The results indicate AE is effective in enhancing cognitive exercising. These promising results suggest that IT may be effective in enhancing cognition, and functional outcome in schizophrenia and consider the potential mechanisms of action.

### 11.1 EFFECT OF INTERVAL TRAINING ON METABOLIC RISK FACTORS IN OVERWEIGHT INDIVIDUALS WITH PSYCHOSIS: A RANDOMIZED CONTROLLED TRIAL

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**Background:** Among adults with psychotic disorders, negative symptoms as unhealthy lifestyle habits contribute to a high prevalence of metabolic syndrome and obesity. Lifestyle interventions, mainly physical activity (PA), has emerged as an essential component. Furthermore, interval training (IT) was found to be efficacious in other populations but poorly studied among people with psychosis. The objective was to determine the effects of a 6-month IT program on metabolic, anthropometric, and psychiatric/functional outcomes.

**Methods:** Randomized controlled trial comparing the effects of a bi-weekly 30 minutes supervised IT program to a waiting list of overweight individuals with psychosis. Body composition and metabolic risk factors (blood pressure, insulin resistance, lipid profile) were measured at baseline and every 3 months. The groups were compared on an intent to treat basis with repeated-measures mixed linear models with the restricted maximum likelihood method of estimation.

**Results:** Sixty-seven individuals (28 control: waiting list; 39 IT intervention) with psychosis (60.6% men, mean age: 31.0 ± 7.2 years old; BMI: 32.0 ± 6.1 kg/m², waist circumference: 107.7 ± 13.3 cm) were included in the study, and 67.2% completed the study. Attendance for the IT sessions was 61.8% and the dropout rate was 32%. IT was associated with significant improvements in waist circumference (-2.72 cm, SE = 1.34; p = 0.04), negative symptoms (-2.93, SE = 1.34; p = 0.03), social (SOFAS) (+5.23, SE = 2.39; p = 0.03) and global functioning (+7.34, SE = 2.05; p < 0.001). The effects of exercise in the first-episode psychosis (FEP) sub-group were similar to those of the entire cohort.

**Discussion:** These promising results suggest that IT may be used as a treatment strategy for the management of metabolic complications and possibly improve social functioning in obese individuals with psychotic disorders. Further studies are needed to understand if IT prevent weight gain and metabolic complications if used before these comorbidities emerge and to understand factors associated with the persistence of exercising.

### 11.2 THE IMPACT OF AEROBIC EXERCISE ON COGNITIVE FUNCTIONING AND BIOMARKERS OF COGNITIVE CHANGE IN INDIVIDUALS WITH SCHIZOPHRENIA

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**Background:** Individuals with schizophrenia (SZ) display substantial cognitive deficits across multiple domains. These deficits have been identified as major determinants of poor functioning and disability, representing a serious public health concern and an important target for interventions. At present, available treatments offer only minimal to limited benefits to ameliorate these deficits. Thus, there remains an urgent need to identify novel treatments for cognitive deficits in people with SZ. Emerging evidence from studies of animals, clinical and non-clinical populations suggest that Aerobic Exercise (AE) is efficacious in improving cognition via up-regulation of Brain-Derived Neurotrophic Factor (BDNF). Yet, the impact of AE on cognition and daily-functioning, and the role of BDNF, have not been investigated in schizophrenia. Additionally, limited information is available on the putative link between inflammation markers to cognitive functioning.

**Methods:** Employing a single-blind RCT design, 33 individuals with schizophrenia were randomized to receive “treatment as usual” (n=17; TAU) or attend a 12-week, 3 times-per-week, 60-minutes AE program (n=16) utilizing active-play video-games (Xbox-360 Kinect) and traditional AE equipment.

**Results:** At baseline, cognitive functioning was associated with serum BDNF (r=.51, p=.01), along with TNF-alpha (r=-.38, p=.03), IL-12 (r=-.36, p=.04) and IL-6 (r=-.33, p=.06). Twenty-six participants completed the study (79%). Following the intervention, the AE participants improved their cognitive functioning (MCCB) by 15.1% (vs. -2.0% in the TAU group; p=.03). Hierarchical multiple-regression analyses indicated changes in AF and serum BDNF predicted 25.4% and 14.6% of the cognitive improvement, respectively. Additionally, changes in aerobic fitness (VO2peak ml/kg/min) correlated with informant-reported improvements in work-related daily-functioning skills (SLOF; r=.51, p=.01). Fidelity with target training intensity, was correlated with cognitive improvement (r=.70, p=.02).

**Discussion:** The results indicate AE is effective in enhancing cognitive and daily functioning skills in people with schizophrenia and provide support for the impact of AE-related BDNF up-regulation on cognition. Additional studies are needed to establish the link between inflammation markers and cognitive functioning and the potential impact of AE on this putative pathway. Overall, low aerobic fitness represents a modifiable risk-factor for cognitive dysfunction in schizophrenia for which AE training offer a relatively safe, non-stigmatizing, and side-effect-free intervention.

### 11.3 CLINICAL AND NEUROBIOLOGICAL EFFECTS OF A CONTINUOUS AEROBIC ENDURANCE TRAINING IN MULTI-EPOISODE SCHIZOPHRENIA PATIENTS

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**Concurrent Symposia**

**Abstracts for the Sixth Biennial SIRS Conference**
11.4 AEROBIC EXERCISE ENHANCES COGNITIVE TRAINING EFFECTS IN FIRST EPISODE SCHIZOPHRENIA: COGNITIVE AND FUNCTIONAL GAINS AND PROMISING BIOLOGICAL MECHANISMS OF ACTION

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Background: The search for treatments to remediate cognitive deficits and their functional outcome consequences remains a critical frontier in schizophrenia. Cognitive training and aerobic exercise both show promising moderate impact on cognition and everyday functioning. Aerobic exercise is hypothesized to increase brain-derived neurotrophic factor (BDNF) and thereby stimulate neurogenesis and synaptic plasticity, leading to increased learning capacity. Systematic cognitive training should take advantage of increased learning capacity and be more effective when combined with aerobic exercise.

Methods: In a recently completed randomized controlled trial, we examined the impact of a 6-month program of Cognitive Training & Exercise (CT&E) compared to Cognitive Training alone (CT) in 47 first-episode schizophrenia outpatients. All participants were provided the same Positive and Negative Syndrome Scale computerized cognitive training, four hours/week, using BrainHQ and SocialVille programs. The CT&E group also participated in total body circuit training exercises to enhance aerobic conditioning. The exercise intensity was in the 60–80% of aerobic capacity range, combining clinical and home-based exercise for a target of 150 minutes per week.

Results: Mixed model analyses demonstrate that the MATRICS Consensus Cognitive Battery Overall Composite improves significantly more by 3 months with CT&E than with CT alone (6.6 vs. 2.2 T-score points, p<.02). Work/school functioning improves substantially more with CT&E than with CT alone by 6 months (p<.001). BDNF is a promising mechanism of action, improving even after 2 weeks and predicting the amount of cognitive gain at 3 months. The magnitude of cognitive gain by 3 months predicts the amount of work/school functioning improvement at 6 months, suggesting a cascade of effects. Analyses by Dr. McEwen show differential increases in cortical thickness in the left dorsal lateral prefrontal gyrus (p=.02) and right superior frontal gyrus (p=.02) over 6 months and increased functional connectivity in the central executive network (p=.04) with CT&E compared to CT alone and correlations of these increases with cognitive and functional outcome gains.

Discussion: We conclude that aerobic exercise significantly enhances the impact of cognitive training on cognition, functional outcome, and frontal cortical thickness in first-episode schizophrenia and that BDNF is a promising mechanism of action for these effects.

12. SYNAPTIC DYSFUNCTION IN SCHIZOPHRENIA: EXPLORATION OF NOVEL HYPOTHESES AND PROMISING NEW LEADS

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Overall Abstract: Accumulating evidence suggests that bioenergetic function is impaired in the brain in schizophrenia. In normal brain, glucose is metabolized to lactate and pyruvate, which are monocarboxylate intermediates that serve as the primary energy source for neurons. Working memory and other cognitive domains are dependent on the shuttling of lactate from astrocytes to neurons. Defects in this complex pathway may underlie cognitive dysfunction in schizophrenia. The focus of this symposium is to present evidence of such defects, and to identify substrates that may be targeted for the development of new treatment strategies. Dr. Laura Rowland (University of Maryland, Baltimore, Maryland, USA) will present evidence of bioenergetic dysfunction in living subjects with schizophrenia. Increased levels of lactate (P<0.05) were present in the ACC in schizophrenia (n=27) compared to controls (n=29). Higher lactate levels were associated with lower scores on the MATRICS Consensus Cognitive Battery. These data establish a direct link between cognition and bioenergetic function in vivo in schizophrenia. Dr. Robert McCullumsmith (University of Cincinnati, Cincinnati, Ohio, USA) will present evidence of alterations in the lactate shuttle and glycolytic enzymes in postmortem samples from schizophrenia (n=20) and control subjects (n=20). Cell-subtype specific changes (P<0.05) in transcripts included increased levels of the lactate transporter MCT4, decreased levels of the glycolytic enzymes PFK1 and hexokinase, and decreased levels of the glucose transporters Glut1 and Glut3. These data suggest attenuated glycolysis in pyramidal neurons, with a shift towards pathways that boost protection from oxidative stress.