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Performances on the Montreal Cognitive Assessment Along the Cardiovascular Disease Continuum

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Abstract

Cardiovascular diseases involve a continuum starting with risk factors, which can progress to coronary heart disease and eventually, to heart failure. Cognitive impairment (CI) is observed as early as cardiovascular risk factors, and in up to 50% of patients with heart failure. Because CI in cardiovascular disease is linked to poorer clinical outcomes, early detection is essential. The Montreal Cognitive Assessment (MoCA) is a screening tool widely used in clinical setting. To date, little is known about MoCA scores along the cardiovascular disease continuum.

Objective: This study compared performances of different cardiovascular disease profiles on the MoCA and its subscores.

Method: Eighty participants (>50 years) from two studies conducted at the Montreal Heart Institute were separated into four groups: low cardiovascular risk factors (<2), high cardiovascular risk factors (>2), coronary heart disease, and stable heart failure. ANCOVAs were performed on the total score and on subscores, with sex, age, and education as covariates.

Results: Group differences were observed on the MoCA total score (heart failure < low cardiovascular risk), verbal fluency (heart failure < low cardiovascular risk), memory (coronary heart disease < low cardiovascular risk), and orientation (coronary heart disease < low and high cardiovascular risk) subscores.

Conclusion: Results suggest that the MoCA, particularly verbal fluency and memory subscores, can detect cognitive changes in later stages of the cardiovascular disease continuum, such as heart failure. Detecting cognitive changes earlier on the cardiovascular disease continuum may require more in depth neuropsychological assessments.

Keywords: Cardiovascular disorders; Cognitive impairment; Screening tests; Cognition; Memory

Introduction

Cardiovascular diseases are responsible for the largest number of deaths worldwide (WHO, 2019). Cardiovascular diseases generally evolve on a continuum, starting with cardiovascular risk factors (e.g., diabetes, hypertension), which may lead to atherosclerotic diseases, such as coronary heart disease, and finally heart failure (Dzau et al., 2006). Early on the continuum, the cardiovascular system is adversely affected by cardiovascular risk factors, which are thought to then trigger a cascade of events (Dzau et al., 2006). Both cardiovascular risk factors and cardiovascular diseases are highly prevalent in Canada: in 2009, 9 in 10 Canadians aged 20 and over lived with at least one cardiovascular risk factor (Dai et al., 2009), whereas 1 in

12 Canadians lived with cardiovascular disease in 2013 (Public Health Agency of Canada, 2018). Therefore, cardiovascular diseases and cardiovascular risk factors represent a significant challenge and burden for the health care system (Tarride et al., 2009). Cardiovascular diseases can cause a variety of negative physiological consequences, among these, cognitive impairment (CI). Both cardiovascular risk factors and cardiovascular diseases have been independently associated with cognitive deficits and increased risk of dementia later in life (Abete et al., 2014). Importantly, CI in the context of cardiovascular diseases has been linked to several negative clinical outcomes such as mortality, rehospitalization, functional decline, and poorer maintenance of disease-related knowledge (Zuccalà et al., 2001, 2003; Agarwal et al., 2016; Salzwedel et al., 2019).

At the beginning of the cardiovascular disease continuum, cardiovascular risk factors have been consistently associated with cognitive deficits, targeting more specifically executive functions, processing speed and memory (Van den Berg et al., 2009). Cardiovascular risk factors developed in midlife, rather than those developed later in life, have been associated with CI and dementia in older age (Knopman et al., 2018; Kivipelto & Ngandu, 2016). As cardiovascular risk factors can develop early in life due to poor lifestyle habits or predisposing genetic factors, their deleterious effects on cognition could potentially accumulate over the years. Moreover, cardiovascular risk factors often co-occur, as such, their accumulation could have detrimental effects on cognition. For instance, an increased Framingham risk score, which assesses cardiovascular risks over the next 10 years and indicates more cardiovascular risk factors, has been associated with an increased decline of global cognition, memory and executive functions (DeRight et al., 2015, Dregan et al., 2013).

Further on the cardiovascular disease continuum, coronary heart disease has also been associated with CI (Abete et al., 2014). First, cross-sectional studies have shown lower scores for global cognition, poorer episodic and short-term memory, slower processing speed, and decreased verbal fluency in individuals with coronary heart disease than in healthy matched controls (Verhaegen et al., 2003; Gayda et al., 2017). Second, longitudinal studies have shown that patients with coronary heart disease not only have lower cognitive scores, but also show faster cognitive decline over the years when compared to healthy adults (Singh-Manoux et al., 2008; Selnes et al., 2009). For instance, Selnes et al. (2009) observed that at baseline, individuals with coronary heart disease had lower motor and psychomotor speed and lower scores on global cognition compared to controls. At their 72-month follow-up, individuals with coronary heart disease showed a steeper decline on tests assessing executive functions, visuospatial memory, visuoconstruction abilities, and global cognition compared to controls. Furthermore, a recent study revealed that CI was not observed immediately after a coronary heart disease diagnosis, but rather at a median of 12 years following its diagnosis (Xie et al., 2019). Hence, CI in the context of coronary heart disease might not appear immediately following a first acute coronary event, but in the following years.

At the end of the cardiovascular disease continuum, heart failure is the first cause of hospitalization in individuals over 65 years of age (Benjamin et al., 2018) and of premature deaths in Western countries (Lloyd-Jones et al., 2002; Roger et al., 2004). Recent reviews estimate that nearly one in two patients with heart failure live with some degree of CI, specifically affecting episodic memory, executive functions and processing speed (Abete et al., 2014; Pressler et al., 2010; Cannon et al., 2017). Importantly, in heart failure patients, CI is an independent predictor of mortality, rehospitalization and rapid functional decline (Huyn et al., 2016; Zuccalà et al., 2001, Zuccalà et al., 2003; Cook et al., 2014). Furthermore, CI is an important factor of reduced disease control related to a lack of patients' self-management and treatment adherence, which may lead to future hospitalizations and acute decompensated heart failure episodes (Dickson et al., 2007; Dolansky et al., 2016).

Altogether, this overview of CI associated with cardiovascular risk factors and cardiovascular disease, along with the high prevalence of these conditions, underlines the need for early detection of CI. The Montreal Cognitive Assessment (MoCA), frequently used in a clinical setting by professionals, is a cognitive screening tool that assesses multiple cognitive functions: short-term memory, visuospatial abilities, executive functions, phonemic fluency, verbal abstraction, attention, concentration, working memory, episodic memory, language and orientation (Nasreddine et al., 2005). Results have shown that the MoCA's subscores can differentiate healthy older adults from adults with mild CI and with dementia (Nasreddine et al., 2005). Interestingly, several authors have concluded that the MoCA is a relevant tool to detect CI in heart failure patients (Davis & Allen, 2013; Huynh et al., 2016; Gelow et al., 2015). To date, most studies assessing the impact of cardiovascular disease on cognition have compared performances of individuals with one type of cardiovascular disease to healthy controls. However, little is still known about cognitive profiles of individuals at different stages of the cardiovascular disease continuum and how they might differ. As a result, the objective of the present study was to compare cognitive performances on the MoCA and its subscores at different stages of the cardiovascular disease continuum. It was hypothesized that a gradient of cognitive functioning on the MoCA would be observed, with the best cognitive performances in participants with low cardiovascular risk (<2 cardiovascular risk factors), followed by participants with high cardiovascular risk (≥ 2 cardiovascular risk factors), participants with coronary heart disease and those with stable heart failure. These differences were expected to be present on the total MoCA score, and on the visuospatial/executive, verbal fluency and memory subscores.

Methods

Participants

Eighty participants aged 50 years and older from two different studies conducted at the Montreal Heart Institute (MHI) and the Preventive Medicine and Physical Activity Centre (Centre EPIC) of the MHI, were recruited through advertisements at the MHI and from physician referrals. In order to be included, participants had to be fluent French or English speakers, right-handed and able to provide written informed consent. The majority of participants were French speakers; only one was an English speaker. The two aforementioned studies were approved by the MHI research ethics board and research was conducted in accordance with the Helsinki Declaration. Participants were included in the low cardiovascular risk group if they had less than two cardiovascular risk factors, whereas participants with two or more cardiovascular risk factors were included in the high cardiovascular risk group. The cardiovascular risk factors taken into account for the current study were hypertension, diabetes mellitus, dyslipidemia, tobacco use, and obesity, which is measured by the body mass index (BMI \geq 30 kg/m²).

Stable coronary heart disease participants were included if they either had previous history of myocardial infarction, coronary angioplasty or coronary artery bypass surgery. Heart failure participants were included if they had all of the following: left ventricular ejection fraction <40% (measured by a multigated acquisition scan, echography or ventriculography within 6 months of their enrolment), New York Heart Association functional class of I–III and if they had underwent a stable drug therapy for at least 6 weeks prior to the study. In addition, heart failure patients were excluded if they had thyroid or pituitary disease, chronic atrial fibrillation, malignant exertional arrhythmias, or symptomatic aortic stenosis. None of the patients had experienced a cardiac arrest. Moreover, participants in each profile were excluded if they had: a progressive neurological or psychiatric disease, a peripheral vascular disease, a history of stroke, chronic diseases such as cancer, infections, or chronic obstructive pulmonary disease, a diagnosis of dementia or severe perceptual deficits.

Materials and Procedure

Participants' global cognitive function was assessed in a baseline visit in each study by a trained psychometrician or a neuropsychologist, using the MoCA, a 30-point paper–pencil test that assesses various cognitive domains in approximately 15 min. For the purpose of the current study, seven cognitive scores were calculated based on the MoCA's version 7.1 subscores developed by Nasreddine et al. (2005). The French and English versions of the MoCA were used; both have been previously validated (Nasreddine et al., 2005). A total of five points were awarded on the visuospatial/executive component assessed by a Modified Trail Making Test (1 point), by the copy of a cube (1 point) and by a clock-drawing task (3 points), for a total of five points. Naming was assessed with the identification of three low-familiarity animal figures (a lion, a rhinoceros and a camel), for a total of three points. Attention was assessed with a forward and backward digit span task (2 points), a letter tapping task (1 point) and a Serial 7-subtraction task (3 points), for a total of six points. Language was assessed by the repetition of two complex sentences (2 points) and by a phonemic fluency task (1 point was awarded if ≥ 11 words were produced in 1 min starting with the letter F in French and in English), for a total of three points. Abstraction was assessed with a two-item similarity task (2 points). Memory was assessed by a 5 min delayed recall of a 5-word list learned previously (5 points). Lastly, orientation in time and place was assessed for a total of six points. The total score on the MoCA was obtained by adding the scores on all these items, for a maximum total of 30 points. In the present study, the raw total score was used.

Data and Statistical Analyses

All analyses were conducted with IBM SPSS Statistics software v25.0 for Mac (IBM, Inc., Chicago, IL, USA). Data distribution was verified using the skewness and kurtosis of all variables according to Curran et al. (1996) recommendations. ANOVAs were performed on baseline characteristics to determine if groups were comparable and nonparametric statistics were used when applicable. ANCOVAs were performed on the total score of the MoCA, on the different subscores, as well as on certain specific items of the subscores (e.g., verbal fluency). Given the multiple comparisons performed, a Benjamini–Hochberg correction was applied to control for the false discovery rate (Benjamini & Hochberg, 1995), rather than a traditional Bonferroni correction (Huang, 2020). The probability of type 1 error increases with multiple comparisons, yet a too severe *p*-value, as in a Bonferroni correction, increases the likelihood of type II error. The Benjamini–Hochberg offers a good compromise; the correction was applied to all ANCOVA *p*-values (Cramer et al., 2016). For a complete description of the Benjamini–Hochberg correction, refer to Supplementary Table 1 for the comparison of *p*-values according to the Benjamini–Hochberg method, with a false discovery rate that was set at 7.5%. An alpha level of .05 was used for other statistical tests. Power calculation indicated

Characteristics	Groups					Group effects			
	Low cardiovascular risk factors $(n = 29)$	High cardiovascular risk factors ($n = 17$)	Coronary heart disease $(n = 18)$	Heart failure $(n = 12)$	F	χ ²	р	η^2	
Age (years)	66.38 (5.27)	68.59 (5.61)	71.11 (3.94)	67.42 (7.49)	2.867		.042*	.107	
Female, n (%)	19.00 (65.52)	10.00 (58.82)	1.00 (5.56)	2.00 (16.67)		21.52	.001***		
Education (years)	15.52 (3.00)	15.76 (4.29)	17.00 (5.36)	15.00 (3.46)	0.737		.534	.030	
NYHA functional class	sification								
Class I, n (%)	1.00 (3.70)	1.00 (6.25)	4.00 (22.22)	4.00 (50.00)					
Class II, n (%)	1.00 (3.45)	4.00 (23.53)	3.00 (16.66)	3.00 (37.50)					
Class III, n (%)	0	0	0	1.00 (12.50)					
Class IV, n (%)	0	0	0	0					
LVEF (%)				27.82 (6.81)	465.486		.001***	.952	
Cardiovascular risk fac	etors								
Hypertension, n (%)	7.00 (24.14)	14.00 (82.35)	12.00 (66.67)	4.00 (36.36)		17.68	.001***		
Diabetes metillus, <i>n</i>	2.00 (6.90)	7.00 (41.18)	5.00 (27.78)	3.00 (27.27)		7.84	.05		
(%) D 1: : 1 : (%)	5 00 (17 24)	12.00 (7(47)	1(00 (00 00)	(00 (50 00)		20.20	001***		
Dyslipidemia, n (%)	5.00 (17.24)	13.00 (76.47)	16.00 (88.89)	6.00 (50.00)		28.20	.001		
Tobacco use, n (%)	3.00 (10.34)	3.00 (17.65)	3.00 (16.67)	2.00 (16.67)		0.99	.80		
Body mass index, (kg/m ²)	26.47 (6.81)	33.08 (3.82)	28.58 (5.06)	26.45 (3.08)	6.09		.001***	.203	

Table 1. Demographic characteristics of study participants

Note: Data are presented as frequencies (percentage) and as means (standard deviation) for these variables: age, education and body mass index. NYHA = New York Heart Association; LVEF = left ventricular ejection fraction.

***p < .001.

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that a sample size of 18 subjects in each group will have 80% power to detect a significant difference in cognitive performances. Eta squared values are reported to appreciate effect size.

Results

Baseline Comparisons

Baseline characteristics for each of the cardiovascular disease groups are presented in Table 1. Significant differences were observed for age F(3, 72) = 2.87, p < .05, and sex $\chi^2(4) = 21.52 \ p < .001$, $\phi = 0.53$. Education was similar among all groups F(3, 72) = 0.74, p = .53. As age, sex and years of education are important factors to take into account when interpreting the MoCA, they were therefore used as covariates in the following analyses (Larouche et al., 2016).

MoCA Scores by Cardiovascular Disease Profile

Table 2 illustrates the mean scores on the MoCA (raw total and subscores) for each cardiovascular disease profile. First, significant differences were observed between cardiovascular disease profiles on their total MoCA scores F(3, 76) = 3.03, p < .05, $\eta^2 = .12$. Post-hoc comparisons indicated that total mean scores for stable heart failure participants (M = 24.92, SD = 2.5) were significantly lower than for those of participants with low cardiovascular risk (M = 27.59, SD = 1.72).

Second, analyses of MoCA subscores showed a group effect in the language subscore, F(3, 76) = 3.00, p < .05, $\eta^2 = .12$; however post-hoc analyses did not allow us to determine where the group differences were located. Moreover, a group difference was observed on the verbal fluency item of the language subscale, F(3, 76) = 3.48, p < .05, $\eta^2 = .13$. Indeed, stable heart failure patients performed significantly lower (M = 0.33; SD = 0.49) than low cardiovascular risk participants (M = 0.83; SD = 0.38). Accordingly, the number of words provided in the verbal fluency condition also differed significantly between groups, F(3, 76) = 5.30, p < .01. Stable heart failure patients evoked fewer words in 60 s (M = 8.50, SD = 2.78) than participants with low cardiovascular risk (M = 13.52, SD = 3.5). The memory subscale also revealed a significant group difference, F(3, 76) = 3.16, p < .05, $\eta^2 = .12$. More precisely, participants with coronary heart disease recalled fewer words on the delayed recall (M = 2.50, SD = 1.69) compared to participants with low cardiovascular risk (M = 3.93, SD = 1.13). CHD and stable HF participants did not

^{*}*p* < .05.

 $i^{**}p < .01.$

Table 2.	Montreal	Cognitive .	Assessment	total and	subscales	scores	means and	standard	deviations
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	Groups	Group effects					
MoCA Scores	Low cardiovascular risk factors $(n = 29)$	High cardiovascular risk factors ($n = 17$)	Coronary heart disease $(n = 18)$	Heart failure $(n = 12)$	F	р	η^2
Total score	27.59 (1.72)	26.65 (2.62)	25.78 (2.44)	24.92 (2.50)	3.033	.035*	.117
Subscales							
Visuospatial/executive	4.59 (0.57)	4.41 (0.94)	4.17 (0.86)	4.00 (1.13)	1.917	.135	.077
Naming	2.90 (0.31)	2.82 (0.39)	3.00 (0.00)	2.83 (0.39)	1.180	.324	.049
Attention	5.72 (0.53)	5.59 (0.62)	5.83 (0.38)	5.42 (0.79)	1.368	.260	.056
Language	2.76 (0.51)	2.29 (0.85)	2.67 (0.49)	2.25 (0.62)	2.999	.036*	.115
Fluency	0.83 (0.38)	0.53 (0.51)	0.67 (0.49)	0.33 (0.49)	3.476	.021*	.131
Number of words	13.52 (3.50)	11.29 (3.35)	11.28 (3.89)	8.50 (2.78)	5.300	.002**	.187
Abstraction	1.83 (0.38)	1.71 (0.69)	1.89 (0.32)	1.50 (0.67)	1.252	.298	.052
Memory	3.93 (1.13)	3.82 (1.19)	2.50 (1.69)	2.83 (1.12)	3.156	.030*	.121
Orientation	6.00 (0.00)	6.00 (0.00)	5.67 (0.49)	5.75 (0.45)	4.463	.006**	.163

Note: Data are presented as mean (standard deviation).

MoCA = Montreal Cognitive Assessment.

*p < .05.

**p < .01.

***p < .001.

differ on the memory subscore. Finally, the orientation subscale also indicated significant differences according to cardiovascular disease profile, F(3, 76) = 4.46, p < .01, $\eta^2 = .16$. Participants with coronary heart disease (M = 5.67, SD = 0.48) had lower scores than those with low cardiovascular risk (M = 6.00, SD = 0.00) and high cardiovascular risk (M = 6.00, SD = 0.00). Finally, there were no group differences in the visuospatial/executive, F(3, 76) = 1.92, p = .14, naming F(3, 76) = 1.18, p = .32, attention F(3, 76) = 1.37, p = .26, or abstraction subscores, F(3, 76) = 1.25, p = .30.

Discussion

The purpose of the present study was to compare cognitive performance of individuals at different stages of the cardiovascular disease continuum using the MoCA. Our results suggest that the MoCA total score and some subscales were indeed useful to differentiate between specific cardiovascular disease profiles at the extreme stages of the continuum.

First, participants with stable heart failure obtained significantly lower MoCA total scores than those with low cardiovascular risk. The difference of total MoCA scores between both groups is not only statistically significant, but is also clinically significant. Indeed, a study by Tan et al. (2017) suggests that a decline of two or more points on the MoCA total score indicates significant clinical decline based on a complete neuropsychological assessment. In our study, low cardiovascular risk and heart failure participants showed an almost 3-point difference on their total MoCA score. On the subscores, stable heart failure patients obtained lower verbal fluency scores and evoked fewer words on this task than participants with low cardiovascular risk. Interestingly, on the memory subscore, significant differences were observed between coronary heart disease and low cardiovascular risk groups, with the former recalling fewer words than the latter. Coronary heart disease and stable heart failure participants, however, did not differ significantly. Similarly, on the orientation subscore, the coronary heart disease group obtained lower scores than the high and low cardiovascular risk groups. Finally, no group differences were found for the visuospatial/executive, naming, attention, and abstraction subscores.

Overall, our results suggest that stable heart failure patients showed the most impaired performances on the MoCA total score, as well as on the verbal fluency subscore. Even though the verbal fluency task is categorized as part of the language subscale in the MoCA, phonological verbal fluency tasks also target executive control abilities. Thus, our results are in line with previous studies finding impaired executive functions in stable heart failure patients, as well as lower global cognitive functioning (e.g., Verhaegen et al., 2003; Pressler et al., 2010; Alagiakrishnan et al., 2017). The poorer memory performances and orientation scores for coronary heart disease participants compared to participants with cardiovascular risk are also consistent with previous studies finding poorer cognitive performances in individuals with coronary heart disease, namely for episodic memory (Gayda et al., 2017). However, contrary to what was expected, we did not observe a gradient of performances between the four groups on the total MoCA score, or either of the visuospatial/executive, fluency and memory recall subscores. This may be explained by the fact that CI along the cardiovascular disease continuum might not follow a linear trend but might rather take place in a stepwise fashion as suggested in Table 2. The lack of cognitive performance gradient may also be due to the fact that the

MoCA, a screening tool, might not be sensitive enough to detect more subtle cognitive deficits earlier on the cardiovascular disease continuum, as those that are associated with cardiovascular risk factors. In this way, the executive/visuospatial subscore of the MoCA, which did not differ according to cardiovascular disease groups, might not be sensitive enough to detect subtle differences in executive function performances. Indeed, the only executive portion per se in this subscore is a short version of the Trail Making Test counting for 1 point, which might lack sufficient sensitivity. Nevertheless, results from the present study suggest that the MoCA can efficiently be used to detect CI across the cardiovascular disease spectrum. Future studies could help clarify the pattern of cognitive deficits specific to cardiovascular diseases by comparing MoCA profiles to a complete neuropsychological assessment.

Limitations and Research Perspectives

Among the limits of the present study, the cross-sectional design must be considered. Indeed, previous studies investigating cognitive functioning in individuals with coronary heart disease, showed mild differences when compared to healthy controls at baseline, whereas increased cognitive decline was observed at follow-up and more precisely on tests targeting executive functions, attention, verbal memory and language (Selnes et al., 2009; Xie et al., 2019). Hence, subtle group differences might not be detected since the present study did not perform a follow-up. Another limit of this study is the relatively small sample size, which could have reduced statistical power and potentially, reduce generalization of results. Future studies with larger and more diverse samples are needed to confirm these results. Furthermore, we cannot exclude a potential bias in the recruitment of female and male participants in this project. Recent publications have stated that women are still underrepresented in clinical research in the field of cardiovascular disease for various reasons, from referral from physicians, to seeking medical help for cardiovascular disease-related symptoms (Norris et al., 2020). To avoid such biases, future studies should include an equal amount of men and women to better understand sex-related differences in cognitive performance, according to cardiovascular profile. Nonetheless the aforementioned limitations, we were able to detect significant cardiovascular disease group differences on the total score and some subscores, mainly among the most extreme groups on the continuum. Moreover, the effect sizes for the significant group differences ranged from medium to large according to Cohen's guideline (1988) for interpreting eta squared values, between .11 and .18 (medium effect size = .06 and large effect size = .16).

Among the strengths of this study are the statistical controls for confounding factors that can influence MoCA score performances, namely age and education (Larouche et al., 2016). Moreover, to our knowledge, this study is one of the first to compare cognitive performances of several groups along the cardiovascular disease continuum.

In conclusion, the MoCA allowed us to detect broad differences between stable heart failure patients and individuals with low cardiovascular risk on the total MoCA score and on the verbal fluency subscore (total words produced). It also detected differences between coronary heart disease and low cardiovascular risk groups on the memory recall subscale, and between coronary heart disease and low and high cardiovascular risk on the orientation subscale. More importantly, in a clinical setting, professionals using the MoCA with patients on the cardiovascular disease continuum should take into consideration that it might not be sensitive enough to detect subtle cognitive changes in its early stages. In this case, cognition should rather be assessed through a complete neuropsychological evaluation. Accordingly, in an effort to prevent cognitive and functional decline in cardiovascular risk factors and following-up on these assessments. Clinicians should emphasize assessments that target memory and executive functions, targeting verbal fluency, as well as more thorough assessments in individuals with cardiovascular disease could help better understand the mechanisms underlying CI (e.g., Ogren et al., 2014, Almeida et al., 2012). Finally, future studies may also include indicators of heart rhythm with electrocardiogram data, as previous studies have found associations between heart rhythm, as well as arrhythmia and cognitive performances (e.g., Vrinceanu et al., 2020).

Supplementary Material

Supplementary material is available at Archives of Clinical Neuropsychology online.

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Conflict of Interest

The authors have no actual or potential conflicts of interest related to this manuscript.

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