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Abstract: Background: Recollection is disrupted in Major Depressive Disorder (MDD), but this disruption can be minimized by focused attention at encoding and retrieval. The neural mechanisms responsible for these clinically important phenomena are unclear. Thus, we used event-related potentials (ERPs) to examine recollection in MDD.

Methods: Twenty-four unmedicated adults with MDD and 24 controls encoded words shown on the left or right (perceptual source) by making animacy or mobility judgments (conceptual source). ERPs were recorded during cued source retrieval, which depends on recollection.

Results: Mobility judgments prompted deeper encoding than animacy judgments, and memory accuracy was characterized by a Group x Cue x Encoding Task interaction: depressed adults were generally less accurate and less confident than controls, but they showed excellent conceptual source memory following deeper encoding. In parallel, a positive parietal ERP deflection that tracks recollection was globally reduced in depression, but sustained left parietal activation was seen during conceptual source judgments for deeply encoded words in MDD.

Conclusions: This study links two reliable effects of depression on recollection to electrophysiological activity over parietal cortex. First, accuracy and confidence were reduced in MDD, and the most reliable ERP correlate of recollection—a positive parietal deflection from 400-800 ms—was blunted. Second, depressed adults showed excellent memory when the encoding and retrieval tasks demanded sustained attention, and this combination elicited lasting left parietal activity. These results link the impact of depression on recollection to parietal circuits that communicate with the hippocampus, highlighting the need for further work on this important topic.

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Dr. Joormann is an expert on cognitive dysfunction in depression.

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Dr. Deldin has a long track record of excellent ERP research focused on depression.

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Dr. Dobbins is a leading researcher on the cognitive neuroscience of episodic retrieval, and he conducted pioneering work focused on dissociating conceptual versus perceptual source memory, which is key to our study.

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Dr. Foti is a leader in novel ERP approaches to depression, and we use advanced ERP techniques to study MDD in this manuscript.

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Dr. Simons developed the experimental paradigm that we adapted for our study, and his group reported the ERP results (in healthy adults) that guided our analytic strategy.

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We found excellent memory in depressed adults when deep encoding was paired with deep retrieval. This result was unexpected but is perfectly in line with work that Dr. Hertel has conducted over the past 20 years; we cite her numerous times as a consequence.

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October 6, 2016

John H. Krystal, M.D.
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Dear Dr. Krystal:

Enclosed please find our manuscript entitled, "**The Impact of Depression on Brain Activity During Source Memory Retrieval**", which we are submitting for consideration as an Archival Report in *Biological Psychiatry*.

The goal of the present study was to fill an important hole in the literature. Specifically, although behavioral research on unipolar depression has consistently revealed episodic memory deficits with key implications for treatment, functional studies of this topic are surprisingly rare. Thus, we conducted an event-related potential (ERP) investigation of source memory retrieval in unmedicated adults with Major Depressive Disorder (MDD) and healthy controls.

We report two main findings, which are informed by extensive work in healthy adults linking successful episodic retrieval with a positive ERP deflection over left parietal cortex. First, we found a significant reduction in this ERP from 400-800 ms in our MDD group, highlighting a neural mechanism that could underlie the episodic memory deficit in depression. Second, we found that depressed adults were exquisitely sensitive to the match between encoding task and retrieval cue. Specifically, although depressed adults were generally less accurate and less confident than controls, they were extremely accurate when cued to retrieve words from a deep encoding condition, and this corresponded to sustained activation of the same sector of left parietal cortex. In other words, depressed adults performed worse than controls except when engaged in conceptual source retrieval, and the variation in their memory accuracy was linked to an ERP that is known to reflect activity in parieto-hippocampal circuits that support recollection.

This is one of the first functional studies of source memory in MDD. Given the clinical importance of memory deficits in depression and the dearth of neuroscientific studies on this topic, we believe the manuscript would appeal to readers of *Biological Psychiatry*; we hope its publication in the journal would spur additional imaging, molecular, and translational research on this critical topic. On the next page we have listed six well-qualified reviewers. Thank you for your time, and we look forward to hearing from you.

Sincerely,

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DEPRESSION MODULATES SOURCE MEMORY

The Impact of Depression on Brain Activity During Source Memory Retrieval

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Abstract

Background: Recollection is disrupted in Major Depressive Disorder (MDD), but this disruption can be minimized by focused attention at encoding and retrieval. The neural mechanisms responsible for these clinically important phenomena are unclear. Thus, we used event-related potentials (ERPs) to examine recollection in MDD.

Methods: Twenty-four unmedicated adults with MDD and 24 controls encoded words shown on the left or right (perceptual source) by making animacy or mobility judgments (conceptual source). ERPs were recorded during cued source retrieval, which depends on recollection.

Results: Mobility judgments prompted deeper encoding than animacy judgments, and memory accuracy was characterized by a *Group x Cue x Encoding Task* interaction: depressed adults were generally less accurate and less confident than controls, but they showed excellent conceptual source memory following deeper encoding. In parallel, a positive parietal ERP deflection that tracks recollection was globally reduced in depression, but sustained left parietal activation was seen during conceptual source judgments for deeply encoded words in MDD.

Conclusions: This study links two reliable effects of depression on recollection to electrophysiological activity over parietal cortex. First, accuracy and confidence were reduced in MDD, and the most reliable ERP correlate of recollection—a positive parietal deflection from 400-800 ms—was blunted. Second, depressed adults showed excellent memory when the encoding and retrieval tasks demanded sustained attention, and this combination elicited lasting left parietal activity. These results link the impact of depression on recollection to parietal circuits that communicate with the hippocampus, highlighting the need for further work on this important topic.

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Introduction

Memory retrieval plays a key role in Major Depressive Disorder (MDD) and, increasingly, in its treatment. Retrieval in depression is “overgeneral” (1): cued to recall specific episodes, depressed adults tend to offer categorical accounts, summaries that convey gist but few details. This lack of precision has consequences, as overgeneral retrieval predicts a longer course of illness (2–4). Moreover, increasing retrieval specificity can decrease hopelessness and brooding rumination, improve problem solving, and lead to sustained remission (5; 6). In short, memory retrieval is impaired in depression and enhancing it can bring lasting relief.

Given these facts, the paucity of data regarding the neurobiology of memory retrieval in depression is astonishing, particularly since episodic retrieval in healthy adults has been studied extensively (7–9). This does not reflect lack of desire; a decade ago, the National Institutes of Mental Health, Aging, and Neurological Disorders and Stroke called for integrated research on depression and memory (10). Furthermore, the nature of the problem is clear. As one might expect from work on overgeneral memory, depression impairs recollection—the retrieval of contextual details specifying the spatiotemporal source of memories (11–14). However, despite dozens of event-related potential (ERP) and functional magnetic resonance imaging (fMRI) studies of recollection in healthy adults, no similar literature in MDD has emerged.

The current study addresses this gap by using ERPs to study source memory in MDD. We adapted a design that dissociates neural systems engaged by conceptual versus perceptual source retrieval (15–17), using neutral stimuli to avoid confounds associated with mood-congruent encoding (18–20). At study, participants viewed words presented on the left or right above a question specifying either an animacy or mobility judgment. At test, they were cued to retrieve the presentation side (perceptual source) and encoding task (conceptual source).

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A recent fMRI/ERP study (15) found that both conceptual and perceptual retrieval elicited the most well-studied ERP marker of recollection: a positive deflection over parietal cortex that extends from about 400-800 ms post-stimulus, often with a left hemisphere maximum, and that is thought to reflect information transfer between the hippocampus and parietal lobes (7). Both forms of retrieval also activated the precuneus and elicited a negative polarity ERP maximal over posterior electrodes and referred to as the late posterior negativity, or LPN (21–23). The LPN extended over left frontal cortex during conceptual retrieval, and this was mirrored by fMRI activation in the dorsolateral PFC.

These findings suggest that retrieval attempts activate parieto-hippocampal circuits, bringing candidate memories to mind and generating the parietal ERP effect. Next, those candidate memories are reviewed until one is selected and endorsed. The review and selection of perceptual memories strongly engages posterior cortical regions, but conceptual retrieval differentially activates left PFC regions that support semantic encoding, elaboration, and selection (24). Because MDD is associated with volumetric loses in hippocampus and PFC (25), and because depressive rumination may occupy left PFC circuits, we anticipated disrupted conceptual source memory in depression.

However, during our analysis it became clear that we had overlooked a key factor. Specifically, several studies report good memory in depression provided attention is sustained at encoding or retrieval (26–30). As detailed below, one of our tasks promoted deeper encoding than the other, and when words from that task were targeted for conceptual source retrieval, the MDD group was quite accurate. Thus, this study highlights neural mechanisms linked to disrupted source memory in MDD, as well as activity that supports recollection when encoding and retrieval conditions are salubrious.

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Materials and Methods

Participants and self-report

Participants (18-62 years old, right-handed, no neurological or unstable medical conditions) were recruited from the community and compensated (\$25/hour), using a protocol approved by the Partners HealthCare Human Research Committee. Participants were screened by phone or online, and we assessed psychiatric history with the MINI International Neuropsychiatric Interview, version 6.0 (31), also administering the Beck Depression Inventory II (BDI-II; 32). Controls had to report no current or past psychiatric conditions. Depressed adults had to report current depression, no history of other DSM-IV Axis I diagnosis (except generalized anxiety, social anxiety, or specific phobia secondary to MDD), no medication use in the past two weeks (six weeks for fluoxetine, six months for neuroleptics), and a BDI-II score \geq 14. Thirty-four controls and 26 depressed adults completed the ERP session. Data from 10 controls and 2 depressed adults were excluded due to excessive artifacts (see below), leaving 24 individuals per group.

We also administered the Mood and Anxiety Symptom Questionnaire (MASQ; 33), the Ruminative Responses Scale (RRS; 34), and the Pittsburgh Sleep Quality Index (PSQI; 35). These probe recent symptoms of depression and anxiety, trait rumination, and sleep quality over the last month, respectively. The Wechsler Test of Adult Reading (WTAR; 36) was used to assess IQ. One control did not complete the MASQ and one depressed participant did not complete the PSQI.

Task

The task was programmed in PsychoPy (37). Due to a hardware change, RT data were not recorded for one control and one depressed participant.

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Stimuli. We used the MRC Psycholinguistic Database (38) to select 25 words from four categories: “living/immobile” (e.g., *oak*), “non-living/immobile” (e.g., *shed*), “living/mobile” (e.g., *dog*), and “non-living/mobile” (e.g., *kite*). ANOVA yielded no differences for number of letters (mean \pm S.D.; 5.27 \pm 1.29) or syllables (1.52 \pm 0.50), frequency (35.58 \pm 79.02), concreteness (598.87 \pm 20.18), or imageability (596.80 \pm 25.31), $p > 0.064$. Words are listed in the Supplement.

Encoding. The task included six encoding-retrieval cycles. Each encoding block included 16 trials (Figure 1, *left*) in which a word appeared on the left or right above one of two questions: “living/non-living?” or “mobile/immobile?” Participants responded by pressing a button. A jittered interval (500-2000 ms) separated the trials.

Counting. Immediately after encoding, a 3-digit number (e.g., 931) was shown and participants counted backwards from that number in steps of three for 30 s. Counting served to disrupt rehearsal and clear working memory (39).

PLEASE INSERT FIGURE 1 ABOUT HERE

Retrieval. Each block comprised 48 trials that included a cue, word, and response screen (Figure 1, *right*). On 16 trials each, the cue was “Side” or “Question” and the word came from the preceding encoding block; these cues prompted perceptual and conceptual source retrieval, respectively. On the remaining trials the cue was “Odd/Even” the word was a numeral between “one” and “ninety-six”, and the participant judged parity. All trials involved reading a cue, interpreting it, and retrieving information, but on Odd/Even trials retrieval was directed at semantic rather than episodic memory. Thus, comparing ERP data from Side or Question trials versus Odd/Even trials should isolate activity mediating episodic retrieval. Presentation order of words and cues was random. The response screen consisted of ‘RESPOND’ printed above the

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word with the numbers 1-5 printed below and corresponding to a choice and level of confidence (Figure 1, *right*). A jittered interval (500-2000 ms) separated the trials.

EEG Recording

The EEG was recorded during retrieval with a 128-sensor HydroCel GSN Electrical Geodesics Inc (EGI) net (sample rate: 1000 Hz, 0.02–100 Hz). Data were referenced to vertex and impedances were kept below 45 k Ω when possible (maximum: 75 k Ω).

Behavioral Analysis

We analyzed trial-level data using linear mixed models implemented with the R (40) library *lme4* (41), as this easily accommodates covariates that might influence memory or depression, such as age and gender (42; 43). Specific models are described below, but in all cases we computed a model with task elements and covariates as fixed effects but without *Group*. We added *Group* in a second model and used likelihood ratio tests to compare model fits. If the second model was a significant improvement, we report its parameters; otherwise, we report parameters from the first model. All models used *Word* and *Subject* as random effects. When modeling encoding accuracy (coded 0 or 1), we used *glmer* with the logit link function. We extracted *p*-values with the R library *lmerTest*.

Encoding. We dropped trials (< 1%) with no response or where RT exceeded the participant's mean \pm 3SD. The first accuracy model included *Encoding Task*, *Side*, *Block*, *Gender*, and *Age*. The first RT model included the same factors plus *Accuracy*. The second models included the same factors plus *Group*.

Retrieval. We dropped trials with no response or where RT exceeded the participant's mean \pm 3SD (< 2%). Next we analyzed the Odd/Even trials. Accuracy on these trials was high (controls: 98.43% \pm 0.12; MDD: 99.13% \pm 0.09), and RT (in ms) was similar between groups

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(controls: 862.58 ± 51 ; MDD: 779.00 ± 48). *Group* did not improve models that included *Block*, *Age*, and *Gender*, χ^2 s < 2.1, p s > 0.14. Thus, Odd/Even trials elicited similar behavior across groups and are suitable as a control condition.

For Side and Question trials, accuracy was coded: incorrect, high confidence = 1; incorrect, low confidence = 2; guess = 3; correct, low confidence = 4; correct, high confidence = 5. Confidence was coded guess = 1, low confidence = 2, high confidence = 3. We computed three models for accuracy and confidence. The first included *Block*, *Cue*, *Encoding Task*, *Encoding Side*, *Age*, and *Gender*. The second added a *Cue* x *Encoding Task* interaction, and the third added a *Group* x *Cue* x *Encoding Task* interaction, plus the main effect and two-way interactions involving *Group*. We used similar models to analyze correct RT.

ERP Analysis

Pre-processing. Pre-processing was conducted with EEGLAB (44) and ERPLAB (45) toolboxes for MATLAB (MathWorks, Natick). EEG data were merged, re-referenced to the average of all electrodes, and filtered (0.1-30 Hz). Bad channels were interpolated, independent components analysis was used to remove activity reflecting blinks, HEOG, and EKG, and the cleaned data were time-locked to word onsets and segmented (-200 to 2000 ms). The pre-stimulus interval was used for baseline correction, and segments where any raw value or the maximum-minimum voltage difference (200 ms intervals, 100 ms sliding window) exceeded 100 μ V were rejected. We used *a priori* criteria of > 18 bad channels or more than 50% of trials rejected to exclude datasets (10 controls, 2 MDD). The mean number of clean segments in each bin defined by *Group* x *Cue* x *Task* ranged from 21-28 for source hits. Guesses were excluded from ERP analysis and there were too few clean segments for analysis of misses.

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Group-level analyses. We first inspected the ERP waveforms associated with correct responses to the Question, Side, and Odd/Even cues, regardless of encoding task. There was a clear group difference in the parietal ERP from 400-800 ms (see Results), thus we extracted mean amplitude data over this window from electrodes in the left (P1, P3, P5, P7) and right (P2, P4, P6, P8) hemispheres for a *Group x Cue x Hemisphere* ANOVA. This focus on a few electrodes in one time window constitutes the traditional approach to ERP analysis used in many studies of recollection (7; 46; 47)

Two additional analyses used a newer approach and focused on difference waves. In the first analysis, we computed “Question minus Odd/Even” and “Side minus Odd/Even” difference waves to isolate activity tracking conceptual and perceptual source retrieval, respectively, closely following prior methods (15). The second analysis was intended to parallel the memory accuracy data, which were characterized by a *Group x Cue x Encoding Task* interaction. To identify activity mediating this interaction, we computed “Question minus Side” difference waves separately for words from the mobility and animacy tasks in each group. For both analyses, we submitted the difference waves to mass univariate analysis (48), focusing on mean amplitudes from 400-800 ms, 800-1400 ms, and 1400-2000 ms. Mass univariate analysis is widely used in fMRI research (49) and here entails a one-sample *t*-test (within-group analysis) or a two-sample *t*-test (between-group analysis) at each electrode. By examining every electrode and multiple time windows, this makes better use of the spatiotemporal richness of ERP data than traditional methods. To correct for multiple comparisons, we used cluster-based permutation (50). All electrodes within 4 cm of each other were considered neighbors, and neighboring electrodes significant at $p < 0.05$ (uncorrected) were considered clusters. The sum of all *p*-values in a cluster constituted its mass. We then performed 2500 permutations, selecting the most extreme

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cluster mass from each permutation to generate a distribution (51) for judging the probability of observing clusters of various sizes. Only clusters significant at $p < 0.05$ (corrected) are reported.

Results

Demographics

There were no group differences in gender, age, education, or estimated IQ (Table 1).

Relative to controls, the MDD group endorsed poorer sleep plus more depression, anxiety, and rumination, with the mean BDI-II score indicating moderate depression.

PLEASE INSERT TABLE 1 ABOUT HERE

Behavior

Encoding. The mobility task was harder than the animacy task, as assessed by percent correct (mobility: 92.42 ± 0.26 ; animacy: 95.85 ± 0.20 ; $Z = -4.91, p < 0.001$) and RT (mobility: $1,801 \pm 552$ ms; animacy: $1,664 \pm 535$ ms; $Z = 10.54, p < 0.001$). Participants were faster when correct (*Accuracy*: $Z = -3.46, p < 0.001$) and RT decreased over the session (*Block*: $Z = -6.38, p < 0.001$). *Group* did not improve the models, χ^2 s < 1.93, $ps > 0.16$, thus depressed and healthy adults performed similarly.

Source accuracy. Source accuracy was influenced by depression and adding *Group* improved the model, $\chi^2 = 26.40, p < 0.001$. There was a *Group* \times *Cue* \times *Encoding Task* interaction, $Z = -2.13, p = 0.033$, which subsumed significant *Cue* \times *Encoding Task* and *Group* \times *Encoding Task* interactions plus main effects of *Cue* and *Encoding Task* ($Zs > 2.7, ps < 0.006$). Figure 2A (left panel) shows that the triple interaction emerged because accuracy under the Side cue did not vary by encoding task, but accuracy under the Question cue was better following mobility versus animacy judgments, with this effect larger in MDD. In the MDD group, a Question minus Side subtraction (Figure 2A, right) was positive for the mobility task but

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negative for the animacy task, $t(23) = 4.47, p < 0.001, d = 0.91$. In controls the Question minus Side subtraction was negative for both tasks but less negative for the mobility task, $t(23) = 2.04, p = 0.053, d = 0.42$. A between-groups test on Question minus Side difference scores for the animacy task was not significant, $t < 1$, but difference scores for the mobility task were more positive in MDD compared to healthy adults, $t(46) = 3.04, p = 0.004, d = 0.88$. In summary, conceptual source memory (prompted by the Question cue) was better following the mobility task versus the animacy task in both groups, but this effect was larger in depressed versus healthy participants. Analysis of hit rates yielded the same findings (see Supplement).

Importantly, this interaction occurred amidst relatively poorer performance by the MDD group. Indeed, pairwise tests showed that depressed adults outperformed controls in the Question/mobility cell of the design, $Z = -1.76, p = 0.08$, but in all other cells accuracy was (non-significantly) higher in controls, Z_s from 0.961-1.792, $p_s > 0.07$. Thus, depressed adults generally performed worse than controls, except for words from the mobility task presented under the Question cue. Finally, the best model included effects of *Age*, $Z = -3.31, p < 0.002$, *Gender*, $Z = 3.32, p < 0.002$, and *Block*, $Z = 3.23, p = 0.001$, reflecting higher accuracy in younger adults, in men, and in later blocks.

PLEASE INSERT FIGURE 2 ABOUT HERE

Source confidence. Figure 2B (top panel) shows that depressed adults were less confident than controls. Accordingly, the model was improved by *Group*, $\chi^2 = 18.46, p = 0.001$, and included a trending *Group* x *Cue* interaction, $Z = -1.65, p = 0.098$, as the difference in confidence was stronger under the Side cue, $Z = 2.42, p = 0.016$, than the Question cue, $Z = 1.14, p = 0.255$. The model included effects of *Cue*, $Z = -5.33, p < 0.001$, *Encoding Task*, $Z = 2.91, p =$

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0.004, and *Block*, $Z = 3.69$, $p < 0.001$, as participants were more confident when responding to the Question cue, to words from the mobility task, and in later blocks.

Source RT. Correct RT was similar across groups, with everyone slower in response to Question vs. Side cues (Figure 2B, bottom). Accordingly, the model was not improved by *Group*, $p = 0.08$, but it included an effect of *Cue*, $Z = -45.51$, $p < 0.001$. There were also effects of *Run*, $Z = -18.82$, $p < 0.001$, *Confidence*, $Z = 21.61$, $p < 0.001$, and *Gender*, $Z = -3.09$, $p = 0.003$, reflecting shorter correct RTs in later blocks, for high confidence responses, and in males.

ERPs

Figure 3 displays waveforms elicited by correct responses to Question, Side, and Odd/Even cues. There was robust activity over parietal electrodes from 400-800 ms in controls that was decreased in MDD, yielding an effect of *Group*, $F(1,46) = 4.35$, $p = 0.043$, $d = 0.40$. There was also an effect of *Cue*, $F(2,92) = 10.37$, $p < 0.001$, with reliable differences between all conditions (REGWQ; Question > Side > Odd/Even, $ps < 0.043$). These data suggest that recollection was strongest under the Question cue and reduced in MDD. In both groups, the LPN is apparent at Oz from 800-2000 ms on Question and Side (but not Odd/Even) trials, and it extends over left frontal cortex on Question trials.

PLEASE INSERT FIGURE 3 ABOUT HERE

To test our *a priori* hypothesis, we subtracted activity on Odd/Even trials from Question and Side trials. Figure 4 shows that the Question condition drove activity over left parietal electrodes from 400-800 ms, although this effect was only reliable in controls (a negative difference over right frontal cortex was only reliable in the MDD group). From 1400-2000 ms, this subtraction revealed a negative difference over left PFC in both groups. By contrast, the Side

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condition elicited an LPN over midline posterior sites from 800-1400 ms. These patterns replicate prior results (15), but between-groups tests yielded no reliable findings.

PLEASE INSERT FIGURE 4 ABOUT HERE

Group x Cue x Encoding Task. Our planned ERP analysis did not reveal group differences, but it was not designed to capture the *Group x Cue x Encoding Task* interaction that characterized source accuracy. To address this limitation, we computed Question minus Side difference waves for words from each encoding task and submitted them to within and between-groups analysis, duplicating our approach to the accuracy data. Figure 5 shows that, in depressed adults, the Question minus Side difference varied drastically by encoding task (see Table 2). Words from the mobility task elicited sustained activation over left parietal cortex, leading to significant effects in all time windows. By contrast, words from the animacy task elicited a negativity over fronto-central sites that was stronger over the left hemisphere; again, significant differences were observed in all time windows. In controls, no significant effects were seen in any time window. Between-groups comparisons revealed reliable differences for the mobility task over left centro-parietal electrodes from 400-800 and 800-1400 ms, with stronger activation in the MDD group. Thus, the Question (minus Side) cue had a strong, task-dependent effect on brain activity in MDD that was muted in controls, paralleling the source accuracy data.

PLEASE INSERT FIGURE 5 AND TABLE 2 ABOUT HERE

Individual Differences

We computed Pearson correlations in the MDD group to determine if variation in depressive severity (BDI-II total), brooding rumination (RRS-Brooding), or sleep disruption (PSQI total) affected source accuracy or ERP amplitudes. We found no relationship with source accuracy, left parietal activity on Question trials averaged over encoding tasks, or left frontal

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activity on Question/animacy trials ($|rs| < 0.31$, $ps > 0.15$). However, as shown in Figure 6, parietal activity isolated by the Question minus Side subtraction for words from the mobility task was negatively correlated with PSQI scores from 400-800 ms and 800-1400 ms ($rs < -0.47$, $ps < 0.02$). To confirm that these results did not simply reflect depressive severity, we computed hierarchical regressions with ERP amplitude as the criterion, entering BDI-II and PSQI scores in steps 1 and 2. PSQI predicted ERP amplitude after accounting for BDI-II (400-800 ms; $\beta = -0.45$, $p = 0.03$; 800-1400 ms; $\beta = -0.49$, $p = 0.03$), and adding PSQI improved both models ($\Delta R^2 > 0.16$, $\Delta Fs > 4.5$, $ps < 0.05$). Thus, ERP amplitude was lowest in those depressed adults who reported chronic sleep disruption, and this effect was not driven by depressive severity.

PLEASE INSERT FIGURE 6 ABOUT HERE

Discussion

This study yielded two sets of behavioral and ERP findings. Relative to controls, depressed adults were less accurate and less confident in their memories, and they showed reduced parietal ERP amplitude from 400-800 ms. The negative effect of MDD on memory was modest, but in addition to reporting lower confidence than controls in all four cells of the design, the depressed adults were numerically less accurate in three cells. Worse performance in 7/8 cells is improbable under the null (binomial test, $p = 0.035$ one-tailed), thus recollection and brain activity indexing recollection were weaker in MDD.

However, depressed adults showed excellent memory for words from the mobility task presented under the Question cue, which we interpret as reflecting sustained attention. At encoding, the mobility task elicited longer RTs and lower accuracy than the animacy task. It is easy to see why—for example, because trees sway in the breeze, deciding whether *oak* is “mobile” is harder than deciding whether an oak is alive—and we think the additional

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consideration needed to render mobility judgments led to deeper encoding. At retrieval, the Question cue elicited longer RTs and more confident responses than the Side cue, suggesting more extended and successful memory searches. Thus, directing conceptual retrieval at words from the mobility task pairs a deep retrieval search with deep encoding. Depressed adults can perform well under these conditions (29; 30), and our ERP data highlight a candidate neural mechanism: sustained recruitment of left parietal cortex, which was otherwise hypoactive.

We speculate that this ERP effect may track relatively effortless recovery of episodic details, because left parietal activity was not observed when words from the animacy task were presented under the Question cue; instead lasting activity over left PFC was seen. Animacy decisions were made quickly at encoding, consistent with shallower encoding in this condition, and accuracy under the Question cue was lower following the animacy versus mobility task (Figure 2A, right). Therefore, the left PFC activity may reflect additional cue elaboration needed to generate candidate memories following relatively poor encoding, or possibly post-retrieval monitoring or selection. Interestingly, the only other imaging study of source memory in MDD we know of reported increased left frontal activation during recollection attempts in depressed adults (52). That study did not manipulate encoding difficulty, but we predict that left PFC activation during source retrieval in MDD will be strongest when encoding is shallowest and recollection is weakest.

Our data may have treatment implications. As described earlier, imprecise retrieval is associated with depression and enhancing retrieval can speed recovery. Consideration of treatment mechanisms suggests an explanation. During cognitive behavioral therapy (CBT), patients recall difficult episodes from their lives and then reappraise them to reduce distress; here the importance of accurate retrieval is self-evident. But patients are also asked to imagine similar

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situations unfolding in the future so they can envision themselves effectively using new coping skills (53). Imagining future events depends on the same parieto-hippocampal circuitry that supports retrieval (54-55), and we have shown that activity in these circuits is blunted in MDD but can recover with adequate support. By extension, we speculate that effective CBT may be associated with improved functioning in parieto-hippocampal circuits. Given links between antidepressant effects and both functional and structural changes in the hippocampus (56), this argument may extend to psychopharmacological interventions as well. Finally, we expect that a sleep intervention would enhance memory retrieval in MDD, based on the negative relationship between sleep quality and ERP amplitudes observed in Figure 6.

In summary, this study provides novel insight into the impact of depression on brain activity during retrieval. The central role of parieto-hippocampal activity in episodic memory is already well-known. These data indicate that the same circuitry may play an important but underappreciated part in depression and its treatment.

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References

1. Williams JMG, Barnhofer T, Crane C, Herman D, Raes F, Watkins E, *et al.* (2007): Autobiographical memory specificity and emotional disorder. *Psychol Bull* 133: 122–148.
2. Brittlebank AD, Scott J, Williams JM, Ferrier IN (1993): Autobiographical memory in depression: state or trait marker? *Br J Psychiatry* 162: 118–121.
3. Peeters F, Wessel I, Merckelbach H, Boon-Vermeeren M (2002): Autobiographical memory specificity and the course of major depressive disorder. *Compr Psychiatry* 43: 344–350.
4. Sumner JA, Griffith JW, Mineka S (2010): Overgeneral autobiographical memory as a predictor of the course of depression: a meta-analysis. *Behav Res Ther* 48: 614–625.
5. Raes F, Williams JMG, Hermans D (2009): Reducing cognitive vulnerability to depression: A preliminary investigation of MEmory Specificity Training (MEST) in inpatients with depressive symptomatology. *J Behav Ther Exp Psychiatry* 40: 24–38.
6. Neshat-Doost HT, Dalgleish T, Yule W, Kalantari M, Ahmadi SJ, Dyregrov A, *et al.* (2013): Enhancing autobiographical memory specificity through cognitive training: an intervention for depression translated from basic science. *Clin Psychol Sci* 1: 84–92.
7. Rugg MD, Curran T (2007): Event-related potentials and recognition memory. *Trends Cogn Sci* 11: 251–257.
8. Eichenbaum H, Yonelinas AP, Ranganath C (2007): The medial temporal lobe and recognition memory. *Annu Rev Neurosci* 30: 123–152.
9. Rugg MD, Vilberg KL (2013): Brain networks underlying episodic memory retrieval. *Curr Opin Neurobiol* 23: 255–260.
10. Steffens DC, Otey E, Alexopoulos GS, Butters MA, Cuthbert B, Ganguli M, *et al.* (2006): Perspectives on depression, mild cognitive impairment, and cognitive decline. *Arch Gen*

DEPRESSION MODULATES SOURCE MEMORY

- Psychiatry* 63: 130-138.
11. Raes F, Hermans D, Williams JMG, Demyttenaere K, Sabbe B, Pieters G, *et al.* (2006): Is overgeneral autobiographical memory an isolated memory phenomenon in major depression? *Memory* 14: 584–594.
 12. MacQueen GM, Galway TM, Hay J, Young LT, Joffe RT (2002): Recollection memory deficits in patients with major depressive disorder predicted by past depressions but not current mood state or treatment status. *Psychol Med* 32: 251–258.
 13. MacQueen GM, Campbell S, McEwen BS, Macdonald K, Amano S, Joffe RT, *et al.* (2003): Course of illness, hippocampal function, and hippocampal volume in major depression. *Proc Natl Acad Sci USA* 100: 1387–1392.
 14. Ramponi C, Barnard P, Nimmo- Smith I (2004): Recollection deficits in dysphoric mood: an effect of schematic models and executive mode? *Memory* 12: 655–670.
 15. Bergström ZM, Henson RN, Taylor JR, Simons JS (2013): Multimodal imaging reveals the spatiotemporal dynamics of recollection. *Neuroimage* 68: 141–153.
 16. Simons JS, Gilbert SJ, Owen AM, Fletcher PC, Burgess PW (2005): Distinct roles for lateral and medial anterior prefrontal cortex in contextual recollection. *J Neurophysiol* 94: 813–820.
 17. Dobbins IG, Wagner AD (2005): Domain-general and domain-sensitive prefrontal mechanisms for recollecting events and detecting novelty. *Cereb Cortex* 15: 1768–1778.
 18. Bower GH (1981): Mood and memory. *Am Psychol* 36: 129–148.
 19. Bower GH (1987): Commentary on mood and memory. *Behav Res Ther* 25: 443–455.
 20. Dillon DG, Dobbins IG, Pizzagalli DA (2014): Weak reward source memory in depression reflects blunted activation of VTA/SN and parahippocampus. *Soc Cogn Affect Neurosci* 9: 1576–1583.

DEPRESSION MODULATES SOURCE MEMORY

21. Johansson M, Mecklinger A (2003): The late posterior negativity in ERP studies of episodic memory: action monitoring and retrieval of attribute conjunctions. *Biol Psychol* 64: 91–117.
22. Mecklinger A, Johansson M, Parra M, Hanslmayr S (2007): Source-retrieval requirements influence late ERP and EEG memory effects. *Brain Res* 1172: 110–123.
23. Cycowicz YM, Friedman D, Snodgrass JG (2001): Remembering the color of objects: an ERP investigation of source memory. *Cereb Cortex* 11: 322–334.
24. Badre D, Wagner AD (2007): Left ventrolateral prefrontal cortex and the cognitive control of memory. *Neuropsychologia* 45: 2883–2901.
25. Treadway MT, Waskom ML, Dillon DG, Holmes AJ, Park MT, Chakravarty MM, *et al.* (2015): Illness progression, recent stress, and morphometry of hippocampal subfields and medial prefrontal cortex in major depression. *Biol Psychiatry* 77: 285–294.
26. Hertel PT (1997): On the contributions of deficient cognitive control to memory impairments in depression. *Cogn Emot* 11: 569–583.
27. Hertel PT, Brozovich F (2010): Cognitive habits and memory distortions in anxiety and depression. *Curr Dir Psychol Sci* 19: 155–160.
28. Hertel PT, Benbow AA, Geraerts E (2012): Brooding deficits in memory: Focusing attention improves subsequent recall. *Cogn Emot* 26: 1516–1525.
29. Hertel PT, Hardin TS (1990): Remembering with and without awareness in a depressed mood: Evidence of deficits in initiative. *J Exp Psychol Gen* 119: 45–59.
30. Hertel PT, Rude SS (1991): Depressive deficits in memory: focusing attention improves subsequent recall. *J Exp Psychol Gen* 120: 301–309.
31. Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, *et al.* (1998): The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of

DEPRESSION MODULATES SOURCE MEMORY

- a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J Clin Psychiatry* 59: 22–33.
32. Beck AT, Steer RA, Brown GK (1996): *Manual for the Beck Depression Inventory-II*. San Antonio, TX: Psychological Corporation.
33. Watson D, Weber K, Assenheimer JS, Clark LA, Strauss ME, McCormick RA (1995): Testing a tripartite model: I. Evaluating the convergent and discriminant validity of anxiety and depression symptom scales. *J Abnorm Psychol* 104: 3–14.
34. Treynor W, Gonzalez R, Nolen-Hoeksema S (2003): Rumination reconsidered : a psychometric analysis. *Cognit Ther Res* 27: 247–259.
35. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ (1989): The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Res* 28: 193–213.
36. Holdnack HA (2001): *Wechsler Test of Adult Reading*: WTAR. San Antonio, TX: Psychological Corporation.
37. Peirce JW (2008): Generating stimuli for neuroscience using PsychoPy. *Front Neuroinform* 2: 10.
38. Coltheart M (1981): The MRC psycholinguistic database. *Q J Exp Psychol Sect A* 33: 497–505.
39. Reitman JS, Higman B, Lifson A, Rosenblum J (1974): Without surreptitious rehearsal, information in short-term memory decays. *J Verbal Learning Verbal Behav* 13: 365–377.
40. R Core Team (2015): R: a language and environment for statistical computing. *R Found Stat Comput*, Vienna, Austria. ISBN 3-900051-07-0, URL <http://www.R-project.org/>.
41. Bates D, Maechler M, Bolker B, Walker S (2015): Fitting linear mixed-effects models using

DEPRESSION MODULATES SOURCE MEMORY

- lme4. *J Stat Softw* 67: 1-48.
42. Mark RE, Rugg MD (1998): Age effects on brain activity associated with episodic memory retrieval. An electrophysiological study. *Brain* 121: 861–873.
43. Nolen-Hoeksema S (2001): Gender differences in depression. *Curr Dir Psychol Sci* 10: 173–176.
44. Delorme A, Makeig S (2004): EEGLAB: An open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *J Neurosci Methods* 134: 9–21.
45. Lopez-Calderon J, Luck SJ (2014): ERPLAB: an open-source toolbox for the analysis of event-related potentials. *Front Hum Neurosci* 8: 213.
46. Hayama HR, Johnson JD, Rugg MD (2008): The relationship between the right frontal old/new ERP effect and post-retrieval monitoring: Specific or non-specific? *Neuropsychologia* 46: 1211–1223.
47. Wilding EL, Rugg MD (1996): An event-related potential study of recognition memory with and without retrieval of source. *Brain* 119: 889–905.
48. Groppe DM, Urbach TP, Kutas M (2011): Mass univariate analysis of event-related brain potentials/fields I: A critical tutorial review. *Psychophysiology* 48: 1711-1725.
49. Friston KJ, Holmes AP, Worsley KJ, Poline J-P, Frith CD, Frackowiak RSJ (1995): Statistical parametric maps in functional imaging: A general linear approach. *Hum Brain Mapp* 2: 189–210.
50. Groppe DM, Urbach TP, Kutas M (2011): Mass univariate analysis of event-related brain potentials/fields II: Simulation studies. *Psychophysiology* 48: 1726–1737.
51. Bullmore ET, Suckling J, Overmeyer S, Rabe-Hesketh S, Taylor E, Brammer MJ (1999): Global, voxel, and cluster tests, by theory and permutation, for a difference between two

DEPRESSION MODULATES SOURCE MEMORY

- groups of structural MR images of the brain. *IEEE Trans Med Imaging* 18: 32–42.
52. van Eijndhoven P, van Wingen G, Fernández G, Rijkema M, Pop-Purceanu M, Verkes RJ, *et al* (2013). Neural basis of recollection in first-episode major depression. *Hum Brain Mapp* 34: 283-294.
53. Holmes EA, Arntz A, Smucker MR (2007): Imagery rescripting in cognitive behaviour therapy: images, treatment techniques and outcomes. *J Behav Ther Exp Psychiatry* 38: 297-305.
54. Addis DR, Pan L, Vu MA, Laiser N, Schacter DL (2009): Constructive episodic simulation of the future and the past: distinct subsystems of a core brain network mediate imagining and remembering. *Neuropsychologia* 47: 2222-2238.
55. Madore KP, Szpunar KK, Addis DR, Schacter DL (2016): Episodic specificity induction imparts activity in a core brain network during construction of imagined future experiences. *Proc Natl Acad Sci USA* 113: 10696-10701.
56. Santarelli L, Saxe M, Gross C, Surget A, Battaglia F, Dulawa S, *et al.* (2003): Requirement of hippocampal neurogenesis for the behavioral effects of antidepressants. *Science* 301: 805-809.
57. Burt DB, Zembar MJ, Niederehe G (1995): Depression and memory impairment: a meta-analysis of the association, its pattern, and specificity. *Psychol Bull* 117: 285-305.

Figure Captions

Figure 1. Encoding (left) and recognition (right) trial structures. Encoding trials began with three centrally presented arrows pointing to the side on which the word would appear. The encoding task was presented next, either “living or non-living?” (animacy judgment) or “mobile or immobile?” (mobility judgment, not shown). Finally, a word was presented directly above the encoding question; participants had 3500 ms to respond. Retrieval trials began with presentation of one of three cues (“Side”, “Question”, or “Odd/Even”). After a 1000 ms delay, a word was presented. On Side and Question trials, the word came from the immediately preceding encoding block, while on Odd/Even trials the word was a numeral (e.g., “seventy-seven”). Finally, a response screen was presented and persisted until the participant responded or 10 seconds had elapsed. The response options for a Side trial are displayed. On Question trials, “left” and “right” were replaced with “living/non-living” and “mobile/immobile”, respectively; on Odd/Even trials they were replaced with “odd” and “even”.

Figure 2. Source memory (A) accuracy, (B, top) confidence, and (B, bottom) correct RT. Bar heights correspond to the mean, error bars = SEM. Asterisks denote $p < 0.05$.

Figure 3. Waveforms elicited by correct responses to the Question (black), Side (red), and Odd/Even (blue) cues. Representative electrodes from the left and right hemisphere are depicted for frontal and parietal scalp; the late posterior negativity (LPN) was maximal at the midline occipital electrode, Oz. Gray shading demarcates the parietal ERP associated with recollection, asterisks indicate reduced parietal activity in depressed adults.

DEPRESSION MODULATES SOURCE MEMORY

Figure 4. Topographical maps of t -values for activity elicited by Question and Side hits, with activity on correct Odd/Even trials subtracted out (one-sample tests against zero). Columns correspond to the three time windows analyzed (400-800, 800-1400, 1400-2000 ms). Electrodes in clusters associated with significant within-group effects are shown in white. Between-group comparisons revealed no differences.

Figure 5. Topographical maps of t -values for Question minus Side difference waves, sorted by group and encoding task. Columns correspond to the three time windows analyzed (400-800, 800-1400, 1400-2000 ms). Electrodes in clusters associated with significant effects are shown in white. Paralleling the behavioral analyses, there were MDD > control differences in response to words from the mobility task but not the animacy task.

Figure 6. ERP amplitudes sensitive to recollection are related to sleep quality in depressed adults. There were significant negative correlations between sleep disturbance as measured by the PSQI (x -axis) and ERP amplitudes captured by the Question minus Side difference wave for words from the mobility task (y -axis) in the 400-800 (left) and 800-1400 (right) ms time windows.

Table 1

[Click here to download Table: BarrickDillon_Table1.docx](#)

SOURCE MEMORY IMPAIRMENT IN DEPRESSION

Table 1. *Demographics and Mean (SD) Self-Report Data*

Variable	Controls	Depressed	<i>P</i>
	<i>n</i> = 24	<i>n</i> = 24	
Gender	13 f, 11 m	15 f, 9 m	0.89
Age	30.58 (11.09)	29.79 (10.62)	0.81
Education (years)	16.92 (1.98)	16.29 (2.44)	0.35
BDI-II	1.29 (2.22)	25.38 (8.69)	< .001
MASQ-GDA	13.04 (2.10)	21.38 (7.04)	< .001
MASQ-AA	17.65 (0.98)	24.00 (8.24)	.001
MASQ-GDD	13.65 (2.08)	38.46 (10.0)	< .001
MASQ-AD	45.61 (12.29)	86.54 (8.74)	< .001
RRS-Dep	17.96 (4.73)	32.96 (4.51)	< .001
RRS-Brood	7.75 (2.38)	12.54 (2.99)	< .001
RRS-Reflect	9.04 (3.80)	12.25 (2.97)	0.002
PSQI	3.00 (2.00)	8.48 (2.73)	< 0.001
WTAR*	116.73 (11.58)	117.09 (7.84)	0.90

Note. f = female, m = male; BDI-II = Beck Depression Inventory II; MASQ = Mood and Anxiety Symptoms Questionnaire (GDD = General Distress: Depressive symptoms, AD = Anhedonic Depression, GDA = General Distress: Anxious symptoms, AA = Anxious Arousal); RRS = Ruminative Response Scale (Dep = depression subscale, Brood = brooding subscale, Reflect = reflection subscale); PSQI = Pittsburgh Sleep Quality Index; WTAR = Wechsler Test of Adult Reading. Statistics reflect between-group *t*-tests except for gender (chi-square). PSQI scores ≤ 5 indicate good sleep quality, scores > 5 indicate poor sleep quality. *WTAR data from non-native English speakers were not analyzed (controls, *n* = 2; MDD, *n* = 2).

Table 2

[Click here to download Table: BarrickDillon_Table2.docx](#)

SOURCE MEMORY IMPAIRMENT IN DEPRESSION

Table 2. *Mass Univariate Analysis of Question minus Side Difference Waves*

Encoding Task	Time Window (ms)	Electrode Numbers in Significant Clusters	Cluster p-value (corrected)
<i>Depressed Group</i>			
Mobility	400-800	40, 42, 46, 47, 50, 51, 52, 53, 57, 58, 59, 60, 61, 65, 66, 67, 69, 70, 71, 74, 75, 83, 90, 91	0.001
	800-1400	42, 47, 51, 52, 53, 57, 58, 59, 60, 61, 62, 65, 66, 67, 68, 69, 70, 71, 72, 74, 75, 76, 77, 78, 82, 83, 89, 90, 91	<0.001
	1400-2000	42, 51, 52, 53, 60, 61, 65, 66, 67, 68, 70, 71	0.010
Animacy	400-800	7, 11, 12, 13, 16, 19, 20, 21, 23, 28, 29, 30, 31, 32, 36	0.021
	800-1400	5, 6, 7, 11, 12, 13, 16, 19, 20, 24, 27, 28, 29, 30, 31, 36, 37, 80, 87, 92, 93, 98, 103, 104, 105, 106, 111, 112, 117, 118, 124	0.003
	1400-2000	7, 11, 12, 13, 19, 20, 24, 29, 30, 31	0.014
<i>Depressed Group minus Healthy Controls</i>			
Mobility	400-800	34, 35, 40, 41, 42, 46, 47, 51, 52, 53	0.028
	800-1400	40, 41, 42, 46, 47, 51, 52, 53, 61	0.026
	1400-2000	None	>.05

Note. No significant effects were observed in healthy controls at any time point. The Depressed-Controls comparison did not reach significance at any time point for the Animacy task. A map showing the position of each electrode on the EGI 128 channel net can be found in the Supplement and at ftp://ftp.evi.com/pub/support/Documents/net_layouts/hcgsn_128.pdf

Figure 1

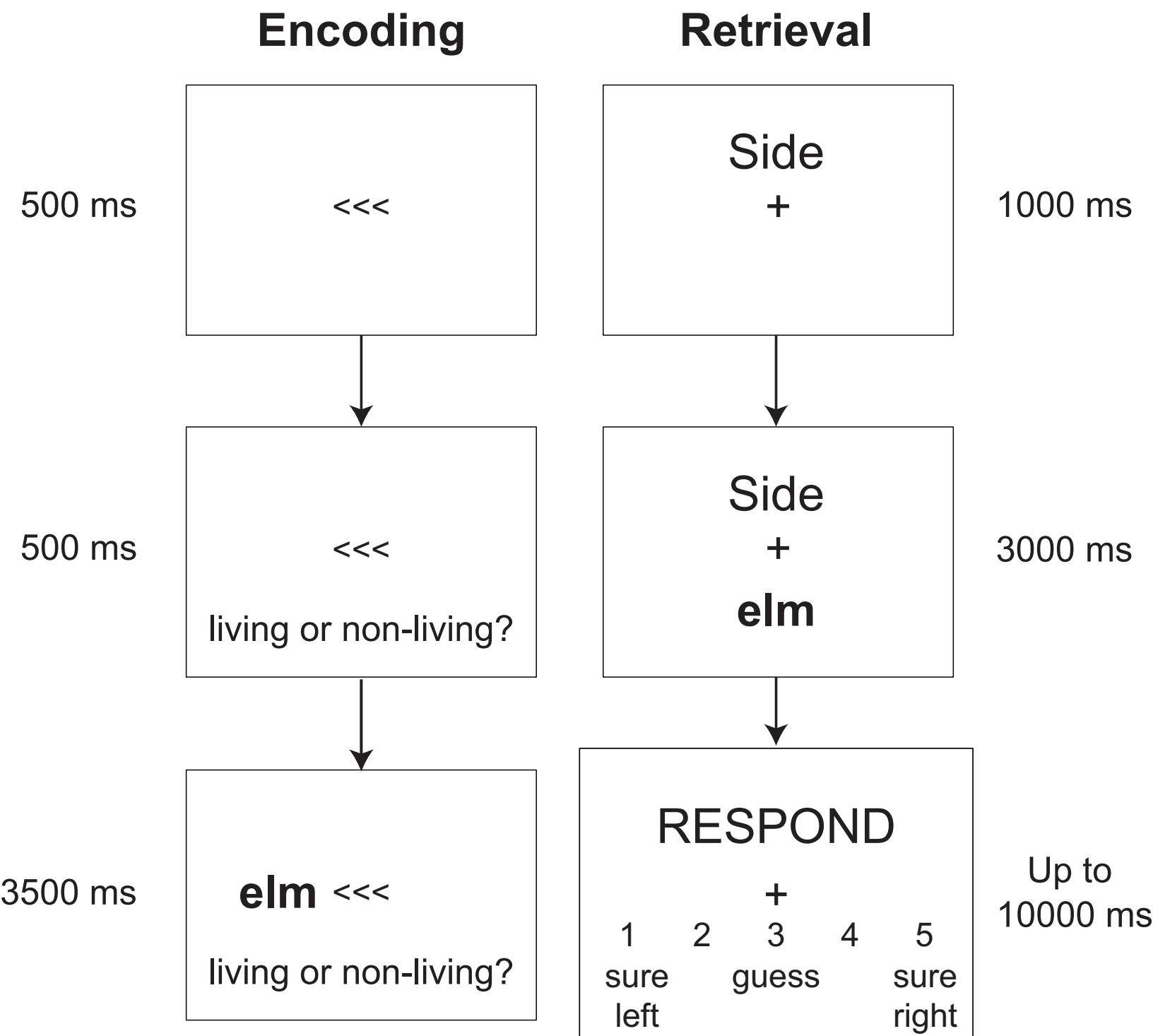


Figure 2

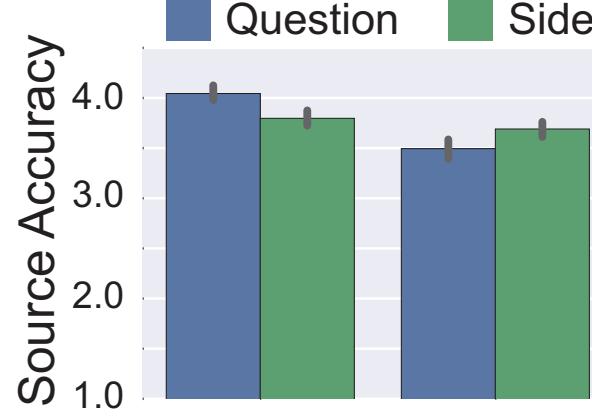
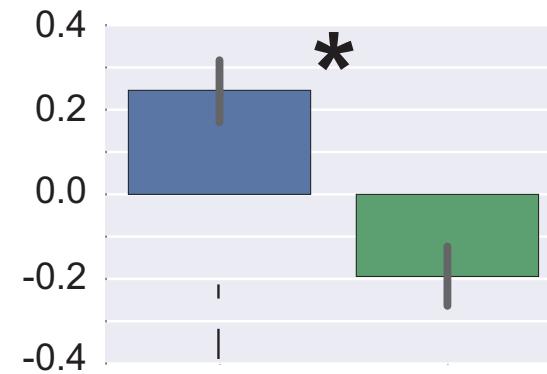
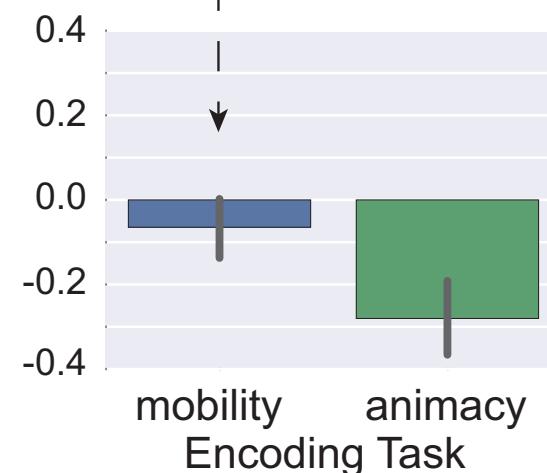
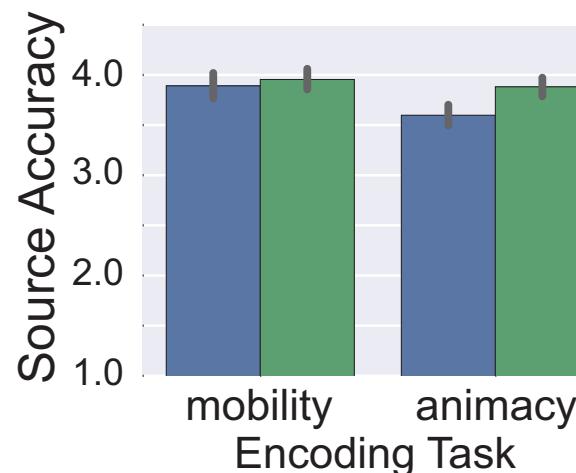
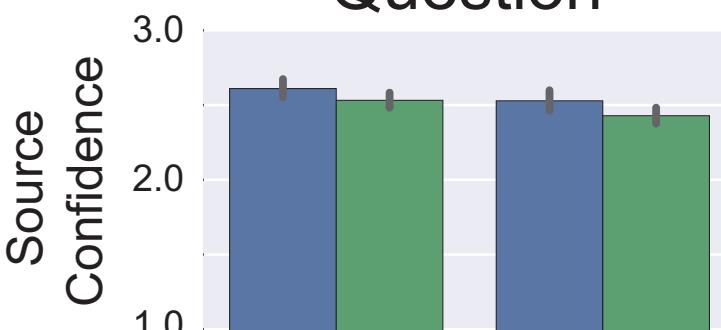
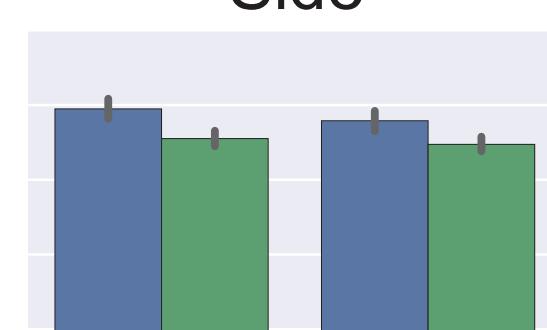
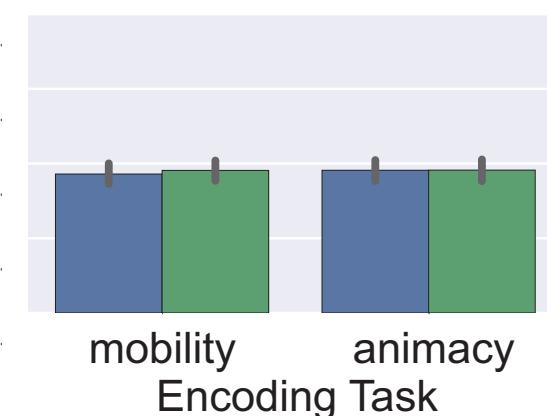
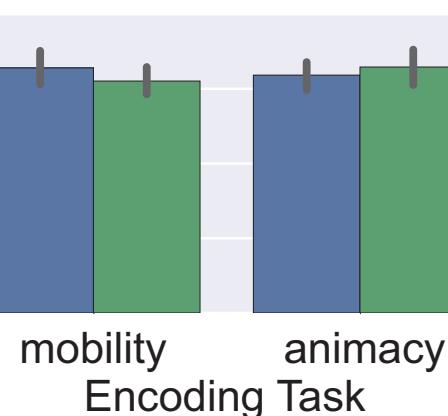
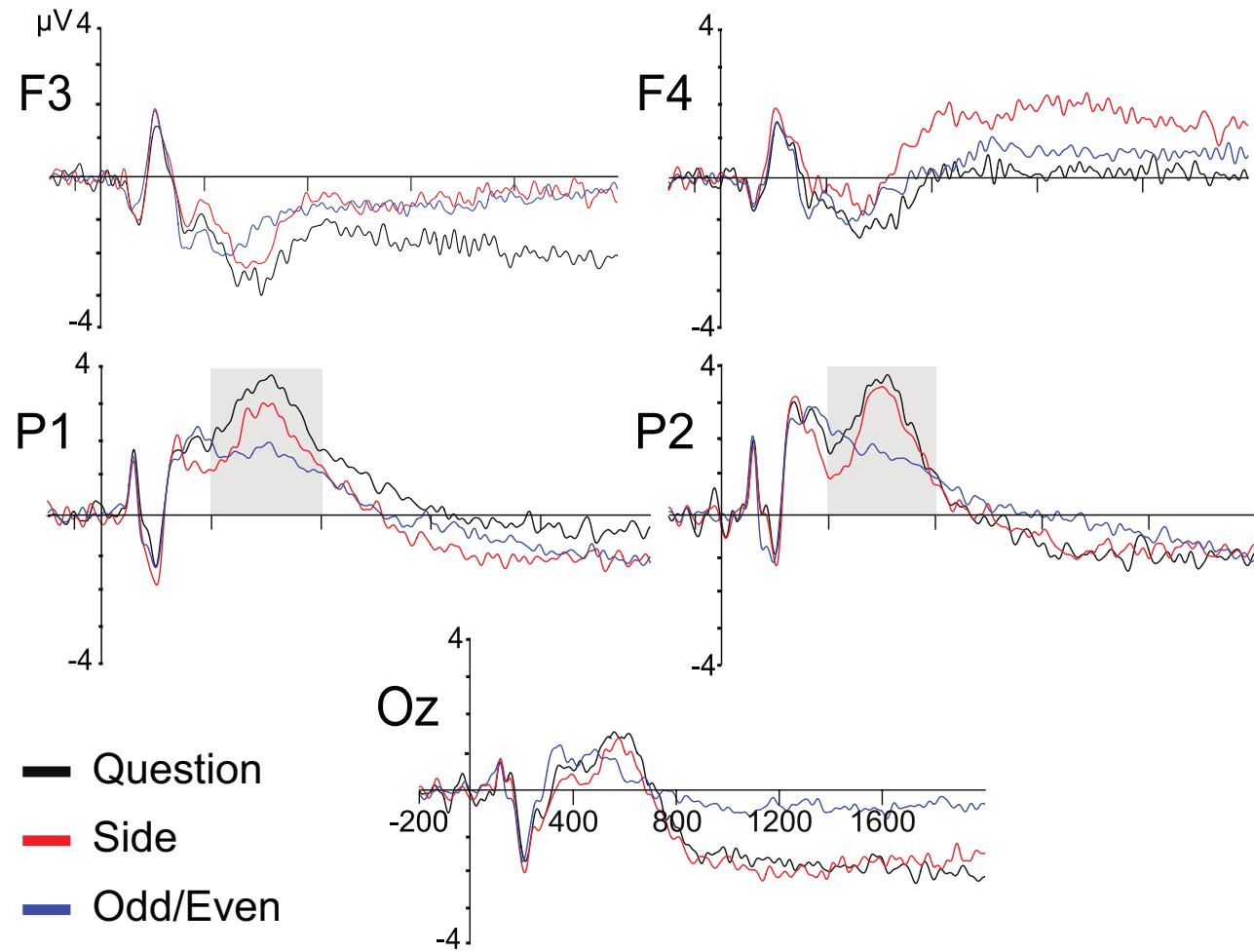
A.**DEPRESSED****Question minus Side****CONTROLS****B.****Controls****Depressed****Question****Side****Correct RT**

Figure 3

CONTROLS



DEPRESSED

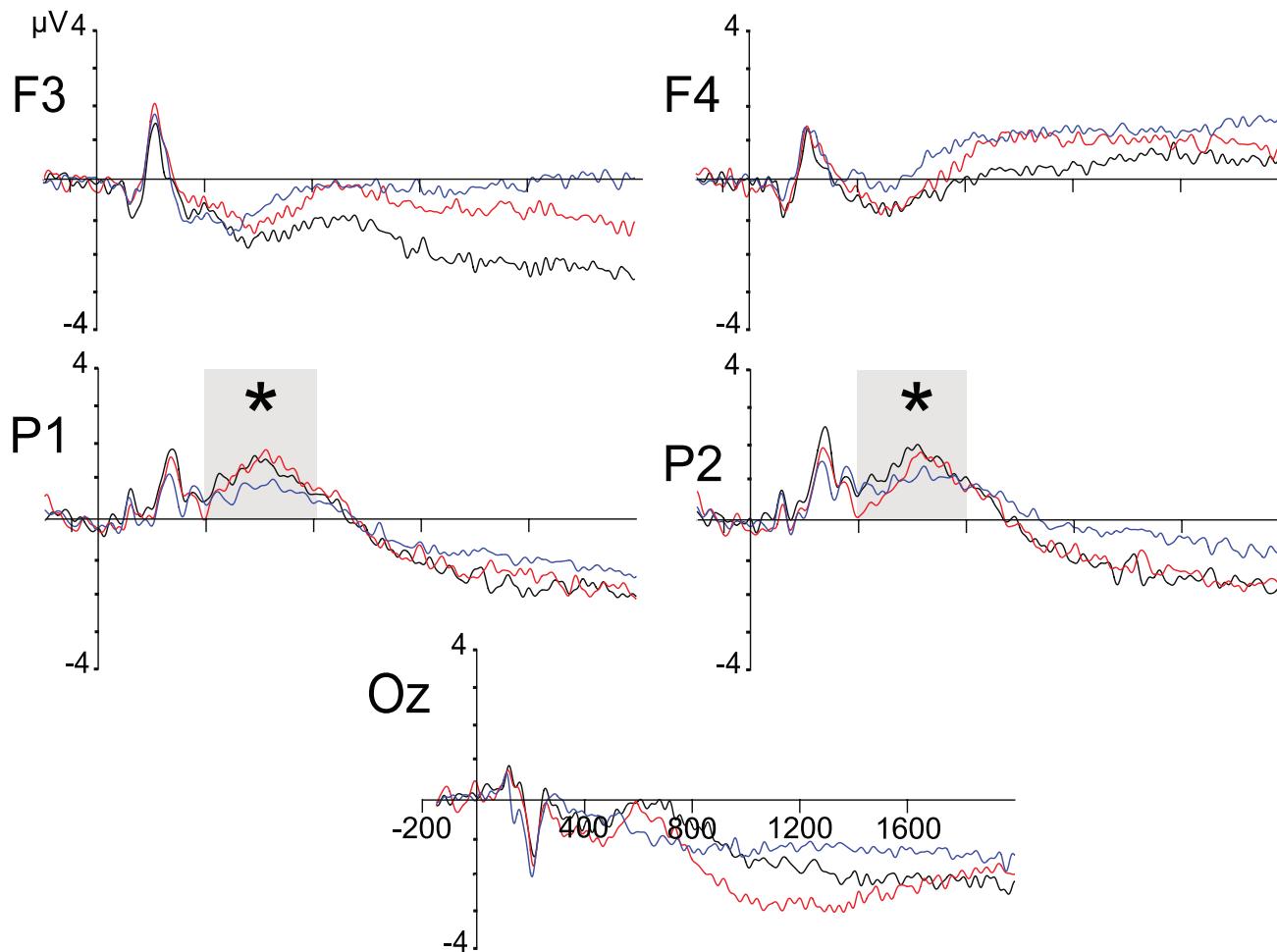
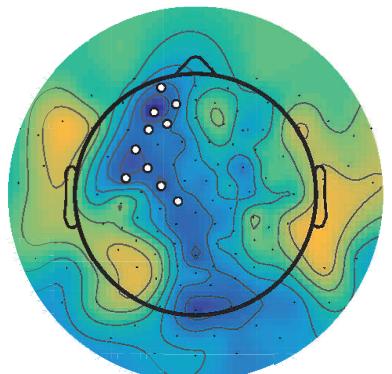
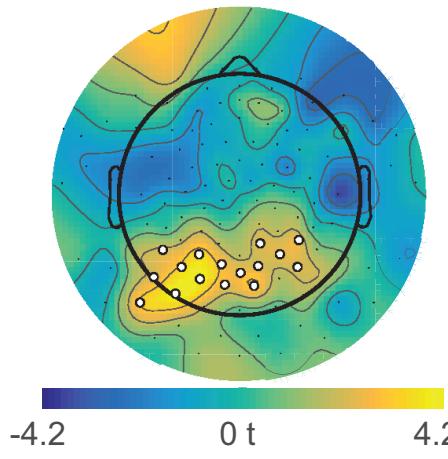


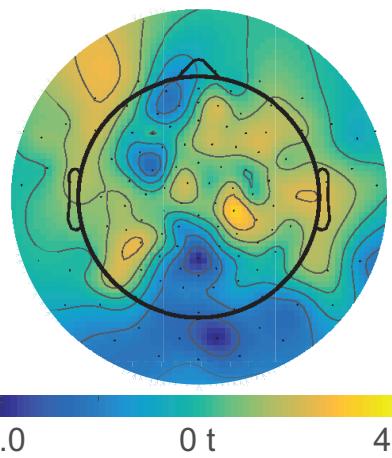
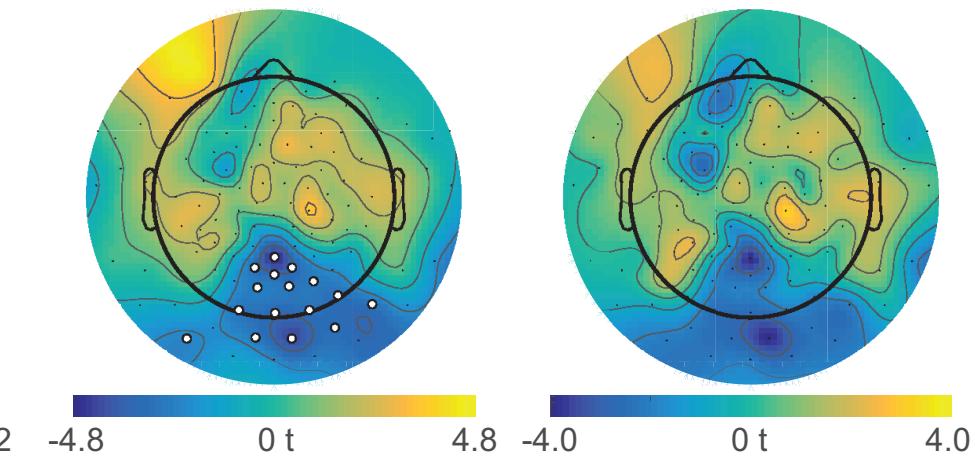
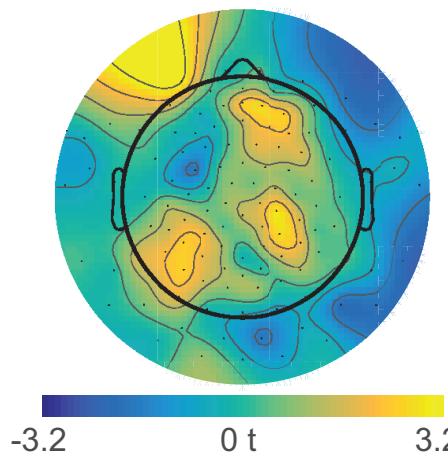
Figure 4

CONTROLS

**Question
minus
Odd/Even**

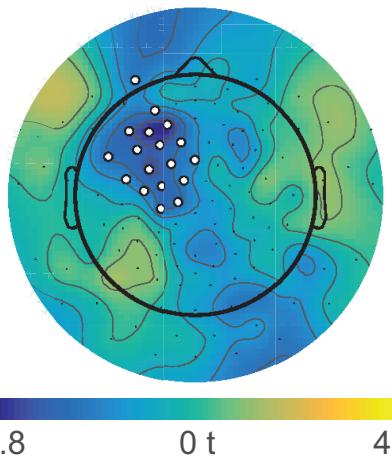
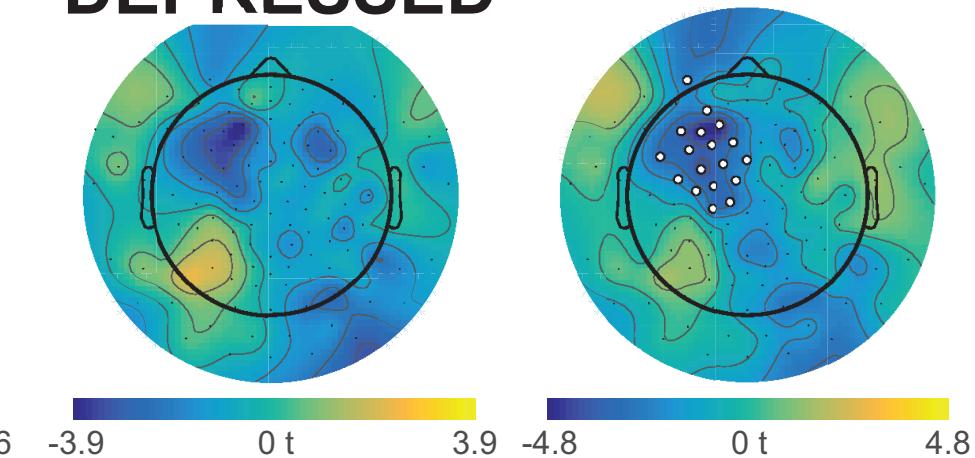
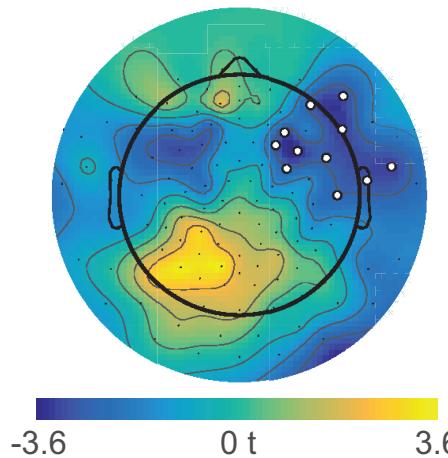


**Side
minus
Odd/Even**

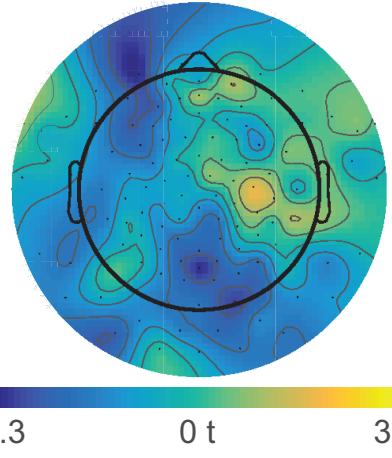
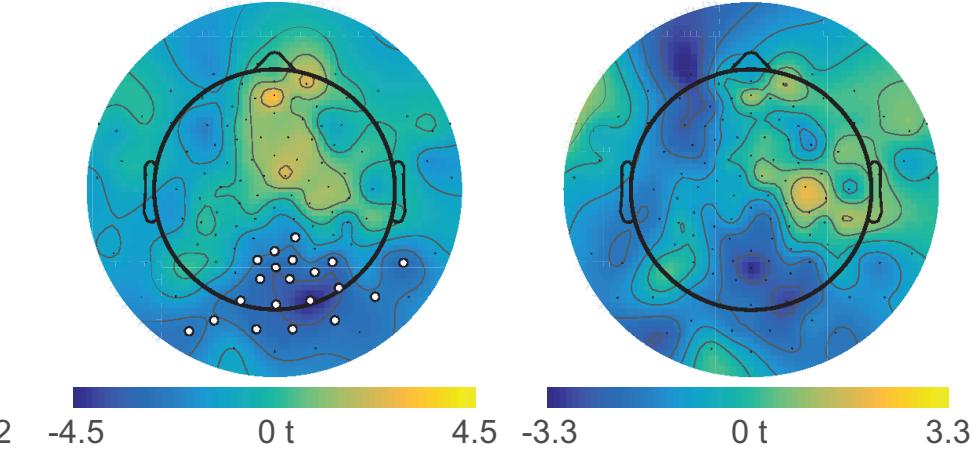
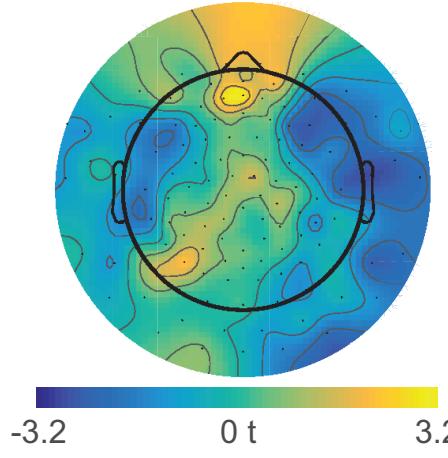


DEPRESSED

**Question
minus
Odd/Even**



**Side
minus
Odd/Even**



400-800 ms

800-1400 ms

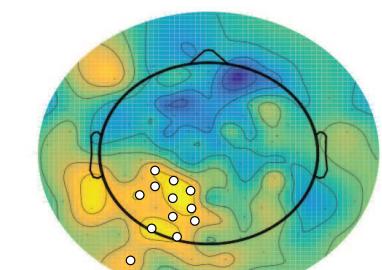
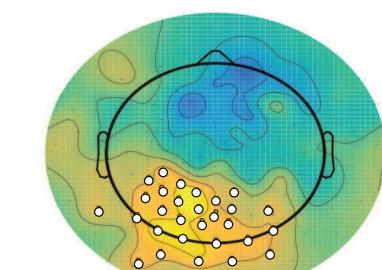
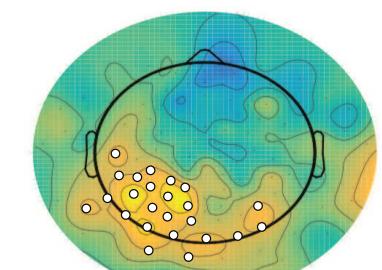
1400-2000 ms

Figure 5

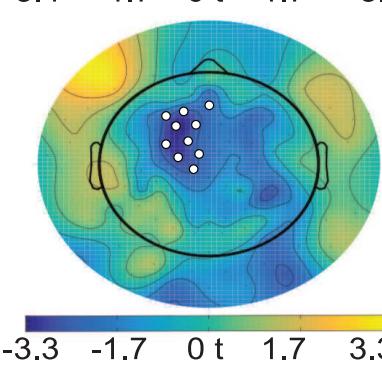
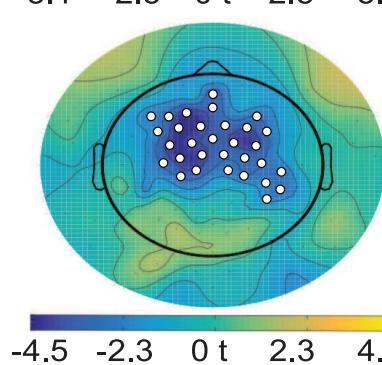
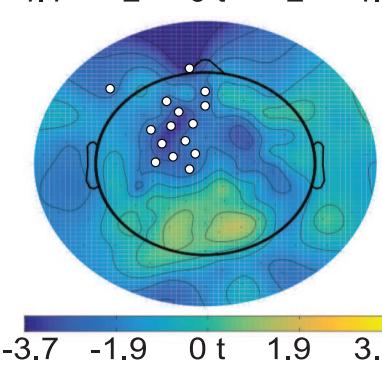
Question minus Side

Depressed

Mobility

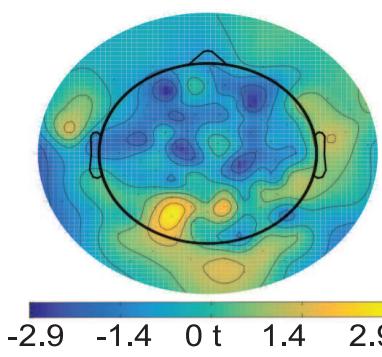
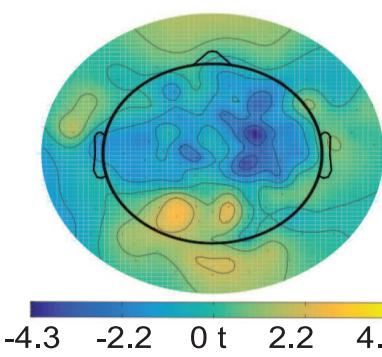
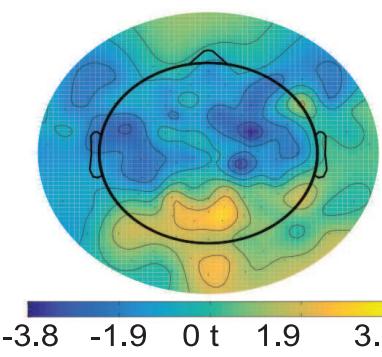


Animacy

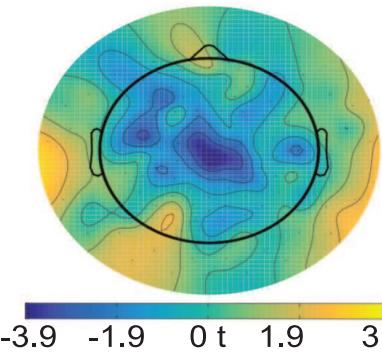
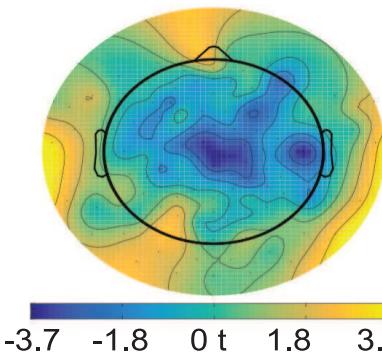
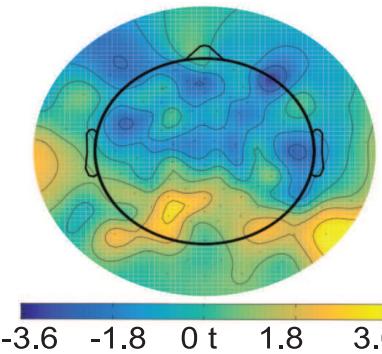


Controls

Mobility

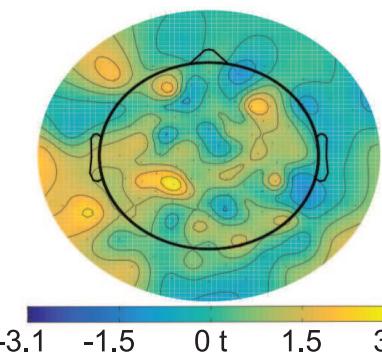
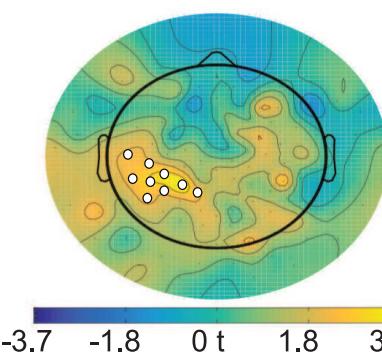
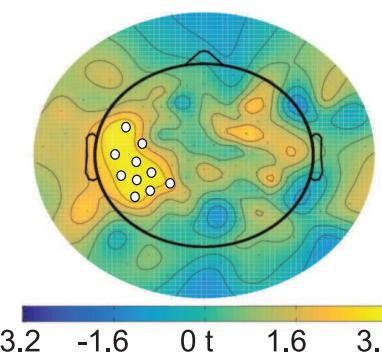


Animacy



Depressed - Controls

Mobility

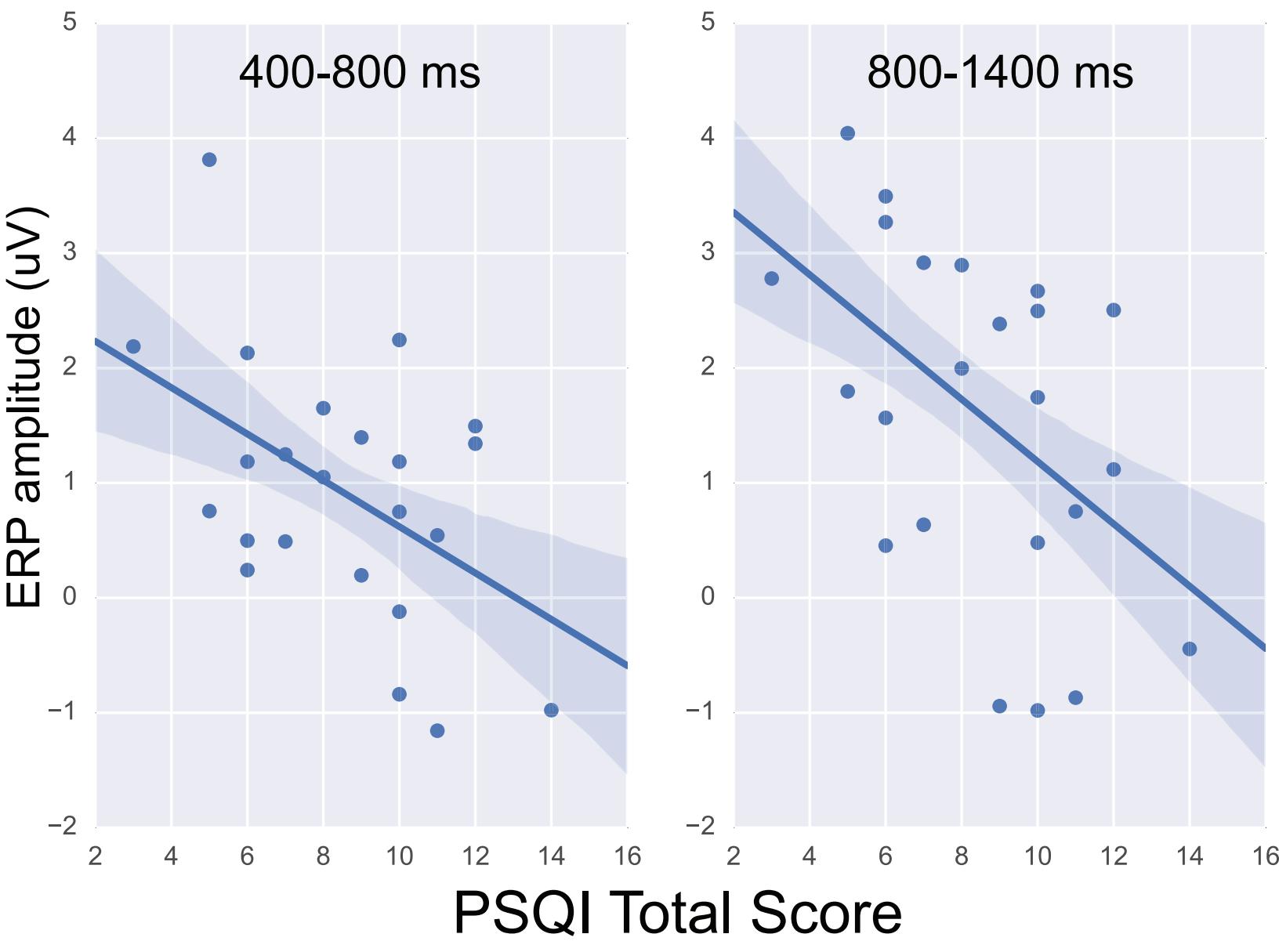


400-800 ms

800-1400 ms

1400-2000 ms

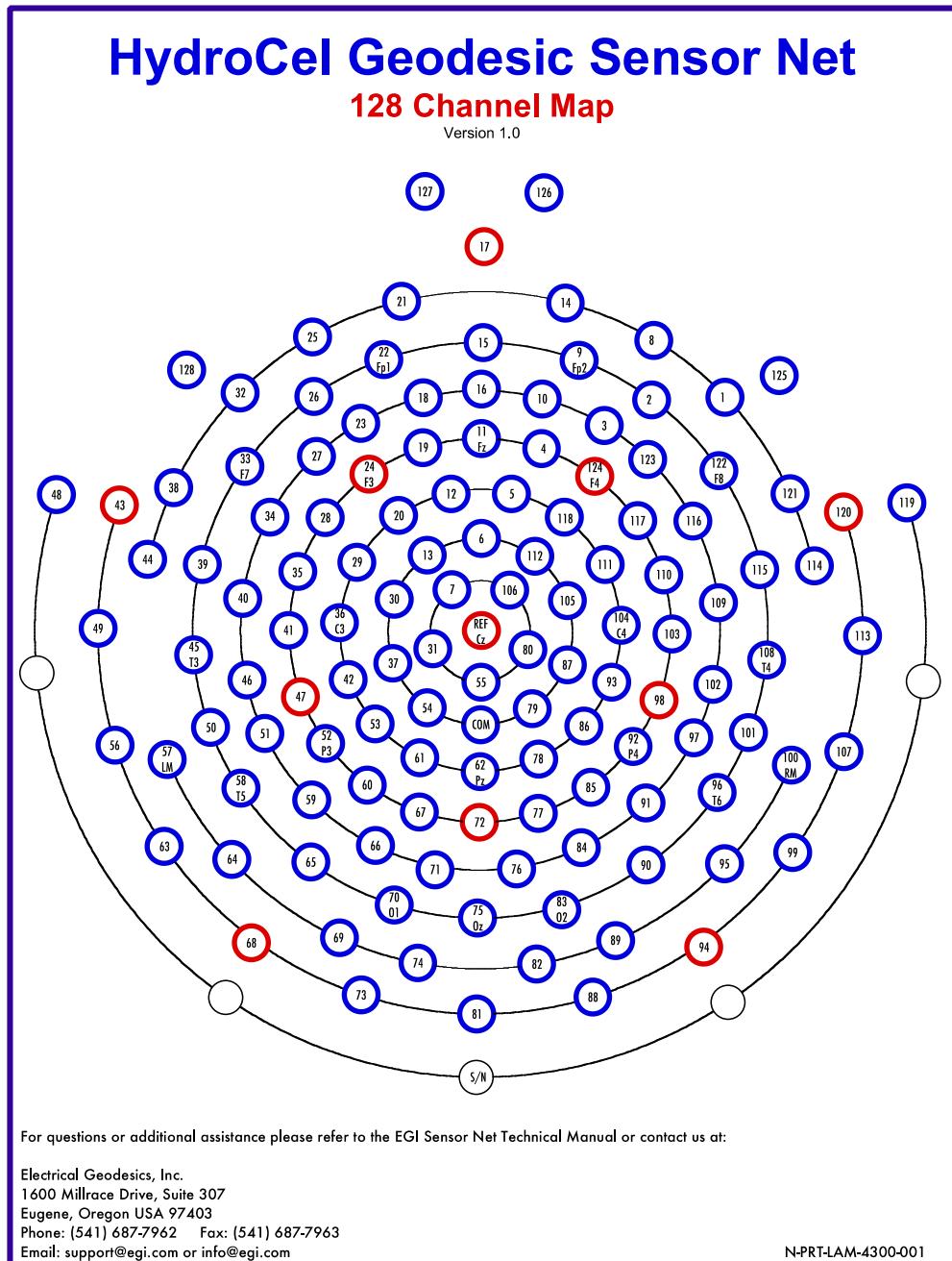
Figure 6



Supplemental Methods**Word Lists**

<i>Living/Immobile</i>	<i>Non-living/Immobile</i>	<i>Living/Mobile</i>	<i>Non-living/Mobile</i>
elm	shed	dog	kite
oak	barn	toad	car
pine	desk	fox	jet
rose	hill	bear	taxi
fern	sink	crow	boat
blossom	bench	moth	bike
peach	house	deer	cart
lily	fence	seal	ship
daisy	hotel	eagle	plane
apple	cabin	pigeon	ferry
pepper	piano	snail	train
grape	bridge	moose	truck
grass	anchor	sheep	yacht
tulip	shower	whale	canoe
birch	garage	snake	kayak
ivy	canyon	spider	moped
shrub	statue	monkey	wagon
clover	church	beaver	rocket
orchid	brick	rabbit	balloon
cherry	glacier	beetle	scooter
mussel	mansion	chicken	tractor
spinach	cottage	sparrow	trolley
willow	boulder	hamster	raft
seaweed	mountain	lobster	trailer
mushroom	oven	squirrel	carriage

Map of Electrode Locations



Supplemental Results

Hit Rate Analysis

Because the ERP analysis focused on hits, we repeated this analysis with hit rates (Table S1). For depressed adults the Question minus Side accuracy subtraction was again more positive for the mobility task (5.03 ± 11.95) versus the animacy task (-8.76 ± 9.82), $t(23) = 3.82, p = 0.001, d = 1.26$. The same was true for controls (mobility: -2.97 ± 9.74 ; animacy: -12.27 ± 14.11 ; $t(23) = 2.83, p = 0.010, d = 0.76$). As before, there was no group difference for the animacy task, $t(46) = 1.00, p = 0.32, d = 0.29$, but Question minus Side difference scores for the mobility task were again larger in depressed adults, $t(46) = 2.54, p = 0.015, d = 0.73$. Thus, the same pattern of results emerged for analysis of hit rates and for accuracy scored ordinally, as in the main text.

SOURCE MEMORY IMPAIRMENT IN DEPRESSION

Table S1. *Mean Hit Rate (% Correct) by Group, Cue, and Encoding Task*

Retrieval Cue	Encoding Task	Hit Rate	SD
<i>Depressed</i>			
Question	Mobility	82.11	9.13
	Animacy	65.19	14.74
Side	Mobility	77.08	10.68
	Animacy	73.95	10.51
<i>Controls</i>			
Question	Mobility	77.00	17.30
	Animacy	66.66	13.88
Side	Mobility	79.97	14.08
	Animacy	78.93	12.73

Note. Guesses were excluded from this analysis.