Association between actigraphy-derived physical activity and cognitive performance in patients with schizophrenia

Li-Jung Chen[1, 2], Andrew Steptoe [2], Ming-Shun Chung[3], Po-Wen Ku[2, 4*]

[1] Department of Exercise Health Science, National Taiwan University of Sport, 271, Lixing Road, Taichung, 404, Taiwan (ljchen@ntupes.edu.tw)

[2] Department of Epidemiology and Public Health, University College London, 1-19 Torrington Place, London WC1E 6BT, UK (a.steptoe@ucl.ac.uk)

[3] Jianan Psychiatric Center, Ministry of Health and Welfare, 80, Lane 870, Zhongshan Road, Tainan 717, Taiwan (mschung3@gmail.com)

[4] Graduate Institute of Sports and Health, National Changhua University of Education, 1, Jin-De Road, Changhua, 500, Taiwan (powen.ku@gmail.com)

Corresponding author: Po-Wen Ku

National Changhua University of Education, Taiwan

No.1, Jinde Rd., Changhua City, 500, Taiwan

Phone: +886 (0) 4 7232105 ext. 1991; E-mail: powen.ku@gmail.com

Word counts in text: 2912; Word counts in abstract: 249; Number of **Tables**: 4

Statements: This work has not been previously published and that is not currently under review elsewhere.

Financial support:

This work was in part supported by the National Taiwan University of Sport and Taiwan Ministry of Science and Technology (102-2410-H-018-041-MY2).

Association between actigraphy-derived physical activity and cognitive performance in patients with schizophrenia

Abstract

Objective: An association between low levels of physical activity and impaired cognitive performance in schizophrenia has been proposed, but most studies have relied on self-report measures of activity. This study examined the association between actigraphy-derived physical activity and cognitive performance adjusting for multiple covariates in patients with schizophrenia.

Methods: Patients with schizophrenia (n=199) were recruited from chronic psychiatric wards, and 60 age-, gender- and BMI-matched comparison participants were recruited from the staff of two hospitals and universities. Physical activity was assessed objectively for 7 days using an Actigraph. Cognitive performance was assessed with the Cognitrone test from the Vienna Test System and the Grooved Pegboard Test. Demographic variables, metabolic parameters, positive and negative symptoms, duration of illness and hospitalization, and medication use were included as covariates. Pearson correlations and multivariable linear regressions were conducted to examine the associations between physical activity levels and cognitive performance.

Results: Patients with schizophrenia were less physically active and had poorer performance on attention/concentration and speed of processing than the comparison group. Patients with schizophrenia who spent more time in light physical activity showed better performance on attention/concentration (Beta=.198, *p*=.020) and speed of processing (Beta=-.169, *p*=.048) tasks than those who were less active. Cognitive performance was also associated with moderate-vigorous physical activity, but the effect was no longer significant once light physical activity had been taken into account.

Conclusion: This study provides evidence for a positive association between objectively measured light physical activity and cognitive performance in people with schizophrenia, after adjustment for multiple confounders.

Keywords: Inactivity; actigraph; accelerometer; psychiatric disorder; cognition

Association between actigraphy-derived physical activity and cognitive performance in patients with schizophrenia

Introduction

Schizophrenia is a chronic and severe mental illness (McGrath et al., 2008, National Institute of Mental Health, 2009), resulting in high economic costs (Wu et al., 2005). People with schizophrenia tend to have a high rate of unemployment (Ramsay et al., 2012), an unhealthy lifestyle (e.g. smoking and physical inactivity) (de Leon and Diaz, 2005, Wichniak et al., 2011, Yamamoto et al., 2011), and poor physical health status (Hausswolff-Juhlin et al., 2009). Side effects of antipsychotic drugs may contribute to an elevated risk of weight gain and the development of metabolic disturbances in schizophrenia (Marder et al., 2014, Malchow et al., 2013, Hägg et al., 2006, Rege, 2008). Moreover, the presence of the metabolic syndrome (MetS) limits physical activity in schizophrenia (Vancampfort et al., 2011), leading to a vicious self-perpetuating cycle of increasing metabolic syndrome and decreasing physical activity among patients with schizophrenia.

The physical health problems and physical activity levels of people with schizophrenia have been widely studied (Vancampfort et al., 2011, Ratliff et al., 2012, Vancampfort et al., 2013). Another critical issue in schizophrenia is cognitive impairment. Cognitive capacity is crucial for functioning in everyday life, since ability to attend to stimuli selectively, maintain concentration on tasks over prolonged periods, use language for communication and self-expression, learn new skills, make decisions, and execute actions are all important (Sharma and Antonova, 2003, Glisky, 2007). These abilities are impaired to some extent in patients with schizophrenia, with deficits in attention, executive function, verbal and visuospatial working memory, and learning and memory having been reported (Sharma and Antonova, 2003). Cognitive deficits are also associated with impaired functional status, work capacity, social behavior, and activities of daily living (Matza et al., 2006, Green, 1996).

The benefits of physical activity for cognitive performance are well documented in healthy populations (Angevaren et al., 2008, McMorris and Hale, 2012, Guiney and Machado, 2013, Verburgh et al., 2014). However, the impact of physical activity on individuals with mental illness has only recently been examined (Richardson et al., 2005, Holley et al., 2011, Zschucke et al., 2013). The available evidence suggests that high physical fitness or more physical activity are associated with better cognitive performance, including executive functioning, verbal working memory, and speed of processing among patients with schizophrenia (Kimhy et al., 2014, Leutwyler et al., 2014). These findings indicate that physical activity might have potential benefits for some domains of cognition in people with schizophrenia.

However, most studies have used self-report measures of physical activity, and these are subject to recall bias (Lindamer et al., 2008). The few studies examining associations between objectively-measured physical activity and cognition in people with schizophrenia have been small scale (Leutwyler et al., 2014, Lindamer et al., 2008). Moreover, potentially confounding factors, such as education levels, body mass index (BMI), MetS parameters, antipsychotic medication, smoking and drinking status have not been controlled (Leutwyler et al., 2014). This study was therefore designed to examine the association between actigraphy-derived physical activity and cognitive performance while adjusting for multiple confounders in people with schizophrenia.

Methods

Participants

Participants were recruited from the chronic psychiatric wards at Jianan Mental Hospital, Taiwan. The diagnosis of schizophrenia was verified by psychiatrists based on the Diagnostic and Statistical Manual Disorders, Fourth Edition. Patients were included if they were stable on antipsychotic medicine and had used the same dosage for at least three months prior to inclusion. Those who were unable to communicate, unable to walk independently, and had neurological disorders were excluded. A total of 200 potential inpatients were suitable for the study. Among them, 199 inpatients provided their written informed consent.

Age-, gender- and BMI-matched comparison participants were recruited from the staffs of two hospitals and universities. Individuals who had no present or past history of psychiatric disorder and were not taking any psychoactive medicines were invited. A total of 60 participants were selected to ensure comparable gender balance, age and BMI ranges to the schizophrenia group. The study was approved by the Institutional Review Board of Jianan Mental Hospital.

Measures

Physical activity

The wActiSleep-BT ActiGraph (Pensacola, FL, USA), was used to assess physical activity levels objectively. This is a tri-axial accelerometer that has been validated and used in previous studies (García-Ortiz et al., 2010, Hansen et al., 2012, Cain et al., 2013, de Moura et al., 2015). Standardized instructions of wearing an accelerometer were provided by research assistants. Participants were asked to wear the accelerometer all day on the wrist of the non-dominant hand for one week and to remove it during bathing or water activities. The accelerometers were initialized, downloaded and analyzed using ActiLife software version 6 (ActiGraph LLC). The sleep period was excluded and the levels of physical activity were defined according to the cut-off points outlined by Freedson (Freedson et al., 1998). Light physical activity was defined as counts between 101 and 1951, and time in moderate-vigorous physical activity (MVPA) was defined as activities≧1952 cpm (Cain et al., 2013, Lindamer et al., 2008). Participants were excluded if the accelerometers were not worn for at least 10 hours per day (excluding sleep period) for at least 5 days (n=38). The average wear time was 13.9±2.1 hours per day for the schizophrenia group and 16.3±1.4 hours per day for the healthy controls.

Cognitive function

Vienna Test System (VTS). The VTS is a computerized neurocognitive function assessment battery consisting of various tests of personality, intelligence, and cognitive function (Schuhfried, 2013). It has been used in previous studies of healthy individuals, people with depression (Deijen et al., 1993, Lee et al., 2003), and people with schizophrenia (Klasik et al., 2011). The Cognitrone test (COG) used in this study is a general ability test assessing attention and concentration. Participants are presented with a series of abstract figures on the computer screen, and make judgments concerning their congruence (Schuhfried, 2013). The number of responses made within the total working time of 7 minutes was recorded.

Grooved Pegboard Test (GPT). The GPT is regarded as a test of manual dexterity, upper-limb motor speed, hand-eye coordination, and speed of processing and has been widely used in previous research (Bezdicek et al., 2014, Belsky et al., 2015, Wang et al., 2011, Nuechterlein et al., 2004). It consists of 25 holes with randomly positioned slots. The task involves inserting pegs into the board in a fixed order and in the correct direction using only one hand. Participants are encouraged to perform the task as quickly as possible, and the total time needed for the test is recorded. In this study, participants were tested twice, once with the dominant hand and once with the non-dominant hand, and the average time taken for the two tests was calculated.

Covariates

Positive and negative syndrome scale (PANSS). The PANSS was developed to assess the severity of positive and negative symptoms and to measure general psychopathology in schizophrenia (Kay et al., 1987). It was completed by the registered nurses looking after each patient with schizophrenia. The 30-item rating scale consists of three subscales: 7-item Positive Symptoms, 7-item Negative Symptoms, and 16-item General Psychopathology. Each item is assessed on a 7-point rating scale ranging from 1 (asymptomatic) to 7 (extremely symptomatic). The PANSS was summed across items, so could range from 7 to 49 for the Positive and Negative Scales and 16 to 112 for the General Psychopathology Scale. Higher scores indicate more severe symptoms.

Medication use. Information about years since illness onset, duration of hospitalization, the use of antipsychotics medication and sleeping pills was collected from hospital records. Antipsychotic medication use was converted into a daily equivalent dosage of chlorpromazine (Gardner et al., 2010), while sedatives were converted to the daily equipotent dosage of Lorazepam, according to the defined daily dose (DDD) of WHO Collaborating Centre for Drug Statistics Methodology (http://www.whocc.no/ddd/definition_and_general_considera/).

Metabolic parameters. Waist circumference, systolic/diastolic blood pressure (SBP/DBP), serum triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and fasting glucose (FG) were obtained through regular health checks in the hospital.

Demographic variables. Data on age, sex, smoking habits, alcohol consumption, and years of schooling were collected. Participants were categorized into two groups: ‘Yes (current/former smoker or drinker)’ and ‘No’ (never). Groups of current and former smoker or alcohol consumer were combined, due to there being few current smokers (n=18) or current alcohol consumers (n=2). Body weight and height were measured in light clothes and body mass index (BMI) was calculated.

Psychiatric nurse practitioners who had completed psychiatric professional training and research ethics training to degree level or higher administered the tests.

Statistical analyses

Descriptive statistics were calculated and Chi-square tests and t-tests were performed to compare schizophrenia and comparison groups. Pearson correlations were used to test the univariate associations between physical activity levels and cognitive performance in each group. To examine the independent association between physical activity levels and cognition, multivariable linear regression analyses were conducted.

Separate regressions were conducted for each of the cognitive measures and groups. Results are presented in terms of standardized (beta) regression coeffients and associated *p* values. All models were adjusted with demographic variables (age, sex, education), behavioral variables (smoking and alcohol consumption), metabolic parameters, and accelerometer wear time in the comparison group. Clinical factors (years since illness onset, duration of hospitalization, medication use, and PANSS) were additional covariates in patients with schizophrenia. All analyses were performed with IBM SPSS statistics 20 and a *p*-value less than 0.05 was considered as statistically significant in this study.

Results

Table 1 shows the descriptive statistics for participants with and without schizophrenia. It can be seen that patients with schizophrenia were aged 44 on average, with a slight majority of men. They were long-term patients averaging 23.8 years since diagnosis, and had been hospitalized for an average of 14.2 months. There was no significant difference between the patients with schizophrenia and the non-psychiatric comparison group in respect to age, sex, and BMI. However, patients with schizophrenia had poorer performance on the GPT and the COG test than the comparison group (all $p<.001$).

Participants with schizophrenia spent 158.6 mins/day in light physical activity, which was significantly fewer than the comparison group (496.0 mins/day). The time spent in MVPA was also less in the schizophrenia group (95.0 mins/day) than the comparison group (154.5 mins/day). The remaining time was spent in sedentary activities. These findings indicate that patients with schizophrenia were less active than the comparison group. Additionally, the schizophrenia group had greater waist circumference, higher TG and FG, and lower HDL-C than the non-psychiatric comparison group (Table 1).

Table 1

The univariate associations between physical activity levels and cognitive performance among patients with schizophrenia and the comparison group are shown in table 2. Significant associations were found between each level of physical activity and all cognitive measures among people with the schizophrenia, so spending more time in any intensity of physical activity was related to better performance on the GPT and COG test. However, no significant association was found between any level of physical activity and the cognitive measures in the comparison group.

Table 2

The fully adjusted linear regressions relating physical activity with cognitive performance in patients with schizophrenia are presented in Table 3. Light physical activity and MVPA were entered separately into regression models. Significant associations were found between the amount of activity at each level of physical activity and the two cognitive measures even after multivariable adjustments (Light: Beta=.224, *p*=.002 in COG, Beta=-.245, *p*=.001 in GPT; MVPA: Beta=.167, *p*=.036 in COG, Beta=-.254, *p*=.001 in GPT, respectively). The results suggest that participating in more light physical activity or MVPA was associated with better cognitive performance among patients with schizophrenia.

Table 3

In order to determine the relative contributions of physical activity levels to cognitive performance, light physical activity and MVPA were simultaneously entered as independent variables into regression models with multivariable adjustments (Table 4). Interestingly, the relationship was stronger for light activity than for MVPA in the schizophrenia group. Patients with schizophrenia who spent more time doing light activity had better performance on COG (Beta=.198, p=.020) and GPT (Beta=-.169, p=.048) tasks. However, MVPA was not associated with any cognitive measures in the presence of light physical activity and other covariates.

No significant association was found in multivariable regression models between levels of physical activity and cognitive performance in the comparison group. The fully adjusted models are shown in Table 4.

Table 4

Discussion

This study showed lower physical activity levels in patients with schizophrenia compared with a non-psychiatric comparison group. Within the schizophrenia group, higher levels of objectively measured light physical activity were associated with better performance on both cognitive tests independently of demographic factors such as age, sex and schooling, physiological risk factors, schizophrenia symptoms, duration of illness and hospitalization, or medication. The amount of MVPA was also associated with cognitive performance, but not after light activity and other covariates were included in the models.

The difference in physical activity between patients with schizophrenia and healthy controls is consistent with the findings from previous research (Yamamoto et al., 2011, Wichniak et al., 2011). However, Lindamer, et al. found no significant difference in physical activity measured with accelerometry between the two groups (Lindamer et al., 2008). One of the reasons might be the age difference of the sample between studies. Lindaner et al. (2008) included older adults (mean age 50.7±6.4), while the mean age of the participants in our study was younger. Moreover, participants in the earlier study were outpatients, whereas our study only included inpatients. The small sample size with valid accelerometry data in the earlier study (16 from people with schizophrenia and 6 from the comparison group) may have resulted in lack of statistical power to make the comparison. Hospitalisation and duration of illness might also contribute to the different findings of other studies (Wichniak et al., 2011).

It should be noted that the people with schizophrenia in this study were all inpatients, while the comparison group was free living. This makes it difficult to conclude whether differences are the result of the mental illness of the patient group, or whether differences are due to restrictions in activity in the hospital environment. The hospital which housed the patients has an indoor gym where patients can play table tennis, basketball, and snooker, and stationary bikes and treadmills are also available. Patients were also encouraged to attend 20-minute stretching and walking sessions in the morning and afternoon. However, with hundreds patients and limited facilities, patients may be restricted in the space and time available to engage in physical activity.

The current study also indicated that spending more time on light activity was associated with better cognitive performance on attention/concentration and processing speed in patients with schizophrenia. The relationship was stronger for light activity than for MVPA. A similar study using objective physical activity measures found significant associations of moderate physical activity with speed of processing and verbal working memory among 30 older schizophrenia participants; however, no significant association between other cognitive measures and physical activity was found (Leutwyler et al., 2014). The inconsistent findings may be due to difference in physical activity categorisation. Sedentary and light activities were combined into one level by Leutwyler et al. (2014). It is more appropriate to separate sedentary from light physical activity, since low activity is commonly found in patients with schizophrenia (Yamamoto et al., 2011), and the association of sedentary and light activities with cognitive performance might differ (Steinberg et al., 2015). We further tested the associations of sedentary and light activity with cognitive performance in the present study (results not shown). The findings confirm that light activity but not sedentary activity was associated with better cognitive performance.

Additionally, no significant association was found between any level of physical activity and either cognitive test in the non-psychiatric comparison group. This contrasts with substantial literature showing positive relationships (Angevaren et al., 2008, McMorris and Hale, 2012, Guiney and Machado, 2013, Verburgh et al., 2014). One of the reasons might be the small size of the comparison group. Moreover, individuals in the comparison group generally had good cognitive performance, leaving little scope for observing any effects of physical activity.

Physical activity interventions may be particularly appealing for individuals with mental illness, in hospital settings, since they are relatively safe, low cost, and easily integrated into daily schedules (Richardson et al., 2005). Studies have shown enhancement in composite cognitive test scores (Kimhy et al., 2015), hippocampal volume, short-term memory (Pajonk et al., 2010), working memory, and speed of processing (Oertel-Knöchel et al., 2014) in patients with schizophrenia after aerobic exercise training, although not all results have been positive (Scheewe et al., 2013, Falkai et al., 2013). However, previous research has mainly focused on the effects of MVPA. Promoting light physical activity might be more feasible than MVPA among patients with schizophrenia, since they spend much of the time in sedentary activities. This study has demonstrated that even light physical activity is associated with better cognitive performance in people with schizophrenia.

The current study provides evidence of positive associations between light physical activity and cognitive performance in patients with schizophrenia after taking multiple potential confounders into account. However, interpretation of the results is limited by the cross-sectional design, which is not able to determine causal relations. All the participants with schizophrenia were long-term psychiatric in-patients, and findings might not generalize to less severe out-patients. Moreover, this study only included two cognitive tests and did not collect information about menstrual status, which may impact cognitive performance and physical activity in female patients. Well-designed prospective cohort studies or randomized controlled trials are needed to establish whether light and moderate physical activity can improve cognitive function among patients with schizophrenia.

Conflict of interest

None

Ethical standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimental and with the Helsinki Declaration of 1975, as revised in 2008.

References

Angevaren, M., Aufdemkampe, G., Verhaar, H. J., Aleman, A. & Vanhees, L. 2008. Physical activity and enhanced fitness to improve cognitive function in older people without known cognitive impairment. *Cochrane Database of Systematic Reviews*, 16**,** CD005381.

Belsky, D. W., Caspi, A., Israel, S., Blumenthal, J. A., Poulton, R. & Moffitt, T. E. 2015. Cardiorespiratory fitness and cognitive function in midlife: Neuroprotection or neuroselection? *Annals of Neurology,* 77**,** 607-617.

Bezdicek, O., Nikolai, T., Hoskovcová, M., Štochl, J., Brožová, H., Dušek , P., Zárubová, K., Jech, R. & Růžička, E. 2014. Grooved pegboard predicates more of cognitive than motor involvement in Parkinson's disease. *Assessment,* 21**,** 723-730.

Cain, K. L., Conway, T. L., Adams, M. A., Husak, L. E. & Sallis, J. F. 2013. Comparison of older and newer generations of ActiGraph accelerometers with the normal filter and the low frequency extension. *International Journal of Behavioral Nutrition and Physical Activity,* 10**,** 51.

De Leon, J. & Diaz, F. J. 2005. A meta-analysis of worldwide studies demonstrates an association between schizophrenia and tobacco smoking behaviors. *Schizophrenia Research,* 76**,** 135-157.

De Moura, B. P., Marins, J. C., Franceschini Sdo, C., Reis, J. S. & Amorim, P. R. 2015. Aerobic exercise did not have compensatory effects on physical activity levels in type 2 diabetes patients. *Journal of Sports Sciences,* 33**,** 545-51.

Deijen, J., Orlebeke, J. & Rijsdijk, F. 1993. Effect of depression on psychomotor skills, eye movements and recognition-memory. *Journal of Affective Disorders,* 29**,** 33-40.

Falkai, P., Malchow, B., Wobrock, T., Gruber, O., Schmitt , A., Honer, W. G., Pajonk, F.-G., Sun, F. & Cannon, T. D. 2013. The effect of aerobic exercise on cortical architecture in patients with chronic schizo- phrenia: A randomized controlled MRI study. *European Archives of Psychiatry and Clinical Neuroscience,* 263**,** 469-473.

Freedson, P. S., Melanson, E. & Sirard, J. 1998. Calibration of the computer science and applications, Inc. accelerometer. *Medicine and Science in Sports and Exercise,* 30**,** 777-781.

García-Ortiz, L., Recio-Rodríguez, J. I., Martín-Cantera, C., Cabrejas-Sánchez, A., Gómez-Arranz, A., González-Viejo, N., Nicolás, E. I., Patino-Alonso, M. C. & Gómez-Marcos, M. A. 2010. Physical exercise, fitness and dietary pattern and their relationship with circadian blood pressure pattern, augmentation index and endothelial dysfunction biological markers: EVIDENT study protocol. *BMC Public Health,* 10**,** 233.

Gardner, D. M., Murphy, A. L., O'Donnell, H., Centorrino, F. & Baldessarini, R. J. 2010. International consensus study of antipsychotic dosing. *American Journal of Psychiatry,* 167**,** 686-693.

Glisky, E. L. 2007. Changes in cognitive function in human aging. *In:* RIDDLE, D. R. (ed.) *Brain aging: Models, methods, and mechanisms.* Boca Raton: CRC Press/Taylor & Francis.

Green, M. F. 1996. What are the functional consequences of neurocognitive deficits in schizophrenia? *American Journal of Psychiatry,* 153**,** 321-330.

Guiney, H. & Machado, L. 2013. Benefits of regular aerobic exercise for executive functioning in healthy populations. *Psychonomic Bulletin and Review,* 20**,** 73-86.

Hägg, S., Lindblom, Y., Mjörndal, T. & Adolfsson, R. 2006. High prevalence of the metabolic syndrome among a Swedish cohort of patients with schizophrenia. *International Clinical Psychopharmacology,* 21**,** 93-98.

Hansen, B. H., Kolle, E., Dyrstad, S. M., Holme, I. & Anderssen, S. A. 2012. Accelerometer-determined physical activity in adults and older people. *Medicine and Science in Sports and Exercise,* 44**,** 266-272.

Hausswolff- Juhlin, V., Bjartveit, M., Lindström, E. & Jones, P. 2009. Schizophrenia and physical health problems. *Acta Psychiatrica Scandinavica,* 119**,** 15-21.

Holley, J., Crone, D., Tyson, P. & Lovell, G. 2011. The effects of physical activity on psychological well- being for those with schizophrenia: A systematic review. *British Journal of Clinical Psychology,* 50**,** 84-105.

Kay, S. R., Flszbein, A. & Opfer, L. A. 1987. The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophrenia Bulletin,* 13**,** 261-276.

Kimhy, D., Vakhrusheva, J., Bartels, M. N., Armstrong, H. F., Ballon, J. S., Khan, S., Chang, R. W., Hansen, M. C., Ayanruoh, L. & Lister, A. 2015. The impact of aerobic exercise on brain-derived neurotrophic factor and neurocognition in individuals with schizophrenia: A single-blind, randomized clinical trial.

Schizophrenia Bulletin, 41**,** 859-868.

Kimhy, D., Vakhrusheva, J., Bartels, M. N., Armstrong, H. F., Ballon, J. S., Khan, S., Chang, R. W., Hansen, M. C., Ayanruoh, L. & Smith, E. E. 2014. Aerobic fitness and body mass index in individuals with schizophrenia: Implications for neurocognition and daily functioning. *Psychiatry Research,* 220**,** 784-791.

Klasik, A., Krysta, K., Krzystanek, M. & Skałacka, K. 2011. Impact of olanzapine on cognitive functions in patients with schizophrenia during an observation period of six months. *Psychiatria Danubina,* 23**,** S83-86.

Lee, H. J., Kim, L. & Suh, K. Y. 2003. Cognitive deterioration and changes of P300 during total sleep deprivation. *Psychiatry and Clinical Neurosciences,* 57**,** 490-496.

Leutwyler, H., Hubbard, E. M., Jeste, D. V., Miller, B. & Vinogradov, S. 2014. Associations of schizophrenia symptoms and neurocognition with physical activity in older adults with schizophrenia. *Biological Research for Nursing,* 16**,** 23-30.

Lindamer, L. A., Mckibbin, C., Norman, G. J., Jordan, L., Harrison, K., Abeyesinhe, S. & Patrick, K. 2008. Assessment of physical activity in middle-aged and older adults with schizophrenia. *Schizophrenia Research,* 104**,** 294-301.

Malchow, B., Reich-Erkelenz, D., Oertel-Knöchel, V., Keller, K., Hasan, A., Schmitt, A., Scheewe, T. W., Cahn, W., Kahn, R. S. & Falkai, P. 2013. The effects of physical exercise in schizophrenia and affective disorders. *European Archives of Psychiatry and Clinical Neuroscience,* 263**,** 451-467.

Marder, S. R., Essock, S. M., Miller, A. L., Buchanan, R. W., Casey, D. E., Davis, J. M., Kane, J. M., Lieberman, J. A., Schooler, N. R. & Covell, N. 2014. Physical health monitoring of patients with schizophrenia. *American Journal of Psychiatry,* 161**,** 1334-1349.

Matza, L. S., Buchanan, R., Purdon, S., Brewster-Jordan, J., Zhao, Y. & Revicki, D. A. 2006. Measuring changes in functional status among patients with schizophrenia: The link with cognitive impairment. *Schizophrenia Bulletin,* 32**,** 666-678.

Mcgrath, J., Saha, S., Chant, D. & Welham, J. 2008. Schizophrenia: A concise overview of incidence, prevalence, and mortality. *Epidemiologic Reviews,* 30**,** 67-76.

Mcmorris, T. & Hale, B. J. 2012. Differential effects of differing intensities of acute exercise on speed and accuracy of cognition: A meta-analytical investigation. *Brain and Cognition,* 80**,** 338-351.

National Institute of Mental Health 2009. Schizophrenia. National Institute of Mental Health: U.S. Depratment of Health and Human Services, National Institute of Mental Health.

Nuechterlein, K. H., Barch, D. M., Gold, J. M., Goldberg, T. E., Green, M. F. & Heaton, R. K. 2004. Identification of separable cognitive factors in schizophrenia. *Schizophrenia Research,* 72**,** 29-39.

Oertel-Knöchel, V., Mehler, P., Thiel, C., Steinbrecher, K., Malchow, B., Tesky, V., Ademmer, K., Prvulovic, D., Banzer, W., Zopf, Y., Schmitt, A. & Hänsel, F. 2014. Effects of aerobic exercise on cognitive performance and individual psychopathology in depressive and schizophrenia patients. *European Archives of Psychiatry and Clinical Neuroscience,* 264**,** 589-604.

Pajonk, F.-G., Wobrock, T., Gruber, O., Scherk, H., Berner, D., Kaizl, I., Kierer, A., Müller, S., Oest, M. & Meyer, T. 2010. Hippocampal plasticity in response to exercise in schizophrenia. *Archives of general psychiatry,* 67**,** 133-143.

Ramsay, C. E., Stewart, T. & Compton, M. T. 2012. Unemployment among patients with newly diagnosed first-episode psychosis: Prevalence and clinical correlates in a US sample. *Social Psychiatry and Psychiatric Epidemiology,* 47**,** 797-803.

Ratliff, J. C., Palmese, L. B., Reutenauer, E. L., Liskov, E., Grilo, C. M. & Tek, C. 2012. The effect of dietary and physical activity pattern on metabolic profile in individuals with schizophrenia: A cross-sectional study. *Comprehensive Rsychiatry,* 53**,** 1028-1033.

Rege, S. 2008. Antipsychotic induced weight gain in schizophrenia: mechanisms and management. *Australian and New Zealand Journal of Psychiatry,* 42**,** 369-381.

Richardson, C. R., Faulkner, G., Mcdevitt, J., Skrinar, G. S., Hutchinson, D. S. & Piette, J. D. 2005. Integrating physical activity into mental health services for persons with serious mental illness. *Psychiatric Services,* 56**,** 324-331.

Scheewe, T. W., Van Haren, N. E., Sarkisyan, G., Schnack, H. G., Brouwer, R. M., De Glint, M., Pol, H. E. H., Backx, F. J., Kahn, R. S. & Cahn, W. 2013. Exercise therapy, cardiorespiratory fitness and their effect on brain volumes: A randomised controlled trial in patients with schizophrenia and healthy controls. *European Neuropsychopharmacology,* 23**,** 675-685.

Schuhfried 2013. *Vienna Test System psychological assessment,* Moedling, Austria, Schuhfried GmbH.

Sharma, T. & Antonova, L. 2003. Cognitive function in schizophrenia: Deficits, functional consequences, and future treatment. *Psychiatric Clinics of North America,* 26**,** 25-40.

Steinberg, S. I., Sammel, M. D., Harel, B. T., Schembri, A., Policastro, C., Bogner, H. R., Negash, S. & Arnold, S. E. 2015. Exercise, sedentary pastimes, and cognitive performance in healthy older adults. *American Journal of Alzheimer's Disease and Other Dementias,* 30**,** 290-298.

Vancampfort, D., De Hert, M., Sweers, K., De Herdt, A., Detraux, J. & Probst, M. 2013.

Diabetes, physical activity participation and exercise capacity in patients with schizophrenia. *Psychiatry and Clinical Neurosciences,* 67**,** 451-456.

Vancampfort, D., Sweers, K., Probst, M., Maurissen, K., Knapen, J., Minguet, P. & De Hert, M. 2011. Association of the metabolic syndrome with physical activity performance in patients with schizophrenia. *Diabetes & Metabolism,* 37**,** 318-323.

Verburgh, L., Königs, M., Scherder, E. J. & Oosterlaan, J. 2014. Physical exercise and executive functions in preadolescent children, adolescents and young adults. *British Journal of Sports Medicine,* 48**,** 973-979.

Wang, Y. C., Magasi, S. R., Bohannon, R. W., Reuben, D. B., Mccreath, H. E., Bubela, D. J., Gershon, R. C. & Rymer, W. Z. 2011. Assessing dexterity function: a comparison of two alternatives for the NIH Toolbox. *Journal of Hand Therapy,* 24**,** 313- 321.

Wichniak, A., Skowerska, A., Chojnacka-Wojtowicz, J., Taflinski, T., Wierzbicka, A., Jernajczyk, W. & Jarema, M. 2011. Actigraphic monitoring of activity and rest in schizophrenic patients treated with olanzapine or risperidone. *Journal of Psychiatric Research,* 45**,** 1381-1386.

Wu, E. Q., Birnbaum, H. G., Shi, L., Ball, D. E., Kessler, R. C., Moulis, M. & Aggarwal, J. 2005. The economic burden of schizophrenia in the United States in 2002.

Journal of Clinical Psychiatry, 66**,** 1122-1129.

Yamamoto, H., Yamamoto, K., Miyaji, S., Yukawa-Inui, M., Hori, T., Tatematsu, S., Yutani, M., Tanaka, K. & Miyaoka, H. 2011. Daily physical activity in patients with schizophrenia. *Kitasato Medical Journal,* 41**,** 145-153.

Zschucke, E., Gaudlitz, K. & Ströhle, A. 2013. Exercise and physical activity in mental disorders: Clinical and experimental evidence. *Journal of Preventive Medicine and Public Health,* 46**,** S12-S21.

Table 1: Characteristics of individuals with and without schizophrenia

Percentages (%) or Means (sd)

	Schizophrenia	Comparison group	*P*
Demographic variables	N=199	N=60	
Age	44.0(9.9)	41.1(9.6)	.052
BMI	24.3(4.3)	23.9(3.7)	.520
Sex (Male) (%)	61.3	56.7	.520
Smoke (Never) (%)	57.3	81.7	.001
Alcohol (Never) (%)	83.4	85.0	.771
Schooling (years)	11.4(2.2)	14.9(3.5)	<.001
MetS [a] parameters			
Waist circumference	86.8(11.1)	81.0(10.5)	<.001
SBP [b]	112.6(13.2)	114.5(11.9)	.303
DBP [c]	71.2(8.8)	73.4(7.0)	.053
TG [d]	133.6(71.7)	106.8(64.3)	.010
HDL-C [e]	47.0(13.3)	54.5(16.1)	.001
FG [f]	100.2(28.8)	93.9(11.3)	.012
Physical activity level			
Light PA (mins/day)	158.6(71.4)	496.0(90.1)	<.001
MVPA (mins/day) [g]	95.0(54.2)	154.5(72.1)	<.001
Cognitive Function			
COG [h]	171.9(100.5)	392.4(134.3)	<.001
GPT (sec) [i]	137.7(45.6)	72.4(32.1)	<.001
PANSS [j]	63.0(20.0)		
PANSS_P	15.4(5.7)		
PANSS_N	16.9(6.2)		
PANSS_G	30.7(10.7)		
Medications (mg/d)			
Chlorpromazine equivalent doses	847.6(783.8)		
Lorazepam equivalent doses	1.1(1.3)		
Years since illness onset	23.8(6.5)		
Duration of hospitalization (month)	14.2(17.0)		

[a]: Metabolic syndrome; [b]: Systolic blood pressure; [c]: Diastolic blood pressure; [d]: Triglyceride; [e]: High-density lipoprotein cholesterol; [f]: Fasting glucose; [g]: Moderate-vigorous physical activity; [h]: Cognitrone; [i]: Grooved Pegboard Test; [j]: Positive and negative syndrome scale.

Table 2: Correlations of physical activity with cognitive performance in people with and without schizophrenia

	Light PA	MVPA	COG	GPT
Patients with schizophrenia				
Light PA	1			
MVPA	.551**	1		
COG	.217**	.300**	1	
GPT	-.287**	-.368**	-.412*	1
Comparison group				
Light PA	1			
MVPA	.153	1		
COG	.172	.125	1	
GPT	-.177	-.224	-.466**	1

MVPA: Moderate-vigorous physical activity; RT: Reaction time;

COG: Cognitrone;

GPT: Grooved Pegboard Test.

**Correlation is significant at the 0.01 level (2-tailed).

Patients with schizophrenia: n=199; Comparison group: n=60

Table 3: Multivariable linear regressions relating cognitive function with physical activity levels in participants with schizophrenia

Variables	Light physical activity						MVPA [g]					
	COG [i]			GPT [j]			COG [i]			GPT [j]		
	R^2	Beta	p	R^2	Beta	p	R^2	Beta	p	R^2	Beta	p
	29.4			28.2			27.4			27.8		
Age		-.264	<.001		.262	<.001		-.229	.003		.203	.009
Sex [a]		.036	.687		-.030	.745		.029	.756		-.013	.885
Smoke [a]		.047	.559		-.060	.457		.047	.569		-.045	.584
Alcohol [a]		-.025	.726		.129	.072		-.031	.666		.136	.059
Schooling		.047	.487		-.092	.184		.072	.295		-.122	.078
MetS parameters												
Waist		.022	.775		.016	.839		.021	.784		.016	.834
SBP [b]		-.227	.014		-.046	.619		-.201	.031		-.070	.446
DBP [c]		.223	.014		.074	.417		.224	.015		.065	.480
TG [d]		.051	.485		-.058	.433		.045	.551		-.048	.523
HDL-C [e]		-.021	.776		.011	.880		.010	.890		-.023	.763
FG [f]		.028	.694		.060	.401		-.007	.923		.099	.162
Physical Activity												
Light		.224	.002		-.245	.001						
MVPA [g]								.167	.036		-.254	.001
PANSS [h]												
PANSS-P		-.151	.068		.249	.003		-.117	.162		.205	.015
PANSS-N		-.316	.005		.181	.106		-.251	.028		.093	.409
PANSS-G		.140	.268		-.141	.271		.092	.470		-.085	.505
Medications												
Chlorpromazine equivalent doses		.154	.026		.094	.179		.142	.043		.104	.137
Lorazepam equivalent doses		-.092	.176		.003	.961		-.101	.144		.021	.766

Years since illness onset	.004	.952	-.012	.864	.017	.819	-.042	.565
Duration of hospitalization (month)	-.115	.098	.007	.922	-.183	.228	-.022	.750

[a]: Dummy variable; [b]: Systolic blood pressure; [c]: Diastolic blood pressure; [d]: Triglyceride; [e]: High-density lipoprotein cholesterol; [f:]: Fasting glucose; [g]: Moderate-vigorous physical activity; [h]: Positive and negative syndrome scale. [i]: Cognitrone; [j]: Grooved Pegboard Test.

Table 4: Multivariable linear regressions relating cognitive function with physical activity levels in participants with and without schizophrenia

Variables	Patients with schizophrenia						Comparison group					
	COG [i]			GPT [j]			COG [i]			GPT [j]		
	R^2	Beta	p	R^2	Beta	p	R^2	Beta	p	R^2	Beta	p
	29.6			29.4			55.8			56.3		
Age		-.250	<.001		.222	.004		-.187	.208		.275	.066
Sex [a]		.032	.727		.016	.861		.214	.165		.122	.423
Smoke [a]		.039	.628		-.039	.635		-.062	.696		-.203	.200
Alcohol [a]		-.026	.720		.131	.066		-.039	.755		.121	.330
Schooling		.052	.451		-.105	.130		.344	.019		-.514	.001
MetS parameters												
Waist		.022	.775		.016	.839		-.059	.705		.138	.375
SBP [b]		-.225	.015		-.050	.591		-.243	.146		-.281	.092
DBP [c]		.227	.013		.062	.491		.130	.345		-.079	.560
TG [d]		.049	.507		-.051	.487		-.100	.502		-.031	.836
HDL-C [e]		-.018	.813		.001	.986		.129	.393		.019	.898
FG [f]		.023	.746		.073	.302		-.317	.006		.178	.107
Physical Activity												
Light		.198	.020		-.169	.048		.034	.791		-.139	.275
MVPA [g]		.054	.551		-.158	.085		.124	.325		-.100	.425
PANSS [h]												
PANSS-P		-.144	.086		.227	.007						
PANSS-N		-.300	.009		.135	.238						
PANSS-G		.133	.296		-.120	.347						
Medications												
Chlorpromazine equivalent doses		.154	.027		.094	.178						
Lorazepam equivalent doses		-.096	.159		.016	.811						
Years since illness onset		.001	.985		-.029	.691						
Duration of		-.114	.101		.005	.947						

hospitalization (month)

[a]: Dummy variable; [b]: Systolic blood pressure; [c]: Diastolic blood pressure; [d]: Triglyceride; [e]: High-density lipoprotein cholesterol; [f]: Fasting glucose; [g]: Moderate-vigorous physical activity; [h]: Positive and negative syndrome scale. [i]: Cognitrone; [j]: Grooved Pegboard Test.