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Short communication

Aerobic exercise and cognitive functioning in schizophrenia: A pilot randomized controlled trial

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ABSTRACT

This pilot randomized controlled trial evaluated the combined effect of individual and group aerobic exercises (AEs) on cognition in schizophrenia. Among 32 randomized patients, 31 were included in the intent-to-treat population: 16 in treatment as usual (TAU) + AE and 15 in TAU groups. Over 12 weeks, patients were given a dose of 2 exercise sessions per week, including 1 individual session and 1 group session. TAU + AE patients showed significant improvements in cognition, intrinsic motivation, psychiatric symptoms, and interpersonal relations. These encouraging findings support the promise of integrated individual and group AEs to improve cognition and other outcomes in schizophrenia.

1. Introduction

Cognition of schizophrenia is a core feature that is a major determinant of functional outcomes (Green et al., 2019; Keefe and Harvey, 2012). Compared to pharmacological approaches, psychosocial treatments for cognitive remediation have produced more encouraging findings (Keefe et al., 2007; McGurk et al., 2007; Woodward et al., 2005; Wykes et al., 2011).

Another intervention option for improving cognition in schizophrenia is the novel non-pharmacological approaches intended to promote neuro-plasticity; that is, physical exercise. Several meta-analyses demonstrated that physical activity, particularly aerobic exercise (AE), is beneficial to improve not only psychiatric symptoms and social functioning but also cognition in schizophrenia (Dauwan et al., 2016; Firth et al., 2017; Rosenbaum et al., 2014). This single-blinded, randomized controlled trial evaluated the integrated effect of individual and group AEs on cognition and other outcome in schizophrenia.

2. Methods

2.1. Participants and procedures

Inclusion criteria were age 20–65 years; psychiatric inpatients; and a DSM-5 diagnosis of schizophrenia or schizoaffective disorder. Exclusion criteria were a diagnosis of alcohol/substance abuse; a known neurological disorder; mental retardation; and likely difficulty with participating in AE due to physical impairment.

Following the baseline assessment, eligible patients were randomized to treatment as usual (TAU) + AE or TAU groups by independent study staff with whom there was no patient contact. Randomization was stratified by sex and age with the use of a computer-generated randomization program.

This study was approved by the ethics committee of the Medical Corporation Seitaikai (0007). All participants provided written informed consent. The study was registered in the University Hospital Medical Information Network Clinical Trials Registry (UMIN-CTR) (UMIN000034910).

2.2. Interventions

The AE program consisted of individual and group programs led by occupational therapists. Patients exercised over 12 weeks, with 2 sessions per week including 1 individual session (60-min duration) and 1 group session (60-min duration). The intensity of each exercise session was individually calibrated at 60% to 80% of aerobic capacity. Patients were required to participate in a minimum of 75% of each session. In the individual AE program, we used exercise equipment, such as a treadmill machine and a stationary bike. In the group AE program, we used exercise videos approved by a certified trainer familiar with the physical health issues of patients with psychiatric disorders.

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Table 1
Changes in outcome scores from baseline to post by treatment group (TAU + AE; TAU alone).

Measure	Time	TAU + AE (n = 16)		TAU (n = 15)		F			η_p^2
		Mean	(SD)	Mean	(SD)	Time	Group	Time × Group	
BACS									
Verbal memory	Baseline	−1.56	(1.16)	−1.84	(0.98)	10.69**	5.55**	2.66	0.19
	Post	−0.77	(0.78)	−1.75	(1.01)				
Working memory	Baseline	−1.42	(1.25)	−1.59	(1.28)	16.18**	4.13*	4.12*	0.26
	Post	−0.68	(1.24)	−1.44	(1.42)				
Motor speed	Baseline	−1.94	(1.32)	−2.55	(1.16)	0.12	0.89	1.41	0.10
	Post	−2.24	(1.46)	−2.18	(1.14)				
Verbal fluency	Baseline	−0.87	(1.14)	−0.75	(1.08)	0.89	6.44**	4.36*	0.28
	Post	0.60	(0.91)	−0.85	(1.24)				
Attention	Baseline	−2.50	(1.30)	−1.71	(1.44)	32.55**	16.57**	19.08**	0.62
	Post	−1.14	(1.27)	−1.69	(1.57)				
Executive functioning	Baseline	−1.90	(1.98)	−2.55	(2.66)	8.00*	10.31**	5.57**	0.33
	Post	−0.68	(1.30)	−2.77	(2.35)				
Composite score	Baseline	−1.75	(1.20)	−1.89	(1.18)	28.19**	13.19**	8.79**	0.43
	Post	−0.98	(0.94)	−1.78	(1.22)				
SCoRS									
Patient total	Baseline	33.27	(14.64)	39.70	(13.57)	2.50	0.93	0.00	0.00
	Post	30.20	(7.54)	36.30	(12.08)				
Patient global rating	Baseline	4.64	(2.58)	5.10	(1.52)	1.21	13.08**	2.51	0.12
	Post	3.70	(1.34)	5.30	(1.16)				
Informant total	Baseline	44.18	(15.95)	38.60	(14.25)	3.64	7.38*	7.07*	0.28
	Post	35.00	(12.27)	40.10	(11.99)				
Informant global rating	Baseline	5.82	(2.44)	5.00	(2.36)	3.07	2.93	3.89	0.18
	Post	4.00	(1.83)	5.10	(2.23)				
Interviewer total	Baseline	44.91	(15.20)	42.60	(9.81)	0.07	2.14	3.81	0.18
	Post	38.80	(10.10)	43.50	(10.71)				
Interviewer global rating	Baseline	6.09	(2.07)	5.80	(1.14)	1.48	0.12	0.65	0.04
	Post	5.30	(1.06)	5.70	(1.57)				
QLS									
QLS score	Baseline	6.24	(2.41)	6.60	(1.67)	39.24**	16.55**	16.39**	0.58
	Post	9.40	(3.44)	7.20	(1.44)				
PANSS									
Positive	Baseline	25.67	(6.44)	25.35	(3.72)	14.44*	4.70*	5.09**	0.30
	Post	21.90	(5.19)	25.00	(5.51)				
Negative	Baseline	27.43	(5.72)	26.00	(3.10)	44.96**	11.10**	14.04**	0.54
	Post	21.40	(5.33)	25.00	(4.35)				
General psychopathology	Baseline	58.62	(9.06)	54.40	(6.34)	4.76	2.46	2.55	0.18
	Post	55.15	(10.00)	53.20	(8.81)				
PANSS total	Baseline	111.71	(19.42)	105.75	(11.33)	17.36**	3.96*	5.17**	0.30
	Post	98.45	(17.39)	103.20	(17.42)				
SANS									
Affective flattening	Baseline	22.00	(10.75)	20.40	(7.23)	7.57*	8.63*	8.90*	0.33
	Post	17.30	(8.25)	20.90	(8.08)				
Alogia	Baseline	16.36	(6.62)	13.70	(5.19)	5.12	4.41	5.12	0.24
	Post	11.70	(4.47)	14.00	(3.68)				
Avolition/apathy	Baseline	13.91	(4.42)	12.80	(3.52)	4.20	8.55*	8.74*	0.34
	Post	10.20	(3.36)	13.10	(3.73)				
Anhedonia/asociality	Baseline	16.00	(5.68)	15.10	(5.15)	3.43	14.88**	8.50*	0.30
	Post	12.00	(4.90)	16.40	(4.14)				
Attention	Baseline	10.73	(4.00)	11.10	(2.85)	10.04*	9.88*	6.33*	0.27
	Post	7.80	(3.19)	9.90	(4.70)				
SANS total	Baseline	77.73	(28.87)	73.10	(20.58)	6.42*	10.38*	8.59*	0.33
	Post	59.00	(21.46)	74.30	(21.47)				
GAF									
GAF score	Baseline	47.62	(6.15)	47.55	(7.75)	20.02**	0.97	2.19	0.15
	Post	52.55	(4.43)	51.35	(5.72)				
LASMI									
Daily living	Baseline	25.38	(7.97)	26.80	(5.75)	22.58**	1.72	1.19	0.09
	Post	20.45	(7.17)	24.40	(7.29)				
Interpersonal relations	Baseline	26.76	(12.78)	26.65	(6.75)	23.71**	6.75**	4.02*	0.25
	Post	17.55	(5.85)	24.90	(8.36)				

*p <0.05, **p < 0.01.
AE, Aerobic exercises; BACS, Brief Assessment of Cognition in Schizophrenia; GAF, Global Assessment of Functioning; LASMI, Life Assessment Scale for the Mentally Ill; PANSS, Positive and Negative Syndrome Scale; QLS, Quality of Life Scale; SANS, Scale for the Assessment of Negative Symptoms; SCoRS, Schizophrenia Cognition Rating Scale; TAU, Treatment as Usual.

All patients received TAU over the course of the study, which included regular meetings with a psychiatrist, medication, case management, and other rehabilitation programs.

2.3. Outcomes

Assessment measures were conducted by trained evaluators who were blind to treatment assignment. Cognition was assessed with the Brief Assessment of Cognition in Schizophrenia (BACS) (Keefe et al.,

2004) and the Schizophrenia Cognition Rating Scale (SCoRS) (Keefe et al., 2006). Intrinsic motivation was assessed based on the sum of the following three items from the Quality of Life Scale (QLS): sense of purpose, motivation, and curiosity (Heinrichs et al., 1984). Social functioning was assessed with the Life Assessment Scale for the Mentally Ill (LASMI) (Iwasaki et al., 1994). Global functioning was assessed with the Global Assessment of Functioning (GAF) scale (American Psychiatric Association, 2000). Psychopathology was assessed with the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987). Negative symptoms were assessed with the Scale for the Assessment of Negative Symptoms (SANS) (Andreason, 1983).

2.4. Statistical analyses

Statistical analyses were performed with JMP13.2.1 for Microsoft Windows (SAS Institute, Cary, NC, USA). Intention-to-treat analysis was conducted. Feasibility assessment was summarized with descriptive statistics. Changes from baseline in BACS and SCoRS were examined using mixed model repeated measures (MMRM) analyses with patients as the random effects and age, sex, baseline scores, baseline QLS score, treatment, assessment time point, and treatment-by-time interaction as the fixed effects. Moreover, we examined changes from baseline in QLS, LASMI, GAF, PANSS, and SANS using MMRM analyses. In these analyses, patients were the random effects, and age, sex, baseline scores, treatment, assessment time point, and treatment-by-time interaction were the fixed effects. Effect sizes were calculated using η_p^2. The significance level was set at $p < 0.05$ for a two-sided test, and Bonferroni correction was applied to the statistical results to reduce the type I errors generated by multiple comparisons.

3. Results

Of 43 patients who were assessed for eligibility, 32 met criteria completion: 16 in TAU + AE and 16 in TAU. One participant dropped out of the TAU alone condition based on a withdrawal of consent to participate. The final sample used for the analyses consisted of 31 patients: 16 in TAU + AE and 15 in TAU.

There were no significant differences between groups in demographics or baseline assessment scores. TAU + AE patients completed an average of 90.00% (mean = 21.6 sessions, SD = 2.50) of AE sessions.

Table 1 showed the MMRM analysis results. It yielded significant treatment-by-time interaction effects on working memory, verbal fluency, attention, executive function, and composite score in BACS; informant total in SCoRS; QLS score; positive, negative, and total in PANSS; affective flattening, avolition/apathy, anhedonia/asociality, attention, total in SANS; and interpersonal relations in LASMI.

4. Discussion

To our knowledge, this is the first randomized trial to demonstrate that integrating individual and group exercise training is feasible for use in a Japanese psychiatric hospital, and that it improves cognition and other outcomes of schizophrenia.

Our results reveal an increase in cognitive performance and a reduction in severity of psychopathology across groups, with the strongest effects being found in patients undergoing AE training. A combination of individual and group AEs may arguably be more effective than TAU alone in the management of cognition, intrinsic motivation, interpersonal relations, and psychopathology in schizophrenia. In addition, this study provides encouraging findings in that the AE intervention for schizophrenia could be feasible at a Japanese psychiatric hospital. This may suggest that there are not any adverse effects in the implementation of AE on schizophrenia.

Several limitations should be noted. First, outcomes were conducted at only 12 weeks following participation in the AE program. Therefore, a follow-up study is needed to evaluate the long-term effects of AE. Second, optimal duration, intensity, frequency, content of physical intervention, and type (individual or group) of each training to maximize cognitive performance was not examined. Third, our results were limited by a small sample size and because the study was conducted at a single site. Finally, the study participants were only inpatients with schizophrenia. Despite these limitations, our preliminary findings provides staunch support for the feasibility of implementing AE and the benefits of AE in improving cognition and other outcomes.

Declaration of Competing Interest

None.

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Supplementary materials

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