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EEG asymmetry and cognitive testing in MCI identification

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Abstract

Background: Finding the baseline resting-state EEG markers for early identification of cognitive decline can contribute to the identification of individuals at risk of further change. Potential applications include identifying participants for clinical trials, early treatment, and evaluation of treatment, accessible even from a community setting.

Methods: Analyses were completed on a sample of 99 (ages 60–90) consensus-diagnosed, community-dwelling African Americans (58 cognitively typical/HC, and 41 mildly cognitively impaired/MCI), who were recruited from the Michigan Alzheimer's Disease Research Center (MADRC) and the Wayne State University Institute of Gerontology. In addition to neuropsychological testing with CogState and Toolbox computerized batteries, resting-state EEGs (rsEEG, eyes closed) were acquired before and after participants were engaged in a visual motion direction discrimination task. rsEEG frontal alpha asymmetry (FAA) and frontal beta asymmetry (FBA) were calculated.

Results: FAA showed no difference across groups for the pre-task resting state. FBA was significantly different between groups, with more asymmetric frontal beta in MCI. Both physiological indices, however, along with computerized neuropsychological tests were significant predictors in logistic regression classification of MCI vs. control participants.

Conclusion: rsEEG asymmetries can contribute significantly to successful discrimination of older persons with MCI from those without, over and above cognitive testing, alone.

Keywords

Resting-state electroencephalography (rsEEG); Frontal alpha asymmetry (FAA); Frontal beta asymmetry (FBA); Mild cognitive impairment (MCI)

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Declaration of competing interest

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1. Introduction

Understanding the psychophysiological correlates of mild cognitive impairment (MCI) is important for several reasons. People diagnosed with MCI, particularly the amnesic subtype (aMCI), transition into Alzheimer's Disease (AD) at a much higher rate than the general older population (Bachman et al., 1993; Petersen et al., 2001), suggesting that in some cases MCI may represent an early stage of decline into dementia (Galluzzi et al., 2001). At the same time, it is important that underrepresented minority populations be included in such research, so that findings can be generalized beyond majority populations (Clark et al., 2019), but this goal remains challenging to meet (Fisher and Kalbaugh, 2011; Erves et al., 2017). Measurement approaches that are less invasive as compared to PET or other related methodologies and can be administered in a community setting may be important factors in identifying people who may benefit from more invasive, expensive procedures.

Recently, Kavcic et al. (2021) reported greater changes in baseline resting-state EEG spectral power after engaging in a motion direction discrimination task in a group of community-dwelling African Americans diagnosed with mild cognitive impairment (MCI) relative to neurologically intact African American controls. In this paper, we report findings from a further analysis of this same data set (R21 AG046637, Kavcic PI) investigating resting-state EEG (rsEEG) changes associated with cognitive decline.

1.1. Known resting-state electrophysiological correlates of MCI

Research going back decades has found dozens of electrophysiological correlates of Alzheimer's disease and MCI in resting state (for review, see Babiloni et al., 2021) and evoked EEG and ERP. A general slowing of oscillatory brain activity, indexed by an increase in delta and theta bands relative to alpha and beta, is seen in normal aging (Hughes and Cayaffa, 1977), is exaggerated in AD (Fernández et al., 2003), and correlates negatively with frontal white matter volume in AD and MCI (Babiloni et al., 2006).

The theta frequency band has a long history of association with both working memory and long-term memory (Klimesch, 1996). Several authors have reported lower resting-state theta in MCI and AD participants compared to neurologically intact comparison groups (Cummins et al., 2008; Finnigan and Robertson, 2011), as well as less event-related synchronization of theta in progressive MCI compared to stable MCI participants (Missonnier et al., 2006).

Babiloni et al. (2010) observed higher delta, lower alpha, and less alpha reactivity (the difference in alpha power between eyes open and eyes closed conditions) in AD and MCI compared to neurologically intact controls. Alpha power deteriorates in amnesic MCI patients relative to controls (Babiloni et al., 2011; Babiloni et al., 2014), and this appears to be related to degeneration of gray matter (Babiloni et al., 2013).

Heuristically, this complex picture can be imperfectly summed up as an exaggerated slowing of oscillatory activity in MCI and AD, which is likely a result of neurodegeneration. However, as discussed below, other popular measures of oscillatory activity, specifically frontal asymmetries, have not been as thoroughly researched in MCI and AD.

1.2. Frontal oscillatory asymmetries

Frontal alpha asymmetry (FAA) is based on the theory that the amplitude of alpha oscillations is inversely related to the degree of information processing activity of underlying cortical tissue (Davidson, 1988; Davidson, 1992). FAA is typically calculated as the difference ln (RIGHT) – ln(LEFT) for a pair of electrodes (Coan and Allen, 2003), with a natural log transform to better conform to a normal distribution (Allen et al., 2004). Since a greater amplitude of alpha corresponds to less activity, a positive FAA corresponds to more activity in the left hemisphere (less alpha) while a negative FAA corresponds to more activity on the right. Although several homologous pairs of electrodes can be used to estimate FAA, the most commonly chosen pair is F3 and F4 (e.g., Davidson et al., 1990; Harmon-Jones and Allen, 1997; Sutton and Davidson, 1997).

When combined with a motivational-emotional dichotomy that is hypothesized to be lateralized in frontal lobes, correlations can be predicted between FAA and behavioral measures of affective-motivational traits and states. The motivational dichotomy corresponding to FAA is not entirely clear, as several have been suggested, including positive vs. negative emotional valence (Davidson et al., 1979), approach vs avoidance motivation (Harmon-Jones and Allen, 1997; Harmon-Jones et al., 2010; Hewig et al., 2006; Sutton and Davidson, 1997) or approach vs. regulatory inhibition (Gable et al., 2018; Lacey et al., 2020), and behavioral activation vs. inhibition (Harmon-Jones and Allen, 1997; Sutton and Davidson, 1997) based on the theory of behavioral activation and inhibition of Gray (1970). In each case, the negative condition is associated with greater right hemisphere activity (i.e., lower alpha on the right and a negative FAA), while the positive condition is associated with greater left hemisphere activity (lower alpha on the left and a positive FAA).

Although it has proven difficult to disentangle these conceptual frameworks, evidence seems to favor a motivational meaning for FAA (Harmon-Jones and Gable, 2018; Rodrigues et al., 2018). In particular a leftward FAA also obtains for anger, a negative emotion but with an approach orientation (Harmon-Jones and Allen, 1998; Harmon-Jones and Gable, 2018), and both right-leaning and left-leaning FAA can be associated with the activation of behavior, whether approach or avoidance (escape), but does not appear to be associated with withholding a behavior (Rodrigues et al., 2018).

There are several reasons to suspect that FAA might be associated with MCI. Neurodegeneration in AD has been found to be asymmetric, and while the side of greatest neurodegeration is unpredictable, it corresponds in meaningful ways to observed deficits (Derflinger et al., 2011; Haxby et al., 1985). For example, greater deterioration of left hemisphere gray matter predicts greater language deficits (Haxby et al., 1985). FAA is predictive of risk for depression (Schaffer et al., 1983; Thibodeau et al., 2006), and depression is sometimes comorbid with MCI and AD (Panza et al., 2009). Further, there is some emerging evidence that mild emotional dysregulation resulting from early degeneration of limbic structures in progressive dementia is characteristic of MCI (Mah et al., 2017; Sturm et al., 2013). Given these associations between MCI and negative affective states, FAA could be predicted to be more negative in MCI compared to intact controls. However, to our knowledge, this is the first attempt to correlate FAA and MCI.

Given the relationship between activity in the beta band and cognitive-emotional processing outlined above, one might wonder whether Frontal beta asymmetry (FBA) might also be related to cognitive decline. FBA is less often investigated, or at least less often reported, than FAA (Ocklenburg et al., 2019), but has an interpretation similar to FAA. Whereas alpha is assumed to be either idling or inhibition of activity (Klimesch et al., 2007; Mathewson et al., 2011) and therefore a relative lack of it to indicate active processing, activity in the beta range is presumed to reflect that activity (Ray and Cole, 1985) and therefore a relatively larger beta power to indicate relatively more processing. Despite the logic, however, FBA, when it has been reported, has had a poor record of success. Lopez-Duran et al. (2012) measured asymmetry in theta, alpha, and beta bands at regions all over the scalp, while participants were watching emotional videos, but failed to find any effect of emotional state or risk of depression on beta asymmetries. Pérez-Edgar et al. (2013) found a relationship between FAA and performance on the dot-probe task, a task designed to measure attentional bias to threatening stimuli, but no such relationship between the dot probe performance and FBA.

1.3. The current data

In this exploratory study, we investigated whether two frontal asymmetries, FAA and FBA, were related to MCI, and if they could add to the predictive ability of two computerized neuropsychological test batteries: CogState (Darby et al., 2002; Fredrickson et al., 2010) and the NIH Toolbox-Cognition (Hammers et al., 2012; Weintraub et al., 2013). The degree to which these instruments distinguish MCI from neurologically intact age-matched controls has already been established (Giordani, 2011; Kairys et al., 2021; Hammers et al., 2012), so we investigated whether the physiological measures used here could increase that discriminability.

Hypotheses: The current state of the literature, along with the available data, suggests several hypotheses. First, if FAA is inversely proportional to neuronal activity, and MCI is characterized by more negative emotional and motivational states, then FAA might differ between people with MCI and controls. Similarly, if the beta is positively associated with underlying neuronal activity, FBA might also be related to MCI, but in the opposite direction. The following hypotheses are possible to test:

Hypothesis 1.: MCI will be associated with FAA, such that MCI participants will have lower FAA scores, corresponding to relatively greater right-hemisphere (negative valence, avoidance motivation) activity.

Hypothesis 2.: MCI will be associated with FBA, such that MCI participants will have higher FBA scores, corresponding to relatively greater right-hemisphere activity.

Hypothesis 3.: Frontal asymmetries (FAA or FBA) will account for unique variability in group membership (MCI vs. control) in the presence of computerized assessments of cognitive functioning.

2. Methods

2.1. Participants

All procedures were approved by the institutional review board of Wayne State University. Participants were community-dwelling African Americans recruited from the volunteer pool of Healthier Black Elders Center (HBEC), a collaboration of the Institute of Gerontology at Wayne State University and the Institute of Social Research at the University of Michigan, and the Michigan Alzheimer's Disease Research Center (MADRC). We attempted to recruit the largest possible sample meeting inclusion criteria from this pool. Participants were recruited based on a screening questionnaire report of having experienced a change in memory in the past year to potentially enrich the sample with participants closer to developing MCI. Originally 129 people from these organization volunteered to participant, but 30 either failed to meet the inclusion criteria or insufficient EEG signal was obtained, leaving a total sample of 99 participants. Of the 41 participants diagnosed as having MCI, there were six males and 35 females, with a mean age of 73.7 years and a standard deviation of 7.2 years. The remaining 58 participants were categorized as neurologically intact controls, with five males and 53 females having a mean age of 71.1 years, with a standard deviation of 6.2 years. The difference in age was not significant, $t(97) = 1.95$, $p = 0.054$. The average number of years of education for the MCI and control groups was $M_{MCI} = 14.46$ and $M_{con} = 15.26$, respectively, and this difference was not significant, $t(97) = 1.64$, $p = 0.103$. Additional demographics, as well as descriptive statistics covering the traditional neuropsychological evaluations used in diagnosis, are presented in Table 1.

2.2. Neuropsychological evaluation

All participants were given computerized cognitive testing on the same day that they sat for an EEG. The Cogstate Brief Battery includes a Detection task (DET) that represents simple attention and reaction time, an Identification task (IDN) that assesses attention and concentration, a 1-Back working memory task (ONB), and One Card learning task (OCL). For Cogstate Brief Battery, acceptable test-retest reliability (Hammers et al., 2011) and validity (Hammers et al., 2012) for older adults have been established. The NIH Toolbox battery (Gershon et al., 2013) of tasks presented on a laptop and includes: Picture Vocabulary, Oral Reading Recognitioin, List Sorting Working Memory, Dimensional Change Card Sort, Pattern Comparison Processing Speed, Flanker Inhibitory Control and Attention, and Picture Sequence Memory tests. In all cases, cognitive testing was done prior to EEG.

Participants also were given the National Alzheimer's Disease Cooperating Centers (NACC) standardized evaluation battery, the Unified Dataset (UDS) (Morris et al., 2006), with these results reviewed in a consensus conference for each participant (see Table 1). These conferences included neurologists, neuropsychologists, nurses, and technicians. Diagnoses were given after applying the following exclusion criteria: psychiatric and sleep disorders, head injury with loss of consciousness longer than 30 min, seizure disorder, learning disability, AIDS, radiation therapy of the brain in the past year, diagnosis of dementia, history of alcoholism or drug abuse, and major medical illness in the past five years. All participants scored at or above 25 on the MMSE. From the consensus conferences,

28 participants were diagnosed as having amnesic mild cognitive impairment (aMCI), 13 as non-amnesic (naMCI), and 58 as neurologically and cognitively intact. Because the naMCI sample was so small, we judged that there would be insufficient statistical power to distinguish among subtypes of MCI and, therefore, collapsed across these subtypes to compare MCI to neurologically intact controls. Computer testing results and functional brain data (fMRI, PET, EEG) were not reviewed as part of the Consensus Conference.

2.3. EEG recording

The electroencephalogram was recorded with a Brain Vision Inc. 64- channel amplifier and Acti Cap (active electrode) high-density system using a modified international 10–20 System of electrode placements. Online reference was FCz, with the ground at AFz, re-referenced offline to average reference. Data were sampled at 500 Hz (32 bit resolution) and bandpass filtered between 0.1 and 70 Hz, 3 dB down, 12 dB roll-off per octave on each side. Impedances were maintained at <10 kΩ, and balanced across all channels within a 5 kΩ range.

All procedures were conducted while participants were seated in a chair adjusted for height, in front of a computer in a dimly lit room. Resting-state EEG measures were taken twice, before and after a motion direction discrimination task (see below). The resting-state EEG was recorded for a minimum of 3 min with eyes open and 3 min with eyes closed. If noisy epochs were observed during recording, an additional time up to approximately 30 s was recorded in order to ensure a minimum of 60 artifact-free 2 s intervals for spectral analysis.

In between recordings of the resting EEG, participants performed a motion direction discrimination task. Stimuli were controlled by a laptop PC using Windows and custom software written by the last author in C, using the Allegro 4 (https://liballeg.org/) programming library and compiled with MinGW (www.mingw.org). Stimuli were moving dots subtending approximately 0.125° of visual angle, presented with a 10° circular aperture with a density of 0.6 dots/deg^2. Dots were white on a dark background. Motion duration was 500 ms, with either rightward or leftward direction on randomly ordered trials and button press responses collected on a laptop.

2.4. EEG processing and frequency analysis

The EEG was inspected offline, and segments containing excessive noise, saturation, or other artifacts were removed. Data were then segmented into 2 s epochs (1024 data points) with a Hanning window, yielding 0.488 Hz resolution. Epochs were automatically rejected if they exceeded 100 mV on any channel. Approximately 90 epochs (range 64–115) were obtained for each participant. Prior to FFT, EEG epochs were transformed into the reference-free current source density (CSD) distribution, which reflects the underlying cortical activity and removes nearly all volume conduction effects (Kayser and Tenke, 2015a, 2015b). In particular this transform has been suggested as better than other reference options for investigating frontal asymmetry (Hagemann et al., 2001). We then estimated power using fast Fourier transform in the traditional bands: delta (2–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), and beta (12–30 Hz). We did not include in power analyses frequencies

>30 Hz due to pericranial musculature electrical activity that can contaminate scalp recorded neuroelectric activity (Whitham et al., 2008).

Frontal alpha asymmetry was computed as the log-transformed difference between electrodes F4 and F3 according to the formula FAA = ln (F4) – ln(F3). These locations were chosen to be consistent with the majority of previous literature (e.g., Davidson et al., 1990; Harmon- Jones and Allen, 1997; Sutton and Davidson, 1997). Frontal beta asymmetry was likewise calculated in exactly the same way using spectral power in the beta range for F4 and F3.

2.5. Data analysis

Data were analyzed with SPSS 26 (IBM, Inc.). FAA and FBA were each analyzed with a 2 (timepoint, pre vs. post) X 2 (group, MCI vs. control) mixed ANOVA. Finally, logistic regression was performed to evaluate whether the physiological measures could add to the ability of the computerized testing variables to classify MCI vs. control participants. In this analysis, age and years of education were entered in a first step, followed by behavioral measures from the computerized testing in a second step, with FAA and FBA entered in a third step. For FAA and FBA, the pre-task measures were used as predictors. Each step was evaluated for goodness of fit using sensitivity, specificity, an area under the ROC curve (AUC), the Kolmogorov-Smirnov statistic, and percent correct classification.

3. Results

3.1. Behavioral results

Table 2 presents the means, standard deviations, and group (MCI vs. control) *t*-tests for the computerized neuropsychological assessments. With the exception of the CogState Identity task and Toolbox flanker task, each measure was significantly worse in MCI than controls.

3.2. Baseline EEG asymmetry results

Conditional means and measures of dispersion for each dependent variable are presented in Table 3. Results of each ANOVA are presented in Table 4. The analysis of FAA revealed no significant main effects or interaction. For FBA, there were main effects of both timepoint, $F(1,94) = 6.63$, $p = 0.012$, and group, $F(1,94) = 8.2$, $p = 0.005$, but no interaction. FBA was shifted leftward after the motion direction discrimination task for both groups, and the MCI participants were more asymmetric than the controls.

Goodness of fit measures for the logistic regression are presented in Table 5, and parameter estimates are presented in Table 6. In the initial step, demographic control factors of age and education level were entered. At the second step the computerized neuropsychological evaluations were entered. Oral Reading from the NIH Toolbox and Det, IDN, and OCL from Cogstate were significant predictors. At the final step, adding in the physiological measures, both FAA and FBA were significant, OCL was no longer a significant predictor, while Card Sorting from the Toolbox was now significant. Fit statistics indicated that overall the model was better with physiological predictors added, with a relatively large increase in sensitivity,

an area under the ROC curve (AUC), and the KS statistic, modest gains in the Cox and Snell pseudo-R^2 and percent correct classification, and a slight decrease in specificity.

The relatively high correlation between FAA and FBA ($r = 0.85$, $p < 0.001$) presents a concern for multicollinearity in the logistic regression model. To assess whether multicollinearity was too extreme, we calculated variance inflation factors for FAA and FBA by regressing each one, one at a time, on the rest of the predicters, and calculating VIF as $1/(1- R^2)$, or in other words, 1/Tolerance. A cutoff of VIF > 10 is typically considered indicative of unacceptable collinearity, although some authors have argued that this is arbitrary (Belsley, 1984), and some have argued that a range of 5–10 could be indicative of problems in logistic regression (Senaviratna and Cooray, 2019). In the case of these two predictors, $VIF_{FAA} = 4.96$, and $VIF_{TBA} = 5.32$.

Handedness can complicate the interpretation of frontal asymmetries. Because we did not use handedness as an exclusion criterion, ten participants were left-handed (approximately matching the population rate of left-handedness). To evaluate whether handedness accounted for our results, we did several additional analyses. First, we determined that handedness was not differentially distributed between MCI and control participants, χ^2 (1) = 2.102, p = 0.147. We then tested whether or not FAA and FBA were significantly different for right and left handers using independent samples t-tests. Left and right handers were not significantly different with respect to either FAA, t(95) = − 1.43, p = 0.157, or FBA, t(95) = − 1.24, p = 0.218. Finally, we regressed group (MCI vs control) on FAA, FBA, and handedness. Both FAA (p = 0.002, Wald = 9.861, Exp(B) = 30.6) and FBA ($p < 0.001$, Wald = 13.21, Exp(B) = 0.026) were significant predictors of group, but handedness was not, p = 0.144, Exp(B) = 0.275.

4. Discussion

In this exploratory analysis, we tested three hypotheses. There was no support for Hypothesis 1, that FAA would be associated with MCI. Although a null result always leaves open the possibility of a Type II error owing to measurement error or inadequate sample size, the estimated effect size indicates that if individuals with MCI have a different FAA than neurologically intact controls, it is a very small difference. This does not completely shut the door to FAA in MCI or Alzheimer's disease. FAA reflects both state and trait variables which have made replications even in the core area of motivation difficult to achieve (see Harmon- Jones and Gable, 2018, for a review). However, this study provides no support to the idea that FAA is associated with MCI.

Hypothesis 2 that participants with MCI would have higher FBA consistent with greater withdrawal motivation was contradicted. MCI were more asymmetric than controls, but with negative FBA indicating relatively greater left frontal activity. In the context of the literature on asymmetric neurodegeneration in AD, this result may be consistent with studies showing greater deficits in the left hemisphere (Loewenstein et al., 1989; Zahn et al., 2004) if we assume an early deficit causes compensatory recruitment or effort, but the majority of studies do not find early or predominant left hemispheric abnormalities (Derflinger et al., 2011). This is consistent with the broader literature on asymmetries and clinical conditions,

where the pattern of abnormalities in asymmetry relative to healthy brains appears to depend in complex and interactive ways with specific symptomology (Mundorf et al., 2021). It may be too early to try to interpret this higher relative beta in MCI vs. controls, but this will be an important direction for future research.

To our knowledge, this is the first report of an association between MCI and FBA. Several studies have reported hemispheric asymmetries in AD based on imaging with MRI, fMRI, and PET studies (for review, see Yang et al., 2017), but only a few studies addressed hemispheric asymmetries in MCI. Furthermore, to the best of our effort, we found only one study evaluating hemispheric asymmetries in MCI with EEG. John et al. (2019) reported asymmetry loss in MCI-AD patients with greater right hemispheric asymmetry, i.e., a larger decline of complexity and/or lower activity in the left hemisphere of the brain than the right, primarily over the parietal lobe. Our result of greater relative beta activity in the left hemisphere complicates this picture, but does not contradict John et al. (2019) because they used much different measures (wavelets, non-linear dynamical systems statistics), and their sample included both MCI and AD participants. Our results, for example, may reflect a compensatory mechanism engaged in early MCI that reverses with decline into AD.

FBA shifted leftward after the motion direction discrimination task for both groups, suggesting that FBA may index a more temporary state rather than a stable trait. This effect may very well depend on the specific task used between measures of resting EEG. It may be fruitful for future research to address changes in FBA with different tasks.

There was support for Hypothesis 3, that the psychophysiological measures used here would contribute significantly to the classification of group membership over and above the neuropsychological predictors alone. A higher level of FAA, corresponding to greater alpha power over the right frontal lobe, increased the likelihood that a participant would be classified as MCI. In contrast, the opposite was the case for FBA, where greater levels of beta over the right hemisphere decreased the likelihood of classification as MCI.

Three observations about the model bear comment, although we cannot draw any firm conclusions without further research and hypothesis testing. First, there was no main effect of group on FAA, yet in the context of the logistic regression it was a powerful predictor accounting for unique variance in group membership. Second, FBA was the single most powerful predictor in the context of the model. Diagnostics indicated that estimation errors from collinearity cannot explain the pattern, so it appears to be an unmasking of the relationship between FAA and MCI. Third, FAA and FBA had opposite signs, indicating that MCI was characterized by greater relative left hemispheric beta and greater relative right hemispheric alpha. This is an empirical pattern uncovered in an exploratory analysis, so the mechanism is unknown. We can speculate that it might reflect compensatory processes in the behavioral activating system (BAS) or approach motivation system. Alternatively, it may reflect disruption of the behavioral inhibition system (BIS), but it is unclear why that would disinhibit only or predominantly the left hemisphere. This brings up many questions about whether this phenomenon would be exaggerated in AD or would reverse as neurodegeneration progresses past the point of compensation.

Also important was the observation that computerized neuropsychological tests were predictive, providing further evidence that this mode of testing may be sufficiently reliable and valid to support future diagnosis and research on MCI and AD. Past research with this population has indicated that Oral Reading test scores were predictive of MCI (Kairys et al., 2021). Our observations replicate that finding and add that along with other neuropsychological tests, FAA and FBA both accounted for significant variability in group membership, over and above cognitive test measures, alone. Interestingly, FAA was not significantly associated with MCI in the ANOVAs (see above), nor by itself, but when added to a model along with FBA, both were predictive. Although the variance inflation factors were within commonly accepted limits, the potential for multicollinearity means that it would be valuable to see this result replicated in independently collected data before too much weight is given to this potentially important finding.

The finding that resting FBA was altered after doing a motion direction discrimination task was incidental and not predicted but fits in with a growing set of findings of resting-state oscillatory dynamics that are altered by sensory-perceptual tasks (Kavcic et al., 2021). FAA, although not statistically significant ($p = 0.06$), was also reduced after the task. Further study is necessary to understand how meaningful such changes might be. Are they purely coincidental and unreplicable, or might the susceptibility to such effects be an index of such characteristics as stability and plasticity?

Frontal theta and delta asymmetries were not investigated in this report. Although both event-related and resting-state theta and delta have been extensively investigated with respect to cognitive functions (Klimesch, 1999; Klimesch et al., 2005; Knyazev, 2007; Tesche and Karhu, 2000), to our knowledge frontal asymmetries in these frequency bands have not been extensively reported. Whether this reflects file drawers full of null results or an important gap in the literature is unclear, but in either case we did not feel that we would have a ready interpretation of any exploratory effects or correlations that might be found.

4.1. Conclusions

We conducted an analysis of common psychophysiological measures, including FAA and FBA, that to our knowledge have not been investigated in relation to MCI. The strongest effect that we found was a group difference in FBA, with MCI being more lateralized than controls. FBA was also shifted rightward after a motion direction discrimination task, and, although not significant, FAA showed a similar rightward shift after the task. Finally, although there was no main effect of group on FAA, FAA was a significant predictor when in a model with FBA, and both FAA and FBA added discriminability after accounting for tasks from two cognitive test batteries. Future research should test the robustness of these findings and potential applications in the diagnosis and evaluation of treatment for neurodegenerative diseases.

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Table 1

Demographics and diagnostic neuropsychological assessments.

	Controls	MCI	t-test	
	M (SD)	M (SD)	t	*p*
Demographics				
Age	71.14 (6.19)	73.68 (7.19)	1.88	0.06
Gender (M, F)	5, 53	6, 35		
Education	15.24 (2,35)	14.49 (2.41)	1.55	0.12
Handedness (L, R)	8, 50	2, 39		
GDS	0.95 (1.39)	0.80 (1.08	0.55	0.14
UDS neurospsych tests				
MMSE	28.75 (1.11)	27.65 (1.53)	4.06	**<0.001**
Logimem	13.14 (3.15)	9.19 (2.97	6.07	**<0.001**
digif	7.91 ((2.05)	7.05 (2.17)	1.94	0.06
digiflen	6.40 (1.19)	5.95 (1.25)	1.79	0.07
digib	6.72 (1.75)	5.16 (1.82)	4.15	**<0.001**
digiblen	5.02 (1.04)	3.97 (1.07)	4.70	**<0.001**
Animals	19.11 (4.49)	15.92 (3.74)	3.78	**<0.001**
veg	15.32 (3.81)	13.08 (3.37)	2.90	**0.004**
traila	36.86 (11.79)	41.22 (13.29)	1.66	0.10
trailarr	0.21 (0.46)	0.19 (0.46)	0.26	0.80
trailb	92.53 (34.76)	157.83 (38.16)	5.24	**<0.001**
trailbrr	0.43 ((0.76)	1.39 (1.63)	3.31	**0.002**
trailbli	24.00 (0.00)	21.08 (5.97)	3.67	**<0.001**
wais	46.52 (9.62)	37.06 (8.71)	4.70	**<0.001**
memnits	11.68 (3.15)	7.16 (2.80)	7.09	**<0.001**
memtime	18.82 (1.96)	21.36 (2.52)	1.40	0.17
boston	26.23 (2.52)	23.59 (4.55)	3.59	**<0.001**

Note. Significant p values are bolded.

Table 2

Descriptive statistics and *t*-tests for computerized neuropsychological tests.

Computerized test	Controls	MCI	t-test	
	M (SD)	M (SD)	t	*p*
CogState				
Detection (lmn)	2.59 (0.08)	2.63 (0.13)	2.05	**0.04**
Identity (lmn)	2.77 (0.09)	2.80 (0.09)	1.87	0.07
One card back (acc)	1.37 (0.17)	1.26 (0.19)	2.87	**0.005**
One card learning (acc)	0.98 (0.09)	0.90 (0.09)	3.80	**<0.001**
Toolbox				
Crystallized composite				
Oral Reading	56.0.84 6.23)	50.56 (8.18)	4.24	**<0.001**
Recognition				
Picture Vocabulary	57.56 (8.45)	49.47 (10.56)	3.46	
Fluid composite				
Picture Sequence	47.93 (13.41)	39.50 (9.48)	3.35	**0.001**
Memory				
Dimensional Change	58.04 (14.56)	48.45 (9.87)	3.59	**<0.001**
Card				
Flanker Inhibitory	52.11 (7.94)	48.90 (8.96)	1.84	0.07
Control				
List Sorting	51.96 (9.07)	45.56 (7.05)	3.67	**<0.001**
Pattern Recognition	51.95 (12.56)	45.03 (10.83)	2.80	**0.006**

Note. Significant p values are bolded. The computerized neuropsychological tests were not used in the diagnosis of MCI. Nevertheless, independent samples *t*-tests indicate that most individual tests in each battery are significantly different between groups.

Table 3

Conditional means for ANOVAs.

Measure	Group	Timepoint	Mean	SE	L 95% CI	U 95% CI
FAA	Control	Pre	0.077	0.068	−0.059	0.212
		Post	0.033	0.079	−0.124	0.191
	MCI	Pre	0.063	0.081	−0.098	0.223
		Post	−0.102	0.094	−0.289	0.084
FBA	Control	Pre	0.100	0.072	−0.042	0.242
		Post	0.007	0.091	−0.175	0.188
	MCI	Pre	−0.159	0.086	−0.329	0.011
		Post	−0.379	0.109	−0.596	−0.162

Note. FAA = frontal alpha asymmetry. FBA = frontal beta asymmetry.

Table 4

ANOVA tables for FAA and FBA.

IV	Statistic	FAA	FBA
Timepoint	F(1,94)	3.652	**6.627**
	p	0.059	**0.012**
	η_p	0.037	0.065
Group	F(1,94)	0.55	**8.204**
	p	0.46	**0.005**
	η_p	0.006	0.079
Timepoint X Group	F(1,94)	1.238	1.088
	p	0.269	0.3
	η_p	0.013	0.011

Note. Mixed ANOVA analysis. Timepoint was within-subjects, group was between-subjects. Significant p values are bolded. FAA = frontal alpha asymmetry, FBA = frontal beta asymmetry, η_p = partial eta squared. Significant effects are bolded.

Table 5

Logistic Regression Goodness of Fit.

	Step 1	Step 2	Step 3
Sensitivity	0.39	0.884	0.833
Specificity	0.862	0.836	0.87
AUC	0.668	0.884	0.933
KS	37.55	62.11	69.85
% Correct	66.7	79.3	83.3
Cox & Snell R^2	0.065	0.435	0.513

Note. AUC = area under ROC curve. KS = Kolmogorov-Smirnov statistic.

Table 6

Logistic regression parameter estimates.

	Step 1			Step 2			Step 3		
Predictor	**β**	**Wald**	**Exp(B)**	**β**	**Wald**	**Exp(B)**	**β**	**Wald**	**Exp(B)**
Age	0.063	3.816	1.065	0.06	1.00	1.06	0.037	0.287	1.037
Education	−0.163	2.866	0.858	0.197	1.476	1.217	0.151	0.721	1.163
TB Card Sort				−0.055	2.883	0.947	**−0.112** *	**6.091**	**0.894**
TB Flanker				0.009	0.035	1.009	0.045	0.814	1.046
TB List Sort				**−0.095** *	**4.282**	**0.910**	− 0.096	3.732	0.908
TB Oral				**−0.196** *	**6.811**	**0.822**	**−0.235** **	**7.958**	**0.790**
TB Pattern				− 0.026	0.642	0.974	− 0.047	1.346	0.954
TB Picture Sequence				− 0.051	2.429	0.950	− 0.010	0.068	0.990
TB Pic Voc				− 0.049	1.324	0.952	− 0.062	1.612	0.940
CS Detect				**0.008** *	**4.902**	**1.008**	**0.009** *	**3.866**	**1.009**
CD Identity				**−0.008** *	**4.839**	**0.992**	**−0.009** *	**4.255**	**0.991**
CS One-Card learning				**−0.003** *	**5.115**	**0.997**	**−0.003** *	**5.072**	**0.997**
CS One-Back				0.003	1.876	1.003	−0.001	0.178	1.001
FAA							**3.493** *	**4.358**	**32.879**
FBA							**−4.438** **	**6.879**	**0.012**
Constant	− 2.625	1.026	0.072	**23.560**	**7.519**	**1.24E+08**	**26.581**	**9.626**	**3.50E+11**

Note. Significant p values are bolded. TB = Toolbox, CS = CogState.

* $p < 0.05$.

** $p < 0.005$.