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Enhanced functional brain network integration in Mild Cognitive Impairment during cognitive task performance: a compensatory mechanism or a result of neural disinhibition?

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Abstract

While previous studies have observed increased global network integration during tasks in persons with mild cognitive impairment (MCI), the association between this integration and actual task performance has remained unexplored. Understanding this link is crucial for uncovering the underlying mechanism behind these changes in network integration and their potential role in MCI. Here, to find such a link, we investigated brain network integration derived from electroencephalography recordings during a visual motion discrimination task in older adults with MCI and those with normal cognition. We focused on a critical period just before stimulus presentation, which is known to be important for task performance. Our results revealed that during this period, MCI patients exhibited increased network integration compared to controls. Interestingly, increased integration was associated with worse task performance in the MCI group, suggesting it was not beneficial. No such association was found in the control group. Notably, this difference existed despite similar overall task performance between the groups. This suboptimal integration pattern during the cognitive task might reflect network de-differentiation due to disinhibition in MCI patients. Collectively, our study highlights the potential of analyzing network integration during tasks to identify cognitive impairment and suggest a distinct role for network integration in MCI patients compared to healthy controls.

Keywords: electroencephalography; mild cognitive impairment; brain network integration; cognitive task; neuropsychology

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Abbreviations

EEG – electroencephalography
MCI – mild cognitive impairment
MST – maximum spanning trees
ICC – intra-class correlation

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1. Introduction

Our cognitive processes emerge from interactions between multiple, distributed brain regions organized into a complex network (Bassett and Bullmore, 2016; Bullmore and Sporns, 2012). A key principle for coherent cognitive processing is the network's ability to integrate specialized and distant brain regions into a unified whole, even without external stimulation (Tononi et al., 1998). Network integration is commonly identified by metrics based on shortest paths between vertices (Bullmore and Sporns, 2009; Fornito et al., 2016). Another feature that characterizes network integration is the presence of critical vertices—vertices that are highly connected to several vertices within other functionally specialized regions. These vertices significantly shorten paths and enhance overall network integration (Tononi et al., 1998).

Emerging evidence suggests atypical patterns of brain network integration in mild cognitive impairment (MCI). MCI represents a critical stage between normal aging and dementia, characterized by noticeable cognitive changes that do not significantly interfere with daily functioning. Individuals with MCI are at an increased risk of developing Alzheimer's disease or other forms of dementia, making early detection and intervention crucial. Research has identified various biomarkers and cognitive assessments to aid in diagnosing and monitoring MCI progression, such as neuroimaging techniques like magnetic resonance imaging and positron emission tomography scans and including electroencephalography (EEG) recordings, as well as neuropsychological tests assessing memory, language, and executive function (Petersen et al., 2018). Understanding the mechanisms underlying MCI involves investigating factors like genetics, lifestyle, and comorbidities such as cardiovascular disease, which may influence its development and progression (Livingston et al., 2020).

Patients with MCI consistently show reduced brain network integration during rest. This is seen in longer shortest paths within various brain network representations, such as weighted graphs (Xu et al., 2014; Wang et al., 2013; Zeng et al., 2015), binary graphs (Kim et al., 2023; Xiang et al., 2013) and maximum spanning trees[1] (Požar et al., 2020). Additionally, there is a loss of critical vertices in MCI patients (Wang et al., 2013; Seo et al., 2013). This decline in integration during rest correlates with cognitive dysfunction in MCI (Wang et al., 2013; Zeng et al., 2015) and suggests a potential limitation in the variety of brain states and transitions between them (Anderson, 2019).

While studies examining brain activity at rest indicate reduced network integration in MCI patients, data from studies involving cognitive tasks suggest the opposite pattern. These studies consistently reveal greater network integration in MCI patients during specific tasks, observed before, during, and after stimulus presentation. For example, Wei et al. (2015) found that MCI patients had reduced path length in binary networks before a stimulus presentation in a selective attention task. This pattern also continued at stimulus onset. Similarly, Buldú et al. (2011) observed reduced path length in weighted networks of MCI patients throughout the cognitive processing in a memory task involving letters and probes. In a visuospatial memory task, Fodor et al. (2021) reported decreased diameter and eccentricity in maximum spanning trees of MCI patients during the retention period. Despite these observations, the meaning of these changes

[1] This study uses the term “maximum spanning tree”, whereas the field of neuroscience typically uses “minimum spanning tree”. Despite this difference in terminology, both terms, when applied to weighted brain networks, refer to a subgraph that connects all vertices without cycles and maximizes the total edge weight. From a mathematical perspective, however, “maximum spanning tree” might be considered more intuitive.

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remains unclear. It could represent a compensatory mechanism to counter cognitive decline (Buldú et al., 2011; Fodor et al., 2021), or it might be a result of neural disinhibition (Fodor et al., 2021). Notably, no studies have investigated the link between this task-related difference in network integration and actual task performance. Understanding this link is crucial for uncovering the underlying mechanism behind these changes in network integration and their potential role in MCI (Scheller et al., 2014).

Here, to find such a link, we investigated brain network integration derived from EEG recordings during a visual motion discrimination task in older adults with MCI and normal cognition. We previously compared brain network organization in these individuals at rest, immediately before and after the same task, using the maximum spanning tree approach. Within what we termed the resting-state task aftereffect design, we found that the task induced a greater increase in global integration from pre- to post-task in MCI patients compared to healthy controls (Požar et al., 2023). In the present study, we therefore used maximum spanning trees to represent and analyze brain networks. We specifically aimed to determine whether these trees effectively capture patterns of abnormal integration in MCI patients before a visual stimulus presentation, compared to healthy controls, and, if so, whether differences in network integration between these groups are associated with individual task performance. Our focus on the period immediately preceding the onset of a stimulus was motivated by previous findings suggesting its importance for subsequent task performance (Linkenkaer-Hansen et al., 2004; Martin et al., 2006; Hanslmayr et al., 2007; Sherwin et al., 2015). We also considered how integration might change throughout the task based on our previous study with the same participants as in this study, which revealed increased global integration from pre-task to post-task resting-state (Požar et al., 2023). Drawing on prior research examining network integration during tasks and in the context of a task aftereffect design, we expected that MCI patients would exhibit greater overall integration during the task compared to controls. Additionally, we predicted a link between aberrant integration during the task and task performance in MCI, but without a specific prediction regarding the direction of this relationship.

2. Material and Methods

2.1 Participants

Ninety non-Hispanic African Americans were recruited out of the volunteer pool of Healthier Black Elders Center, a joint collaboration between Wayne State University's Institute of Gerontology and University of Michigan's and the Wayne State University's Institutes of Social Research and the Michigan Alzheimer's Disease Research Center (MADRC). Participants were enrolled based on their responses to a question included in the health screening forms asking if they believed they had experienced a change in memory or other cognitive areas over the past year, but not so severe as to interfere with their ability to complete daily activities. Inclusion criteria were age 65 years or older, a research diagnosis consistent with National Alzheimer's Coordinating Center-defined criteria (see below), and accompaniment by a knowledgeable informant (e.g., child, spouse, or partner). Study partners completed measures of functional ability and neurobehavioral symptoms with a trained staff member (e.g., study coordinator). All participants were allowed to wear their appropriate corrective prescription. Following a neurological and physical health screening examination, in order to exclude individuals with a history of stroke, TBI, DSM-IV-TR psychiatric disorder, intellectual disability, and on any psychoactive medication that may affect cognition, volunteers were enrolled in the MADRC and underwent a neuropsychological examination by

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a trained technician as stipulated in the uniform data set (UDS, version 2) of the National Alzheimer's Coordinating Center (Weintraub et al., 2009). Diagnosis of the participants was carried out at a consensus meeting consisting of at least one neuropsychologist and two neurologists, as well as other MADRC support staff using the UDS criteria. Of 90 participants 39 were determined to meet MCI criteria. Normal controls were in good health and had a normal neurological examination with no history of central nervous system disease and no memory-related complaints or cognitive impairments on neuropsychological testing. For participants who scored in the impaired range on UDS testing and demonstrated subjective complaints but lack evidence of functional decline based on self-report and informant ratings needed for a diagnosis for dementia, clinicians rendered a diagnosis of MCI according to the revised Peterson criteria (Petersen, 2004). All participants were consented and procedures were approved by the Wayne State University Research Subjects Review Board (IRB: 095914A) and the University of Michigan Medical School Review Board (see Table 2 for demographics of the participants).

2.2 Motion direction discrimination task

In this experiment, participants performed a left-right, global visual motion discrimination task using random dot stimuli (for a schematic illustration see Fig. 1). On each trial, participants were asked to focus on a fixation dot subtending approximately 0.5˚ of visual angle during a fixation period of random length that varied between 2 to 3 s with uniform distribution. A fixation period was followed by the onset of a random dot stimulus. The stimulus had a circular aperture 10˚ in radius and consisted of a cloud of stationary white dots on a black background, each subtending 0.125˚ of visual angle. Dot density was approximately 0.6 dots/deg^2. After a random interval that varied between 1 to 2 s with uniform distribution, the dots began to move either to the left or the right for 0.5 s, followed by another 0.5 with the dots remaining static. Participants identified the direction of motion for the target only by pressing one of two buttons on a computer mouse: they pressed the left button for leftward motion with their left index finger and the right button for rightward motion with their right index finger, as quickly and accurately as possible. This procedure was repeated 240 times. To familiarize themselves with the task and to adapt visual motion mechanisms, participants completed 25 practice trials. The stimuli were presented on a computer monitor controlled by custom C language software compiled with MinGW (http://www.mingw.org) on a Windows 10 system.

2.3 EEG recording and processing

We recorded scalp electroencephalographic activity during the motion direction discrimination task with Brain Vision (Brain Vision, Inc.) equipment. We used a high-density 64-channel ActiCap system following the International 10-20 system. The recording locations included eight midline sites, with the FCz electrode as an on-line reference and a ground at midline location AFz. Low and high pass filter settings were 0.1 and 70 Hz Hz, respectively. The cutoff frequencies for these filters were set at 3 dB down; the roll-off was 12 dB per octave at both sides. Impedances were maintained below 10 kΩ for each channel and balanced across all channels within a 5 kΩ range. The data were sampled at 500 Hz with 32-bit resolution.

After recording, we inspected the data by using Brain Vision Analyzer 2.2. Initially, we applied an off-line raw data inspection procedure to identify and remove segments of EEG recording that were contaminated with excessive noise, saturation, or lack of EEG signal activity. Where needed, we applied independent component analyses to correct for eyeblinks and/or lateral eyes

movements. The visually detected bad channels were interpolated using the spherical method. Data were then segmented into 2-s epochs during the fixation period, capturing the brain activity from two seconds before the stimulus presentation to the stimulus onset. Epochs were identified as acceptable by an automatic artifact rejection procedure, using a rejection criterion of 100 mV on any channel affected by artifacts (muscular, instrumental).

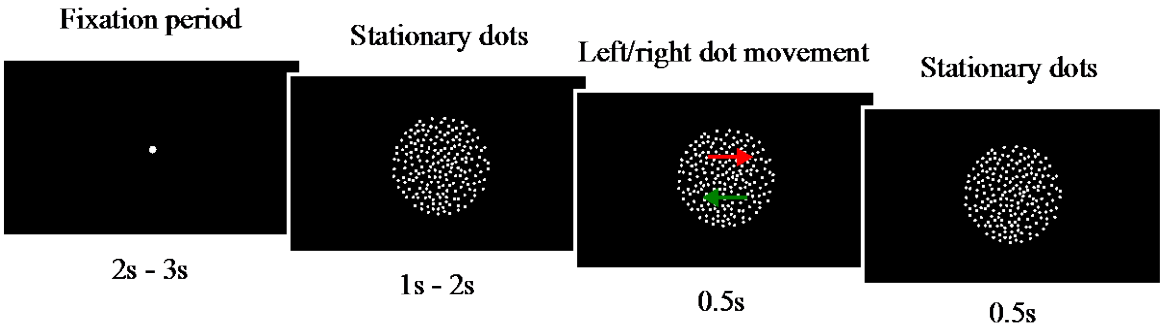


Figure 1: A left-right, global motion direction discrimination task design.

To examine how integration might change throughout the task, we divided the task into three equal sections with the first, second and last representing early, middle and late task phase, respectively. For each subject and for each phase, 30 artifact-free epochs were used to compute functional connectivity in five frequency bands: delta (0.5-4 Hz), theta (4-8 Hz), lower alpha (8-10 Hz), upper alpha (10-13 Hz) and beta (13-20 Hz). For each epoch, functional connectivity between each pair of channels was assessed using the phase lag index (Stam et al., 2007) and stored in a 64× 64 functional connectivity matrix.

2.4 Maximum spanning tree analysis

A functional connectivity matrix models the brain as a *weighted graph*. Vertices in this brain graph represent electrodes, while edges between them represent the relationship between those electrodes, weighted by the strength of their functional connectivity. Each functional connectivity matrix was used as input for Kruskal's algorithm (Kruskal, 1956) to compute a *maximum spanning tree* (MST) of the brain graph. An MST is a subgraph that connects all vertices without cycles and maximizes the total edge weight. All the resulting trees had 64 vertices and 63 edges, and their corresponding edge weights were disregarded in further analyses. This step ensured any potential differences in connection density or strength between participants were excluded from consideration. To assess network integration, we then calculated several MST measures: the leaf number, eccentricity, and degree. Table 1 shows an overview of these measures. For consistent interpretation, all measures were normalized by their maximal possible values, yielding values ranging from 0 to 1. We included mean eccentricity and maximum degree over all vertices as global characteristics in the statistical analyses. We used the NetworkX Python library (Hagberg et al., 2008) to compute MSTs and the corresponding topological measures.

Trees can exhibit two topological extremes. In one extreme, a single central node connects to all others. This extreme maximizes integration by having the highest possible maximum degree and leaf number while minimizing mean eccentricity for a fixed number of vertices in the tree. The other extreme involves two specific vertices, each with only one connection, while all remaining vertices connect to exactly two others. This extreme minimizes integration, resulting

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in the smallest possible maximum degree and leaf number, while maximizing mean eccentricity for a fixed number of vertices in the tree. Overall, highly integrated networks have large maximum degree and leaf number and small mean eccentricity, while less integrated networks have small maximum degree and leaf number and large mean eccentricity.

Table 1: Basic measures on a tree.

Tree measure	Explanation
Degree	The degree of a vertex is the number of edges connected to it. It measures local importance of a vertex in a tree.
Leaf number	The number of vertices with degree 1. It provides information about network centralization.
Distance	The distance between two vertices in a tree is the number of edges on the path between them (note that there is a unique path between any two vertices in a tree).
Eccentricity	The eccentricity of a vertex in a tree is the greatest distance from that vertex to any other vertex in a tree. It measures relative importance of a vertex for global communication.

2.5 Statistical analysis

All statistical analyses were performed using MATLAB (The Mathworks, Inc). First, MST measures were averaged across the epochs per subject prior to statistical analysis. Then, outliers in MST measures for each frequency band were detected and excluded from the subsequent analyses. To find outlier values, we used interquartile range. For each graph measure, a participant was removed if he or she was an outlier at one or more of the phases. All results include the number of usable participants for each graph measure (for detailed information see Supplementary Table 1).

To investigate changes in the integration, a linear mixed model was fitted to the data for each MST measure (leaf number, maximum degree, mean eccentricity) and each frequency band. Each model included, as fixed-effect predictors, the factors phase (Early, Middle, Late, coded as −1, 0, and 1), group (Control, MST, coded as -1 and 1), and their interaction. Age, gender and education were included as covariates. Each model also included a random intercept term for the effect of the phase for each subject. A correction for multiple comparisons across frequency bands was performed by the false discovery rate (FDR) (Benjamini and Hochberg, 1995). When appropriate, post hoc tests were performed by an unpaired permutation test for group differences, and a paired-permutation test was performed for phase differences. These multiple comparisons were corrected using FDR. The FDR-corrected p values less than 0.05 were considered to be statistically significant.

To investigate the relationship between the task performance and the characteristics of network topology, we computed the Pearson correlation coefficients between the reaction time and MST measures, averaged over all three phases. Only those MST measures that showed statistically significant group effect were investigated in the correlation analysis. To test between-group differences in correlation coefficients, we applied the Fisher's Z-test.

We further investigated how consistent participants' MST measures were within each task phase. Consistency here refers to whether the rank order of participants' measures remained similar across phases. To assess this, we calculated the intra-class correlation coefficient (ICC), using the two-way mixed-effect designed for consistency with multiple measurements.

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3. Results

The demographic characteristics of participants and discrimination task are given in Table 2. The Motion direction discrimination task did not differ significantly between the groups.

3.1 Functional brain reorganization during task performance

In the delta band, we detected significant effects of phase for all outcomes (leaf number: $p_{FDR} = 0.0003$; maximum degree: $p_{FDR} = 0.002$; mean eccentricity: $p_{FDR} = 0.02$). We did not find significant effects of group or interaction for any MST measure (leaf number: $p_{FDR} > 0.19$; maximum degree: $p_{FDR} > 0.38$; mean eccentricity: $p_{FDR} > 0.16$). During the period before stimulus presentation, participants' leaf number and the maximum degree increased steadily with task progress, whereas the mean eccentricity showed the opposite pattern (2A-C, Supplementary Table 1). The pairwise comparison revealed that participants' maximum degree during "Late" phase was significantly higher than during "Early" phase (paired permutation test, two-sided: $p_{FDR} = 0.0009$) and "Middle" phase (paired permutation test, two-sided: $p_{FDR} = 0.045$). In addition, participants' leaf number was significantly higher during "Late" phase than during "Early" phase (paired permutation test, two-sided: $p_{FDR} = 0.0018$). More details of the pairwise comparisons are shown in Supplementary Table 2.

Table 2: Demographic characteristics and discrimination task of control and MCI subject groups.

	Controls ($N = 51$)		MCI ($N = 39$)		
	Mean	SD	Mean	SD	p value*
Age (years)	71.25	6.19	73.08	6.73	0.1375
Education (years)	15.27	2.28	14.38	2.46	0.068
Gender (% female)	96	-	85	-	-
MDDT (RT)	0.7532	0.1465	0.7411	0.1193	0.3533
Accuracy (%)	95	-	93	-	-
Error rate	0.04	-	0.06	-	-

MDDT (RT), Motion Direction Discrimination Task (reaction time); SD, standard deviation.

*The value was obtained using Mann-Whitney U-tests for independent samples.

In the theta band, we detected significant effects of phase for all outcomes (leaf number: $p_{FDR} < 0.0001$; maximum degree: $p_{FDR} = 0.0001$; mean eccentricity: $p_{FDR} = 0.0045$). Moreover, a significant effect of group was observed for leaf number ($p_{FDR} = 0.045$), whereas no differences in other two measures were observed (maximum degree: $p_{FDR} = 0.63$; mean eccentricity: $p_{FDR} = 0.13$). We did not find significant effects of interaction for any MST measure (leaf number: $p_{FDR} = 0.92$; maximum degree: $p_{FDR} = 0.84$; mean eccentricity: $p_{FDR} = 0.61$). During the period before stimulus presentation, participants' leaf number and maximum degree increased with task progress, whereas mean eccentricity showed the opposite pattern (Fig. 2D-F, Supplementary Table 1). The pairwise comparison revealed that participants' maximum degree and leaf number were significantly higher during "Late" phase than during "Early" phase (paired permutation test, two-sided: $p_{FDR} < 0.0001$) and

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"Middle" phase (paired permutation test, two-sided: $p_{FDR} < 0.0027$), whereas participants' mean eccentricity was significantly lower during "Late" phase than during "Early" phase (paired permutation test, two-sided: $p_{FDR} = 0.003$). Participants' leaf number was also significantly higher during "Middle" phase then during "Early" phase (paired permutation test, two-sided: $p_{FDR} = 0.025$). More details of the pairwise comparisons are shown in Supplementary Table 2. Compared to healthy controls, the MCI group had significantly higher leaf number during all phases ("Early": $p_{FDR} = 0.0043$; "Middle": $p_{FDR} = 0.037$; "Late": $p_{FDR} = 0.0375$) (Fig. 2D, Supplementary Table 3).

In the lower alpha band, we detected significant effects of phase for all outcomes (leaf number: $p_{FDR} < 0.0001$; maximum degree: $p_{FDR} = 0.0003$; mean eccentricity: $p_{FDR} = 0.02$). Moreover, a significant effect of group was observed for maximum degree ($p_{FDR} = 0.028$) and mean eccentricity ($p_{FDR} = 0.04$), whereas no differences in leaf number was observed ($p_{FDR} = 0.19$). We did not find significant effects of interaction for any MST measure (leaf number: $p_{FDR} = 0.59$; maximum degree: $p_{FDR} = 0.84$; mean eccentricity: $p_{FDR} = 0.31$). During the period before stimulus presentation, participants' leaf number and maximum degree increased with task progress, whereas mean eccentricity showed the opposite pattern (Fig. 2G-I, Supplementary Table 1). The pairwise comparison revealed that participants' maximum degree and leaf number were significantly higher during "Late" phase than during "Early" phase (paired permutation test, two-sided: $p_{FDR} < 0.0006$) and "Middle" phase (paired permutation test, two-sided: $p_{FDR} < 0.0018$), whereas participants' mean eccentricity was significantly lower during "Late" phase than during "Early" phase (paired permutation test, two-sided: $p_{FDR} = 0.03$) and "Middle" phase (paired permutation test, two-sided: $p_{FDR} < 0.03$). More details of the pairwise comparisons are shown in Supplementary Table 2. Compared to healthy controls, the MCI group had significantly higher maximum degree during all phases ("Early": $p_{FDR} = 0.03$; "Middle": $p_{FDR} = 0.02$; "Late": $p_{FDR} = 0.02$,; Fig. 2H, Supplementary Table 3) and lower mean eccentricity with significant change during "Early" phase ($p_{FDR} = 0.001$; Fig. 2I, Supplementary Table 3).

In the upper alpha band, we detected significant effects of phase for all outcomes (leaf number: $p_{FDR} < 0.0001$; maximum degree: $p_{FDR} = 0.046$; mean eccentricity: $p_{FDR} = 0.02$). We did not find significant effects of group or interaction for any MST measure (leaf number: $p_{FDR} > 0.19$; maximum degree: $p_{FDR} > 0.38$; mean eccentricity: $p_{FDR} > 0.13$). During the period before stimulus presentation, participants' leaf number increased steadily with task progress, whereas mean eccentricity showed the opposite pattern. In addition, participants displayed an inverted U-shaped curve of maximum degree with task progress (Fig. 2J-L, Supplementary Table 1). The pairwise comparison revealed that participants' maximum degree and leaf number were significantly higher during "Middle" phase than during "Early" phase (paired permutation test, two-sided: $p_{FDR} < 0.015$), whereas participants' mean eccentricity was significantly lower during "Late" phase than during "Early" phase (paired permutation test, two-sided: $p_{FDR} = 0.0495$). Participants' leaf number was also significantly higher during "Late" phase then during "Early" phase (paired permutation test, two-sided: $p_{FDR} < 0.0001$). More details of the pairwise comparisons are shown in Supplementary Table 2.

In the beta band, we did not find significant effects of phase, group or interaction for any MST measure (leaf number: $p_{FDR} > 0.11$; maximum degree: $p_{FDR} > 0.25$; mean eccentricity: $p_{FDR} = 0.13$).

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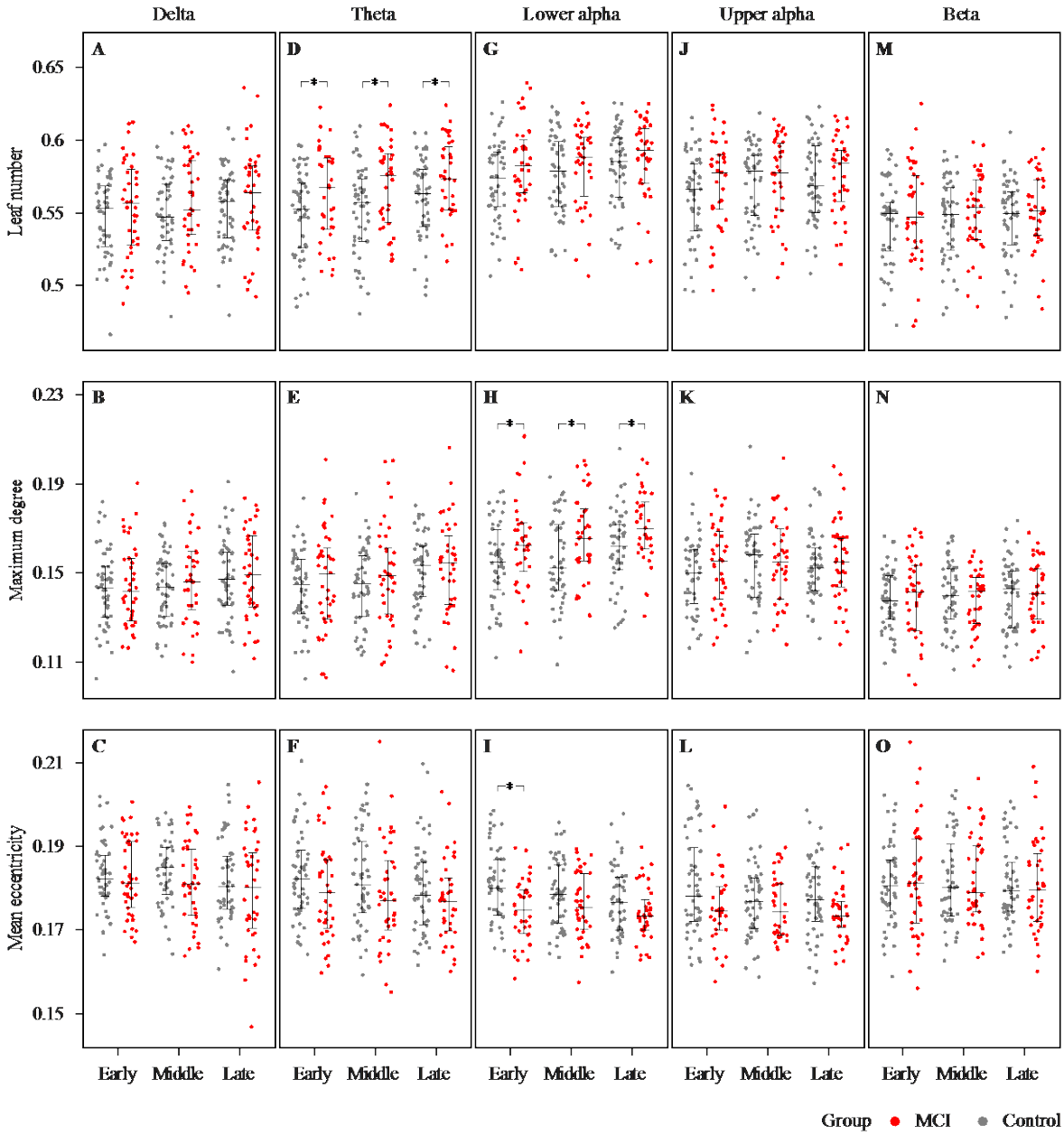


Figure 2: Leaf number (first row panels), maximum vertex degree (second row panels) and mean eccentricity (third row panels) across phases and groups for each frequency band. Each dot represents the value of one participant at particular phase ("Early", "Middle", "Late") and group (red: MCI, gray: control) in the delta band (**A**-**C**), theta band (**D**-**F**), lower alpha band (**G**-**I**), upper alpha band (**J**-**L**), and beta band (**M**-**O**). The median of each group is denoted as a black horizontal bar; error bars around this median denote the interquartile range. Asterisks indicate the significance level of post hoc tests across groups, false discovery rate corrected p values less than 0.05 were considered significant. MCI = mild cognitive impairment.

3.2 Brain-behaviour relationships

In the theta band, leaf number, averaged over all three phases, correlated positively with reaction time (Pearson's correlation test: $p = 0.006$; Fig. 3A) in the MCI group. In the control group, in contrast, this relationship was not significant (Pearson's correlation test: $p = 0.54$). The correlation coefficients were significantly different between groups (Fisher's Z-test, $p =$

0.01). In the lower alpha band, we found the same correlation pattern for maximum degree, averaged over all three phases (Pearson's correlation test, MCI: $p = 0.005$; Controls: $p = 0.08$; Fisher's Z-test, $p = 0.001$; Fig. 3B), whereas no significant correlations were observed for eccentricity, averaged over all three phases (Pearson's correlation test, MCI: $p = 0.19$, Controls: $p = 0.91$). More details of brain-behavior relationships, separately for each of the three phases, are shown in Supplementary Table 4.

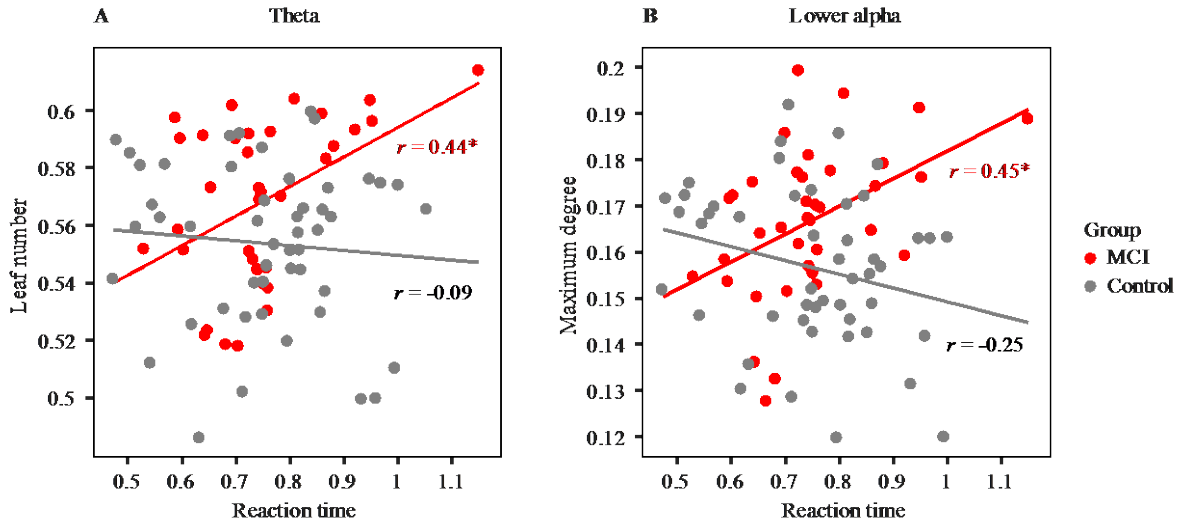


Figure 3: Brain-behaviour relationships. (**A**) Scatterplots illustrate correlations between reaction time and leaf number in the theta band, averaged over all three phases, within each group (red: MCI, gray: control) (**B**) Scatterplots illustrate correlations between reaction time and maximum degree in the lower alpha band, averaged over all three phases, within each group (red: MCI, gray: control). Asterisks indicate significant correlations; p values less than 0.05 were considered significant. r = correlation coefficient, MCI = mild cognitive impairment.

3.3 Consistency of MST measures across phases

The consistency of each MST metric was excellent (ICC $>$ 0.77) according to Cicchetti (1994) in each frequency band for both groups, except for fair consistency (ICC = 0.53) of mean eccentricity in the lower alpha for the MCI group. A full list of ICC values and their 95% confidence intervals are given in Supplementary Table 5.

4. Discussion

While previous studies have observed increased network integration during tasks in individuals with MCI, the association between this integration and actual task performance has remained unexplored. The present study is the first to investigate this link, demonstrating a relationship between network integration during task engagement and performance in MCI patients.

We have demonstrated that network integration during the whole task was significantly different between MCI and control groups. During periods before stimulus presentation,

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patients with MCI exhibited significantly lower mean eccentricity and higher maximum degree in the lower alpha frequency band, and significantly higher leaf number in the theta frequency band, compared to controls, indicating a more integrated, centralized topology. This finding aligns with previous research demonstrating increased network integration in MCI patients during various stages of cognitive tasks, including the period before stimulus presentation, task performance, and retention period of cognitive tasks (Buldú et al., 2011; Fodor et al., 2021; Wei et al., 2015). Furthermore, it is compatible with our prior analysis of this sample, which revealed a greater increase in global network integration from pre- to post-task resting-state in MCI patients compared to controls (Požar et al., 2023). Considering that brain network integration arises from intricate interaction between specialized brain regions, each responsible for specific functions (Genon et al., 2018, van den Heuvel and Sporns, 2013), the shift towards a more integrated network topology in MCI might reflect excessive recruitment of diverse brain areas to accomplish a given task that healthy controls could manage with more focused activation.

A recent study suggests that older adults benefit from a more integrated network organization during task performance compared to younger adults (Crowell et al., 2020). Perhaps surprisingly, we have shown that increased network integration during periods before stimulus presentation was related to worse performance in the MCI group. Specifically, higher leaf number in the theta band and higher maximum degree in the lower alpha band correlated with longer reaction times in the MCI group. No such association was found in the control group. Notably, this difference existed despite similar overall task performance between the groups. This suggests that network integration likely plays a distinct functional role in MCI, even when performance seems unaffected.

Two potential explanations exist for increased network integration during tasks, depending on the level of performance achieved. Compensation proposes that recruiting additional brain regions after initial impairment improves performance (Fornito et al., 2015). Conversely, when increased integration does not benefit performance, it might indicate network de-differentiation due to enhanced neural noise or an excitation-inhibition imbalance (Fornito et al., 2015). De-differentiation disrupts the functional specialization of task-related regions, leading to non-selective recruitment of irrelevant brain areas. Though our motion discrimination task showed no performance difference between the MCI and control group, our results support the latter interpretation. The MCI group displayed greater network integration during the task than controls, but performance declined with increased integration, indicating a non-beneficial effect. The significant group difference in the brain-behavior relationship further confirms dysfunctional integration in MCI. Therefore, de-differentiation, rather than compensation, is a more likely explanation for the observed network reorganization in MCI patients. This suboptimal integration pattern during cognitive tasks might reflect disinhibition in these patients (Fodor et al., 2021). Additionally, the observed over-centralization of brain networks in MCI raises the possibility that essential vertices become overloaded during a task, leading to increased network vulnerability (de Haan et al., 2012). Future research is needed to clarify the mechanisms involved.

We have shown that functional brain network organization dynamically reconfigures throughout the task. This dynamic pattern has been consistent between both groups and seen to some extent, except for the beta frequency band, in all other four frequency bands prior to stimulus onset. Specifically, regardless of the group, we observed that the leaf number and maximum degree generally increased, while mean eccentricity decreased from the early to the late phase of the task. These differences accumulated further with time, with additional

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increases in leaf number and maximum degree alongside a continued decrease in mean eccentricity. These results suggest that longer task durations shift brain networks in older adults towards a less optimal integrated network architecture, potentially requiring costly infrastructure (Meunier, 2010). Similar patterns have been observed in studies exploring the effects of cognitive fatigue on functional network organization. Li et al. (2019) investigated brain network changes by studying participants performing a short mental arithmetic task twice, with a more demanding task in between to induce mental fatigue. The study revealed a significant decrease in characteristic path length during the second task compared to the first, suggesting that mental fatigue, induced by a demanding cognitive task, leads to increased network integration. Zhong et al. (2022) reported similar findings with increased network integration after mental fatigue. Interestingly, Ioannucci et al. (2019) introduced neural fatigue related to overwork, caused by keeping specific neural assemblies active over a prolonged period of time. This alignment suggests that our study participants and individuals experiencing fatigue might exhibit comparable brain dynamics, where more widespread activity is needed to complete the same task in the later stages.

This study investigated brain networks in sensor space, using the phase lag index to measure functional connectivity since it minimizes the effects of volume conduction (Stam et al., 2007). We utilized MST analysis to assess network topological properties. This method overcomes the challenges of thresholding and normalization faced by conventional approaches. Notably, our results indicated that MST metrics remained highly consistent throughout the three task phases. Furthermore, MST analysis revealed sensitivity to changes in global network integration within the MCI group during the task. To directly localize brain regions critical for task performance, source space analysis would be a valuable addition to future investigations. Additionally, anatomical-functional mapping with functional magnetic resonance imaging might be useful for precisely identifying brain areas with enhanced integration during visual motion discrimination or other cognitive tasks vulnerable to neurological decline (e.g., memory or executive processing). For tasks specifically involving visual discrimination, techniques such as magnetic resonance spectroscopy could offer valuable insights into the dynamic balance between excitation and inhibition in brain areas like hMT+/V5, which are critical for visual decision-making.

While our study has many strengths, a higher percentage of female participants limits its generalizability. As in our study, research on aging often suffers from a significant gender disparity, with too few male participants included in studies. This imbalance can limit our understanding of how aging processes affect men, potentially skewing conclusions drawn from research findings. For instance, studies investigating cardiovascular health or cognitive decline may not accurately represent the male population's experiences and needs. Addressing this disparity in the future is crucial for developing targeted interventions and treatments that cater to both sexes, ensuring equitable healthcare outcomes as we confront the challenges of an aging population (Gorska-Ciebiada et al., 2020).

Our results highlight the potential of analyzing network integration during task performance for early detection of cognitive impairment. Consistent with previous research, we observed increased network integration in patients with MCI compared to neurologically healthy elderly individuals while performing a specific task. However, our novel finding lies in the distinct brain-behavior relationships between the two groups. While lower task performance in the MCI group was associated with higher network integration, no such correlation existed for the control group. Together, our results suggest that MCI disrupts network integration during the period before stimulus presentation, likely not as a compensatory mechanism, but rather as a

process of network de-differentiation, where distinct brain regions lose their specialized roles and become more interconnected in a less effective manner.

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Conflict of Interest Statement

The authors declare no competing or financial interests. of the manuscript.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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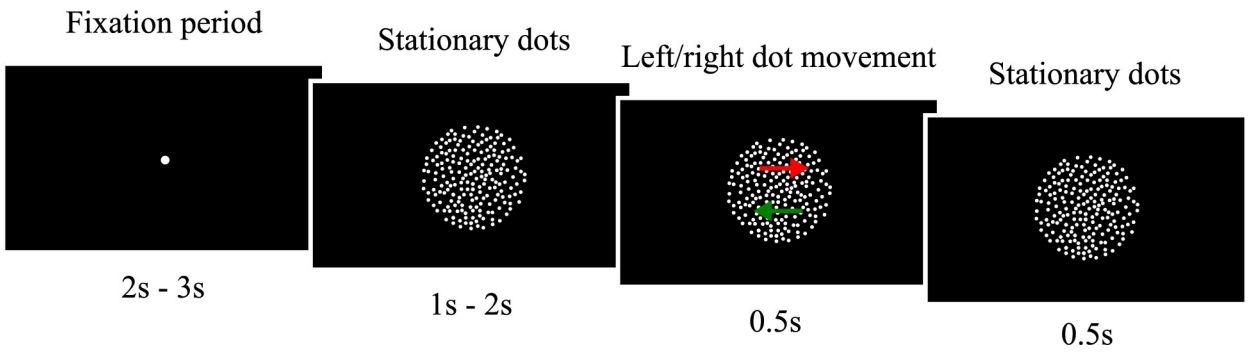


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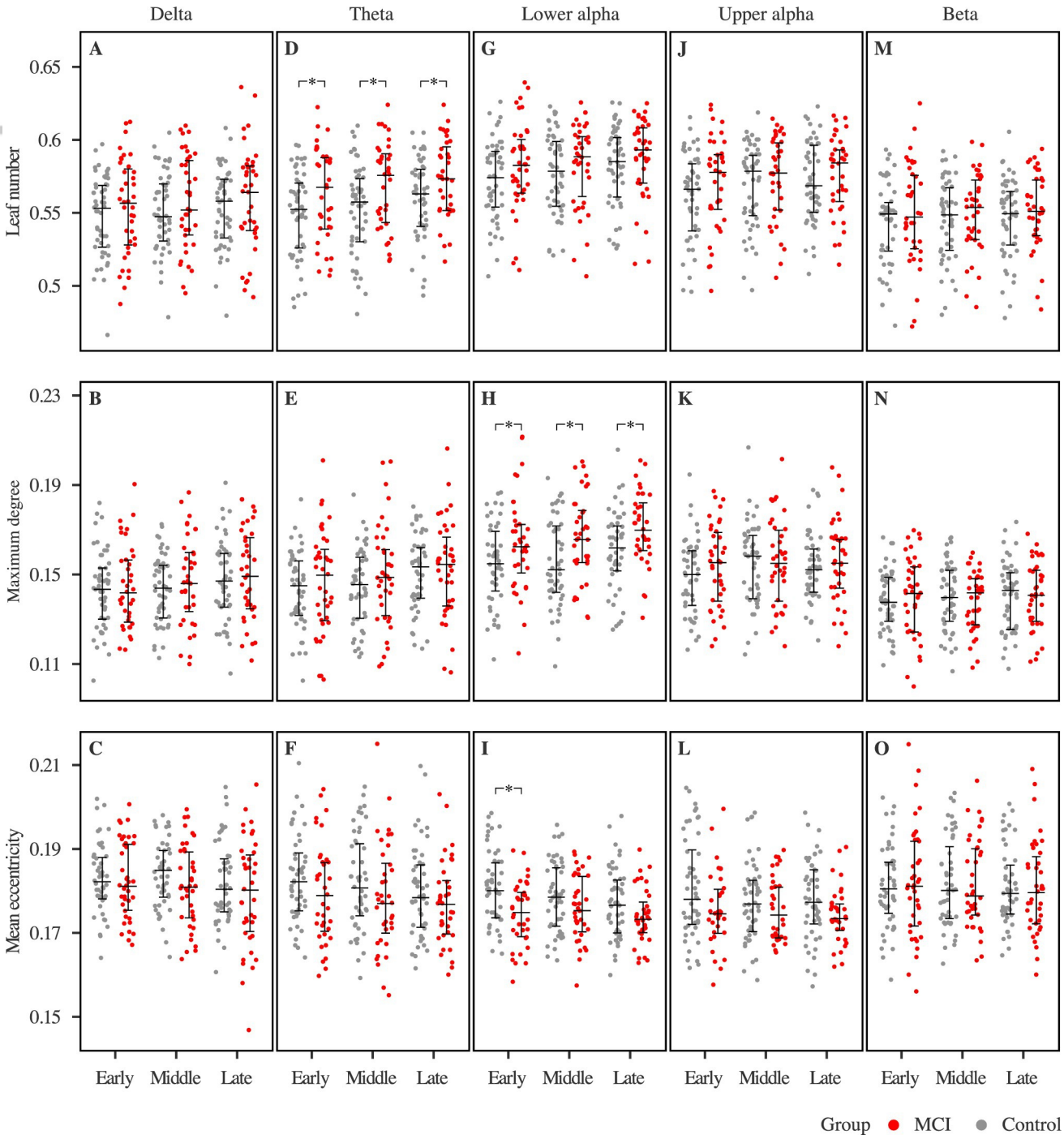


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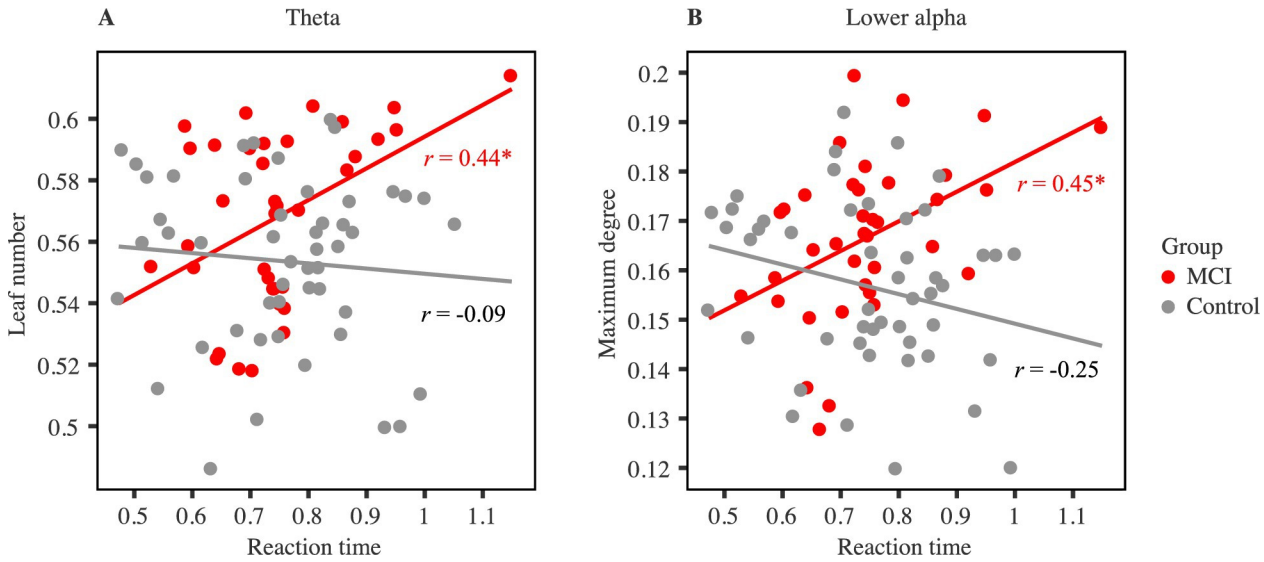
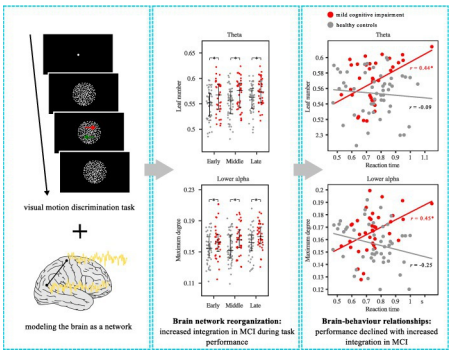


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