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Incongruent changes in heart rate variability and body weight after discontinuing aerobic exercise in patients with schizophrenia

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ABSTRACT

A bidirectional connection exists between obesity and altered heart rate variability (HRV). Schizophrenia has been associated with a high risk of obesity and decreased vagal modulation. Few studies have examined the link between obesity and HRV in patients with schizophrenia. The aim of this study was to investigate the effects of aerobic exercise on body weight and HRV, and if so, whether these effects could be sustained after discontinuation of exercise training. A total of 18 overweight patients with schizophrenia completed an 8-week moderate-intensity aerobic exercise program conducted twice weekly for 50 min. Body weight and heart rate variability were measured at baseline, week 8, and 4 weeks after discontinuation of exercise training. Compared with the control group (15 overweight patients with schizophrenia without exercise training), the exercise group had reduced 2.3 kg at week 8. Furthermore, the exercise program increased the low frequency, high frequency, and low frequency plus high frequency of HRV. However, after discontinuation of the exercise program for 4 weeks, the changes in body weight and the HRV parameters diverged. All of the HRV parameters returned to their baseline values, but no change was seen in the reduced body weight. This suggests that HRV analysis is a more sensitive tool to detect health conditions in patients with schizophrenia. Although exercise is an easy and effective way to prevent and improve health problems, mental health providers might have underestimated the benefits of exercise in daily clinical practice. A regular exercise program should be considered as an essential part of treatment strategies for patients with schizophrenia.

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1. Introduction

Obesity is a chronic, serious, and complex medical condition. It affects not only physical and psychological conditions but also social dimensions in all ages and socioeconomic groups. A large body of evidence suggests that overweight and obesity confer risks of several medical illnesses such as type 2 diabetes (Chan et al., 1994), hypertension (DeMarco et al., 2014), stroke (Suk et al., 2003), and certain forms of cancers (Ligibel et al., 2014). Moreover, among the components of metabolic syndrome, obesity is the major driving force that leads to cardiovascular diseases (CVD) (Kahn et al., 2005). In this regard, obesity research that translates scientific discoveries into positive health outcomes remains an international priority.

Autonomic imbalance is characterized by hyperactive sympathetic and hypoactive parasympathetic systems (Thayer et al., 2010). It serves as the final common pathway to CVD. Evidence suggests that patients with schizophrenia have high rates of obesity and CVD mortality (Hennekens et al., 2005), and their life expectancy is 20 years less than that of the general population (Chang et al., 2011). Indeed, CVD stands as a major precipitating factor to a high rate of sudden unexpected death in schizophrenia (Koponen et al., 2008). Until now, several studies have examined the link between schizophrenia and autonomic imbalance, pointing out a disease-associated decrease in vagal modulation (Bar et al., 2007; Boettger et al., 2006; Toichi et al., 1999).

Effective exercise is essential to healthy weight loss, and regular exercise can improve heart rate variability (HRV) and vagal modulation (Routledge et al., 2010; Zoppini et al., 2007). An important fact is that exercise may also benefit individuals with mental illness. A review article by Stathopoulou et al. (2006) highlights exercise as a powerful intervention for clinical depression. Accumulating evidence supports that regular exercise programs improve the physical and psychiatric conditions of patients with schizophrenia (Gorczynski and Faulkner, 2010). In recent decades, measurement of HRV as a noninvasive tool has been extensively used to assess the schizophrenia-inherent autonomic

Abbreviations: HRV, heart rate variability; CVD, cardiovascular diseases; BMI, body mass index; ECG, electrocardiography; VLF, very low frequency; LF, low frequency; HF, high frequency; TP, total power; LF/HF, the ratio of LF to HF; MRR, mean RR intervals; MNN, the mean of all normal-to-normal interbeat intervals; VAR, the variance of the RR intervals.

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dysregulation (Bar et al., 2010). As obesity is associated with altered HRV (Piestrzeniewicz et al., 2008) and weight loss improves HRV (Karason et al., 1999; Poirier et al., 2003), it would be interesting to investigate the link between obesity and HRV in schizophrenia.

However, little attention has been paid to the effects of exercise on weight loss and HRV in patients with schizophrenia. Previous studies reported that mental health providers might have neglected exercise intervention as an effective treatment for people with mental illness (Callaghan, 2004), despite its non-pharmacological and cost-effective properties. This issue is particularly important for patients with schizophrenia, as the estimated incidence rate of overweight or obesity in this population is 40–60% (Catapano and Castle, 2004; Citrome and Vreeland, 2008; Coodin, 2001). A pilot study recruited 6 patients with schizophrenia and reported that exercise could increase fitness levels, exercise tolerance, energy levels, and upper body and hand grip strength levels (Fogarty et al., 2004). In this regard, we investigated whether these findings could be replicated by using a larger sample of patients with schizophrenia. The primary outcome of this study was an assessment the effects of 8-week aerobic exercise on body weight and HRV parameters in overweight people with schizophrenia. The secondary outcome was determining whether the exercise-associated weight loss or HRV changes could be maintained after discontinuation of the exercise programs.

2. Material and methods

2.1. Participants

The experimental protocol was approved by the Institutional Review Board for the Protection of Human Subjects at the Tri-Service General Hospital, National Defense Medical Center in Taipei, Taiwan (TSGHIRB No: BT101-03). Between 2012 and 2013, psychiatric outpatients who were undergoing rehabilitation in the Beitou Branch of Tri-Service General Hospital were eligible to participate. The participants were required to be fully capable of comprehending the study's purpose, procedure, treatment, risks and possible benefits, alternative treatment, and their right to refuse to participate in this study. All the participants provided written informed consent and were free to withdraw their participation at any time. The inclusion criteria were as follows: (1) age between 20 and 60 years; (2) meeting the diagnostic criteria for schizophrenia according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (26); (3) a body mass index (BMI) exceeding 25 kg/m^2; (4) receiving day-care service support for >6 months; and (5) motivated to join the study group.

Individuals were excluded if they had a systolic blood pressure of >180 mm Hg or a diastolic blood pressure of >110 mm Hg; if they had a history of a significant medical disorder such as heart disease, diabetes, CVD, liver or renal disease, endocrinopathies, neurological disorders, or cancer; if they met the criteria for substance-related disorders, including those from nicotine and alcohol abuse; if they were involved in a special dietary or special physical exercise program for weight reduction; and if they lost >5% of body weight within 3 months. Betel nut chewing, cigarette smoking, and alcohol drinking were not allowed during the study.

A series of examinations were performed, including complete physical examination, routine biochemical panel, complete blood count, urinary test, stool study, chest radiography, and electrocardiography (ECG). The height (cm) and weight (kg) of each participant were measured by using a standard balance beam scale. The medical charts were systematically reviewed in order to confirm that all participants met the above-mentioned operational criteria.

All patients in the day-care center were screed for the study participation ($n = 60$), and 33 met all eligibility criteria. The eligible participants were assigned randomly into an exercise group ($n = 18$) and a control group ($n = 15$) consisting of sex-, age- and baseline BMI-matched subjects. All the participants were assessed at three time points as follows: at baseline, week 8 (the end of the 8-week aerobic exercise program), and week 12 (1-month follow-up after the program).

A dance-based aerobic exercise program was conducted with an intensity between 60% and 79% of maximal heart rate. The moderate-intensity exercise program was group-based and performed twice a week for 8 weeks. An exercise session comprised 50 min aerobic dance, preceded by a 10-min warm-up and followed by a 10-min cool-down. The warm-up was to aid in the transition from rest to exercise, and the cool-down was to help the body return to near resting levels. The sessions were conducted by a certified physical fitness instructor in the multi-purpose room in the day-care center. Participants in the control group were asked to continue with their usual lives and did not receive any of these exercises. All the psychotropic drugs were unchanged throughout course of the study.

2.2. Measurements of heart rate variability

Detailed procedures of the analysis of HRV have been reported previously and are only briefly summarized here (Kuo et al., 1999; Liu et al., 2003). Prior to the measurements, the participants were instructed to refrain from caffeine consumption for 24 h and from exercising and heavy eating for at least 8 h. All the participants had a usual breakfast on the day of the study to ensure standardization of the ECG recordings. After the participants had rested for 15 min in a quiet, air-conditioned room, ECG recording for the analysis of beat-to-beat HRV was started under standardized conditions. The subjects were asked to relax, breathe naturally, and move as little as possible. Experimental procedures were performed between 0900 and 1100 h. The HRV Monitor (V1.89) was manufactured by Yang Ying Inc. (Taipei, Taiwan).

A 288-s signal sequence of the telemetrically transmitted lead I ECG was recorded. As the HRV indexes are greatly influenced by breathing frequency (Hayano et al., 1994), we ensured that the subjects were breathing at a normal respiratory rate of 12–15 breaths/min by recording the respiratory movements to avoid respiratory interference during the HRV measurement (Hayano et al., 1991). The raw ECG signals were amplified with a gain of 1000 and were band-pass filtered (0.68–16 Hz). Signals were then recorded with an 8-bit analog-to-digital converter at a sampling rate of 512 Hz. The digitized ECG signals were analyzed online and simultaneously stored on removable hard disks for offline verification. Signal acquisition, and data storage and processing were performed via a general-purpose personal computer. Our computer algorithm identified each QRS complex and rejected each ventricular premature complex or noise according to its likelihood in a standard QRS template. Stationary RR values were resampled and interpolated at a rate of 7.11 Hz to produce continuity in the time domain.

The frequency-domain analysis was performed by a nonparametric method of fast Fourier transformation. The direct current component was deleted, and a Hamming window was used to attenuate the leakage effect. For each time segment (288 s; 2048 data points), our algorithm estimated the power spectrum density based on the Fourier transformation. The resulting power spectrum was corrected for attenuation due to the sampling and Hamming window. The power spectrum was subsequently quantified into standard frequency-domain measurements, including very low frequency (VLF; <0.04 Hz), low frequency (LF; 0.04–0.15 Hz), HF (0.15–0.40 Hz), total power (TP), the ratio of LF to HF (LF/HF), and LF plus HF. The spectral components of HRV were analyzed as absolute units through the logarithm transformed data (ln ms^2). The changes in LF and HF power were also analyzed in units normalized to TP (nu). The time-domain parameters were the mean RR intervals (MRR), the mean of all normal-to-normal interbeat intervals (MNN), and the variance of the RR intervals (VAR). The time-domain parameters were measured in milliseconds (ms). All HRV analyses were performed by a trained research nurse blinded to the protocol. Individuals who showed no predominantly regular sinus rhythm or those who had sustained atrial arrhythmias, such as atrial fibrillation or >5% ectopic complexes, were excluded from further analysis.

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