

Exploring effects of exercise on the functional connectome in patients with schizophrenia [Abstract]

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neural substrate of schizophrenia, is due to interactions with epigenetic changes that reflect environmental influence. By demonstrating the moderating role of schizotypy on the association between BDNF methylation and changes in the DMN-FPN network FC, this study provides pivotal neurobiological data substantiating the stress-vulnerability model of developing schizophrenia.

Conflict of interest

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Altered functional connectivity patterns in schizophrenia – a possible link between psychopathology and decreased physical fitness?

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Introduction: Obesity, weight gain and decreased physical fitness often co-occur with psychiatric disorders, especially schizophrenia. These comorbidities constitute important predisposing factors for cardiovascular disorders and lower life expectancies of patients. Dopaminergic neurotransmission might play a major role in the context of weight gain in schizophrenia [1], as it currently poses the main target of antipsychotic medication, which is known to cause an increase of appetite. Moreover, it mediates reward processes, regulates energy expenditure and is further linked to weight gain of otherwise healthy obese patients [2]. **Objectives:** We hypothesize that alterations of the reward system lead to weight gain and lower physical fitness in patients compared to a group of healthy participants, indexed by less muscular strength, more body fat and lower aerobic capacity (VO₂max). With this study, we aim to establish a link between psychopathology and physical fitness to contribute to the development of alternative treatment options.

Methods: We will investigate 50 schizophrenic patients and 50 healthy volunteers, matched by gender and age. We have established a neuroimaging battery of two standardized fMRI tasks and a resting state measurement. We use a monetary incentive delay task [3] to probe reward anticipation as well as a delay-discounting-paradigm [4] to test orbitofrontal evaluation strategies. Anthropometric measures further provide us with information about body fat, muscular strength and maximal oxygen capacity in order to characterize the physical fitness status of the participants.

Psychopathology is assessed by the Positive and Negative Syndrome Scale, the Calgary Depression Scale for Schizophrenia as well as by self-rating scales, such as the Chapman Scale of Physical and Social Anhedonia and the WHO Disability Assessment Schedule. Furthermore, we record diet, eating behavior and physical activity by using standardized questionnaires.

Results: Up to now, we have measured 35 patients (age = 40.6 ± 14.42) as well as 30 gender and age- matched healthy volunteers (age = 39.8 ± 15.25). First tendencies reveal no differences as to body fat between the two groups. Physical fitness is, however, significantly lower in the patient- (VO₂max = 29.7 ± 16.4) compared to the healthy subject group (VO₂max = 41.6 ± 9.7 , p-value = 0.012). A principal component analysis (PCA) of the fitness test variables revealed two factors, we interpreted as 'physical fitness' and 'physical condition', that were used for further analyses. The resting state analysis yielded altered seed-to-voxel functional connectivity (FC) between reward areas and the rest of the brain in the patient group compared to healthy individuals. Decreased FC could be linked to psychopathology, while increased FC positively correlated with the physical fitness variable of the PCA.

Conclusion: Our resting state analysis indicates that alterations in reward mediating brain areas might constitute the link between weight gain and decreased physical fitness in schizophrenia. Although there are other factors contributing to weight gain, the reward system regulates behavioural responses and might thus represent a target for behavioural interventions in the future, such as fitness and lifestyle therapies. Our follow-up analysis of the two fMRI reward tasks might give further insights.

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Exploring effects of exercise on the functional connectome in patients with schizophrenia

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Introduction: Schizophrenia is accompanied by widespread alterations in static functional connectivity associated with symptom severity and cognitive deficits. Improvements in aerobic fitness have been demonstrated to ameliorate symptomatology and cognition in people with schizophrenia, but the intermediary role of macroscale connectivity patterns remains unknown. Particularly, even the general association between aerobic fitness and global functional connectivity patterns in patients with schizophrenia has not been studied to date. Consequently, we do not know to which particular functional connections aerobic fitness is generally linked in schizophrenia and thus cannot derive hypotheses on behaviorally relevant, regional connectivity adaptations induced by aerobic exercise interventions.

Objective: Therefore, we aim to explore the relation between aerobic fitness and the functional connectome in individuals with schizophrenia. Further, we investigate clinical and cognitive relevance of the identified fitness-connectivity links.

Methods: Patients diagnosed with schizophrenia in accordance to the DSM IV were included in this cross-sectional resting-state fMRI analysis. A stepwise lactate threshold test was utilized to measure aerobic fitness. The functional connectome was examined using two global approaches: Focusing on the functional organization of the human brain, we computed functional connectivity within and between core intrinsic connectivity networks. Considering the anatomical perspective, we assessed functional connectivity between different regions of interest. Multilevel Bayesian partial correlations between aerobic fitness and the functional connectome as well as between static functional connectivity patterns and clinical and cognitive outcome were performed. Preliminary causal inferences were enabled based on mediation analyses.

Results: Aerobic fitness was linked to static functional connectivity within and between several prominent intrinsic connectivity networks such as the default-mode, the fronto-parietal or the basal ganglia network. Additionally, aerobic fitness was associated with functional connectivity between multiple anatomical regions of interest across the whole brain, especially within the cerebellum. With regard to clinical relevance of those interrelations, static functional connectivity between the subcortical nuclei and the cerebellum as well as between temporal seeds mediated the attenuating relation between aerobic fitness and total symptom severity. Functional connections between cerebellar seeds affected the positive link between aerobic fitness and global cognition, while the functional interplay between central and limbic seeds drove the beneficial association between aerobic fitness and emotion recognition.

Conclusion: The current study provides first insights into the interactions between aerobic fitness, the functional connectome and clinical and cognitive outcome in people with schizophrenia, but causal interpretations are preliminary. Further interventional aerobic exercise studies are needed to replicate the current findings and to enable conclusive causal inferences. Future aerobic exercise studies can build upon our findings and examine if adaptations of the functional connections that have been linked to aerobic fitness in the current study also mediate positive effects of exercise interventions on psychopathology and cognition in individuals with schizophrenia. Consequently, the present investigation represents the first step to identify functional brain mechanisms that drive exercise effects in psychiatric populations.

Conflict of interest

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Psychometric instruments for the assessment of creativity in patients with bipolar disorder – a systematic review

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Introduction: Bipolar disorder (BD) is a serious mood disorder characterized by the occurrence of episodes of both mania and major depression [1]. This disorder has long been associated with the concept of creativity being associated with manic phases. Essentially, studying the biographies of well-known artists with BD, time periods of productivity correlate with periods of mania. [2,3].

The goal of our literature review was to focus on assessment tools that can objectively measure creativity in bipolar patients in order to be able to confirm or deny the hypothesis that mania aids creativity.

Methods: A systematic review of the available literature was performed using the PubMed and ClinicalTrials.gov databases (April 2012-2022). We used the following search terms: "bipolar disorder", AND "creativity" AND "scales". Studies were included if patients were diagnosed with BD or as having a low/high risk for BD, and used scales to assess creativity. Studies included > 20 participants. After the screening and selection processes, 6 studies met our inclusion criteria.

Results: 1.The Barron's Welsh Art Scale (BWAS), a nonverbal measure of creativity, was used in two studies. Participants are asked to draw pictures and these are subsequently evaluated using scales based on Freudian primary processes (symbolization, condensation, and substitution) and secondary processes (logic, rational thinking). Study 1 (BD): mania (n=41 patients), depressive (n=25). Study 2, low vs. high risk for BD (n=30). The BWAS identified creative talent regardless of intelligence, personal strength, gender, or background.

2. One study assessed inspiration (considered to foster creativity) by utilizing the Scale of External and Internal Sources of Inspiration-EISI (n=708 students). The total, auto, and prosocial EISI subscales of the EISI were independently associated with clinically established risk of BD and with current symptoms of mania.

3. The Voluntarily Engaged Set of Statistically Unlikely Activities (WASSUP) is a measure of the tendency to set implausibly high goals. Study 1 (BD, n=22): WASSUP scores were significantly correlated with creativity. Study 2 (risk BD, n=221 undergraduates: mania risk associated with greater ambition.

4. The Carson Creative Achievement Questionnaire (CAQ) (n=1 study, risk; n=1 study, BD) captures creative achievement throughout life. Creative achievement not correlated with mood changes but related with mania risk.

5. The Adjectives Checklist Creative Personality Scale (ACL-CPS), a self-assessment of creative personality characteristics (n=1 study, BD risk). ACL-CPS scores associated with hypomanic traits (n=297).

6. The Compound Remote Associates (CRA) scale (n=1 study, BD risk), developed to measure creative insight into problem solving. CRA scores not associated with mania risk (n=297)

Conclusions: Different scales used for the purpose of confirming the role of bipolar disorder, especially the manic phase, in creativity have shown potential usefulness in a small number of studies, revealing a potential objective relationship between BD and creativity particularly in its manic phase. It would make sense to conduct a longitudinal study comparing the utility of these scales in current artists known to suffer creative and non-creative periods in their careers.

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At clinical high risk for psychosis – diagnostic challenge: a case study

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Introduction: Early detection and treatment of psychosis already in the prodromal stage have become widely accepted goals in psychiatry during the last two decades. Patients at clinical high risk (CHR) for psychosis include individuals at ultra-high risk for psychosis and/or those with primary symptoms and often present with non-psychotic clinical symptoms and disorders such as anxiety and depression at baseline, as well as psychosocial impairment, which seem to persist even in patients without transition to psychosis.

The study aims to present a patient at clinical high-risk for psychosis with various concomitant clinical presentations and symptoms.

Case presentation: An adolescent male, age 15, was admitted to our department with following symptoms: obsessions and excessive compulsions, ritualized eating followed by severe loss of appetite and progressive weight loss (BMI 13.8), complete loss of interest and pleasure, feeling of emptiness, high level of anxiety, social withdrawal up to complete isolation, loss of initiative, passivity, poor and quiet speech, insomnia, which all resulted in severe psychosocial impairment and the dependence on other people. During hospitalization, negative symptoms were observed (affective flattening, alogia, anhedonia, avolition) and poor rapport. None of the positive symptoms have been reported nor suspected in behavior but could not be ruled out. Data collected regarding family background were poor but could indicate possible Bipolar disorder in the patient's late mother. Premorbid characteristics pointed to traits of Anxious personality disorder. Clinical presentation met the criteria for Obsessive Compulsive Disorder, Major Depressive disorder and Attenuated Psychosis Syndrome, supported by psychological and clinical assessment (The Patient Health Questionnaire-9, Children's Global Assessment Scale, Comprehensive Assessment of At-Risk Mental States, Positive and Negative Syndrome Scale). At some point during treatment, clinical presentation also met the criteria for Avoidant Restrictive Food Intake Disorder. Somatic examinations and laboratory analysis did not show any abnormalities except malnutrition and hypotrophia. In addition, magnetic resonance imaging did not show any abnormalities. Psychopharmacological treatment (sertraline, risperidone and mirtazapine, switched to clomipramine and olanzapine) resulted in reduction of obsessive-compulsive symptoms, significantly reduced level of anxiety and led to sleep improvement, better appetite and weight gain (BMI 16.3). Psychosocial functioning improved to the point that the patient could take care of himself, but negative symptoms persisted.

Conclusion: Patients at clinical high risk (CHR) for psychosis often present with