control group. Conversely, the HC group did not show significantly greater brain activation during source memory performance compared to item memory, in any brain region, compared to individuals with OCD. These relationships are depicted in figure 2 and 3.

ROI Analysis

Based on the results of the whole brain analysis, regions of activation in the left medial PFC, premotor cortex/dorsolateral prefrontal cortex, posterior bilateral cingulate cortices, and right parietal were selected and percent signal change from baseline was calculated for each condition (Target Hits and Source Correct).

The OCD group exhibited greater source verses item memory effects in the left medial PFC (x, y, z = -10, 46, 15) when compared to the control group. Further examination of the data revealed that in left medial PFC this significant interaction was driven by a greater decrease in activation in the OCD group during correct recognition of targets compared to the HC group.

Greater source memory verses item memory effects were also observed for the OCD group compared to the HC group in the right premotor cortex/dorsolateral PFC (x, y, z = 32, 4, 36). Examination of these data revealed, that this significant interaction was driven by the HC group compared to the OCD group exhibiting increased activation during correct recognition of targets. The HC also exhibited greater activation during target correct verses source correct trials, while no differences between target correct and source correct trials were observed for the OCD group. Thus, the HC group exhibited greater target correct effects in this region.

Next, individuals with OCD exhibited greater source memory verses item memory effects in posterior bilateral cingulate cortices when compared to the control group. Based on whole brain analysis, percent signal change in the posterior bilateral cingulate cortices (x, y, z = 5, -47, 24; x, y, z = -13, -44, 27), for source correct and target hit trials verses baseline was calculated (See Figure 3). Examination of these data revealed that the significant interaction was driven by increased activation in the bilateral cortices in the OCD group compared to the HC during source correct. In the bilateral posterior cingulated cortices, the OCD group exhibited increased activation compared to the HC for source correct. The OCD group exhibited deactivation in the right cingulate cortex region during correct object recognition, while the HC exhibited deactivation during both correct target and source recall. In the left posterior cingulate, the OCD group exhibited increased activation for source recognition, and deactivation during object recognition. The HC group exhibited the opposite pattern, with increased activation for object

recognition, and decreased activation during source recall. Thus, the OCD group exhibited greater source memory effects in the bilateral posterior cingulate cortices, while the HC group exhibited greater object memory effects in left posterior cingulate cortex region.

Finally, the OCD group exhibited greater source memory verses item memory effects in the right parietal lobe (x, y, z =29, -65, 39) when compared to the control group. Examination of these data revealed that the significant interaction was driven by increased activation during object recognition in the HC group compared to the OCD group. Examination of percent signal change data for the right parietal lobe revealed greater activation during target correct responses compared to source correct for the HC group compared to the OCD group, which exhibited the greater activation for source correct verses target correct. Thus, the HC engaged this region to a greater extent during correct object recognition.

Discussion

In this study we sought to examine object and source memory in individuals with OCD using an ecologically valid paradigm. Contrary to our hypotheses, no differences were observed between the OCD and CNT group in terms of behavioral performance. These results are consistent with some past studies (Constans, et al., 1995; McNally & Kohlbeck, 1993; Moritz, et al., 2006). Results of this study do not support the theory that individuals with OCD exhibit behavioral impairments in object and source memory on an ecologically valid task. While no significant differences were found between the two groups in terms of behavioral performance, individuals with OCD exhibited different patterns of task related activation in the left medial prefrontal, right premotor cortex/dorsolateral PFC, parietal lobe, and posterior cingulate cortical areas relative to healthy controls during correct source memory recognition verses object recognition. Thus, even when no differences in behavioral performance were observed,

differences were found in brain regions supporting task performance. The absence of performance differences is advantageous in terms of simplifying interpretation of the neuroimaging results, because differences in the observed neural correlates of memory between the two groups cannot be attributed to differences in overall performance (Morcom, Li, & Rugg, 2007). The medial prefrontal, dorsolateral prefrontal cortex, parietal lobe, and posterior cingulate cortical areas have been implicated in memory (Fan, Gay Snodgrass, & Bilder, 2003; Suzuki & Amaral, 1994), as well as neurobiological processes underlying OCD (Busatto et al., 2000; Friedlander & Desrocher, 2006; Rauch, Dougherty, et al., 2001; Rauch, Makris, et al., 2001).

Medial Prefrontal Cortex

The OCD and HC groups exhibited differential activation in the medial prefrontal cortex during correct source verses object recognition. Examination of differences in the left medial PFC, revealed a greater reduction in activation in the OCD group during correct object recognition (vs. source judgments) compared to the HC group, suggesting that the OCD group exhibited a greater reduction in activation in this region during object recognition compared to the control group. The medial prefrontal cortex serves executive functions that are essential for behavioral flexibility, action monitoring, and behavioral control (Passetti, Chudasama, & Robbins, 2002). Prefrontal cortex dysfunction has been identified as a key neurobiological correlate of cognitive inflexibility and behavioral disinhibition associated with neuropsychiatric disorders such as obsessive-compulsive disorder. The important role of the medial PFC in top-down cognitive control mechanisms is particularly well documented (Narayanan & Laubach, 2006; Passetti, et al., 2002). A greater reduction in activation in this region, may suggest diminished flexibility and action monitoring. The findings of the present study are consistent with a previous study that found decreased medial PFC activation in individuals with OCD, and

their unaffected relatives compared to healthy control subjects during a working memory task, despite no differences in behavioral performance (Chamberlain et al., 2008). The findings of decreased activation in the medial PFC observed in this study suggest that OCD disrupts of the engagement of regions that support behavioral control and cognitive flexibility.

Premotor/Dorsolateral Prefrontal Cortex

The HC group exhibited greater activation in a brain region including both premotor cortex and dorsolateral prefrontal cortex (DLPFC) during correct object recognition compared to the OCD group, suggesting that the HC group engaged this region to a greater extent during object recognition compared to the OCD group. The DLPFC is involved in motor planning, working memory, and anticipating actions. The present study found reduced activation in this region during correct object recognition in individuals with OCD compared to the HC group, which may reflect greater action planning in the healthy control group compared to the OCD group during object recognition. This finding is consistent with previous studies that found decreased DLPFC activation associated with impaired planning capacity in OCD patients (Schlosser et al., 2010; van den Heuvel et al., 2005). Past studies have also reported decreased activation in premotor regions in individuals with OCD (den Braber et al., 2010). For example, a study examining brain activation during the Tower of London planning paradigm in twins concordant and discordant for OC symptoms (den Braber, et al., 2010), observed reduced activation in the premotor cortex for the high OC symptom group, despite intact behavioral performance.

Posterior Cingulate Cortex

The OCD group exhibited greater source memory effects in the posterior bilateral cingulate cortices compared to the healthy control group. The posterior cingulate cortex plays a

key role in memory, as it has particularly strong reciprocal connections with medial temporal lobe memory structures, including the entorhinal and parahippocampal cortices (Morris, Pandya, & Petrides, 1999; Suzuki & Amaral, 1994). Previous imaging studies have found the posterior cingulate cortex to be activated during naturally acquired autobiographical memory retrieval (Andreasen et al., 1995; Maddock, Garrett, & Buonocore, 2001). Although neurobiological models of OCD have emphasized the role of orbitofrontal cortex, anterior cingulate cortex, and the caudate nucleus, several functional imaging studies have also pointed to a role for posterior cingulate cortex in OCD (Busatto, et al., 2000; Rauch, Dougherty, et al., 2001; Rauch, Makris, et al., 2001). For example, a study examining preoperative predictors of treatment for OCD patients undergoing an anterior cingulotomy found that preoperative glucose metabolic rates in the right posterior cingulate cortex significantly correlated with subsequent reduction in OCD symptom severity following anterior cingulotomy (Rauch, Dougherty, et al., 2001). A positive correlation between regional cerebral blood flow in the posterior cingulate cortex and subsequent symptomatic improvement following treatment with serotonergic reuptake inhibitor (SRIs) treatment has also been reported (Rauch et al., 2002). In the present study, increased activation was observed in the bilateral posterior cingulated cortices. This "hyperactivation" may be a compensatory, and adaptive response during source recognition (e.g.,Cabeza, Anderson, Locantore, & McIntosh, 2002; Cabeza et al., 1997; Park et al., 2004), since behavioral performance was maintained.

Deactivation exhibited by the HC group in the bilateral posterior cingulate cortices during source recognition may reflect the active suppression of processing that would otherwise interfere with or divert resources from successful retrieval. If OCD impairs inhibition, as has been proposed, lack of inhibition may reflect lack of suppression of irrelevant details of the

learning episode or failure of inhibition in individuals with OCD. Further data are needed to test this possibility. It is also be possible to account for some of the group differences in terms of differences in the cognitive strategies and operations employed by individuals with OCD and HC participants during memory retrieval.

Parietal Cortex

Differences between the OCD group and HC were also observed in the parietal cortex. Specifically, the HC group exhibited greater activation for target correct compared to the OCD group. The parietal cortex is one of the regions most frequently activated during episodic retrieval (Cabeza & Nyberg, 2000). Several studies found that certain parietal regions, specifically the superior parietal region, show greater activity for recollection than for familiarity (Eldridge, Knowlton, Furmanski, Bookheimer, & Engel, 2000; Henson, Rugg, Shallice, Josephs, & Dolan, 1999). This region is thought to be involved in the voluntary allocation of attention, and is associated with top-down (attention guided by goals) processes supporting retrieval search, monitoring and verification. As such, dysfunction related to this region does not always translate in deficits in behavioral performance. Past studies examining object and source performance in individuals with parietal lesions, revealed intact object and source memory. However, subjects with parietal lesions reported decreased vividness and lack of confidence in their memory, despite intact behavioral performance (Davidson et al., 2008). The present study found reduced activation in this region during correct object recognition in individuals with OCD compared to controls, which may reflect greater attention driven recollection in the healthy control group compared to the OCD group. The finding of reduced activation is consistent with other studies, including findings from a study examining brain activation during the Tower of London planning paradigm in twins concordant and discordant for OC symptoms (den Braber, et

al., 2010), which observed reduced activation in this region for the high OC symptom group, despite intact behavioral performance.

Strengths/Limitations and Future Directions

Strengths of the study include the exclusion of individuals with OCD who met criteria for other axis I disorders. Groups were also carefully matched in terms of gender, age, education, handedness (all right), and general cognitive ability. The absence of performance differences is advantageous in terms of simplifying interpretation of the neuroimaging results, because differences in the observed neural correlates of memory between the two groups cannot be attributed to differences in overall performance (Morcom, et al., 2007). Some limitations of the study include, the limited sample size, and exclusion of males. Gender differences in object and source memory have been reported in previous studies (De Goede & Postma, 2008; Lejbak, Vrbancic, & Crossley, 2009; Voyer, Postma, Brake, & Imperato-McGinley, 2007; Wang & Fu, 2010). Because past studies suggest that males and females process context information differently (Piefke & Fink, 2005), collapsing males and females into statistical comparison may bias fMRI results. Future studies may examine gender differences in neural correlates of memory between male and females with OCD. A further limitation includes the inclusion of individuals with OCD who were taking an SSRI medication. It should be noted that individuals who were taking antidepressant medication were on a stable dose for at least two months prior to scanning. While it is possible that antidepressant medication may impact the findings of this study, a study comparing neuropsychological performance between SSRI medicated and un-medicated individuals with OCD found no differences between the two groups on a comprehensive battery of neuropsychological tests (Mataix-Cols, et al., 2002). Additionally, a study examining the effects of an SSRI (escitalopram) found no significant effects on

performance or the hemodynamic response during working memory tasks. (Rose, Simonotto, Spencer, & Ebmeier, 2006). Therefore, it is not likely the observed differences between the two groups were due to medication effects.

Another possible limitation of the study is that the OCD group included individuals with mixed symptom types. It is possible that impairments may be specific to symptom type. For example, some studies suggest that OCD impairments may be more consistent in patients with primarily checking concerns (Omori et al., 2007). Future studies may investigate neural correlates of memory in more homogenous subgroups of individuals with OCD.

Conclusions

Results of this study suggest that despite no differences in terms of behavioral performance, individuals with OCD exhibited different patterns of task related brain activation. While the level of performance was matched between individuals with OCD and healthy controls, the groups differentially recruited several brain regions to support source recognition. Differences between the OCD and HC groups emerged in brain regions known to play a role in planning, anticipating actions, and cognitive flexibility, such as the DLPFC and MPFC, as well as brain regions related to episodic retrieval, such as the bilateral cingulate cortices, and regions involved in top down processes supporting retrieval (attention guided by goals), such as the parietal cortex.

The findings of decreased activation in the medial PFC observed in this study suggest that OCD may disrupt the engagement of regions that support behavioral control and cognitive flexibility. Decreased DLPFC activation observed in the OCD group during object recognition may reflect impaired motor planning, a finding that is consistent with past research suggesting impaired planning capacity in OCD patients (Schlosser, et al., 2010; van den Heuvel, et al.,

2005). Increased activation in the parietal region during correct object recognition in healthy individuals compared to the individuals with OCD observed in this study, may reflect greater attention driven recollection in the healthy control group compared to the OCD group. Failure to modulate the bilateral cingulate cortices was also observed in the OCD group, which may reflect a compensatory, and adaptive response in the OCD group during source memory recognition.

In some situations, individuals with OCD lack confidence in their memory, even when accuracy is normal (Hermans, et al., 2008). Results of this study suggest that even when behavioral performance is unaffected, differences exist in terms of the underlying neural correlates related to memory in OCD. Future studies should examine how these differences relate to memory confidence and doubt. Increased understanding of the role of neural processes related to memory and cognitive processing in OCD may lead to increased understanding of this debilitating disorder, and more targeted interventions.

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Table 1. Demographics

	OCD Mean (SD)	HC Mean (SD)	t	df	p
Age	25.1 (8.6)	26.7(9.7)	.47	31	.64
Education	15.1 (1.6)	15.3(1.9)	.28	31	.78
WASI	119.3(10.1)	120.2(5.0)	.33	21.6	.75
OCI-R	32.3(13.2)	5.0(8.2)	-7.1	24.8	.0000001
YBOCS	18.9(3.6)	.89(1.4)	-18.9	19.3	.0000001
DOCS	24.5(9.8)	2.7(2.9)	-8.5	17.4	.0000001
BAI	14.2(7.1)	2.6(3.0)	-5.8	19.1	.00001
BDI	16.6(10.5)	2.7(3.9)	-5.0	18.8	.00009

Note. WASI= Wechsler Abbreviated Scale of Intelligence; OCI-R=Obsessive Compulsive Inventory Revised Version; YBOCS= Yale Brown Obsessive Compulsive Scale-Self Report Version; DOCS= Dimensional Obsessive Compulsive Scale; BAI= Beck Anxiety Inventory; BDI-II= Beck Depression Inventory-Second Edition

Table 2. Behavioral Performance

	OCD Mean (SD)	HC Mean (SD)	t	df	p
Target % Accuracy	85.9 (4.5)	82.3(11.9)	1.2	20.7	.26
Distracter % Accuracy	86.1 (11.2)	86.9(8.4)	-.239	31	.81
Object Discriminability	86.0 (6.0)	84.6 (7.8)	-.57	31	.57
Target Response Time (ms)	1851(232)	1778(248)	-.86	31	.40
Distracter Response Time (ms)	2265(434)	2114(273)	-1.18	31	.25
Source % Accuracy	76.3 (22.1)	81.5(14.4)	-.79	31	.43
Source Reaction Time	1560(355)	1377 (244)	-1.7	31	.10

Table 3. Regions of Significant activation for Random Effects GLM Contrast of Source Hit verses Target Hit, OCD verses HC

Regions Reaching Significance During GLM Contrasts of OCD > Healthy Control

		Talairach Coordinates					
Region and Contrast	L/R	X	Y	Z	Voxels	*t*	*P value*
Source Hit vs. Target Hit							
A priori							
Left Medial Prefrontal Cortex	L	-10	46	15	7	3.63	.0010
Premotor cortex/Dorsolateral prefrontal cortex	R	32	4	36	12	4.04	.00034
Right Posterior Cingulate Cortex	R	5	-47	24	11	4.02	.00035
Left Posterior Cingulate Cortex	L	-13	-44	27	13	4.26	.00018
Post hoc							
Right Parietal Lobe	R	29	-65	39	7	3.45	.0016

Figure 1. Object and source memory fMRI paradigm: Participants viewed pictures of objects, which were present in the rooms during encoding (targets) and some that were not (distracters). They were asked to indicate (using a response button) whether each object was old or new, and also for objects that were identified as "old" to indicate the source (which room the object seen in). The order of these responses choices was counterbalanced between participants. A variable length of fixation was viewed between trials. Target and distracter objects were counter balanced across participants.

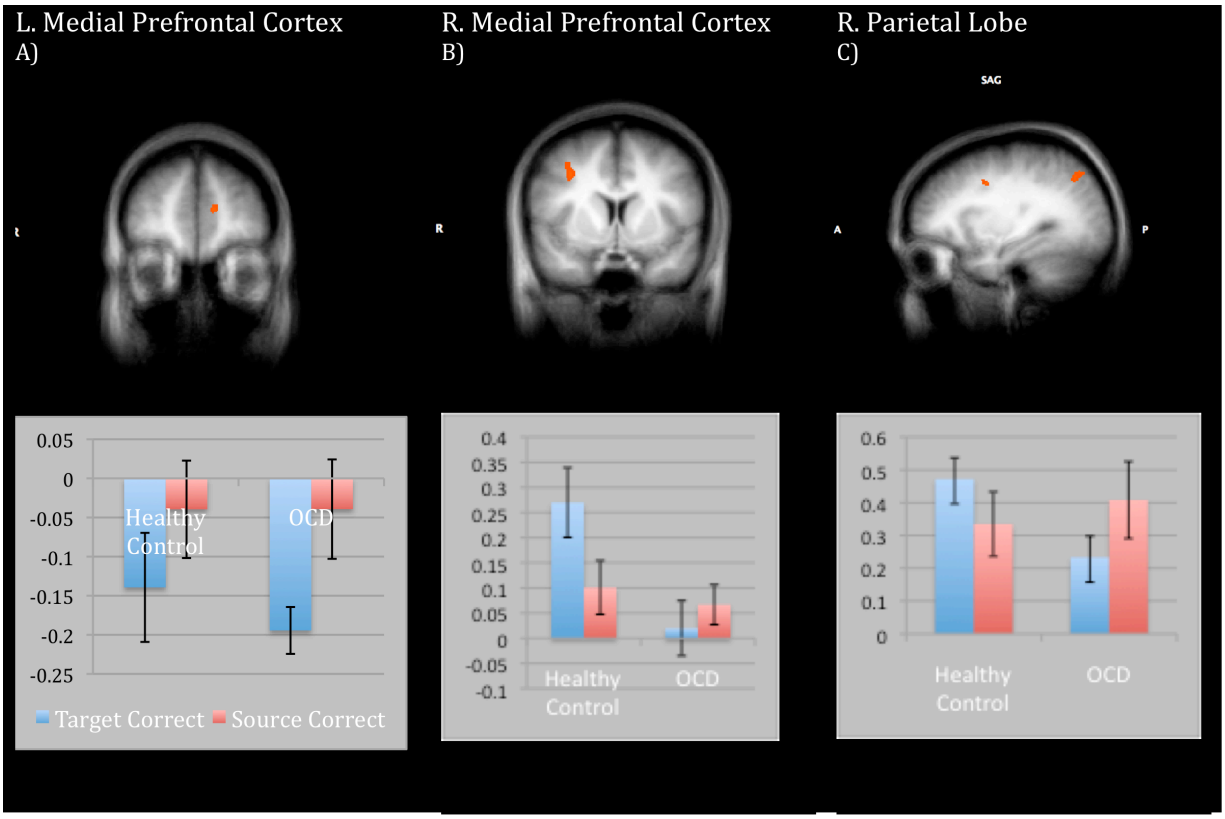

Figure 2. Comparison of Source Correct verses Target Hits by OCD verses HC groups. Mean percent signal change in the maximally activated voxel for each cluster was extracted and calculated for each condition. Areas of activation were found in the A) left medial PFC (x, y, z = -10, 46, 15), B) right premotor cortex/DLPFC (x, y, z = 32, 4, 36), and C) the right parietal lobe (x, y, z = 29, -65, 39).

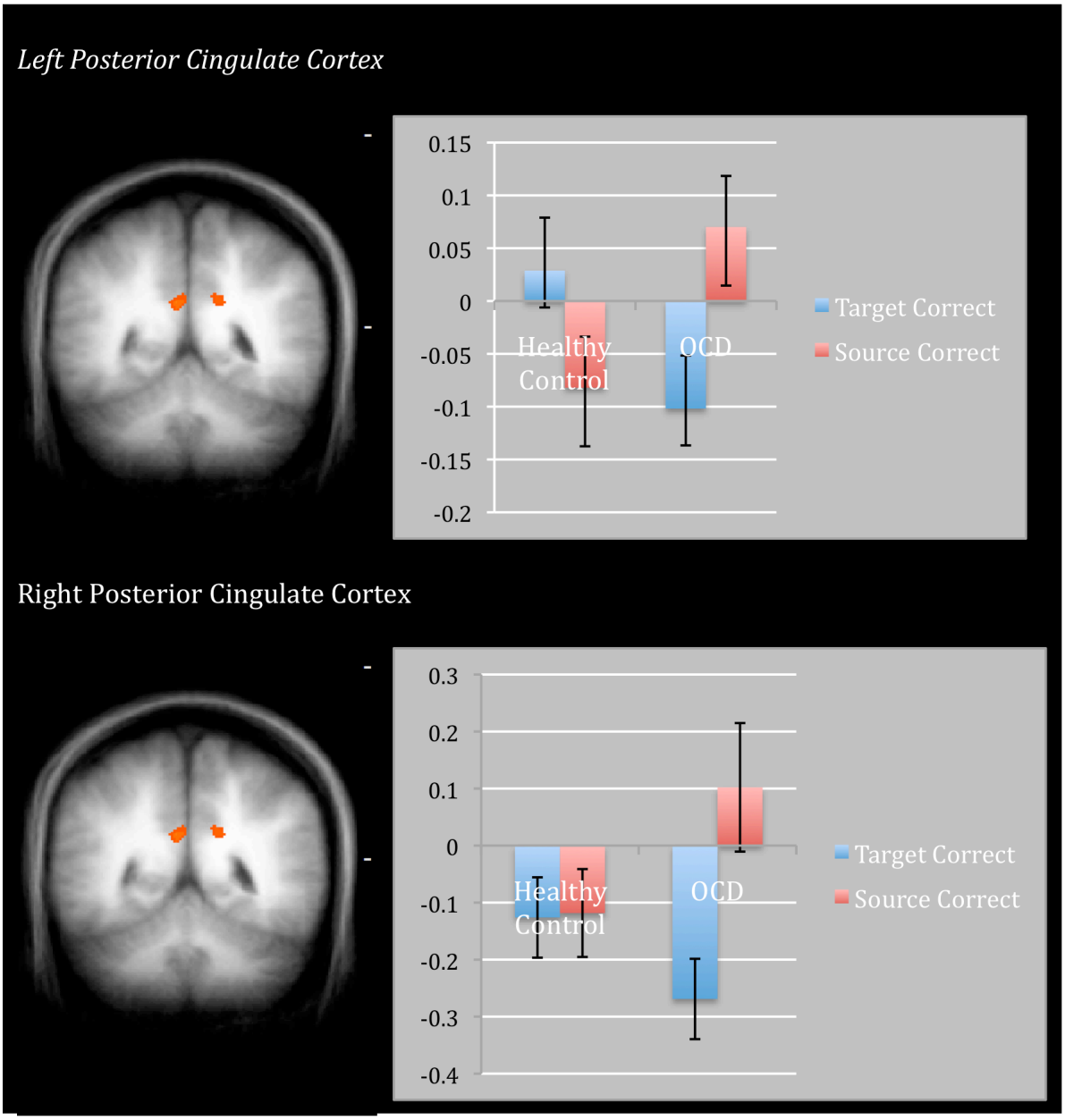

Figure 3. Comparison of Source Correct verses Target Hits, OCD verses HC. Mean percent signal change in the maximally activated voxel of each cluster was extracted for each condition. Clusters of activation shown for the bilateral cingulated cortices A) Left Cingulate Cortex (x, y, z = -13, -44, 27), and B) Right Cingulate Cortex (x, y, z = -5,-47, 24).