The effect of high-intensity interval training on executive function in adolescents hospitalized for a mental illness.

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ABSTRACT

Introduction: Impaired inhibitory control, one of the core executive functions, is common among individuals with mental illness. However, inhibitory control is essential for successful treatment and recovery. Inhibitory control is extremely vulnerable to developmental disruption during adolescence, a time when mental illness is first diagnosed. An acute bout of exercise has been shown to improve inhibitory control in healthy adolescents, however, to our knowledge there are no studies evaluating this effect in adolescents with mental illness.

Purpose: The primary goal of this project was to examine the effect of an acute bout of high-intensity interval training on inhibitory control immediately, and 30 minutes following exercise in adolescents hospitalized for mental illness. The secondary goal was to assess the feasibility of using this type of exercise as an adjunct to current treatment.

Methods: Participants were recruited through the inpatient mental health unit at the Children's Hospital of Eastern Ontario. They performed exercise and control conditions in a randomized, counterbalanced manner. The Colour-Word Stroop Task was assessed pre, post, and 30-minutes-post on both days. The exercise condition included a 12 minute HIIT circuit, consisting of body weight exercises performed in a 1:1 work to rest ratio. The control condition involved reading magazines. Repeated-measures ANOVA evaluated changes in Interference Cost, the reaction time cost of responding to trials where the ink and colour do not match, and overall accuracy. Feasibility was assessed through recruitment and completion rates, as well as changes in affect and acceptability of the high-intensity interval training.

Results: There was a significant interaction between condition and time for the Interference Cost measure, $F(1.6,43.3)=13.6$, $p<.0001$, $\eta^2=.34$. Interference Cost was similar for both conditions at baseline ($M_{diff} = 12.4 \pm 11.11$, $p=.28$). Interference Cost was significantly reduced immediately (M_{diff} = 78.8±14.91, $p<.001$) and 30-minutes post-exercise (M_{diff} = 59.6±15.14, $p=.001$) compared to control. Response accuracy did not differ by time, $F(2,54)=.14$, $p<=.87$, $\eta^2=.01$ nor condition, $F(1,27)=2.25$, $p=.15$, $\eta^2=.08$. After exercise, participants increased positive affect (mean difference = 4.3±8.09, $p=.009$) and were willing to perform the exercise before therapy sessions (rating = 6.4±2.75 out of 10).

Conclusion: These findings suggest that high-intensity interval training could be used to improve inhibitory control in adolescents with mental illness, which has the potential to enhance the efficacy of their treatment. Future research should determine the impact of individual factors, such as diagnosis, medication, age of illness onset, length of hospitalization, and treatment history, on inhibitory control improvement after exercise.

RATIONALE

1.1 Demand for Mental Health Treatment Exceeds Supply

As many as 1 in 5 children and youth in Ontario will experience some form of mental illness[1]. Specifically, 70% of mental health problems have their onset during childhood or adolescence[2]. Unfortunately, resources to help youth with mental health disorders are extremely limited, and 5 out of 6 kids will not receive the treatment they need due to long wait times for counselling and therapy[1]. Wait times to see a psychologist in Ontario are commonly six months to one year[3,4]. Therefore, improving the effectiveness and implementation of mental health treatment for youth is a priority in Canadian health care.

1.2 Improve Treatment Availability through Enhanced Treatment Effectiveness

It has recently been identified that poor mental health is associated with impairments in executive function[5,6]. However, successful participation in mental health therapy requires executive function to be intact[7]. Therefore, the effectiveness of mental health treatments could theoretically be enhanced by improving the executive functioning of patients before therapy sessions. Recent systematic reviews and meta-analyses have demonstrated that acute exercise bouts can lead to improved executive functioning in healthy youth[8,9]. These findings have been applied to academic settings to demonstrate that exercise is beneficial for school performance[9]. However, few studies have explored the benefits of exercise on adolescents with mental illness and to our knowledge, none have investigated executive function outcomes. Thus, there is a critical need for additional research examining the relationship linking exercise and executive function in adolescents with mental illness. If exercise could improve the efficacy of mental health therapy by means of enhanced executive functioning, then it would be a simple, inexpensive, and valuable non-pharmacologic tool to aid in treatment.

LITERATURE REVIEW

2.1 What is Executive Function?

Executive function (EF) is a multifaceted construct involving highly interdependent top-down cognitive processes responsible for motivating actions of self-regulation and goal directed action[10]. There are three core EFs[11]: inhibitory control, working memory and cognitive flexibility. These EFs are essential for mental and physical health; success in school and career; quality of life; and cognitive, social, and psychological development[10]. Inhibitory control (IC) is the ability to control one's attention, behaviour, thoughts, and emotions to override a strong internal predisposition to do what is most appropriate[10]. Working memory is the ability to temporarily store information in the mind and manipulate it to form relevant representations[10]. Cognitive flexibility is the ability to multitask and to adjust one's perspective in response to changes in circumstance[10]. The prefrontal cortex was originally implicated as the key area of the brain for mediation of executive function though lesion[12] and functional neuroimaging studies[13,14]. More recently, it has been established that the frontal lobes facilitate the integration of information between complex networks in the brain for EF[15].

There is much overlap between the core EFs and proper functioning generally relies on interdependence between EFs. These domains have been suggested to be separable components, but not completely independent[10]. For example, the use of cognitive flexibility to change perspectives first requires deactivating the previous perspective using IC, followed by forming a new perspective using working memory. In addition, the use of working memory to relate multiple ideas together requires IC to resist internal and external distractions. IC can also aid working memory by keeping limited mental workspace from becoming overly cluttered by suppressing irrelevant thoughts. All aspects of EF are important for higher-order cognition; however, it has been proposed that IC may be foundational for all EFs to operate properly[11].

2.2 Developmental Reasons to Target Adolescence

EF follows a developmental trajectory from infancy to young adulthood. The most rapid improvement in EF occurs during preschool ages 3 to 6[16]. In middle childhood, these abilities are refined to meet increased academic and social demands[17]. By the time children reach adolescence, it is assumed that they have developed the executive function skills necessary to be successful within their environment. However, there is often inconsistent application of executive function skills in adolescence which may be due to the process of synaptic pruning in the prefrontal cortex[17]. In the human cortex, the period of peak synaptic plasticity occurs during early childhood, which is then followed by a period of robust synaptic elimination during adolescence. Synaptic elimination in adolescence is thought to account for the decline in gray matter volume, which has been detected in longitudinal magnetic resonance imaging (MRI) studies[18]. However, there is an optimal level of synaptic pruning that is essential to normal development and too much cortical thinning during adolescence has been shown to be associated with diseased states such as ADHD and other psychiatric disorders[18,19].

2.3 Risk for Mental Illness during Adolescence

Due to the ongoing synaptic reorganization of the brain, the impact of environmental factors on the frontal lobes is hypothesised to be greater during adolescence[18,19,20]. It is also proposed that EFs are extremely vulnerable to developmental disruption during adolescence and therefore deficits in EF may be a contributing factor to psychopathology[21,22]. In addition, it has been suggested that the gap between the onset of emotional changes and the full maturation of IC may contribute to a window of risk for emotional dysregulation and potentially deleterious impulsive actions in early adolescence[23]. Theories regarding mental health risk during adolescence are supported by data indicating that nearly half of mental disorders have their onset before age 14 and 75% before age 25[19].

2.4 Executive Function and Mental Illness

It has been identified that there are transdiagnostic impairments in EF and common structural perturbations in the brain among individuals with mental illness regardless of their specific diagnosis[5,6]. Deficits in EF, have been found in major depressive disorder (MDD)[24], post-traumatic stress disorder[25], bipolar disorder[26], obsessive-compulsive disorder[24], and schizophrenia[27]. There is support that IC impairments are the most pronounced EF deficit for patients with MDD[24], post-traumatic stress disorder[28] and substance abuse disorders[28,29]. In non-clinical samples, trait anxiety, especially anxious apprehension (worry) is associated with impairments in EF, and in particular IC[30,31]. In clinical populations with anxiety disorders, mainly obsessive compulsive disorder and post-traumatic stress disorder, these disorders are associated with EF deficits[32,33,34]. However, the less studied anxiety disorders which include generalized anxiety disorder, social anxiety disorder, and panic disorder, have yielded mixed results[33]. EF deficits are especially problematic in individuals with mental illness since it has been linked to increased risk of suicidality[35] and difficulty controlling thoughts about self-harm[36].

There is some evidence that executive dysfunction may make mental illnesses more difficult to treat[31]. Greater impairment in pre-therapy EF has been found to predict worse treatment response to Cognitive Behavioural Therapy[37,38,39]. One explanation is that EF is required to engage effectively in treatment strategies, which include restructuring exercises, formulating and implementing behavioural plans, and monitor their own cognition and behavior.

EF has also been shown to predict pharmacotherapy response in individuals with depression, schizophrenia, obsessive compulsive disorder, and bipolar disorder[31]. Although the precise reasons are unclear, it has been suggested that medication compliance is likely the cause rather than neurobiological explanations. These findings suggest that success in mental health treatment is dependent on EF, however, there are currently few interventions targeted at improving EF.

2.4 Executive Function and Exercise

The benefits of exercise on physical health outcomes have been widely established[40,41]. More recently, the benefit of exercise on cognitive health has gained significant interest. Regular exercise, as well as acute bouts of exercise, are associated with enhanced neuro-electric processes in the brain and improved EF[42]. As such, exercise is thought to be an effective way of taking advantage of the brain's natural plasticity to provide cognitive benefits[43]. Past research has primarily focused on the benefits of exercise for improving EF in relation to academic performance. There is strong evidence that physical fitness is positively associated with EF performance in youth[44,45,46]. Acute bouts of exercise[49] and chronic exercise interventions[47,48] have been shown to improve EF in youth.

Aerobic activities have the strongest evidence for the benefits of acute exercise[49,50], with most studies focused on moderate intensity aerobic activities[50,51]. However, high-intensity interval training (HIIT) has gained recent interest as a time-efficient approach and effective training protocol in children and adolescents[52,53]. HIIT refers to repeated bouts of short-to-moderate duration exercise (i.e. 10 seconds to 5 minutes) completed at an intensity greater than anaerobic threshold, interspersed with recovery periods or light-intensity work[54]. Cooper et al (2016) found that sprint training improved adolescents' IC performance both immediately and 45 minutes after exercise[55]. HIIT circuit training has also been shown to improve adolescents' IC immediately, 30 minutes, and 60 minutes post-exercise[56]. Recent studies in adults have suggested that HIIT may, in fact, be superior to aerobic exercise for improving EF. HIIT was superior to Continuous Aerobic Exercise (CAE) for improving IC on a Flanker task and the neural efficiency of executive areas in the brain[57]. Improvement in IC, measured by a Stroop Task, was also sustained for a longer time after HIIT compared to CAE[58].

To our knowledge, there are no previous studies that have investigated whether exercise can improve EF in adolescents hospitalized for a mental illness. In populations without mental illness, lower EF at baseline has led to greater improvement in EF post-exercise compared to having a higher EF[59,60,61]. Thus, we postulate that individuals with mental illness, known to have executive dysfunction, could greatly benefit from exercise-based interventions. Evidence to support this speculation can be drawn from studies showing that exercise can improve EF impairments in patients with attention-deficit/hyperactive disorder (ADHD)[62,63]. The next step is to examine the impact of exercise on EF among individuals with other psychiatric disorders.

2.5 Feasibility of HIIT for Adolescents with Mental Illness

Feasibility is often used to determine whether an intervention warrants further testing based on its appropriateness or sustainability[64]. Populations with serious mental illness face substantial illness-related barriers to exercise including poor physical health, sedation effects of psychiatric medications, low self-confidence, low-energy, and disorganization[65,66]. As a result, patients with mental illness referred for exercise programs have lower attendance and completion rates compared to patients with physical health problems[67,68]. However, systematic reviews and meta-analyses support that exercise is just as feasible compared to pharmacological or psychological treatments for patients with serious mental illness[69,70]. Dropout rates for aerobic exercise (delivered on average 3 times/week, 45 minute sessions of moderate intensity, and total duration of 9.2 weeks) and non-exercise interventions were shown to be similar for adults with MDD, 14.8% and 14.5%, respectively[71]. In addition, dropout rates for exercise (mostly moderate to vigorous aerobic exercise, ranging from 5-12 weeks) and control interventions were comparable for adolescents and young adults with MDD, 11% and 18% respectively[72]. Furthermore, studies of inpatient populations with mental illness demonstrate exercise is safe and well tolerated across a range of conditions[73].

Enjoyment, motivation and affect responses to exercise are also important components when examining feasibility. Affect experienced during physical activity has been shown to predict future engagement in that activity and overall physical activity participation[74,75,76]. In addition, studies applying the self-determination theory framework demonstrate a positive association between intrinsic motivation, which exists when the behaviour is enjoyable, and long-term physical activity engagement[77,78]. Previous research examining the psychological responses to exercise in non-clinical populations has demonstrated a negative relationship between exercise intensity and affect/enjoyment[79,80]. However, the majority of research examining this relationship has compared vigorous-intensity CAE to low- and moderate-intensity CAE[81,82].

On the other hand, recent reviews found that HIIT is a viable alternative to traditional exercise as affect, enjoyment, and preference were found to be equal or greater than CAE[83,84,85,86].In addition, some patients may find HIIT to be more enjoyable than traditional endurance training due to the short bursts of activity and the overall shorter duration[86,87,88]. Even for adults with mental illness, HIIT exercise has been shown to be just as feasible as CAE[89,90]. Adults with unipolar depression randomized to a 4-week intervention of either HIIT or CAE showed similar dropout rates, self-determined exercise motivation, and positive affective response during and after the training sessions[89]. Another study showed that inactive adults with mental illness had similar attendance and withdrawal rates between HIIT and CAE groups[90]. Furthermore, these patients were equally satisfied with their group allocation, enjoyment of the exercise, and even their confidence at continuing the exercise without supervision[90].

There is no research examining the feasibility of HIIT for adolescents with mental illness. However, recent studies in healthy adolescents have found HIIT to produce greater enjoyment than CAE due to elevated feelings of reward, excitement and success[91,92]. Due to the limited evidence in adolescents with mental illness, it is inconclusive whether HIIT is feasible for these patients, especially in an inpatient setting.

RESEARCH PROBLEM & GOALS

Successful treatment of mental illness requires EFs to be intact, although EF deficits are common among these patients. The goal of this project was to determine the effect of an acute bout of exercise on EF immediately, and 30 minutes following exercise in adolescents hospitalized for a mental illness. We hypothesized that exercise would improve EF in patients with mental illness. Most of the existing literature focuses on cognitive effects immediately after exercise, however, we chose to explore whether cognitive benefits would be sustained for a short duration after exercise, as this would be applicable for therapy. The 30-minute time interval between post-exercise tests were chosen based on previous literature that demonstrated improved EF was maintained 30 minutes after exercise[55,58]. Of the three core EFs, we chose to examine IC since it has been found to be impaired among populations with diverse forms of mental illness[7,28,31].

The proposed study used an acute bout of HIIT due to its time efficient nature and evidence supporting the use of HIIT to improve IC in adolescents[55,56].The recent literature has demonstrated that healthy adolescents can improve their IC following HIIT[55,56]. However, the feasibility, enjoyment and affect response of HIIT for adolescents with mental illness is unknown. Thus, the current study examined whether HIIT could improve IC adolescents hospitalized for a mental illness and whether HIIT was feasible for an inpatient setting.

Specific Study Objectives:

First Objective: Determine if an acute bout of HIIT can improve IC in adolescents hospitalized for a mental illness immediately and 30-minutes post-exercise.

Second Objective: Examine the feasibility of performing HIIT before therapy for adolescents hospitalized with a mental illness.

PILOT STUDY

Purpose: A pilot study was conducted prior to the main study to investigate the efficacy of the proposed assessment protocol. This study used a modified version of the exercise protocol described by Ludyga (2018) in which adolescents performed body weight circuit training exercises in a 1:1 work to rest ratio[56]. This type of exercise was favourable to other forms of high-intensity interval training since there is no equipment required. The main purpose of the pilot study was to perform the exercise protocol in adolescents hospitalized for a mental illness to ensure that this type of exercise would be intense enough to raise participant's heart rates to at least 80% of their predicted HR max while being well tolerated.

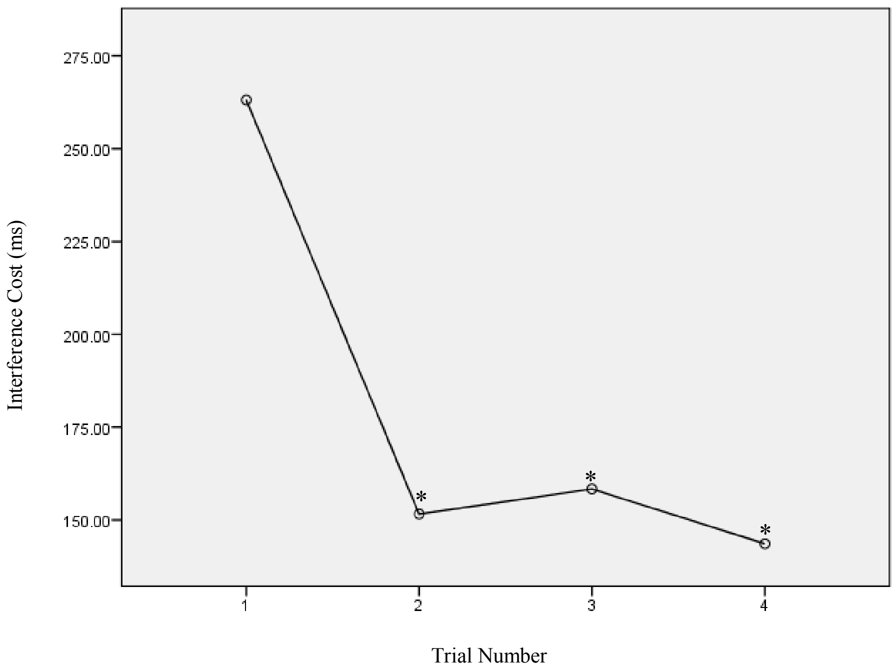
The second reason for the pilot study was to determine how many practice trials of the Stroop test would be required for individuals to learn the task. There are many variations of the Stroop Task that can be used to assess IC. The main study used a validated version of the Colour-Word Stroop Task (CWST) created on PsyToolkit[93]. To determine the appropriate number of practice trials for the main study, CWST performance in the participants of the pilot study were assessed to identify when learning plateaus.

Methods: Participant recruitment and consent was the same as the main study described in the main study article (methods). Participants who consented were asked to do two assessment sessions over two consecutive days. The first assessment consisted of performing 1 practice trial and 3 regular trials of the CWST. On the second day, participants performed 3 trials of the CWST as well as the exercise intervention from the main study article (methods). We asked participants to perform 4 CWST in total to identify when learning would plateau.

To assess tolerability, we examined how many participants were able to successfully complete the 12 minute circuit training exercise. Mean HR was calculated during the exercise to determine whether a minimum of 80% of HR max was achieved. Reaction time data were analyzed using SPSS version 25.0 (IBM Corp, 2017). Interference Cost for the Stroop Colour-Word Test was calculated using the following equation: Interference Cost = [RT of incongruent task−RT of neutral task], where RT is reaction time in seconds. To determine how many trials were required to learn the CWST, repeated measures analysis of variance (ANOVA) were performed for the 4 trials.

Results: All 7 participants in the pilot study successfully completed the exercise protocol. All 7 participant's HR was in a range above 80% of their predicted maximum HR [208 – (Age x 0.7)][94] with a mean HR of 172.6 ± 4.6. For reaction time data, Interference Cost differed significantly between time points ($F(3,21) = 25.26$, $p<.001$). Post-hoc test with Bonferonni correction revealed that Interference Cost was significantly lower for time point 2 (mean difference = 111.5 ± 15.67, $p<.001$), time point 3 (mean difference = 104.8 ± 21.92, $p=.002$), and time point 4 (mean difference = 119.5 ± 18.88, $p<.001$) compared to the first-time point. There was no difference between time points 2 and 3 (p=.57), 2 and 4 (p=.55), or 3 and 4 (p=.24). We concluded that one practice trial was sufficient to learn how to do the CWST (Figure A).

Figure A**.** Interference Cost (ms) over 4 tirals for the Stroop Task



Note. *Interference cost significantly different from baseline.

MAIN STUDY ARTICLE

Manuscript Title: The Effect of High-Intensity Interval Training on Executive Function in Adolescents Hospitalized for a Mental Illness

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Contributions:

JL- study design, data collection, data analysis, writing, review and editing

AB – study design, review and editing

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PL – study design, data analysis, review and editing

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Abstract

Introduction: Inhibitory control is essential for treatment of, and recovery from mental illness. An acute bout of exercise has been shown to improve inhibitory control in healthy adolescents.

Purpose: The primary goal was to examine the effect of an acute bout of high-intensity interval training on inhibitory control immediately, and 30 minutes post-exercise in adolescents hospitalized for a mental illness.

Methods: Participants were recruited through at the Children's Hospital of Eastern Ontario. Participants performed exercise and control conditions in a randomized, counterbalanced manner. The Colour-Word Stroop Task (CWST) assessed Interference Cost (reaction time) pre, post, and 30-minutes post for each condition (exercise / control). The exercise condition included a 12 minute HIIT circuit, consisting of body weight exercises performed in a 1:1 work to rest ratio. The control condition involved reading magazines. Repeated-measures ANOVA evaluated changes in the interference cost and accuracy measures of the CWST.

Results: There was a significant interaction between condition and time for the interference cost measure, $F(1.6,43.3)=13.6$, $p<.0001$, $\eta^2=.34$. Interference costs at baseline were similar between exercise and control conditions ($M_{diff} = 12.4\pm11.11$, $p=.28$). Interference cost was significantly reduced immediately after exercise ($M_{diff} = 78.8\pm14.91$, $p<.001$) and 30-minutes after exercise ($M_{diff} = 59.6\pm15.14$, $p=.001$) compared to control. Accuracy did not differ by time, $F(2,54)=.14$, $p<=.87$, $\eta^2=.01$ nor condition, $F(1,27)=2.25$, $p=.15$, $\eta^2=.08$.

Conclusion: HIIT was able to improve inhibitory control in adolescents with mental illness by increasing their response efficiency rather than improving the overall ability to respond correctly.

Introduction

It has been identified that mental illness is associated with impairments in executive function (EF), regardless of the specific diagnosis[1,2]. Deficits in EF, particularly impairments in inhibitory control (IC), occur in major depressive disorder[3], post-traumatic stress disorder[4], bipolar disorder[5], obsessive-compulsive disorder[6], and schizophrenia[7]. EF deficits in patients with mental illness have been linked to increased risk of suicidality[8] due to difficulties controlling thoughts about self-harm[9]. Furthermore, successful participation in mental health therapy is dependent on EF being intact[10] since executive dysfunction has been shown to reduce responsiveness to pharmacological treatments[10] and Cognitive Behavioural Therapy [11–13].

There is a period of robust synaptic elimination in the cortex during adolescence[14]. It is proposed that EFs are extremely vulnerable to developmental disruption during this time, which may be a contributing factor to psychopathology in adolescence[15–17]. This theory is supported by data indicating nearly half of mental disorders have their onset before age 14 and 75% before age 25[15]. Therefore, targeting EFs during this critical period of development may have important implications for improving treatment outcomes in adolescents with mental illness.

Acute bouts of aerobic exercise lead to improved EF in healthy adolescents [18–20],[21,22]. High-intensity interval training (HIIT) has gained recent interest as a time-efficient approach to exercise training in children and adolescents[23,24]. Initial studies suggest that HIIT may be superior to continuous aerobic exercise (CAE) at moderate intensity for improving and sustaining EF[25–27]. Recent studies support the feasibility of HIIT for adults with mental illness since HIIT and CAE showed similar attendance and withdrawal rates, changes in self-determined exercise motivation from baseline to post-intervention, as well as similar positive affective response during and after the training sessions[28,29]. However, it is unknown whether HIIT is feasible at an inpatient clinic for adolescent with mental illness.

Although deficits in EF are an established comorbidity in all types of mental illness[3–6], few studies have explored the effects of exercise on this population. The goal of this study was to determine whether an acute bout of HIIT exercise could improve EF, immediately and 30 minutes following exercise among adolescents hospitalized for a mental illness. The specific aspect of EF we chose to assess was inhibitory control (IC), the ability to control one's attention, behaviour, thoughts, and emotions to override a strong internal predisposition[30]. We hypothesized that an acute bout of HIIT would improve IC immediately, and 30 minutes post-exercise in adolescents hospitalized for a mental illness. The secondary objective of this study was to assess the feasibility of the HIIT intervention based on recruitment and completion rates, as well as post-exercise enjoyment and changes in affect.

Methods

A total of 28 participants were recruited through the inpatient mental health unit at the Children's Hospital of Eastern Ontario (CHEO). In previous research among healthy adolescents, Stroop task performance significantly improved by 60 ± 37 ms following an acute bout of high intensity sprints[19]. Based on this finding, and using alpha level of 5% and a beta level of 20%, it was calculated that a sample of 28 participants would provide the statistical power to identify a change in reaction time of 60 ms following exercise. Since the improvement in IC from exercise is greater among those with the lowest initial scores, and adolescents with mental illness are known to have low IC, we expected that the response to exercise in our patient population would be at least as large as that observed in healthy adolescents.

Participants were eligible if they were male or female, between the ages of 14 and 17, and hospitalized for treatment of one or multiple of the following mental illnesses: major depressive disorder, anxiety disorders, obsessive compulsive disorder, bipolar disorder, or schizophrenia. All disorders were grouped together since it has been identified that there is a trans-diagnostic pattern of executive dysfunction across all mental illness[1,2]. Exclusion criteria included having a physical disability or neurodevelopmental disorder.

Permission to approach potential study participants was obtained from the psychiatrist responsible for their care at CHEO. The study activities were clearly described to and approved by each psychiatrist before recruitment began. Participants were also screened based on their clinic nurse's perception of patient suitability. If patients were found to be suitable and willing to participate, they gave informed consent and completed the Get Active Questionnaire, a screening tool created by the Canadian Society for Exercise Physiology (CSEP) to identify underlying health conditions that may be contraindications to participating in vigorous physical activity[31].

Study Design: All aspects of patient recruitment, consent and data collection were done at CHEO. Participants were required to do two 1-hour assessment sessions over two consecutive days, 24 hours apart. On one of the days, the participant performed an acute bout of circuit training (exercise condition) and on the other day the participant would read magazines (control condition). The order of the conditions was randomized and counterbalanced. For exercise and control conditions, IC was measured using a Colour-Word Stroop Task (CWST) at 3 time points: baseline (0 minute), immediately after the exercise/control condition (20 minutes), and 30-minutes post-exercise/control condition (50 minutes after baseline)[a]. On the first day, participants

[a] We chose to administer a 30-minute, rather than a 60-minute post Stroop test to improve patients' adherence to the study protocols as we expected that resting for 60-minutes may have been difficult.

performed 1 practice trial of the CWST; the next trial was recorded as the baseline measure (0 minute) of IC. Between the 0 and 20-minute CWST, participants in the exercise condition performed the exercise intervention and participants in the control condition read magazines. All study participants, exercise and control, read magazines between the 20 and 50-minute Stroop tasks. On the second day, participants who did the exercise condition initially performed the control condition, and participants who did the control condition initially performed the exercise condition. Participants were instructed to follow standard exercise testing procedures, including no vigorous PA or caffeine on the day of testing[32], and nothing to eat 1 hour prior to testing.

Exercise Intervention: Participants performed 12 minutes of circuit training consisting of 4 full body exercises: jumping jacks, modified burpies, side jumps, and high knees. These exercises were repeated 3 times, using a 1:1 work to rest ratio of 30 seconds of work and 30 seconds of rest. This circuit was modified from a study by Ludyga and colleagues (2018) that demonstrated healthy adolescents had improved IC immediately and 60 minutes after exercise[18]. In Ludyga's exercise protocol, adolescents performed 16 minutes of circuit training at a 1:1 work to rest ratio. However, we decided to reduce the amount of exercise to 12 minutes (including rest intervals) so that our sample of patients could feasibly complete the exercise. Participant heart rate (HR) was monitored throughout the exercise using a Polar Heart Rate Monitor (model FT4; Polar Electro, Finland) and recorded after each period of work. Participants were encouraged to keep their HR at or above 80% of their predicted maximum HR [(208 – (0.7 x Age)][33]. After each round of exercise, participants were also asked to provide a rating of perceived exertion (RPE), using the OMNI scale for children as reference[34].

Colour-Word Stroop Task: The CWST is a widely used, standardized assessment of IC that directly measures an individual's ability to inhibit habitual responses during a decision-making task[35]. The CWST was performed manually on a laptop using PsyToolKit Software[36]. Each trial consisted of a fixation cross presented in the center of the screen for 500 ms, followed by a stimulus which remained on the screen until the response was given. Stimuli consisted of either a colour word (BLUE, RED, GREEN, or YELLOW) or 4X's in a row (e.g. XXXX) written in blue, red, green, or yellow ink. Participants were instructed to identify the ink color of the word as quickly and accurately as possible. The compatibility between the identity of the word and its color is manipulated, yielding 36 compatible trials (e.g., the word red printed in red ink), 36 incompatible trials (e.g., the word red printed in blue ink) and 36 neutral trials (e.g., XXXX printed in blue ink). The words for each task were presented in random order. Participant responses were considered correct between 300 ms and 2000 ms. The minimum response time was set at 300 ms since perceptual processing of a Stroop task stimulus, evident by the P300 event-related potential, has been shown to be greater than 300 ms[37]. This infers that response times before 300 ms would be a premature response. A response limit was set based on a meta-analysis of Stroop response times in individuals with Attention Deficit Hyperactivity Disorder, who have known impairments in IC[38]. Response times in these individuals were shown to have an upper limit of 2000 ms, excluding outliers. In the present study, accuracy and reaction time data for the Stroop task were recorded on the PsyToolKit Software[36]. Task performance was assessed by interference cost, the reaction time cost of responding to the task when the ink color and word do not match, as well as overall accuracy, in which incorrect colour selections and timed out responses were considered as errors.

Questionnaires: The Habitual Activity Estimation Scale (HAES)[35] was completed by participants to estimate their physical activity levels for a typical weekday prior to entering the hospital. The HAES has been shown to be a valid and reliable assessment of physical activity in pediatric populations with chronic illness, which can be easily completed in 15 minutes by self-report (35 & wells). However, the administration of the HAES in the present study was atypical since participants' recall of a 'typical weekday' varied depending on when they were admitted to the hospital in relation to completing the HAES. Participants documented the amount of time spent awake in each of 4 categories: inactive (lying down), somewhat inactive (sitting down), somewhat-active (walking), and very active (breathing hard and sweating). Participants also recorded wake-up, bedtimes, and meal times. Time spent in each category per day was calculated in minutes. The inactive and somewhat inactive categories were combined to describe sedentary behaviour. The somewhat-active and very active categories were used to described light activity and moderate-to-vigorous physical activity (MVPA), respectively[39]. Participants' affect was assessed before and after exercise using the Positive Affect Negative Affect Schedule (PANAS)[40]. The PANAS is a relatively short and simple measure which makes it suitable for completing it before and after the exercise intervention. In addition, the PANAS has previously been used to assess changes in affect following exercise in populations with mental illness (Heggelund 2014). The PANAS is comprised of 10 positive and 10 negative adjective words in which participants must rate their affective state from 1 (not at all) to 5 (extremely). The sums of the 10 positive and 10 negative ratings are separately calculated for the total positive and negative affect scores. Finally, we assessed participants' perception of whether they would be (a) willing to perform HIIT prior to therapy if HIIT is found to be beneficial (b) their enjoyment of the HIIT session compared to other forms of exercise, and (c) how likely they would be physically active on most days of the week once discharged, on a scale from 1-10 where 1 was not likely or not enjoyable and 10 was very likely or very enjoyable.

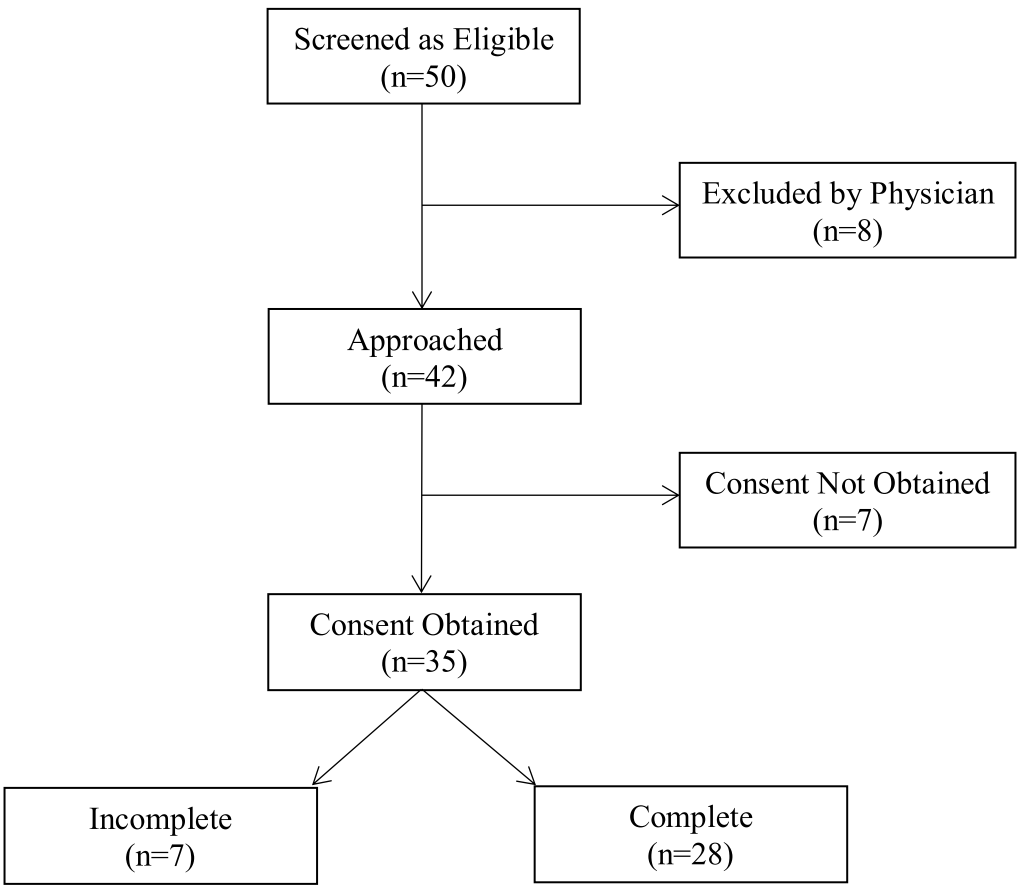
Statistical Testing: Data were analyzed using SPSS version 25.0 (IBM Corp, 2017). Reaction time (RT) data were expressed as a mean with standard error for incompatible and neutral trials. Interference Cost for the CWST was calculated using the following equation: Interference Cost = [(RT of incongruent task−RT of neutral task]. Preliminary analyses were conducted to ensure participant factors did not differ between groups (performed exercise first or the control first). Univariate analyses also examined whether the observed effects differed depending on participant characteristics. RTs (incompatible and neutral), Interference Cost, and accuracy were analyzed using separate repeated-measures analyses of variance (ANOVA) where within subject factors were session time (0/20/50 min) and condition (exercise/control). Feasibility of the HIIT intervention was quantified by recruitment/ completion rates and reasons for withdrawal, as well as descriptive statistics for ratings of enjoyment and willingness to perform HIIT before therapy. Finally, a two factor repeated measures ANOVA assessed the changes in the PANAS scores from pre- to post-exercise.

Results

Preliminary Results: Participant recruitment is described in Figure 1. Participant demographics and calculated estimates for sedentary time, light activity, and MVPA are described in Table 1. Almost 1/3 of our sample (8/28 or 29%) reported less than 60 minutes of MVPA per day, and 6 of these 8 participants reported 0 minutes of MVPA per day. Participant factors did not differ between the groups (Table 1). There were no differences in the physiological response to exercise (HR) and RPE between groups (Table 2). The mean decrease in Interference Cost from pre- to post-exercise was 99.9 ms ± 72.86. Univariate analyses revealed that improvement in Interference Cost after exercise was not associated with participant order of trial condition, sex, baseline Interference Cost, enjoyment of HITT, or MVPA (Table 3).

Participants less likely to perform physical activity once discharged had significantly greater improvement in Interference Cost post-exercise. Although not significant, a lower likelihood of performing HIIT before therapy was related to greater improvement in Interference Cost post-exercise (Table 3).

Figure 1. Participant Screening and Recruitment Flow Chart



Note. Excluded by Physician = patients had an eating disorder (n=2), too acutely ill (n=1), or getting discharged (n=5); Consent not Obtained = patients not interested in participating in the study (n=3) or getting discharged before study could be completed (n=4); Incomplete = patients did not complete the exercise session (n=2) or got discharged after first day of testing (n=5).

Table 1. Participant Demographics

		Exercise First (n=14)	Control First (n=14)	Total Sample (n=28)	P-value
Age		15.4±.85	15.6±1.00	15.5±.92	.68
Gender					
	Male:Female	4:10	4:10	8:20	
Diagnosis					
	MDD/SI	10	13	23	
	GAD	2	1	3	
	PTSD	1	0	1	
	BD	1	0	1	
HAES (min/day)					
	Sedentary	494.3±109.42	486.2±188.21	490.2 ± 151.46	.89
	Light Activity	295.0±137.73	356.6±216.44	325.9 ±180.75	.38
	MVPA	114.9±78.67	105.9±93.46	110.4 ±84.89	.79
Questionnaire:					
1. Exercise before therapy		6.9±2.88	5.9±2.64	6.4±2.75	.38
2. Enjoyment of exercise		5.9±2.14	5.6±1.95	5.7±2.02	.72
3. PA once discharged?		6.4±2.41	6.1±2.99	6.2±2.67	.78

Note. MDD/SI = Major Depressive Disorder/ Suicidal Ideation; GAD = Generalized Anxiety Disorder; PTSD = Post-Traumatic Stress Disorder: BD = Bipolar Disorder. HAES = Habitual Activity Estimation Scale (Hay 2006). MVPA = moderate-to-vigorous physical activity.

Table 2. Participants' Heart Rate and Perceived Exertion during Exercise

		Exercise First	Exercise Second	Total	P-value
Heart Rate (beats per minute)	Round 1	172.5±8.91	168.3±10.03	170.4±9.56	.24
	Round 2	176.8±.39	174.5±11.63	175.6±10.02	.56
	Round 3	179.2±8.60	179.7±10.59	179.5±9.24	.89
RPE (rated on a scale from 1-10)	Round1	5.7±1.64	5.7±1.38	5.7±1.49	1.00
	Round 2	7.8±1.58	7.5±1.34	7.6±1.45	.61
	Round 3	8.8±1.37	8.9±1.14	8.9±1.24	.77

Note. RPE = Rate of Perceived Excursion; P-value using independent t-test.

Table 3. Univariate Effect of Participant Characteristics on Change in Interference Cost

		Beta ± SE	F-value	P-value	Adjusted R^2
Participant Characteristics	Control first	11.7±27.97	.18	.68	.03
	Female Sex	36.4±30.23	1.45	.24	.02
	Higher baseline IntC	0.3±0.23	1.7	.20	.06
	Less likely to do HIIT before	9.1±4.87	3.5	.07	.12
	Lower Enjoyment of HIIT	5.6±7.00	.64	.43	.02
	Less likely to do physical activity after discharge	10.1±4.97	4.10	.05	.14
	Lower MVPA	0.2±0.17	.94	.34	.04

Note. Higher baseline IntC = more interference cost on baseline Stroop task; Lower MVPA = less moderate-to-vigorous physical activity per day estimated using the Habitual Activity Estimation Scale (Hay 2006)

Interference Cost: There was a significant interaction between condition and time for Interference Cost, $F(1.6,43.3)=13.6$, $p<.0001$, $\eta^2=.34$ (Figure 2a). The within subject effects were deconstructed by examining the effect of time at each group level. For the exercise condition, Interference Cost significantly reduced from pre to post ($M_{diff}= 85.3\pm12.06$, $p<.001$) and from pre to 30-minute post ($M_{diff} = 84.2\pm11.44$, $p<.001$), with no difference from post to 30-minute post ($M_{diff}=1.1\pm12.06$, $p=1.00$). For the control condition, Interference Cost did not change from pre- to post ($M_{diff} = 1.9\pm12.49$, $p=1.00$), from pre to 30-min post ($M_{diff} = 12.2\pm9.25$, $p=.59$) or from post to 30-min post ($M_{diff} = 14.1\pm14.34$, $p=1.00$). Between subject effects were deconstructed by examining the effect of condition at each time point. There was no difference in Interference Cost between exercise and control conditions at pre-test ($M_{diff} = 12.4\pm11.11$, $p=.28$). However, Interference Cost was significantly reduced in the exercise condition compared to the control condition at the post test ($M_{diff} = 78.8\pm14.91$, $p<.001$) and the 30-minute post-test ($M_{diff} = 59.6\pm15.14$, $p=.001$).

Accuracy: Participant accuracy on the CWST did not differ by condition, $F(1,27)=2.25$, $p=.15$, $\eta^2=.08$, or time, $F(2,54)=.14$, $p=.87$, $\eta^2=.005$ (Figure 2b).

Figure 2a. Colour-Word Stroop Task Interference Cost

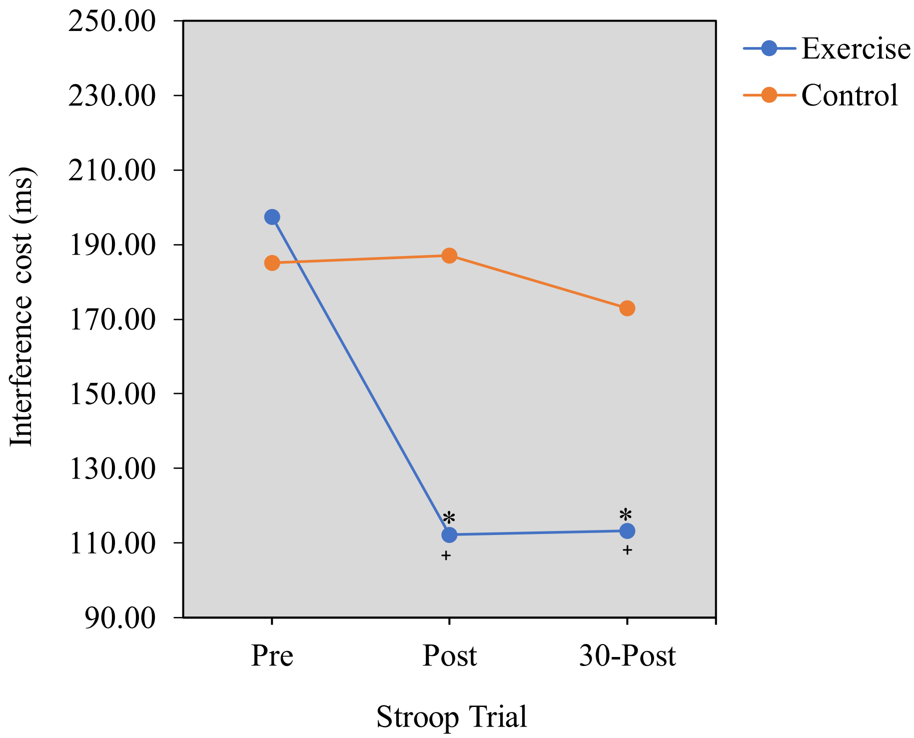
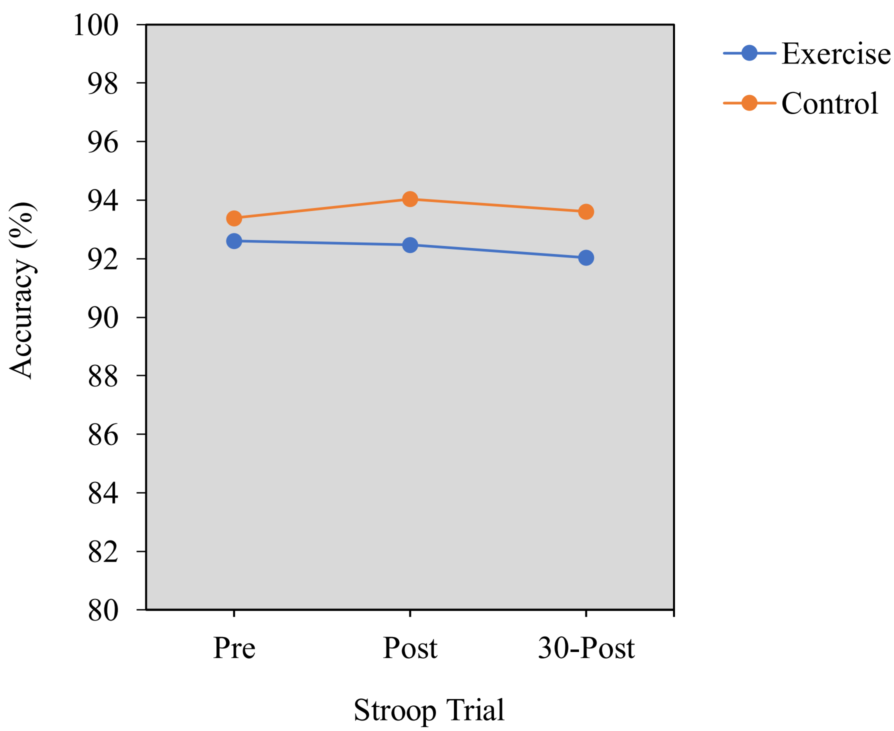


Figure 2b. Colour-Word Stroop Task Accuracy



Note. *significantly reduced from pre-exercise trial (p<.05); +significantly lower than control condition (p<.05)

Feasibility: Participant recruitment and reasons for removal are described in Figure 1. Of the 50 eligible patients, 42 patients (84%) were approached to participate, and of those 42, consent was obtained by 35 patients (83%), and a total of 28 patients who completed the study (80%). The main reason for removal from the study was due to participants being discharged from the hospital. Only 2 participants were removed from the final analysis because they were not able to complete the total HIIT session due to fatigue. Average ratings for the questions regarding enjoyment of HIIT compared to other forms of exercise and willingness to do HIIT before therapy are described in Table 1. Frequencies of participant ratings are demonstrated in Figure 3a and 3b. There was a significant interaction between time and affect scale [$F(1,27) = 13.54$, $p=.001$] for the PANAS (Figure 4). Within subject effects were deconstructed by examining the differences between the positive and negative affect scores at each time point. At baseline, there were no differences between scores ($M_{diff} = .14 \pm 14.6$, $p=.96$). After exercise, positive affect was significantly higher than negative affect ($M_{diff} = 6.9 \pm 15.2$, $p=.02$).

Figure 3 a. Perceived enjoyment of HIIT compared to other forms of Exercise

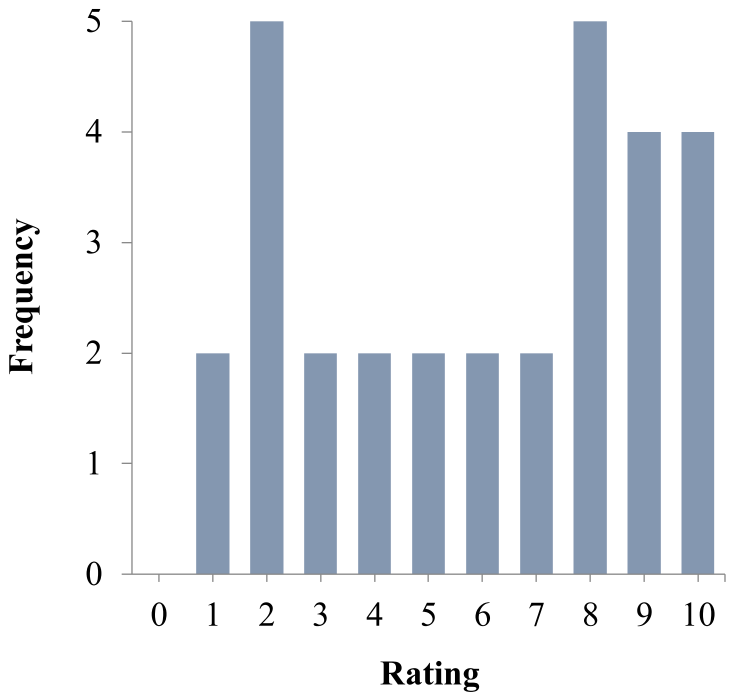


Figure 3 b. Willingness to do HIIT before therapy if there is a benefit

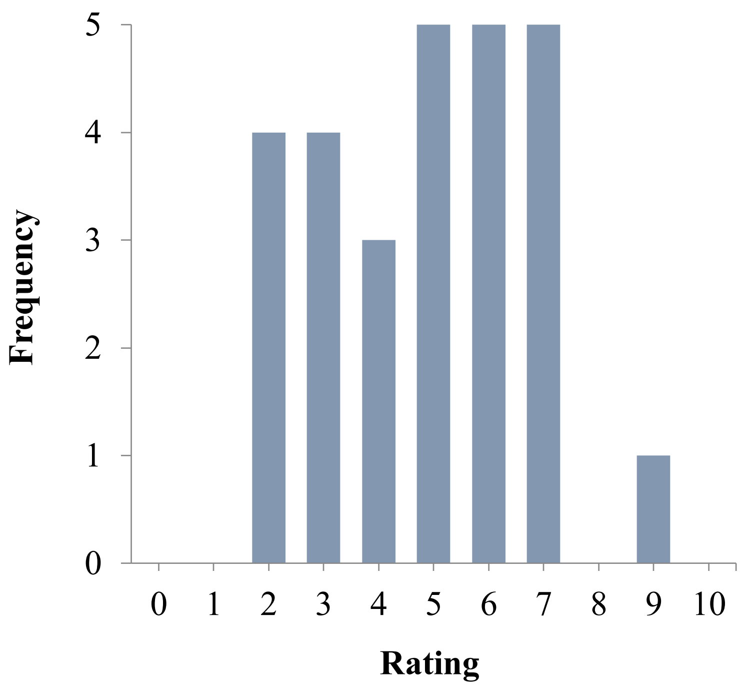
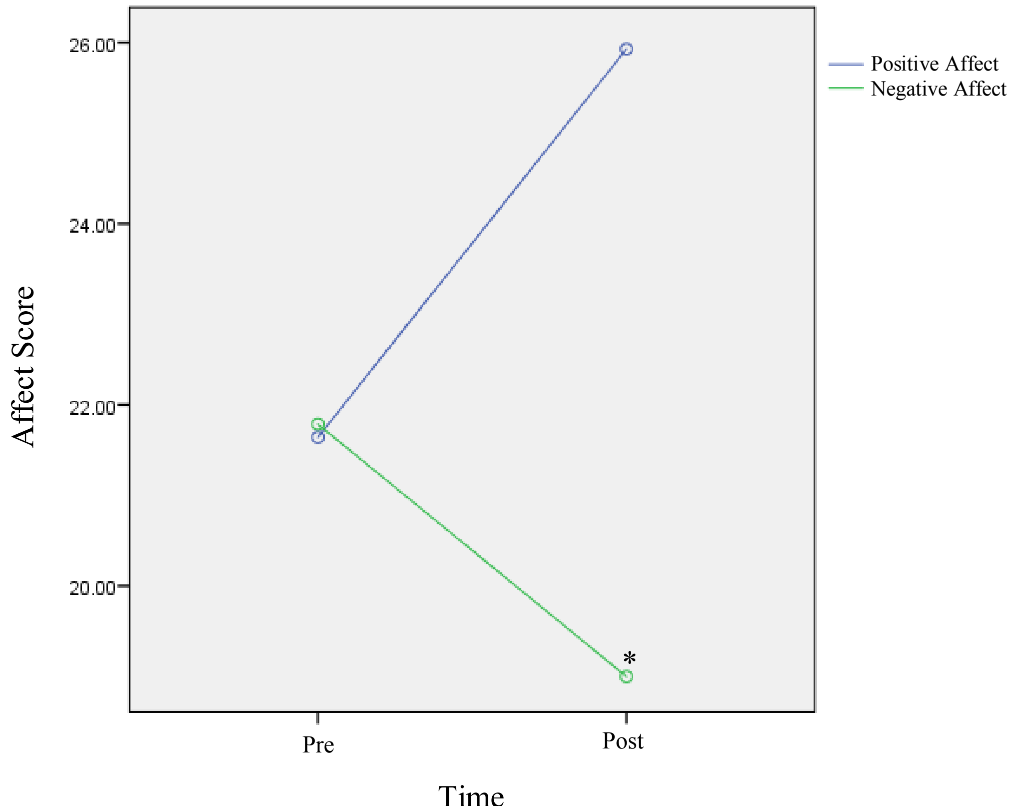


Figure 4. Change in Positive and Negative Affect after Exercise



Note.*Negative affect score significantly different ($p<.05$) from positive affect score.

Discussion

The main finding of this study was that in contrast to the control condition, exercise improved patients' Interference Cost measure. Interference Cost on the CWST decreased after HIIT due to faster RT during incongruent trials. Furthermore, these cognitive benefits were sustained 30 minutes after exercise. These results suggest that HIIT can improve IC in adolescents hospitalized for a mental illness, specifically their efficiency on a task when there are conflicting stimuli presented. There were no group-specific changes in accuracy over time suggesting that improvements in CWST performance reflected greater effectiveness while inhibiting a response, rather than improvements in response accuracy. In addition, HIIT was demonstrated to be feasible since 82% of patients approached for the study consented to participate and 80% of patients who consented completed the study. The main reason for consent not being obtained or participation was incomplete was due to discharge from the hospital, 60% and 71% respectively. Furthermore, positive affect was significantly higher than negative affect post-exercise. There was a bimodal distribution for enjoyment of HIIT compared to other forms of exercise; however, almost half of our participants (46%) rated HIIT as 8 or above. Finally, willingness to perform HIIT before therapy, if HIIT was found to be helpful, was rated a mean of 6.4 out of 10.

Previous research had found that an acute bout of HIIT can improve IC in healthy adolescents[18–20]. Our findings demonstrate that exercise benefits on IC can also be seen in adolescents hospitalized for mental illness, particularly those with MDD (since this comprised 82% of our sample). There is support for the effectiveness of exercise interventions for reducing symptoms of depression among adolescents with clinical depression[41]. Although cognitive impairment is a major factor in relapse[42] and functional outcomes[43] in MDD, comparatively less research has examined the cognitive benefits of exercise. We chose to examine the IC benefits of exercise since IC impairments are not only present in the acute phases of depression[3], they have also been shown to persist in remission[44]. Furthermore, IC impairments are recognized as common symptoms of depression, including the inability to focus, concentrate or make decisions[45]. However, research examining the immediate effect of exercise on IC in MDD is limited, with only few studies in adults examining changes in IC following acute moderate-aerobic exercise[46,47]. This study adds to the growing literature on the acute exercise effects of inhibitory control for adolescents with mental illness. In addition, these findings provide preliminary evidence that HIIT is feasible for adolescents hospitalized for mental illness.

Improvements in RT have been most commonly used to describe changes in IC during Stroop Tasks[18,19], however, the current study also sought to examine changes in accuracy. Our findings revealed that exercise enhanced IC through improvements in RT rather than accuracy. We speculate that our patients' experienced ceiling effects in which high baseline accuracy (92.5 % ± 5.38) prevented further improvements after exercise. In healthy adolescents, the effects of HIIT on IC has also been characterized by enhanced RT, rather than accuracy for Stroop[19] and Flanker tasks[18]. Similarly, authors reported high baseline accuracy for Stroop (pre-exercise accuracy for the colour-interference trials was 95.8 % ± 5.2)[19] and Flanker tasks (figure displays pre-exercise accuracy rates above 92.5% for incongruent trials)[18]. We hypothesize that ceiling effects may have arisen due to insufficient task difficulty. Participants in our study who performed the CWST had 2000 ms to respond to each trial. Healthy adolescents who did not improve accuracy on the Flanker task also had 2000 ms to respond to each trial[18]. In contrast, healthy adolescents were shown to improve accuracy on a Flanker task that had a response window of only 1000 ms, following a 5 minute bout of exercise (either at 50, 65, and 80% of maximal intensity)[48]. We speculate that if our participants only had 1000 ms to respond to each trial, we may have observed improvements in accuracy. While our findings support HIIT improved our patients' response efficiency, improving accuracy may be more clinically relevant for individuals with depression who are impaired at decision making[45]. Future research should continue to examine IC performance as it relates to changes in accuracy using sufficiently difficult IC tasks in order to mitigate ceiling effects.

To our knowledge, there has been no previous research documenting the acute benefits of exercise on IC in adolescents with depression. Several studies do however support these benefits in adults with depression. Performing 30 minutes of moderate CAE improved mean RTs on

Stroop tasks in adult outpatients with MDD (n=24, 42.2 ± 12.2 years)[46] and elderly patients with MDD (n=10, age=71.5 ± 6.0 years)[47]. Interestingly, findings for the IC benefits of exercise in healthy populations are not as consistent[22]. Studies in healthy children and adolescents found that an acute bout of moderate CAE was not able to improve IC on a Flanker task[49,50]. One explanation is that research suggests acute exercise facilitates IC in those who need it the most, i.e. low-performers improve more than high-performers[51]. One of the major limitations in studies examining the benefits of exercise on global cognition in depression is that cognitive impairment is not a prerequisite for study participation[52]. This has been proposed to lead to an underestimation of the impact of long-term exercise interventions on cognition. While MDD is characterized by difficulty inhibiting negative thoughts and emotions[53], the disorder affects each individual differently and thus severity of cognitive impairments vary. For example, it has been estimated that approximately 28-37% of depressed individuals score between 1-2 SD below healthy controls, and 16-39% score 2 SD or greater[54]. Since more severe depressive symptoms are related to a higher degree of dysfunctional cognitions[55], we suspect our patients had low levels of IC at baseline and thus responded positively to treatment. However, future research should pre-screen for cognitive impairment as samples could notably vary in their degree of cognitive dysfunction which may affect the impact of exercise on IC.

Neuroimaging techniques have allowed researchers to infer neural substrates in the brain by which an acute bout of exercise improves IC. Studies using functional near-infrared spectroscopy (fNIRS) in healthy individuals have revealed that an acute bout of low[56], moderate[57] , or high-intensity exercise[58] increased activation of the left-dorsolateral prefrontal cortex (DLPFC) in conjunction with improved Stroop performance. As such, exercise is hypothesized to facilitate IC by enhancing cortical activations in the DLPFC[59]. However, these techniques do not provide us with the physiological processes underlying the increase in blood flow to the DLPFC. One of the leading hypotheses is that exercise engages arousal mechanisms which release neurotransmitters into the pre-frontal cortex and other areas involved in cognition[60]. Since hypofrontality, i.e. reduced activity of the DLPFC, is one of the characteristics of cognitive dysfunction in psychiatric disorders[10] , we speculate that exercise may enhance DLPFC activity mediated change in IC in our patients.

Feasibility: Our findings suggest that a single session of HIIT before therapy may be feasible for adolescent mental health inpatients. The main reason patients did not consent or withdrew after the first day of testing was discharge from the hospital. Since patients in our study had to go through physician approval, nurse approval, and informed consent, the process from initial recruitment to participation was not efficient. We expect that more patients would have participated if HIIT were implemented as part of regular treatment.

In our sample, we found that HIIT had a positive influence on affect. These findings are corroborated by research in non-clinical populations that show that post-exercise enjoyment, affect and preference for HIIT are equal to CAE[61–63]. However, 2 of the 35 participants who consented were removed from the final analysis since they were unable to complete the exercise. Although this is a small portion of our sample, it will be important for future studies to determine whether a modified exercise protocol would be more suitable for certain patients.

Strengths and Limitations: This study provides preliminary evidence that HIIT can improve IC in adolescents hospitalized for a mental illness. A major strength of this study was the use of a randomized crossover design. Since each participant acted as his/her own control, the study design minimized the extent to which individual factors may have influenced the results. Although our sample size was large enough to test the proposed research question, it was not large enough to perform meaningful subgroup analyses which would have allowed us to assess moderators of IC improvement after exercise. For instance, 24/28 of our participants had a diagnosis of MDD; as such we could not assess the impact of diagnosis on the results. Furthermore, we did not consider differences in medication, length of hospitalization stay, age of illness onset, history of relapse, or past treatments. Interestingly, our results support the idea that acute exercise facilitates IC in those who need it the most since participants who rated themselves as less likely to perform exercise before therapy or to exercise when discharged had the greatest improvement in Interference Cost post-exercise.

Conclusion

With 5 out of 6 youth with mental illness not receiving the treatment they need due to long wait times for counselling and therapy[64], the demand for mental health treatment far exceeds our resources. This study provides preliminary evidence that HIIT is feasible and could be used to improve inhibitory control, with the greatest benefit accruing to those who are less physically active. Further research appears warranted to investigate whether HIIT prior to therapy could improve the efficacy of mental health treatment for adolescents with mental illness through enhanced cognitive pathways, improvements in mood, enhanced patient focus or a reduction of impulsive behaviours. Additional research is required to determine the optimal exercise type and intensity for enhanced IC and participant enjoyment, the impact of individual factors (e.g., diagnosis, medication, age of illness onset, length of hospitalization, and treatment history).

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GLOBAL DISCUSSION

6.1 Exercise, Cognition, and Mental Health

Psychiatric conditions have traditionally been characterized as emotional in nature, with cognitive symptoms being comparatively overlooked. It is now understood that cognitive dysfunctions are just as pronounced in mental health disorders and are even related to the persistence of symptoms, including emotional dysregulation and rumination[95]. Cognitive impairment is also one of the main predictors of relapse and there is evidence that impairments continue beyond remission[96]. With little positive feedback for the development of pro-cognitive drugs[95], non-pharmacological strategies have become the focus for attenuating these cognitive deficits. Based on the development of disease patterns, depression is expected to be the second highest contributing factor to the global burden of disease in 2030[97]. As such, most of the research in this field is focused on patients with depression.

To date, evidence for the cognition-enhancing effects of exercise in MDD remains equivocal. Recently published meta-analyses do not support the pro-cognitive effects of exercise in MDD[98,99]. However, these results must be interpreted with caution since most of the studies assessed cognition as secondary or tertiary outcomes, and therefore these studies were not correctly powered for cognitive outcomes. It is also important to note that data were pooled together from different cognitive measures, which vary in reliably for detecting cognitive changes. Furthermore, there was a lack of homogeneity in samples, with respect to diagnosis and symptom severity, as well as the type of exercise performed. Finally, studies did not require patients to have cognitive impairment at baseline, which may have underestimated the impact of exercise on impaired cognition. There is more consistent evidence for the antidepressant effects of exercise training on individuals with depression[100,101,102]. However, improvement in affect/

mood alone is not enough since cognitive impairment is a major factor in relapse[103] and poor functional outcomes[104].

Relative to healthy individuals, depression elicits numerous physiological changes in the brain which may contribute to cognitive dysfunction[24]. Neuroplasticity is the brains capacity to change and reorganize itself in response to internal/external influences[105]; this explains how the brain adopts maladaptive patterns of functioning in depression. Fortunately, the consequences of neuroplasticity can also be adaptive. Exercise is hypothesized to be one method of harnessing neuroplasticity to counteract the cognitive decline that occurs in patients with depression. There is emerging evidence that physical exercise in combination with other forms of treatment, such as cognitive behavioural therapy[106], meditation[107] or mental relaxation training[108], is effective at improving cognition in individuals with depression. These results suggest that combining two interventions, which both promote neuroplastic changes, can have additive and synergistic effects on cognition. This was the premise underlying the current project; we hypothesized that the combination of exercise and psychotherapy would be more effective for improving cognition in patients with mental illness than each method alone. The next step for this programme of research is to assess whether there are cumulative effects on IC if HIIT and therapy are performed in succession. It will also be important to determine whether improvements in IC performance after HIIT are applicable to real world functioning and lead to better outcomes in therapy.

6.2 Feasibility of Implementing HIIT into Mental Health Treatment

The second aim of this project was to assess the feasibility of implementing HIIT exercise into inpatient mental health treatment. In the current study, the major barrier to participation was the high turnover of patients discharged from hospital. Of the 42 eligible patients, 7 did not consent to participate in the study: 3/7 due to not being interested and 4/7 due to imminent discharge (Figure 1). Of the 35 patients that consented to the study, 2 participants were not able to finish the HIIT protocol due to fatigue and 5 participants were excluded from the analysis because they were discharged prior to completing both testing sessions. Since this study required physician consent and nurse screening before patients could be approached, recruitment time contributed to the number of patients discharged before participating in the study. As such, we do not expect discharges to decrease participation if pre-therapy HIIT is performed as a regular part of treatment.

After participants performed the exercise condition, we asked participants to answer three questions regarding their willingness to do HIIT before therapy if HIIT was found to be beneficial and their enjoyment of the HIIT compared to other exercise (Figure 3 a and b). Participants' ratings showed a bimodal distribution in response to enjoyment of HIIT compared to other forms of exercise. Interestingly, a recent study showed 100% (8/8) of the participants randomized to HIIT found the exercise enjoyable compared to only 63% (5/8) in the CAE[90]. However, their study recruited participants via advertisements, private clinician referrals, and the outpatient unit. In contrast, our participants were only recruited through the inpatient mental health unit. Differences in participant recruitment, age, and severity of illness may have contributed to our heterogeneous findings. In addition, we speculate that the distinction between participants who rated enjoyment high versus low could have been due to previous engagement in sports or physical activity, data which were not collected in the current study.

The most important consideration in support of using HIIT as an intervention is that performing the exercise did not contribute towards participants' negative feelings and emotions. Fortunately, performing the HIIT improved most participants' positive affect (n=19/28 improved, n=6/28 decreased, n=3 did not change) and reduced their negative affect (n=25/28 improved, n=3/28 did not change (Figure 4). The benefit of high intensity exercise on improving mood in patients with depression has been documented after a single session of exercise[109] and after long-term interventions[110]. Interestingly, the immediate benefits of acute exercise on mood in women with depression have been found to be similar for light, moderate, and hard intensity exercise[111].

One factor which may have contributed to our study's high rate of participation was that patients were hospitalized. This hypothesis is corroborated by the results of a meta-analysis by Stubbs et al (2016), which found dropout rates for RCT's with exercise were lower for inpatients compared to outpatients[112]. We expect that since inpatients are confined to the hospital, they are more willing to take part in research since they have limited access to other activities. Interestingly, the dropout rates from meta-analysis on exercise RCT's was found to be relatively low among all people with depression at 15.2%[85]. This is further evidence for the acceptability of patients with depression to exercise as part of treatment.

6.3 Assumptions

It is important to understand that these findings are based on the assumption that CWST performance represents a persons' level of IC. In this task, it is assumed that reading the word is an overlearned cognitive process and will be the automatic response when participants are instructed to name the ink colour. During the incongruent trials, participants must resolve this cognitive interference when the word and the colour do not match. Since it is presumed that there is no response competition for neutral trials (XXXX written in blue, red, or green), incongruent trial RT is compared to neutral trial RT to determine Int C. Congruent trials are still important to include in the task to decrease the likelihood that subjects use the suppression strategy, i.e. avoid reading the word by not focusing on gaze. Instead, subjects are more likely to split their attention between reading and colour naming dimensions when congruent trials are used in the task[113].

Impulsivity is thought to be a manifestation of impaired inhibitory control processes at the behavioural level that leads to impulsive actions[114]. Rumination is also proposed to be a consequence of inhibitory control deficits; however, instead of impulsive actions, individuals are not able to inhibit persistent negative information from entering and remaining in their working memory[115]. There are currently mixed findings on whether inhibitory control task performance is associated with behavioural measures of impulsivity. Previous studies in patients with borderline personality disorder[116] and Bulimia Nervosa[117] have demonstrated associations between Stroop performance and the Barratt Impulsivity Scale. Whereas research in patients with bipolar disorder have shown no association between Stroop performance and the Barratt Impulsivity Scale[118,119]. There is stronger support for the positive association between rumination and impaired inhibitory control for adult[120] and adolescent samples[121]. These findings suggest that there may be some translation between inhibitory control performance and real world inhibitory functioning.

6.4 Limitations

The use of the CWST is one of the main limitations in this research. Since there are many variations of the Stroop task, it is difficult to make comparisons between different studies assessing IC. Recently, the Emotional Stroop Task has become commonly used in psychopathology research, where instead of having words of different colours, the words are now affective words related to the disorder[122]. However, this modified version of the Stroop is different from the original Stroop because it is based on the idea that individuals will actively attend to the words consistent with their feelings. The Stroop task and its variations are not only representative of IC; it also requires other functions, such as cognitive flexibility. Thus, it is difficult to know whether Stroop performance represents IC or overall cognitive ability.

In addition, examining clinical populations also has its own limitations. In our sample of patients, there were several factors that could have influenced how individuals responded to the exercise. For instance, patients in our study differed by their medications, days hospitalized, number of relapses, and treatment histories. Furthermore, we were not able to look at differences between diagnostic groups since the majority of our patients had MDD. Finally, participants' ability to recall a 'typical week' for the HAES may have been influenced by the length of their hospital stay prior to the study. We expect that this limitation may have contributed to participants' overall high level of estimated MVPA.

6.5 Strengths

So far, little is known about the effect of acute exercise on cognition in adolescents with mental illness. This study contributes to the current literature by demonstrating that exercise is feasible for adolescents hospitalized with mental illness and that patients are willing to perform high intensity interval training (HIIT). The major strength of this study was the use of a randomized crossover design. Since participants act as their own control, this minimizes the extent to which individual factors may influence the impact of the intervention. Furthermore, we used a baseline measurement of IC, rather than just taking the scores after the exercise intervention. Our ability to pilot test also contributed to the quality of our study design, as we determined the number practice trials required for the CWST and that there was no learning effect over two days.

6.6 Implications and Significance

With 5 out of 6 kids not receiving the treatment they need due to long wait times for counselling and therapy[1], the demand for mental health treatment far exceeds our resources. The results of this study provide preliminary evidence that a single session of HIIT can improve IC. Improving IC has the potential to optimize treatment though cognitive pathways, i.e. and through positive changes in mood and affect. Research in this field should continue to target adolescence to reduce the risk of morbidities throughout the lifespan. Furthermore, early interventions during adolescence may have the greatest impact from a neurobiological perspective, since the brain is still developing[123]. There should also be a focus on inpatients with mental illness since they have the most pronounced cognitive deficits, with more hospitalizations being associated with more severe cognitive impairments[124].

We hope this research will generate discussion of the potential benefits of implementing physical activity or exercise into the mental health treatments offered to youth. However, rigorous validation of the impact of the proposed changes on therapeutic outcomes is required before changes in health care policy are warranted. The first step would be to determine the optimal exercise type, intensity and duration that would elicit the greatest cognitive improvement. Additional studies examining how long the acute benefits of exercise would last are warranted, as current studies have only tested participants for 1 hour after exercise. There is also the consideration of what type of exercise would be the most enjoyable to participants, and whether enjoyment and cognitive enhancements will coincide. It is especially important to determine whether improvements in cognition (in the laboratory) lead to improved outcomes in therapy (in the real word), such as enhanced focus and a reduction of impulsive thoughts and behaviours. Future research should also determine the impact of individual factors, such as diagnosis, medication, length of hospitalization, and treatment history, on the improvement on EF after exercise.

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APPENDICES

1. Feasibility and Enjoyment Questions
2. PANAS Questionnaire
3. HAES Questionnaire
4. University of Ottawa Ethics approval

Appendix 1

1. If our research suggests that the circuit training you just performed improves your ability to participate in your therapy sessions, how likely is it that you would do the circuit training before each therapy session:

1 2 3 4 5 6 7 8 9 10

Not likely Very likely

2. In comparison to other forms of exercise, rate your level of enjoyment in performing this circuit training:

1 2 3 4 5 6 7 8 9 10

Not enjoyable Very enjoyable

3. How likely are you to do physical activity on most days of the week once you are discharged?

1 2 3 4 5 6 7 8 9 10

Not likely Very likely

Appendix 2

PANAS Questionnaire

This scale consists of a number of words that describe different feelings and emotions. Read each item and then list the number from the scale below next to each word. **Indicate to what extent you feel this way right now, that is, at the present moment *OR* indicate the extent you have felt this way over the past week (circle the instructions you followed when taking this measure)**

1	2	3	4	5
Very Slightly or Not at All	A Little	Moderately	Quite a Bit	Extremely

__________ 1. Interested	__________ 11. Irritable
__________ 2. Distressed	__________ 12. Alert
__________ 3. Excited	__________ 13. Ashamed
__________ 4. Upset	__________ 14. Inspired
__________ 5. Strong	__________ 15. Nervous
__________ 6. Guilty	__________ 16. Determined
__________ 7. Scared	__________ 17. Attentive
__________ 8. Hostile	__________ 18. Jittery
__________ 9. Enthusiastic	__________ 19. Active
__________ 10. Proud	__________ 20. Afraid

THE HAES (HABITUAL ACTIVITY ESTIMATION SCALE)

This questionnaire will ask you questions about your daily activities. Please read all of the instructions carefully and answer each question as truthfully as you can.

Name: ____

Date: __________________________

INSTRUCTIONS (please read!)

Please recall the activities of *one typical weekday* (choose from Tuesday, Wednesday or Thursday) and *one typical Saturday* within the past 2 weeks. For each given time period, please estimate the percentage of time that you spent in each of 4 different activity levels. For each of the time periods, the total time spent in all activity levels must add up to 100%.

The different activity levels are described below:

ACTIVITY LEVEL DESCRIPTIONS

These descriptions give you examples of activities that are typical of each activity level. You should refer back to these descriptions as often as you need when completing your estimates.

a) **inactive** – *lying down*, sleeping, resting, napping

b) **somewhat inactive** – *sitting*, reading, watching television, playing video games, time in front of the computer, playing games or activities which are mostly done sitting down

c) **somewhat active** – *walking*, shopping, light household chores

d) **very active** – *running*, jumping, skipping, bicycling, skating, swimming, games that require lots of movement and make you breathe hard and exert yourself

Following is a sample of a completed time period:

SAMPLE

From when you finished breakfast until when you started lunch, please estimate the percentage of time that you spent in each of the following activity levels:

a) inactive	5% (i.e., having a nap)
b) somewhat inactive	60% (i.e., watching TV)
c) somewhat active	25% (i.e., shopping)
d) very active	10% (i.e., riding a bicycle)
TOTAL	100%

WEEKDAY ACTIVITY

For *one typical weekday in the past 2 weeks*, (choose from one of Tuesday, Wednesday or Thursday), please answer the following questions as accurately as possible in the spaces provided.

1. At what time did you get out of bed in the morning? ______
2. At what time did you start eating breakfast? ______
3. How long did you spend eating breakfast? ______ minutes
4. At what time did you start eating lunch? ______
5. How long did you spend eating lunch? ______ minutes
6. At what time did you start eating supper? ______
7. How long did you spend eating supper? ______ minutes
8. At what time did you go to bed that evening? ______

For the *typical weekday* that you are referring to, please estimate the percentage of time that you spent in each activity level.

9. After getting out of bed until starting breakfast:

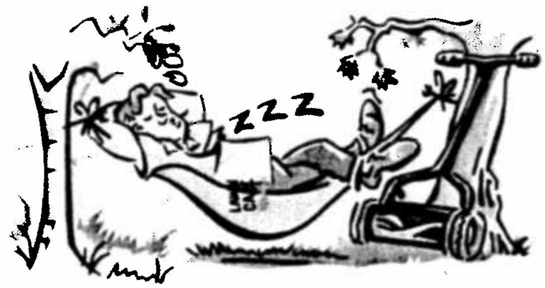
a) inactive _______ %

b) somewhat inactive _______ %

c) somewhat active _______ %

d) very active _______ %

TOTAL	100 %



INACTIVE

10. After finishing breakfast until starting lunch:

a) inactive _______ %

b) somewhat inactive _______ %

c) somewhat active _______ %

d) very active _______ %

TOTAL	100 %

SOMEWHAT INACTIVE

11. After finishing lunch until starting supper:

a) inactive _______ %

b) somewhat inactive _______ %

c) somewhat active _______ %

d) very active _______ %

TOTAL	100 %

SOMEWHAT ACTIVE

12. After finishing supper until bedtime:

a) inactive _______ %

b) somewhat inactive _______ %

c) somewhat active _______ %

d) very active _______ %

TOTAL	100 %

VERY ACTIVE

13. For the *typical weekday* that this questionnaire has asked you about, please rate your overall level of activity (please circle one response only):

a) very inactive
b) inactive
c) somewhat inactive
d) somewhat active
e) active
f) very active

14. Is this "typical" Tuesday, Wednesday or Thursday that you described in this questionnaire (please circle one response only):

a) a lot like most weekdays
b) a little bit like most weekdays
c) a little bit different from most weekdays
d) a lot different from most weekdays

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Office of Research Ethics and Integrity

Lettre d'approbation administrative I Letter of administrative approval

Numéro de dossier / Ethics File Number	H-10-18-1297
Titre du projet / Project Title	The effect of high-intensity interval training on executive functions in adolescents hospitalized for a mental illness
Type de projet / Project Type	Thèse de maîtrise / Master's thesis
CÉR primaire / Primary REB	CHEO / CHEO
Statut du projet / Project Status	Approuvé / Approved
Date d'approbation (jj/mm/aaaa) / Approval Date (dd/mm/yyyy)	26/10/2018
Date d'expiration (jj/mm/aaaa) / Expiry Date (dd/mm/yyyy)	15/07/2019

Équipe de recherche / Research Team

Chercheur / Researcher	Affiliation	Role
Jacqueline LEE	École des sciences de l'activité physique / School of Human Kinetics	Chercheur Principal / Principal Investigator
Patricia LONGMUIR	Département de pédiatrie / Department of Paediatrics	Superviseur / Supervisor

Conditions spéciales ou commentaires / Special conditions or comments:

CHEO REB File #18/91X

Université d'Ottawa
Bureau d'éthique et d'intégrité de la recherche

University of Ottawa
Office of Research Ethics and Integrity

L'Université d'Ottawa a signé une Entente, conforme aux exigences de la plus récente version de l'EPTC et tout autre règlement ou législation applicable, permettant au CÉR ci-haut nommé d'être désigné comme CÉR primaire pour les projets de recherche où

1) les activités principales de recherche sont menées sous l'autorité ou sous les auspices de l'établissement lié au CÉR primaire et

2) Une partie du projet est également réalisé sous l'autorité ou sous les auspices de l'Université d'Ottawa.

Cette lettre confirme que l'Université d'Ottawa a autorisé que le CÉR primaire soit le CÉR officiel pour l'évaluation et la supervision de ce projet de recherche. Ceci n'est pas une approbation éthique.

Afin de nous aider à garder votre dossier à jour, veuillez soumettre une copie de toutes demandes de modification, renouvellement d'approbation éthique etc. soumis à et approuvé par le CÉR primaire dès qu'elles sont disponibles.

Cette approbation administrative est valide pour la durée indiquée ci-haut et est sujette aux conditions énumérées dans la section intitulée « Conditions spéciales ou commentaires ».

The University of Ottawa has signed an Agreement, compliant with current TCPS guidelines and any other applicable guidelines or legislation regarding multisite review, allowing the REB named above to serve as Board of Record (BoR) for research projects where

1) the main research activities are conducted within the auspices or jurisdiction of the BoR's institution and

2) parts of the project are also conducted under the jurisdiction or auspices of the University of Ottawa.

This letter confirms that the University of Ottawa has authorized the REB named above to serve as Board of Record for the review and oversight of this research project. This is not an REB approval.

In order to help us keep your file up to date, please submit a copy of all amendment requests, project renewals or any other changes submitted to and approved by the BoR, as they become available.

Administrative approval is valid for the period indicated above and is subject to the conditions listed in the section entitled «Special conditions or comments».

Catherine PAQUET
Directeur / Director
Pour/For **Daniel LAGAREC** Président(e) du/ Chair of the **Comité d'éthique de la recherche en sciences sociales et humanités / Social Sciences and Humanities Research Ethics Board**