The development of aperiodic neural activity in the human brain

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Abstract

The neurophysiological mechanisms supporting brain maturation are fundamental to attention and memory capacity across the lifespan. Human brain regions develop at different rates, with many regions developing into the third and fourth decades of life. Here, in this preregistered study (https://osf.io/gsru7), we analyzed intracranial EEG (iEEG) recordings from widespread brain regions in a large developmental cohort. Using task-based (i.e., attention to-be-remembered visual stimuli) and task-free (resting-state) data from 101 children and adults (5.93 – 54.00 years, 63 males; *n* electrodes = 5691), we mapped aperiodic ($1/f$-like) activity, a proxy of excitation:inhibition (E:I) balance with steeper slopes indexing inhibition and flatter slopes indexing excitation. We reveal that aperiodic slopes flatten with age into young adulthood in both association and sensorimotor cortices, challenging models of early sensorimotor development based on brain structure. In prefrontal cortex (PFC), attentional state modulated age effects, revealing steeper task-based than task-free slopes in adults and the opposite in children, consistent with the development of cognitive control. Age-related differences in task-based slopes also explained age-related gains in memory performance, linking the development of PFC cognitive control to the development of memory. Last, with additional structural imaging measures, we reveal that age-related differences in gray matter volume are differentially associated with aperiodic slopes in association and sensorimotor cortices. Our findings establish developmental trajectories of aperiodic activity in localized brain regions and illuminate the development of PFC inhibitory control during adolescence in the development of attention and memory.

Keywords: aperiodic $1/f$ activity; brain development; gray matter; memory; resting-state; intracranial electroencephalography.

Introduction

Human brain regions develop at different rates, with many regions developing into the third and fourth decades of life, followed by gradual declines in volume throughout adulthood (Bethlehem et al., 2022; Gogtay et al., 2004; Grydeland et al., 2019). Understanding the complexities of human brain development requires a comprehensive investigation into the intricate interplay between electrophysiological dynamics, brain structure, and behavior across the lifespan. Despite the importance of this endeavor to basic and translational neuroscience, research has been limited by a paucity of methods capable of studying human brain function with high spatial and temporal precision and focused on narrow age ranges. Further, non-oscillatory, aperiodic activity has yet to be fully characterized from a developmental perspective (cf. Favaro et al., 2023; Hill et al., 2022; Schaworonkow & Voytek, 2021; Tröndle et al., 2022). Consequently, the manifestation of age-related differences in aperiodic activity and their relation to brain structure and cognition remains unknown.

The aperiodic component of the electrophysiological power spectrum, characterized by its spectral slope and offset (Donoghue et al., 2020; Wen & Liu, 2016), is hypothesized to reflect the balance between excitation and inhibition (E:I) of neuronal populations (Ahmad et al., 2022; van Nifterick et al., 2023). A flatter slope and lower offset are posited to reflect increased excitatory neuronal population spiking (Manning et al., 2009; Miller et al., 2012). Converging computational (Donoghue et al., 2020; Gao et al., 2017) and pharmacological (Irene Gonzalez-Burgos et al., 2023; Molina et al., 2020; Salvatore et al., 2024; Wiest et al., 2023) work indicates that steeper slopes reflect increased inhibitory signaling (i.e., elevated GABAergic or reduced glutamatergic activity), while flatter slopes reflect dominance of excitatory signaling.

The balance of excitatory and inhibitory neural activity is a fundamental property of healthy brain function (Turrigiano & Nelson, 2004). Indeed, an optimal level of E:I balance is proposed to safeguard against hyper-synchronization, with E:I imbalance implicated in neurodevelopmental disorders, such as schizophrenia and autism (Earl et al., 2024; Pani et al., 2022; Shuffrey et al., 2022) and generalized learning disabilities (Fernandez & Garner, 2007). Studies using scalp electroencephalography (EEG) during passive (i.e., task-free) states have consistently demonstrated a flattening of the slope and a downward shift in the offset with advancing age throughout adulthood (Donoghue et al., 2020; Merkin et al., 2023; Voytek et al., 2015; Waschke et al., 2017). Such age-related flattening in task-free aperiodic activity predicts declines in memory performance (Voytek et al., 2015) and alterations in stimulus-related neurophysiological responses, such as inter-trial alpha phase clustering during visual spatial discrimination in the elderly (Tran et al., 2020). By contrast, flatter task-based aperiodic slopes are associated with enhanced memory and learning in healthy young adults (Cross et al., 2022; Lendner et al., 2023), hinting at a nuanced interplay between aperiodic activity, attentional state, and age. Thus, understanding the development of aperiodic activity and its modulation by attentional states with high spatial precision is necessary to understand brain development and cognitive function across the lifespan.

To date, developmental studies of aperiodic activity have relied on scalp EEG (Cellier et al., 2021; Favaro et al., 2023; Hill et al., 2022; Schaworonkow & Voytek, 2021). Yet, scalp-EEG is limited in spatial resolution and cannot reliably characterize regionally precise neurophysiological activity (Ofen et al., 2019). To overcome these limitations, we analyzed rare intracranial EEG (iEEG) data from an exceptionally large developmental cohort of neurosurgical patients aged 5 to 54 years undergoing invasive monitoring for seizure management. In contrast to noninvasive neuroimaging, iEEG provides both spatially localized information and the high temporal precision needed to examine neurophysiology (Johnson et al., 2020; Johnson & Knight, 2015; Parvizi & Kastner, 2018), and is thus an invaluable tool for investigating mechanisms of cognitive and brain maturation (Johnson, Tang, et al., 2018; Johnson, Yin, et al., 2022; Johnson & Knight, 2023; Ofen et al., 2019;

Yin et al., 2020, 2023). iEEG provides rich and novel measures of neurophysiology including low-frequency periodic and aperiodic activity, and high-frequency broadband activity reflecting neuronal population activity (Leszczyński et al., 2020; Nir et al., 2007; Ray et al., 2008; Rich & Wallis, 2017; Watson et al., 2018). Thus, iEEG enables unique discoveries of the neurophysiological mechanisms of cognitive and brain maturation in humans.

In this preregistered study (https://osf.io/gsru7), we sought to define regionally precise, brain-wide developmental trajectories of aperiodic activity in task-based and task-free states (Figures 1A, 1B). In addition to mapping aperiodic activity across development, we defined the relationship between regionally precise aperiodic activity and cortical structure (Figure 1C). Measures of regional gray matter volume (GMV) and electrophysiological activity show substantial overlap in relation to cognition, pathology (Hunt et al., 2016; Schölvinck et al., 2013), and age (Doval et al., 2024; Overbye et al., 2018; Sui et al., 2014; Whitford et al., 2007), which suggests that they may be jointly explained by shared factors, such as myelination and synaptogenesis. Thus, examining structure-function coupling can provide context to understand novel electrophysiological findings, such as iEEG measures of aperiodic activity by age, based on well-documented age-related variability in regional brain structure (Bethlehem et al., 2022; Gogtay et al., 2004; Groeschel et al., 2010). Based on reports of age-related variability in global scalp EEG-derived aperiodic activity (Cellier et al., 2021; Finley et al., 2022; Hill et al., 2022; Schaworonkow & Voytek, 2021; Thuwal et al., 2021) and in brain structure demonstrating that sensorimotor regions mature earlier than association regions (Gogtay et al., 2004; Grydeland et al., 2019; Hill et al., 2010; Sydnor et al., 2021), we hypothesized that: (a) in association cortices, the aperiodic slope flattens with age into young adulthood; (b) in sensorimotor cortices, the aperiodic slope flattens with age into adolescence; (c) attentional state (task-based vs. task-free) modulates age effects observed in (a) and (b), and; (d) age-related differences in aperiodic activity are modulated by regional GMV.

We first reveal a gradient in aperiodic activity across the brain, suggesting heightened inhibition in inferior lateral posterior regions and heightened excitation in superior medial frontal regions. We then establish developmental trajectories of aperiodic activity, revealing a flattening of the slope and a downward shift in the offset from childhood to young adulthood in both association and sensorimotor cortices, challenging our hypothesis that aperiodic activity stabilizes before young adulthood in sensorimotor cortices. We further reveal how attentional state modulates age effects in select regions including prefrontal cortex (PFC) and establish predictive links between task-based aperiodic activity in PFC and individual memory outcomes. We last uncover novel associations between cortical structure and function, highlighting how aperiodic slopes in PFC are modulated by age-related variability in GMV. Taken together, we offer critical insights into the intricate interplay between aperiodic neural activity, cortical structure, and behavior from childhood to middle age and illuminate the development of PFC inhibitory control during adolescence in the development of attention and memory.

Results

iEEG memory and brain volume measures generalize to healthy populations

One hundred and one neurosurgical patients participated (mean age = 19.25, range = 5.93 – 54.00 years; 63 males). Patients were selected based on above-chance behavioral performance on two visual memory recognition tasks (mean normalized accuracy = 0.54, SD = 0.25, range = 0.01 – 1.00; $\beta = 0.54$, SE = 0.02, $p = \leq .001$) and/or if there was a task-free recording available. Those with major lesions, prior surgical resections, noted developmental delays, or neuropsychological memory test scores <80 were considered ineligible. Analysis of recognition accuracy by age indicated a positive association ($\beta = 0.90$, SE = 0.16, $p = \leq .001$, $R^2 = .27$; see Figure 1C), indicating that iEEG patients exhibit the expected developmental trajectory of improved memory from age 5-30 years, consistent

with age-matched, healthy controls (Johnson, Yin, et al., 2022, 2022; Ofen et al., 2007, 2019). Analysis of global GMV by age indicated a negative association (β = -46.56, SE = 9.36, p = $\leq$.001, R^2 = .20; Figure 1C), further demonstrating that iEEG patients show the developmental trajectory of decreased GMV from age 5 to 54 years, consistent with well-documented decreases in GMV from childhood through adulthood in healthy individuals (Bethlehem et al., 2022; Gogtay et al., 2004; Groeschel et al., 2010; Wilke et al., 2007). These demonstrations provide converging evidence that the results of our iEEG analyses generalize to healthy populations (Hill et al., 2020; Johnson & Knight, 2023).

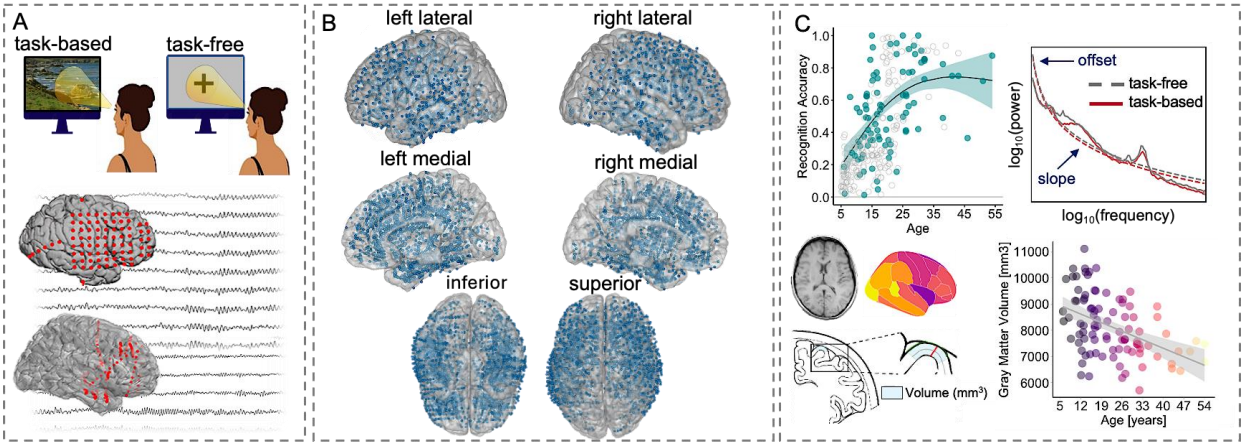

Figure 1. Design, channel coverage, and key variables. (A) Intracranial neurophysiological activity was recorded using electrocorticography (ECoG; middle) and stereoelectroencephalography (sEEG; bottom) during both task-based (top left) and task-free wake states (top right). **(B)** Seizure- and artifact-free intracranial channel placements (n = 5691) across all patients (n = 101) in MNI space. **(C)** Schematic of key dependent and independent variables. Top left: iEEG patients (teal; n = 81) show the expected developmental trajectory of improved memory recognition from ~5 – 30 years of age ($p \leq$.001) and fall in the range of age-matched, healthy controls (gray; n = 221). Top right: power spectral density plot illustrating the periodic (oscillatory) components over and above the aperiodic ($1/f$-like) component in task-free (dashed) and task-based (solid) conditions. The offset (i.e., y-intercept) and slope (exponent) make up the aperiodic component when power (y-axis) and frequency (x-axis) are represented in log-log space. Bottom left: TI MRI obtained for each patient, parcellation of cortical regions based on the Desikan-Killiany-Tourville atlas, and GMV estimation (adapted from Bethlehem et al., 2022). Bottom right: age-related differences in global GMV (mm^3) in our cohort, showing the expected developmental trajectory of decreased GMV from ~5 – 54 years of age ($p \leq$.001).

Aperiodic activity differs by brain region

Prior to testing hypotheses, we first characterized regional differences in aperiodic activity by implemented linear mixed-effects models, regressing region onto the aperiodic slope and offset while regressing out attentional state (task-based, task-free) and age, treating participants and nested channels as random intercepts (Johnson & Knight, 2023). Regions of interest (ROI) were defined based on the Desikan-Killiany-Tourville (DKT) atlas (Klein & Tourville, 2012). We revealed a gradient of steeper slopes in inferior lateral posterior regions to flatter slopes in superior medial frontal regions ($\chi2(19)$ = 1038.30, $p \leq$ 0.001; Figure 2A). The aperiodic offset exhibited a similar pattern ($\chi2(19)$ = 484.70, $p \leq$ 0.001; Figure 2B). These results extend previous reports of a posterior-to-anterior gradient in task-free E:I balance based on fMRI, i.e., Hurst exponent (Fotiadis et al., 2023) and magnetoencephalography (MEG) aperiodic component (Mahjoory et al., 2020). Our data demonstrate that aperiodic activity varies between localized brain regions to higher degree than previously reported.

Second, to characterize relationships between regional GMV and aperiodic activity (i.e., structure-function coupling), we implemented linear mixed-effects models, regressing region and GMV onto the aperiodic slope and offset while regressing out attentional state and age, treating

participants and nested channels as random intercepts (Johnson & Knight, 2023). We revealed regionally specific relationships between aperiodic activity and GMV (Figure 2C and Figure 2D). We observed a significant positive correlation with slope and GMV in rostral middle frontal gyrus (r = 0.27, p = 0.02, 95% CI = [0.04, 0.48]), and a significant negative correlation in inferior temporal cortex (r = -0.22, p = 0.03, 95% CI = [-0.40, -0.01]). The offset also correlated positively with GMV in lateral orbitofrontal cortex (r = 0.32 , p = 0.03, 95% CI = [0.03, 0.57]), superior temporal cortex (r = 0.30, p = 0.01, 95% CI = [0.06, 0.50]), and rostral (r = 0.36, p = 0.009, 95% CI = [0.09, 0.57]) and caudal (r = 0.24, p = 0.03, 95% CI = [0.02, 0.44]) middle frontal gyri, and correlated negatively with GMV in inferior temporal cortex (r = -0.25 , p = 0.03, 95% CI = [-0.45, -0.02]). These results reveal opposing structure-function coupling between localized frontotemporal regions and indicate that there is not a clear one-to-one mapping between GMV and aperiodic activity.

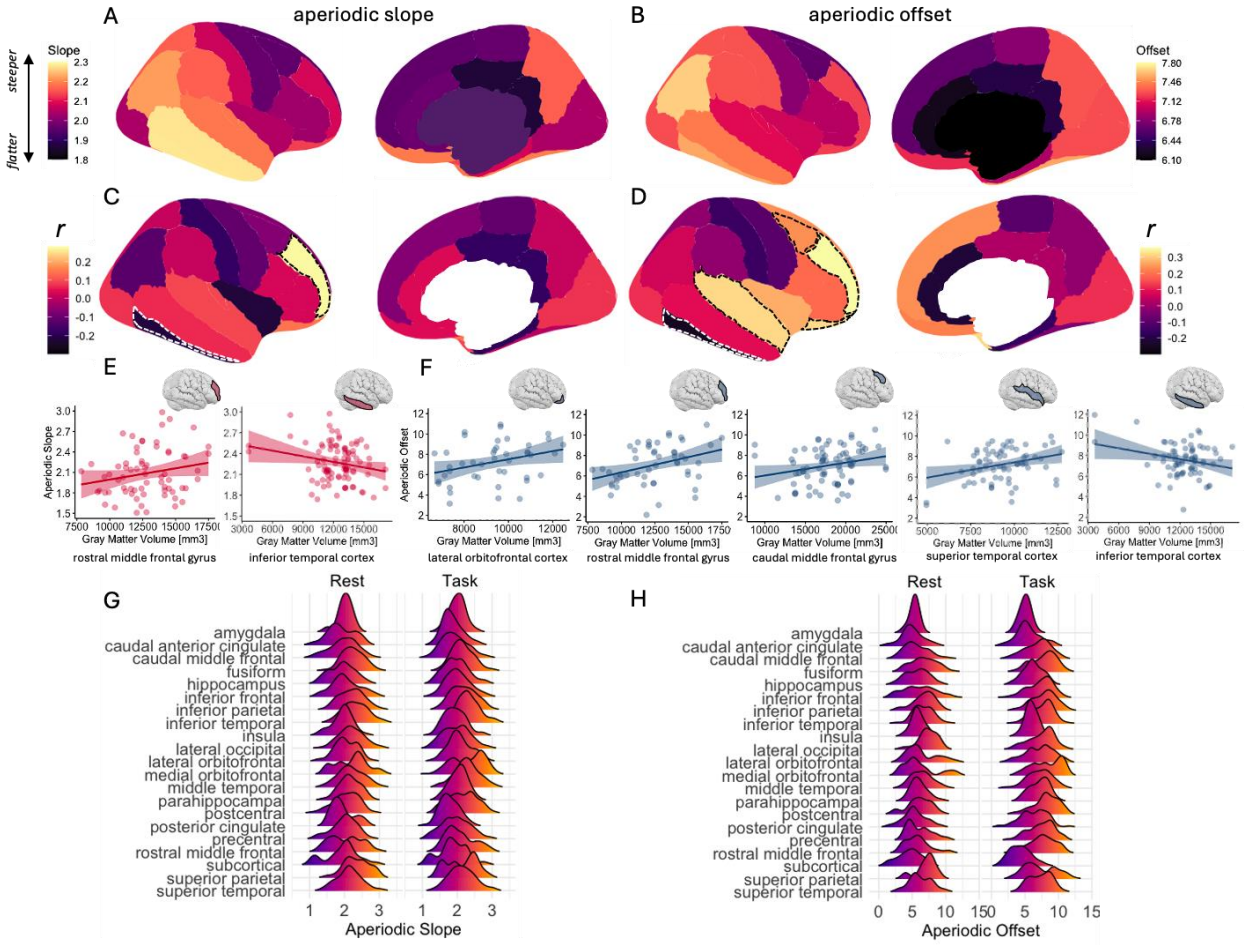

Figure 2. Regional differences in the aperiodic slope and offset and their correlation with GMV. Top row: Brain-wide standardized means of the regional aperiodic slope (**A**; left) and offset (**B**; right). Warmer colors/higher values indicate steeper slopes and higher offsets, respectively. Middle row: brain-wide correlations (Pearson r) between regional GMV (mm^3) and aperiodic slopes (**C**; left) and offsets (**D**; right). Warmer colors/higher values indicate positive correlations; cooler colors/lower values indicate negative correlations. Note that the area corresponding to subcortical space is white as no analysis of subcortical GMV was performed. Regions with statistically significant correlations (p < 0.05) are indicated by dashed borders. Bottom row: scatterplots illustrating relationships between GMV (x-axis) and aperiodic slopes (**E**; y-axis; red) and offsets (**F**; y-axis; blue) in regions with statistically significant correlations. Individual data points represent single participant data averaged across channels for each representative ROI. Shading shows the standard error. (**G**) Ridgeline plot illustrating the distribution of aperiodic slopes (x-axis; higher values denote a steeper slope) by region (y-axis) and condition (left: task-free; right: task-based). **(H)** Same as **(G)** for the aperiodic offset (x-axis; higher values denote a higher offset).

Aperiodic activity stabilizes in young adulthood in associative and sensorimotor cortices

Having demonstrated that aperiodic activity differs by brain region, we sought to establish developmental trajectories of aperiodic activity between association and sensorimotor cortices. We first examined hypotheses a, that in association cortices, the aperiodic slope flattens with age into young adulthood, and b, that in sensorimotor cortices, the aperiodic slope flattens with age into adolescence (see Table S1 in the supplementary materials for a summary of association and sensorimotor regions). We implemented nonlinear mixed-effects regressions, modeling aperiodic activity as a function of age (fit with two splines) and cortex type (association, sensorimotor), treating participant and DKT region as random effects on the intercept, and channel nested under participant. For the aperiodic slope, we revealed a significant age × cortex type interaction (β = 0.20, SE = 0.05, p < 0.001; age: β = -0.57, SE = 0.18, p = 0.002; cortex type: β = -0.02, SE = 0.04, p = 0.59), demonstrating that the slope flattens with age into young adulthood, with greater flattening in sensorimotor compared to association cortices between 15 – 35 years of age (β = 0.23, SE = 0.11, p = 0.03; Figure 3A). For the aperiodic offset, while there was no interaction between age and region (β = -0.16, SE = 0.55, p = .76) nor a main effect of region (β = -0.21, SE = 0.16, p = 0.20), we revealed a significant main effect of age, whereby the offset downshifted from 5 – 30 years of age (first spline term; β = -6.06, SE = 0.85, $p \leq 0.001$) before stabilizing thereafter (second spline term; β = -1.15, SE = 0.84, p = 0.17; Figure 3B). These results support our prediction that the aperiodic slope and offset flatten and downshift with age into young adulthood in association cortices. These results are contrary to our prediction that aperiodic activity stabilizes with age into adolescence in sensorimotor cortices; however, the difference in flattening suggests dissociable trajectories between association and sensorimotor cortices.

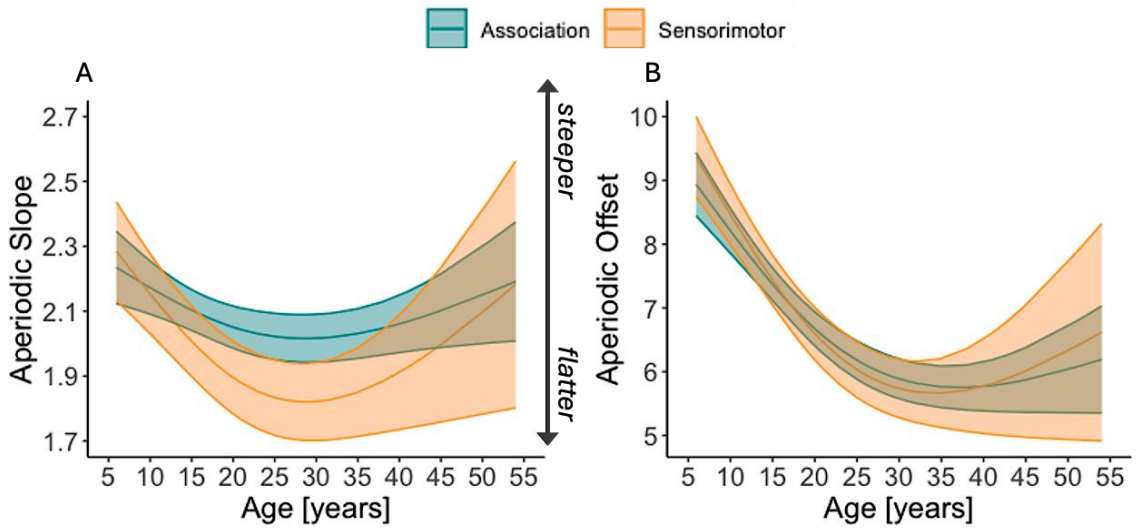

Figure 3. Age-related differences in aperiodic activity between association and sensorimotor cortices. (A) Modeled effects for differences in the aperiodic slope (y-axis; higher values denote a steeper slope) and age (x-axis). **(B)** Modeled effects for differences in the aperiodic offset (y-axis: higher values denote a higher offset) and age (x-axis). In both **(A)** and **(B)**, association cortices are presented in teal and sensorimotor cortices in orange. Shaded regions indicate the 83% confidence interval.

Regional aperiodic neural activity differs by age and attentional state

We next sought to establish developmental trajectories of aperiodic activity within localized brain regions and test hypothesis c, that age effects would differ between attentional states. To identify regional age effects in aperiodic activity and whether they differ by attentional state, we implemented separate linear mixed-effects models for each ROI. Our strategy for each analysis was to fit a model to the dependent variable of interest (i.e., aperiodic slope or offset) and regress the estimates onto age

(in years), attentional state (task-based, task-free), and the interaction of age and attentional state. All models were fit with by-participant and by-task random intercepts, with channel nested under participant.

For the aperiodic slope, we revealed a main effect of age in caudal anterior cingulate cortex (β = -0.01, SE = 0.004, p_{adj} = 0.03), and significant age × attentional state interactions in caudal middle frontal gyrus (cMFG; β = -0.003, SE = 0.001, p_{adj} = 0.007; age: β = -0.005, SE = 0.004, p_{adj} = 0.41; task: β = 0.09, SE = 0.02, $p_{adj} \leq 0.001$) and rostral middle frontal gyrus (rMFG; β = -0.004, SE = 0.001, p_{adj} = 0.04; age: β = -0.01, SE = 0.004, p_{adj} = 0.02; task: β = 0.09, SE = 0.03, p_{adj} = 0.37). In both cMFG and rMFG, task-free slopes are steeper than task-based slopes in children and the opposite is observed in adults; the direction of differences reverses around age 18 – 20 years (Figure 4B). If flatter slopes imply more excitation, and increased excitation in the PFC reflects activation of inhibitory cognitive control, then these results are consistent with increased inhibitory control during task engagement in adolescence (Keller et al., 2023; Larsen et al., 2023; Sydnor et al., 2021; Sydnor et al., 2023) and mirror the development of domain-general cognitive control (Tervo-Clemmens et al., 2023). These results also support our hypothesis that attentional state modulates age-related flattening of the aperiodic slope (see S1 in supplementary materials for aperiodic offset results). For visualizations of the main effects of age and condition on the aperiodic slope, see Figures S3 and S4, respectively.

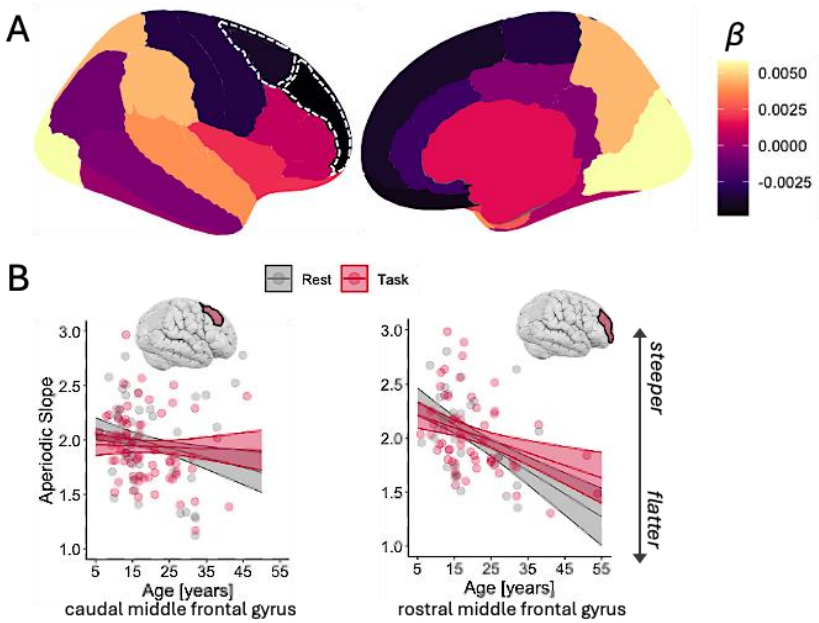

Figure 4. Regions with a significant interaction between age and attentional state on aperiodic activity. (A) Brain-wide age and condition interactions on regional aperiodic slopes. Regions with statistically significant interactions between age and attentional state (*FDR* < 0.05) are indicated by dashed borders. **(B)** Scatterplots illustrating interactions between age (x-axis; in years) and attentional state (red = task-based; gray = task-free) on the aperiodic slope (y-axis; higher values denote a steeper slope) in regions with statistically significant interactions. Individual data points represent single participant data averaged across channels for each representative ROI. Shading shows 83% CIs.

Task-based aperiodic activity in association cortices predicts individual memory outcomes

Having demonstrated that memory performance improves with age, with marked variability among adolescents (Figure 1C), we examined whether age interacts with regionally specific task-based and task-free aperiodic slopes, respectively, to predict memory performance. For each analysis, we fit a general linear model to recognition accuracy and regressed the estimates onto age (in years) and aperiodic slopes (task-based or task-free), and the interaction of age and slope. For task-based slopes,

we observed age × slope interactions in rMFG (β = 0.02, SE = 0.01, p = 0.03; age: β = -0.02, SE = 0.01, p = 0.14; slope: β = -0.76, SE = 0.23, p = 0.001; Figure 5A left) and fusiform gyrus (β = -0.03, SE = 0.01, p = 0.005; age: β = 0.08, SE = 0.02, p = 0.001; slope: β = 0.64, SE = 0.27, p = 0.02; Figure 5A right). In rMFG, memory performance increased with age and an age-related flattening of the aperiodic slope. Although overall steeper slopes were observed in children, relatively flatter slopes in children and adolescents were associated with relatively superior memory. By contrast, in fusiform gyrus, flatter slopes were associated with inferior memory in children but superior memory in adolescents and adults. There were no significant main effects of the task-free slope or interactions between the task-free slope and age on memory performance (all p >.05). For visualization of main effects of task-based and task-free slopes on memory, see Figure S7 and Figure S9, respectively. For aperiodic offset results, see S2 in the supplementary material.

Taken together, our results elucidate how age-dependent effects on aperiodic slopes in PFC and fusiform gyrus, and age-invariant effects on aperiodic offsets in PFC and inferior parietal cortex predict individual memory performance (S2 and Figure S2). These effects were evident exclusively during task-based states, thus linking aperiodic activity during attention to to-be-remembered visual information to an individual's memory for that information. From this perspective, the aperiodic slope may serve as a key marker of typical and atypical memory development, while the offset may reflect an age-invariant neural marker of successful memory encoding (Figure S2).

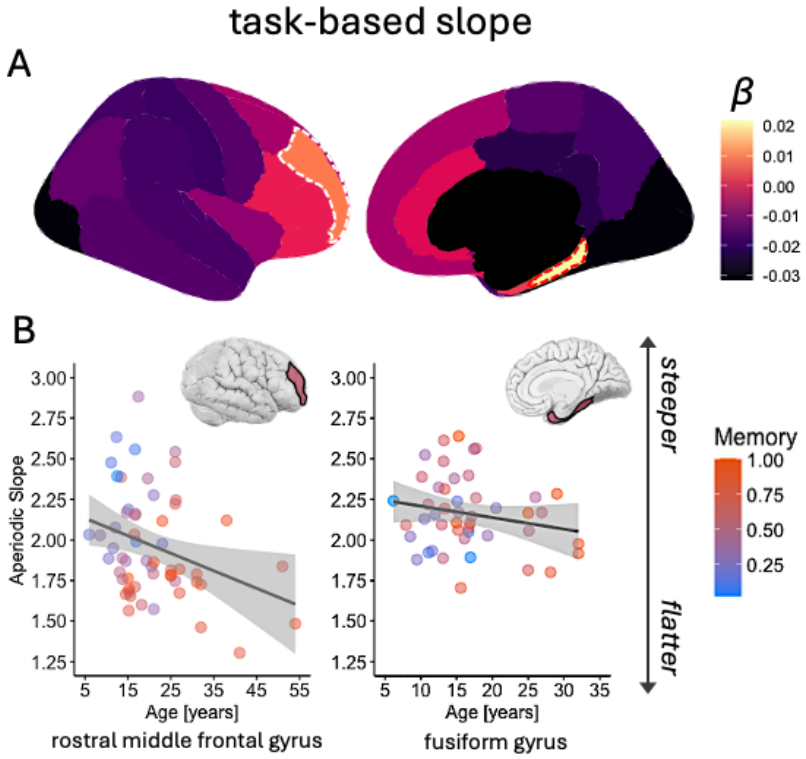

Figure 5. Regions with a significant effect of task-based aperiodic activity on memory performance. (A) Brain-wide slope and age interactions on memory. Regions with statistically significant interactions between the task-based slope and age (p < 0.05) are indicated by dashed borders. **(B)** Scatterplots illustrating interactions between task-based slopes (y-axis; higher values denote a steeper slope) and age (x-axis; in years) on memory (z-scale; warmer colors denote higher memory recognition accuracy) in regions with statistically significant interactions. Individual data points represent single participant data averaged across channels for each representative ROI. Shading shows the standard error.

Gray matter volume and age interact to predict aperiodic activity in select brain regions

Thus far, we have established that aperiodic slopes in PFC differ by age and attentional state and predict age-related variability in memory outcomes, whereas slopes in sensorimotor regions do not differ by attentional state or predict age-related variability in memory outcomes. Last, we focus on structure-function relationships. Before testing hypothesis d, that age-related differences in aperiodic activity are modulated by regional GMV, we sought to replicate previous reports of age-related reductions in regional GMV (Bethlehem et al., 2022; Gogtay et al., 2004; Groeschel et al., 2010). Having demonstrated that global GMV decreases with age in our cohort (Figure 1C), we examined GMV by ROI. We implemented a linear mixed-effects model, regressing region and age onto GMV, treating participants as random intercepts. Our model confirmed a significant main effect of region ($\chi2(19) = 11081.98$, $p \leq 0.001$) and revealed an age × region interaction ($\chi2(19) = 92.05$, $p \leq 0.001$; Figure 5). Gray matter volume was reduced with age in lateral orbitofrontal cortex ($r = -0.61$, $p < 0.001$, 95% CI = [-0.77, -0.35]), mOFC ($r = -0.60$, $p = 0.001$, 95% CI = [-0.81, -0.27]), rMFG ($r = -0.38$, $p = 0.007$, 95% CI = [-0.61, -0.11]), cMFG ($r = -0.42$, $p <.001$, 95% CI = [-0.60, -0.20]), inferior frontal gyrus ($r = -0.35$, $p = 0.01$, 95% CI = [-0.57, -0.09]), superior temporal cortex ($r = -0.45$, $p < 0.001$, 95% CI = [-0.64, -0.22]), middle temporal cortex ($r = -0.31$, $p = 0.01$, 95% CI = [-0.51, -0.07]), posterior cingulate cortex ($r = -0.36$, $p = 0.04$, 95% CI = [-0.62, -0.02]), and inferior parietal cortex ($r = -0.54$, $p < 0.001$, 95% CI = [-0.70, -0.33]; Figure 6A and 6B). These results replicate previous reports of age-related reductions in GMV in association cortices starting in childhood (Bethlehem et al., 2022; Gogtay et al., 2004; Groeschel et al., 2010).

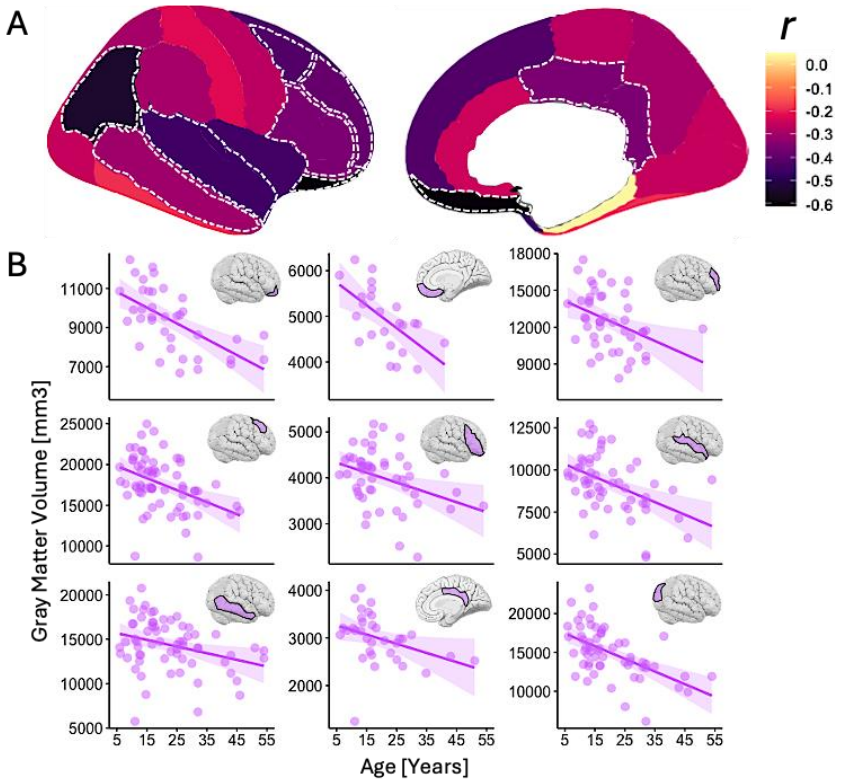

Figure 6. Regions with a significant effect of age on GMV. (A) Brain-wide correlations (Pearson *r*) between regional GMV (mm^3) and age (in years). Warmer colors/higher values indicate positive correlations and cooler colors/lower values indicate negative correlations. Note that the area corresponding to subcortical space is white as no analysis of subcortical GMV was performed. Regions with statistically significant correlations ($p < 0.05$) are indicated by dashed borders. **(B)** Scatterplots illustrating relationships between GMV (y-axis) and age (x-axis) in regions with statistically significant correlations.

To test whether age-related differences in aperiodic activity are modulated by regional GMV, we fit mixed-effects models to task-based aperiodic activity (slope or offset) and regressed these estimates onto age (in years), GMV, and the interaction between age and GMV. All models were fit with by-participant and by-task random intercepts, with channel nested under participant. We revealed age × GMV interactions on task-based aperiodic slopes in inferior frontal gyrus ($\beta = 2.15 \times 10^{-5}$, SE $= 9.77 \times 10^{-6}$, $p = 0.03$; age: $\beta = -0.09$, SE $= 0.04$, $p = 0.02$; GMV: $\beta = -0.0004$, SE $= 0.0002$, $p = 0.03$), posterior cingulate cortex ($\beta = -5.44 \times 10^{-5}$, SE $= 1.71 \times 10^{-5}$, $p = 0.003$; age: $\beta = 0.14$, SE $= 0.04$, $p = 0.004$; GMV: $\beta = 0.0007$, SE $= 0.0002$, $p = 0.01$), and inferior parietal cortex ($\beta = -3.93 \times 10^{-6}$, SE $= 1.50 \times 10^{-6}$, $p = 0.01$; age: $\beta = 0.04$, SE $= 0.02$, $p = 0.02$; GMV: $\beta = 6.24 \times 10^{-5}$, SE $= 2.90 \times 10^{-5}$, $p = 0.03$), three of the regions where GMV was reduced with age (see Figure 6), as well as postcentral gyrus ($\beta = -1.07 \times 10^{-5}$, SE $= 3.78 \times 10^{-6}$, $p = 0.007$; age: $\beta = 0.10$, SE $= 0.03$, $p = 0.007$; GMV: $\beta = 0.0001$, SE $= 6.30 \times 10^{-5}$, $p = 0.03$; Figure 7). In inferior frontal gyrus, task-based aperiodic slopes flattened with age and reductions in GMV; flatter slopes were associated with higher GMV in children and lower GMV in adults. In posterior cingulate cortex, inferior parietal cortex, and postcentral gyrus, while there was no relationship between task-based slopes and GMV in children, flatter slopes were associated with higher GMV in adults (for visualizations of the main effects of age and GMV on aperiodic slopes, see Figure S9 and S10, respectively). There were no significant age × GMV interactions on task-based aperiodic offsets (all $p > .05$; for visualizations of the non-significant main effects of age and GMV on aperiodic offsets, see Figure S13 and S14, respectively).

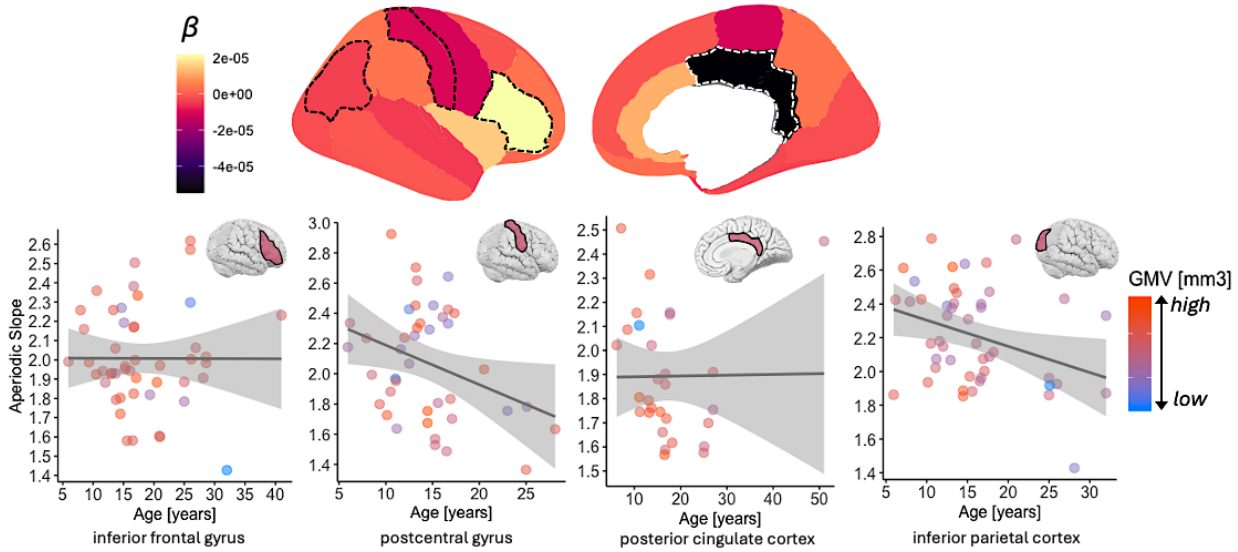

Figure 7. Regions with a significant interaction between age and GMV on the aperiodic slope. (A) Top row: Brain-wide GMV and age interactions on regional aperiodic slopes. Regions with statistically significant interactions between age and GMV (*FDR* < 0.05) are indicated by dashed borders. Bottom row: scatterplots illustrating interactions between age (x-axis; in years) and GMV (z-scale; warmer colors denote higher GMV) on the aperiodic slopes (y-axis; higher values denote a steeper slope) in regions with statistically significant interactions. Individual data points represent single participant data averaged across channels for each representative ROI. Shading shows the standard error.

Discussion

We mapped aperiodic activity – a proposed marker of E:I balance – from childhood to late middle adulthood. Our findings demonstrate: (I) a gradient of slopes from inferior lateral to superior medial regions, suggesting heightened inhibition in inferior lateral temporal regions and heightened

excitation in superior medial frontal regions (Figure 2); (II) a U-shaped relationship in slopes by age, suggesting heightening excitation into young adulthood followed by heightening inhibition into middle adulthood (Figure 3); (III) a flattening of PFC slopes with advancing age, with more pronounced flattening in task-free states, suggesting that age-related increases in excitation are task-dependent (Figure 4); (IV) PFC-derived aperiodic slopes during task-based states predict age-related variability in memory (Figure 5); and (V) higher GMV that is associated with steeper slopes across age in PFC, but flatter slopes in sensorimotor cortices (Figure 7). In sum, these findings reveal regional and attentional differences in E:I balance from early childhood to late middle adulthood and establish E:I balance in PFC as a mechanism of memory development (for a schematic summary of the main results, see Figure 8).

E:I balance stabilizes in association and sensorimotor cortices in adulthood

The spatiotemporal patterning of cortical maturation progresses from sensorimotor to higher-order association cortices, characterized by heightened plasticity in late-maturing association regions, potentially influencing higher-order cognition in adulthood (Sydnor et al., 2021). Based on these observations, we hypothesized that aperiodic activity would follow similar developmental trajectories, such that it would stabilize during adolescence in sensorimotor cortices and during young adulthood in association cortices. Indeed, we revealed that the aperiodic slope and offset flatten and downshift from childhood to young adulthood in association cortices. However, contrary to dominant models of brain development based on structural measures (Gogtay et al., 2004; Grydeland et al., 2019; Sydnor et al., 2021), we found that aperiodic activity in sensorimotor cortices does not stabilize until young adulthood. We further revealed that the magnitude of flattening is greater in sensorimotor than association cortices during adolescence and young adulthood. Our findings establish that the development of aperiodic activity in sensorimotor regions does not mirror the development of cortical structure and suggest that the development of E:I balance in sensorimotor regions follows a protracted trajectory into adulthood.

Attention modulates E:I balance by age in prefrontal cortex

Scalp-EEG studies have consistently demonstrated an age-related flattening and downshifting of the aperiodic slope and offset, respectively, often with a frontal-central distribution (Bornkessel-Schlesewsky, Alday, et al., 2022; Favaro et al., 2023; McSweeney et al., 2023; Merkin et al., 2023; Ouyang et al., 2020; Schaworonkow & Voytek, 2021; Thuwal et al., 2021). To our knowledge, only one iEEG study has examined age-related aperiodic slope variability, demonstrating an age-related flattening of the slope in the visual cortex of 15 patients aged 15 – 53 years (Voytek et al., 2015). Little is known regarding regional differences in the slope and offset. We found that subregions of PFC, namely caudal and rostral MFG, exhibit a flattening of the aperiodic slope across age. We further reveal that the age-related flattening of the slope is modulated by attentional state, with less pronounced flattening for task-based relative to task-free states. This finding can be interpreted in the context of PFC inhibitory control: a central role of the PFC is to exert cognitive control in the service of behavior, partially by modulating activity in regions further upstream, such as visual cortex and MTL (Gazit et al., 2020; Miller & Cohen, 2001; Noudoost & Moore, 2011). The difference between task-states also emerges at roughly 18 to 20 years of age, revealing the aperiodic slope as a potential marker of the development of cognitive control in adolescence. Functionally, steeper on-task slopes, suggesting increased inhibition, have been proposed to reflect the maintenance of top-down predictions (Cross et al., 2022; Dave et al., 2018) and support information integration (Bornkessel-Schlesewsky, Sharrad, et al., 2022; Sheehan et al., 2018). By contrast, flatter slopes have been associated with slower processing speed (Ouyang et al., 2020), and poorer visual working (Donoghue et al., 2020) and visuomotor (Immink, Cross et al., 2021) memory, albeit these studies analyzed task-free slopes.

Our findings suggest that the PFC gains flexibility in inhibitory control with age, exerting increased inhibition during the processing of external, task-relevant information.

Our exploratory analyses of the aperiodic offset revealed a decrease with age, with task-free offsets showing a more pronounced decline than task-based offsets in more anterior regions, and the reverse in more posterior regions. Lower offsets are hypothesized to reflect increased neuronal population activity (Manning et al., 2009; Miller et al., 2012). Accordingly, previous work has demonstrated that the offset is higher in task-free states (e.g., during sleep; Favaro et al., 2023; Lendner et al., 2023) and downshifts from ages 2 – 17 years in an anterior-to-posterior gradient (Favaro et al., 2023). Here, we extend previous reports by demonstrating a broad-band voltage reduction from childhood to middle late adulthood in frontal, MTL and occipital regions. Reductions in the offset, and thus overall power reductions, may covary with synaptic pruning, as lower synaptic density is likely related to lower EEG power (Larsen et al., 2022; McKeon et al., 2024). From this perspective, region-specific age-related reductions in the offset may indicate synaptic refinement, with overall power differing as a function of task-state.

E:I balance during memory encoding predicts subsequent memory performance

Do age-related differences in aperiodic activity predict age-related differences in memory? Prior work on aperiodic activity has reported mixed findings in relating the slope and offset to various aspects of cognition. Steeper task-free slopes have been associated with faster reaction times in young adults and improved recognition accuracy during initial learning (Immink, Cross et al., 2021). However, in the same study, flatter slopes and higher offsets were associated with improved recognition with increasing task exposure. In a similar study with young adults, flatter task-free slopes and higher offsets were associated with improved decision-making performance (Dziego et al., 2023). Of the studies examining task-based aperiodic activity, flatter slopes have been associated with improved learning of an artificial language in young adults aged 18 – 40 years (Cross et al., 2022), but lower working memory performance with age from 15 – 53 years (Voytek et al., 2015). Critically, past work has either focused on task-based or task-free aperiodic activity and cognition without accounting for differences between task-states, and it is unknown how task-based differences in localized brain regions relate to behavior by age.

Here, we overcame this limitation by mapping task-based and task-free aperiodic slopes and offsets by age to behavior on a region-by-region basis. We observed opposing age-dependent relationships between aperiodic slopes and memory in MFG and fusiform gyrus, which likely stems from their distinct functional roles and development (Rosen et al., 2018; Tang et al., 2018). In MFG – a region core to executive functions and cognitive control and which undergoes protracted development (Fuster, 2002; Ridderinkhof et al., 2004) – children with steeper slopes exhibited worse memory performance. This finding suggests that excessive neural inhibition (Donoghue et al., 2020; Voytek et al., 2015) in MFG during childhood may hinder attentional control. Indeed, ADHD-diagnosed, medication naïve children exhibit steeper slopes than their typically developing counterparts (Robertson et al., 2019), as do individuals with schizophrenia (Molina et al., 2020; Peterson et al., 2023), suggesting that underdeveloped inhibition in childhood results in inefficient neural communication and disrupted coordination, manifesting in poorer memory outcomes.

As individuals age, structural and functional changes in MFG (i.e., synaptic pruning, changes in neurotransmitter levels [GABAergic interneurons, glutamate]; Kolk & Rakic, 2022), likely lead to a flattening of aperiodic slopes (McKeon et al., 2024; Sukenik et al., 2021). Flatter slopes have been likened to increased neural "noise" (Bornkessel-Schlesewsky, Alday, et al., 2022; Bornkessel-Schlesewsky, Sharrad, et al., 2022; Dave et al., 2018; Voytek et al., 2015), due to increased levels of aberrant neural firing in the absence of a slower modulatory oscillation (Voytek et al., 2015; Voytek & Knight, 2015). We observed that flatter slopes in MFG during adulthood were less related to memory

outcomes than in children, likely due to the emergence of compensatory neural recruitment and altered cognitive strategies (Braver et al., 2009; Cabeza et al., 2018; Spreng & Turner, 2019). Conversely, in fusiform gyrus, a higher-order visual region that supports detailed visual memory encoding (Ofen et al., 2007; Rosen et al., 2018), children with steeper slopes had superior memory. Enhanced inhibition in fusiform gyrus during childhood may be advantageous for the rapid encoding of detailed visual information, consistent with theoretical models positing that increased inhibition provides homeostatic control to restore network stability and helps to protect overlapping memories from interference (Barron, 2021), thus facilitating successful episodic memory formation (Axmacher et al., 2008). Inversely, during adulthood, age-related declines in synaptic density and myelination may result in flatter slopes, increased neural noise, and decreased inhibition. This shift towards increased neural "noise" could be an adaptive response to maintain visual memory performance. Indeed, flatter slopes have been proposed to index greater "complexity" within biological systems (Amigó et al., 2004; Medel et al., 2023), likely indicating informationally-rich neural processing (Sheehan et al., 2018). By contrast, steeper slopes have been argued to support faster information processing (Cross et al., 2022; Dziego et al., 2023), which may not always be advantageous in processing complex sensory information, particularly with advancing age.

Interestingly, we did not observe significant relationships between task-free slopes and memory performance. This apparent discrepancy with past findings can likely be explained by differences in experimental task designs and inter-regional source mixing inherent to scalp-EEG, where signals from multiple cortical areas are mixed due to volume conduction (Musall et al., 2014; Palva et al., 2018). Scalp-EEG, with its relatively low spatial resolution, could mask region-specific relationships between aperiodic slopes and behavior, explaining discrepancies with previous findings. Although source localization techniques can help mitigate these issues, they are limited in resolving precise cortical sources (Buzsaki, 2006; Nunez & Srinivasan, 2006). Further, previous work has focused on mapping intrinsic, task-free aperiodic activity onto trait-like measures of cognition (e.g., processing speed, verbal ability; Euler et al., 2024; Montemurro et al., 2024; Pi et al., 2024) or tasks that do not measure episodic or working memory (Bornkessel-Schlesewsky, Sharrad, et al., 2022; Dziego et al., 2023; Immink et al., 2021). Our findings demonstrate that aperiodic activity during the encoding of visual stimuli predicts recognition of those stimuli, a direct relationship that did not survive on a region-by-region basis with intrinsic (i.e., task-free) activity.

We further observed that lower task-based offsets were associated with better memory after accounting for the effect of age (Figure S2). In MFG and inferior parietal cortex, lower offsets were associated with improved recognition accuracy. This is in apparent contrast with previous work, wherein higher task-free offsets are associated with better behavioral performance (Immink et al., 2021) and better decision-making outcomes (Dziego et al., 2023). From this perspective, task-based offsets may facilitate memory independent of age, reflecting more stable basal neural activity. This stability may reflect better regulation of neural resources, allowing for more efficient processing of incoming information, and a brain state conducive to optimal cognitive functioning. Indeed, the two regions with negative associations between the offset and memory performance are key nodes in the frontoparietal network, a system at the interface of memory processes and attentional orientation to task-relevant information (Fischer et al., 2021).

E:I balance is associated with age-related variability in gray matter volume

Finally, having established that aperiodic activity differs by age and attentional state and that activity during task performance predicts memory outcomes, we mapped task-based aperiodic activity onto GMV across age. We reveal that in inferior frontal gyrus (IFG), lower GMV is associated with steeper aperiodic slopes during childhood, whereas the inverse relationship is observed during

adulthood. This suggests that premature cortical GMV pruning may precipitate an early steepening of aperiodic slopes, potentially leading to premature inhibitory processes and poorer memory outcomes.

Mechanistically, the observed relationship between GMV and aperiodic slopes in IFG can be interpreted through the lens of synaptic pruning and cortical maturation (Larsen et al., 2022; Legon et al., 2016). During childhood, accelerated pruning is posited to lead to reductions in GMV and a steepening of aperiodic slopes. This premature steepening may reflect E:I imbalance, adversely affecting cognitive functions such as memory encoding. In adulthood, however, the stabilization of synaptic networks and maintenance of GMV may facilitate flatter aperiodic slopes, indicative of a more balanced and established cortical state. Our findings suggest that E:I mechanisms may be disrupted by early reductions in regional GMV during childhood, leading to alterations in aperiodic activity.

By contrast, in postcentral gyrus (i.e., primary motor cortex), we observed that lower GMV is associated with flatter slopes during childhood and steeper slopes during adulthood. This is in addition to the finding that sensorimotor cortical development – as indexed by E:I balance – stabilizes during young adulthood, challenging models of early sensorimotor development based on cortical structure (Bethlehem et al., 2022; Larsen et al., 2022). The differential relationship between GMV and aperiodic slopes in association versus sensorimotor cortices by age highlights the complex interplay between structural and functional maturation. Indeed, rates of GMV development vary across brain regions (Bethlehem et al., 2022; Gogtay et al., 2004; Grydeland et al., 2019; Hill et al., 2010), as do rates of aperiodic activity development (Favaro et al., 2023; Hill et al., 2022; Schaworonkow & Voytek, 2021). Here, we identify the brain regions where these rates align and those where they diverge. Future research should further examine relationships between aperiodic activity and brain structure to elucidate the mechanisms by which structure-function development impacts the development of higher-order cognition.

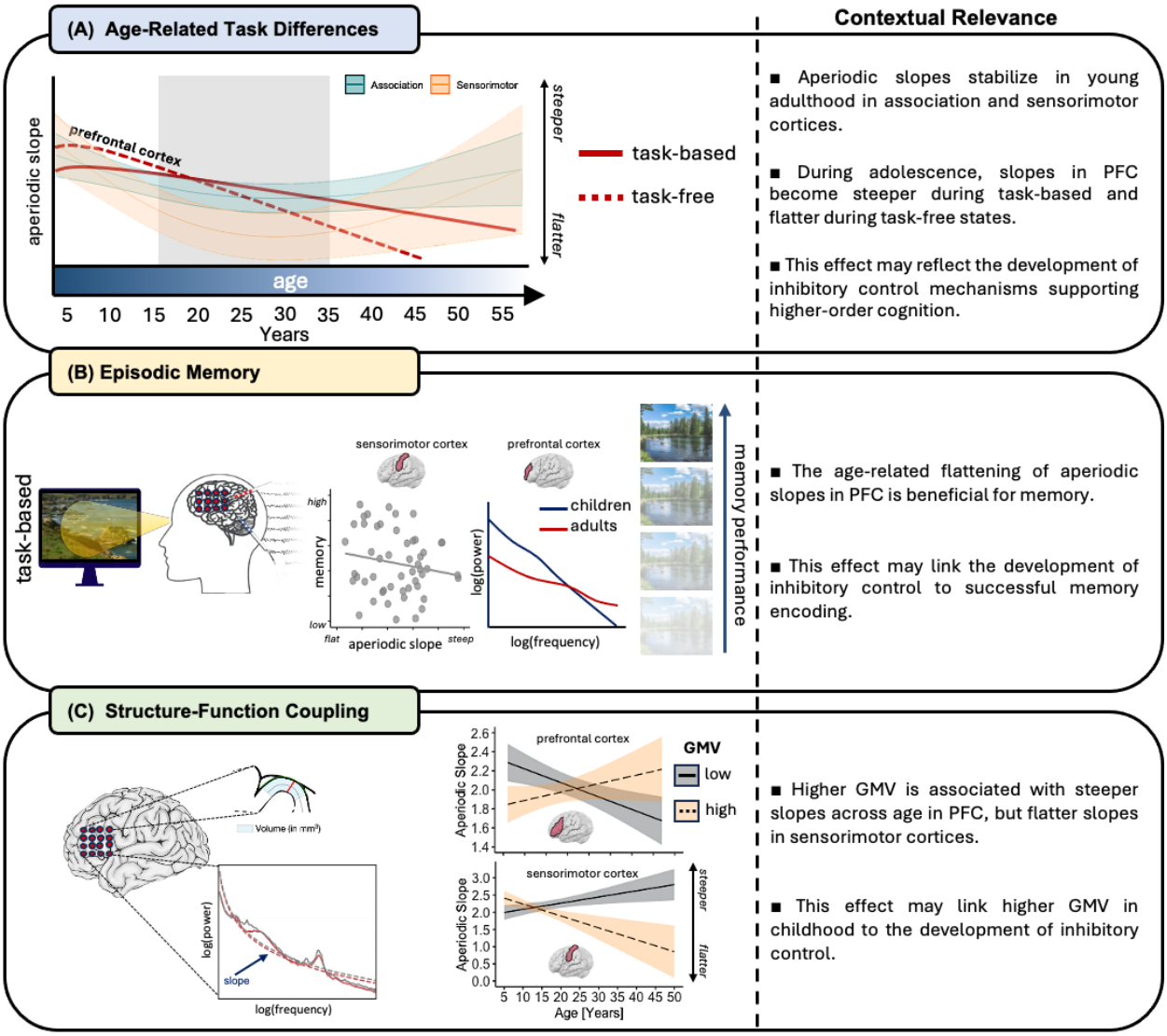

Figure 8. Aperiodic activity stabilizes in young adulthood, differs by age and attentional state, predicts age-related variability in episodic memory, and is associated with age-related variability in GMV. (A) Aperiodic slopes in sensorimotor (orange) and association (teal) cortices flatten from age 5 – 25 years and steepen thereafter. Note that the flattening is more pronounced in sensorimotor than association cortices in adolescence and young adulthood (gray shading). Regarding attentional state (i.e., task-based vs. task-free) differences in aperiodic activity, in PFC, task-free (dashed red) slopes are steeper (i.e., greater inhibition) than task-based (solid red) slopes in children, and the inverse is observed in adults. Effects reverse at approximately ~18 – 20 years of age, likely reflecting the development of inhibitory control. **(B)** PFC-derived aperiodic slopes during task-based but not task-free states predicted age-related variability in memory performance, whereby the age-related flattening of aperiodic slopes was associated with age-related improvements in memory. Flatter sensorimotor cortical slopes were not associated with better memory performance after accounting for age. **(C)** Modeling the relationship between brain volume and aperiodic slopes revealed differential age-related differences in structure-function coupling. In PFC, lower GVM was associated with steeper slopes in childhood and flatter slopes in adulthood. In sensorimotor cortices, slopes were steeper in childhood regardless of GMV; in adolescence and adulthood, lower GMV was associated with steeper slopes and higher GMV was associated with flatter slopes.

Limitations and future directions

We have revealed regional age-related variations in aperiodic neural activity dependent upon task-state. Our findings suggest that brain development may be best understood as a diverse set of

regionally independent trajectories, partially indexed by aperiodic activity. However, as iEEG data are cross-sectional, we were unable to follow these putative trajectories through time. A critical next step will be to establish the potential utility of aperiodic activity in elucidating longitudinal changes in regional structure-function relationships (Ofen et al., 2019). As such, future studies, focusing *a priori* on the regions we identified (e.g., MFG), could capitalize on the spatio-temporal precision and capacity to perform multi-visit longitudinal studies with, for example, MEG.

While our cohort is representative of typical development and the use of iEEG affords precise spatiotemporal precision, iEEG samples are comprised of pharmacoresistant epilepsy patients, potentially limiting the generalizability of our findings (Johnson & Knight, 2023). For this reason, it is important to note that our sample demonstrated typical age-related gains in memory performance and age-related differences in global GMV (Figure 1C) that are consistent with healthy cohorts (Bethlehem et al., 2022). An additional limitation is the relatively lower representation of older individuals within our sample, a common observation in iEEG investigations, and the relatively lower representation of patients with task-free (n = 65) compared to task-based (n = 81) data. Nonetheless, the current results underscore maturation within MFG, and this effect was present across our entire age range of ~5 to 54 years. To obtain larger samples across age, future research may seek to increase sample sizes through multi-site collaboration and data sharing (Johnson, Yin, et al., 2022; Johnson & Knight, 2023).

We also found no significant age-related difference in aperiodic activity in the hippocampus in relation to attentional state, or in predicting individual memory performance. Given that our study examined memory, these results may be somewhat surprising. However, it is possible that oscillatory activity in the hippocampus exhibits effects related to attentional state and memory outcomes, consistent with ample literature on hippocampal theta oscillations (Herweg et al., 2020; Lega et al., 2012). Future research should directly investigate this hypothesis. Lastly, with our task-based versus task-free contrast as a starting point, future research may also aim to examine additional attentional states, such as sleep versus wake states. The aperiodic slope and offset systematically shift as a function of sleep stage, which has recently been shown to differ across development (Favaro et al., 2023). However, it is unknown whether there are region-specific differences in sleep-based aperiodic activity, whether these regional differences relate to the development of higher-order cognition, and whether sleep-based aperiodic activity changes concomitantly with wake-related aperiodic dynamics.

Implications

Historically, neuroscientific research has predominantly focused on young adults aged 18-40 years, largely overlooking the influence of age on brain dynamics. This practice has resulted in a significant knowledge gap regarding brain development. Addressing this gap is crucial due to its profound clinical implications across various domains, including neurodevelopmental disorders, traumatic brain injury, stroke, age-related cognitive decline, and neurodegenerative diseases, as well as advancements in neural prosthetics for injury, stroke, or disease management. Our study addresses this knowledge gap by elucidating the trajectory of aperiodic electrophysiological dynamics and their associations with brain structure and memory across development, from childhood into late middle adulthood. Previous attempts to characterize these dynamics have been constrained by limitations in imprecise spatiotemporal measurements and relatively small sample sizes. To overcome these challenges, we adopted a comprehensive approach. Firstly, we employed iEEG to delineate developmental neurophysiology with exceptional precision. Secondly, we applied sophisticated analyses of aperiodic components in iEEG data to establish novel connections between aperiodic activity and developmental variations in memory. Thirdly, we explored the relationship between aperiodic components and GMV. Lastly, we leveraged an exceptionally large iEEG dataset to detect subtle effects that may have been undetected in smaller cohorts.

Understanding how cortical maturation influences memory encoding processes is also fundamental to cognitive function and daily performance, given well-documented changes in brain structure and function over the lifespan. Furthermore, elucidating the impact of brain development on memory formation across different life stages holds promise for early detection and intervention strategies targeting the emergence of both neurodevelopmental disorders and age-related memory decline. Identifying markers of healthy brain development and aging is crucial for detecting dysfunction in age-related pathologies, which often manifest gradually over many years before exhibiting overt behavioral symptoms. In this context, our findings may contribute to the prevention or delay of pathological aging, offering significant health benefits, particularly considering the limitations and risks associated with current pharmacological treatments. Additionally, our study lays the groundwork for investigating memory dysfunction in psychiatric disorders, many of which emerge during adolescence and young adulthood, and which show deviations in aperiodic activity from healthy populations (Earl et al., 2024; Fernandez & Garner, 2007; Pani et al., 2022; Shuffrey et al., 2022).

Conclusions

We reveal that aperiodic neural activity follows the same developmental time course across young adulthood in both sensorimotor and association cortices, challenging models of early sensorimotor development based on measures of brain structure. We also isolate attentional state and age-related differences in the aperiodic slope to PFC, demonstrating that task-based slopes are steeper, reflecting greater inhibition, and that this difference emerges during adolescence. We further establish the functional role of PFC-derived slopes in memory, revealing that age-related improvements in memory outcomes are associated with the age-related flattening of aperiodic slopes. The aperiodic offset, by contrast, which reflects overall neuronal spiking, predicts memory outcomes irrespective of age. Lastly, we characterized, for the first time, the relationship between age-related differences in aperiodic activity and brain structure, identifying region-specific trajectories in structure-function relationships during development. Taken together, our findings establish brain-wide maps in aperiodic neural activity, its relation to age-related variability in memory, and novel structure-function relationships, findings which are critical for understanding brain development and aging in both health and disease.

Methods

Participants. Participants were 101 neurosurgical patients aged 5.93 – 54.00 years (63 males; mean age = 19.25) undergoing iEEG monitoring as part of clinical seizure management. Those with major lesions, prior surgical resections, noted developmental delays, or neuropsychological memory test scores <80 were considered ineligible. Patients were recruited from Northwestern Memorial Hospital, the Ann & Robert H. Lurie Children's Hospital of Chicago, St. Louis Children's Hospital, University of California, Irvine Medical Center, University of California, Davis Medical Center, University of California, San Francisco Benioff Children's Hospital, Children's Hospital of Michigan, and Nationwide Children's Hospital, University of California, San Diego, Rady Children's Hospital, Mount Sinai Hospital, California Pacific Medical Centre, and University of California, San Francisco Medical Centre. Written informed consent was obtained from participants aged 18 years and older and from the guardians of participants aged under 18 years. Written assent was obtained from participants aged 13 – 17 years and oral assent was obtained from younger children. All procedures were approved by the Institutional Review Board at each hospital in accordance with the Declaration of Helsinki. Given that electrode positioning in these participants was based on clinical necessity rather than for experimental reasons, *a priori* power analyses were not performed. Human iEEG research is limited by the availability of neurosurgical patients. From this perspective, the majority of iEEG work has

been based on relatively small sample sizes and could not consider age-related or other sources of inter-individual variability (Johnson & Knight, 2023).

Experimental design. Task-based iEEG data were derived from the encoding phase of two visual memory recognition tasks that have been used extensively to study memory in adults and children across neuroimaging modalities, including iEEG. In the blocked-trial paradigm, participants encode a set of 40 indoor and outdoor scenes and classify each as indoor/outdoor in preparation for a self-paced old/new recognition test of all 40 studied scenes intermixed with 20 new scenes as foils (Chai et al., 2010, 2014; Johnson, Tang, et al., 2018; Johnson, Yin, et al., 2022; Ofen et al., 2007, 2012, 2019; Tang et al., 2018; Yin et al., 2020, 2023). In the single trial paradigm, participants encode three shapes in a specific spatiotemporal sequence in preparation for a self-paced old/new recognition test of sequences that match exactly or mismatch on one dimension (i.e., shape identity, spatial position, or temporal order; cf. Davoudi et al., 2021; Dezfouli et al., 2021; Johnson, Adams, et al., 2018; Johnson, Chang, et al., 2022; Johnson et al., 2017, 2019). Both paradigms use visual stimuli to avoid potential confounds on memory with verbal material in children. The encoding phases of the two paradigms are similar because, in both paradigms, participants encode visual stimuli (3000ms, 500-1500ms inter-trial interval) in preparation for a self-paced, two-alternative forced choice recognition test. We ensured that on-task data reflected task engagement by only analyzing iEEG data during the viewing of stimuli that were attended during encoding, as indexed by a correct indoor/outdoor classification of each scene in the blocked-trial paradigm and correct old/new classification of each sequence in the single-trial paradigm (Johnson, Tang, et al., 2018; Johnson, Yin, et al., 2022; Yin et al., 2020). For a schematic of both visual memory tasks, see Figure S15. For task-free data, participants were instructed to sit quietly with their eyes open, fixating on the center of a computer monitor for five minutes. If no formal task-free task was administered, task-free data was taken from natural rest in continuous 24/7 iEEG recordings.

Behavioral analysis. Both visual memory tasks test memory in a two-alternative forced choice design, permitting the use of similar measures of memory performance across tasks. For both tasks, for all participants, we calculated the hit rate (i.e., number of previously studied stimuli that were correctly recognized as old/match out of all studied stimuli) and false alarm rate (number of new stimuli presented that were incorrectly identified as old/match out of all new/mismatched stimuli). Performance accuracy was calculated as hit rate minus false alarm rate to equate measures across memory tasks and correct for differences in an individual's tendency to respond old/match or new/mismatch, respectively. For a summary of behavioral performance, see Figure 1C.

iEEG acquisition and pre-processing. iEEG data were recorded at a sampling rate of 200-5000 Hz using Nihon Kohden JE120 Neurofax or Natus Quantum LTM recording systems interfaced with the BCI2000 software. Data acquired >1000 Hz were resampled to 1000 Hz after the fact. As described below, spectral analysis was performed up to 60 Hz. Thus, the lowest sampling rate of 200 is well over the minimum Nyquist frequency required for analysis (i.e., 2 cycles/frequency = 120 Hz). For consistency, all data from both visual memory tasks and from task-free recordings were pre-processed using the same procedures. Raw electrophysiological data were filtered with 0.1-Hz high-pass and 300-Hz low-pass finite impulse response filters, and 60-Hz line noise harmonics were removed using a discrete Fourier transform. Task-based continuous data were demeaned and epoched into 3s trials (i.e., 0-3s from scene or study sequence onset). Continuous task-free data were also demeaned and transformed into 3s epochs with 25% overlap. All epoched data were manually inspected blind to electrode locations and experimental task parameters. Electrodes overlying seizure onset zones and electrodes and epochs displaying epileptiform activity or artifactual signal (from poor contact, machine noise, etc.) were excluded. Neighboring electrodes within the same anatomical structure were bipolar montage re-referenced using consistent conventions (ECoG, anterior –

posterior; sEEG, deep – surface). For ECoG grids, electrodes were referenced to neighboring electrodes on a row-by-row basis. An electrode was discarded if it did not have an adjacent neighbor, its neighbor was in a different anatomical structure, or both it and its neighbor were in white matter. Bipolar referencing yielded virtual channels that were located midway between the original physical electrodes. Data were then manually re-inspected to reject any trials with residual noise. Pre-processing routines used functions from the FieldTrip toolbox for MATLAB (Oostenveld et al., 2011). All results were based on analysis of non-pathologic, artifact-free channels, ensuring that data represented healthy cortical tissue (Rossini et al., 2017).

Aperiodic neural activity. The irregular-resampling auto-spectral analysis method (Wen & Liu, 2016) (IRASA) was used to estimate the $1/f$ power-law exponent. IRASA estimates the aperiodic (random fractal) component of neural time series data by resampling the signal at multiple non-integer factors h and their reciprocals $1/h$. As this resampling procedure systematically shifts narrowband peaks away from their original location along the frequency spectrum, averaging the spectral densities of the resampled series attenuates peak components while preserving the $1/f$ distribution of the fractal component. The exponent summarizing the slope of aperiodic spectral activity is then calculated by fitting a linear regression to the estimated fractal component in log-log space. Using the YASA toolbox (Vallat & Walker, 2021) v.0.6.3 implemented in MNE-Python (Gramfort et al., 2013) v.1.3.1, we fit a power-law function to each fractal estimate within the frequency range of 1 – 60 Hz. For each epoch, channel, and task, the inverse slope of the power-law function was taken as the trial-level estimate of the $1/f$ exponent. The aperiodic offset (i.e., intercept of the power-law function) was also extracted, which reflects the initial amplitude of the power-law.

iEEG localization. Macro-electrodes were surgically implanted for extra-operative recording based solely on clinical need. The electrodes were subdural electrode grids or strips with 10 mm spacing or stereoelectroencephalography electrodes with 5-10 mm spacing. Anatomical locations were determined by co-registering post-implantation computed tomography coordinates to pre-operative magnetic resonance (MR) images, as implemented in FieldTrip (Stolk et al., 2018), FreeSurfer (Fischl, 2012), iELVis (Groppe et al., 2017) or VERA (Adamek et al., 2022). Electrode locations were then projected into standard MNI space and bipolar channel locations (see preprocessing) were projected at the midpoint between their contributing electrodes. Based on these MNI coordinates, the *R* package *label4MRI* v1.2 (https://github.com/yunshiuan/label4MRI) was used to categorize each channel into its corresponding Brodmann area, which were then grouped according to the DKT atlas (Klein & Tourville, 2012).

Structural imaging and regional gray matter volume. T1-weighted MRI scans were acquired as part of routine preoperative procedures. Parcellation of cortex into regions of interest (ROI) was performed based on standard procedures implemented within FreeSurfer (Fischl, 2012). Regional GMVs were then estimated based on the DKT atlas (Klein & Tourville, 2012). GMV from each ROI was calculated using FreeSurfer (Fischl, 2012). Volumes were calculated for left and right ROIs and averaged across hemispheres for analysis.

Statistical analysis. Data were imported into *R* version 4.2.3 (R Core Team, 2020) with the aid of the *tidyverse* package (Wickham et al., 2019) and analyzed using linear and nonlinear mixed-effects models fit by restricted maximum likelihood (REML) using *lme4* (Bates, 2010) and *splines* (R Core Team, 2020). *P*-values were estimated using the summary function from the *lmerTest* package, which is based on Satterthwaite's degrees of freedom (Kuznetsova et al., 2017), and effects were plotted using the package gg*effects* (Lüdecke, 2018) and *ggplot2* (Wickham & Wickham, 2016). Statistical significance was adjusted using the False Discovery Rate with an alpha threshold of .05 in analyses modeling aperiodic activity on a region-by-region basis testing hypothesis b. Task was entered as an

unordered factor using sum-to-zero contrast coding and age was specified as a continuous predictor. In our preregistration, we specified that we would apply cubic splines to age to model potential non-linear effects of age on aperiodic activity for each ROI, as well as a random effect of task-free recording type (eyes open vs eyes closed). However, in doing so, models indicated nonconvergence or singular fit. To reduce model complexity, we modeled age as a linear predictor and removed task-free recording type as a random effect in our analysis of each ROI. For analyses testing hypotheses a and b, where we tested differences in association and sensorimotor cortices, we had sufficient power to model nonlinear differences. Also note that when contrast coding is explicitly described, the need for post-hoc testing is eliminated (for a detailed discussion of contrast coding in linear mixed-effects regressions, please see (Brehm & Alday, 2022). Further, for modeled effects, an 83% confidence interval (CI) threshold was used given that this approach corresponds to the 5% significance level with non-overlapping estimates (Austin & Hux, 2002; MacGregor-Fors & Payton, 2013). In order to isolate outliers, we used Tukey's method (Tukey, 1977), which identifies outliers as exceeding ±1.5 × inter-quartile range. The packages *ggseg* (Mowinckel & Vidal-Piñeiro, 2020) and *ggsegDKT* were used to generate cortical plots based on DKT atlas nomenclature. Hypotheses a and b were tested using the following formula:

$$EEG_i = \beta_0 + \beta_1 ns(age, 2)_i * \beta_2 region_i + channel/subject_{0i} + \epsilon,$$

where *EEG* is the aperiodic estimate; *age* is age in years modeled with two spline terms, and *region* encodes association and sensorimotor cortices; *channel* encodes region-specific channels nested under the random intercept of *participant*, and *participant* is the random intercept term of participant ID. To test hypothesis c, we employed the following model equation on a region-by-region basis:

$$EEG_i = \beta_0 + \beta_1 condition_i * \beta_2 age_i + channel/subject_{0i} + task_{0i} + \epsilon,$$

where *EEG* is the aperiodic estimate; *condition* encodes task-based and task-free recordings, age is age in years as a linear predictor; *channel* encodes region-specific channels nested under *participant*, and *participant* is participant ID, while *task* is a random intercept encoding whether the recording is derived from the working memory or scene recognition tasks.

Our exploratory analyses focused on relationships between GMV, behavioral performance, and aperiodic estimates derived from task-based and task-free recordings. Here, our primary exploratory research questions were whether:

i) regional age-related variability in aperiodic neural activity predicts variability in memory performance, and;
ii) regional age-related variability in GMV predicts regional variability in aperiodic neural activity.

These exploratory analyses were examined with general linear models with the following formulae:

$$\text{(a)} \quad memory_i = \beta_0 + \beta_1 age_i * \beta_2 EEG_i + \epsilon,$$

where *memory* is performance on the visual memory task(s), *age* is age in years, and *EEG* is the aperiodic estimate from each ROI.

$$\text{(b)} \quad EEG_i = \beta_0 + \beta_1 age_i * \beta_2 volume_i + channel/subject_{0i} + task_{0i} + \epsilon,$$

Here, *EEG* is the aperiodic estimate; *age* is age in years; *volume* is regional GMV in mm^3; *channel* encodes ROI-specific channels; *participant* is participant ID; *task* encodes whether the task recording was from the scene recognition or working memory task. As with the other models, each ROI was applied to the model equation described above. *Participant* was modeled as a random effect on the intercept, while *channel* was nested under participant. *Task* were also specified as a random effect on the intercept.

Note that in our preregistration, we stated that we would include task (task-based, task-free) in all models examining the interaction between GMV and age on aperiodic activity. However, all models indicated nonconvergence or singular fits. To reduce model complexity, we examined aperiodic activity during task-based states only.

A final exploratory analysis examined the aperiodic offset. Here, we submitted the aperiodic offset to the same models that we specified for the slope, with the following formulae (the description of each fixed and random effect structure is described for the model equations presented above):

(a) $offset_i = \beta_0 + \beta_1 condition_i * \beta_2 age_i + channel/subject_{0i} + task_{0i} + \epsilon,$
(b) $memory_i = \beta_0 + \beta_1 age_i * \beta_2 offset + \epsilon,$
(c) $offset = \beta_0 + \beta_1 age_i * \beta_2 volume_i + channel/subject_{0i} + task_{0i} + \epsilon,$

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