Age-Related Changes in the Neural Dynamics of Memory Encoding Processes

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Abstract

We examined oscillatory power in electroencephalographic recordings obtained while younger (18-30 years) and older (60+ years) adults studied lists of words for later recall. Power changed in a highly consistent way from word-to-word across the study period. Above 14 Hz, there were virtually no age differences in these neural gradients. But gradients below 14 Hz reliably discriminated between age groups. Older adults with the best memory performance showed the largest departures from the younger adult pattern of neural activity. These results suggest that age differences in the dynamics of neural activity across an encoding period reflect changes in cognitive processing that may compensate for age-related decline.

Age-Related Changes in the Neural Dynamics of Memory Encoding Processes

Memory impairments are among the most common complaints of older adults [1]. Much effort has been devoted to identifying the neurocognitive causes of age related memory decline [2, 3]. But one potential source of age differences has received little attention: the ability to sustain encoding processes across series of events or items that unfold over time [4]. For example, the people you meet during a job interview, the grocery list your spouse dictates over the phone, or which of your medications you have already taken today.

Researchers have studied this aspect of memory using the free recall task, in which participants study a list of sequentially presented items (e.g., words) and then recall the items in any order. The nature of the encoding processes participants engage changes from item-to-item as the list is studied [5]. These dynamics unfold in the brain without any obvious behavioral correlates—they can only be inferred from which items are subsequently remembered and forgotten. Perhaps for this reason, most cognitive aging theories are silent about the contribution of encoding dynamics to memory impairments [6, 3, 7, 8].

But any process that changes across encoding should leave its signature in neural activity. Here we examine neural recordings taken while participants study lists and test for age differences in gradients of neural activity across the encoding period.

Method

The data are from the Penn Electrophysiology of Encoding and Retrieval Study (PEERS), an ongoing project aiming to assemble a large database on memory ability in older and younger adults. The full methods of the PEERS, including some manipulations that we do not consider here, are described in the supplemental materials.

Participants

The present analyses are based on the 172 younger adults (age 17–30) and 36 older adults (age 61-85 years) who had completed Experiment 1 of PEERS as of September 2015. Participants were recruited through a two–stage process. First, we recruited right-handed native English speakers for a single session. Participants who did not make an excess of eye movements during item presentation epochs of the introductory session and had a recall probability of less than 0.8 were invited to participate in the full study. Approximately half of the subjects recruited for the preliminary session move on to the full study. Older adults were pre-screened for signs of pathology using a detailed medical history and the Short Blessed Test [9].

PEERS Experiment

Participants completed 7 sessions of the free recall task. Each session included 16 free recall lists. For each list, 16 words were presented one at a time on a computer screen followed by an immediate free recall test. Each stimulus was drawn from a pool of 1638 words such that within each list, varying degrees of semantic relatedness occurred at both adjacent and distant serial positions.

For each list, there was a 1500 ms delay before the first word appeared on-screen. Each item was on-screen for 3000 ms, followed by jittered inter-stimulus interval of $800 - -1200$ ms (uniform distribution). Each word was accompanied by a cue to perform one of two encoding tasks ("Will this item fit into a shoebox?" or "Does this word refer to something living or not living?") or no encoding task. After the last item in the list, the participant was then given 75 seconds to recall aloud any of the just-presented items.

Electrophysiological recordings and data processing

We used Netstation to record EEG from Geodesic Sensor Nets (Electrical Geodesics, Inc.) with 129 electrodes digitized at 500 Hz by either the Net Amps 200 or 300 amplifier

and referenced to Cz. Recordings were then rereferenced to the average of all electrodes except those with high impedance or poor scalp contact. To eliminate electrical line noise, a fourth order 2 Hz stopband butterworth notch filter was applied at 60 Hz. To correct artifacts such as eye blinks or electrodes with poor contacts we used independent component analysis [ICA, 10] and an artifact detection/correction algorithm based on [11], which is described in the supplemental material.

To compute spectral power, the corrected independent components were projected back into EEG sensor space and the time series for an entire session was convolved with Morlet wavelets (wave number = 6) at each of 60 frequencies logarithmically spaced between 2 Hz and 200 Hz. The resulting power time series were downsampled to 10 Hz. We then defined encoding events by extracting the time period from -200 ms to 3000 ms relative to each item's presentation. For each frequency, a participant's raw power values were z-scored across encoding events separately for each session and each encoding task (no-task, single-task, and task-shift) to remove the effects of these variables. Z-scored power was then averaged across the -200 ms to 3000 ms encoding interval to provide one power value for each study event.

Results

Figure 1A shows the gradient of spectral power across serial positions in six frequency bands. For younger adults, these gradients are in close agreement with those found in previous work [12]. In the 16–26 Hz, 28–42 Hz, and 44–200 Hz bands, both younger and older adults show high initial power followed by a rapid decline across serial positions, with little age difference. By contrast, the 2–3 Hz, 4–8 Hz, and 10–14 Hz bands all show clear age differences. Just as at higher frequencies, older adults exhibit a steep decline in power across serial positions at lower frequencies, but younger adults exhibit a shallower decline (in the 2–3 Hz band) or a net increase across serial positions (in the 4–8 Hz and 10–14 Hz bands). That is, older adults show higher power than younger adults early in a study list,

but the age difference reverses for late-list items.

To determine if these neural gradients reliably predict age, we began by condensing the gradients into a single number for each participant by computing the change from the power level at the first serial position to the average power of the last 5 items:

$$\Delta_{EEG} = \frac{\sum_{i=k}^{LL} SP_i}{LL - k + 1} - SP_1, \tag{1}$$

where SP_i is power during the i^{th} list item, LL is the total number of items in a list (here $LL = 16$), and k is the first item included in the late-item average ($k = 5$ for the analyses reported here). We then tested whether Δ_{EEG} distinguishes older from younger adults by examining receiver operating characteristic (ROC) curves created by varying the criterion value of Δ_{EEG} used to classify a participant as younger versus older. These curves (Figure 1B) show that the 2–3 Hz, 4–8 Hz, and 10–14 Hz gradients were all highly robust biomarkers of age group. Significance was assessed by finding where the area under the curve (AUC) for the actual ROC curves lay in a null AUC distribution formed by permuting Δ_{EEG} across participants 50000 times and computing a ROC for each permuted dataset.

How do these age differences in neural dynamics relate to age age differences in memory ability? To explore this question, we conducted a median split analysis comparing the older adults with the highest memory scores to the older adults with the lowest memory scores (see the inset in the first panel of Figure 2). As shown in Figure 2, these subgroups showed distinct neural gradients.

In the 2–3 Hz, 4–8 Hz, and 10–14 Hz bands, the older adults with the largest memory impairments showed neural gradients that were more similar to the younger adult pattern of shallowly decreasing (2–3 Hz) or gradual increasing (4–8 Hz and 10–14 Hz) power across serial positions. That is, the best preforming older adults looked *least* like younger adults at the neural level. A similar situation is observed at higher frequencies. Young adults

show a steep decrease in power in the 28–42 Hz and 46–200 Hz bands, as do the impaired older adults. But the non-impaired older adults show a shallower decrease. Again, the non-impaired older adults depart most strikingly from the younger adult pattern of neural dynamics.

ROC analyses on Δ_{EEG} values, analogous to those reported in Figure 1, revealed that no individual frequency band reliably discriminated impaired from non-impaired older adults ($.06 < p < .20$). However, the younger adult pattern is not fully described by any individual frequency band, instead it is characterized by gradual increases across serial positions at 10–14 Hz and sharp decreases for higher frequencies. To capture this pattern we computed the difference between Δ_{EEG} in each lower frequency band, F_i, and the 46–100 Hz band:

$$\Delta_{EEG_{F_i}} - \Delta_{EEG_{44-200Hz}}. \tag{2}$$

Figure 3A compares this measure among younger adults, impaired older adults, and non-impaired older adults for each of the frequency bands. To ease interpretation the $\Delta_{EEG_{F_i}} - \Delta_{EEG_{44-200Hz}}$ values, the small curves next to each data point show the full gradients across serial positions for the current frequency (F_i, solid lines) and 44–200 Hz (dotted lines). $\Delta_{EEG_{F_i}} - \Delta_{EEG_{44-200Hz}}$ represents the difference in the rate of change of these two gradients. At all frequencies, the impaired older adults are numerically closer to the younger adult pattern than are the non-impaired older adults. We conducted an ROC analysis on the ability of this measure to distinguish the two older adult subgroups. The measure for the 2–3 Hz, 4–8 Hz, and 10–14 Hz bands robustly discriminated impaired from non-impaired older adults (Figure 3B). That is, larger deviation from the younger adult pattern of neural dynamics across an encoding episode is a biomarker of successful aging.

Discussion

We found evidence of age differences in how neural activity changes while encoding a series of events. For both older and younger adults, high frequency oscillatory power

(16–200 Hz) declined rapidly across events [12]. By contrast, power at lower frequencies showed marked age differences. Whereas older adults exhibited rapid power declines at both high and low frequencies, younger adults exhibited shallower decreases (2–3 Hz) and even rapid increases (10–14 Hz) at low frequencies. The rate and direction of change of the gradient at these low frequencies was a highly robust biomarker of age, as revealed by ROC analyses. These results add neural dynamics across encoding periods to the growing list of age differences in electrophysiology [13, 2, 14, 15, 16, 17]. Intriguingly, older adults who preformed best on the memory task showed the largest deviation from the young adult pattern, particularly in the 4–14 Hz range. This finding complements previous work that has suggested that some aspects of age-related change in processing compensates for, rather than contributes to, behavioral impairments [18, 19, 20, 21, 22].

In this brief report, we provide evidence for the general hypothesis that there are age differences in the neural dynamics of encoding. We hope these preliminary results will be useful both in guiding basic science and in designing assessments to detect signs of memory impairment. To conclude we highlight two important questions for future work and provide some speculations on promising answers.

The first question is which cognitive processes are linked to the observed age difference in neural dynamics? Two general categories of processes strike us as likely candidates: processes that become less efficient as the list progresses with time due to fatigue [e.g., 5] and processes that ramp up as the list goes on such as rehearsing early item in the list.

The second question is why would age differences in such processes compensate for, rather than exacerbate, memory impairment? In the case of fading efficiency, if older adults are aware they will fatigue across a list, it might make sense for them to strongly engage encoding processes for early items to ensure that at least some items are well-encoded. In the case of rehearsal, it is known that older adults are less likely to rehearse items [23], perhaps because they are impaired at the retrieval processes [4] needed

to think back to early list items [24]. If rehearsal is likely to fail, older adults may be well-served by instead focusing on encoding the current item. Indeed, alpha power (corresponding to the 10–14 Hz band used here) has been linked to holding more items in mind [25] and increases in 10–14 Hz power younger adults show across a list may be an index of elaborative encoding or rehearsal [12]. Therefore, the lack of 10–14 Hz increases in our group of non-impaired older adults may indicate that they are not attempting to engage in elaborative encoding or rehearsal.

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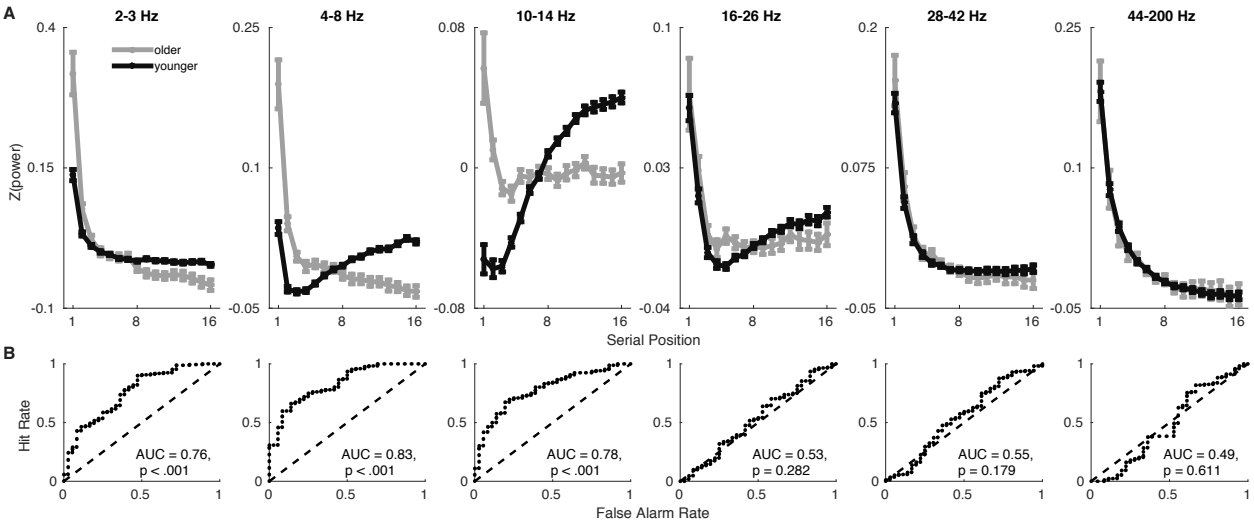

Figure 1. **A.** Spectral power in six frequency bands across serial positions for younger adults versus older adults. Error bars are one standard error of the mean. **B.** ROC curves created by varying the threshold value of Δ_{EEG} (the change from the power level at the first serial position to the average power of the last 5 items) used to classify a participant as a younger or older adult. Significance was assessed by comparing the observed AUC value with a null distribution created by permuting Δ_{EEG} values across participants 50000 times and running the analysis on each permuted dataset.

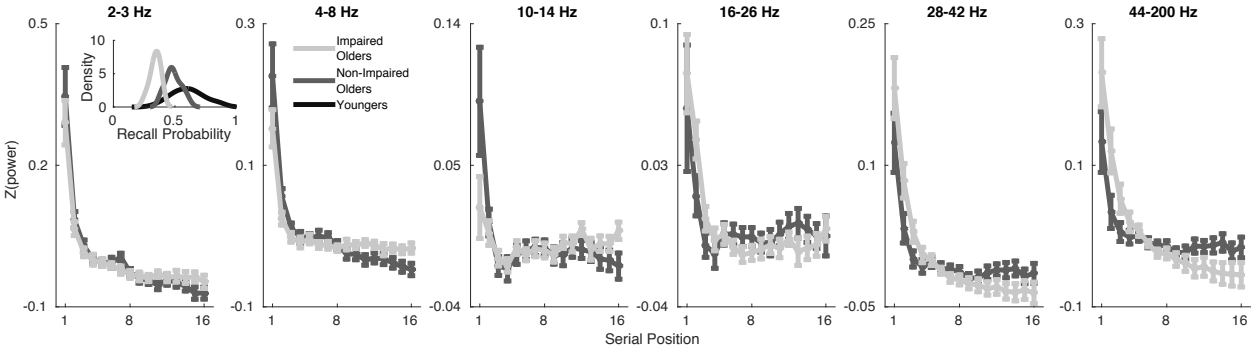

Figure 2. Spectral power in 6 frequency bands across serial positions for older adults with recall probabilities above (non-impaired) versus below (impaired) the older adult median. Error bars are one standard error of the mean. The inset in the first panel shows kernel density estimates of the distributions of overall probability of recall values for each group.

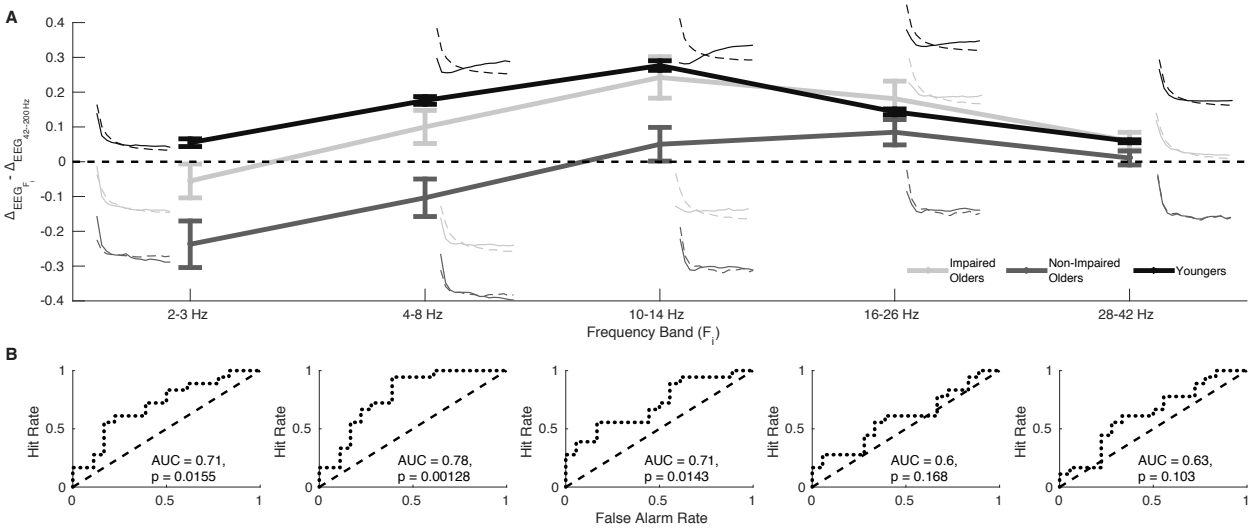

Figure 3. **A.** Mean values of $\Delta_{EEG_{F_i}} - \Delta_{EEG_{44-200Hz}}$ for the 2–3 Hz, 4–8 Hz, 10–14 Hz, 16–26 Hz, and 28–42 Hz bands for the younger adults, older adults with recall probabilities above (non-impaired) the older adult median, and older adults below (impaired) the older adult median. Error bars are one standard error of the mean. To ease interpretation the $\Delta_{EEG_{F_i}} - \Delta_{EEG_{44-200Hz}}$ values, the small curves next to each data point show the full gradients across serial positions for the current frequency (F_i, solid lines) and 44–200 Hz (dotted lines). $\Delta_{EEG_{F_i}} - \Delta_{EEG_{44-200Hz}}$ represents the difference in the rate of change of these two gradients. **B.** ROC curves created by varying the threshold value of $\Delta_{EEG_{F_i}} - \Delta_{EEG_{44-200Hz}}$ used to classify a participant as an impaired versus a non-impaired older adult. Significance was assessed by comparing the observed AUC value with a null distribution created by permuting $\Delta_{EEG_{F_i}} - \Delta_{EEG_{44-200Hz}}$ values across participants 50000 times and running the analysis on each permuted dataset.