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Frontal-posterior coherence and cognitive function in older adults☆

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ABSTRACT

The reliable measurement of brain health and cognitive function is essential in mitigating the negative effects associated with cognitive decline through early and accurate diagnosis of change. The present research explored the relationship between EEG coherence for electrodes within frontal and posterior regions, as well as coherence between frontal and posterior electrodes and performance on standard neuropsychological measures of memory and executive function. EEG coherence for eyes-closed resting-state EEG activity was calculated for delta, theta, alpha, beta, and gamma frequency bands. Participants ($N = 66$; mean age $= 67.15$ years) had their resting-state EEGs recorded and completed a neuropsychological battery that assessed memory and executive function, two cognitive domains that are significantly affected during aging. A positive relationship was observed between coherence within the frontal region and performance on measures of memory and executive function for delta and beta frequency bands. In addition, an inverse relationship was observed for coherence between frontal and posterior electrode pairs, particularly within the theta frequency band, and performance on Digit Span Sequencing, a measure of working memory. The present research supports a more substantial link between EEG coherence, rather than spectral power, and cognitive function. Continued study in this area may enable EEG to be applied broadly as a diagnostic measure of cognitive ability.

1. Introduction

In spite of the importance of early detection in mitigating the effects of cognitive decline in aging, decline is often detected too late. Though cognitive changes can be detected in laboratory testing in healthy adults in their 20s and 30s (Salthouse, 2009), rates of self-reported decline vary widely in older adults (Centers for Disease Control and Prevention, 2013; Fritsch et al., 2014). The disparity between cognitive performance in the laboratory and the subjective experiences of the individual suggests that decline likely progresses for decades prior to recognition. According to the NIH, physical changes in the brain may precede the cognitive and behavioral changes that impact daily life by as much as 20 years (NIH, 2011; see also Sperling et al., 2011). This preclinical period, prior to observable symptoms, has been identified as the most effective period for intervention to limit the impact of brain changes on the individual (Sperling et al., 2011).

Although self-reports of cognitive function vary in accuracy, changes in the physical brain during aging can be reliably detected with brain imaging methods, such as EEG and MRI (see Lemaitre et al., 2012; Sala-Llonch, Bartrés-Faz, & Jungué, 2015). Research using MRI has identified reductions in brain volume and decreases in neuronal density in healthy older adults when compared to younger adults (Driscoll et al., 2009; Scahill et al., 2003), with these reductions more pronounced in individuals with mild cognitive impairment (MCI) and Alzheimer's disease (AD; Schuff et al., 2009). In addition, research using EEG has revealed several age-related electrical changes in the brain, including a reduction in high-frequency electrical activity coupled with an increase in low-frequency electrical activity (Babiloni et al., 2006a; Klimesch, 1999), as well as reduced electrical synchronization throughout the brain (Vecchio et al., 2014), changes more pronounced in older adults with MCI and AD (Knyazeva et al., 2010; Jelles et al., 2008). Though neuroimaging measures are sensitive to changes in the brain, cost and accessibility limits their implementation in routine screenings for decline, with standard neuropsychological assessment tools and observer reports remaining the norm (e.g., Lin et al., 2013; Rajan et al., 2015).

Changes in brain connectivity may be more effective than other measures of brain function in detecting cognitive change during typical and atypical aging. Age-related decline in brain network activity measured with fMRI has been tied to a decline in verbal fluency (Dong et al., 2012), working memory, and executive function (Damoiseaux et al., 2008). Moreover, neurodegenerative disorders, such as AD and MCI have been referred to as disorders of connectivity (Sala-Llonch et al., 2015; Tóth et al., 2014), with reductions in EEG coherence observed across frequency bands (delta through gamma) for both local (e.g., frontal regions) and distant brain regions (e.g., between frontal and posterior regions; Locatelli et al., 1998; McBride et al., 2013). EEG coherence is a measure of the electrical synchronization between regions of the brain and an indicator of the functional connectivity of the underlying regions (Thatcher, North, Biver, 2005). To assess connectivity, EEG coherence

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can be measured during task-directed cognition (e.g., Sauseng, Klimesch, Schabus, & Doppelmayr, 2005), or during a resting state, when the individual is awake, but not involved in task-directed cognition (e.g., Hata et al., 2016). Assessing the resting-state has wide appeal because the measure can be completed in individuals whose cognitive ability or native language precludes testing with standard neuropsychological assessments (see Rosazza & Minati, 2011, for a review). Further, because EEG is significantly less expensive than other imaging methods (e.g., fMRI, PET), it is feasible to test larger groups, with the possibility of retesting to track longitudinal change (Babiloni et al., 2016).

Explorations of the brain's resting-state networks using fMRI have identified changes in network connectivity during typical aging (Sala-Llonch et al., 2015). Older adults demonstrate reduced network connectivity compared to younger adults, particularly in the default mode network (DMN) and the brain's attention networks (see Ferreira & Busatto, 2013 for a review; see also Sala-Llonch et al., 2015). The DMN is a set of brain regions including medial prefrontal cortex, medial and lateral temporal lobes, posterior cingulate, and posterior inferior parietal lobes that increase in activation during rest or internally directed cognition, and deactivate during externally focused, task-directed cognition (Spreng et al., 2010). In contrast, the frontoparietal attention network (FPAN) includes lateral prefrontal cortex, dorsal anterior cingulate, anterior inferior parietal lobes, as well as precuneus and anterior insula, and plays an important role in memory and executive function (Vincent et al., 2008). Both the DMN and FPAN have been associated with cognitive change in aging (Damoiseaux et al., 2008; Shaw, Schultz, Sperling, & Hedden, 2015). In addition to the age-related decreases in brain connectivity noted above, an increase in local connectivity has been recorded within frontal regions (Davis et al., 2008; Turner & Spreng, 2012) and in some cases the parietal regions (Toussaint et al., 2014) during aging. Considered together, a global decrease in network connectivity, coupled with an increase in local network connectivity, accompanies the transition into older age.

The utility of resting-state EEG as an indicator of brain function is contingent upon our increased understanding of how quantitative EEG measures are associated with performance on standard neuropsychological assessments. Existing research has linked quantitative EEG measures, such as spectral power, to neuropsychological assessment scores in older adults (e.g., Finnigan & Robertson, 2011; Roca-Stappung et al., 2012). Researchers have observed relationships between EEG spectral power and individual peak alpha frequency and cognitive function in areas such as global cognition (Babiloni et al., 2006a; Finnigan & Robertson, 2011), verbal fluency (Brickman et al., 2005), working memory (Clark et al., 2004), and IQ (Grandy et al., 2013; Roca-Stappung et al., 2012). To date, limited research has explored age-related connectivity changes in the brain or the relation between connectivity changes and performance on neuropsychological measures of cognitive function. Resting-state fMRI research has observed significant relationships between resting-state network connectivity and cognitive performance, such as memory and executive function (see Sala-Llonch et al., 2015, for a review). In this research, reductions in connectivity at rest for DMN and FPAN were associated with weaker task performance for memory, processing speed, and executive function, with stronger relationships observed for the FPAN (Shaw et al., 2015).

Specific to resting-state EEG connectivity, the relationship between coherence and IQ has been explored in younger and middle-aged adults (Silberstein et al., 2004; Thatcher et al., 2005). Thatcher et al., (2005) observed lower coherence within and between brain regions in individuals with higher IQ scores, which the researchers interpreted as evidence for greater brain complexity in individuals with higher IQs. In a recent study, Vecchio et al. (2016) explored the relationship between resting-state network connectivity and memory performance on the Digit Span (Wechsler, 2008) in AD and MCI participants, and a control group of healthy older adults. Network connectivity was assessed using a measure of small-world organization, which quantifies connectivity within local brain regions and the interconnectedness among those local regions. Participants with higher small-world organization values (higher values indicate less overall network organization) within the gamma frequency band demonstrated stronger performance on the Digit Span, suggesting that brain connectivity in the gamma band is an important factor in maintaining memory function.

Prior research has suggested that coherence between frontal and posterior brain regions may be particularly important to overall cognitive function (e.g., Babiloni et al., 2006a; Sauseng et al., 2005; Shaw et al., 2015). Sauseng et al. (2005) reported an increase in task-related coherence within posterior and between frontal and posterior brain regions as young adults performed the difficult trials in a working memory task, supporting a link between the FPAN and working memory function. When exploring age-related changes in connectivity in resting-state MRI and its link to cognition, Shaw et al. (2015) determined that connectivity within the FPAN was uniquely related to executive function performance, even after controlling for effects associated with other resting-state networks. Further, the FPAN mediated relationships between connectivity in other networks (e.g., DMN and salience network) and performance on measures of episodic memory, executive function and processing speed. Altered connectivity between distant brain regions, such as the frontal and parietal regions, has been consistently observed in MCI and AD groups (see Babiloni et al., 2016, for a review). Decreases in synchronization likelihood, a measure of linear and nonlinear connectivity, are evident between frontal and parietal regions in MCI and AD patient groups when compared to older adults experiencing typical aging, with greater reductions evident in individuals with the weakest scores on the MMSE (Babiloni et al., 2006b; Tóth et al., 2014). Together, these findings suggest that coherence within and between frontal and posterior brain regions may be of value in understanding the health of the physical brain and the potential for sustained cognition during aging.

The present research explored the relationship between resting-state EEG coherence within and between frontal and posterior brain regions and measures of cognitive ability that targeted executive function and memory. Older adults with no prior history of dementia had their resting-state EEG activity recorded and, in a separate session, completed a neuropsychological battery comprised of executive function and memory measures. Memory and executive function are two cognitive domains that decline during typical aging and in which an acceleration in the rate of decline is predictive of subsequent dementia five to ten years prior to diagnosis (e.g., Grober et al., 2008; Howieson et al., 2008). Memory measures evaluated long-term and short-term memory components, to include working memory. Because prior research has identified an important role for the FPAN in memory and executive function processes (Vincent et al., 2008), we expected that the FPAN would underlie important EEG coherence findings here. Consistent with existing research reporting differences in brain coherence in healthy older adults versus individuals with AD and MCI (e.g., Babiloni et al., in press; Jelles et al., 2008; Stam et al., 2005), we predicted that higher resting-state EEG coherence within frontal and posterior regions, and between these regions, would be associated with stronger performance on neuropsychological assessments.

In addition, we predicted several unique relationships between neuropsychological test performance and EEG coherence in specific frequency bands. An extensive body of research has established a clear relationship between task-related theta power and coherence and the specific working memory demands of the task (Jensen & Tesche, 2002; Sauseng et al., 2010; Toth et al., 2012). Therefore, we predicted that resting-state theta coherence would correlate with performance on the Digit Span subtests that placed the greatest demands on working memory, in this case the Backwards and Sequencing subtests. Further, in light of prior research that specifically identified resting-state gamma coherence as a correlate of memory performance on the Forward and Backward subtests of the Digit Span in older adults (Vecchio et al., 2016), we expected to replicate this effect in the gamma frequency band. Finally, increased delta synchronization has been observed during memory encoding and maintenance in a range of memory tasks, including working memory and episodic memory (e.g., Imperatori et al., 2014; Toth et al., 2012), as well as during tasks that require sustained concentration (Harmony, 2013). Therefore, we predicted that delta, more so than other frequencies, would be associated with performance on the California Verbal Learning Test (Delis et al., 2000), a measure of long-term memory, and would also be related to performance on the Verbal Fluency Measures (Delis et al., 2001) of executive function, which require the rapid and targeted retrieval of category members.

2. Material and methods

2.1. Participants

Data were collected from 100 participants from southern New Jersey. Participants were volunteers recruited via newspaper advertisement (they were not paid for their involvement), were right handed (as verified by scores on the Edinburgh Handedness Inventory; Oldfield, 1971), had normal or corrected hearing and vision, and no prior history of dementia. To increase the likelihood that we were testing adults experiencing normal aging, we excluded participants who self-reported any history of traumatic brain injury, stroke, or neurological disorder; two or more concussions; a history of drug or alcohol abuse; or the current use of medications for the treatment of anxiety or depression. Further, we excluded participants with scores <26 on the Mini Mental State Examination – 2nd Edition (MMSE-2; Folstein et al., 2010). Scores <26 on the MMSE are generally considered indicative of MCI (e.g., Vertesi et al., 2001). After applying the above criteria, data from 66 participants were retained for analysis. Forty-two members of the sample were female (63.63%), and the majority of participants tested were Caucasian (95%). Participants' mean age was 67.15 years ($SD = 9.16$). Additional demographics are reported in Table 1.

2.2. Materials

2.2.1. EEG

EEG data were recorded using a HydroCel Geodesic Sensor Net, with Cz reference (Electrical Geodesics, Inc.). Sensor impedance levels were below 50 KΩ, appropriate for use with the Net Amps 300 high-impedance amplifier. Data were sampled at 250 Hz, and filtered using an analog 0.1–0.100 Hz bandpass filter. Three minutes of eyes-closed data were recorded from each participant using Net Station 4.2 software. Data from the 19 channels in the 10–20 electrode system of placement were exported from Net Station for artifact removal and data reduction using Neuroguide 2.6.5 (Applied Neuroscience, Inc.; Thatcher, 2015). Data were re-referenced to linked mastoids and each participant's EEG record was visually inspected for artifact and the first 90 s of clean EGG data were selected for additional processing.

All coherence calculations were performed in Neuroguide for the following frequency bands: delta (1.0–4.0 Hz), theta (4.0–8.0 Hz), alpha (8.0–12.0 Hz), beta (12.5–25.0 Hz) and gamma (30.0–50.0 Hz) (see Thatcher, 2012). As described in Thatcher (2012), coherence was calculated as the spectral cross correlation between electrodes, normalized by the electrodes' power spectra.

A selection of frontal and posterior electrodes were include in the coherence analyses and mirrored the array used by Sauseng et al. (2005) in their research exploring coherence within and between frontal and posterior brain regions. Frontal electrodes included frontal pole electrodes FP1 and FP2, as well as frontal electrodes F3, F4, and Fz. Posterior electrodes included parietal electrodes P3, P4, and Pz, as well as occipital electrodes O1, and O2 (see Fig. 1). Coherence was calculated for electrode pairs within the frontal region and separately for electrode pairs within the posterior region. In addition, coherence between frontal and posterior electrode pairs was explored by examining each frontal electrode in combination with each of the five posterior electrodes (for FP1: FP1-P3, FP1-P4, FP1-Pz, FP1-O1, FP1-O2). In sum, 45 coherence values were calculated per frequency band, 10 coherence values within each region, frontal and posterior, and 25 between frontal and posterior regions.

Table 1
Descriptive statistics – demographics.

Variable	Frequency	Mean	Range	SE	SD
Gender					
Male	24 (36.4%)				
Female	42 (63.6%)				
Age		67.15	50–88	1.128	9.162
Education (years)		15.18	8–20	0.339	2.751
WAIS-II (FSIQ-2)		111.23	81–139	1.608	13.064
MMSE-II		28.29	26–30	0.161	1.310
Clock drawing					
Normal	58 (87.9%)				
Abnormal	8 (12.1%)				

2.2.2. Neuropsychological measures

The neuropsychological battery administered in conjunction with the present research contained measures of global cognition (MMSE-2 (Folstein et al., 2010) and The Clock Drawing Test (Strauss et al., 2006)), intelligence (WAIS-II (Wechsler, 2011), memory and executive function. Table 1 contains the descriptive statistics for all neuropsychological measures. The memory and executive function measures are detailed below.

2.2.2.1. Memory. The Digit Span subtest of the Wechsler Adult Intelligence Scale-Fourth Edition (WAIS – IV; Wechsler, 2008) and the California Verbal Learning Test – Second Edition (CVLT-II; Delis et al., 2000) were administered to assess working memory and long-term memory function. For the Digit Span, individuals were read a series of numbers and were asked to repeat those numbers in the same order (forward), in reverse order (backwards) or in ascending order (sequencing), for the respective sections of the assessment.

The CVLT-II (Delis et al., 2000) is an assessment of learning (memory encoding) and retention (memory storage) of verbal material in long-term memory. Specifically, individuals were asked to learn a list of 16 words from four categories in five trials, with each trial including list

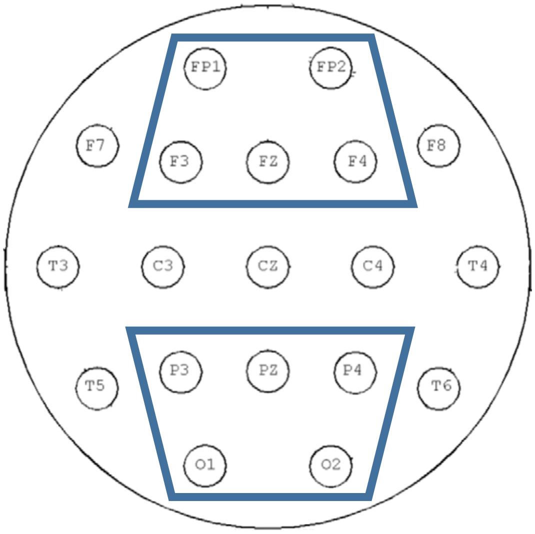


Fig. 1. Frontal and posterior electrode array Frontal and posterior electrodes included in the coherence analyses. Frontal electrodes included frontal pole electrodes FP1 and FP2, as well as frontal electrodes F3, F4, and Fz. Posterior electrodes included parietal electrodes P3, P4, and Pz, as well as occipital electrodes O1 and O2.

presentation and list recall, and to subsequently recall those words after a brief distractor task (short-term recall) and again after a 20-min delay (long-term recall). For the current research, the number of items recalled during the encoding phase for trials 1–5 were summed to generate a CVLT-II Trials I–V score. In addition, the total number of list items recalled after the 20-min delay (CVLT-II Delayed Recall) and the total number of errors during the delayed recognition test (CVLT-II False Positives) were included as measures of long-term memory.

2.2.2.2. Executive function. To determine participants' abilities in flexible thinking, strategy use, and related processes, participants completed the Delis-Kaplan Executive Function System (D-KEFS) Verbal Fluency Test (Delis et al., 2001), as well as The Trail Making Test (Reitan & Wolfson, 1993). In the first portion of the Verbal Fluency Test, Letter Fluency, participants were asked to generate as many words as possible that began with a specific letter in 60 s, with three letter trials provided. In the second phase, Category Fluency, participants were asked to generate as many category members as possible in 60 s, with two category trials presented. Finally, in the final phase, Category Switching, participants were asked to generate words from two different categories simultaneously, alternating back and forth between the categories. In the present research, the total number of unique, correct responses were summed to generate total scores for Letter Fluency and Category Fluency.

The Trail Making Test (Reitan & Wolfson, 1993) is part of the standard administration of the Halstead-Reitan Neuropsychological Test Battery. In Trails A, individuals are asked to connect, in numerical order, encircled numbers that are randomly presented on a page. Then, in Trails B, participants are asked to connect encircled numbers and letters in alternating order (e.g., 1 to A, A to 2, 2 to B). Both trials were timed and Trails A and Trails B completion times were used as performance indicators.

2.3. Procedure

The research procedure for the project was approved by Stockton University's Institutional Review Board. Participants completed two research sessions each lasting 1–1.5 h in duration, scheduled 1–2 weeks apart (mean intersession interval = 9.2 days; *SD* = 4.09). All participants completed the EEG recording and self-report measures as part of Session 1, followed by the neuropsychological assessments of thinking and memory in Session 2. Session 1 began with participants providing written informed consent. Experimenters then reviewed participants' responses on a comprehensive demographics form completed at home by participants prior to the session that included questions about health, activities of daily life, and general demographics. After this was complete, participants had their eyes-closed, resting-state EEG activity recorded for 3min. Prior to the recording, participants were asked to sit in a relaxed position and to keep their minds free from other thoughts. Participants were visually monitored for adherence to the instructions, as well as drowsiness during the recording session. After the EEG recording concluded, participants completed four self-report measures of mood and cognition. Scores on the self-report measures were not analyzed further and are not detailed in this report.

The battery of neuropsychological measures was administered during Session 2. All participants completed the neuropsychological measures in the same order: (a) MMSE-II, (b) Digit Span, (c) CVLT-II, (d) Trails A and B, (e) WASI-II – Matrix Reasoning Subscale, (f) The Clock Drawing Test, (g) CVLT-II – 20-min delayed recall and recognition, (h) WASI-II – Verbal Subscale, and (i) Verbal Fluency. After completing the assessments, participants were debriefed, thanked for their participation, and the session concluded. We note that participants who scored 2.0 or more standard deviations below their age-appropriate mean on any one assessment, or 1.5 standard deviations below their age-appropriate mean on two or more assessments, were sent a letter recommending a follow-up assessment in the community.

Table 2
Descriptive statistics – neuropsychological assessments.

Variable	Mean	Range	SE	SD
Digit Span Forward	11.53	7–16	0.287	2.335
Digit Span Backward	8.56	4–14	0.287	2.334
Digit Span Sequencing	8.06	4–12	0.188	1.528
Digit Span Total	28.15	18–39	0.612	4.971
CVLT-II Trials I-V	46.94	23–77	1.227	9.969
CVLT-II Delayed Recall	10.05	2–16	0.388	3.150
CLVT-II False Positives	2.80	0–14	0.442	3.592
Letter Fluency	41.32	15–86	1.606	13.044
Category Fluency	39.58	16–56	0.987	8.017
Trails A Time (seconds)	30.97	14.04–65.24	1.229	9.912
Trails B Time (seconds)	71.51	33.47–148.31	3.218	26.144

3. Results

3.1. Neuropsychological data

Descriptive statistics for all neuropsychological assessment variables used in our analyses are available in Table 2. To streamline the interpretation of significant relationships, scores on Trails A and Trails B (completion time in seconds) and CVLT-II False Positives (number of items incorrectly recognized as study-list items) were inverted prior to analysis so that higher scores reflected stronger cognitive function for all assessment variables in the dataset. In addition, we tested all neuropsychological variables for violations of normality and linearity. The measure of CVLT-II False Positives was positively skewed and subject to a base 10 logarithmic transformation to ensure a normal distribution prior to data analysis (Tabachnick & Fidell, 2013). Explorations for univariate outliers revealed no outliers for the neuropsychological variables.

3.2. Analysis overview

Power spectra for the frontal and posterior electrodes are presented in Fig. 2. Partial correlation analyses controlling for age were used to explore the relation between neuropsychological test performance and measures of EEG coherence, while controlling for any effects on this relationship that stem from age. Because the sample size in our analyses was small for partial correlation ($N = 66$), we focused on correlation results associated with a medium effect size or higher ($r_p > |0.30|$) and a significance level <0.01 (two-tailed). In an attempt to distinguish contributions from the frontoparietal attention and default mode networks for significant correlation results between coherence and test performance, William's t tests (Weaver & Wuensch, 2013) were conducted to compare the strength of the correlations between midline and lateral frontal electrode pairs and neuropsychological test performance. Finally, in addition to analyses exploring coherence, we examined the relationship between absolute power and cognitive performance for the frontal and posterior electrode sites included in the coherence analyses presented below.

To test our hypotheses that coherence would be positively correlated with neuropsychological test performance, we explored the relationship between each measure of cognitive function and coherence, for delta, theta, alpha, beta, and gamma frequency bands. Significant partial correlations between coherence and neuropsychological test performance are reported in Table 3. All electrode pairs presented in bold reflect r_p values of 0.30 or higher, with pairs presented in red indicating inverse relationships between the electrode pair's coherence and the associated neuropsychological assessment. A graphical representation of the relationships is included in Fig. 3. Finally, when significant relationships were observed between coherence and neuropsychological measures, the partial correlation result for the strongest outcome is presented in detail, along with a scatterplot reflecting the pairwise relationship for participants. (See Fig. 4.)

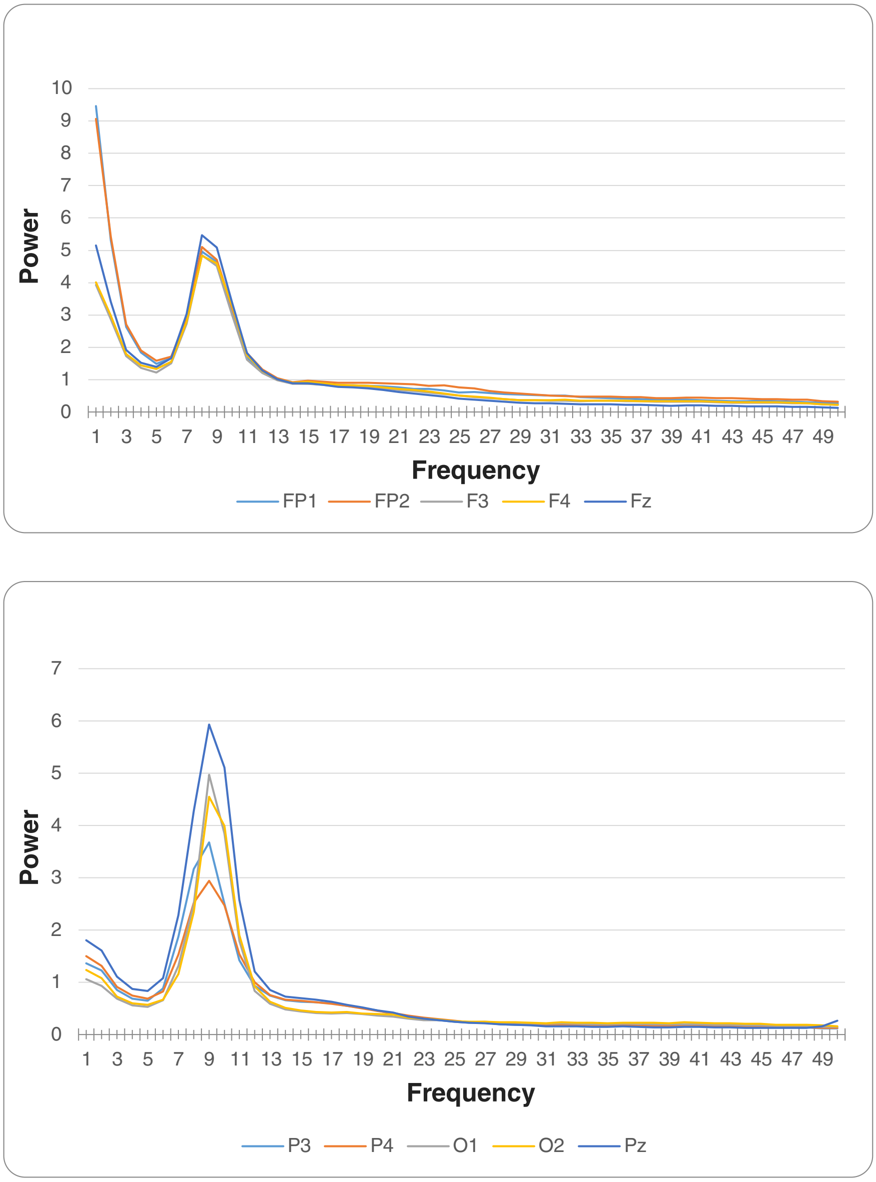


Fig. 2. Power spectra for frontal and posterior electrodes.

3.3. Memory results

3.3.1. Digit span

We explored the relationship between EEG coherence and scores on the Digit Span, a measure of working memory function. Performance on the Digit Span Forward subtest was positively correlated with frontal coherence for beta and gamma frequency bands, with the strongest relationship evident in the gamma frequency band (F4-Fz; $r_p = 0.428$, $p < 0.001$). No significant relationships were detected between Backward Digit Span performance and coherence. Digit Span Sequencing performance, however, was significantly correlated with frontal beta coherence, posterior gamma coherence, and coherence between frontal and posterior electrode locations for all frequency bands, with the exception of alpha. Digit Span Sequencing scores were positively correlated with frontal beta coherence (FP1-F3; $r_p = 0.326$, $p = 0.008$), but negatively correlated with posterior gamma coherence (P4-O1; $r_p = -0.367$, $p = 0.003$). Coherence for frontal-posterior electrode combinations across frequency bands was negatively correlated with task performance, with the strongest pattern emerging for the theta frequency band (F3-O2; $r_p = -0.417$, $p < 0.001$).

3.3.2. CVLT-Ii

Next, we assessed the relationship between EEG coherence and performance on the CVLT-II, a measure of long-term memory. No significant relationships were observed between CVLT-II Trials I–V or CVLT-II Delayed Recall and coherence for any of the frequency bands. Partial correlations of |0.30| or higher were present between CVLT-II Trials I–V scores and frontal delta coherence, but these relationships failed to achieve the 0.01 significance threshold. We did observe significant positive correlations between CVLT-False Positive scores and frontal and posterior delta coherence (frontal: FP1-F3; $r_p = 0.332$, $p = 0.007$; posterior: P4-O2; $r_p = 0.333$, $p = 0.007$), but we failed to find relationships between CVLT-II False Positive scores and coherence for any of the remaining frequency bands.

3.3.3. Memory summary

Greater resting-state EEG coherence among frontal electrode pairs for the beta frequency band was associated with stronger task performance for Forward and Sequencing subtests of the Digit Span. In addition, lower coherence values between frontal and posterior electrode pairs was associated with stronger task

Table 3
Partial correlations (controlling for age) between coherence and assessment scores.

	Digit span			CVLT			Verbal fluency		Trails	
Frequency	**Forward**	**Backward**	**Sequencing**	**Trials I–V**	**Recall**	**False positives**	**Letter**	**Category**	**Trails A**	**Trails B**
Delta										
Frontal		FP1-F4	F4-Fz	FP1-F3 **FP1-Fz** **FP2-F4** FP2-Fz F4-Fz	FP1-Fz F4-Fz	**FP1-F3**** **FP1-Fz** FP2-Fz F3-Fz F4-Fz	F3-Fz	FP1-F3 FP2-F3 F3-F4 **F3-Fz***** **F4-Fz****	F3-Fz	F3-Fz **F4-Fz****
Posterior			P4-O1		O2-Pz	**P3-O2**** **P3-Pz** **P4-O2**** **O2-Pz**				
Frontal-Posterior			FP1-F4 FP1-O2 FP1-Pz **F3-O1**** **F3-O2**** Fz-O1							FP1-Pz FP2-P4 FP2-Pz F3-Pz
Theta										
Frontal	FP1-Fz							F3-Fz		
Posterior		P4-O2	P3-P4 **P4-O1**** O1-O2							
Frontal-posterior			**FP1-P3**** **FP1-P4***** FP1-O1 **FP1-O2**** **FP1-Pz**** **FP2-P3**** **FP2-P4**** **FP2-O2***** **FP2-Pz**** F3-P3 **F3-P4**** **F3-O1***** **F3-O2***** F3-Pz F4-P3 F4-P4 **F4-O1**** **F4-O2***** F4-Pz Fz-P3 **Fz-P4**** **Fz-O1**** **Fz-O2***** Fz-Pz						FP1-O1 **FP2-O1*** F3-O2 **F4-O1**** F4-O2 Fz-O1	FP2-O1
Alpha										
Frontal							FP1-F3 F3-Fz	FP1-F3		
Posterior						P4-O2				
Frontal-Posterior		F4-P4 Fz-P4								
Beta										
Frontal	FP1-F3 FP1-F4 FP1-Fz		**FP1-F3**** FP1-Fz FP2-F4				F3-Fz		FP1-Fz F3-Fz	FP1-FP2 **FP1-F3**** FP1-F4

Table 3 (*continued*)

	Digit Span			CVLT			Verbal Fluency		Trails	
Frequency	**Forward**	**Backward**	**Sequencing**	**Trials I–V**	**Recall**	**False Positives**	**Letter**	**Category**	**Trails A**	**Trails B**
	FP2-F3 **FP2-F4**** FP2-Fz F3-Fz **F4-Fz****									**FP1-Fz***** **FP2-F3** FP2-F4 **FP2-Fz****
Posterior			P3-P4 **P4-O1**** **O1-O2****							
Frontal-posterior			**FP1-P4**** **FP1-Pz** PF2-P3 FP2-P4 FP2-Pz **F3-P4**** F3-O1 F3-O2 **F3-Pz** F4-P3 **F4-O2**** F4-Pz **Fz-P4**** Fz-O1 **Fz-O2**** **Fz-Pz**							
Gamma										
Frontal	FP1-FP2 **FP1-F4**** FP1-Fz **FP2-F3**** **FP2-F4***** FP2-Fz **F3-F4**** **F3-Fz**** **F4-Fz*****									
Posterior			**P3-P4** **P4-O1**** **O1-O2**** O1-Pz							
Frontal-Posterior			F3-P4 F3-O1 F3-O2 F4-O1 F4-O2 F4-Pz **Fz-O1** **Fz-O2**** Fz-Pz							

$^{**}p < .01$, $^{***}p < .001$

Results include all partial correlations between coherence and neuropsychological assessment scoreswith significance levels of .05 or lower. All results presented in bold show relationships with medium effect sizes (r_p= .30) or higher. Electrode pairs presented in red indicate inverse relationships.

Results include all partial correlations between coherence and neuropsychological assessment scores with significance levels of 0.05 or lower. All results presented in bold show relationships with medium effect sizes ($r_p = 0.30$) or higher. Electrode pairs presented in red indicate inverse relationships.

performance for the more challenging Digit Span Sequencing trials, but unrelated to performance for Forward and Backward subtests. In contrast, for long-term memory, greater resting-state EEG coherence in the delta frequency band within frontal and posterior regions was associated with stronger task performance, reflected in fewer CVLT-II False Positive errors during the delayed recognition test.

3.4. Executive function results

3.4.1. Verbal fluency

No significant relationships were observed between Letter Fluency performance and any of the resting-state EEG coherence measures. However, a significant positive correlation was found between Category Fluency scores and frontal coherence in the delta frequency band (F3-

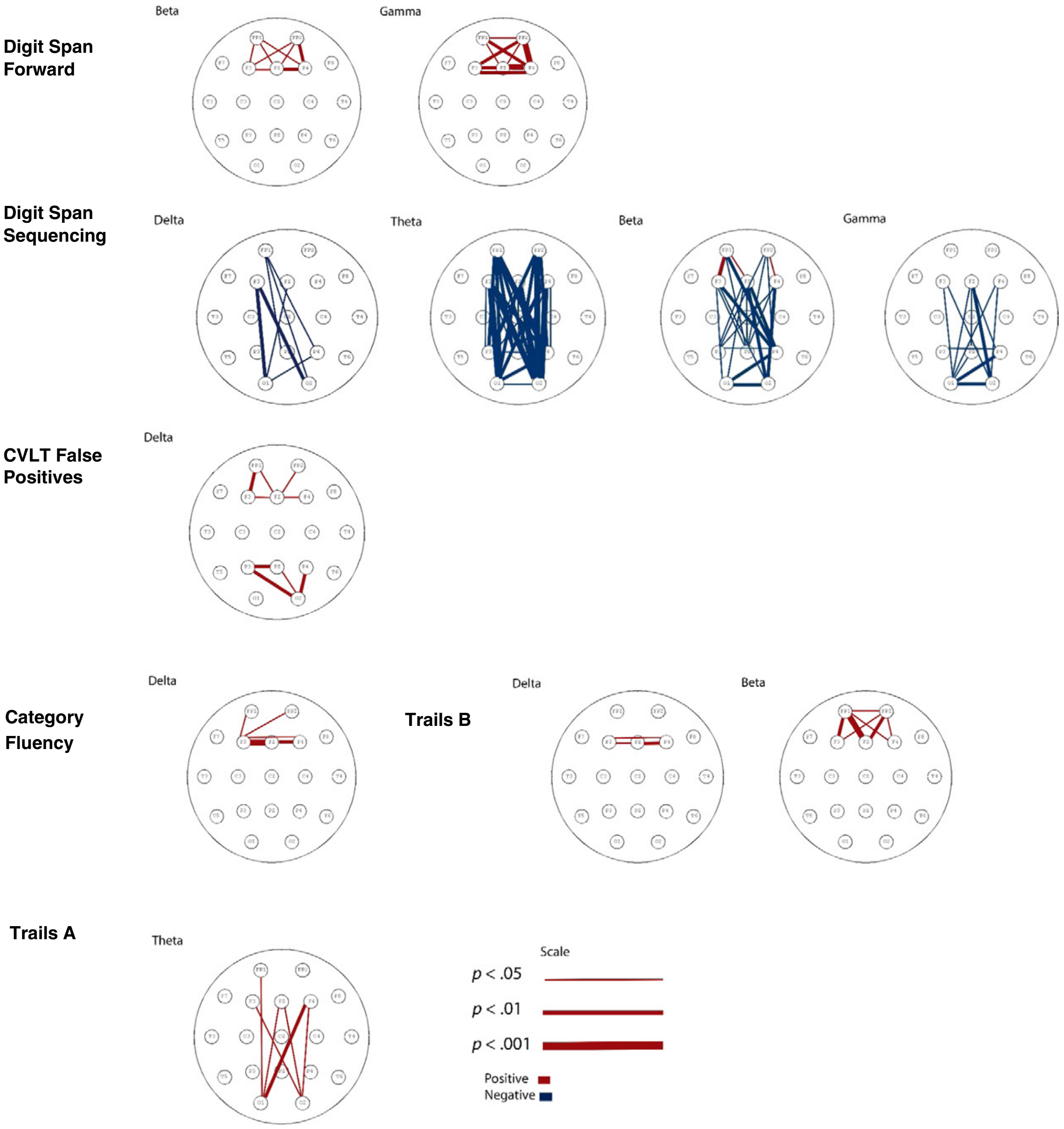


Fig. 3. Coherence and neuropsychological assessment scores. Significant partial correlations between coherence and neuropsychological assessment scores by frequency band. We observed significant positive correlations between frontal coherence and assessment scores for delta and CVLT – False Positives, Category Fluency, and Trails B; for beta and Digit Span Forward and Trails B; and for gamma and Digit Span Forward. Significant positive correlations were found between posterior coherence for delta and CVLT – False Positives, while significant negative relationships were observed between posterior gamma coherence and Digit Span Sequencing. Finally, significant inverse relationships were observed for coherence between frontal and posterior regions and Digit Span Sequencing for delta, theta, beta and gamma frequency bands.

Fz; $r_p = 0.407$, $p = 0.001$). No other significant relationships between Category Fluency and coherence were detected.

3.4.2. Trails B

Finally, Trails B scores were positively correlated with frontal coherence in delta and beta frequency bands, with the strongest relationships emerging for the beta frequency band (FP1-Fz; $r_p = 0.425$, $p < 0.001$). Significant relationships were not detected outside the frontal region for delta or beta frequency bands, and no significant relationships were observed between Trails B completion times and coherence for any other frequency.

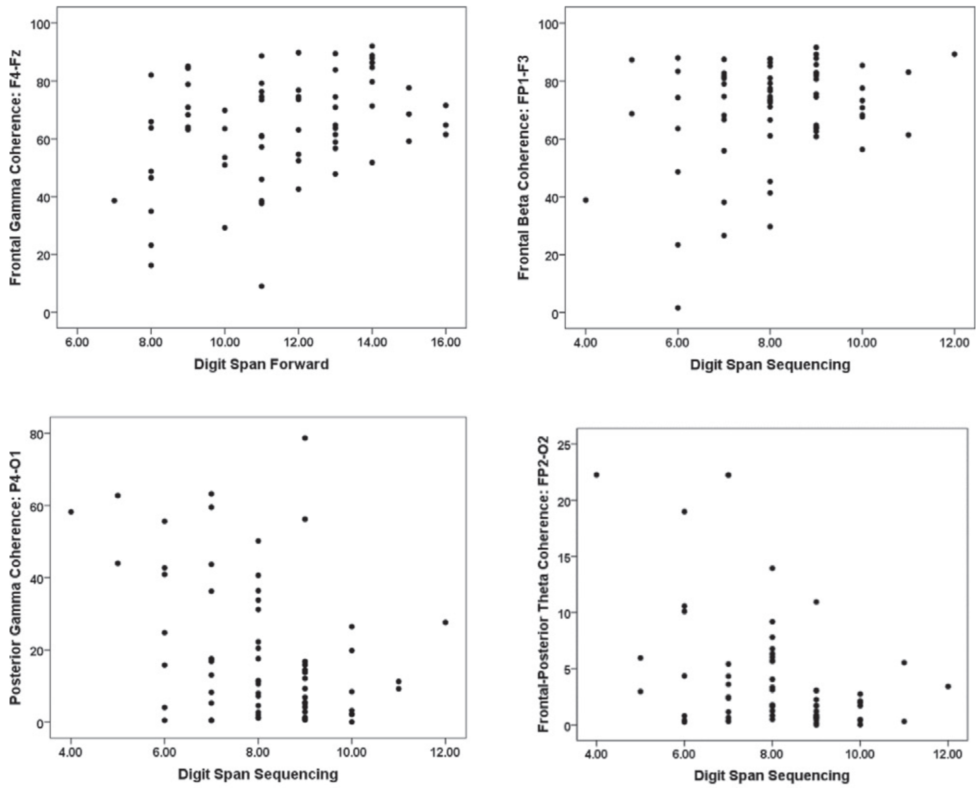
3.4.3. Trails A

We note that performance on Trails A, a measure of processing speed rather than executive function, was positively correlated with theta coherence between frontal and posterior brain regions (F4-O1; $r_p = 0.336$, $p = 0.007$). This was the only significant relationship observed between Trails A completion times and coherence.

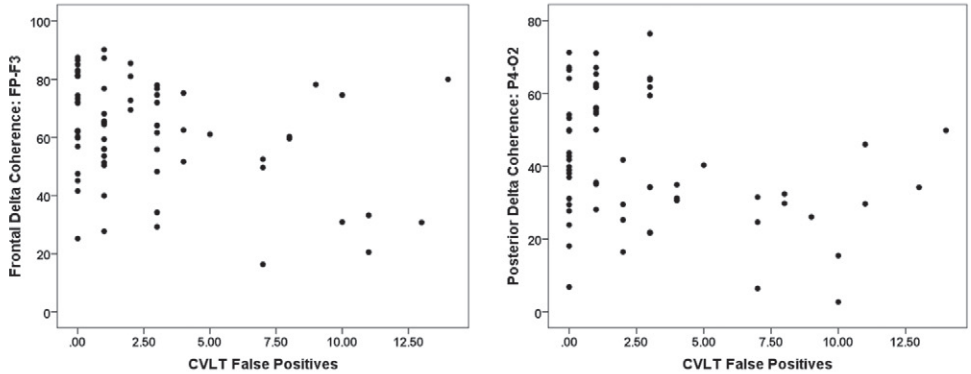
3.4.4. Executive function summary

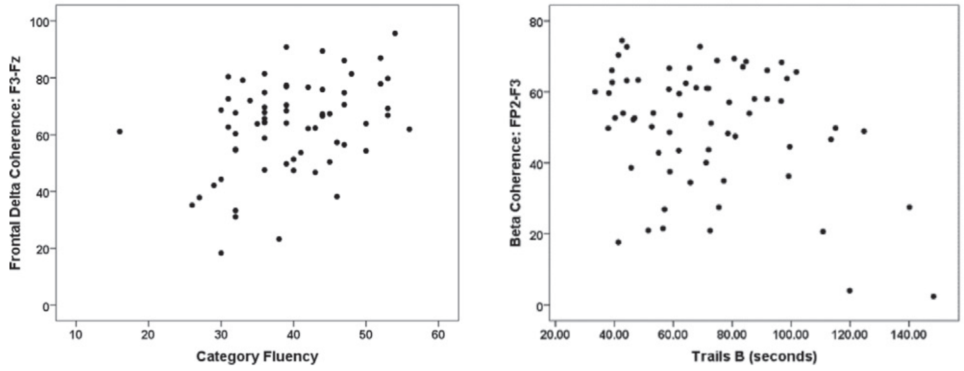
Strong performance on the Category Fluency task was associated with greater delta coherence within the frontal region of the brain. Increased frontal delta coherence was also related to improved completion times on Trails B, as was coherence in the beta frequency band.

Digit Span



CVLT




Verbal Fluency

Trails B

Fig. 4. Scatterplots reflecting relationships between coherence and neuropsychological test performance.

3.5. Medial and lateral coherence and cognitive function

To determine if significant relationships between frontal coherence and cognitive function are more likely attributed to the frontoparietal attention network (FPAN) or the default mode network (DMN), the strength of the relationships between medial (Fz-FP1 and Fz-FP2) and lateral (F3-F7 and F4-F8) electrode pairs and neuropsychological test performance were compared using William's tests for non-independent correlations (see Weaver & Wuensch, 2013, for a review). Specifically, the strength of the relationships for medial and lateral electrode pairs were tested separated for each hemisphere, comparing the coherence between Fz-FP1 and F3-F7 pairs in the left hemisphere and Fz-FP2 and F4-F8 pairs in the right hemisphere. Prior to alpha correction, significant differences were observed between medial and lateral electrode pairs in the left hemisphere and Category Fluency scores in theta and alpha frequency bands (theta: $t(63) = -2.89$, $p = 0.005$; alpha: $t(63) = -2.31$, $p = 0.024$). In addition, right medial and lateral differences were observed for the Backwards subtest of the Digit Span and Trails B completion times in the theta frequency band (Digit Span: $t(63) = -2.02$, $p = 0.048$; Trails B: $t(63) = -2.20$, $p = 0.032$). In the beta frequency band, significant differences were observed between medial and lateral left frontal pairs and CVLT Delayed Recall performance ($t(63) = -2.17$, $p = 0.034$), as well as between medial and lateral right frontal pairs and CVLT Trials 1-V scores ($t(63) = -2.59$, $p = 0.012$). Finally, in the gamma band, differences were observed between medial and lateral right frontal electrode sites and performance on CVLT Trials I—V ($t(63) = -2.96$, $p = 0.004$), as well as CVLT Delayed Recall ($t(63) = -2.18$, $p = 0.033$). No significant differences were found for the delta frequency band. For all significant differences noted above, the relationship between coherence for lateral electrode pairs and test performance was stronger than the relationship between coherence for medial electrode pairs and test performance. Although this pattern generally supports the FPAN over the DMN as a correlate of test performance, we note that none of the above relationships remained significant when using a corrected alpha level for multiple comparisons.

3.6 Power and cognitive function

To assist in our interpretation of the coherence results above, we explored the relationship between absolute power at the five frontal and five posterior electrode locations in the design and cognitive function (see Table 4). Using partial correlation analyses, as were used in our coherence analyses above, two clusters of significant relationships emerged. The first was a significant inverse relationship between posterior delta power and performance on CVLT-II Trials I–V and CVLT-II Delayed Recall. For coherence, however, relationships between delta coherence and CVLT performance were limited to positive relationships between CVLT-II False Positives scores and coherence for frontal and posterior regions.

Lower delta power over posterior electrode sites was also correlated with enhanced performance on Trails A, the measure of processing speed. For coherence, however, performance on this measure was unrelated to delta coherence for frontal or posterior regions.

Finally, there was a cluster of effects between beta power at frontal and posterior electrode sites and performance on the CVLT-II. An inverse relationship between beta power and task performance for CVLT-II Trials I–V and CVLT-II Delayed Recall scores suggests that higher scores on the long-term memory assessment were associated with lower beta power in these regions; however, none of the relationships for beta power was significant at the 0.01 significance threshold.

4. Discussion

Our primary objective was to explore the relationship between resting-state EEG coherence and neuropsychological test performance to assess the value of EEG coherence as an indicator of brain health and cognitive ability; in doing so we found a number of significant relationships. Consistent with our prediction, increased coherence among frontal electrodes was associated with stronger cognitive function. This pattern was detected between delta coherence and CVLT False Positive, Category Fluency, and Trails B scores; between beta coherence and Forward and Sequencing subtests of the Digit Span, and Trails B scores; and between gamma coherence and the Forward subtest of the Digit Span. However, the findings for the relationship between posterior coherence and cognitive function were mixed. Although posterior delta coherence was positively correlated with CVLT False Positive scores, posterior gamma coherence was inversely related to performance on the Sequencing subtest of the Digit Span. Finally, contrary to our prediction, we observed an inverse relationship between frontal-posterior coherence and performance on the Sequencing subtest of the Digit Span. This relationship was strongest in the theta frequency band and present for all frequencies except alpha. We consider these findings in turn below.

In the present research, resting-state delta coherence among frontal electrode sites was significantly related to long-term memory and verbal fluency performance, relationships we believe are driven by the important role of strategy use in these tasks. The frontal lobes contribute significantly to the application of strategies during memory encoding and retrieval, with the dorsolateral prefrontal cortex performing a larger role in memory encoding and retrieval when the content to be remembered is presented without context, as in word lists (see Baldo & Shimamura, 2002; Fletcher et al., 1998). Like most assessments of long-term memory, the CVLT requires the individual to learn a list of words from several different categories, with performance contingent on the individual's ability to identify the relevant categories during study-list presentation and to use these categories to facilitate encoding and subsequent retrieval. Strategy use is also essential to successful performance on the Category Fluency task, where the application of strategies is needed to facilitate the organized retrieval of target items while simultaneously remembering which targets have already been offered as responses. Finally, we note that posterior brain regions, including the inferior parietal lobe, intraparietal sulcus, and precuneus have been associated with memory retrieval processes (Wagner et al., 2005), and may underlie the positive relationship between posterior delta coherence and CVLT retrieval accuracy observed in the present research.

As in the delta frequency band, several relationships were observed between beta coherence and cognitive function. Resting-state beta coherence among frontal electrode sites was associated with performance on short-term and working memory components of the Digit Span and the Trails B measure of executive function, relationships that may stem from beta's role in attention and response inhibition. Prior research has associated activity in the beta frequency band with visual attention (Bekisz & Wróbel, 2003), task-directed arousal (Güntekin et al., 2013), and response inhibition (Huster et al., 2013). Güntekin et al. (2013) reported global increases in beta power and synchronization for target trials during the oddball task, which the researchers interpreted as a shift to a task-ready state for target trials. Therefore, we speculate that the link between beta coherence and Digit Span performance in the present research may reflect the role of beta in the modulation of attention necessary to encode and manipulate content in memory. Prior research has also observed increases in beta power and coherence between the inferior frontal lobes and motor cortices during successful response inhibitions in the go/no-go task (e.g., Swann et al., 2012). Further, research has recently established a relationship between greater resting-state beta power over the right frontal lobe and improved performance on a figural version of the Trail Making Test (Foster et al., 2015). Trails B requires an individual to connect a series of numbers and letters in ascending order, while alternating between numbers and letters in the progression (e.g., A-1-B-2). In light of the above findings, we suggest that frontal beta coherence in the brain at rest may be an indicator of an individual's ability to inhibit competing responses during task-directed cognition.

Table 4
Partial correlations (controlling for age) between absolute power and assessment scores.

	Digit span			CVLT			Verbal fluency		Trails	
Frequency	**Forward**	**Backward**	**Sequencing**	**Trials I–V**	**Recall**	**False positives**	**Letter**	**Category**	**Trails A**	**Trails B**
					Delta					
Frontal				F4						
Posterior				P3 **P4**** **Pz**** O2	P3 **P4**** **O2****	O2			**P3**** **P4** **Pz**** **O2****	**O2**
					Alpha					
Frontal										
Posterior				P4						
					Beta					
Frontal				F3 F4 Fz	F3 **F4** Fz					**FP2**
Posterior				P3 **P4** O2	P3 **P3** Pz **O2**	P4				
					Gamma					
Frontal	**FP1****	FP2		F3	F3					FP1 **PF2****
Posterior		O2		O2	O2		O2		P3 Pz	

** *p*< .01

Results include all partial correlations with significance levels of .05 or lower. All results presented in bold show relationships with medium effect sizes (*r*= .30) or higher. All significant correlations between absolute power and test performance reflected inverse relationships.

Results include all partial correlations with significance levels of 0.05 or lower. All results presented in bold show relationships with medium effect sizes ($r = 0.30$) or higher. All significant correlations between absolute power and test performance reflected inverse relationships.

Unlike the broader roles of delta and beta coherence in cognitive function noted above, the relationship between resting-state gamma coherence and cognitive performance in the present research was limited to short-term and working memory components of the Digit Span. The positive relationship we detected between frontal gamma coherence and performance on the Forward subtest of the Digit Span extends prior research reported by Vecchio et al. (2016) that identified connectivity in the gamma frequency band as a correlate of short-term memory performance. Though we identified a positive relationship between frontal gamma coherence and Forward Digit Span scores, we also observed an inverse relationship between gamma coherence over posterior electrode sites and Sequencing Digit Span scores. Gamma activity has been generally associated with episodic encoding and retrieval and specifically linked to the maintenance phase of working memory (Roux & Uhlhaas, 2014), with gamma activity during the maintenance interval associated with the right intraparietal lobe and left dorsolateral and medial prefrontal cortex (Roux et al., 2012). Thus, lower resting-state gamma coherence over posterior regions in the present research may be associated with posterior memory regions and reflect an individual's ability for memory maintenance during cognition.

For delta, beta, and gamma coherence, a pattern emerged in which greater local coherence within frontal regions was associated with superior performance on measures of cognitive function. Several theories have been proposed to explain how the increased local connectivity that occurs in older adults (Sala-Llonch et al., 2015) is related to cognition. One suggestion is that an increase in regional connectivity (e.g., within the frontal lobes) during healthy aging could be a compensatory mechanism (Turner & Spreng, 2012), recruiting more of the region in support of sustained cognition, though other theories have interpreted this increase as evidence for a loss of specialized processing within the region (Park et al., 2004). In prior research, Vecchio et al. (2014) interpreted the increase in coherence in their participants in delta and theta frequency bands as a reflection of cognitive decline. Although Vecchio et al. speculate that the increase in coherence in slower brain frequencies is a byproduct of disconnection that occurs as the brain ages, our findings support a favorable relationship between increased local delta coherence within frontal and posterior regions and cognitive function in long-term memory and executive function domains. In line with other reports (see Babiloni et al., in press, for a review), our findings indicate that sustained local coherence in frontal regions is essential in the ability to maintain strong cognition and that the deterioration of local coherence is a significant contributor to cognitive decline.

Regarding long-distance coherence, we observed an inverse relationship between working memory capacity on the Sequencing subtest of the Digit Span and coherence between frontal and posterior brain regions that was strongest in the theta frequency band. Although greater task-related theta power and coherence have been observed in prior research in participants during the completion of tasks with greater working memory demands (e.g., Benchenane et al., 2011; Douw et al., 2011; Sauseng et al., 2005), there is some evidence that an inverse relationship may exist between resting-state theta activity and working memory capacity (Euler et al., 2016; Thatcher et al., 2005). For example, greater frontal-posterior theta coherence recorded during the resting state has been associated with weaker cognitive performance (Thatcher et al., 2005), a pattern we observed in the present research. In addition, Euler et al. (2016) observed lower phase scaling for theta power in resting-state EEG across scalp locations in individuals with the strongest working memory performance. Scaling is a measure of the correlation of spectral power over longer temporal periods, with higher values indicating greater consistency over time. Although counter to the established positive relationship between task-related theta and working memory demands, Euler et al. suggest that the temporal independence of theta in individuals with the strongest working memory performance may reveal the existence of increased theta resources during cognition in these individuals. Though these findings do not directly inform our findings for an inverse relationship between linear coherence and working memory performance, they do suggest that the relationship between resting-state theta coherence and working memory capacity may differ from the relationships observed to date between working memory performance and task-related theta activity.

In light of prior research linking the frontoparietal attention network to memory and executive function (Vincent et al., 2008), we attempted to determine if the frontal coherence relationships in the present research were associated with frontoparietal or default mode networks. To do so, we directly compared the relationships between coherence for midline and lateral electrode pairs in each hemisphere, but failed to observe significant differences in the strength of midline versus lateral electrodes pairs and neuropsychological test performance after alpha correction. We note, however, that the spatial resolution possible with EEG may have limited our ability to ascertain if the coherence relationships observed in the present research were specifically associated with resting-state connectivity in the FPAN or the DMN. Upon closer review of our results, we did observe instances of stronger correlations between select assessments and coherence for medial rather than lateral electrode pairs (e.g., Trails B and medial beta coherence), as well as instances of stronger correlations between assessments and coherence for lateral rather than medial electrode pairs (e.g., Category Fluency and lateral delta coherence); however, the magnitude of these differences was not sufficient to achieve significance. Because we have observed significant relationships between coherence and neuropsychological test performance for electrodes that are more medial than lateral in location, particularly in the theta band (see Fig. 3), these relationships could be associated at least in part with the DMN rather than the FPAN (see Scheeringa et al., 2008). Future research using simultaneous fMRI and EEG methods (e.g., Balsters et al., 2013; Scheeringa et al., 2008) would be more successful in determining the independent contributions of individual resting-state networks to cognitive function.

To determine how spectral power contributed to our coherence findings, we tested potential relationships between power and cognitive function. In doing so we observed fewer significant correlations than were evident in our explorations of coherence. We did observe significant inverse relationships between posterior delta power and performance on the CVLT, long-term memory assessment. Prior research has associated greater posterior delta power at rest with increased activity in networks devoted to visual processing, measured with fMRI (Mantini et al., 2007). Lower resting-state delta power in high memory performers in the present research may suggest that weaker activation in visual processing networks at rest is beneficial for internal concentration during task-directed cognition. Beyond delta power, there was a trend for inverse relationships between beta power over frontal sites and memory function, but these relationships were not statistically significant. Of importance, the significant power relationships observed in the present research were comprised of inverse relationships between power and cognition, whereas, with few exceptions, significant relationships between coherence within frontal and posterior regions and cognition were positive.

The above coherence findings align with the findings of prior research that explored differences in EEG coherence between healthy older adults and patient groups with MCI and AD (e.g., Jelles et al., 2008; Stam et al., 2005). A consistent observation in prior research has been that older adults experiencing atypical cognitive decline demonstrate reduced coherence throughout the brain when compared to age-matched controls (e.g., Adler et al., 2003; Babiloni et al., 2006b; Koenig et al., 2005; Stam et al., 2005). In the present research, greater local coherence in frontal regions, particularly in delta and beta frequency bands, was observed in participants who exhibited the strongest performance on memory and executive function measures. However, we also observed that lower coherence between frontal and posterior brain regions was associated with superior working memory performance. Although older adults with normal cognition have been shown to possess greater brain-wide coherence than older adults experiencing clinical decline (Koenig et al., 2005; Stam et al., 2005), it is less clear which coherence patterns accompany the strongest cognitive function among healthy older adults. In healthy young adults, superior cognitive performance has been associated with reductions in task-related brain activity and brain-wide coherence, reflecting neural efficiency (Cheung et al., 2014; Steffener & Stern, 2012; Thatcher et al., 2005). It should be noted that older adults with higher IQ scores and more years of education have also shown reductions in brain activity in DMN and posterior attention networks in the brain at rest (Bastin et al., 2012). Our findings demonstrate that greater frontal coherence, particularly in delta and beta frequencies, coupled with greater independence of distant brain regions may be most advantageous to cognitive function in older adult experiencing healthy aging.

We do note several limitations in the present research. The final sample size available ($N = 66$), limited the power of our analyses and the ability to explore the present dataset using more comprehensive statistical analyses. In addition, we note that our sample ranged in age from 50 to 88 years, with the majority of participants between 65 and 70 years. Considering prior research that has revealed changes in brain coherence with aging (Ferreira & Busatto, 2013), we elected to use age as a covariate in our design to isolate the relationships between cognition and coherence, removing possible influences on these relationships from age. Because trajectories of decline suggest that the physical brain is changing a decade or more before symptoms of decline are apparent (see Sperling et al., 2011), exploration of coherence changes in a younger sample is needed to have a clearer reflection of the value of coherence in predicting subsequent decline. We plan to conduct a second study that incorporates a wider age range, to include middle-aged adults as participants. Beyond the limitations in age, our sample was relatively homogeneous in composition. The majority of participants were Caucasian and had completed at least a high-school degree or its equivalent. Therefore, it is unclear how these findings will extend to diverse participant groups for whom differences may exist in the impact of health variables (e.g., hypertension rates), socioeconomic status, and education on the structure and function of the physical brain (see Thies & Bleiler, 2013). Finally, we note that our methods examined relationships between cognitive function and linear coherence, using a small group of scalp electrodes. Further research examining these relationships using more sensitive measures, such as high-density EEG coherence analyses, eLORETA or graph theory analyses (e.g., Hata et al., 2016; Spreng et al., 2013; Vecchio et al., 2014) could further elucidate the connectivity patterns described above.

The ability to predict the onset of cognitive decline at the earliest point possible is an essential step in mitigating the effects of aging on the physical brain. As noted above, our findings provide a set of relationships between resting-state EEG coherence and neuropsychological test performance associated with superior cognitive function that offers an initial representation of brain coherence in healthy aging. Further refinement of these relationships may position EEG as a valuable tool in monitoring cognitive function over time and in the early detection of decline. Toward this end, there are several factors related to the present research that must be explored in greater detail to clarify and extend our findings. First, the participants in our research were primarily older adults, ranging in age from 55 to 88 years, with the majority of participants between 65 and 70 years of age, suggesting the need to study a younger, more diverse sample. It will also be important to explore longitudinally, how coherence in the brain changes during healthy aging and as older adults transition from normal cognition into MCI, in a manner similar to existing longitudinal research exploring coherence changes in AD patients over time (see Babiloni et al., 2013; Knyazeva et al., 2013). Finally, our detection of an association between cognitive function and coherence, within the frontal region and between frontal and posterior brain regions, requires replication and extension in a larger, more diverse sample, so that the effectiveness of EEG coherence within and between frontal and posterior regions, specifically, can be more fully understood as an indicator of brain health and cognition.

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