European Psychiatry 61 (2019) 72–78

Contents lists available at ScienceDirect

European Psychiatry

journal homepage: http://www.europsy-journal.com

Original article

Physical performance is more strongly associated with cognition in schizophrenia than psychiatric symptoms

Jiheon Kim[a,1], Ji-Hyeon Shin[b,1], Jeh-Kwang Ryu[c], Jae Hoon Jung[a], Chan-Hyung Kim[d], Hwa-Bock Lee[e], Do Hoon Kim[a], Sang-Kyu Lee[a], Daeyoung Roh[a,*]

[a] Mind-neuromodulation Laboratory and Department of Psychiatry, Chuncheon Sacred Heart Hospital, Hallym University College of Medicine, 77 Sakju-ro, Chuncheon, Gangwon-Do, 24253, Republic of Korea
[b] Department of Otolaryngology-Head and Neck Surgery, College of Medicine, The Catholic University of Korea, 271 Cheonbo-ro, Uijeongbu, Gyungki-Do, 11765, Republic of Korea
[c] Institute for Cognitive Science, College of Humanities, Seoul National University, 1 Gwanak-ro, Gwanak-Gu, Seoul, 08826, Republic of Korea
[d] Department of Psychiatry, Severance Hospital, Yonsei University College of Medicine, 50-1 Yonsei-ro, Seodaemun-Gu, Seoul, 03722, Republic of Korea
[e] Gwangmyeong Mental Health Welfare Center, 613 Ori-ro, Gwangmyeong-si, Gyungki-do, 14303, Republic of Korea

ARTICLE INFO

Article history:
Received 13 March 2019
Received in revised form 24 June 2019
Accepted 27 June 2019
Available online 23 July 2019

Keywords:
Schizophrenia
Cardiorespiratory fitness
Functional mobility
Supine to standing test
Neurocognition
Physical performance

ABSTRACT

Background: Although neurocognitive dysfunction and physical performance are known to be impaired in patients with schizophrenia, evidence regarding the relationship between these two domains remains insufficient. Thus, we aimed to investigate the relationship between various physical performance domains and cognitive domains in individuals with schizophrenia, while considering other disorder-related clinical symptoms.
Methods: Sixty patients with schizophrenia participated in the study. Cardiorespiratory fitness and functional mobility were evaluated using the step test and supine-to-standing (STS) test, respectively. Executive function and working memory were assessed using the Stroop task and Sternberg working memory (SWM) task, respectively. Clinical symptoms were evaluated using the Brief Psychiatric Rating Scale, Beck Depression Inventory, and State-Trait Anxiety Inventory. Multivariate analyses were performed to adjust for relevant covariates and identify predictive factors associated with neurocognition.
Results: Multiple regression analysis revealed that the step test index was most strongly associated with reaction time in the Stroop task ($\beta = 0.434$, $p = 0.001$) and SWM task ($\beta = 0.331$, $p = 0.026$), while STS test time was most strongly associated with accuracy on the Stoop task ($\beta = -0.418$, $p = 0.001$) and SWM task ($\beta = -0.383$, $p = 0.007$). Total cholesterol levels were positively associated with Stroop task accuracy ($\beta = -0.307$, $p = 0.018$) after controlling for other clinical correlates. However, clinical symptoms were not associated with any variables in Stroop or SWM task.
Conclusions: The present findings demonstrate the relationship between physical performance and neurocognition in patients with schizophrenia. Considering that these factors are modifiable, exercise intervention may help to improve cognitive symptoms in patients with schizophrenia, thereby leading to improvements in function and prognosis.

1. Introduction

Schizophrenia is among the world's most debilitating illnesses [1]. Despite the striking nature of psychotic symptoms in schizophrenia, neurocognitive dysfunction is recognized as a core feature of the condition. These deficits are present from the first psychotic episode or earlier, impairing functional recovery and resulting in substantial socio-occupational disability [2,3]. The most pronounced cognitive impairments among patients with schizophrenia are associated with memory, executive function, and processing speed [4,5]. Furthermore, antipsychotic medications have little impact on cognition [6], and other pharmacological approaches for the treatment of these deficits have demonstrated limited success [7].

Physical performance is defined as the ability to satisfactorily perform muscular work, and is influenced by both physical capacity and motor abilities [8]. Various components of

* Corresponding author.
E-mail address: omydoc@naver.com (D. Roh).
[1] These first authors contributed equally to this work.

http://dx.doi.org/10.1016/j.eurpsy.2019.06.010
0924-9338/

physical performance are significantly correlated with everyday functioning, including strength, flexibility, balance, mobility, motor coordination, muscle mechanics, and cardiorespiratory fitness. Among these, cardiorespiratory fitness [9] and functional mobility [10] are notably impaired in patients with schizophrenia.

Profoundly low cardiorespiratory fitness (CRF; i.e., the ability of the circulatory and respiratory systems to supply oxygen to working muscles during sustained physical activity [11]) is present from the first psychotic episode in patients with schizophrenia [12]. Low CRF is a strong and independent predictor of cardiovascular disease (CVD; [13]), which is the largest single cause of death among patients with schizophrenia [14]. In addition, low CRF has been associated with cognitive dysfunction in the general population [15,16], and several studies have also reported this relationship in patients with schizophrenia [17–21].

Functional mobility is defined as the capacity to move through the environment (e.g., standing, bending, walking) in order to perform activities of daily living (ADLs) [22]. Functional mobility has emerged as a useful clinical marker for predicting overall health decline [23], disability in ADLs [24], and health-related quality of life [22]. Furthermore, poorer mobility is independently associated with poorer executive function [25], memory [26], and global cognition [27]. Thus, there is a growing interest in the development of a brief and easy-to- task for the assessment of functional mobility.

Rising from the floor, which can be assessed using the supine-to-standing (STS) test, is a basic functional mobility task that requires appropriate levels of muscle strength, joint coordination, balance, and flexibility. Previous studies have indicated that STS results exhibit a significant correlation with measures of typical functional mobility (e.g., gait speed and timed up-and-go (TUG) test results) and are a significant predictor of failing health and function in older adults [28,29]. Because the STS test is less than 1 min in duration and requires no specialized equipment or training, it is relatively simpler than other tests for functional mobility [29,30]. In this respect, STS will be useful in measuring functional mobility in schizophrenia patients. However, to our knowledge, no studies have investigated STS test results in patients with schizophrenia, although a few studies [31–33] have explored the relationship between cognitive function and functional mobility in patients with schizophrenia.

As stated above, while several studies have examined the relationship between CRF or functional mobility and a single domain of cognition in patients with schizophrenia, no studies to date have investigated how individual physical performance domains (e.g., CRF, functional mobility) are associated with different cognitive domains in this patient population. Furthermore, there is a need to consider the association between cognitive function and disorder-related clinical symptoms in patients with schizophrenia. Both depression and psychotic symptoms appear to negatively affect memory and psychomotor speed [18,34]. In addition, health indicators such as total cholesterol levels and body mass index (BMI) may impact neurocognition in patients with schizophrenia [35,36].

In the present study, we aimed to investigate the relationship between physical performance (i.e., CRF and functional mobility) and cognitive function (i.e., executive function and working memory) in individuals with schizophrenia. We hypothesized that poorer physical performance would be associated with lower cognitive function after adjusting for factors that are known to affect both physical performance and cognitive function in patients with schizophrenia.

2. Methods

2.1. Participants

Patients aged 18–60 with a primary diagnosis of schizophrenia or schizoaffective disorder were recruited via posters placed in local hospitals with psychiatric units and community mental health centers, and via advertisements in local newspapers. Some patients were also referred by other local health professionals.

Participants were eligible for the study if they had a diagnosis of schizophrenia or schizoaffective disorder according to the Diagnostic and Statistical Manual for Mental Disorders, 4th Edition, Text Revision (DSM-IV-TR), received antipsychotic treatment, and were at least 18 years old. Face-to-face diagnostic interviews were conducted by a psychiatric/mental health nurse and a board-certified psychiatrist who reviewed the history, symptoms, and psychosocial function of each patient using all available sources of information, in accordance with DSM-IV-TR criteria. All participants were required to be on a stable dose and dosing regimen of antipsychotics for at least 4 weeks prior to assessment. Participants were excluded if they had participated in any exercise program in the 3 months o before the start of the study or displayed evidence of significant cardiovascular, neuromuscular, endocrine, or other somatic/substance use disorders that would prevent safe participation.

A total of 65 participants were screened, five of whom failed to meet initial eligibility criteria.

2.2. Procedure

The present cross-sectional study included 60 patients diagnosed with schizophrenia. All procedures were approved by the Investigational Review Board of Severance Mental Health Hospital. All participants provided written informed consent. Participants were required to perform all assessments between 10 a.m. and 4 p.m. on the same day, in the following order: psychiatric measures, cognitive tasks, and physical performance tasks. The time interval between the administration of assessments ranged from 15 min to 1 h.

2.3. Demographic information

Demographic characteristics (age, sex, years of education) and baseline clinical data (age at onset, duration of illness, number of hospital admissions, antipsychotic dosing (PDD:DDD ratio), total cholesterol, and BMI were collected.

2.3.1. Antipsychotic dosing

To calculate doses of antipsychotic drugs, the prescribed daily dose (PDD) in milligrams was divided by the defined daily dose (DDD) to yield a PDD:DDD ratio. DDD is defined as the assumed average maintenance dose per day for a drug used for its main indication in adults.

2.4. Clinical symptoms

Clinical symptoms were determined via interviews and self-report questionnaires.

2.4.1. Brief psychiatric rating scale (BPRS)

The BPRS is an 18-item, semi-structured introductory interview that is completed by the interviewer [37]. Each item is rated on a scale from 0 to 6. Scores between 15 and 30 indicate minor symptoms, while those above 30 indicate major symptoms. Previous studies have demonstrated the reliability of the BPRS in Korean patients [38].

2.4.2. Beck depression inventory (BDI)

The BDI was used to assess depressive symptoms [39]. The BDI is a 21-item self-report inventory that asks participants to choose the one statement that best describes their feelings during the past 2 weeks. The Korean version of the BDI has been identified as both valid and reliable [40].

2.4.3. State-trait anxiety inventory (STAI)

The STAI is a self-rated instrument that contains two 20-item subscales for the measurement of anxiety [41]. One scale measures state anxiety, while the other measures trait anxiety. A standardized Korean version of the STAI has been developed by Han and colleagues [42].

2.5. Neurocognitive function

2.5.1. Stroop word-color test

The Stroop Word-Color Test was used to assess components of executive function representing a person's ability to deal with conflicting stimuli [43]. This test involves pairs of conflicting stimuli that are presented simultaneously (i.e., the name of one color printed in another color). In the congruous condition, participants are required to read the names of colors printed in black ink (W) and to name diff ;erent color patches (C). Conversely, in the color-word (CW) condition, color-words are printed in an inconsistent color ink. Thus, in this incongruent condition, participants are required to name the color of the ink instead of reading the word.

2.5.2. Sternberg working memory task (SWM)

The classic SWM task [44] was administered using Inquisit 5.0.13.0 (Millisecond Software, LLC Seattle, WA). Each trial of the task consisted of a set of two to five white digits presented in a sequence (1200 ms each). A yellow probe digit appeared 2500 ms after the last digit (maintenance period), at which point participants were required to press an appropriate button indicating whether it had been present in the previously displayed sequence. Participants were provided with visual feedback regarding the accuracy of their responses. Task sessions were divided into equally distributed "in" (probe present in the memory sequence) and "out" (probe not present in the memory sequence) trials (120 trials in total, preceded by 15 training trials).

2.6. Physical performance

2.6.1. Step test

Measuring post-exercise recovery heart rate (HR) after a step test is a common method for determining cardiorespiratory (CR) fitness. The present study used the 3-minute YMCA step test (American College of Sports Medicine, 2006), which involves stepping at a rate of 24 steps/minute for 3 min. Following exercise, HR was counted for 1 min with the participant in the seated position. Low post-exercise recovery HR is considered indicative of good CRF.

2.6.2. STS test

The STS test is used to assess a person's ability to transition from a supine position to a standing position. Previous studies have utilized the STS test to evaluate functional mobility [45] and physical performance [29] in older adults and patients with neurodegenerative conditions. Beginning from a mat on the floor, participants were instructed to rise from the supine position at a comfortable rate, using any motions they desired. The administrator measures the amount of time it takes to rise from the supine position. The STS test has been associated with excellent test-retest reliability (intraclass correlation coefficient = 0.9) [46].

2.7. Statistical analysis

We first analyzed the demographic and clinical characteristics of participants using descriptive statistics. Multiple regression analyses were then used to adjust for relevant covariates and identify predictive factors associated with neurocognitive function. After performing univariate analyses to identify the associated factors, multivariate analyses were conducted using Stroop Word-Color test and SWM task results as the dependent variables. Analyses were performed using SPSS version 18.0 (SPSS, Chicago, NJ, USA). The level of statistical significance was set at $p < 0.05$.

3. Results

3.1. Descriptive statistics

A total of 60 participants were included in the analysis. Demographic information, clinical characteristics, physical performance, and cognitive function results are presented in Table 1.

3.2. Correlation analysis

Table 2 presents the associations between neurocognitive function and the following factors: demographic information, clinical characteristics, and physical performance. Stroop CW response latency (RL) was positively correlated with age ($p = 0.005$), age at onset ($p = 0.047$), and step test results (index) ($p = 0.009$). In addition, Stroop CW correct rate (CR) was negatively correlated with age ($p = 0.004$), duration of illness ($p < 0.001$), number of hospital admissions ($p = 0.024$), and STS test results ($p < 0.001$). SWM RL was positively correlated with age ($p = 0.006$), duration of illness ($p = 0.03$), BDI ($p = 0.001$) results, and step test results (index) ($p = 0.026$). Our findings also indicated that SWM CR was inversely correlated with age ($p = 0.027$) and STS test results ($p = 0.007$).

The results of additional analyses based on Global Assessment of Functioning (GAF) scores are shown in STable 1,2, and 3. In the high-functioning group, we observed significant positive correlations between the step text index and response latency in the Stroop CW and SWM tasks. STS test time was also correlated with

Table 1
Demographic information, clinical symptoms, physical performance, and cognitive function of participants (N = 60).

Attribute	Mean	SD
Male n = 35 (58.3%), female n = 25		
Age (years)	38.9	10.1
Years of education	14.1	3.0
Age at onset (years)	24.1	7.9
Duration of illness (years)	14.7	10.1
No. of hospital admissions	4.5	10.5
PDD:DDD ratio	2.2	1.0
Total cholesterol (mg/dl)	185.9	48.8
BMI (kg/m^2)	27.4	5.2
BPRS, total	42.3	15.9
BDI	17.6	11.0
SAI	45.6	9.4
TAI	48.6	10.3
Stroop CW RL	2039.0	1151.5
Stroop CW CR (%)	78.6	27.3
Sternberg WM RL	2570.6	1808.6
Sternberg WM CR (%)	62.9	20.8
Step test (index)	105.1	15.1
STS test (s)	3.1	0.8

DDD, defined daily dose; PDD, prescribed daily dose; BMI, Body mass index; BPRS, Brief Psychiatric Rating Scale; BDI, Beck Depression Inventory; SAI, State Anxiety Inventory; TAI, Trait Anxiety Inventory; CW, Color-word condition; RL, response latency; CR, correct rate; WM, working memory task; STS, supine-to-standing.

Table 2
Association between neurocognitive function and demographic characteristics, clinical symptoms, and physical performance.

	Stroop CW RL	Stroop CW CR	Sternberg WM RL	Sternberg WM CR
Age	0.376**	−0.383**	0.366**	−0.300*
Sex	−0.214	−0.123	−0.176	−0.002
Age at onset	0.272*	−0.01	0.024	−0.132
Duration of illness	0.156	−0.471**	0.296*	−0.196
No. of hospital admissions	−0.087	−0.306*	0.049	−0.064
Years of education	−0.028	0.111	−0.043	−0.124
PDD:DDD ratio	0.166	0.068	0.137	−0.034
Total cholesterol	−0.223	0.072	0.016	−0.051
BMI	−0.038	−0.253	0.015	−0.035
BPRS, total	−0.016	0.206	0.119	0.035
BDI	0.244	−0.078	0.333*	−0.22
SAI	0.072	−0.135	0.114	0.074
TAI	0.092	−0.119	0.135	−0.03
Step test (index)	0.362**	−0.062	0.311*	−0.099
STS test (s)	0.148	−0.526**	0.211	−0.383**

CW, color-word condition; RL, response latency; CR, correct rate; WM, working memory task; DDD, defined daily dose; PDD, prescribed daily dose; BMI, body mass index; BPRS, Brief Psychiatric Rating Scale; BDI, Beck Depression Inventory; SAI, State Anxiety Inventory; TAI, Trait Anxiety Inventory; STS, supine-to-standing.
Pearson's correlation coefficients: **Correlation is significant at the 0.01 level (2-tailed). *Correlation is significant at the 0.05 level (2-tailed).

SWM CR in this group. In the low-functioning group, STS test results were strongly correlated with Stoop task CR.

3.3. Multiple regression analysis

Multivariable linear regression was applied to determine which factors were associated with Stroop CW test and SWM test results (Table 3). Significantly associated variables by univariate analyses above were included as independent variables. Our analysis revealed that age at onset, total cholesterol, and step test results (index) were significantly associated with Stroop CW RL, while the duration of illness and STS time (s) were significantly associated with Stroop CW CR. Step test results (index) were the only significant predictor of RL in the SWM task, while STS time (s) was the only significant predictor of SWM CR. Step test results were positively associated with both Stroop CW RL and SWM RL, while STS test results were negatively associated with both Stroop CW CR and SWM CR. However, clinical symptoms were not associated with any variables in Stroop or SWM task.

4. Discussion

In the present study, we aimed to investigate the associations between physical performance and neurocognition among patients with schizophrenia. Our findings indicated that poorer functional mobility as determined by the STS test was associated with lower accuracy on executive function and working memory tasks after adjusting for other clinical correlates. Furthermore, poorer CRF as determined by the step test was associated with slower performance on these two cognitive tasks. In addition, total cholesterol levels and the duration of illness were significantly associated with latency and accuracy on the executive function task, respectively.

Recent studies involving the general population and older adults have demonstrated that functional mobility is associated with cognitive function, including executive function and memory [25,26,47,48]. Although there is also evidence to support this relationship in patients with schizophrenia, previous studies are limited in that they included particular sub-groups of patients only (e.g., older adults, early schizophrenia) [31,32] or utilized subjective measures only [33]. However, our study demonstrated that, when related variables including age and clinical symptoms are considered, the objective STS is the most explanatory factor for cognitive domains such as executive function and memory. Although such findings suggest a close relationship between mobility and cognition in patients with schizophrenia, follow-up studies are required to verify our results.

Previous research has indicated that the STS is useful for evaluating functional mobility and ADL performance in older adults and patients with Parkinson's disease [45,46], as well as those undergoing neurological rehabilitation [49]. Similarly, the STS may be useful in patients with schizophrenia due to the impact of sedentary behavior and low levels of physical activity in this population [50]. The STS is advantageous in that it is more efficient

Table 3
Multivariable linear regression analysis.

	Stroop CW						Sternberg WM					
	RL			CR			RL			CR		
	R^2	Beta	P	R^2	Beta	P	R^2	Beta	P	R^2	Beta	P
	0.301			0.396			0.097			0.147		
Age		0.128	0.370		−0.623	0.536		0.230	0.113		−0.166	0.255
Age at onset		0.266	**0.034**		–	–		–	–		–	–
Duration of illness		–	–		−0.361	**0.005**		0.185	0.193		–	–
No. of hospital admission		–	–		0.106	0.481		–	–		–	–
Total cholesterol		−0.307	**0.018**		–	–		–	–		–	–
BDI		–	–		0.031	0.812		0.132	0.363		−0.091	0.516
Step test (index)		0.434	**0.001**		–	–		0.331	**0.026**		–	–
STS test (s)		–	–		−0.418	**0.001**		–	–		−0.383	**0.007**

Note: Bold values are statistically significant.
CW, color-word condition; RL, response Latency; CR, correct rate; WM, working memory task; BDI, Beck Depression Inventory; STS, supine-to-standing.

than other functional mobility tasks, requiring less time and space than the TUG test or measurements of gait speed. In addition, the STS test is easy to understand and requires no specific training for evaluators, making it ideal for patients with schizophrenia. Taken together, the accumulated evidence suggests that the STS represents a quick, easy method for assessing functional mobility in patients with schizophrenia in both clinical and practical settings.

Given the complexity of functional mobility, it is not surprising that multiple cognitive functions are associated with performance in this domain. Among the multiple brain regions associated with mobility, the cuneus not only controls limb movement, but also processes and memorizes environmental information [51]. The prefrontal cortex is responsible for executive function and is known to be active during the planning and initiation of a series of actions [52]. Previous studies have reported abnormalities in neural synchrony in the cuneus of patients with schizophrenia [53], along with hypofrontality [54]. Thus, it is possible that dysfunction of this region exerts a negative impact on the series of processes involved in rising from the floor. However, the cause-effect relationship between mobility and neurocognition remains to be elucidated.

In accordance with our findings, previous studies have demonstrated an association between CRF and executive function/memory in patients with schizophrenia [17–21]. Recently evidence also indicates that adult neurogenesis may be reduced in patients with schizophrenia, which in turn may contribute to impaired cortical-to-hippocampal connectivity [55]. However, some investigators have found that improving CRF through aerobic exercise increases levels of neural growth factors (e.g., brain-derived neurotrophic factor (BDNF)) in patients with schizophrenia, helping to support the survival of existing neurons and encouraging the growth and differentiation of new neurons and synapses [19,18–21,56]. Aerobic exercise promotes neurogenesis and synaptic plasticity, exerting positive effects on neurocognition in schizophrenia. The resulting improvements in CRF lead to increases in the number of synapses in the frontal and parietal gray matter [11], which play a role in resolving the response competition elicited by incongruence response cues (e.g., Stroop task). In addition, a study by Pajonk and colleagues [20] reported that improving CRF increases levels of metabolic and synaptic plasticity-related proteins in the hippocampus, which may contribute to improved cognition, particularly with regard to short-term memory.

Interestingly, higher total cholesterol levels were associated with better performance on cognitive tasks after controlling for other clinical symptoms. Similarly, Elias and colleagues [57] observed that total cholesterol levels are positively correlated with cognitive function in healthy adults. Some researchers have speculated that serum cholesterol concentrations play a role in synthesizing neurotransmitters and forming neuronal membranes [58]. Plasma cholesterol also enhances cognitive function by modifying brain membrane fatty acid composition and altering physiological properties to activate membrane neurotransmitter receptors [59]. Krakowski and Czobor [35] revealed that increases in cholesterol levels were associated with improved cognition in patients with schizophrenia receiving antipsychotics. When taken with these previous results, our findings suggest that physical health factors, including cholesterol levels and physical performance, are closely related to cognitive function in patients with schizophrenia.

In the present study, longer duration of illness was associated with poorer performance on the Stroop task. It is well established that longer durations of illness among patients with schizophrenia are associated with greater impairments in higher-order cognitive functions such as attention and executive function. For example, using a battery of standardized neuropsychological tests, Smet and colleagues [60] reported that patients with a longer duration of illness exhibited significantly greater impairments in executive function as determined using the Trail-Making Test and Wisconsin Card Sort Test. In addition, in a study by Albus and colleagues [61], patients with chronic schizophrenia exhibited poorer performance on measures of visuomotor processing, attention, and executive function (abstraction/flexibility) when compared to patients with first-episode schizophrenia.

The present study demonstrated robust associations between physical performance and neurocognition. While previous studies focused on a single component (e.g., CRF), we also considered functional mobility, which is closely related to the functional outcomes of schizophrenia as well as CRF. In addition, our findings indicated that total cholesterol level is significantly associated with cognitive function. Moreover, unlike previous studies, we also controlled for the effects of other disorder-related clinical correlates (e.g., psychotic symptoms, depression). Our findings suggest that addressing physical health factors may improve cognitive function in patients with schizophrenia. Because direct treatment of cognitive dysfunction remains difficult [18], the clinical value of our findings cannot be understated, as we have identified modifiable factors that may impact neurocognition. While antipsychotic medications can improve psychotic symptoms, their impact on cognitive dysfunction is limited [62]. Furthermore, non-pharmacological interventions such as cognitive remediation therapy exert only minor effects, which are eventually lost over time [63]. In the future, exercise intervention may help to improve cognitive symptoms in patients with schizophrenia, thereby leading to improvements in function and prognosis [64].

Given several limitations of the present study, our findings should be interpreted with caution. First, although the STS test has been used to evaluate functional mobility in other clinical populations, the test has not yet been standardized for the assessment of patients with schizophrenia. Subsequent studies should aim to replicate our findings using this tool. Second, the structured diagnostic tools were not used, but diagnostic verification was double-checked by two psychiatric practitioners. Third, although the time of day at which neurocognitive tests are administered may influence performance among patients with schizophrenia [65], cognitive tasks were not administered at the exact same time in the present study. Fourth, the generalizability of our findings may be limited due to a small sample size and the inclusion of patients with chronic schizophrenia with a rather long duration of illness. Finally, as the study was cross-sectional, no causal correlations could be established. Interaction effects may exist, as better cognitive abilities may provide better opportunities for a healthy lifestyle. Further studies are also required to investigate the mechanisms underlying schizophrenia symptoms.

5. Conclusion

The results of the present study demonstrate the relationship between physical performance and neurocognition in patients with schizophrenia. Functional mobility and CRF were correlated with accuracy and RT during cognitive tasks including the Stoop and Sternberg task, respectively. In addition, total cholesterol levels were positively associated with Stroop task accuracy, after controlling for clinical symptoms (e.g., psychotic symptoms). These findings suggest that physical performance is closely associated with neurocognition among patients with schizophrenia. Given that these factors are modifiable, exercise intervention may help to improve cognitive symptoms in patients with schizophrenia, thereby leading to improvements in function and prognosis. Subsequent studies should aim to clarify the mechanisms underlying the association between physical health and neurocognition in individuals with schizophrenia.

Funding

This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (NRF-2018R1C1B6005103) and Hallym University Research Fund.

Contributors

Roh designed the study and structured this manuscript. Ryu wrote the protocol of exercise programs. Jung, Kim CH and Kim DH managed the literature searches and analyses (including the statistical analysis). Lee HB and Lee SK contributed to the interpretation of the results. Shin and Kim J wrote the first draft of the manuscript. Shin and Kim J managed and contributed equally the entire this study process. All authors contributed to and have approved the final manuscript.

Declaration of Competing Interest

The authors declare that they have no competing interests.

Acknowledgment

None.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.eurpsy.2019.06.010.

References

[1] Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990–2020: global burden of disease study. Lancet 1997;349:1498–504.
[2] Bagney A, Rodriguez-Jimenez R, Martinez-Gras I, Sanchez-Morla EM, Santos JL, Jimenez-Arriero MA, et al. Negative symptoms and executive function in schizophrenia: does their relationship change with illness duration? Psychopathology 2013;46:241–8.
[3] Green MF, Kern RS, Braff DL, Mintz J. Neurocognitive deficits and functional outcome in schizophrenia: are we measuring the "right stuff"? Schizophr Bull 2000;26:119–36.
[4] Dickinson D, Ragland JD, Gold JM, Gur RC. General and specific cognitive deficits in schizophrenia: Goliath defeats David? Biol Psychiatr 2008;64:823–7.
[5] Nuechterlein KH, Barch DM, Gold JM, Goldberg TE, Green MF, Heaton RK. Identification of separable cognitive factors in schizophrenia. Schizophr Res 2004;72:29–39.
[6] Goldberg TE, Goldman RS, Burdick KE, Malhotra AK, Lencz T, Patel RC, et al. Cognitive improvement after treatment with second-generation antipsychotic medications in first-episode schizophrenia: is it a practice effect? Arch Gen Psychiat 2007;64:1115–22.
[7] Keefe RS, Buchanan RW, Marder SR, Schooler NR, Dugar A, Zivkov M, et al. Clinical trials of potential cognitive-enhancing drugs in schizophrenia: what have we learned so far? Schizophr Bull 2011;39:417–35.
[8] Bouchard C, Shephard RJ, Stephens T, Sutton J, McPherson B. May 29-June 3, 1988, Toronto, CanadaExercise, fitness, and health: a consensus of current knowledge: proceedings of the International Conference on Exercise, fitness, and health1990. Exercise, fitness, and health: a consensus of current knowledge: proceedings of the International Conference on Exercise, fitness, and health 1990 Exercise, fitness, and health: a consensus of current knowledge: proceedings of the International Conference on Exercise, fitness, and health, May 29-June 3, 1988, Toronto, Canada: Human Kinetics Publishers.
[9] Strassnig M, Brar JS, Ganguli R. Low cardiorespiratory fitness and physical functional capacity in obese patients with schizophrenia. Schizophr Res 2011;126:103–9.
[10] Viertiö S, Sainio P, Koskinen S, Perälä J, Saarni SI, Sihvonen M, et al. Mobility limitations in persons with psychotic disorder: findings from a population-based survey. Soc Psychiatr Epidemiol 2009;44:325–32.
[11] Colcombe SJ, Kramer AF, Erickson KI, Scalf P, McAuley E, Cohen NJ, et al. Cardiovascular fitness, cortical plasticity, and aging. Pro Natl Acad Scie 2004;101:3316–21.
[12] Vancampfort D, Rosenbaum S, Probst M, Soundy A, Mitchell A, De Hert M, et al. Promotion of cardiorespiratory fitness in schizophrenia: a clinical overview and meta-analysis. Acta Psychiatr Scand 2015;132:131–43.
[13] Laursen TM, Nordentoft M, Mortensen PB. Excess early mortality in schizophrenia. Annu Rev Clinical Psychol 2014;10:425–48.
[14] Hennekens CH, Hennekens AR, Hollar D, Casey DE. Schizophrenia and increased risks of cardiovascular disease. Am Heart J 2005;150:1115–21.
[15] Voss MW, Chaddock L, Kim JS, VanPatter M, Pontifex MB, Raine LB, et al. Aerobic fitness is associated with greater efficiency of the network underlying cognitive control in preadolescent children. Neuroscience 2011;199:166–76.
[16] Etnier JL, Nowell PM, Landers DM, Sibley BA. A meta-regression to examine the relationship between aerobic fitness and cognitive performance. Brain Res Rev 2006;52:119–30.
[17] Kimhy D, Vakhrusheva J, Bartels MN, Armstrong HF, Ballon JS, Khan S, et al. Aerobic fitness and body mass index in individuals with schizophrenia: implications for neurocognition and daily functioning. Psychiatry Res 2014;220:784–91.
[18] Holmen TL, Egeland J, Andersen E, Bigseth TT, Engh JA. The association between cardio-respiratory fitness and cognition in schizophrenia. Schizophr Res 2018;193:418–22.
[19] Kimhy D, Vakhrusheva J, Bartels MN, Armstrong HF, Ballon JS, Khan S, et al. The impact of aerobic exercise on brain-derived neurotrophic factor and neurocognition in individuals with schizophrenia: a single-blind, randomized clinical trial. Schizophr Bull 2015;41:859–68.
[20] Pajonk F-G, Wobrock T, Gruber O, Scherk H, Berner D, Kaizl I, et al. Hippocampal plasticity in response to exercise in schizophrenia. Arch Gen Psychiat 2010;67:133–43.
[21] Firth J, Stubbs B, Rosenbaum S, Vancampfort D, Malchow B, Schuch F, et al. Aerobic exercise improves cognitive functioning in people with schizophrenia: a systematic review and meta-analysis. Schizophr Bull 2017;43:546–56.
[22] Forhan M, Gill SV. Obesity, functional mobility and quality of life. Best Pract Res Clin Endocrinol Metab 2013;27:129–37.
[23] Viccaro LJ, Perera S, Studenski SA. Is timed up and go better than gait speed in predicting health, function, and falls in older adults? J Am Geriatr Soc 2011;59:887–92.
[24] Huang EJ, Reichardt LF. Neurotrophins: roles in neuronal development and function. Annu Rev Neurosci 2001;24:677–736.
[25] McGough EL, Kelly VE, Logsdon RG, McCurry SM, Cochrane BB, Engel JM, et al. Associations between physical performance and executive function in older adults with mild cognitive impairment: gait speed and the timed "up & go" test. Phys Ther 2011;91:1198–207.
[26] Kimura N, Kazui H, Kubo Y, Yoshida T, Ishida Y, Miyoshi N, et al. Memory and physical mobility in physically and cognitively-independent elderly people. Geriatr Gerontol Int 2007;7:258–65.
[27] Mun-San Kwan M, Lin S-I, Chen C-H, Close JC, Lord SR. Sensorimotor function, balance abilities and pain influence timed up and go performance in older community-living people. Aging Clin Exp Res 2011;23:196–201.
[28] Bergland A, Laake K. Concurrent and predictive validity of "getting up from lying on the floor". Aging Clin Exp Res 2005;17:181–5.
[29] Klima DW, Anderson C, Samrah D, Patel D, Chui K, Newton R. Standing from the floor in community-dwelling older adults. J Aging Phys Act 2016;24:207–13.
[30] Tiedemann A, Shimada H, Sherrington C, Murray S, Lord S. The comparative ability of eight functional mobility tests for predicting falls in community-dwelling older people. Age Ageing 2008;37:430–5.
[31] Leutwyler H, Hubbard E, Jeste D, Miller B, Vinogradov S. Association between schizophrenia symptoms and neurocognition on mobility in older adults with schizophrenia. Aging Ment Health 2014;18:1006–12.
[32] Lallart E, Jouvent R, Herrmann FR, Beauchet O, Allali G. Gait and motor imagery of gait in early schizophrenia. Psychiatry Res 2012;198:366–70.
[33] Chwastiak LA, Rosenheck RA, McEvoy JP, Keefe RS, Swartz MS, Lieberman JA. Special section on CATIE baseline data: interrelationships of psychiatric symptom severity, medical comorbidity, and functioning in schizophrenia. Psychiatr Serv 2006;57:1102–9.
[34] Douglas KM, Porter RJ. Longitudinal assessment of neuropsychological function in major depression. Aust N Z J Psychiatry 2009;43:1105–17.
[35] Krakowski M, Czobor P. Cholesterol and cognition in schizophrenia: a double-blind study of patients randomized to clozapine, olanzapine and haloperidol. Schizophr Res 2011;130:27–33.
[36] Rashid NAA, Lim J, Lam M, Chong S-A, Keefe RS, Lee J. Unraveling the relationship between obesity, schizophrenia and cognition. Schizophr Res 2013;151:107–12.
[37] Overall JE, Gorham DR. The brief psychiatric rating scale. Psychol Rep 1962;10:799–812.
[38] Kim M, Lee B, Jeon Y. Reliability of Korean brief psychiatric rating scale (BPRS): comparison of interrater reliability between the two rating methods and correlation of BPRS and SCL-90 self-report test. Kor J Clin Psychol 2003;22:685–98.
[39] Beck AT, Steer RA, Carbin MG. Psychometric properties of the Beck Depression Inventory: twenty-five years of evaluation. Clin Psychol Rev 1988;8:77–100.
[40] Lee Y. A study of the reliability and the validity of the BDI, SDS, and MMPI-D scales. Kor J Clin Psychol 1991;10:98–113.
[41] Spielberger CD. State-Trait anxiety inventory. Corsini Encycl Psychol 2010;1-.
[42] Han D-W, Lee C-H, Tack J. The standardization of the spielberger stait and trait anxiety inventory. J Stud Guidance 1993;10:214–22.
[43] Stroop JR. Studies of interference in serial verbal reactions. J Exp Psychol 1935;18:643.
[44] Sternberg S. High-speed scanning in human memory. Science 1966;153:652–4.
[45] Schenkman M, Ellis T, Christiansen C, Barón AE, Tickle-Degnen L, Hall DA, et al. Profile of functional limitations and task performance among people with early-and middle-stage Parkinson disease. Phys Ther 2011;91:1339–54.

[46] Alexander N, Galecki A, Nyquist L, Hofmeyer M, Grunawalt J, Grenier M, et al. Chair and bed rise performance in ADL-impaired congregate housing residents. J Am Geriatr Soc 2000;48:526–33.
[47] Demnitz N, Zsoldos E, Mahmood A, Mackay CE, Kivimäki M, Singh-Manoux A, et al. Associations between mobility, cognition, and brain structure in healthy older adults. Front Aging Neurosci 2017;9:155.
[48] Donoghue OA, Horgan NF, Savva GM, Cronin H, O'regan C, Kenny RA. Association between timed Up-and-Go and memory, executive function, and processing speed. J Am Geriatr Soc 2012;60:1681–6.
[49] Schenkman M, Cutson TM, Kuchibhatla M, Chandler J, Pieper CF, Ray L, et al. Exercise to improve spinal flexibility and function for people with Parkinson's disease: a randomized, controlled trial. J Am Geriatr Soc 1998;46:1207–16.
[50] Vancampfort D, Firth J, Schuch FB, Rosenbaum S, Mugisha J, Hallgren M, et al. Sedentary behavior and physical activity levels in people with schizophrenia, bipolar disorder and major depressive disorder: a global systematic review and meta-analysis. World Psychiatry 2017;16:308–15.
[51] Beloozerova IN, Sirota MG. Integration of motor and visual information in the parietal area 5 during locomotion. J Neurophysiol 2003;90:961–71.
[52] Frith CD, Friston K, Liddle PF, Frackowiak RS. Willed action and the prefrontal cortex in man: a study with PET. Proc R Soc Lond Ser B: Bio Sci 1991;244:241–6.
[53] Hoptman MJ, Zuo X-N, Butler PD, Javitt DC, D'Angelo D, Mauro CJ, et al. Amplitude of low-frequency oscillations in schizophrenia: a resting state fMRI study. Schizophr Res 2010;117:13–20.
[54] Davidson LL, Heinrichs RW. Quantification of frontal and temporal lobe brain-imaging findings in schizophrenia: a meta-analysis. Psychiatry Res Neuroimaging 2003;122:69–87.
[55] Reif A, Fritzen S, Finger M, Strobel A, Lauer M, Schmitt A, et al. Neural stem cell proliferation is decreased in schizophrenia, but not in depression. Mol Psychiatr 2006;11:514.
[56] Vakhrusheva J, Marino B, Stroup TS, Kimhy D. Aerobic exercise in people with schizophrenia: neural and neurocognitive benefits. Curr Behav Neurosci Rep 2016;3:165–75.
[57] Elias PK, Elias MF, D'agostino RB, Sullivan LM, Wolf PA. Serum cholesterol and cognitive performance in the Framingham Heart Study. Psychosom Med 2005;67:24–30.
[58] Hibbeln JR, Umhau JC, George DT, Shoaf SE, Linnoila M, Salem Jr N. Plasma total cholesterol concentrations do not predict cerebrospinal fluid neurotransmitter metabolites: implications for the biophysical role of highly unsaturated fatty acids. Am J Clin Nutr 2000;71:331S–8S.
[59] Burger K, Gimpl G, Fahrenholz F. Regulation of receptor function by cholesterol. CMLS-Cell Mol Life Sci 2000;57:1577–92.
[60] Smet I, Tandon R, Goldman R, Decker L, Lelli G, Berent S. Chronicity and neuropsychological dysfunction in schizophrenia. Biol Psychiatr 1996;39:579.
[61] Albus M, Hubmann W, Ehrenberg C, Forcht U, Mohr F, Sobizack N, et al. Neuropsychological impairment in first-episode and chronic schizophrenic patients. Eur Arch Psych Clin Neurosci 1996;246:249–55.
[62] Hasan A, Falkai P, Wobrock T, Lieberman J, Glenthoj B, Gattaz WF, et al. World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for biological treatment of schizophrenia, part 2: update 2012 on the long-term treatment of schizophrenia and management of antipsychotic-induced side effects. World J Biol Psychiatry 2013;(14):2–44.
[63] Wykes T, Huddy V, Cellard C, McGurk SR, Czobor P. A meta-analysis of cognitive remediation for schizophrenia: methodology and effect sizes. Ame J Psychiatry 2011;168:472–85.
[64] Sommer IE, Kahn RS. The magic of movement; the potential of exercise to improve cognition. US: Oxford University Press; 2015.
[65] D'Reaux RA, Neumann CS, Rhymer KN. Time of day of testing and neuropsychological performance of schizophrenic patients and healthy controls. Schizophr Res 2000;45: 157-156.