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Exploring the cognitive connectome in patients with mild cognitive impairment and healthy older adults

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Abstract

Introduction. Studies on aging and cognitive impairment using graph theory metrics have revealed insights into network efficiency, hub regions, and cognitive module organization. The purpose of the present study was to use the cognitive connectome in a group of patients with MCI (mild cognitive impairment) and healthy controls (HC). ***Materials and methods.*** The study included two groups, MCI-group (n = 48) and HC (n = 48), female/male ratio of 42/6 in MCI-group and 44/4 in HC, mean ages 76.8 ± 5.5 years in MCI-group and 75.5 ± 6.2 years in HC. The research utilized diagnostic screening tests (MoCA, MMSE, GDS), neuropsychological assessment (Comprehensive Trail Making Test, Verbal fluency test), and graph analysis to construct a cognitive connectome. Newman's algorithm was employed to identify cognitive modules. ***Results.*** Significant differences were observed between the groups in screening tests, Verbal fluency test, and CTMT performances and cognitive modules ($p<0.01$). No significant differences were found in global network measures, including efficiency, transitivity, modularity between the MCI and control group. ***Conclusions.*** The study identified fewer, yet more intricate cognitive modules in the MCI group compared to the control group. However, these findings should be interpreted cautiously as the connectome was constructed using subtests from screening tests, which might have resulted in a network structure different from those reported in other studies. *Geriatria 2024;18:149-162. doi: 10.53139/G.20241820*

Keywords: mild cognitive impairment, cognitive connectome, graph theory, cognitive decline

Introduction

Brain function relies on the efficient communication between different functional brain systems. The anatomical basis facilitating neural communication and integration is the 'connectome'—a intricate network of structural connections within a nervous system. The primary objective of the connectomics field is to comprehend how the network organization of the connectome correlates with the brain's ability for neural processing and overall brain function [1,2]. Topological changes in the brain's structural connectome associated with normal aging, offering potential structural foundations for cognitive aging and valuable imaging markers for predicting individual cognitive functions in the elderly [3]. Alterations in the connectome have been observed in various neurological disorders [4]. The relationship between reliability ("connectivity fingerprinting") and validity (associations with disease-related biomarkers) still lacks definitive answers [5].

The network science approach, specifically graph theory, stands out as a potent mathematical framework for investigating the functional architecture of the human brain [6,7]. The use of graph theory and network topology has made it possible to describe the brain's functional connections using a small number of indicators that have a biological interpretation [8,9]. In neuroscience, descriptive metrics that provide insights into both local and global characteristics of network structure have been extensively employed across various data sets encompassing structural and functional information from diverse species. These examinations consistently uncover nonrandom topological features, including elevated clustering, abbreviated path lengths, and the presence of network communities (modules)

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connected by highly central hub nodes [10]. The topological role of each node within the network can be assessed using graph theory metrics, which gauge the node's connectivity within its own module and with other modules. This metric categorizes nodes into two groups: connector nodes, characterized by numerous global edges spanning multiple modules, and local nodes, primarily associated with within-module edges. Connector nodes are believed to facilitate access to information across diverse modules, potentially integrating or coordinating connectivity among them, while local nodes support the specialized functions within individual modules [11]. The brain network is a representation where nodes correspond to neurons, and edges symbolize the axonal connections between these neurons [12]. The modules in the brain are indicative of the inherent structural connectivity framework, wherein a significant portion of the functional connections within a module corresponds to direct anatomical connections [13,14]. Human brain imaging data revealed the presence of a structural wiring network characterized by modularity, where there is strong connectivity within modules and relatively weaker connectivity between modules [4]. Genes play a strong and preferential role in shaping functionally valuable, metabolically costly connections between connectome nodes [15]. Connecting nodes tie modules together, processing signals between them at all times, generating between different areas of the brain a personalized model of its activity described by cognitive and behavioral characteristics [16]. There are disproportionately more connections between modules performing related cognitive functions than between modules involved in completely different processes. Neural networks exhibit a community structure in which nodes form clusters or communities, and connections within communities are stronger than connections between members of different communities [11,17]. By working within local modules, the brain saves energy by operating over short distances and also allows the system to evolve faster and adapt to a changing environment (one module can change or duplicate itself independently of the others, and there is no risk that other well-adapted modules will change or be lost in the process) [11].

Graph theory has been widely applied to neuroimaging data in the field of aging [18,19]. Studies on brain connectivity have demonstrated that regions with extensive connections, often referred to as 'hub' regions, are especially susceptible to Alzheimer's pathology, exhibiting notable amyloid-β deposition in the early stages. Recently, it has been observed that heightened local neuronal activity contributes to an increased deposition of amyloid [20]. Post-hoc analysis of regional synchrony using MRI (magnetic resonance imaging - MRI) in patients with mild AD (Alzheimer's disease - AD) revealed increased synchrony involving frontal cortex areas, and overall decreases concentrated in parietal and occipital areas. This pattern effectively translated into a global decrease in functional long--distance connections between frontal and posterior brain areas [21]. MCI (mild cognitive impairment), a prodromal state of AD (for certain patients), is characterized by the disorganization of functional hubs and the modular structure of the default-mode network. Notably, changes in functional connectivity have been proposed as potential markers for identifying MCI and individuals at risk of developing AD [4].

Transferring the idea of a connectome from the field of neuroimaging to the field of cognitive data, or the creation of a "**cognitive connectome,**" is currently the subject of intense research. This approach is expected to yield important new insights into the organization of human cognition. This step is justified in order to better understand the behavioral consequences of a thoroughly studied brain connections in the context of neuroimaging studies [13,22]. One study discovered that the structural connectome of the brain experiences a notable decline in topological efficiency, modularity, and hub integration during the process of normal aging (n=633, cognitively healthy elderly individuals), particularly in the frontal, parietal, and superior temporal regions. Significantly, the study revealed a positive correlation between network efficiency and attention, as well as executive function in elderly individuals. Furthermore, network efficiency played a crucial mediating role in the age-related decline of these cognitive functions [4]. Garcia-Cabello et al., [23], examined 334 cognitively unimpaired individuals categorized into early-middle-age (37-50 years, n = 110), late-middle-age (51-64 years, n = 106), and elderly (65-78 years, n = 118) groups. Cognitive networks were constructed from 47 cognitive variables for each age group using graph theory. Comparative analyses of global and nodal graph measures revealed a cognitive connectome characterized by five modules: verbal memory, visual memory-visuospatial abilities, procedural memory, executive-premotor functions, and processing speed. The elderly group exhibited reduced transitivity and average strength, along with increased global efficiency compared to the

early-middle-age group. Nodal analyses underscored the pivotal role of executive functions and processing speed in elucidating the distinctions between age groups. Gonzalez-Burgos et al. [24] explored compensation mechanisms for age-related differences in verbal fluency using graph theory. Their study highlights the potential of graph theory as a valuable approach for investigating cognitive aging, presenting an alternative to other multivariate methods like random forest analysis or orthogonal partial least squares to latent structures [24,25]. Notably, only four previous studies, outside the realm of normal aging, have applied graph theory to cognitive data. Among these, three investigations focused on children with epilepsy [26,27], while another study explored neurological patients with diverse etiologies [28].

One of the conclusions of past studies [23] using the cognitive connectome suggested that future studies should also consider patients with cognitive impairment. Therefore, the purpose of this study was to use graph analysis in patients with MCI. Clinical practice is often associated with time constraints, therefore the purpose of this study was to use the subscale scores of the various screening tests and verify their usefulness using graph analysis. The aim of the study was to answer the question of whether there were differences between MCI patients and controls in terms of the number of modules and network parameters.

Material and methods

Study Design, Setting, and Duration

The research was carried out on 98 individuals admitted to the John Paul II Geriatric Hospital in Katowice (Poland) between 2016 and 2018. The individuals were hospitalized for a thorough geriatric assessment. The study received approval from the Bioethics Committee for Scientific Research at the Jerzy Kukuczka Academy of Physical Education in Katowice (Resolution No. 2/1/2015). Initially, 106 patients were screened; however, 8 patients were excluded from the final analysis due to statistically significant differences in age and education between the study groups. Participants provided voluntary and informed consent, receiving blank informed consent forms and supplementary materials explaining the study's purpose and procedures. All participants meeting the inclusion and exclusion criteria who agreed to take part were enrolled in the study. Only those patients with no missing outcome were included in the analysis. To determine the optimal sample size for the study, a power analysis was performed, considering a significance level of $\alpha = 0.05$, a targeted power of 0.90, and an anticipated effect size (Cohen's d) of 0.67. The outcome of the power analysis revealed that a minimum sample size of 48 was necessary to achieve the specified power level. All the participants were assigned to 2 groups of 48 patients each by diagnosis:

- A group of patients with a diagnosis of MCI (MCI-group) based on criteria,
- A group of patients without a cognitive impairment, constituting the control group (HC – healthy control).

Study Inclusion, Exclusion, and Diagnostic Criteria

The study enrolled participants aged 60 years and older, all of whom were right-handed and native Polish speakers. Prior research and recommendations suggest that the MoCA scale is particularly effective in detecting mild cognitive impairment (MCI). Some studies propose improved diagnostic accuracy by using multiple screening tests, albeit moderately, for patient categorization. Therefore, two screening tests, MoCA and MMSE, were employed based on this rationale [29,30].

Screening tests can be combined either in parallel or serial connection. In a parallel combination, a patient is categorized based on scoring below the cutoff point on at least one test. Data from our study support the notion that combining MMSE and MoCA in parallel enhances sensitivity [30]. Hence, this criterion was adopted in our study: individuals scoring below the cutoff on either MMSE or MoCA were classified as having MCI. The score range for MCI was 19-25 on the MoCA scale and 24-26 on the MMSE, based on previous research conducted on the older Polish population [31]. Normal cognition was defined as MoCA scores of 26–30 and MMSE scores of 27-30, adjusted for age and education level [32].

Exclusion criteria comprised visual impairments, diagnosed dementia, behavioral disorders, impairment of activities of daily living (ADL <3 points), history of stroke, traumatic brain injury, frailty syndrome, Parkinson's syndrome, illiteracy, mental disorders (including depression assessed with the Geriatric Depression Scale), schizophrenia, alcohol dependence syndrome.

Data Collection and Instruments Used

The initial assessment of patients in the geriatric ward comprised the administration of several tests, including the Montreal Cognitive Assessment (MoCA), Mini-Mental State Examination (MMSE), and Geriatric

Depression Scale (GDS). Following this, a comprehensive neuropsychological evaluation was conducted, incorporating tests such as the Comprehensive Trail Making Test (CTMT) and Verbal Fluency Test. These two stages of assessment were separated by a minimum of two days. Throughout the study, various variables potentially influencing the results, such as stress severity, progression of physical rehabilitation, and the somatic condition of patients, were consistently monitored. Both the initial and follow-up examinations were conducted by a psychologist in an office setting.

Neuropsychological assessment

In the present study, we used individual scores collected by diagnostic screening tests (MMSE, MoCA) and taking into account individual tasks related to specific cognitive domains (subscales of a given cognitive domain, e.g., memory in the MMSE). The literature has pointed to the usefulness of this type of analysis of scores within a given domain in estimating progression to dementia (in MoCA it is Memory Index Score) [33]. Some screening tests (e.g., ACE III) present scores of individual subscales in addition to the total score, which can be useful in analyzing the profile of cognitive impairment [34].

In order to increase the number of variables, individual trials of the CTMT were included in further analyses. Below is a brief description of the tests that assess cognitive function:

Comprehensive Trail Making Test (CTMT)—a psychological test of the ability to focus attention on visual–spatial material—assesses visual search ability, psychomotor speed, as well as the ability to switch attention between stimuli of different types, which is one of the manifestations of working memory and executive functions. The CTMT was developed to extend the original TMT test, provided a more accurate assessment of cognitive functions, and was more comprehensive than the standard version of the TMT. Trail 1 is similar to Part A of the TMT. Trail 5 in the CTMT is similar to part B of the TMT. The direction of lines in the CTMT is much more complex and varied than in the original TMT, requiring a greater performance of executive functions, including cognitive control and behavioral monitoring, the aforementioned psychomotor speed, and performance of visuospatial processes. The CTMT includes five trails that present varying levels of complexity and difficulty, and a variable number of distractors. In Trail 1, the patient draws a line to connect in order the numbers 1 through 25, each contained in a plain, black circle. In Trail 2, the patient draws a line to connect in order the numbers 1 through 25, each contained in a plain, black circle (29 empty distractor circles appear on the same page). In Trail 3, the examinee draws a line to connect in order the numbers 1 through 25; 13 empty distractor circles and 19 distractor circles containing irrelevant line drawing appear on the same page. In the following section, in Trail 4, the patient draws a line to connect in order the numbers 1 through 20, where 1 of the numbers is presented as Arabic numerals (e.g., 1 and 7) and the remaining numbers are spelled out in the English language form (e.g., "nine"). In Trail 4, there are circles with numbers and boxes with words; the words in the boxes are number words (for example, "nine"). The patient's task is to draw a line from 1 to 2 and so on, connecting the circles to the boxes in the correct order. In Trail 5, the patient draws a line to connect in alternating sequences the numbers 1 through 13 and the letters A through L, beginning with 1 and drawing a line to A, then 2, then B, and so on until all the numbers and letters are connected (15 empty distractor circles appear on the same page). The patient has to ignore all the circles where there are no letters or digits. For all the trails the patient's task is to connect the points as rapidly as possible. Errors defined as marking a number or letter out of sequence were pointed out, but they were not converted to any form of standardized or scaled score. An error had a negative impact on the examinee's score because the corrections added to the time needed to complete each trail. According to the author, the CTMT test can be performed on patients between the ages of 11 and 74 years, who can understand the directions for the subtest, who are able to formulate the necessary responses, and who can pass the practice items. Although the patients who participated in our study were older (>74 years), they met all the requirements listed above in the test manual to be eligible for the study. The interpretation used the overall score, which was the sum of all the raw scores, expressed in seconds from each part.

Verbal fluency test—the patient is given 60 second to produce as many unique words as possible within a semantic category (e.g., animals—semantic fluency) or starting with a given letter (e.g., F, A, S—phonemic phonetic fluency). Executive functions, semantic retrieval, processing speed, and working memory are involved in verbal fluency tasks. In our study, we used semantic fluency (category: animals) and phonetic fluency (words

beginning with the letter "K"). The performance indicator was the number of words given by the patient.

Graph Analysis

All cognitive variables detailed in Table I were selected as the nodes to construct the network constituting the cognitive connectome. These variables were extracted from the screening tests – MoCA and MMSE (A). Based on these variables, a hypothetical model of modules was developed to account for each cognitive domain (B).

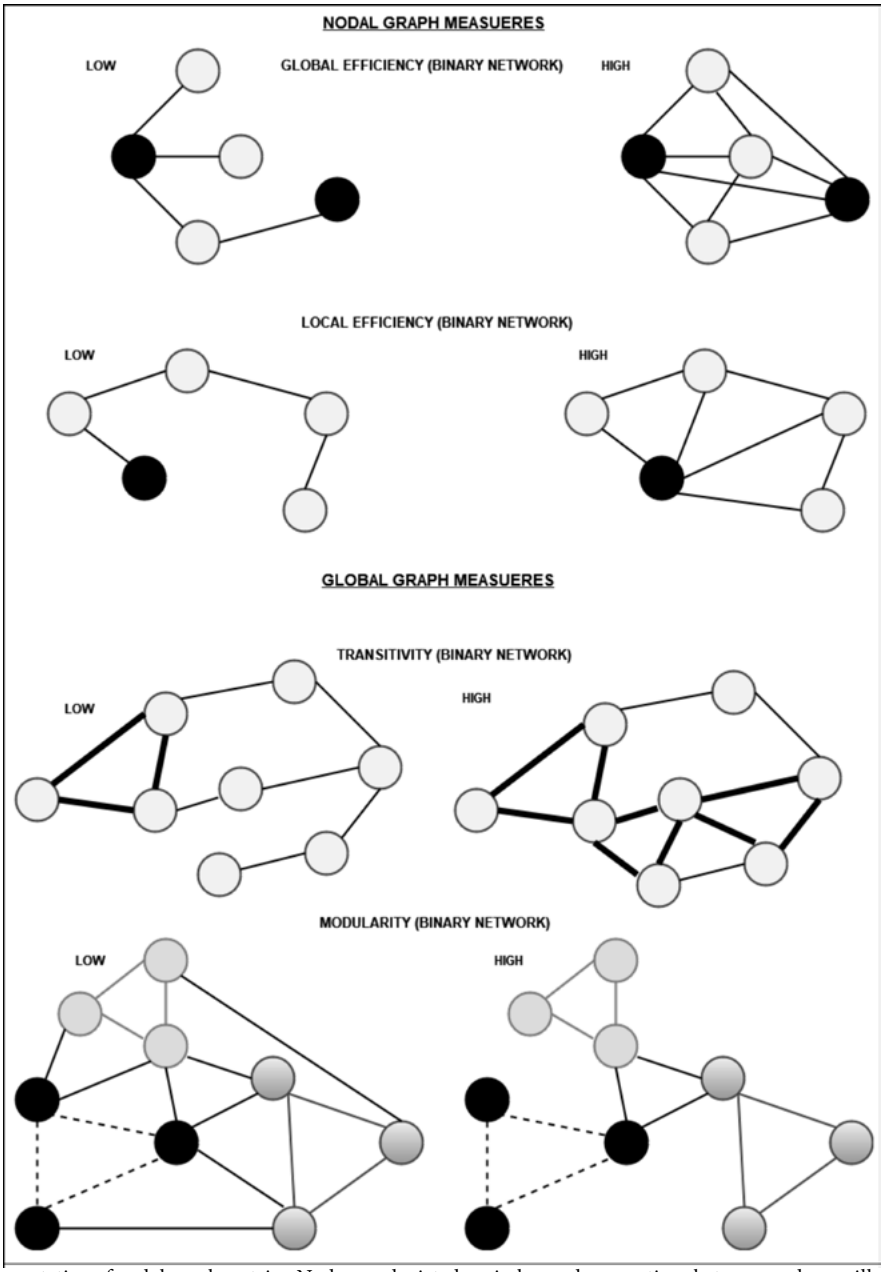
The interconnections among nodes were computed using matrices of Spearman's correlation coefficients between each node pair. These matrices were transformed into binary form by applying a threshold to the correlation coefficients within the range of 15% to 50% of connections, with a step size of 1%. This approach aimed to eliminate disconnected networks (densities below 15%) and random topologies (densities above 50%, where the small-world index approached). Comparisons of network topologies were conducted across this density range. While results from global graph measures were presented across all densities, nodal graph measures were considered throughout all densities but reported specifically at the median density (30%) for simplicity and in accordance with established practices to represent the entire range of densities [35,36]. Figure 1 presents a visual representation of the nodal graph measures analyzed in this study. These measures include nodal global efficiency, local efficiency, computed from binary networks at various densities. Additionally, nodal strength, derived from the weighted network before binarization, is also featured. Nodal global efficiency represents the average of the inverse shortest path length from a node to all other nodes in the network. Local efficiency quantifies the global efficiency of a node within the subgraph formed by its neighbors. Nodal strength is defined as the sum of the weights of all edges connected to a given node. The characteristics of selected network parameters are described in Figure 1.

Statistical Analysis

Graph analysis is based on correlation, and for this reason all the variables that were collected during the study were included. A total number of 14 variables were obtained and used for further analysis. All cognitive variables detailed in Table II were selected as the nodes to construct the network constituting the cognitive connectome. The table shows the cognitive variables used as nodes in the network construction (A). In addition, the table shows the cognitive variables included in each of the different cognitive modules based on Newman's

Table I. Cognitive variables extracted from screening and neuropsychological tests and presented in major cognitive domains

Cognitive variables included as the nodes in graph analysis (A)	Score range / indicators	(B) Modules created from from other studies (human)
MMSE-Memory	0-6	Memory
MoCa-Memory	0-5	
MMSE-Language	0-8	Language
MoCa-Language	0-6	
MMSE-Attention	0-5	Attention
MoCa-Attention	0-5	
MoCa-Visual-spatial functions	0-5	Visual-spatial functions
Semantic fluency	Number of words	Executive functions
Phonetic fluency	Number of words	
CTMT 4	time (s)	
CTMT 5	time (s)	
CTMT 1	time (s)	Processing speed
CTMT 2	time (s)	
CTMT 3	time (s)	



Diagrammatic representation of nodal graph metrics. Nodes are depicted as circles, and connections between nodes are illustrated by edges. In the global efficiency, the circles represent the nodes, with the connections showing the less efficient connectivity between the two black nodes on the left compared to the more efficient connectivity on the right (multiple one- and two-step connections between the black nodes). Moving to the local efficiency section, it demonstrates less efficient connectivity between the black node and all other nodes on the left (only one connection) and more efficient connectivity on the right (four connections). The schematic representation of global graph metrics involves circles denoting nodes and edges indicating connections. The transitivity metric measures the number of triangles in a network, with the left panel illustrating lower transitivity (one triangle) and the right panel depicting higher transitivity (three triangles). In the modularity panel, three modules are shown, and the left part indicates less clear division into separate communities (high between-module connectivity relative to within-module connectivity: low modularity), while the right part demonstrates a clearer division (low between-module connectivity relative to within-module connectivity: high modularity). Parentheses note the use of binary networks for transitivity and modularity global measures [23].

Figure 1. Schematic representation of global and nodal graph measures

algorithm (B, C). The Newman algorithm [37] is a method of analyzing the structure of a network to detect communities or modules in graphs. The main goal of the algorithm is to find the distribution of nodes in the network so as to increase the density of connections within communities and at the same time reduce the density of connections between communities. Newman's algorithm is popular in the analysis of social networks, biological networks, or other network structures. The modular structures that result from this algorithm help identify important communities or groups in a network, which can lead to a better understanding of network structure and function. Only Newman's algorithm was used. Another commonly used Louvain algorithm is prone to creating communities with poor connectivity, and in extreme cases communities can even be disconnected, especially when the algorithm is executed iteratively [38].

The statistical analysis was conducted using Python version 3. Descriptive analyses were provided for demographic and cognitive data, and results were analyzed by groups. The normality of parameter distribution was assessed using the Shapiro–Wilk test. Subsequently, the t-test (or Welch's test for unpaired samples with unequal variances) was applied when applicable; otherwise, the Wilcoxon test was utilized. Spearman's rank correlation was employed to determine the correlation coefficient. The statistical significance threshold was set at $p < 0.05$. The sample size was calculated in accordance, with the logical logical justifications as proposed by Lakens [39].

Results

The study groups exhibited no significant differences in age and education. Patients with MCI scored worse on screening tests (MMSE and MoCA) compared to those in the control group ($p<0.01$). Statistically significant disparities were observed between Group I (MCI) and HC-group regarding the number of words spoken in the Verbal fluency test for both semantic and phonetic criteria ($p<0.01$). Patients with MCI reported a lower number of words, aligning with the specified criteria. Additionally, significant distinctions were noted between the MCI group and control patients on the CTMT ($p<0.01$), with patients with MCI taking longer to complete the test. Statistically significant differences were also obtained between the study groups in terms of

Table II. Cognitive variables included in each group

Cognitive variables included as the nodes in graph analysis (A)	(B) modules generated from Newman's algorithm – MCI group	(C) modules generated from Newman's algorithm – HC
MMSE-Memory	Variables in Community 1: MMSE_ Memory, MoCA_Memory, MMSE_ Language, MoCA_Language, MMSE_Attention, MoCA_Attention, MoCA_Visuospatial, Phonetic_ Fluency, Semantic_Fluency	Variables in Community 1: MoCA_Memory, MMSE_ Language, MMSE_Attention, MoCA_Attention, MoCA_ Visuospatial, Semantic_Fluency
MoCa-Memory		
MMSE-Language	Variables in Community 2: CTMT1, CTMT2, CTMT3, CTMT4, CTMT5	Variables in Community 2: MMSE_Memory, CTMT1, CTMT2, CTMT3, CTMT4, CTMT5
MoCa-Language		
MMSE-Attention		Variables in Community 3: MoCA_Language, Phonetic_ Fluency
MoCa-Attention		
MoCa-Visual-spatial functions		
Semantic fluency		
Phonetic fluency		
CTMT 1		
CTMT 2		
CTMT 3		
CTMT 4		
CTMT 5		

memory module (p<0.01), attention (p<0.01), visuospatial function (p<0.01), and language function (p<0.01). Detailed data can be found in Table III. The results of the neuropsychological tests are presented in Figure 2.

The modules shown were generated using data from the literature (not using Newman's algorithm).

In Spearman correlation coefficient analysis between individual subscales of screening tests and neuropsy-

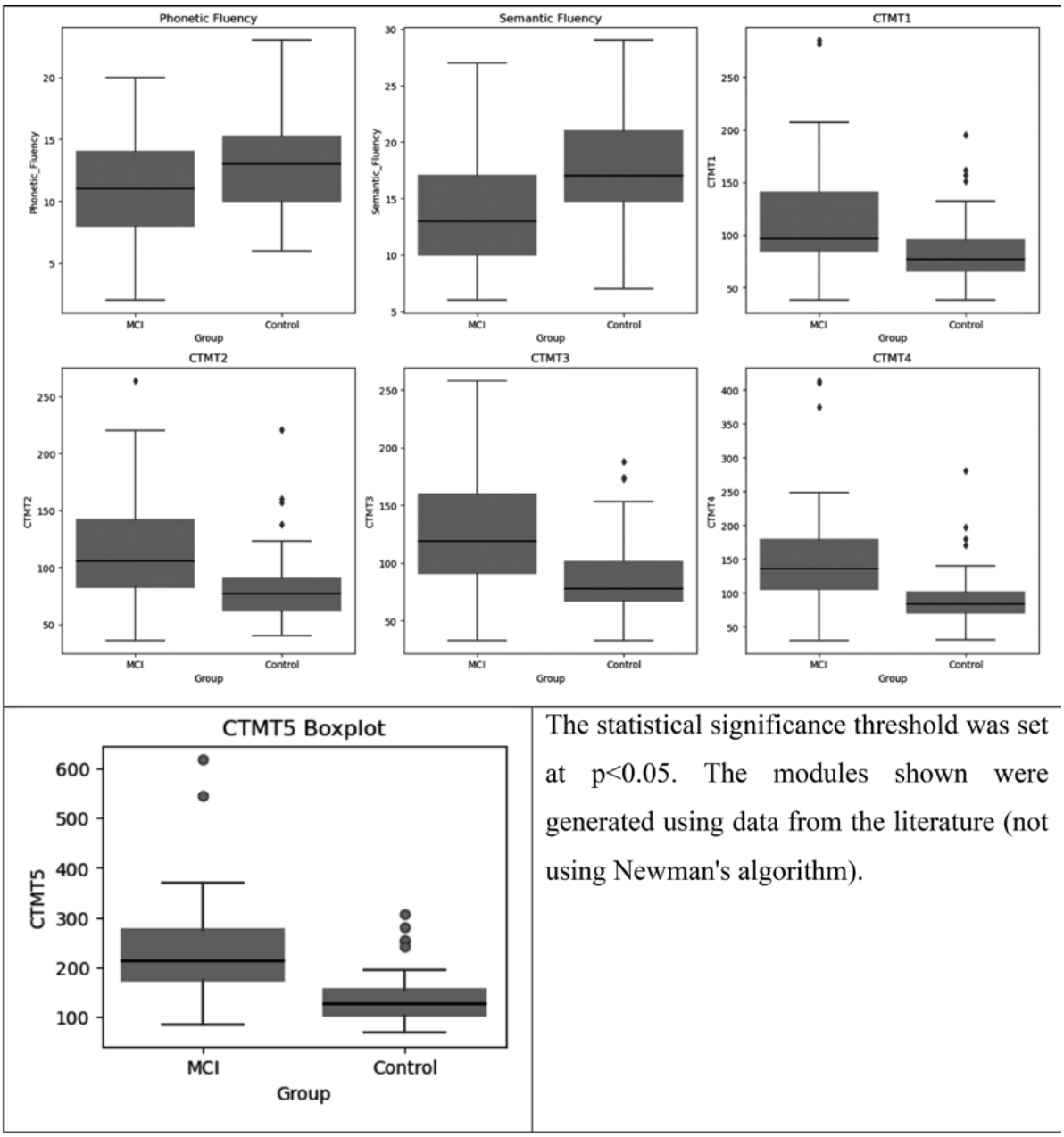


Figure 2. Comparison of MCI patient modules and HC group

Table III. Sociodemographic variables, screening and neuropsychological test results

	MCI	HC	p value
	M (SD)	M (SD)	
Age (years)	76.83 (5.57)	75.54 (6.21)	0.28
Sex (male/female)	(8/40)	(4/44)	
Education (years)	10.22 (3.10)	10.84 (2.25)	0.29
MMSE	28.33 (2.02)	29.18 (0.95)	p<0.01 **
MoCA	22.77 (2.24)	27.75 (1.80)	p<0.01 **
Semantic fluency	13.79 (4.65)	17.85 (5.12)	p<0.01 **
Phonetic fluency	11.08 (4.21)	13.25 (4.11)	p<0.01 **
CTMT Trail 1	114.87 (52.22)	85.27 (32.53)	p<0.01 **
CTMT Trail 2	120.79 (50.77)	83.58 (33.28)	p<0.01 **
CTMT Trail 3	127.02 (51.07)	88.10 (34.04)	p<0.01 **
CTMT Trail 4	153.39 (81.63)	93.14 (43.96)	p<0.01 **
CTMT Trail 5	233.75 (102.78)	136.56 (54.19)	p<0.01 **
Memory module	3.69 (2.05)	4.66 (1.21)	p<0.01 **
Attention module	4.27 (1.13)	4.94 (0.82)	p<0.01 **
Language module	5.98 (1.71)	6.57 (1.47)	p<0.01
Visual-spatial functions	3.47 (1.16)	4.62 (0.60)	p<0.01

MMSE = Mini-Mental State Examination, MoCA = Montreal Cognitive Assessment, CDT = Clock Drawing Test, CTMT = Comphrensive Trail Making Test, p = statistical significance (*p < 05. **p < .01).

chological tests, statistically significant correlations were obtained between some of the variables in the MCI group. A statistically significant correlation was obtained between MoCA_Memory scores and CTMT5 test performance time (p=0.03). The results obtained suggest that a higher MoCA_Memory score is associated with a shorter CTMT Trail 5 performance time. A statistically significant correlation was found between MoCA_Language scores and the phonetic_fluency test (p<0.01), the results indicate that a higher MoCA_Language subscale score is associated with a higher score in phonetic fluency. A statistically significant correlation was observed between MoCA_Visuospatial scores and CTMT Trail 5 test performance time (p=0.02), this implies that better visual--spatial function on the MoCA_Visuospatial subscale is associated with shorter CTMT Trail 5 test performance time. A statistically significant correlation was observed between phonetic fluency scores and semantic fluency (p=0.01). There was a statistically significant correlation between phonetic fluency scores and the score on the CTMT Trail 1 test (p=0.04). A statistically significant correlation was observed between phonetic fluency scores and the score on the CTMT Trail 4 test (p=0.02). A smaller number of words, was associated with longer time to complete the various parts of the CTMT. There was a statistically significant correlation between semantic fluency scores and the CTMT Trail 1 (p<0.01), CTMT Trail 2 (p<0.01), CTMT Trail 3 (p<0.01), CTMT Trail 4 (p=0.01), CTMT Trail 5 (p<0.01). A lower semantic fluency score was associated with longer time to complete all parts of the CTMT. Correlations between the CTMT parts were to be expected and were therefore not included in the description. The data are presented in the correlation matrix (Figure 3). Correlation matrices were generated for MCI group. The color bar serves as an indicator of the strength of Spearman's correlation coefficients, with lighter colors indicating weaker correlations and darker colors indicating stronger correlations.

No statistically significant differences were obtained between the study groups in terms of global efficiency, local efficiency, transitivity, modularity (p>0.05). The data are presented in Table IV.

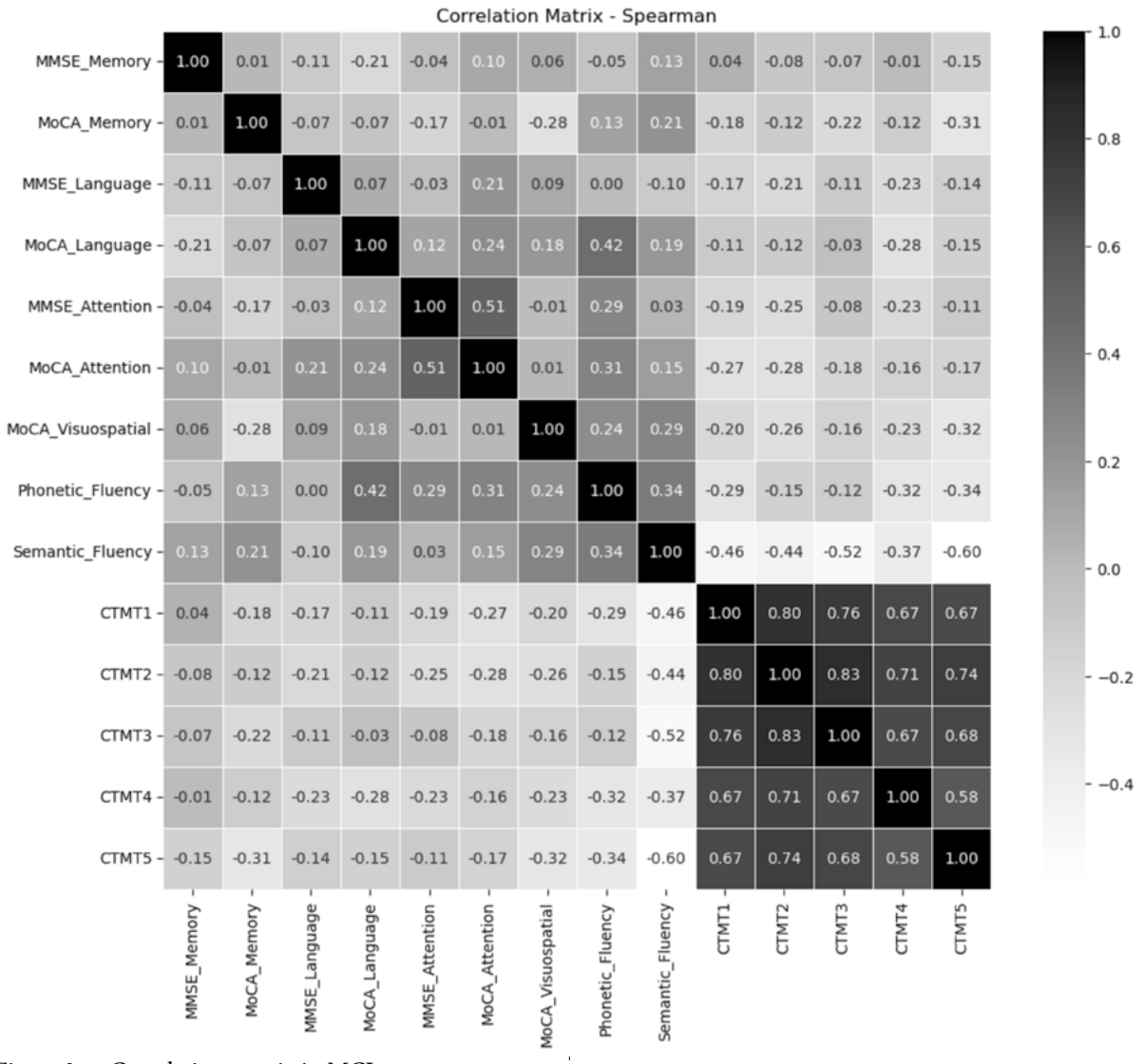


Figure 3. Correlation matrix in MCI group

Table IV. Differences in global network measures from the cognitive connectome across groups

	MCI (n=48)	HC (n=48)	p value
Newman algorithm			
Average Strength	3.85	4.28	n.s
Global Efficiency	0.39	0.59	n.s
Local Efficiency	0.84	0.65	n.s
Transitivity	0.70	0.65	n.s
Modularity	0.46	0.34	n.s
n.s - non-significant results.			

Discussion

The study was designed to examine the cognitive connectome in patients with MCI and healthy older adults using various cognitive tests and graph theory. Statistical analysis showed significant differences between MCI patients and controls in several cognitive areas, including memory, attention, visuospatial function and language function. Verbal fluency tests (both semantic and phonetic) showed that MCI patients provided fewer words and took longer to complete CTMT tests, indicating deficits in executive function and speed of information processing. Correlation analysis using Spearman's coefficient revealed significant relationships between scores on individual cognitive tests and scores on other neuropsychological tests in the MCI group. Higher scores on MoCA_Memory were found to be associated with shorter performance on the CTMT5. It was also noted that better visuospatial function on the MoCA_Visuospatial subscale was associated with shorter CTMT5 test performance time. Significant correlations also occurred between phonetic fluency scores and semantic fluency scores, as well as various parts of the CTMT test, indicating that lower verbal fluency is associated with longer performance time on these tests. The results obtained may be related to executive deficits in the studied group of MCI patients, which is also confirmed by the results of other studies [40]. Both executive function and processing speed are considered major domains affecting aging and contributing to cognitive impairment in diseases [41]. The results of other study, suggest that hippocampal atrophy impacts both episodic and semantic memory, whereas alterations in white matter are linked to fluctuations in processing speed [40]. It is hypothesized that the age-related decline in cognitive processing speed significantly contributes to observed differences in cognitive functioning among the older. Slower cognitive processing in older individuals suggests that they handle a smaller volume of information within a specific timeframe. This notion indicates that information processing comprises separate stages, each tied to different cognitive functions, and response latency reflects the combined duration of these stages [42].

The purpose of this study was to apply the concept of cognitive connectome to neuropsychological data. In the present study, fewer modules were observed in the MCI group than in the control group. In analyzing the communities for the MCI patient group and the control group using Newman's algorithm, differences in the structure of the cognitive function communities can also be seen. For patients with MCI, Module 1 included variables related to memory, language, attention, visual-spatial functions and executive functions (Verbal fluency test). Module 2, on the other hand, was more concerned with psychomotor speed and executive functions (CTMT). In contrast, in the control group, Module 1 focused on memory, language, attention, visual-spatial functions and executive functions. Module 2 in the control group included memory, psychomotor speed and executive functions (CTMT), while module 3 considered language and executive functions (phonetic fluency). Findings from the analysis suggest that the communities in the MCI group are more cumulative and cover a wider range of cognitive functions, while in the control group the communities appear more specialized. These differences may reflect differing mechanisms of aging and the impact on different aspects of cognitive function. Reducing the number of modules in the group of patients with MCI can also be considered an attempt to compensate, in this view, reducing the number of modules allows for a lower cost of network maintenance (dense network in one module). In the control group, attention is particularly drawn to executive functions as main cognitive domain, which are present in all modules and thus may translate into greater cognitive performance, compared to patients with MCI. In this view, the names of the different modules can be modified (table I) and a new approach can be proposed, in which they are not treated in an isolated way (as has already been proposed by other researchers [23], but as diads and complexes of cognitive functions (table II). Attention may be drawn to the difference in the organization of modular structure in the study groups based on Newman's algorithm and data from the literature (table I versus table II). Newman's algorithm is one of many approaches to detecting modular structures in networks, and in the present study it provided additional insight into the network topology of patients with MCI and preserved cognitive performance. Of note is the similarity of Module 1 in the MCI group and the control group (table II), where several cognitive functions were grouped together. Another study also observed a combination of processing speed and (verbal) memory measurements in a single module in healthy elderly (better processing speed managed to keep a higher performance in verbal memory) [23]. In the control group, a module combining memory, executive functions and psychomotor speed was extracted. Other research has also highlighted the importance of processing speed in older adults, suggesting that it

serves as a potential compensatory mechanism in addition to the well-established role of executive functions [43-44]. The results of one study indicated that healthy older adults with higher processing speed scored better on verbal memory [23]. Nodal network analyses confirm the key involvement of executive functions in late middle-aged individuals, while emphasizing the importance of processing speed in older adults [43-44]. Executive functions and psychomotor speed can enhance the performance of other cognitive functions, such as memory, and language functions. Executive dysfunctions can compound memory problems (lack of use of memorization strategies) and affect language functions (effective searching of the semantic lexicon and planning of speech).

Some similarities can be noted between the cognitive conectome and the one that was created from neuroimaging data. Meunier and colleagues [45] conducted a comparison between groups of younger and older adults, using modularity maximization on a single scale to identify modules for both groups. They found that the older group, compared to the younger group, showed fewer modules that covered groups of brain areas. These findings were confirmed by Geerligs et al., [46], who compared the populations of younger and older participants, reporting a decrease in modularity resulting from a reduction in internal connectivity in the control, relevance network and somatomotor modules, while inter-module connections increased. A study by Betzel et al., [47] indicated decreased modularity with age in modules related to cognitive control (executive function dimension) and attention.

The study did not obtain significant differences between the research groups in terms of graph parameters such as global efficiency, local efficiency, transitivity and modularity. This may be due to several factors. First, the individual components of the screening tests may not vary enough to affect graph parameters in a statistically significant way. The variability of results in these tests may be too small to affect network structures. Second, cognitive functions are complex and multidimensional. Graph parameters such as global and local efficiency, transitivity and modularity may not be sensitive enough to capture subtle differences between groups. Complex cognitive networks may require more sophisticated analysis tools that account for a wider range of variables and interactions among them.

Limitations

Subscales from screening tests (MMSE, MoCA) and only two neuropsychological tests (CTMT and Verbal Fluency Test) were used to build the connectome. The network was built on the basis of a correlation matrix, and, there were correlations between individual subscales, which could therefore be higher (the internal accuracy required for test construction) than if „separate" neuropsychological tests were included in the analysis. Future studies may find it useful to use longer screening tests (e.g., ACE III) or more neuropsychological tests. It should be noted that the network was built on a small number of variables, being components of the screening tests (only subscales, not a separate diagnostic tool) or individual parts of the test (Trail 1, 2, etc. in CTMT), which may have affected the network topology and the results obtained. Some modules may be due to the nature of the data collected (example: the MoCA's letter fluency test as part of the language subscale). In future studies, it may be useful to monitor the cognitive connectome longitudinally in different clinical groups (MCI, dementia).

Conclusions

The study revealed a smaller number of more complex cognitive modules in the MCI group compared to the control group, although the results should be approached with caution because subtests from screening tests were used to build the connectome, which may have determined a network structure that differed from that observed in other studies. It seems that graph theory and the cognitive connectome may allow additional insights into the complex interactions of cognitive functions and mechanisms of aging, allowing for a better understanding of these issues.

Conflict of interest
None

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