

<https://doi.org/10.1038/s41514-025-00263-8>

Age-related alterations in alpha and beta oscillations support preservation of semantic processing in healthy aging



Megan C. Hall¹, Maggie P. Rempe^{1,2}, Chloe C. Casagrande¹, Ryan J. Glesinger¹, Nathan M. Petro¹, Grant M. Garrison¹, Jason A. John¹, Sarah M. Dietz¹, Mikki Schantell¹, Hua Bai¹, Yasra Arif¹, Christine M. Embury¹, Seth Bashford¹, Hannah J. Okelberry¹, Aubrie J. Petts¹, Elizabeth L. Keifer¹, Pamela E. May-Weeks², Giorgia Picci^{1,3}, Elizabeth Heinrichs-Graham^{1,3} & Tony W. Wilson^{1,2,3} ✉

Semantic processing remains relatively preserved during healthy aging, but the mechanisms are poorly understood. Herein, we use dynamic functional mapping based on magnetoencephalography to examine the neural oscillations serving semantic processing across the adult lifespan ($N = 154$; 21–87 years). Task-related oscillatory dynamics were imaged using a beamformer and whole-brain linear mixed-effects (LME) models were calculated with age and task condition (semantically-related or -unrelated) as factors. LMEs revealed significant age-by-condition interactions on alpha and beta activity in multiple regions, which generally reflected stronger responses with increasing age and/or in the semantically-related condition across regions (p values < 0.005 , corrected). Follow-up mediation analyses of these interaction clusters indicated that left perisylvian alpha responses suppressed the effect of age on verbal fluency ($p = 0.014$), with larger conditional differences in this region supporting preserved fluency with increasing age. Our findings provide novel insight on age-related neurophysiological adaptations that support preservation of semantic processing.

Navigating the world requires being able to comprehend, synthesize, and understand the meaning of words and objects. Semantic processing encompasses the ability to understand visual and auditory input and connect this information to internal and external concepts. In the laboratory, semantic processing can be measured in many ways, including through the viewing of ambiguous words with contextual cues^{1–5}, matching pictures and words⁶, and through tasks that require matching of words that are congruent or incongruent with one another^{6,7}. Semantic processing is broadly thought to occur in a distributed, left-lateralized brain network, with some differences based on the task design. For example, while auditory word processing begins in the bilateral superior temporal cortex, visual word processing begins in the primary visual cortex and becomes more strongly left-lateralized very rapidly⁸. However, such differences are typically limited to the early sensory transformations, with later processing converging in regions of the left temporal and inferior frontal regions^{7–9}. Specifically, studies using semantic anomalies have shown neural responses across the left ventral frontotemporal cortices^{2–4}, and those using ambiguous words and/or semantic control paradigms have shown activation in left-lateralized regions of the ventrolateral prefrontal cortex (PFC), inferior frontal gyrus

(IFG), angular gyrus, and left posterior middle temporal gyrus (MTG)^{1,5,10–16}. Importantly, semantic processing and language more generally typically remains intact or even improves during healthy aging, but can become degraded in certain neurological conditions such as semantic aphasia or dementia^{10,15,17}. However, whether the neurophysiology underlying semantic processing evolves during healthy aging to maintain such performance levels remains far less understood.

The United States population has grown exponentially older, with adults over 65 years expected to make up 23% of the total population by 2054¹⁸; thus, understanding the impact of aging on cognitive and brain health is essential. One influential theory of brain aging is the hemispheric asymmetry reduction in older adults model (HAROLD)¹⁹. The HAROLD model postulates that neural activity, especially in the prefrontal cortex, becomes less lateralized in older adults. Supporting the tenets of HAROLD in the context of semantic processing, prior research has found that older adults activate language-related cortices more bilaterally relative to their younger peers during semantic processing³. A related view without the emphasis on hemispheric lateralization is the neural dedifferentiation hypothesis. This theory suggests that neural regions become less specialized

¹Institute for Human Neuroscience, Boys Town National Research Hospital, Boys Town, NE, USA. ²College of Medicine, University of Nebraska Medical Center (UNMC), Omaha, NE, USA. ³Department of Pharmacology & Neuroscience, Creighton University, Omaha, NE, USA. ✉e-mail: tony.wilson@boystown.org

for a given cognitive function with older age, which may contribute to the observed decrease in lateralized neural activity with age²⁰. Another influential theory of brain and cognitive aging is the compensation-related utilization of neural circuits hypothesis (CRUNCH)²¹. A key aspect of the CRUNCH model is that older adults tend to hyperactivate some brain regions (relative to younger adults) in order to maintain high performance levels on cognitive tasks, until the task becomes too difficult, at which point activation and performance declines. Finally, there is also the posterior to anterior shift in aging (PASA) model, which is based on studies showing a decrease in occipital activity and an increase in PFC activity with aging^{22,23}. These theories have recently been elaborated upon to include some of the complexities of reserve, maintenance, and compensation, and the differential roles that socioecological, socioeconomic, and biological factors play throughout the aging process^{24,25}.

These theories of brain aging have played a prominent role in understanding how semantic processing changes with healthy aging. For example, a meta-analysis of 47 functional neuroimaging studies showed that while both older and younger adults exhibit left-lateralized neural activation during semantic processing, older adults tend to show less activity in semantic control regions such as the left IFG and MTG, along with greater activation in right-hemispheric frontal and parietal regions, lending support to the HAROLD model²⁶. Similarly, in a semantic judgement task using magnetoencephalography (MEG), the left inferior PFC was found to be more active in younger relative to older adults who tended to recruit the bilateral temporoparietal cortices and left anterior temporal lobe (ATL) more strongly²⁷. Likewise, a recent fMRI study of object naming showed that younger adults more strongly activated the left IFG relative to their older peers, although the reverse pattern was observed in the left MTG and left hippocampus²⁸. Other studies have focused on how brain networks serving semantic processing change with healthy aging. For example²⁹, showed that increased network segregation during a semantic fluency fMRI task was associated with higher accuracy and faster reaction time in younger adults, while such segregation was associated with poorer performance in older adults.

While the majority of research on semantic processing has used fMRI, a handful of studies have used MEG or electroencephalography (EEG) to examine potential changes in neural oscillatory activity. These studies have generally shown stronger alpha/beta oscillations (i.e., greater event-related desynchronization [ERD]) during semantic processing, with some studies also showing theta and gamma oscillations^{30–33}. For example, left-lateralized alpha and beta oscillations have been observed in the ventral and lateral frontotemporal regions in response to semantic anomalies and with words occurring later in a sentence^{2–5,7,9}. These left-lateralized alpha/beta oscillations are stronger (i.e., greater ERD) when viewing sentences as opposed to word lists, with responses emerging in bilateral occipito-parietal, left frontal, and left temporal areas, and later spreading to right frontal and parietal regions⁹. Specifically, in their word analysis, Lam and colleagues⁹ found that alpha/beta power tends to decrease more strongly (i.e., greater ERD) in the left hemisphere when viewing words in a sentence relative to words in a list. Further, when comparing word processing within a sentence, there was stronger alpha/beta oscillations (i.e., greater ERD) in left-lateralized regions when viewing later relative to earlier words in a sentence, while the opposite was true for right-lateralized regions⁹. During MEG, Rempe and colleagues⁷ also observed a sustained alpha response during a semantic processing task. This response was associated with task performance; specifically, stronger alpha oscillations (i.e., stronger ERD) predicted shorter reaction times during semantic processing trials⁷. Thus, in addition to being important for semantic memory and information integration, left-lateralized alpha oscillations may play a key role in performance of semantic processing tasks⁷.

Despite the vast research focused on semantic processing, few studies have focused on age-related changes in semantic processing using MEG. Therefore, the primary goals of the current study were to examine the impact of healthy aging on behavioral performance and the underlying neural oscillations during a semantic processing task using dynamic functional mapping with MEG. Specifically, a large sample of healthy adults ages

21–87 years old performed a semantic judgement task during MEG, whereby they viewed a prime word followed by a target word that was either related or unrelated. Outside the MEG scanner, participants also completed neuropsychological assessments that included the Controlled Oral Word Association Test (COWAT) F-A-S and Animals to measure phonemic and semantic fluency. Consistent with previous research, we expected robust left-lateralized alpha and beta oscillatory responses (i.e., ERDs) following the target word. We hypothesized that these responses would be stronger when viewing related words, indicating deeper engagement of semantic representations during related word pairs. Further, consistent with a recent study on semantic and spatial judgments in healthy aging³⁴, we also hypothesized that the strength of alpha and beta oscillations would increase with age (i.e., greater ERD) in task-related brain regions and that this would help support preserved performance levels in older adults, in agreement with the CRUNCH model. Finally, prior MEG research using this task in young adults has indicated bilateral activity with stronger responses in left hemispheric language areas³⁵, and we predicted this left hemispheric dominance would remain, but that bilateral recruitment may be increased in older adults, consistent with the HAROLD model. Thus, we expected that aspects of both CRUNCH and HAROLD would be supported by our results, such that older adults would have stronger neural responses in task-related cortices, that these responses would be more bilateral, and that stronger left hemispheric responses would aid in maintaining cognitive performance with healthy aging. Conversely, we did not expect our results to support key elements of PASA, nor the neural dedifferentiation hypothesis.

Results

Behavioral analysis

Of the 163 enrollees (Table S1), nine were excluded due to low accuracy (<75% averaged across conditions) on the semantic MEG task ($n = 2$), technical difficulties ($n = 1$), and excessive artifacts in their MEG scan ($n = 6$). The remaining 154 participants were included in primary data analyses ($M_{\text{age}} = 49.72$, $SD_{\text{age}} = 15.30$, $\text{range}_{\text{age}} = 21–87$, $N_{\text{female}} = 79$; Table 1; Figure S1). Analyses involving the verbal fluency assessments were based on 147 participants ($M_{\text{age}} = 50.50$, $SD_{\text{age}} = 14.83$, $\text{range}_{\text{age}} = 21–87$, $N_{\text{female}} = 74$), as four did not complete both the COWAT F-A-S and Animals and three others scored less than 2.5 SDs below the mean on the average verbal fluency score.

Participants performed well on the semantic MEG task, responding accurately to about 95% of all trials (related: 95.06% [3.97%]; unrelated: 95.8% [5.19%]). Reaction time was calculated using the onset of the target word and a complete breakdown of accuracy and reaction time by condition is provided in Table 1. A repeated measures ANOVA with age as a between-subjects factor and condition as a within-subjects factor showed that age, but not condition, significantly impacted accuracy (condition: $F(1, 152) = 1.45$, $p = 0.230$; age: $F(1, 152) = 4.47$, $p = 0.036$), with accuracy improving with increasing age. In contrast, there was a significant effect of condition, but not age on reaction time (condition: $F(1, 152) = 17.51$, $p < 0.001$; age: $F(1, 152) = 2.19$, $p = 0.141$; Fig. 1b), with faster responses during semantically related compared to unrelated word pairs (related: 841.81 ms (128.85); unrelated: 985.35 ms (181.90)). The interaction of age and condition was not significant for accuracy ($F(1, 152) = 0.45$, $p = 0.503$) or reaction time ($F(1, 152) = 0.12$, $p = 0.727$).

Sensor-level analysis

To identify significant oscillatory responses serving task processing, the MEG time series data were transformed into the time-frequency domain and statistical analyses focused on the target interval were conducted on the sensor-level time-frequency spectrograms across both conditions and all participants. These analyses included paired t-tests against baseline per pixel, with significant clusters of pixels being subjected to nonparametric permutation testing to control for multiple comparisons. These tests revealed significant decreases in alpha (8–14 Hz) and beta (14–26 Hz) power relative to baseline (i.e., greater ERDs; $p < 0.001$, corrected; Fig. 2) across a large number of MEG sensors bilaterally that started about 250 ms

Table 1 | Participant Demographics and Behavior

Demographics	Full sample	
	<i>n</i>	%
Gender		
Female	79	51
Male	75	49
Age		
21–36 years	39	25
37–61 years	77	50
62–87 years	38	25
Race		
American Indian/Alaska Native	2	1
Black/African American	14	9
Asian	7	5
White	128	83
Multiple	3	2
Ethnicity		
Hispanic or Latino	12	8
Not Hispanic or Latino	142	92
Handedness		
Right	145	94
Left	9	6
Behavioral Statistics	Full sample	
	<i>M</i>	<i>SD</i>
Accuracy (%)		
Related	95.058	3.971
Unrelated	95.812	5.191
Reaction Time (ms)		
Related	841.810	128.845
Unrelated	985.353	181.902

Age groups are shown based on the first and third quartiles of the sample, but all statistical analyses treated age as a continuous variable and the subgroups were only used for visualization/interpretation of interaction effects.

after target onset (1000 ms after prime onset) and were sustained for 500 ms (i.e., 1000–1500 ms). There were also strong theta responses following the onset of each visual stimulus, but these transient responses were largely evoked (i.e., phase-locked to the stimulus). Given our focus on oscillatory activity, we did not further examine these neural responses in the current study, but plan to report these in future work focusing on how aging affects time domain visual signals.

Beamformer analysis

To determine the neural regions most active during semantic processing, the sensor-level time-frequency bins described in Section “Sensor-level analysis” were imaged using a time-frequency resolved beamformer. The resulting whole-brain maps per neural oscillatory response were then grand-averaged across both conditions and all participants (Fig. 2) as a data quality check and to identify regions exhibiting the strongest responses. Alpha (8–14 Hz) and beta (14–26 Hz) oscillations (i.e., ERDs) from 1000–1500 ms post-prime onset extended across a wide area of occipital, parietal, and temporal cortices and were mostly left-lateralized. The condition-specific maps were then used to perform whole-brain statistics investigating conditional and age effects.

Whole-brain linear mixed effects models

We next ran whole-brain linear mixed effects (LME) models to examine age-by-condition interactions, with age as a continuous covariate of interest

and condition as a within-subjects factor with two levels (i.e., related and unrelated). The resulting maps were thresholded at $p < 0.005$ and a cluster-extent threshold of $k > 4$ voxels (i.e., 256 mm³) was used to account for multiple comparisons. The whole-brain LME models revealed several brain regions that exhibited significant interaction effects of age and condition. For alpha, this included the right early visual cortex (Fig. 3; $F(1, 148) = 10.16$, $p < 0.005$, $k = 17$), left perisylvian cortex ($F(1, 148) = 9.49$, $p < 0.005$, $k = 27$), right inferior parietal ($F(1, 148) = 10.09$, $p < 0.005$, $k = 15$), and left anterior cingulate ($F(1, 148) = 8.51$, $p < 0.005$, $k = 10$). Likewise, neural oscillatory responses in the beta range showed a significant interaction effect of age and condition in the left supramarginal (Fig. 4; $F(1, 146) = 10.10$, $p < 0.005$, $k = 78$). With the exception of the right early visual cortex, each of these regions exhibited stronger oscillatory responses (i.e., greater ERD) as age increased, with the slopes being steeper in the related compared to the unrelated condition in the left perisylvian, left anterior cingulate, and left supramarginal, and the opposite pattern being observed in the right inferior parietal (i.e., unrelated steeper than related). Scatterplots showing these patterns for each region are provided in Supplementary Fig. S2.

Next, we investigated the main effects of age alone, controlling for condition. The alpha maps showed main effects of age across an extended region, with the main peak in the right superior parietal (Fig. 5; $F(1, 148) = 65.77$, $p < 0.005$, corrected). In the beta maps, there were also significant main effects of age extending across most of the cortex, with main peaks in the left superior frontal (Fig. 5; $F(1, 146) = 64.34$, $p < 0.005$, corrected) and right middle cingulate ($F(1, 146) = 69.74$, $p < 0.005$, corrected). For each of these peaks, oscillatory responses increased with age (i.e., stronger ERD with increasing age). Beyond these main peaks, there were several subpeaks in each map, including alpha subpeaks in bilateral inferior frontal cortices, left inferior parietal, and right posterior temporal, as well as beta subpeaks in the right inferior frontal and right sensorimotor cortices ($p < 0.005$, corrected). These are shown in Fig. S3 of the supplemental materials.

Finally, we investigated the main effects of condition alone controlling for age. Neural responses in the alpha range showed significant conditional differences that extended broadly, with main peaks in the right parieto-occipital (Fig. 6; $F(1, 149) = 21.35$, $p < 0.005$, corrected), left MTG ($F(1, 149) = 69.90$, $p < 0.005$, corrected), left medial parietal ($F(1, 149) = 16.89$, $p < 0.005$, corrected), right hippocampus ($F(1, 149) = 54.77$, $p < 0.005$, corrected), and left temporoparietal junction (TPJ; $F(1, 149) = 55.25$, $p < 0.005$, corrected), such that alpha oscillations were stronger (i.e., greater ERD) during the related compared to the unrelated condition. In addition, there were also significant subpeaks across the right temporal cortices and the left inferior frontal gyrus ($p < 0.005$, corrected; Fig. S3 in the Supplementary materials). Likewise, stronger beta oscillations (i.e., greater ERD) during the related relative to the unrelated condition were found across an extended region of the cortex, with main peaks in the left MTG (Fig. 7; $F(1, 147) = 72.89$, $p < 0.005$, corrected), left TPJ ($F(1, 147) = 70.42$, $p < 0.005$, corrected), right angular gyrus ($F(1, 147) = 26.35$, $p < 0.005$, corrected), left supramarginal ($F(1, 147) = 67.24$, $p < 0.005$, corrected), and right MTG ($F(1, 147) = 19.78$, $p < 0.005$, corrected). In contrast, beta oscillations in the right IFG showed the opposite pattern, with stronger responses (i.e., stronger ERD) during the unrelated compared to the related condition (Fig. 7; $F(1, 147) = 29.13$, $p < 0.005$, corrected). Finally, there were also significant beta subpeaks in the right temporal cortices and the right inferior frontal gyrus ($p < 0.005$, corrected; Fig. S3), with the effects in both subpeaks matching their neighboring main peaks.

Mediation model using cognitive assessment

Finally, given our results and that of others that semantic processing remains robust with healthy aging, we ran an exploratory analysis to identify whether this effect was mediated by oscillatory changes with aging. Participants completed cognitive assessments of verbal fluency, including the COWAT F-A-S ($M = 42.95$, $SD = 11.79$) and Animals ($M = 22.93$, $SD = 5.41$). As described in Section “Cognitive Assessment”, raw scores were first z-scored across the sample per assessment and then averaged together ($M = 0.01$,

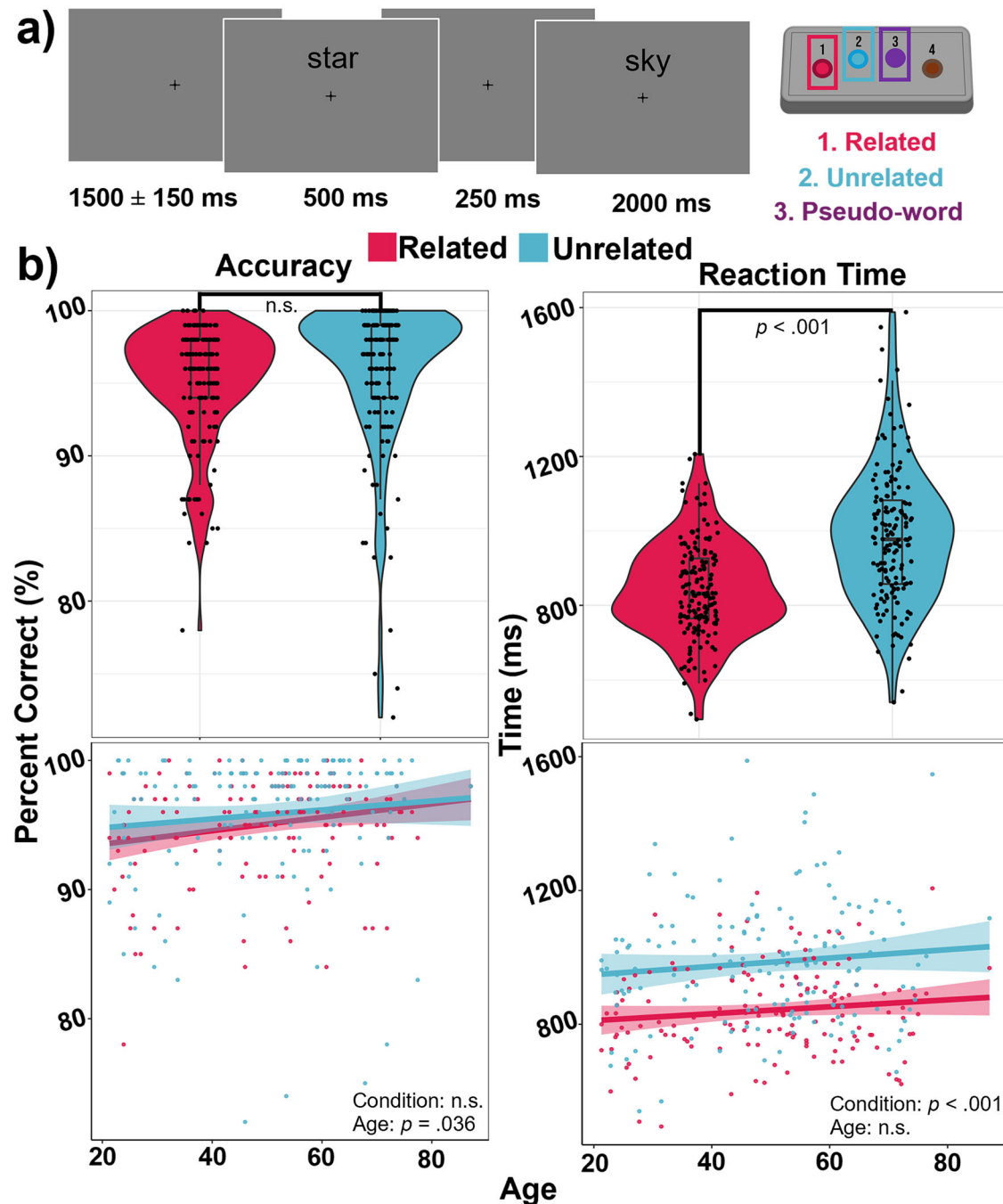


Fig. 1 | Semantic relatedness judgement paradigm and behavioral performance. **a** Each trial started with the presentation of a central fixation cross for 1500 (± 150) ms followed by the appearance of a prime word above the fixation cross for 500 ms, which then disappeared leaving only the fixation cross for 250 ms. Finally, a second (target) word appeared above the fixation cross for 2000 ms and participants

were instructed to respond with a button press as to whether the target word was related (right index) or unrelated (right middle) to the prime or was a pseudoword (right ring finger). **b** Accuracy (left) did not differ by condition but did differ with age ($p = 0.036$), whereas reaction time (right) differed by condition ($p < 0.001$) but not by age.

$SD = 0.89$) as a measure of verbal fluency, unadjusted for age. Mediation analyses (see Section “Statistical Analyses”) were run using a structural equation modeling framework to directly test indirect effects³⁶. A separate model using the difference score (i.e., unrelated—related) for each of the five significant age-by-condition interaction peaks assessed for a mediating relationship between age and verbal fluency. Our findings indicated a significant suppression effect of conditional alpha oscillatory differences in the left perisylvian cortex on the relationship between age and verbal fluency (Fig. 8; Average Causal Mediated Effect [ACME] = 0.003, $p = 0.014$, 95% CI [0.0007, 0.01]; see Table S2 for a correlation table including all variables used in mediation models), and a significant direct effect of age on verbal fluency

(Average Direct Effect [ADE] = -0.019 , $p < 0.001$, 95% CI [-0.028 , -0.01]). These effects were such that older age was associated with stronger conditional differences in alpha oscillatory activity in the left perisylvian cortex and worse verbal fluency scores. However, conditional differences in the left perisylvian cortex suppressed the effect of age on verbal fluency, such that larger conditional alpha differences in the left perisylvian were associated with preserved verbal fluency. In other words, larger conditional alpha differences in the left perisylvian significantly weakened the relationship between older age and worse verbal fluency scores. For all other peaks detected in the whole-brain LMEs for alpha and beta, only the direct effect of age on verbal fluency was significant (alpha right early visual cortex:

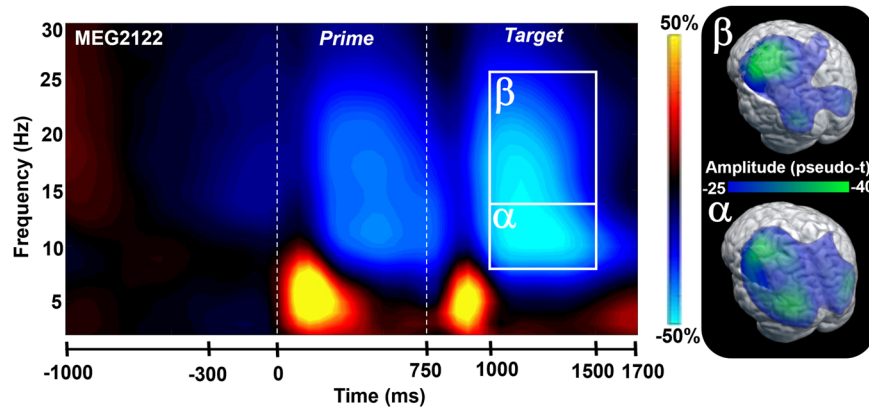


Fig. 2 | Sensor-level analyses of neural oscillatory activity. (left): MEG time-frequency spectrogram from the medial occipito-parietal area with time (ms) on the x-axis and frequency (Hz) on the y-axis. The onset of the prime word was 0 ms and the onset of the target word was 750 ms. Power is shown in percentage change units relative to the baseline period (−1000 to −300 ms). Data has been averaged across all trials and participants. We observed significant alpha (8–14 Hz) and beta (14–26 Hz) oscillations from 1000–1500 ms after prime onset ($p < 0.001$, corrected).

The white boxes denote these time-frequency windows, which were used for the beamformer imaging analyses. (right): After imaging each significant time-frequency window with a beamformer, grand averages were computed across all participants and conditions. The sustained alpha (bottom) and beta (top) oscillatory responses extended across a large region encompassing parietal, temporal, and occipital cortices, which were largely lateralized to the left hemisphere.

ADE = −0.016, $p < 0.001$, 95% CI [−0.03, −0.01]; alpha right inferior parietal: ADE = −0.015, $p = 0.004$, 95% CI [−0.03, −0.01]; alpha left anterior cingulate: ADE = −0.017, $p = 0.002$, 95% CI [−0.03, −0.01]; beta left supramarginal: ADE = −0.018, $p = 0.002$, 95% CI [−0.03, −0.01]. Finally, while this was an exploratory analysis, all findings remained at a FDR corrected level of $p = 0.05$.

Discussion

In the current study, we examined how aging affects the neural oscillatory dynamics underlying semantic processing in a large sample of 21–87 year-old healthy adults. Specifically, we sought to understand how judgments of semantic relatedness and the underlying oscillatory dynamics change with age. We found a sustained decrease in power relative to baseline (i.e., ERD) in both alpha (8–14 Hz) and beta (14–26 Hz) starting 250 ms after onset of the to-be-judged target word, which was sustained for about 500 ms. Whole-brain LME models focused on the interaction of age and task condition indicated stronger alpha and beta oscillations (i.e., greater ERD) with increasing age and/or in the related compared to the unrelated condition across a collection of brain regions. Specifically, alpha responses in the left perisylvian cortex and anterior cingulate and beta responses in the left supramarginal gyrus became stronger with increasing age (i.e., greater ERD) and the age-related slopes were steeper in the related relative to unrelated condition. Alpha responses also became stronger with increasing age (i.e., greater ERD) in the right inferior parietal, but in this region the slope was steeper for unrelated compared to related words. Conversely, alpha responses became weaker with age in the early right visual cortex, and this decline was steeper for related words. Whole-brain LME models also revealed multiple neural responses impacted by age alone, such that there were stronger alpha and beta oscillations (i.e., stronger ERD) as age increased in the right superior parietal (alpha) and the left superior frontal and right middle cingulate (beta). Whole-brain LME models also revealed significant conditional differences in alpha and beta bilaterally, with nearly all activity being stronger (i.e. greater ERD) in the semantically related relative to the unrelated condition. The only exception was for beta in the right IFG, where stronger oscillatory activity (i.e., stronger ERD) was found in the unrelated condition. Further analysis using the peak activity from our age-by-condition LME models revealed a significant suppression effect of conditional differences in left perisylvian alpha activity on the relationship between age and verbal fluency. Specifically, older age was associated with worse verbal fluency, but larger conditional differences in left perisylvian alpha suppressed this effect, suggesting that modulation of alpha activity allows for higher verbal fluency scores despite the impact of age. Below, we

discuss the implications of these findings for understanding the neural correlates underlying verbal fluency and how neurophysiological activity changes with age.

Behaviorally, we found that semantic processing was largely preserved in healthy aging, as accuracy significantly increased with advancing age and reaction time did not statistically differ with age, but participants were faster during semantically related relative to unrelated trials. Regarding the aging effect, this is contrary to the results of a meta-analysis on semantic processing, which found that younger adults tended to outperform older adults in the majority of studies; however, in many of the included studies the effect sizes were small and the groups did not statistically differ²⁶. Further, in six of the 29 studies examined for behavioral differences, the older adults outperformed the younger adults²⁶. Regarding the faster reaction time during related compared to unrelated trials, this of course would be expected and reflects the well-known semantic priming effect^{37–45}.

Regarding the neural data, our most interesting findings were that multiple brain regions exhibited significant oscillatory changes as a function of age, while others showed age-by-condition interactions. Specifically, age alone impacted alpha and beta oscillations across an extended area of the cortex, with alpha peaking in the right superior parietal and beta responses peaking in the left superior frontal and right middle cingulate. Across all three areas, oscillatory activity became much stronger (i.e., stronger ERD) with increasing age. Such stronger neural responses with increasing age were also observed across a collection of subpeaks in these extended clusters, including areas of the bilateral inferior frontal cortices, left inferior parietal, and right posterior temporal in the alpha range, as well as right inferior frontal and sensorimotor cortices in the beta range. Prior research has shown that spontaneous alpha and beta activity during rest significantly increases across the lifespan in adults⁴⁶. Thus, the pattern of stronger oscillatory responses (i.e., stronger ERD) found in the current study may reflect that stronger responses are needed to overcome the elevated spontaneous activity that is observed with increasing age, with the peaks indicating areas that are most involved in semantic search processes that would be common across both conditions. This overall pattern extended into our age-by-condition interactions, as we generally found stronger alpha oscillations (i.e., greater ERD) with increasing age and this relationship was steeper during related compared to unrelated trials in the left perisylvian and left anterior cingulate. The same pattern was observed for beta oscillations in the left supramarginal (i.e., the strength of the ERD increased with age and the effect was stronger in the related condition). A similar effect was observed in the right inferior parietal, except that the significant increase in alpha ERD with age was steeper in the unrelated relative to the related

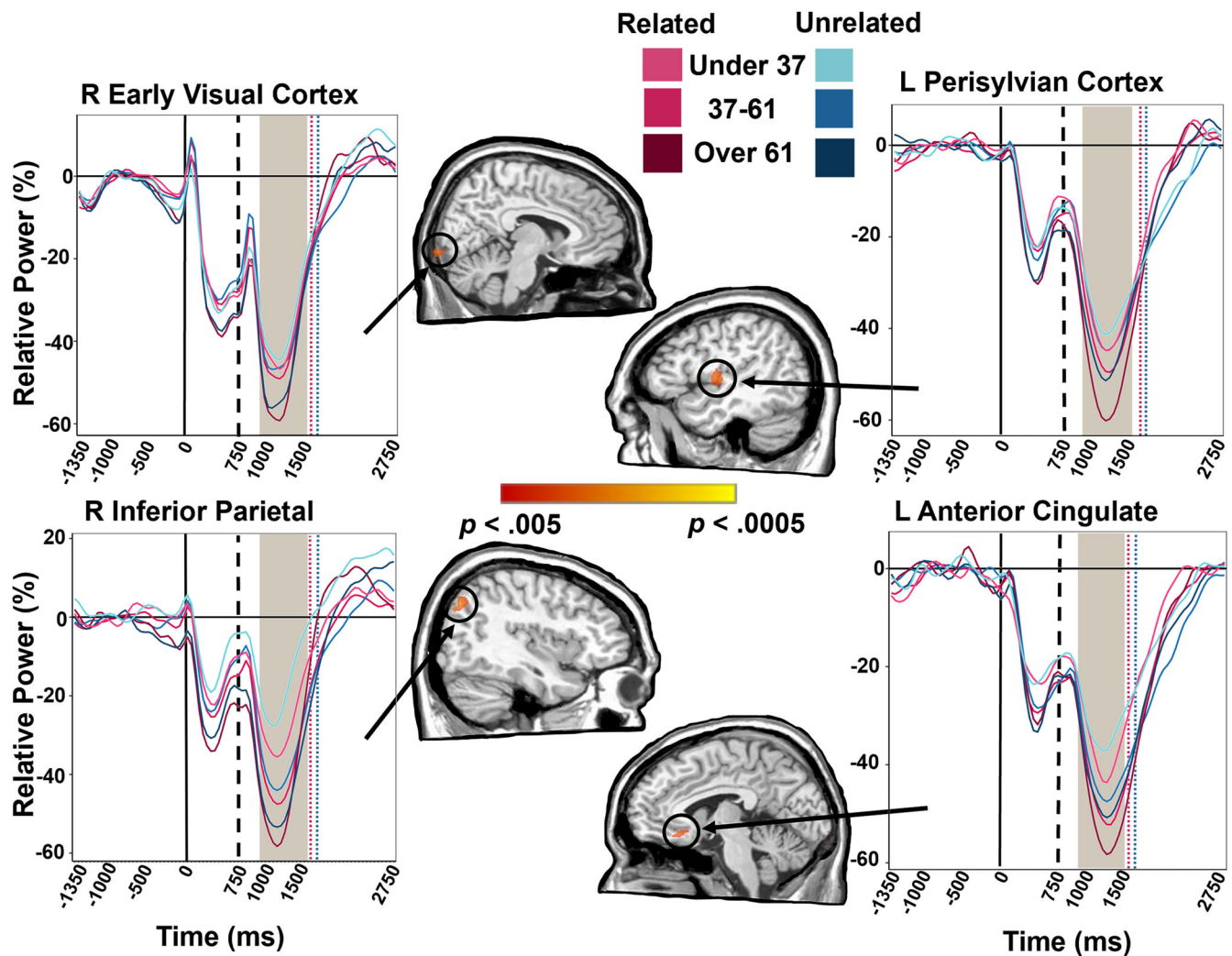


Fig. 3 | Interaction of age and condition on alpha oscillations. Whole-brain linear mixed-effects (LME) modeling revealed significant interaction effects of age and condition in several regions in the alpha band. These regions included the early right visual cortex, left perisylvian cortex, right inferior parietal, and left anterior cingulate. All maps have been thresholded at $p < 0.005$, corrected. Time series have been extracted from the peak voxel of each cluster and are shown by condition (related = pink, unrelated = blue) and age (younger = lighter). Age has been binned based on the 1st and 3rd quartile of our entire sample. In each plot, the solid black line indicates prime onset at 0 ms, the dashed black line indicates target onset at 750 ms, the pink (related) and blue (unrelated) dashed lines indicate the mean reaction time

per condition, and the time period used in the beamformer analysis (1000–1500 ms) is shaded. In the two left hemispheric regions, the interaction reflected a stronger oscillatory response (i.e., greater ERD) as age increased, which was steeper in the related compared to the unrelated condition ($p < 0.005$, corrected). In the right inferior parietal, the interaction also reflected stronger alpha oscillations (i.e., greater ERD) with increasing age, but the relationship was stronger in the unrelated compared to related condition. Finally, the opposite effect was found in the right early visual cortex, such that alpha oscillations became weaker with increasing age (i.e., less ERD) with the effect being stronger in the related condition.

condition. For these interactions, we propose that the additive conditional component reflects accentuated neural responses supporting task performance in the older adults. Altogether, these findings support our primary hypotheses about stronger responses in bilateral regions with increasing age, and corroborate key tenets of the CRUNCH model in which older adults generally have stronger neural responses in task-related brain regions compared to younger adults when performance levels are comparable²¹. Importantly, these results are also partially consistent with the HAROLD model and dedifferentiation hypothesis, as we observed increased oscillatory responses in right hemispheric regions with increasing age. To our knowledge, the current study is the first to extend these models to semantic processing in the context of neural oscillatory activity in healthy aging. Thus far, semantic processing studies have mainly focused on normative young adults using fMRI. The current work is the largest MEG study of semantic processing to date and uses an age range (21–87 years) that extends over the entire adult lifespan. Future studies should continue to examine semantic processing during the aging process and in neurological disease using

advanced neuroimaging techniques such as MEG to further elucidate the underlying neurophysiology of semantic processing. In particular, future studies could examine whether the effects observed here extend to evoked brain responses in the time domain.

Another important finding in the current study was that modulation of alpha activity in the left perisylvian cortex was associated with better verbal fluency, despite age. The left perisylvian cortex is a critical hub in the left-lateralized language network and has been implicated in language processing in the healthy brain^{47–50}, as well as primary progressive aphasia and dyslexia^{51,52}. Our current results extend these findings by showing that condition-wise alpha modulation is compensatory toward sustained verbal fluency performance with increasing age. In other words, those who exhibited the largest difference in left perisylvian alpha oscillations during the processing of semantically related relative to unrelated stimuli showed the smallest age-related decrements in verbal fluency. More broadly, our findings supported the view that verbal fluency generally decreases with age, which some have suggested may reflect a general slowing with age, as verbal fluency requires

Fig. 4 | Interaction of age and condition on beta oscillations. Whole-brain linear mixed-effects (LME) modeling revealed a significant age by condition interaction effect in the left supramarginal in the beta band, such that there were stronger beta oscillations (i.e., greater ERD) as age increased, and this response was stronger in the related compared to the unrelated condition ($p < 0.005$, corrected). The brain map has been thresholded at $p < 0.005$, corrected. Time series have been extracted from the peak voxel and are shown by condition (related = pink, unrelated = blue) and age (younger = lighter). Age is binned based on the 1st and 3rd quartile of our entire sample. In each plot, the solid black line indicates prime onset at 0 ms, the dashed black line indicates target onset at 750 ms, the pink (related) and blue (unrelated) dashed lines indicate the mean reaction time per condition, and the time period used in the beamformer analysis (1000–1500 ms) is shaded.

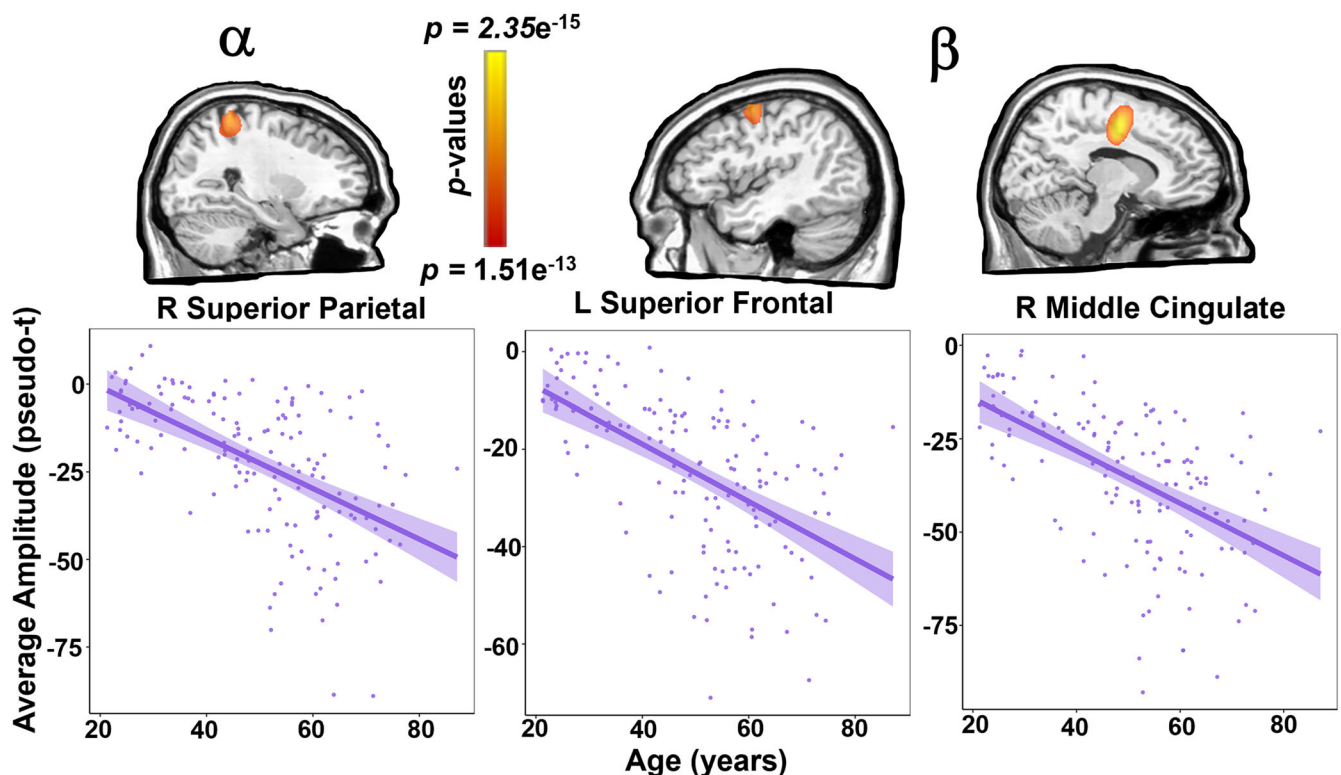
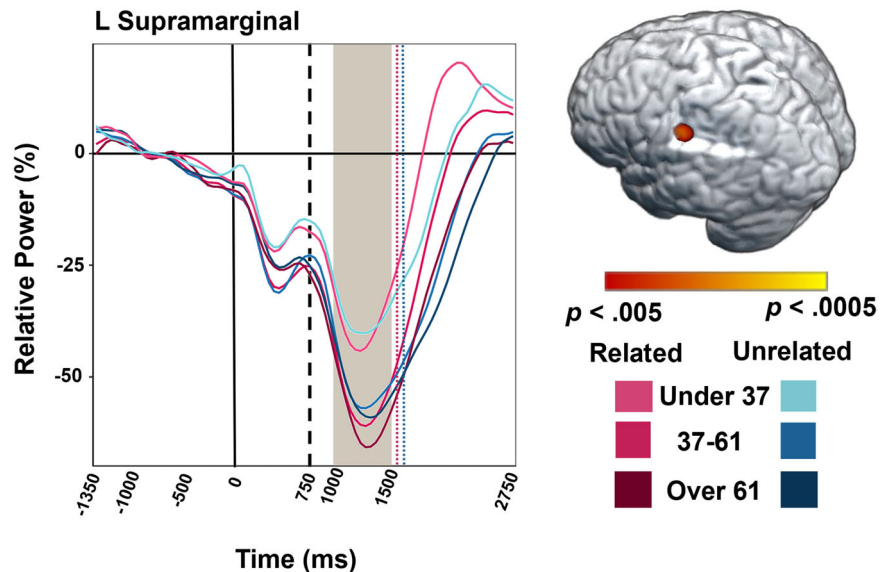


Fig. 5 | Alpha and beta oscillations increase with age. (top): Whole-brain linear mixed-effects models revealed significant main effects of age in the right superior parietal in the alpha band and in the left superior frontal and right middle cingulate in the beta band, such that there were stronger oscillatory responses (i.e., greater ERD) as age increased across related and unrelated conditions (all p values < 0.005 , corrected). Note that the brain maps are shown at a higher threshold to improve

visualization of the peak responses. Maps showing subpeaks that were also significant at the $p < 0.005$, corrected, threshold are provided in Fig. S3 within the supplemental materials. (bottom): A regression line representing the distribution of the average amplitude across conditions (y-axis) is plotted by age (x-axis) for each peak. The solid line indicates the line of best fit for the effect of age on amplitude; light purple shading around this line indicates the standard error.

the retrieval of words from memory^{53,54}. Importantly, multiple recent studies have shown that alpha oscillations can be modulated by transcranial electrical stimulation methods^{55–60}, which could suggest therapeutic applications targeting cortical alpha rhythms. However, results of this analysis should be interpreted with caution, as the analysis was exploratory. Future studies should aim to replicate these results and continue to examine the interaction of neural activity and language processing with age.

Finally, we also found conditional task differences extending across many brain regions. With the exception of beta activity in the right IFG, these effects reflected stronger alpha and beta oscillations (i.e., greater ERD) during semantically related relative to unrelated trials. Regions exhibiting such effects in the alpha range included the right parieto-occipital, left MTG, left parietal, right hippocampus, and left TPJ, while those exhibiting effects in the beta range included the bilateral MTG, left TPJ, right angular gyrus,

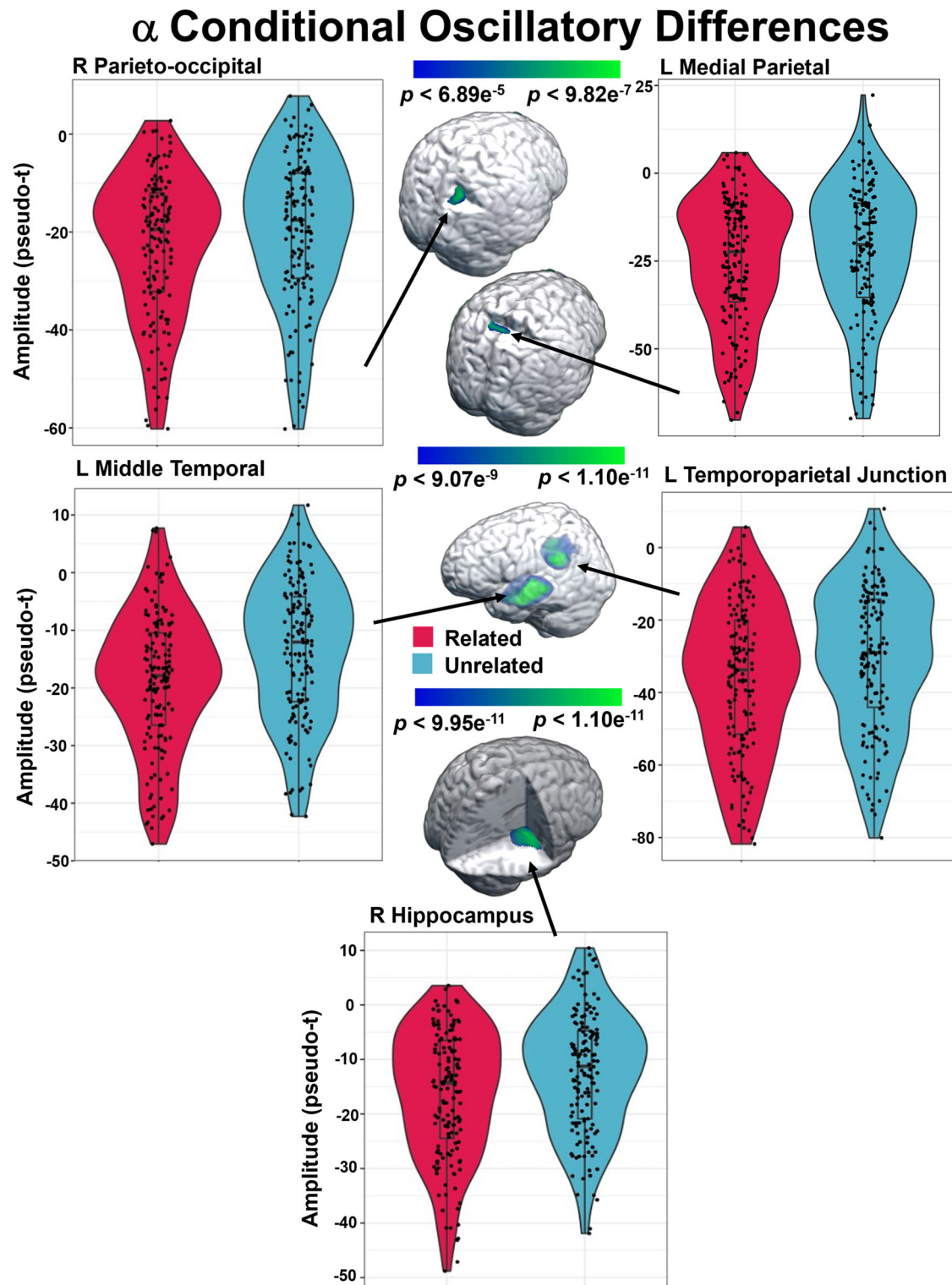


Fig. 6 | Conditional task differences in alpha oscillatory activity. Whole-brain linear mixed-effects (LME) modeling revealed significant conditional differences in alpha power in the right parieto-occipital, left middle temporal gyrus (MTG), left medial parietal, right hippocampus, and left temporoparietal junction (TPJ), such that there were stronger alpha oscillations (i.e., greater ERD) during the related compared to the unrelated condition (all p values < 0.005 , corrected). Violin plots show the distribution of the amplitude values at the peak voxel (y-axis) for each

significant cluster by condition (x-axis), with dots representing individual responses. Within each violin, box plots show the median value of the amplitude with vertical lines representing values below the 25th percentile or above the 75th percentile. Note that the brain maps are shown at different thresholds to improve visualization of the peak responses. Maps showing subpeaks that were also significant at the $p < 0.005$, corrected, threshold are provided in Fig. S3 within the supplemental materials and included regions in the right temporal and left inferior frontal cortices.

β Conditional Oscillatory Differences

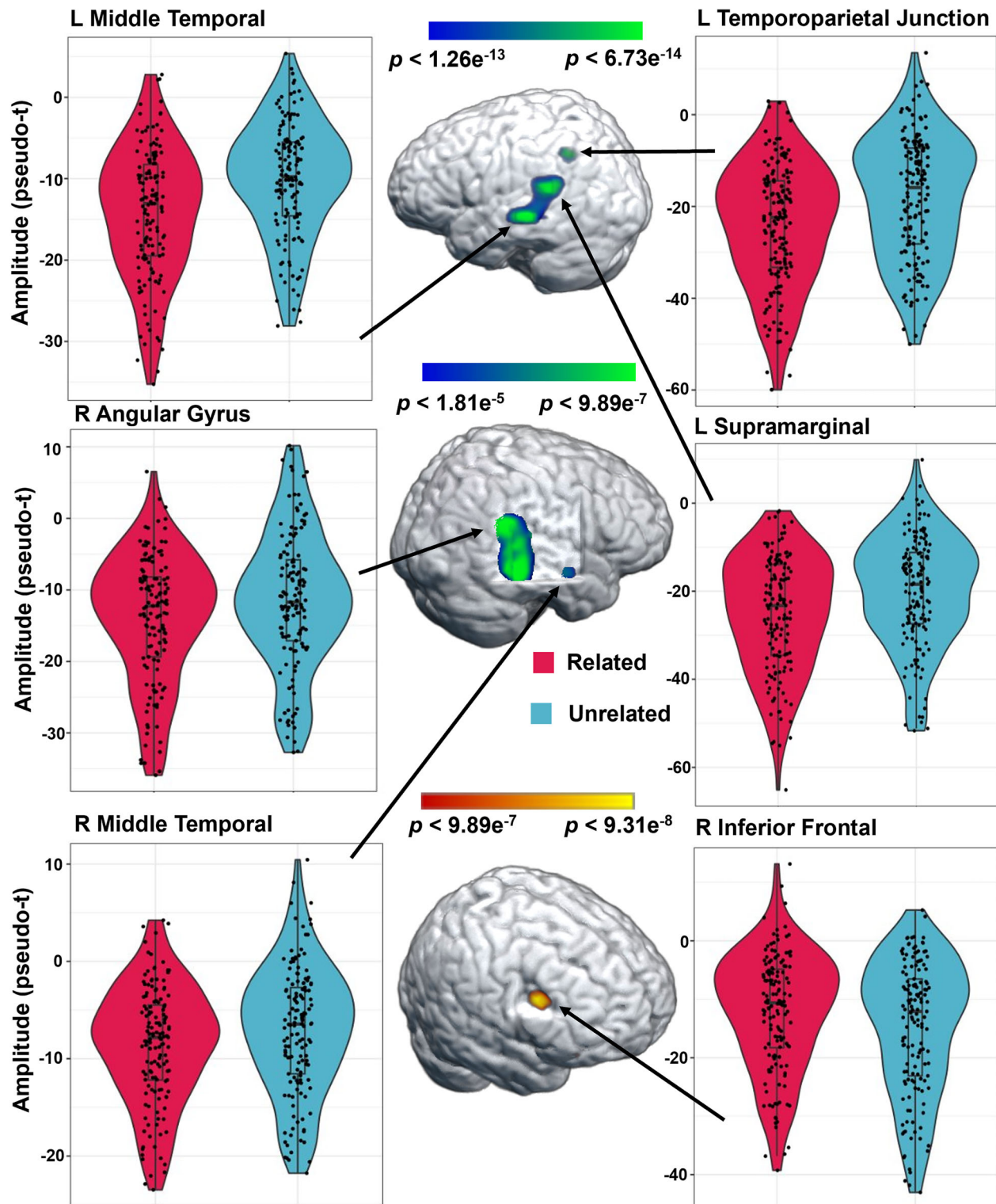


Fig. 7 | Conditional task differences in beta oscillatory activity. Whole-brain linear mixed-effects (LME) modeling revealed significant conditional differences in beta power in the left middle temporal gyrus (MTG), left temporoparietal junction (TPJ), right angular gyrus, left supramarginal, and right MTG, such that there were stronger beta oscillations (i.e., greater ERD) during the related compared to the unrelated condition (all p values < 0.005 , corrected). Additionally, the opposite pattern was observed in the right inferior frontal gyrus (IFG), with stronger beta oscillations during the unrelated condition ($p < 0.005$, corrected). Violin plots are

formatted similar to Fig. 6 and show the distribution of the amplitude values at the peak voxel (y-axis) plotted by condition (x-axis) for each significant cluster, with dots representing individual responses per condition. Note that the brain maps are shown at different thresholds to improve visualization of the peak responses. Maps showing subpeaks that were also significant at the $p < 0.005$, corrected, threshold are provided in Fig. S3 within the supplemental materials and included regions in the right temporal and right inferior frontal cortices, with directionality that matched their neighboring main peak.

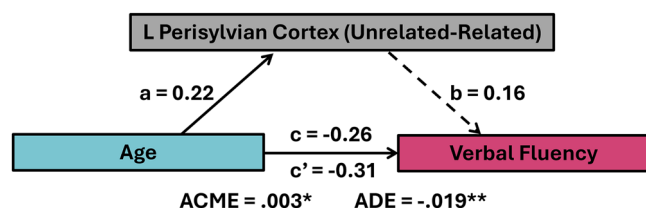


Fig. 8 | The effect of age on verbal fluency is suppressed by alpha oscillations in the left perisylvian cortex. A mediation analysis was conducted on each of the statistically significant interaction peaks found in our linear-mixed effects (LME) models. The difference score (unrelated-related) was used for each peak. Age significantly predicted the difference score for the left perisylvian cortex and scores on our verbal fluency assessments. While alpha activity in the left perisylvian cortex did not significantly predict verbal fluency scores, it significantly suppressed the effect of age on verbal fluency ($\beta = -0.31$, $p = 0.0002$; ACME = 0.003; ADE = -0.019), such that larger conditional differences in left perisylvian alpha were associated with preserved verbal fluency with increasing age. * $p < 0.05$ ** $p < 0.001$.

and left supramarginal. There were also alpha subpeaks in the left inferior frontal gyrus and right lateral temporal cortices, as well as a beta subpeak in the right posterior temporal that followed the same pattern. These findings are somewhat supportive of prior research using fMRI, which has pinpointed a well-established left-lateralized network associated with semantic processing, while right-lateralized activity has been associated with word memory and retrieval⁶¹. Specifically, past research has established a left-lateralized network supporting semantic processing and in the current study we extend these findings to show more bilateral neural recruitment, which may be indicative of slightly different language-related functions per hemisphere. In addition, a collection of electrophysiological studies have linked left-lateralized alpha and beta oscillations in the ventral and lateral frontotemporal region to semantic anomalies, including unexpected words occurring later in a sentence^{2-5,9}. These left-lateralized alpha and beta oscillations are generally stronger when viewing sentences as opposed to word lists, with neural responses first emerging in bilateral occipito-parietal, left frontal, and left temporal areas, with later processing in right frontal and parietal regions⁹. In previous work, we demonstrated stronger alpha oscillations (i.e., greater ERD) across a collection of left perisylvian regions during semantic compared to length judgments, with structural equation modeling showing that the strength of alpha oscillations in these areas accounted for 44% of the variance in reaction time differences between semantic and length judgments⁷. Thus, beyond being important for semantic processing, left-lateralized alpha may be critical to performance during semantic processing tasks⁷. Finally, recent work from our lab using the same semantic relatedness judgment task as the current study with a normative young adult population found similar results, with stronger increases in alpha and beta oscillations (i.e., greater ERD) occurring in the related vs the unrelated condition across many of these same regions⁶².

While this study contributes substantially to our understanding of the neurophysiology underlying semantic processing during aging, it is not without limitations. First, while our task was designed to use emotionally neutral words, participants could have perceived some words as being emotionally salient which may have biased some of our results. However, since this should have affected the conditions equally, we think it is unlikely that our results were differentially influenced by such emotional associations. Second, prior research has shown that sociodemographic and lifestyle factors can influence semantic processing. We did not control for these factors, as we were solely focused on the impact of healthy aging and purposefully enrolled participants who were representative of the local community. Nonetheless, we feel this is an important question and future work should examine the neural dynamics and circuitry underlying semantic processing with sociodemographic and lifestyle factors as covariates of interest. It is possible that these factors influence the specific brain regions involved in semantic judgments. Finally, our mediation analysis focused on verbal fluency, inclusive of both phonemic and semantic fluency. Prior

research has found slight differences in phonemic and semantic fluency⁶³, and future research should examine these separately as well as together.

In conclusion, the current study used advanced MEG imaging to quantify the neural oscillations serving semantic processing during healthy aging. In agreement with many prior studies, we found that semantic processing was fully preserved with aging, as behaviorally our older participants performed as well or better than younger participants. Interestingly, while behavior was preserved, we found widespread differences in the underlying neural dynamics, with neural oscillations in the alpha and beta ranges becoming stronger (i.e., greater ERD) with increasing age across many brain regions, with this effect being significantly accentuated in the semantically related compared to unrelated condition in key brain regions. In addition, such oscillations increased in strength (i.e., stronger ERD) with aging irrespective of condition across extended cortical regions, and a widespread, distributed group of brain regions exhibited stronger alpha and beta oscillations (i.e., stronger ERD) during semantically related relative to unrelated trials regardless of age. Finally, our mediation analyses suggested that left perisylvian alpha may play a critical role in the preservation of semantic processing with increasing age. These findings extend prior research and provide critical new insight on the role of oscillatory activity in semantic processing and its preservation during healthy aging.

Methods

Participants

One-hundred and sixty-three healthy adult participants were included in this study ($M_{\text{age}} = 49.64$ years, $SD_{\text{age}} = 15.12$, $\text{range}_{\text{age}} = 21-87$ years, $N_{\text{female}} = 82$; Table S1). Initial exclusionary criteria included any medical illness affecting CNS function, neurological or psychiatric disorder, history of head trauma, current substance misuse, and presence of any type of ferromagnetic implanted material. The study protocol was approved by the Boys Town National Research Hospital's Institutional Review Board and all ethical regulations relevant to human research participants were followed in accordance with the Declaration of Helsinki. Written and informed consent was obtained from all participants after a full description of the study was provided.

Experimental Paradigm

Participants performed a semantic relatedness judgement task during MEG recording (Fig. 1a). They were instructed to fixate on a crosshair presented in the center of the screen throughout the task. Each trial began with the presentation of a central fixation crosshair for 1500 ms (± 150 ms). Then, a prime word appeared at the top of the screen for 500 ms, followed by another fixation crosshair for 250 ms. Finally, a second (target) word appeared at the top of the screen for 2000 ms. Participants were instructed to respond based on whether the prime word was related semantically to the target word (right index finger), semantically unrelated (right middle finger), or a pseudoword (right ring finger). Each trial lasted 4250 ms (± 150 ms) and there was a total of 210 trials (i.e., 100 semantically related, 100 semantically unrelated, and 10 pseudowords) resulting in a total run-time of approximately 14.88 mins. All participants completed a brief practice session of the task prior to MEG recording to ensure adherence to task instructions. Related (e.g., star-sky) and unrelated (e.g., game-gorilla) prime-target pairs were presented pseudorandomly and were taken from the word list of the Semantic Priming Project⁶⁴. All words were restricted to 3–4 letters in length to prevent excessive eye movement and were balanced for length, frequency of use, part of speech, and number of orthographic neighbors across conditions. Words which could elicit strong emotions or require above-average education level were not included. Pseudo-word trials were included to help minimize mental sets and promote cognitive flexibility. They were not included in the MEG or behavioral analyses.

MEG data acquisition

Participants were seated in a non-magnetic chair within a two-layer VACOSHIELD magnetically-shielded room (Vacuumschmelze, Hanau, Germany). A MEGIN Neo MEG system (Helsinki, Finland) equipped with

306 sensors, including 204 planar gradiometers and 102 magnetometers, was used to sample neuromagnetic responses continuously at 1 kHz with an acquisition bandwidth of 0.1 – 330 Hz. Participants were monitored by a real-time audio-video feed from inside the shielded room throughout MEG data acquisition. Data from each participant were individually corrected for head movement and noise reduced using the signal space separation method with a temporal extension (correlation limit: 980; correlation window duration: 6 seconds; mainline frequency: 60 Hz)⁶⁵.

Structural MRI and MEG coregistration

Before MEG recording, five coils were attached to the participant's head and localized, together with the 3 fiducial points (i.e., nasion, left and right preauriculars) and scalp surface, with a 3D digitizer (Fastrak; Polhemus Navigator Sciences, Colchester, VT). Once the participant was positioned for MEG recording, an electric current with a unique frequency label (e.g., 322 Hz) was fed to each of the five coils. This induced a measurable magnetic field and allowed each coil to be localized in reference to the sensors throughout the recording session. Since coil locations were also known in head coordinates, all MEG measurements could be transformed into a common coordinate system. With this coordinate system, each participant's MEG data were co-registered with their structural T1-weighted MRI data prior to source space analyses using BESA MRI (Version 3.0; BESA GmbH, Gräfelfing, Germany). All structural MRI data were acquired on a 3 T Siemens Prisma magnet using a 32-channel head coil with the following parameters: TR: 2400 ms; TE: 2.05 ms; field of view: 256 mm; matrix: 256 × 256; slice thickness: 1 mm with no gap; voxel size: 1.0 × 1.0 × 1.0 mm; acquisition plane: sagittal; flip angle: 8 degrees. These anatomical images were aligned parallel to the anterior and posterior commissures and transformed into standardized space. Following source analysis (i.e., beamforming), each participant's 4.0 × 4.0 × 4.0 mm MEG functional images were also transformed into standardized space using the transform that was previously applied to the structural MRI volume and spatially resampled.

MEG time-frequency transformation and statistics

MEG preprocessing and imaging were completed using the Brain Electrical Source Analysis (BESA V7.1) software. Cardiac and eye-blink artifacts were manually removed from the MEG data prior to statistical analysis using signal-space projection (SSP)⁶⁶, which was accounted for during source reconstruction. The continuous magnetic time series was divided into epochs of 4100 ms duration, with the prime word onset being defined as 0 ms and the baseline being defined as -1000 to -300 ms prior to prime onset. Epochs containing artifacts were rejected based on individual amplitude and gradient thresholds. The average amplitude threshold was 1164.29 ($SD = 329.29$) fT/cm and the average gradient threshold was 420.52 ($SD = 199.78$) fT/(cm*ms) across all participants and conditions. Further, only trials where participants responded correctly were used for analysis. Note that we used individually determined thresholds based on the signal distribution for both amplitude and gradient to account for variance across participants in head size and distance between the brain and the MEG sensor array, which greatly affects raw MEG signal amplitudes. On average, 87.13 ($SD = 5.29$) related and 87.39 ($SD = 6.46$) unrelated trials remained after artifact rejection and were used in subsequent analyses. Importantly, the number of trials did not differ between the related and unrelated conditions ($p > 0.05$) and were not correlated with age ($p_{\text{related}} > 0.05$, $p_{\text{unrelated}} > 0.05$).

Artifact-free epochs were transformed into the time-frequency domain from 2 to 30 Hz using complex demodulation with a resolution of 1 Hz and 50 ms. The resulting spectral power estimations per sensor were averaged over trials to generate time-frequency plots of mean spectral density⁶⁷. These sensor-level data were then normalized per time-frequency bin using the respective bin's baseline power, which was calculated as the mean power during the -1000 ms to -300 ms time period. The specific time-frequency windows used for imaging were determined by statistical analysis of the sensor-level spectrograms across all participants and all trials, restricted to the entire array of gradiometers. To reduce the risk of false positive results

while maintaining reasonable sensitivity, a two-stage procedure was followed to control for Type I error. In the first stage, paired-samples *t*-tests against baseline were conducted on each data point and the output spectrogram of *t*-values was thresholded at $p < 0.05$ to define time-frequency bins containing potentially significant oscillatory deviations relative to baseline across all participants and both conditions. In the second stage, time-frequency bins that survived the threshold were clustered with temporally, spectrally, and/or spatially neighboring bins with *t*-values that were also above the ($p < 0.05$) threshold, and a cluster value was derived by summing all of the *t*-values of all data points in the cluster. Nonparametric permutation testing was then used to derive a distribution of cluster-values, and the significance level of the observed clusters (from stage 1) were tested directly using this distribution^{68,69}. For each comparison, 10,000 permutations were computed to build a distribution of cluster values. Based on these analyses, only the time-frequency windows that contained significant oscillatory events ($p < 0.001$) across all trials and participants were subjected to imaging, and these source images were then used to test our hypothesized effects. Further methodological details are available⁷⁰.

MEG source imaging and statistics

Cortical responses were imaged using dynamic imaging of coherent sources (DICS)⁷¹, a time-frequency-resolved extension of the linearly constrained minimum variance (LCMV) beamformer⁷², which applies spatial filters to time-frequency sensor data to calculate voxel-wise source power for the entire brain volume. The single images are derived from the cross spectral densities of all combinations of MEG gradiometers averaged over the time-frequency range of interest, and the solution of the forward problem for each location on a grid specified by input voxel space. Such images are typically referred to as pseudo-*t* maps, with units (pseudo-*t*) that reflect noise-normalized power differences (i.e., active vs. passive) per voxel. Following convention, we computed noise-normalized source power per voxel (4.0 × 4.0 × 4.0 mm) in each participant using active (i.e., task) and passive (i.e., baseline) periods of equal duration and bandwidth⁷³. The resulting 3D maps of brain activity were averaged across all participants and both conditions to assess the anatomical basis of the significant oscillatory responses identified through the sensor-level analysis and used in whole-brain statistical analyses to assess our primary hypotheses.

Cognitive assessment

Participants completed phonemic (Controlled Oral Word Association Test [COWAT], letters F-A-S) and semantic (Animals) tasks outside of the scanner to measure verbal fluency⁷⁴. Scores were adjusted for age and education level and averaged together to create a single score to assess verbal fluency performance. Since age was a covariate of interest in the analyses, demographically uncorrected scores were used for analyses with neural data. For the neurobehavioral analyses, raw scores from the COWAT F-A-S and Animals tasks were transformed into *z*-scores across the sample and then averaged together to create a metric of verbal fluency.

Statistical analyses

To evaluate the interaction of age and condition on neural oscillatory responses, whole-brain linear mixed-effects (LME) models were calculated for alpha and beta separately with age (continuous between-subjects factor) and task condition (within-subjects factor with 2 levels; i.e., semantically related and unrelated) using custom functions in MATLAB. In addition, whole-brain LMEs were calculated using age and condition as main effects without an interaction term to evaluate the impacts of age and condition, controlling for the other, on the voxel-wise whole-brain maps. On the resulting images, we employed an alpha threshold of $p < 0.005$ and cluster-extent threshold of $k > 4$ voxels (i.e., 256 mm³), although significant clusters were generally much larger. Finally, an exploratory mediation analysis was conducted to better understand the effect of age on verbal fluency using the regional peaks identified through our age-by-condition interaction LME models. Specifically, we computed four mediation models in the alpha band and one in the beta band, corresponding to the age-by-condition interaction

peaks. For these analyses, we used conditional difference scores (unrelated-related) for each significant age-by-condition peak to determine the mediating effect of brain activity on the relationship between age and verbal fluency (see Section “Cognitive Assessment”). Specifically, the *mediation* package in R was used to test the indirect and direct effects of peak oscillatory activity on verbal fluency using bias-corrected bootstrapping procedures with 1000 samples³⁶. While these mediation analyses were exploratory, significant models remained significant at $p = 0.05$ following correction using the false discovery rate (FDR) method.

Data availability

All data are publicly available via the Collaborative Informatics and Neuroimaging Suite (COINS; <https://coins.trendscenter.org/>) upon request.

Received: 9 May 2025; Accepted: 25 July 2025;

Published online: 06 August 2025

References

- Hoffman, P., Jefferies, E. & Lambon Ralph, M. A. Ventrolateral prefrontal cortex plays an executive regulation role in comprehension of abstract words: convergent neuropsychological and repetitive TMS evidence. *J. Neurosci.* **30**, 15450–15456 (2010).
- Kielar, A., Panamsky, L., Links, K. A. & Meltzer, J. A. Localization of electrophysiological responses to semantic and syntactic anomalies in language comprehension with MEG. *NeuroImage* **105**, 507–524 (2015).
- Kielar, A., Deschamps, T., Jokel, R. & Meltzer, J. A. Functional reorganization of language networks for semantics and syntax in chronic stroke: evidence from MEG. *Hum. Brain Mapp.* **37**, 2869–2893 (2016).
- Kielar, A., Deschamps, T., Jokel, R. & Meltzer, J. A. Abnormal language-related oscillatory responses in primary progressive aphasia. *NeuroImage Clin.* **18**, 560–574 (2018).
- Mollo, G., Jefferies, E., Cornelissen, P. & Gennari, S. P. Context-dependent lexical ambiguity resolution: MEG evidence for the time-course of activity in left inferior frontal gyrus and posterior middle temporal gyrus. *Brain Lang.* **177–178**, 23–36 (2018).
- Thompson-Schill, S. L., D’Esposito, M., Aguirre, G. K. & Farah, M. J. Role of left inferior prefrontal cortex in retrieval of semantic knowledge: a reevaluation. *Proc. Natl. Acad. Sci. USA* **94**, 14792–14797 (1997).
- Rempe, M. P. et al. Alpha oscillations in left perisylvian cortices support semantic processing and predict performance. *Cereb. Cortex* **32**, 5376–5387 (2022).
- Marinkovic, K. et al. Spatiotemporal dynamics of modality-specific and supramodal word processing. *Neuron* **38**, 487–497 (2003).
- Lam, N. H. L., Schoffelen, J.-M., Uddén, J., Hultén, A. & Hagoort, P. Neural activity during sentence processing as reflected in theta, alpha, beta, and gamma oscillations. *NeuroImage* **142**, 43–54 (2016).
- Binney, R. J., Embleton, K. V., Jefferies, E., Parker, G. J. M. & Lambon Ralph, M. A. The ventral and inferolateral aspects of the anterior temporal lobe are crucial in semantic memory: evidence from a novel direct comparison of distortion-corrected fMRI, rTMS, and semantic dementia. *Cereb. Cortex* **20**, 2728–2738 (2010).
- Davey, J. et al. Automatic and controlled semantic retrieval: tms reveals distinct contributions of posterior middle temporal gyrus and angular gyrus. *J. Neurosci.* **35**, 15230–15239 (2015).
- Hoffman, P., Binney, R. J. & Lambon Ralph, M. A. Differing contributions of inferior prefrontal and anterior temporal cortex to concrete and abstract conceptual knowledge. *Cortex* **63**, 250–266 (2015).
- Jefferies, E. The neural basis of semantic cognition: Converging evidence from neuropsychology, neuroimaging and TMS. *Cortex* **49**, 611–625 (2013).
- McDonald, C. R. et al. Multimodal imaging of repetition priming: Using fMRI, MEG, and intracranial EEG to reveal spatiotemporal profiles of word processing. *NeuroImage* **53**, 707–717 (2010).
- Noonan, K. A., Jefferies, E., Corbett, F. & Lambon Ralph, M. A. Elucidating the nature of deregulated semantic cognition in semantic aphasia: evidence for the roles of prefrontal and temporo-parietal cortices. *J. Cogn. Neurosci.* **22**, 1597–1613 (2010).
- Noonan, K. A., Jefferies, E., Visser, M. & Lambon Ralph, M. A. Going beyond inferior prefrontal involvement in semantic control: evidence for the additional contribution of dorsal angular gyrus and posterior middle temporal cortex. *J. Cogn. Neurosci.* **25**, 1824–1850 (2013).
- Thompson, H. E., Henshall, L. & Jefferies, E. The role of the right hemisphere in semantic control: A case-series comparison of right and left hemisphere stroke. *Neuropsychologia* **85**, 44–61 (2016).
- Schaeffer, K. U.S. centenarian population is projected to quadruple over the next 30 years. *Pew Res. Center*. <https://www.pewresearch.org/short-reads/2024/01/09/us-centenarian-population-is-projected-to-quadruple-over-the-next-30-years/> (2024).
- Cabeza, R. Hemispheric asymmetry reduction in older adults: the HAROLD model. *Psychol. Aging* **17**, 85–100 (2002).
- Koen, J. D. & Rugg, M. D. Neural dedifferentiation in the aging brain. *Trends Cogn. Sci.* **23**, 547–559 (2019).
- Reuter-Lorenz, P. A. & Cappell, K. A. Neurocognitive aging and the compensation hypothesis. *Curr. Dir. Psychol. Sci.* **17**, 177–182 (2008).
- Dennis, N. A. & Cabeza, R. Neuroimaging of healthy cognitive aging. In *The Handbook of Aging and Cognition* (Psychology Press, 2007).
- Grady, C. L. et al. Age-related changes in cortical blood flow activation during visual processing of faces and location. *J. Neurosci.* **14**, 1450–1462 (1994).
- Cabeza, R. et al. Cognitive neuroscience of healthy aging: maintenance, reserve, and compensation. *Nat. Rev. Neurosci.* **19**, 701–710 (2018).
- Grady, C. Trends in neurocognitive aging. *Nat. Rev. Neurosci.* **13**, 491–505 (2012).
- Hoffman, P. & Morcom, A. M. Age-related changes in the neural networks supporting semantic cognition: a meta-analysis of 47 functional neuroimaging studies. *Neurosci. Biobehav. Rev.* **84**, 134–150 (2018).
- Lacombe, J., Jolicoeur, P., Grimault, S., Pineault, J. & Joubert, S. Neural changes associated with semantic processing in healthy aging despite intact behavioral performance. *Brain Lang.* **149**, 118–127 (2015).
- Alves, M., Figueiredo, P. & Raposo, A. Semantic cognition in healthy ageing: neural signatures of representation and control mechanisms in naming typical and atypical objects. *Neuropsychologia* **184**, 108545 (2023).
- Martin, S., Williams, K. A., Saur, D. & Hartwigsen, G. Age-related reorganization of functional network architecture in semantic cognition. *Cereb. Cortex* **33**, 4886–4903 (2023).
- Klimesch, W., Schimke, H. & Schwaiger, J. Episodic and semantic memory: an analysis in the EEG theta and alpha band. *Electroencephalogr. Clin. Neurophysiol.* **91**, 428–441 (1994).
- Klimesch, W., Doppelmayr, M., Pachinger, T. & Russeger, H. Event-related desynchronization in the alpha band and the processing of semantic information. *Cogn. Brain Res.* **6**, 83–94 (1997).
- Maguire, M. J., Brier, M. R. & Ferree, T. C. EEG theta and alpha responses reveal qualitative differences in processing taxonomic versus thematic semantic relationships. *Brain Lang.* **114**, 16–25 (2010).
- Röhm, D., Klimesch, W., Haider, H. & Doppelmayr, M. The role of theta and alpha oscillations for language comprehension in the human electroencephalogram. *Neurosci. Lett.* **310**, 137–140 (2001).
- Rempe, M. P. et al. Hemisphere- and condition-specific alpha oscillations support semantic and spatial cognition in aging. *GeroScience*. <https://doi.org/10.1007/s11357-025-01651-4> (2025)

35. Rempe, M. P. et al. Hippocampal and cortical oscillatory dynamics reflect semantic processing and predict behavioural performance. *J. Physiol.* **603**, 3089–3106 (2025).
36. Preacher, K. J. & Hayes, A. F. Asymptotic and resampling strategies for assessing and comparing indirect effects in multiple mediator models. *Behav. Res. Methods* **40**, 879–891 (2008).
37. Brown, C. & Hagoort, P. The processing nature of the n400: evidence from masked priming. *J. Cogn. Neurosci.* **5**, 34–44 (1993).
38. Kutas, M. & Federmeier, K. D. Electrophysiology reveals semantic memory use in language comprehension. *Trends Cogn. Sci.* **4**, 463–470 (2000).
39. Kutas, M. & Federmeier, K. D. Thirty years and counting: finding meaning in the N400 component of the event related brain potential (ERP). *Annu. Rev. Psychol.* **62**, 621–647 (2011).
40. Kutas, M. & Hillyard, S. A. Reading senseless sentences: brain potentials reflect semantic incongruity. *Science* **207**, 203–205 (1980).
41. Lau, E. F., Phillips, C. & Poeppel, D. A cortical network for semantics: (de)constructing the N400. *Nat. Rev. Neurosci.* **9**, 920–933 (2008).
42. Lau, E. F., Weber, K., Gramfort, A., Hämäläinen, M. S. & Kuperberg, G. R. Spatiotemporal signatures of lexical–semantic prediction. *Cereb. Cortex* **26**, 1377–1387 (2016).
43. Lucas, M. Semantic priming without association: a meta-analytic review. *Psychon. Bull. Rev.* **7**, 618–630 (2000).
44. Nobre, A. C. & McCarthy, G. Language-related field potentials in the anterior-medial temporal lobe: II. Effects of word type and semantic priming. *J. Neurosci.* **15**, 1090–1098 (1995).
45. Plaut, D. C. & Booth, J. R. Individual and developmental differences in semantic priming: empirical and computational support for a single-mechanism account of lexical processing. *Psychol. Rev.* **107**, 786–823 (2000).
46. Rempe, M. P. et al. Spontaneous cortical dynamics from the first years to the golden years. *Proc. Natl. Acad. Sci. USA* **120**, e2212776120 (2023).
47. Heinrichs-Graham, E. & Wilson, T. W. Spatiotemporal oscillatory dynamics during the encoding and maintenance phases of a visual working memory task. *Cortex J. Devoted Study Nerv. Syst. Behav.* **69**, 121–130 (2015).
48. Wilson, T. W., Leuthold, A. C., Lewis, S. M., Georgopoulos, A. P. & Pardo, P. J. Cognitive dimensions of orthographic stimuli affect occipitotemporal dynamics. *Exp. Brain Res. Exp. Hirnforsch. Exp. Cereb.* **167**, 141–147 (2005).
49. Wilson, T. W., Leuthold, A. C., Lewis, S. M., Georgopoulos, A. P. & Pardo, P. J. The time and space of lexicality: a neuromagnetic view. *Exp. Brain Res. Exp. Hirnforsch. Exp. Cereb.* **162**, 1–13 (2005).
50. Wilson, T. W. et al. Reading in a deep orthography: neuromagnetic evidence for dual-mechanisms. *Exp. Brain Res. Exp. Hirnforsch. Exp. Cereb.* **180**, 247–262 (2007).
51. Rimrodt, S. L., Peterson, D. J., Denckla, M. B., Kaufmann, W. E. & Cutting, L. E. White matter microstructural differences linked to left perisylvian language network in children with dyslexia. *Cortex* **46**, 739–749 (2010).
52. Sonty, S. P. et al. Primary progressive aphasia: PPA and the language network. *Ann. Neurol.* **53**, 35–49 (2003).
53. Kempler, D., TENG, E., Dick, M., TAUSSIG, I. & DAVIS, D. The effects of age, education, and ethnicity on verbal fluency. *J. Int. Neuropsychol. Soc.* **4**, 531–538 (1998).
54. Nebes, R. D. & Madden, D. J. Different patterns of cognitive slowing produced by Alzheimer’s disease and normal aging. *Psychol. Aging* **3**, 102–104 (1988).
55. Arif, Y. et al. High-definition transcranial direct current stimulation of the occipital cortices induces polarity dependent effects within the brain regions serving attentional reorientation. *Hum. Brain Mapp.* **43**, 1930–1940 (2022).
56. Arif, Y. et al. High-definition transcranial direct current stimulation of the parietal cortices modulates the neural dynamics underlying verbal working memory. *Hum. Brain Mapp.* **45**, e70001 (2024).
57. Koshy, S. M. et al. Multielectrode transcranial electrical stimulation of the left and right prefrontal cortices differentially impacts verbal working memory neural circuitry. *Cereb. Cortex* **30**, 2389–2400 (2020).
58. McDermott, T. J. et al. tDCS modulates behavioral performance and the neural oscillatory dynamics serving visual selective attention. *Hum. Brain Mapp.* **40**, 729–740 (2019).
59. Wiesman, A. I. et al. Polarity-dependent modulation of multi-spectral neuronal activity by transcranial direct current stimulation. *Cortex* **108**, 222–233 (2018).
60. Wilson, T. W., McDermott, T. J., Mills, M. S., Coolidge, N. M. & Heinrichs-Graham, E. tDCS Modulates visual gamma oscillations and basal alpha activity in occipital cortices: evidence from MEG. *Cereb. Cortex* **28**, 1597–1609 (2018).
61. Ries, S. K., Dronkers, N. F. & Knight, R. T. Choosing words: :Left hemisphere, right hemisphere, or both? Perspective on the lateralization of word retrieval. *Ann. N.Y. Acad. Sci.* **1369**, 111–131 (2016).
62. Rempe, M. P. et al. Hippocampal and cortical oscillatory dynamics reflect semantic processing and predict behavioral performance. *J. Physiol.* **603**, 3089–3106 (2025).
63. Meinzer, M. et al. Neural signatures of semantic and phonemic fluency in young and old adults. *J. Cogn. Neurosci.* **21**, 2007–2018 (2009).
64. Hutchison, K. A. et al. The semantic priming project. *Behav. Res. Methods* **45**, 1099–1114 (2013).
65. Taulu, S. & Simola, J. Spatiotemporal signal space separation method for rejecting nearby interference in MEG measurements. *Phys. Med. Biol.* **51**, 1759–1768 (2006).
66. Uusitalo, M. A. & Ilmoniemi, R. J. Signal-space projection method for separating MEG or EEG into components. *Med. Biol. Eng. Comput.* **35**, 135–140 (1997).
67. Kovach, C. K. & Gander, P. E. The demodulated band transform. *J. Neurosci. Methods* **261**, 135–154 (2016).
68. Ernst, M. D. Permutation methods: a basis for exact inference. *Stat. Sci.* **19**, 676–685 (2004).
69. Maris, E. & Oostenveld, R. Nonparametric statistical testing of EEG- and MEG-data. *J. Neurosci. Methods* **164**, 177–190 (2007).
70. Wiesman, A. I. & Wilson, T. W. Attention modulates the gating of primary somatosensory oscillations. *NeuroImage* **211**, 116610 (2020).
71. Gross, J. et al. Dynamic imaging of coherent sources: studying neural interactions in the human brain. *Proc. Natl. Acad. Sci. USA* **98**, 694–699 (2001).
72. Van Veen, B. D., Van Drongelen, W., Yuchtman, M. & Suzuki, A. Localization of brain electrical activity via linearly constrained minimum variance spatial filtering. *IEEE Trans. Biomed. Eng.* **44**, 867–880 (1997).
73. Hillebrand, A., Singh, K. D., Holliday, I. E., Furlong, P. L. & Barnes, G. R. A new approach to neuroimaging with magnetoencephalography. *Hum. Brain Mapp.* **25**, 199–211 (2005).
74. Benton, A. L., Hamsher, D. S. K. & Sivan, A. B. *Controlled Oral Word Association Test (COWAT)*. <https://doi.org/10.1037/t10132-000> (1983).

Acknowledgements

This study was supported by the National Institutes of Health (NIH) through grants R01-DA056223 (TWW), R01-DA059877 (TWW), R01-DA059542 (TWW), R01-NS141729 (TWW), S10-OD028751 (TWW), P20-GM144641 (TWW), and F31-DA056296 (MS). The funders had no role in study design, data collection, analysis, decision to publish, or manuscript preparation. We want to thank the participants for volunteering to participate in the study and our staff and local collaborators for contributing to the work.

Author contributions

Conceptualization: T.W.W., E.H.G., and G.P.; Data Collection: G.M.G., R.J.G., H.J.O., A.J.P., and J.A.J.; Methodology and Software: M.P.R., C.M.E., C.C.C., N.M.P., Y.A., S.B., M.S., P.E.M.-W., E.H.G., and H.B.; Formal Analysis: M.C.H., M.P.R., Y.A., G.P., S.M.D., M.S., and E.L.K.; Writing-original draft: M.C.H., M.P.R., and T.W.W.; Reviewing and Editing: all authors; Supervision, Resources, and Funding Acquisition: T.W.W. All authors approved the final version for publication and can certify that no other individuals not listed as authors have made substantial contributions to the paper.

Competing interests

The authors declare no competing interests.

Additional information

Supplementary information The online version contains supplementary material available at <https://doi.org/10.1038/s41514-025-00263-8>.

Correspondence and requests for materials should be addressed to Tony W. Wilson.

Reprints and permissions information is available at <http://www.nature.com/reprints>

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Open Access This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by-nc-nd/4.0/>.

© The Author(s) 2025