

Differences in EEG oscillations between normal aging and mild cognitive impairment during semantic memory retrieval

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Abstract

Semantic memory remains relatively stable with normal cognitive aging and declines in early stages of neurodegenerative disease. We measured electroencephalography (EEG) oscillatory correlates of semantic memory retrieval to examine the effects of normal and pathological aging. Twenty-nine cognitively healthy young adults (YA), 22 cognitively healthy aging adults (HA), and 20 patients with mild cognitive impairment (MCI) completed a semantic memory retrieval task with concurrent EEG recording in which they judged whether two words (features of objects) led to retrieval of an object (retrieval) or not (non-retrieval). Event-related power changes contrasting the two conditions (retrieval vs. non-retrieval) within theta, alpha, low-beta, and high-beta EEG frequency bands were analyzed across time to examine normal aging (YA versus HA) and pathological aging effects (HA versus MCI). Though no behavioral differences between the cognitively healthy groups were observed, we found later theta and alpha power differences between conditions only in YA, and a high-beta power difference between conditions only in HA. For pathological aging effects, we found reduced accuracy in MCI. While we found different EEG patterns of early beta power differences between conditions in MCI compared to HA, a low-beta power difference between conditions was found only in HA. We conclude that the aging brain relies on faster (beta) oscillations during the semantic memory task. With pathological aging, retrieval accuracy declines and patterns of beta oscillation changes. The findings improve understanding on age-related neural mechanisms underlying semantic memory and have implications for early detection of pathological aging.

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Semantic memory remains relatively stable with normal cognitive aging and declines in early stages of neurodegenerative disease. We measured electroencephalography (EEG) oscillatory correlates of semantic memory retrieval to examine the effects of normal and pathological aging. Twenty-nine cognitively healthy young adults (YA), 22 cognitively healthy aging adults (HA), and 20 patients with mild cognitive impairment (MCI) completed a semantic memory retrieval task with concurrent EEG recording in which they judged whether two words (features of objects) led to retrieval of an object (retrieval) or not (non-retrieval). Event-related power changes contrasting the two conditions (retrieval vs. non-retrieval) within theta, alpha, low-beta, and high-beta EEG frequency bands were analyzed across time to examine normal aging (YA versus HA) and pathological aging effects (HA versus MCI). Though no behavioral differences between the cognitively healthy groups were observed, we found later theta and alpha power differences between conditions only in YA, and a high-beta power difference between conditions only in HA. For pathological aging effects, we found reduced accuracy in MCI. While we found different EEG patterns of early beta power differences between conditions in MCI compared to HA, a low-beta power difference between conditions was found only in HA. We conclude that the aging brain relies on faster (beta) oscillations during the semantic memory task. With pathological aging, retrieval accuracy declines and patterns of beta oscillation changes. The findings improve understanding on age-related neural mechanisms underlying semantic memory and have implications for early detection of pathological aging.

Key words: aging, MCI, semantic memory, semantic retrieval, EEG, time-frequency

1. INTRODUCTION

Semantic memory is relatively preserved with normal cognitive aging but declines in early stages of Alzheimer’s disease and related dementia (AD-RD) including mild cognitive impairment (MCI) (Salmon et al., 1999; Gainotti et al., 2014; Kraut et al., 2006, 2007; Gustavson et al., 2020). Although cognitively healthy older adults experience some challenges with word retrieval (e.g., recalling names) and engage additional neural resources compared to younger controls (Shafra et al., 2010; Baciou et al., 2016; Haitas et al., 2021), their semantic knowledge remains intact (Verhaegen & Poncelet, 2013; Nicholas et al., 1985). In contrast, older adults with MCI and AD-RD have semantic memory deficits that may go beyond word retrieval issues and can involve degradation of semantic knowledge (Dudas et al., 2005; Joubert et al., 2021). With disease progression from MCI to AD-RD, there is more noticeable semantic memory deterioration (Pelgrim et al., 2021; Aschenbrenner et al., 2015; Almeida & Radanovic, 2022). The majority of this research has been conducted using naming tasks (e.g., confrontational naming, verbal fluency, associations). One of the major challenges in understanding the nature of alterations in semantic memory in MCI and AD-RD relates to difficulty in determining whether deterioration is in word retrieval, accessing semantic memory, or semantic knowledge *per se*.

A semantic memory task that examines access to semantic knowledge without requiring overt word retrieval is thus ideal to investigate changes in semantic memory retrieval associated with normal versus pathological aging. We designed the Semantic Object Retrieval Task (SORT), which examines how objects are retrieved via explicit evaluation of object-associated features (Kraut et al. 2002; Kraut et al., 2006, 2007). In the SORT paradigm, the features (e.g., “humps” and “desert”) normally facilitate retrieval of an object (e.g., “camel”). While participants are not required to overtly recall the word (e.g., “camel”), they are asked to judge whether the features bring to mind a particular object by pushing the ‘yes’ or ‘no’ button on the response box. Our task is distinct from tasks involving semantic priming, contextual constraints, etc. where

participants are asked to judge semantic relatedness between stimuli or if stimuli share a category (probed as individual words/pictures or in the context of a sentence; Kiefer, 2001; Kutas & Federmeier, 2000; Wlotko et al., 2010). In contrast, we explicitly require participants to judge whether the stimuli evoke retrieval of a specific object and not just relatedness.

Electroencephalogram (EEG), with its millisecond temporal resolution and direct measure of post-synaptic neuronal activity, is a useful tool to study neural dynamics associated with semantic memory (Chiang et al., 2016, 2020). Previously, on EEG-based semantic object memory retrieval test (SORT), we observed differences in event-related potentials (ERPs) between (1) cognitively normal younger and older adults, and (2) individuals with MCI and cognitively normal older controls. A frontal ERP between 800-1000 ms differentiated retrieval from non-retrieval trials in cognitively normal older adults but not in younger adults, which was posited to relate to a more extensive search during the non-retrieval trials with aging (Chiang et al., 2014). A similar fronto-parietal potential between 950-1050 ms differentiated retrieval from non-retrieval trials in individuals with MCI but not in cognitively normal age- and education-matched controls (Chiang et al., 2015), suggesting a differentiation between normal and pathological aging in semantic search. This fronto-parietal activity was also found to be correlated with episodic memory performance. Those with worse performance on the logical memory subtest (immediate and delayed recall) of Wechsler Memory Scale-Third Edition (Wechsler, 1997) had a delayed fronto-parietal ERP effect, supporting the value of this task in differentiating normal and pathological aging. Despite the utility of ERPs for examining the temporal unfolding of neural activity, non phase-locked and time-locked activity is treated as noise during averaging of ERPs and thus information that could provide useful information about the underlying neurophysiological process is not included. The current study was motivated by the additional insights that time-frequency EEG analysis (Roach et al., 2008; Cavanagh & Frank, 2014) may provide about semantic memory related to the SORT task, and aimed at examining differences in neural dynamics that could inform how semantic memory functions differ from normal to pathological aging.

Prior EEG studies using time-frequency analysis have suggested functional roles of low and high beta (12-20 and 20-30 Hz, respectively) in lexical semantic retrieval (Bakker et al., 2015; Bastiaansen and Hagoort, 2006; Slotnick et al., 2002; Lewis & Bastiaansen, 2015; Weiss & Mueller, 2012). While theta (4-8 Hz) and alpha (8-12 Hz) oscillations have been linked to word or sentence processing (Bakker et al., 2015; Bastiaansen and Hagoort, 2006; Li & Yang, 2013; Shahin et al., 2009; Chiang et al., 2016). Also, the slower frequency bands (theta, alpha) are thought to be associated with domain-general processes such as cognitive control and attentional demands during semantic processing (Cavanagh & Frank, 2014; Klimesch, 2012). How these different frequency bands specifically relate to semantic memory processing is still under scrutiny; therefore, the current study examined oscillatory dynamics in all three frequency bands (theta, alpha, high/low beta) during the SORT task.

The current literature on EEG oscillations related to semantic memory mostly involves studies on young adults. There are a few EEG studies examining time-frequency responses directly elicited by semantic tasks in normal aging or pathological aging (e.g., MCI) (Markiewicz et al., 2021; Poullisse et al., 2020; Packard et al., 2020; Mazaheri et al., 2018), and none have compared such effects across normal and pathological aging. Since there is not sufficient literature to guide an adequately-informed *a priori* hypothesis to focus on specific frequency bands or time frames, we used a data-driven approach based on permutation tests to examine neural oscillations on the SORT task.

Our goals were to examine (1) normal aging effects by comparing younger to cognitively normal older adults and (2) pathological aging effects by comparing cognitively normal older adults to individuals with MCI. Our general hypothesis was that changes would be observable at the neural level with no differences in behavioral performance for normal aging effects. In contrast, we expected changes both in task performance and neural oscillations in older adults with MCI compared to their age- and education-matched cognitively normal controls.

2. METHODS

2.1 Participants

The study included three groups of participants including younger adults [YA] (Total N = 29, 11 males, mean age of 21.3 ± 2.5 years, mean education of 14.2 ± 1.2 years), cognitively healthy older adults [HA] (total N = 22, 5 males, mean age of 63.9 ± 6.4 years, mean education of 17 ± 1.6 years), and individuals with a diagnosis of mild cognitive impairment [MCI] (total N = 20, 10 males, mean age of 67.8 ± 8.2 years, mean education of 16 ± 2.4 years; Clinical Dementia Rating of 0.5). All participants were native English speakers with no history of learning disabilities, stroke, major psychiatric illness, alcoholism or substance abuse, or uncorrected hearing or vision loss. All MCI participants met Petersen criteria (Petersen et al., 2009), by consensus diagnosis among clinicians or research investigators, including the following: (1) cognitive concerns reported by the patient and/or corroborated by a reliable informant, (2) cognitive impairments verified by objective measures, (3) relative independence in performing daily functions, and (4) did not meet dementia criteria. Both amnesic (N = 16) and non-amnesic (N = 4) MCI patients were included. The HA and MCI groups had no statistical differences in age and education. Performance on selected neuropsychological tests for HA and MCI is presented in Table 1. Informed consent was obtained from all participants in accordance with the protocols approved by the Institutional Review Boards of The University of Texas at Dallas and The University of Texas Southwestern Medical Center. Experiments with participants were performed in accordance with the ethical standards of the Committee on Human Experimentation of these institutions and with the Helsinki Declaration of 1975.

2.2 EEG task and procedures

All participants completed the SORT task which has been described in prior publications (Chiang et al., 2014, 2015). SORT consists of word pairs presented simultaneously representing two conditions: retrieval condition and non-retrieval condition. The retrieval condition includes 56 word pairs which facilitate retrieval of a particular object from memory (e.g., the pair ‘humps’ and ‘desert’ facilitate retrieval of the concept ‘camel’). The non-retrieval condition contains 56 word pairs which come from the same set of words, but which are randomly paired and thus do not lead to memory retrieval of any object (e.g., ‘humps’ and ‘monitor’ do not facilitate retrieval of a specific item). Retrieval and non-retrieval word pairs were randomly sequenced to create two different versions of the task, which were randomly assigned and counterbalanced across participants. Word pairs appeared simultaneously on the screen with one word above the other for a total of three seconds. A fixation target (+) was presented at the center of the screen for three seconds between each word pair. Participants were asked to decide if each pair led to object retrieval by pushing either a ‘yes’ or ‘no’ button on a response pad using their right index and middle finger, respectively.

Participants received the following instructions prior to the EEG task: “You are going to see two words. These represent features that are related to objects. Push the button under your index finger if the two words combine to bring to mind some particular object. If the two words do not combine to bring to mind a particular object, push the button under your middle finger.” Participants were encouraged to respond as quickly and accurately as possible. Response time (RT) and accuracy were recorded for each trial. Responses recorded outside the window of 300-3000 ms were labeled as incorrect. The entire task took approximately 11 minutes. The stimuli were presented on an LCD screen using Stim software (Compumedics Neuroscan, USA) and placed about 46 inches from the participant. The two words in each pair spanned approximately 5° of both vertical and horizontal visual angles, with the horizontal measure varying slightly by word length. All the words were presented against a white background in black, lower-case, Times New Roman font (size 72).

2.3 EEG data acquisition and preprocessing

EEG was continuously recorded from a 64-electrode EEG cap (Neuroscan Quikcap) via a Neuroscan Syn-Amps2 amplifier using Scan 4.5 software (Compumedics Neuroscan, USA; sampling rate: 1 kHz, DC-200 Hz) while subjects performed the SORT task. The reference electrode was placed between Cz and CPz at the midline. A bipolar vertical electrooculogram (VEOG) was recorded for the left eye. EEG data from electrodes with impedance exceeding 10–20 k Ω were discarded from further processing and most impedances

were less than 5–10 k Ω . Poorly functioning electrodes were excluded manually by visual inspection of the raw data. Data from fewer than 5% of electrodes were rejected; the number of rejected electrodes did not differ significantly across groups (YA vs HA, $t(49) = 0.15$, $p = 0.881$; HA vs MCI, $t(40) = 0.44$, $p = 0.663$). An algorithm computing the average based on spherical splines fitted to the data was then applied to interpolate EEG data to the sites of the bad electrodes identified (Ferree et al., 2009).

The continuous EEG data were high-pass filtered at 1 Hz and subsequently low-pass filtered at 40 Hz using a finite impulse response filter. Independent component analysis (ICA) was then applied to the filtered continuous EEG data to identify artifacts (muscle, eye, and heart) using the EEGLAB toolbox (Delorme and Makeig, 2004) running under MATLAB 2021 (MathWorks, Natick, MA, USA). Components with >70% probability of representing an artifact were automatically removed (ICLabel, Pion-Tonachini et al., 2019). Subsequently, ICA components of each individual’s data were visually examined and artifacts not identified previously by the algorithm were removed manually to complete data cleaning. After this step, EEG data were segmented for retrieval and non-retrieval conditions into multiple EEG epochs (-1000 to 3000 ms, time-locked to the stimulus onset). Epochs having a peak amplitude of $\pm 75 \mu\text{V}$ between -500ms and 2000 ms post stimulus onset (highly associated with artifacts) were rejected and epochs with extreme values (based on standard deviation > 5) were excluded by rejection algorithms in EEGLAB using joint probability and kurtosis of activity. The average (accepted trials / all correct trials) epochs retained for retrieval and non-retrieval conditions respectively were $88.3 \pm 5.8 \%$ (42.3 ± 4.1 trials) and $89 \pm 6.6 \%$ (42.7 ± 5.2 trials) in the YA group, $91 \pm 5.3 \%$ (44.7 ± 4.2 trials) and $91.9 \pm 4.1 \%$ (44.8 ± 4.4 trials) in the HA group, and $88.6 \pm 5.8 \%$ (39.3 ± 4 trials) and $88.3 \pm 7.5 \%$ (40.3 ± 7.6 trials) in the MCI group.

2.4 EEG Time-Frequency analysis

EEG epochs underwent spectral decomposition using Morlet wavelets to extract power data for frequencies from 4 to 30 Hz (with approximately 1 Hz intervals). Three cycles were set for the lowest frequency and cycles increased linearly with frequency scaled at 0.5 using EEGLAB `newtimef()` function (‘cycles’, [3 0.5]; Delorme and Makeig, 2004). Temporal resolution was around 36-37 ms per time frame. Baseline correction within each 1 Hz frequency interval was performed for each single trial by subtracting the average power between -600 and -100 ms pre-stimulus onset from each time point post-stimulus onset to calculate event-related spectral perturbation (ERSP) using the gain model (Grandchamp and Delorme, 2011). The power data were then logarithmically converted to decibel (dB) for further statistical analysis. Increase in power relative to baseline represents event-related synchronization (ERS), while lower power relative to baseline represents event-related desynchronization (ERD).

2.5 Statistical Analysis

For SORT performance, we utilized repeated measures general linear models (GLM; IBM SPSS Statistics 28.0) with group as a between-subject factor (two group comparisons: YA vs HA, or HA vs MCI) and conditions as a within subject factor (retrieval vs non-retrieval). RT and accuracy data were analyzed separately. Post-hoc comparisons were adjusted with Bonferroni correction. Significant results were reported when $p < 0.05$.

EEG data were analyzed for theta (4–8 Hz), alpha (8–12 Hz), low beta (12–20 Hz), and high beta (20–30 Hz) frequency bands with mean values calculated from each frequency range, based on canonical classification from prior EEG studies (Weiss & Mueller, 2012; Poullisse et al., 2020; Markiewicz et al., 2021). In order to examine differences in individual alpha frequency (IAF), given different age groups, we performed peak frequency extraction within the frequency range 7-14 Hz from epochs between -750 to 2500 ms to stimulus onset, for each individual across conditions (Klimesch, 1999). We ran a repeated measures GLM and did not find any significant effects (no effects of group, condition, or group by condition interaction), thus ruling out that individual alpha differences affected our analysis, and supporting the use of the standard window.

Permutation tests ($N = 2000$) were performed to compare group data, for difference between retrieval and non-retrieval conditions, based on two-tailed independent t-tests. These tests were performed to assess (1) normal aging effects by comparing YA to HA groups and (2) pathological aging effects by comparing HA to

MCI groups, for all electrodes ($N = 62$) and all windows ($N = 26$) spanning from 188 to 1105 ms post stimulus onset. We chose this time window given that prior studies have shown effects within this time window on the SORT task (Chiang et al., 2014, 2015, 2016, 2020). A False Discovery Rate (FDR) < 0.05 from permutation tests was considered significant, which is a robust statistical approach commonly adopted in functional imaging studies to avoid excessive false negative results, so further corrections for multiple comparisons were not applied. Additionally, we tested conditional effects (retrieval vs non-retrieval conditions) within each group separately, based on permutation tests ($N = 2000$) using two-tailed paired-t tests, thresholded at FDR < 0.05 . These results are presented in the supplementary materials since condition effects are not related to our primary research questions.

Post hoc analysis was performed based on the mean power scores extracted within the time window at the electrodes showing significant results, using 2-tailed paired-t tests to compare conditions (retrieval vs non-retrievals). Significant results were reported if $p < 0.05$.

3. RESULTS

3.1 Normal aging effects (YA vs HA comparison)

3.1.1 Behavioral results. For RT (measured in ms), main effect of condition was significant, $F(1,49) = 78.418$, $p < .001$, with participants taking longer to respond to non-retrieval (mean RT = 1562, SD = 345) compared to retrieval (mean RT = 1296, SD = 235) conditions. Main effect of group was not significant, $F(1,49) = 3.798$, $p = .057$. No significant interaction between condition and group was found, $F(1,49) = .126$, $p = .724$. For accuracy, main effect of condition was significant, $F(1,49) = 4.657$, $p = .036$, with participants performing better on non-retrieval (mean accuracy = 88 %, SD = 9.1 %) compared to retrieval (mean accuracy = 84.7 %, SD = 6.9 %) conditions. Main effect of group was not significant, $F(1,49) = 0.761$, $p = 0.387$. No significant interaction between condition and group was found, $F(1,49) = 0.196$, $p = 0.66$. Group averaged RT and accuracy scores for each condition are listed in Table 2 and plotted in Figure 1.

3.1.2 EEG results. Permutation tests on ERSPs (difference between retrieval and non-retrieval conditions) between YA and HA showed three different effects (FDR < 0.05). First, there was greater theta ERS near the left/midline parietal electrode (P1) from 628 to 701 ms post-stimulus onset in non-retrieval compared to retrieval conditions in YA, $t(28) = 3.841$, $p < 0.001$, Cohen's $d = 1.06$ (retrieval: 1.96 ± 1.49 dB, non-retrieval: 2.72 ± 1.48 dB), but not in HA, $t(21) = 1.772$, $p = 0.091$ (retrieval: 2.25 ± 1.75 dB, non-retrieval: 1.76 ± 2.3 dB) (Figure 2.1). Second, there was greater alpha ERD near the left centro-parietal electrode (CP3) from 555-591 ms post-stimulus onset in retrieval compared to non-retrieval conditions in YA, $t(28) = 3.744$, $p < 0.001$, Cohen's $d = 1.17$ (retrieval: -0.32 ± 1.81 dB, non-retrieval: 0.5 ± 2.13 dB), but not in HA, $t(21) = 0.889$, $p = 0.384$ (retrieval: 0.14 ± 3.05 dB, non-retrieval: -0.09 ± 3 dB) (Figure 2.2). Third, there was greater high beta ERS near the right parietal electrode (P8) from 444-481 ms post-stimulus onset in non-retrieval compared to retrieval in HA, $t(21) = 2.32$, $p = 0.03$, Cohen's $d = 0.85$ (retrieval: 0.11 ± 1.1 dB, non-retrieval: 0.53 ± 0.77 dB), but not in YA, $t(28) = 1.305$, $p = 0.202$ (retrieval: 0.82 ± 0.69 dB, non-retrieval: 0.63 ± 0.76 dB) (Figure 2.3).

For reference, group-averaged ERSPs in different frequency bands in each condition is illustrated in Supplementary Figures 1 (YA) and 2 (HA). The differences in ERSPs between conditions within each group are included in Supplementary Figures 4 (YA) and 5 (HA). Results from all time frames (including windows with non-significant effects) for normal aging effects (YA versus HA) can be found in Supplementary Figure 7.

3.2 Pathological aging effects (HA vs MCI group comparison)

3.2.1 Behavioral results. For RT (measured in ms), main effect of condition was significant, $F(1,40) = 58.107$, $p < .001$, with participants taking longer to respond to non-retrieval (mean RT = 1704, SD = 346) compared to retrieval (mean RT = 1439, SD = 257) conditions. Main effect of group was not significant, $F(1,40) = 1.988$, $p = 0.166$. No significant interaction between condition and group was found, $F(1,40) =$

0.146, $p = 0.688$. For accuracy, main effect of condition was significant, $F(1,40) = 4.684$, $p = .036$, with participants performing better on non-retrieval (mean accuracy = 86 %, SD = 11.9 %) compared to retrieval (mean accuracy = 82.2 %, SD = 8.3 %) conditions. Main effect of group was also significant, $F(1,40) = 7.401$, $p = 0.01$, with HA more accurate (mean accuracy = 87.24 %, SD = 7.5 %) than MCI (mean accuracy = 80.7 %, SD = 12 %). No significant interaction between condition and group was found, $F(1,40) = 0.598$, $p = 0.444$. Group averaged RT and accuracy scores for each condition are listed in Table 2 and plotted in Figure 1.

3.2.2 EEG results. Permutation tests on ERSPs (difference between retrieval and non-retrieval conditions) between HA and MCI showed two different effects. First, greater low beta ERS near the right frontal electrode (F2) from 444-481 ms post-stimulus onset was observed in retrieval compared to non-retrieval conditions for HA, $t(21) = 3.136$, $p = 0.005$, Cohen's $d = 1.01$ (retrieval: 0.56 ± 1.51 dB, non-retrieval: -0.11 ± 1.34 dB), but not in MCI, $t(19) = 1.292$, $p = 0.212$ (retrieval: 0.24 ± 1.28 dB, non-retrieval: 0.65 ± 1.74 dB) (Figure 3.1). In addition, greater high beta ERS in the left fronto-temporal electrode (FT7) during 224-261 ms post-stimulus onset was observed in non-retrieval compared to retrieval conditions in MCI, $t(19) = 2.173$, $p = 0.043$, Cohen's $d = 0.83$ (retrieval: 0.58 ± 0.58 dB, non-retrieval: 0.99 ± 0.93 dB), with a reverse pattern noted in HA, $t(21) = 2.097$, $p = 0.048$, Cohen's $d = 0.87$ (retrieval: 1.03 ± 0.71 dB, non-retrieval: -0.65 ± 0.55 dB) (Figure 3.2).

For reference, group-averaged ERSPs in different frequency bands in each condition is illustrated in Supplementary Figures 2 (HA) and 3 (MCI). The differences in ERSPs between conditions within each group are included in Supplementary Figures 5 (HA) and 6 (YA). Results from all time frames (including windows with non-significant effects) for pathological aging effects (HA versus MCI) can be found in Supplementary Figure 8.

4. DISCUSSION

By utilizing a semantic memory paradigm that did not require explicit word retrieval, we were able to identify different patterns of EEG oscillations between normal aging versus pathological aging. When comparing YA and HA groups, no significant behavioral differences were seen but three within-group condition effects were identified on EEG measures: differences in (1) theta ERS and (2) alpha ERD between conditions were observed in YA but not in HA after 500 ms post-stimulus onset, and (3) a difference in high beta band ERS between conditions in the HA group but not in YA group during 400-500 ms post-stimulus onset. When individuals with MCI were compared to HA, they performed worse than HA across conditions accompanied by two EEG effects: (1) a difference in low beta ERS between conditions was observed in the HA group but not in the MCI group during 400-500 ms post-stimulus onset and (2) a difference in high beta ERS between conditions, divergent in pattern, was noted between MCI and HA between 224-261 ms post-stimulus onset.

Our behavioral data showed preserved accuracy and RT in the HA group compared to the YA group consistent with findings from our prior studies and the literature supporting relatively preserved access to semantic memory with normal aging, (Chiang et al., 2014; Verhaegen & Poncelet, 2013; Rönnlund et al., 2015). However, differences between YA and HA groups observed on EEG suggest early age-related changes emerge between conditions during 400 and 500 ms post-stimulus onset. The HA group showed differences in high beta between retrieval and non-retrieval conditions relative to the YA group. High beta has been associated with retrieval of semantic information (Slotnick et al., 2002; Ferree et al., 2009; Hart et al., 2013; Lewis & Bastiaansen, 2015; Weiss & Mueller, 2012). Differences across conditions observed in the HA group suggest recruitment of additional neural resources, mediated by high beta activity, to support varying demands related to semantic processing between the two conditions. In contrast to HA, the YA group showed differences across conditions after 500 ms post-stimulus onset in theta and alpha frequency power. In particular, consistent with our prior findings within similar time windows (Chiang et al., 2016; Ferree et al., 2009; Hart et al., 2013), YA demonstrated increased alpha ERD during retrieval compared to non-retrieval conditions, which might be linked to semantic integration of features which lead to object memory activation. In the subsequent time window (628 to 701 ms post-stimulus onset), YA had higher theta ERS during non-retrieval compared to retrieval conditions, which might be related to enhanced search for potential feature integration

prior to making a final judgment (Yes/No response on button push). In HA, the loss of such differentiation in theta and alpha responses (as shown in Supplemental Figures 2 & 5) might suggest age-related neurophysiological alterations on both retrieval and non-retrieval conditions as processing related to the task continues. However, these neural alterations in HA at later time frames do not seem to be enough to impact task performance, which also implicates that the earlier high beta differential effects in HA may be a compensatory mechanism to support semantic memory function. Given that both retrieval and non-retrieval conditions elicited similar magnitude of changes in neural responses (i.e., alpha ERD and theta ERS) in older adults, this finding is consistent with the literature that suggests dedifferentiation and reduced segregation in neural activity in healthy aging (Koen & Rugg, 2019; Martin et al., 2022).

Our task was able to differentiate the HA group from individuals with MCI on behavioral task performance as well as EEG measures. Consistent with our hypothesis, lower accuracy was noted in the MCI group compared to the healthy older adult group, suggesting impaired semantic memory performance, which has been reported in our prior studies and the literature (Chiang et al., 2015; Kraut et al., 2007; Dudas et al., 2005; Joubert et al., 2021). We also found greater low beta ERS in retrieval compared to non-retrieval conditions in the HA group but not in the MCI group in earlier time windows (< 500 ms post stimulus onset). These findings suggest that while the HA group differentially allocates neural resources, mediated by low beta, across the two conditions, these differentiations are lost in the MCI group. Interestingly, within the first 300 ms post-stimulus onset, both groups showed differences in high beta power across conditions, albeit different in patterns. While the HA group had higher high beta power in retrieval compared to non-retrieval conditions, an opposite direction was observed in the MCI group with non-retrieval greater than retrieval conditions. It is unclear what this reverse pattern indicates, but these findings suggest that HA and MCI groups may use different strategies to retrieve or process semantic information during the task. Nevertheless, the MCI group shows patterns of neural oscillations that can be differentiated from the HA group on the SORT task and these alterations may be indicative of early neural decompensation, as suggested in prior studies (Woodard et al., 2009; Barbeau et al., 2012; Pistono et al., 2021).

Overall, with age, there is a shift in differentiation across conditions (retrieval vs non-retrieval) from slower frequencies (alpha, theta) to faster frequencies (low and high beta) on the SORT paradigm. The transition from slower to faster brain oscillatory responses may be a sign of aging in general. While both normal and pathological aging effects were specifically identified in high beta power, the YA and HA groups differed in the time frame of 444-481 ms post stimulus onset, which is later than the time frame of 224-261 ms which differentiates the HA and MCI groups. It is possible that alterations in high beta in the earlier time window is a sign of pathological aging, while high beta in the later time window reflects normal aging. Given the evidence that integration of semantic memory was thought to be associated with high beta frequency (25-30 Hz) activity from both the cortex and thalamus during the SORT task (Slotnick et al., 2002; Hart et al., 2013), it is plausible that differential changes in cortico-thalamo-cortical synchronization (Crosson, 2021) may underlie the changes we found in high beta frequency in normal versus pathological aging, though during an earlier time frame. It has been shown that changes in thalamic function and cortico-thalamo-cortical connectivity can occur in normal aging (Goldstone et al., 2018; Fama & Sullivan, 2015) as well as in MCI (Hahn et al., 2016; Zhou et al., 2013; Aggleton et al., 2016). Future work that combines EEG and MRI techniques would be useful to explore these possibilities.

Behavioral measures of semantic memory (e.g., semantic/category fluency) have already shown promising predictive value in risk of progression to MCI and dementia (Sutin et al., 2019; Gustavson et al., 2020). EEG markers of semantic memory will provide additional insights given that neural changes may precede behavioral changes in pathological aging (Olichney et al., 2002; Jack et al., 2013). An important implication of our study is that these brain oscillatory responses can potentially be used as outcome measures to assess efficacy of interventions (e.g., cognitive training, pharmacological treatment) in order to gain a mechanistic view. Furthermore, with the advent of non-invasive brain stimulation methods, these oscillatory brain responses may serve as targets that can be modulated directly by electrical stimulation to stabilize compensatory processes or to interfere pathological processes, and thus to maintain or even improve cognitive function in aging populations (Grover et al., 2022).

5. CONCLUSION

In conclusion, our findings implicate a shift in neural dynamics from young to older adults on semantic memory retrieval assessed with SORT. Beta oscillations may suggest an age-related reorganization of the semantic neural network as a compensatory mechanism in normal aging. The decline and change in pattern of this beta activity observed in MCI could serve as a sensitive biomarker for detecting early disease processes. We recognize that this data examines group level differences and future work is necessary to examine how these markers can be utilized at the individual level to differentiate normal versus pathological aging. Also, longitudinal studies would be warranted in the future to understand if changes in these brain oscillatory responses can predict disease progression. To our knowledge, our study is the first to directly examine both normal and pathological aging effects to demonstrate EEG oscillatory changes during semantic memory retrieval.

Conflict of interest statement

The authors declare no conflicts of interest.

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Data availability statement

Data available on request from the corresponding author.

Author contributions

H.-S. C., M.A.K., J.H.Jr., and R.M. conceived and designed the study. H.-S.C., E.A.L. and R.M. performed data processing, data analysis and interpreted the results. M.A.K. and J.H.Jr. supervised data analysis and interpretation of the results. All authors took part in writing the manuscript, and contributed intellectual input. All the authors have read and approved the final version of the manuscript

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