A review of the evidence and recommendations for the development and implementation of onTRACK: A peer-driven program providing alternative and complimentary behavioural therapies for young adults with mental illness

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Plain Language Summary

Purpose

There has been a recent accumulation of research suggesting that activities such as exercise, meditation, and yoga, can help to alleviate symptoms associated with mental illness [1-4]. It has been well established that exercise improves physical health in most individuals whether healthy or unhealthy (with some exceptions for the latter), as well as the well-being and cognitive performance of healthy individuals [5].

This review was conducted in order to evaluate if and how complimentary or alternative behavioural therapies (CABTs; i.e., exercise, mindfulness meditation, and yoga), could benefit young adults with a mood and/or anxiety disorder. We also wanted to address other related questions. We will reformulate our main questions here:

- Can CABTs benefit young adults experiencing mental health challenges?
    - Also, what specific benefits do they have?
- If they do provide benefits, how should CABTs be organized and delivered in order to maximize their beneficial effects?
    - What safety considerations should we keep in mind?

These questions were addressed in order to help guide the development, design, and delivery of a program called ONTrack. ONTrack is a project that was established by Stella's Place in collaboration with the Miles Nadal Jewish Community Center, and aims to provide young adults with mental illness the opportunity to participate in activities providing holistic benefits for mental health—that is, benefits which not only help to manage symptoms or prevent relapse, but which also have positive impacts on other aspects of well-being. For example, we considered things like general physical fitness, relationships, community, and resilience.

Key Findings

Overall, the evidence suggests that exercise, mindfulness, and yoga can each be of benefit to young adults with mood or anxiety disorders [2, 3, 10-12]. The suitability of exercise, mindfulness, or yoga as an alternative to standard interventions (e.g., medication) depends on the severity of one's symptoms.

Individuals with mental illness who participate in CABT group-structured programs can derive important social-relational benefits [13, 14]. CABTs can also mitigate adverse effects associated with medications, counteract negative lifestyle changes (e.g., becoming more sedentary and socially isolated) [13, 15]. CABTs also have positive effects on brain function and improve cognition [10, 16].

Evidence suggests that the antidepressant or antianxiety effects of exercise are optimized when regimens are structured in accordance with public-health guidelines proposed by the American College of Sports Medicine (ACMS) [2]. Most significant findings reported in the

literature have involved forms of aerobic exercise. The majority of evidence demonstrating the positive effects of meditation on the health and well-being of individuals with mood or anxiety disorders was based on studies in which the intervention was based on the Mindfulness-Based Stress Reduction program developed by Jon Kabat-Zinn [10, 18-20]. There are potential adverse effects associated with CABTs which need to be considered before engaging in these activities. For example, mindfulness meditation has been known to trigger episodes of psychosis and mania [22]. Individuals with may be at risk when experiencing significant symptoms of psychosis.

Main Program Recommendations

- In cases of severe depression or anxiety, exercise should only be considered as a form of *supplementary* treatment (not an alternative) to standard forms of treatment (i.e. pharmacotherapy or psychotherapy). In cases of mild to moderate depression or anxiety, on the other hand, a regular and structured exercise regimen *may* serve as a viable *alternative* treatment.
- It is recommended that activities involving aerobic exercise (AEX) constitute the core of the ONTrack program, but incorporating some components of resistance training may help to broaden its appeal.
- Exercise activities should provide opportunities for both group-level and personal engagement. Group activities foster community and social connection; however, offering only group activities imposes too much structure which could undermine autonomy and motivation [23].
- AEX programs should follow recommendations made by ACMS: One-hundred fifty minutes of moderate-intensity exercise per week, which can be, "met through 30-60 minutes of moderate-intensity exercise (five days per week) or 20-60 minutes of vigorous-intensity exercise (three days per week) [24]." For mood disorders, particularly unipolar depressive disorders, the guidelines proposed by the National Institute of Clinical Excellence may also want to be considered [25].
- It is advised that all potential program participants be strongly encouraged to consult with a physician if they should have any doubt regarding their personal safety in performing moderate to high intensity exercise or sport.
- It is recommended that interventions of mindfulness meditation for mood or anxiety disorders follow the Mindfulness-Based Stress Reduction (MBSR) program developed by Jon Kabat-Zinn. Program developers and coordinators are referred to the following sources for detailed information on the program [26, 27].
- It is unclear that as a complementary therapeutic intervention, if one type or branch of yoga is superior to others. The inclusion of the ethical/spiritual dimensions of yoga into the practice yield better outcomes than yoga treated merely as a form of exercise and stretching [28].
- Practitioners guiding meditation sessions, yoga, and related mind-body techniques should be familiar with the potential AEs associated with meditation and should also (ideally) be able to identify warning signs.

Introduction

Terminology

For the purpose of this review, the phrase *young adult* is chiefly reserved for individuals aged 18 to 29 years. Unless otherwise noted, the reader can assume that '*young adult*' refers to this age group or an age group which is otherwise subsumed by it. Owing to semantic disparities among different organizations, governmental agencies, research groups, etc., the phrase *young adult* will on occasion be used in a manner that departs from the definition indicated above. It has been determined that in order to present the clearest picture on the subject matter, occasional flexibility in the definition of *young adult* is warranted, and will ultimately provide more information than what may otherwise be lost. Cases in which the phrase is used while with a different definition—with an age range falling outside of 18-29—will be noted, with the referent age group specified within parentheses. Also, for the purpose of this review, the phrase *early adulthood* should be regarded as synonymous with *young adulthood*.

Rationale

There has recently been a recent accumulation of empirical research suggesting that alternative behavioural therapies, such as exercise (e.g., running and resistance training), meditation (e.g., mindfulness and loving-kindness), and several forms of yoga, can effectively alleviate the symptoms associated with psychiatric disorders ranging from major depressive disorder (MDD), social anxiety disorder (SAD), to schizophrenia (SCZ) [3, 29, 30]. There is also an abundance of epidemiologic evidence suggesting that young adults who regularly engage in exercise are at lower risk of developing mental illness [31-33], though see [34]. Individuals are also able to derive important benefits to their well-being from the social aspects of exercise-related activities or sport [14]. Moreover, practices such as mindfulness meditation (MM) and aerobic exercise (AEX) can enhance pharmacological response, shorten illness duration, and prevent relapse [35, 36].

Epidemiology of Mental Illness among Young Adults

- Worldwide, young adults are affected by mental illness at a disproportionately higher rate compared to the general population [6].
- The 12 month prevalence rate of mental illness among Ontarian young adults (aged 15-24) has been estimated at 16.8-25% [7-9]
- Psychiatric disorders are the largest contributor to the global population risk of suicide [17], and suicide is cited as the second leading cause of death among Canadian young adults 15-24 years-of-age [21].
- The majority of psychiatric disorders have an age-at-onset in late adolescence or early adulthood.
- Data on specific 12 month and lifetime prevalence rates associated with common psychiatric disorders among Ontarian young adults is shown in *Table I* (next page).

Table I. 12 month and lifetime prevalence of psychiatric and substance-use disorders among young adults (aged 15-24) living in Ontario[a,b].

	12 Month		Lifetime	
Psychiatric Disorder	Rate (%)	95% CI	Rate (%)	95% CI
Any (except social phobia)[c]	16.8	13.9-19.7	27.3	23.9-30.8
Any Mood Disorder	7.8	5.6-10.1	11.7	9.3-14.1
Major Depression	6.6	4.6-8.6	9.6	7.4-11.9
Bipolar Disorder	2.4[d]	1.2-3.6[d]	4.0[d]	2.6-5.4[d]
Generalized Anxiety	1.5[d]	0.7-2.2[d]	5.5	3.8-7.2
Social Anxiety Disorder[c]	10.4	____	16.1	____
Any SUD	10.7	8.2-13.1	18.7	15.4-21.9
Alcohol Abuse/Dep	6.3	4.5-8.2	13.1	10.3-15.9
Cannabis Abuse/Dep	4.9[d]	5.8-10.1[d]	10.3	7.9-12.8
Other Abuse/Dep	1.7[d]	0.7-2.8[d]	3.5[d]	2-4.9[d]

Data from Statistics Canada [8], with the exception of social phobia (see note below). [a]*12 month prevalence* is the proportion of individuals within a population that has the disease/illness at any point during a specified 12 month period; [b]*Lifetime prevalence* refers to the proportion of the population that has or has ever had the disease/illness at the time of assessment. [c]Data obtained cross-sectionally by the Ontario Community Health Survey Mental Health Supplement, as referenced in Stein & Kean [37]. [d]High coefficient of variation—interpret/use with caution; Abbreviations: CI = Confidence interval; SUD = Substance use disorder; Dep = Dependence

Here, we survey the literature to assess how such alternative therapies, or related lifestyle practices, can be optimally utilized by young adults experiencing mental health challenges to benefit themselves. We have conducted this review in order to inform the development and implementation of an evidence-based, peer-driven program dubbed 'ONTrack, which aims to provide a holistic approach to wellness and recovery (while fostering resilience, self-determination, and social connectedness) specifically tailored to young adults. That being said, we consider the evidence within the backdrop of three core areas of need/concern which have been identified as being particularly relevant to young adults with mental illness. We begin by outlining these areas.

Core Areas of Need or Concern for Young Adults with Mental Illness

(1) Ongoing psychosocial and neurobiological development

When asked about the most significant events shaping the course of their life, the majority of older adults will recount experiences from their early adulthood [38]. Young adulthood represents a critical stage of psychological development, especially with respect to identity formation. Traditional theories of identity formation have tended to focus on adolescence, when in fact the most important phases of identity formation occur during the late teens and twenties [38]. Granted, substantial changes in demographic trends in the last several decades, especially within industrialized societies, have partly contributed to this disparity [39, 40]. As Arnett [38]

The substantial psychological change that accompanies young adulthood underscores the need for our communities to undertake initiatives that support young adults experiencing mental health challenges…

points out, there has been a considerable extension to the time in which young adults have the opportunity for, "exploration in the areas of work, love, and worldviews." It is for this reason that Arnett prefers the expression emerging adulthood over young adulthood to describe this demographic. It is through the process of shaping one's identity that he or she ultimately comes to define themselves within the context of their relationships, communities, and society at large. The substantial psychological change that accompanies early adulthood underscores the need for our communities to undertake initiatives that support young adults experiencing mental health challenges by providing them with opportunities to engage in activities that enrich their psychological development and facilitate the formation of a secure and healthy identity.

Not only does psychosocial development persist into young adulthood, but neurobiological development continues as well. The myelination of neurons (i.e. brain cells) —a process in which a fatty tissue envelops the 'connecting' segments of neurons so as to allow efficient communication within the nervous system— in a brain region known as the prefrontal cortex does not finish until approximately age 25 [41, 42]. Full maturation of the PFC is integral to cognitive functions such as impulse control, planning, and decision making [43]. The notion of post-adolescent neural development is consistent with behavioural differences observed when comparing individuals in their late teens to those in their mid-twenties. On average, 18 year-olds show poorer performance on a gambling task compared to 25 year-olds. This related to differences in risk-seeking behaviour in which 18 year-olds make riskier (and disadvantageous) bets compared to 25 year-olds [44].

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The occurrence of mental illness, such as MDD and SAD, may impede or disrupt post-adolescent neural development. (However, it has also been proposed that the origins of mood and anxiety disorders are themselves neurodevelopmental by nature; for example, see [45].) There is an abundance of evidence demonstrating aberrant activity of the prefrontal cortex in depressed and anxious individuals [46-48]. For example, neuroimaging studies have found that a large portion of individuals with MDD exhibit hyperactivity in the ventromedial PFC (vmPFC; an area of the brain involved in emotion regulation) and hypoactivity in the dorsolateral PFC (dlPFC; a brain region linked to rational thought and problem solving) in comparison to healthy controls [49]. Moreover, the negative impact of chronic stress on the prefrontal cortex and neurodevelopment has been well documented [50, 51], and mood and anxiety disorders are well characterized as disorders of a dysregulated stress response [52, 53]. Thus, it stands to reason that the disrupted brain activity and chronic stress associated with mood and anxiety disorders may negatively affect post-adolescent neural development.

(2) Negative lifestyle changes and auxiliary health effects

Compared to the general population, individuals with mental illness engage in significantly lower amounts of exercise and general physical activity [54-59]. There are numerous barriers to physical activity in the context of mental illness, such as fear of leaving one's residence, anhedonia (i.e. lack of motivation), fatigue, medication side-effects, and a lack of self-efficacy, to name a few examples.

Although other factors are also involved (as we shall see below) this is one reason that individuals with mood disorders are at higher than normal risk of developing metabolic abnormalities (e.g., insulin resistance, overweight and obesity), even among young adults [55]. Later in adulthood, this often translates into the development of diabetes type 2 and cardiovascular disease (CVD) [60].

As can be observed based on the prevalence data in Table I, substance use/dependence is a serious problem among young adults. In fact, it is the most pervasive mental health problem encountered by Ontarian young adults. However, SUDs are highly comorbid—that is, they commonly occur in conjunction with other forms of mental illness [52]. Importantly, SUDs among young adults (aged 18-30) primarily develop *after* the onset of a mood or anxiety disorder [61]. This suggests that young adults are frequently turning to alcohol and other drugs as a means to cope with illness symptoms and impairment in psychosocial function. Social isolation is another example of an auxiliary problem arising from mental illness which can impede psychosocial development and decrease quality of life.

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(3) Insufficient efficacy and adverse effects associated with pharmacotherapy

Although pharmacological treatments for mental illness have been proven effective, approximately only a 1/3 of individuals fully respond to first-line psychotropic interventions. Another1/3 shows only a partial response and will experience persistent residual symptoms. Another 1/3 fails to respond at all, even after trying several different pharmacological trials [29, 62-64].

In addition to a lack of efficacy, many psychotropic drugs are associated with adverse effects (AEs) which can cause metabolic disturbances, such as weight gain and glucose dysregulation, thereby increasing risk of diabetes and cardiovascular disease. Antidepressants (i.e. mirtazapine and paroxetine), mood stabilizers (i.e. lithium and valporate), and almost all antipsychotics, especially the so-called second-generation 'atypical' antipsychotics (SGAs), all have the potential to induce metabolic abnormalities [65-67].

Psychotropic drugs are also commonly associated with other AEs, including insomnia, sedation, and sexual dysfunction, to name a few [68-70]. Even if core symptoms of the disorder are managed, the persistence of AEs can lead to impairments in other areas of life, which can potentially become their own source of stress depression and/or anxiety. Sexual dysfunction, for

example, can be particularly distressing and frustrating for young adults, as many of them are just beginning to explore their sexuality. Another example is weight-gain, which can lead to a negative body image and reductions to self-esteem. It is for this reason that AEs are a major cause of treatment discontinuation and non-compliance [65, 70]

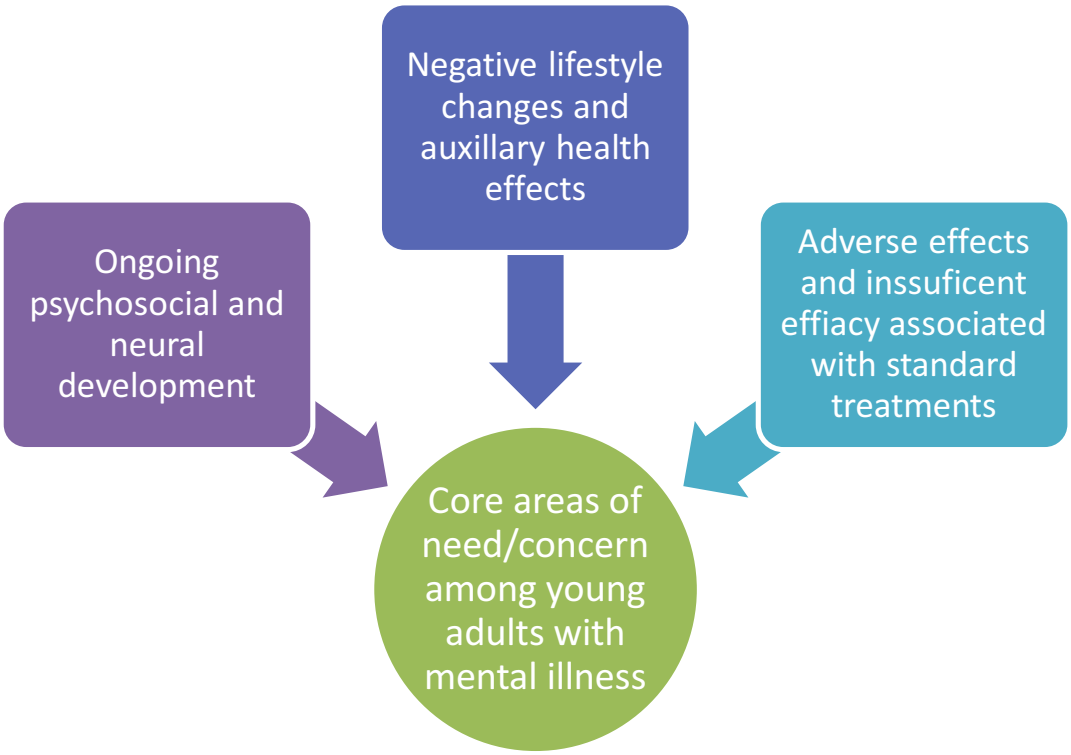

Figure 1. Core areas of need or concern among young adults with mental illness. It is proposed that complimentary and/or alternative behavioural therapies (namely exercise, meditation, and yoga), if structured appropriately, can benefit young adults with mental illness by alleviating symptoms, supporting ongoing psychosocial and neural development, counteracting negative lifestyle changes or auxiliary problems caused by mental illness, and by mitigating adverse effects associated with the psychotropic drugs which are used to treat these conditions. Importantly, these *complimentary* treatments augment standard treatments, which often fail to fully resolve symptoms.

Getting ONTraxk: The Role of Complimentary/Alternative Therapies in a Peer-Driven Program to Support Young Adults with Mental Illness

Please refer to *Table II* for an overview of the results on the effectiveness of exercise, mindfulness, and yoga for mood disorders. Please refer to *Table III* for an overview of the results on the effectiveness of exercise, mindfulness, and yoga for anxiety disorders. Note: The *methods* section is presented at the end of this document.

Exercise

i. Recommended Indications

a) Depression and Depressive Symptoms Associated with Mood Disorders (Excludes Perinatal Depression)

b) Anxiety Disorders (Generalized Anxiety Disorder, Panic Disorder, and Social Anxiety Disorder Generalized Anxiety Disorder)

- The overall evidence suggests that exercise can be an effective complementary or alternative behavioural treatment for depressive symptoms associated with mood disorders (e.g., MDD, bipolar disorder, dysthymia, etc.) and anxiety symptoms associated with anxiety disorders.
    - In cases of severe depression or anxiety, exercise should only be considered as a form of *supplementary* treatment (not an alternative) to standard forms of treatment (i.e. pharmacotherapy or psychotherapy).
    - In cases of mild to moderate depression or anxiety, on the other hand, a regular and structured exercise regimen *may* serve as a viable *alternative* treatment.

ii. Type(s) and Structure (e.g., frequency, intensity, group vs. home setting, etc.)

- The majority of empirical evidence in support of exercise having beneficial effects for individuals with mental illness (e.g., symptom reduction and improved well-being) is derived from studies on aerobic exercise (hereafter, AEX), such as running or cycling [2, 30, 71]. However, there is also evidence suggesting that resistance training can also benefit individuals with mood or anxiety disorders [72].
    - That said, it is recommended that activities involving AEX constitute the core of the ONTrack program.
    - Still, it may be worthwhile to consider including components of resistance training, as this may broaden the appeal of the program. It may also improve retention rates for individuals who struggle with cardiovascular fitness, but who otherwise excel in terms of their muscular endurance.
- In terms of structuring and organizing exercise regimens so as to derive optimal therapeutic (i.e. antidepressant) benefits, a number of guidelines have been proposed by professional societies and researchers.
- With respect to depressive symptoms associated with mood disorders, a recent systematic review and meta-analysis published by the Cochrane Library concluded that studies showing the greatest benefits to mental-health had designed interventions in accordance with recommendations proposed by the American College of Sports Medicine [2]:
    - One-hundred fifty minutes of moderate-intensity exercise per week, which can be, “met through 30-60 minutes of moderate-intensity exercise (five days per week) or 20-60 minutes of vigorous-intensity exercise (three days per week) [24].”

    - Moreover, evidence suggests that individuals are more likely to maintain a moderate-intensity exercise regimen compared to a vigorous or low intensity exercise regimen [72].
    - This is finding is also supported by observational data derived by Mata and colleagues via experience sampling [73]. They also identified a *dose response effect*—that is, periods of moderate or high-intensity physical activity were associated with greater positive affect than periods of low-intensity activity. This is consistent with previous reports from Dunn and colleagues [71, 74].
- Guidelines from the National Institute for Health and Clinical Excellence (NICE) recommend that structured physical activity programs for the treatment of mild to moderate depression (or persistent subthreshold symptoms) should [25]:
    - Be delivered within a group setting with support from a competent practitioner
    - Should usually involve at least three sessions per week (lasting from 45 minutes to an hour) for at least 10-14 weeks
- To the best of our knowledge, there has yet to be any guidelines established by professional societies or expert panels on the use of exercise as a complimentary or alternative therapeutic intervention for anxiety disorders.
    - However, most studies to date have designed exercise interventions for anxiety disorders with program variables approximating the ACMS guidelines previously mentioned [24].

iii. Risks and Adverse Effects (AEs)

- The most common AEs associated with exercise are minor musculoskeletal injuries [2]. However, there is no evidence suggesting that the risk of minor (or serious) musculoskeletal injuries is any different from that of healthy participants. That being said, it seems that with proper instruction and/or guidance, the risk of injury is minimal.
- Very few, if any, risks/adverse effects related specifically to the symptomatology of mood disorders or anxiety disorders have been identified.
    - There is some anecdotal evidence derived from a qualitative study suggesting that exercise can exacerbate symptoms of mania [75]. Still, while some participants have claimed that exercise heightens symptoms of mania or hypomania, others have cited exercise as a useful tool for self-regulation and relaxation during episodes of mania or hypomania.
        - More research is needed to clarify any potential interactions between exercise and the phase of BP illness, as well as when and if these interactions help or harm individuals with BPDs. At present, the evidence seems to be in favour of positive outcomes over negative ones.
- There is a risk of AEs associated with interactions between exercise and drugs prescribed for the treatment of mood or anxiety disorders, as well as other concurrent psychiatric or non-psychiatric conditions. However, an in depth report on these interactions is far

beyond the scope of this review. For a comprehensive treatment of this subject, the reader is referred elsewhere [76]. We do, however, report on a few notable findings that came to light during the review process:

  - One report suggested that AEX was accompanied by a worsening of side-effects associated with the SSRI sertraline (Zoloft) [2].
  - Dehydration presents a particular problem for individuals receiving lithium therapy, as lithium retention (in response to dehydration) can result in the accumulation of toxic levels of the drug. That said, it is particularly important that individuals receiving lithium therapy remain adequately hydrated during periods of exertion [77].

- It is advised that all potential program participants be strongly encouraged to consult with a physician if they should have any doubt regarding their personal safety in performing moderate to high intensity exercise or sport.
- It is important to note that prospective participants may have a comorbid medical condition that is contraindicated with exercise or sport (see [9] for a detailed list). Hopefully they are aware of that.
- While the program developers and coordinators should do everything in their power to inform individuals of potential risks and contraindications outlined here (and in referenced materials), participants will ultimately have to assume liability for their own safety. Necessary legal documentation (e.g., liability release waiver) should be acquired.

iv. Other Benefits, Relationship to Core Areas, and Additional Program Considerations

- For individuals who have recovered from MDD, exercise promotes resilience to negative mood induction via repeated exposure to emotional stressors, and can thereby potentially mitigate the likelihood of relapse [78].
- Group exercise and sport simultaneously afford opportunities to promote identity formation and to counteract issues related to social isolation:
  - Exercise in the form of team sports or games aimed at achieving a ***common goal*** (e.g. “capture the flag”) are most likely to encourage interaction among peers.
  - However, similar social benefits may be derived from other forms of exercise held in group settings in which the activity itself does not necessitate direct social interaction [13, 79].
  - Activities that involve both AEX and opportunities for social interaction (in context of achieving common goals) are important as they can create and instill a sense of community within participants. Community is essential to the process of identity formation [80, 81].
  - Independent exercise activities are equally important; only offering structured or group activities may prevent the expression of autonomy needed to sustain motivation. Furthermore, individuals with social anxiety disorder or agoraphobia

may feel too overwhelmed to participate in group activities and could be discouraged.

- Evidence suggests that exercise upregulates levels of brain-derived neurotrophic factor (BDNF), a biological molecule essential for neural health and development [82, 83]. Furthermore, BDNF has neuroprotective effects which mitigate the negative effects of stress on the brain [84]. Increased BDNF has also been associated with improvements in cognition (e.g., learning and memory).

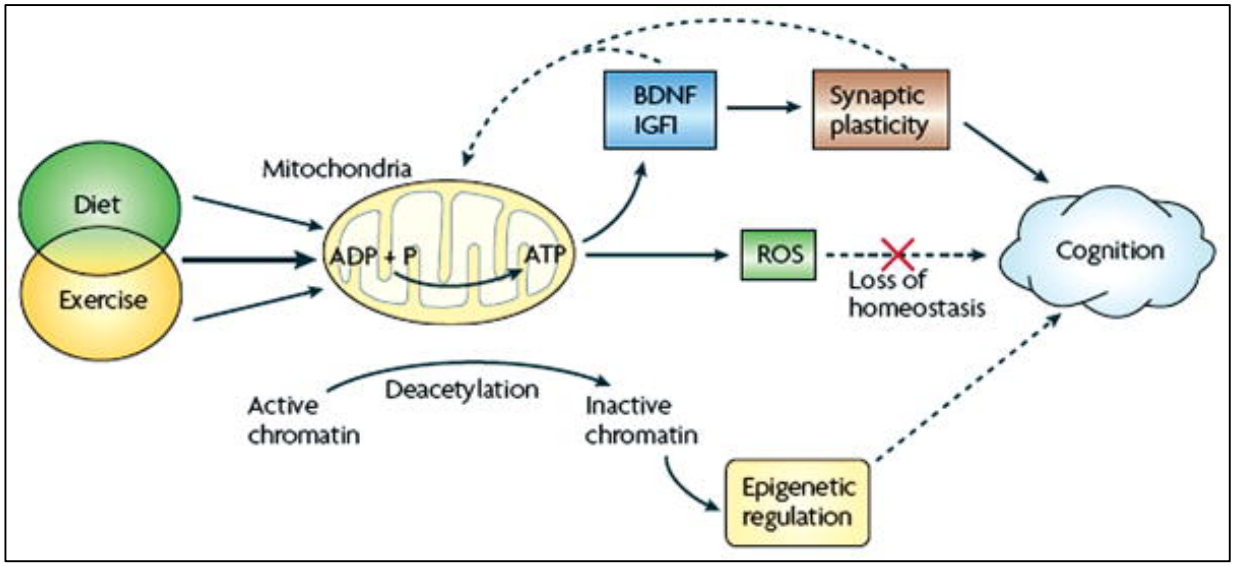

Figure 2. Hypothetical mechanism through which exercise improves cognition. Exercise, in combination with proper diet may have specific regulatory effects on mitochondrial energy production (ATP). ATP is integral for maintaining proper neuron function. Certain energy evets elicited by exercise activate pathways leading to the production of brain-derived neurotrophic factor (BDNF) and insulin-like growth factor 1 (IGF1). BDNF and IGF1 support synaptic plasticity, a process essential for developing and strengthening connections between neurons. The strengthening and formation of new neural connections underlie improvements in cognitive capacity, such as verbal memory and attention. Exercise and proper diet counteracts excess energy production that results from high caloric diets. Excess energy results in the formation of reactive oxygen species (ROS), which can disrupt cellular homeostasis. ROS are implicated in the development of mental disorders. Exercise and diet may also modulate epigenetic levels of control. Epigenetic regulation directly affects levels of genetic expression. Adapted from Gomez-Pinilla & Hillman [85].

- Exercise can also mitigate various adverse effects associated with psychotropic drugs used to treat mood and anxiety disorders.
- There has been mixed evidence as to whether exercise actually leads to improvements in the overall quality of life for persons with mental illness [5].

v. Limitations of Evidence & Caveats

- Common genetic factors

    - The need for caution in interpreting data derived from correlational or epidemiological studies is highlighted by De Moor and colleagues [34] who show that genetic factors predisposing tendencies to engage in exercise behaviour also explain resilience to depressive symptoms.
    - However, their study does not necessarily contradict findings from RCTs, as their methodology does not allow the extension of these findings as a counterargument to *prescribed* or *structured* exercise regimens or sport engagement.

- One meta-analysis which examined 10 studies suggests that the antidepressant effects of exercise may possibly be limited to elderly populations and individuals with mild depressive symptoms [86].
    - Nevertheless, the relatively small number of studies included in this meta-analysis restricts the strength of this claim. To the best of our knowledge, there are no comparative studies of age-specific effects on exercise outcomes in the context of mental illness. In fact, there is a paucity of high quality RCTs limited to young adult populations (of any range between 15-29 years).

Meditation & Yoga (Hatha)

i. Recommended Indications

a) Depression and Depressive Symptoms Associated with Mood Disorders (Excludes Perinatal Depression)

b) Anxiety Disorders (Generalized Anxiety Disorder, Panic Disorder, and Social Anxiety Disorder)

ii. Type(s) and Structure (e.g., frequency, intensity, group vs. home setting, etc.)

- In considering the evidence reviewed [10, 18-20, 27, 29, 87] (see *Table III* for the details on a selection of the studies reviewed), it is recommended that interventions of mindfulness meditation for mood or anxiety disorders follow the Mindfulness-Based Stress Reduction (MBSR) program developed by Jon Kabat-Zinn
    - Program developers and coordinators are referred to the following sources for detailed information on the program [26, 27].
- Mindfulness meditation has also been integrated with cognitive behavioural therapy to constitute what is known as mindfulness-based cognitive behavioural therapy (MBCT). Incidentally, the development of MBCT was informed by the techniques proposed by Kabat-Zinn [26, 27]. Cognitive behavioural therapy (CBT) requires meta-cognitive, or introspective, awareness. It was apt to combine a technique that actively cultivates meta-cognitive awareness with CBT, as this should theoretically improve its success by allowing patients to pay better attention (non-judgmentally) to and identify their thought distortions. Participants who have practiced and are familiar with CBT may find that cultivating a meditation practice can facilitate CBT.

- There is support for yoga having beneficial effects as a complementary intervention for mood or anxiety disorders.
- With respect to yoga, a number of different forms and styles have been examined in relation to mood or anxiety disorders. At this point in time, it is not evident that one style or branch of yoga is more effective than others in terms of benefiting individuals with anxiety or mood disorders.
    - From a logical standpoint, it seems that a complex form of yoga that integrates elements of breath work, posture, physical activity, and meditation would be the most effective.
    - A randomized-control trial exclusively involving young adult participants experiencing mild depression or anxiety showed that Iyengar was effective at reducing symptoms and improving mood [4]. It may also modulate levels of cortisol, a stress hormone that is typically elevated within depressed patients. However, participants in this study were not derived from a clinical population and were selected solely based on measures of self-report.
    - The inclusion of the ethical components of yoga grounded within its spiritual tradition has been shown to be superior to the common Western practice of yoga, which more or less tends to treat it as a form of exercise and stretching [28]. Participants within the integrated yoga group involving a spiritual/ethical component reported lower anxiety levels and had a greater decrease in cortisol levels compared to the 'yoga as exercise group'.

iii. Risks and Adverse Effects (AEs)

- Physical AEs:
    - Meditation and yoga can both involve sustaining certain postures that are usually unfamiliar to novices.
    - The ability to assume certain postures might require greater flexibility than an individual currently has. Thus, it is important that beginning students do not overdue themselves, as this may potentially cause muscle strains or other musculoskeletal injuries.
- Psychological AEs:
    - The psychological AEs associated with meditation or yogic practices have tended to be downplayed, if not completely ignored, by the popular media. However, there are a number of potential AEs that prospective (and current) students and teachers should be made aware of. The following set of adverse effects have been reported in association with meditation and yogic practices [88, 89]:
        - Non-severe AEs: anxiety, tension, reduced motivation, boredom (usually acute and limited to the meditation session or parts thereof, but not exclusively)
        - Severe AEs: confusion and disorientation, dissociation, impaired reality testing (psychosis-like symptoms), panic, grandiosity, 'destructive behaviour', suicidal ideation, vivid recall of traumatic experiences

    - Numerous psychiatric case reports have described cases of meditation-induced psychosis [22].
        - Individuals with previous psychiatric history (especially past episodes of psychosis), sleep deprivation, or who are malnourished are at the greatest risk of meditation-induced psychosis.
- Practitioners guiding meditation sessions, yoga, and related mind-body techniques should be familiar with the potential AEs associated with meditation and should also (ideally) be able to identify warning signs.
    - If the practitioner is unable to provide guidance to an individual within the context of the meditative experience, he or she should be able to refer that person to a more seasoned practitioner who can provide such guidance (for example, Philip V Starkman of Toronto, a psycho-spiritual therapist).
    - This is not to say that a participant should not also speak with their physician, but they may also wish to approach the problem within the context of the spiritual tradition within which mindfulness meditation is grounded.
- Fortunately, the severe AEs listed here are relatively uncommon. Nevertheless, they represent a concern that practitioners should be aware of.
- While the program developers and coordinators should do everything in their power to inform individuals of the potential risks and contraindications outlined here (and in referenced materials), participants will ultimately have to assume liability for their own safety. Necessary legal documentation (e.g., liability release waiver) should be acquired.

iv. Other Benefits, Relationship to Core Areas, and Additional Program Considerations

- Mindfulness meditation, especially when combined with CBT, has been widely recognized as an effective means for preventing the recurrence of depressive episodes [90, 91]. Similarly, yoga has also been shown to be effective in preventing relapse [92].
- Mindfulness meditation increases attentional control and can thereby improve impulse-control and emotion-regulation. Neuroimaging studies have demonstrated that improvement in these cognitive functions as a result of mindfulness meditation is correlated with increased activation within areas of the prefrontal cortex that have been implicated in these cognitive functions [10, 11, 18].
    - It was mentioned that young adults do not attain full brain maturation until approximately age 25 and that the PFC is one of the last regions of the brain to finish developing [41]. Moreover, this has been directly correlated with age-specific differences in risk-seeking behaviour and emotion-regulation [41, 44].
    - Mindfulness meditation may serve to support post-adolescent neurodevelopmental processes attenuated by functional and structural brain abnormalities associated with mood and anxiety disorders. .
- Mindfulness and yoga have both been shown to enhance cognitive functions and may thereby help to mitigate cognitive impairment associated with depression, bipolar disorder, anxiety, or drugs used for their treatment.

v. Limitations of Evidence & Caveats

Several of the studies reviewed and considered within the evidence have samples comprised of non-adult populations. Owing to the paucity of the studies exclusively examining young adult samples, however, a compromise was required to attain enough evidence to make reasonable assessments for program recommendations and considerations. Although unlikely given the criteria applied in study selection (see methods), age-specific-effects cannot be completely ruled out.

Methods

The US National Library of Medicine MEDLINE (Ovid) database was searched using the following combination of key-terms or matched subject-headings: (Depression or Major Depression or Bipolar Disorder or Schizophrenia or Psychotic Disorders or Anxiety Disorders or Obsessive-Compulsive Disorder or Phobic Disorders) AND (Exercise or Exercise Therapy or Mindfulness or Meditation or Yoga). The following limits were imposed: English language and humans"1990 –Current; and "Young Adult and adult (19-24 and 19-44)" and (Journal Article or Meta-Analysis or Review or Systematic Reviews). The search strategy yielded an initial 946 hits. After the removal of duplicates, 887 papers remained. Exclusion criteria included: 1) Publication not peer-reviewed; 2) Commentaries, letters-to-the-editor, or perspective pieces; 2) Study samples with co-morbid medical conditions (e.g., cardiovascular disease, cancer, Alzheimer's disease, traumatic brain injury, etc.); and 3) Pediatric or geriatric samples or a mean-sample-age > 40 years; or 4) Articles tangentially or not at all related to mental illness and alternative therapies were also excluded. The second and third exclusion criteria were not applied in the case of meta-analyses, in which case it was necessary that at least 50% of the studies included had a mean sample age ≤40 year, no more than 15% of studies involved patients with concurrent non-psychiatric illness, and that metaregression analyses were performed in order to assess potential confounding effects by these variables. After exclusion criteria were applied, 74 articles remained. Reference lists of retained publications were screened for other potentially relevant studies. Owing to an abundance of literature, emphasis is placed on major depressive disorder and anxiety disorders, as these are among the most common mental disorders afflicting young adults (for which data is available). Nevertheless, some consideration is also given to bipolar disorders.

Table II. Studies on the effectiveness of alternative and/or complimentary behavioural therapies for mood disorders or related symptoms

Study	Diagnosis & Participants	Intervention(s)	Main Outcome Measure(s)	Significance
De Moor et al. [34] Cross-sectional study on data collected during a period of up to 11 yrs.	Anxious and depressive symptoms (ADS); *N* = 15, 961; After exclusion criteria and selection, ~ 6200 twin pairs per cross-sectional analysis with (Age *M* = 27.9 yr., *SD* = 8.0) Mostly Caucasian;	Population based (cross-sectional and longitudinal) study; not an intervention per se. Looked at monozygotic (MZ) and dizygotic (DZ) twins to try and parse apart a causal effect of exercise on ADS from genetic factors correlated with exercise behaviour.	Survey data about leisure - time exercise (MET hours per week based on type, frequency, and duration); 4 scales (e.g., young adult self-report scale) of ADS.	Small associations best explained by common genetic factors with opposite effects on exercise behav and ADS. In MZ twins, the twin who exercised more *did not* display ↓ ADS than the co-twin who exercised less; ↑ exercise participation did not predict ↓ ADS; suggests epidemiological studies should be interpreted with caution
Mata et al. [73] Observational; 7-8 days	MDD (DSM–IV & score > 14 on BDI); *N* = 106; (Age *M* = 26.8, *SD* = 6.4) MDD *n* =53; healthy control *n* = 53	Observational study; prompts delivered via a hand-held device assessing current or recent physical activity (PA), and associated positive affect and negative affect	Positive (+) & negative (-) affect after PA. PA was measured in metabolic task equivalent (MET) minutes.	Participants w/ MDD and controls reported higher levels of (+) affect at prompts after PA vs. prompts after inactive periods; MDD group in particular showed a dose-response effect of PA on (+) affect: longer duration and/or higher intensity of PA ↑ (+) affect significantly more than short duration and/or lower intensity PA.
*Dunn et al. [71]; RCT, 12 weeks	MDD (DSM-IV) of mild to moderate severity (HRSD-17); *N* = 80; (Age *M* = 35.9, *SD* = 6.4) 70% female	(1) Low dose AEX (7 kcal/kg /week) at 3x/week; (2) Low dose AEX at 5x/week; (3) Public-health dose (17.5 kcal/kg/week) 3x/week; (4) Public health dose 5x/week; (5) Exercise placebo ctrl, ~25 min stretching 3x/week	Change in score from baseline on the 17-item Hamilton Rating Scale for Depression (HRSD-17)	Sig main effect of energy expenditure in reducing HRSD-17 scores at 12 weeks was sig. Adjusted mean HRSD-17 scores at 12 weeks were reduced 47% from baseline for public-health dose, compared with 30% for low dose and 29% for control; absence of sig main effect for exercise frequency at 12 weeks
Bartholomew et al. [93]; RCT, 1 day	Onset of MDD (DSM-IV); No concurrent drug therapy or psychiatric diagnosis; *N* = 40; M/F: 15/25 (Age *M* = 38.1)	(1) Single bout of AEX (fast walking on treadmill) at 60–70% of age-predicted maximal heart rate for 30 min; (2) 30-min period of quiet rest (control)	Profile of Mood States and Subjective Exercise Experiences Scale delivered 5 min before, and 5, 30, and 60 min post-intervention	Both groups reported similar reductions in measures of psychological distress, depression, confusion, fatigue, tension, and anger. Only the exercise group, however, reported a significant increase in positive well-being and vigor.

Abbreviations: AEX = Aerobic exercise; ADS = Anxious and depressive symptoms; BDI = Beck Depression Inventory; Behav = Behaviour; DSM-IV = Diagnostics and Statistical Manual for Mental Disorders 4th Edition; HRSD = Hamilton Rating Scale for Depression; ICD-10 = International Classification of Diseases 10; MDD = Major depressive disorder; PA = Physical activity

Table II. Continued

Study	Diagnosis & Participants	Intervention(s)	Main Outcome Measure(s)	Significance
*Silveira et al., [86]; Meta-Analysis of 10 studies.	MDD (DSM-IV, ICD-10, RDC, and CIS); *N* = 758;	(1) AEX, (2) Resistance training (RET); (3) AEX + pharmacotherapy; (4) RET + pharmacotherapy (5) Pharmacotherapy alone; Also considered frequency, intensity, or if AEX was supervised or unsupervised.	HRSD; yes/no outcomes were also used for the proportion of remission (% reduction of MDD symptoms below the cutoff) and response (at least 50% decrease from initial score)	Statistically sig difference between AEX and control (p = 0.001), and trending sig when comparing RET with control (0.06); combined sig *P* < 0.001. Metaregression analyses showed that only elderly subjects and patients with mild depressive symptoms present a better treatment response with AEX compared to controls.
*Rosenbaum et al. [30]; Meta-analysis of 20 studies	Any mental illness diagnosed with DSM-IV or ICD-10 criteria (except SCZ, anorexia nervosa or dysthymia).	AEX (13), Yoga (1), Tai-chi (2), RET (1), AEX + RET (2) , Exercise counselling, and lifestyle change programs with a large component dedicated to AEX	Standardized mean differences[a] (SMDs) of HRSD, GDI, EPN, DASS, IDS, CES-D	There was a sig large pooled effect of physical activity on depressive symptoms (SMD = 0.8; 95% CI: 0.47-1.13; *P* < 0.001). Larger effect for interventions that met ACSM aerobic training guidelines. Smaller in high quality studies.
*Cooney et al., [2]; Meta-analysis	Depression made by any diagnosis or of any severity; *N* = 1356 from a total of 37 RCTs.	Exercise as defined by ACSM: "Planned, structured and repetitive bodily movement done to improve or maintain one or more components of physical fitness [72]." (Excludes Yoga)	Pooled SMDs across numerous scales and outcomes, but mainly BDI and HRSD	Pooled SMD for the main outcome of depression at post-treatment was -0.62 (95% CI: -0.81 to -0.42), suggesting a modest clinical effect. "…The evidence about whether exerciser for depression improves quality of life is inconclusive [2]."
*Cramer et al., [12]; Meta-analysis of 12 RCTs.	MDD or elevated levels of depression (DSM-IV; ICD-10, HRSD, BDI, CES-D and others); *N* = 619; Median Age: 33.7	(1) Complex forms of yoga integrating PA with breath techniques & meditation. (2) Exercise based yoga without breath or mediation exercises. (3) Breath, lifestyle or meditation practice grounded in Yoga, but no PA.	SMDs of changes in severity of depression (originally measured with BDI, HRSD, etc.) Remission rates	For depression severity, "there was moderate evidence for short-term effects of yoga compared to usual care (SMD = −0.69; 95% CI: −0.99, −0.39; P < .001), and limited evidence compared to relaxation (SMD = −0.62; 95% CI −1.03, −0.22; P = .003), and aerobic exercise (SMD = −0.59; 95% CI −0.99, −0.18; P = .004) [12]."

[a]SMD allows different outcome measures to be compared via score standardization: (Intervention Improvement (*M*) - Placebo Improve-ment (*M*)) / (Standard Deviation).
[c]The Cooney et al., [2] meta-analysis included four studies of patients with concurrent physical health problems (e.g., CVD). Abbreviations: AEX = Aerobic exercise; ACSM = American College of Sports Medicine; BDI = Beck Depression Inventory; CES-D = Centre for Epidemiologic Studies Depression Scale; DASS = Depression Anxiety and Stress Scale; EPDS = Edinburgh Postnatal Depression Scale; GDI = Geriatric Depression Index; HRSD = Hamilton Rating Scale for Depression; PA = Physical activity; RDC = Research diagnostic criteria; RET = Resistance training; *Should be weighted more heavily when considering program development.

Table II. Continued

Study	Diagnosis & Participants	Intervention(s)	Main Outcome Measure(s)	Significance
Salehi et al., [82]; RCT; 6 weeks (first 2 wks just SSRI)	Treatment Resistant MDD (DSM-IV, BDI ≥ 30, HRSD ≥ 25); *N* = 60 (Age *M* = 31.45, *SD* = 6.75); 31.6% females	(1) Electroconvulsive therapy (ECT) only; (2) ECT & AEX; (3) AEX only; All groups received concurrent citalopram (SSRI) at 40 mg/day	Change in BDI and HRSD from baseline. Change in serum brain-derived neurotrophic factor levels from baseline.	Sig ↑ in BDNF levels across time in all three study conditions. At post-intervention, the ECT group showed sig higher BDNF levels com-pared to the ECT + AEX and the AEX conditions. Sig ↓ in depression in each group, though the ECT + AEX condition led to a sig greater decrease for either ECT or AEX alone.
Woolery et al. [4]; RCT; 5 weeks	Mild depression as reported by BDI. *N* = 28 (Age *M* = 21.5, *SD* = 3.23)	(1) 2 x 1-hour Iyengar yoga classes per wk for 5 conse-cutive weeks; (2) Waitlist control	Changes from baseline in self-reported measures (BDI, State-Trait Anxiety Inventory, and Profile of Mood States) and morning cortisol levels	Sig ↓ in symptoms of depression and trait anxiety were observed by the middle of the intervention and persisted until the end. Following yoga classes, participants reported acute elevations in mood and ↓ fatigue.
Ives-Deliperi et al., [11]; RCT; 8 weeks	Bipolar Disorder (I or II) (DSM-IV) *N* = 33; (Age *M* = 35.4 yr., *SD* = 8.3) BPD (*n* = 23, age *M* = 37.6, *SD* = 9.3) HCs (*n* = 10, age *M* = 30.2 *SD* = 5.3)	Bipolar participants were assigned to either (1) MBCT for 8 weeks (BPT group); or (2) waitlist control (BPW group); fMRI imaging occurred at the same intervals for each condition	Change from baseline in 1) Self-report measures (FFMQ, BAI, SOSI, DWERS); and 2) Mindfulness-related brain activity	MBCT resulted in Sig ↓ in anxiety and emotion dysregulation and enhancements to mindfulness and executive function in the BPT group, but not in the BPW group. Sig ↑ BOLD signal in mPFC and PCC in the BPT group, compared to the BPW group. The activity pattern appeared more similar to HCs; Changes were correlated with improve-ments in cognition and emotion regulation
Mata et al., [78] RCT, 1 session	Recovered from MDD, (i.e. MDD-R group) (SCID) MDD-R (*n* = 41, age *M* = 38.61, *SD* = 11.28); Matched healthy controls (*n* = 40)	(1) Exercise condition, 15 minutes of moderate intensity stationary cycling; (2) No exercise condition, 15 minutes of quiet rest	Resistance to negative mood induction (sad film), as measured by changes from baseline scores on BDI-II and a study specific scale to assess affect.	Results suggest that exercise can serve build resilience such that individuals are less prone to depressed affect when exposed to repeated emotional stressors.

Abbreviations: AEX = Aerobic exercise; BAI = Becks Anxiety Index; BDNF = Brain-derived neurotrophic factor; BDI-II = Beck Depression Inventory II; BOLD = Blood oxygenated dependent level signal; BPD = Bipolar disorder; DWERS = Difficulties with Emotion Regulation Scale; ECT = Electroconvulsive therapy; FFMQ = Five-Facet Mindfulness Questionnaire; HRSD = Hamilton Rating Scale for Depression; HC = Healthy controls; MBCT =Mindfulness-based cognitive therapy MDD = Major depressive disorder; mPFC = Medial prefrontal cortex; PCC = Posterior cingulate cortex, RCT = Randomized controlled trial; SCID = Structured Clinical Interview for DSM-IV; Sig = Significant/significantly; SOSI = Symptoms of Stress Inventory;

Table III. Studies on the effectiveness of alternative and/or complimentary behavioural therapies for anxiety disorders or symptoms

Study	Diagnosis & Participant Data	Intervention(s)	Main Outcome Measure(s)	Significance
Herring et al., [94]; RCT; 6 Weeks	GAD (DSM-IV) in sedentary females; *N = 30*; (Age *M* = 23.5, *SD* = 5.9); Concurrent pharmacotherapy; Concurrent SAD was common.	2 weeks: (1) Aerobic exercise (AEX); (2) Resistance training (RET); or (3) Waitlist control	Remission; Change in 'worry' from baseline measured at 2, 4, and 6 weeks with the Penn State Worry Questionnaire [95]	Remission rates were 60%, 40%, and 30% for RET, AEX, and WL, respectively; AEX & RET increasingly (*Sig*) reduced worry symptoms across time whereas worry did not change for WL group.
Hoge et al. [19]	GAD (DSM-IV); *N = 89;*	(1) Mindfulness-Based Stress Reduction (as described in [27]) (2) Control, "Stress Management Education"	Change from baseline on: Hamilton Anxiety Scale; CGI-Illness Severity; BAI, Stress Reactivity Test	Sig improvement at post-intervention on CGI-IS and BAI compared to control. Sig improvement on a stress-reactivity test. Suggests ↑ resilience.
Goldin et al., [96]; Clinical Trial; Total duration not specified	Generalized SAD (DSM-IV); *N* = 14; (*M* = 35.2 yr., *SD* = 11.9); Ethnically diverse	(1) MBSR as described in [26, 27];	Emotion reactivity and regulation of negative self-beliefs; fMRI; Liebowitz Social Anxiety Scale (Self-Report) [97]; BDI, other scales	From baseline to post-MBSR patients had sig ↓ social anxiety, depression, rumination, and state anxiety, as well as ↑ self-esteem. fMRI: Sig ↓ amygdala (implicated in (-) emotion) activity and ↑ regions involved in attentional deployment and mindfulness
Jazaieri et al., [20]; RCT 2 month; w/ follow- up	Generalized SAD (DSM-IV); *N* = 56; (Age *M* = 32.8 yr., *SD* = 8.4);	(1) AEX, 1 group & 2 individual sessions of moderate intensity; (2) MBSR as described in [26]; or (3) Untreated generalized SAD controls; (4) healthy controls	Liebowitz Social Anxiety Scale (Self-Report) [97]; Social Interaction Anxiety Scale [98], BDI, PSS-4, RSS, SLS, SCS	Both MBSR and AEX led to sig and comparable changes in clinical symptoms and well-being (e.g., life-satisfaction) both immediately after the intervention and at 3 months post-intervention.
Goldin et al., [10]; RCT; 2 months	As described above for Jazaieri et al., [20]; (same sample)	As described above for Jazaieri et al., [20] (outcomes assessed based on the same exp. manipulation)	Change from baseline self-report of negative self-belief reactivity. fMRI to assess changes in emotion & attention related brain activity	Self-report: Sig post-intervention improvement for both AEX & MBSR groups; fMRI: only MBSR yielded Sig greater 1) ↓ (-) emotion & 2) ↑ activity of attention-related brain regions; Suggests ↑ emotion regulation

Abbreviations: AEX = Aerobic exercise; BDI = Beck Depression Inventory; CGI = Clinical Global Impression; DSM-IV = Diagnostics and Statistical Manual of Mental Disorders 4th Ed.; fMRI = Functional magnetic resonance imaging; GAD = Generalized anxiety disorder; MBSR = Mindfulness-based Stress Reduction; PANAS = Positive and Negative Affect Schedule; PEP = Post-event processing; PSS-4 = Perceived Stress Scale (4th version); RCT = Randomized controlled trial; RET = Resistance training; RSS = Rosenberg Self-Esteem Scale; SAD = Social anxiety disorder; SCS = Self-Compassion Scale; SD = Standard deviation; Sig = Significant/significantly; SLS =

Satisfaction with Life Scale; WL = Waitlist (control)

Table III. Continued

Study	Diagnosis & Participant Data	Intervention(s)	Main Outcome Measure(s)	Significance
Cassin & Rector, [99]; RCT	Generalized SAD (DSM-IV); *N* = 57; (Age *M* = 35.1, *SD* = 13.4), 57.9% male; 59% with comorbid psychiatric disorder.	(1) Mindfulness training; (2) Distraction training; (3) No training (control)	Visual analogue scale (self-report) rating of distress during post-event processing induction); PANAS	Mindfulness group showed a significant decline in PEP related distress rating from baseline compared to distraction training or no training (control) groups.
Kocovski et al., [100]; RCT 12 wk; 3 mo-nth follow up	Generalized SAD (DSM-IV-TR) *N* = 100; (Age: *M* = 34 yrs.) 54% female	(1) Mindfulness and acceptance based group therapy (MAGT); (2) standard group CBT; (3) Waitlist control	Social Phobia Inventory (SPIN), LSAS; Clinical Global Impression (CGI) impro-ement and severity scales	MAGT and group CBT significantly improved generalized SAD compared to control, but did not differ from one another in efficacy.
Shikatani et al., [101]; RCT 1 day; 2 day follow-up	SAD (DSM-IV); *N* = 56; (Age *M* = 24.5 yr., SD = 7.2); ~70% female	(1) Single session (~40 min) of cognitive restructuring training; (2) Single session (~40 min) of mindfulness training; (3) Control condition	Rumination related to a speaking task recorded on video; SPIN, Personal Report of Confidence as a Speaker, Skin conductance level	Participants in the cognitive restructuring and mindfulness conditions reported comparably (sig) ↓ PEP and improved affect as compared to the control condition. No sig differences in skin conductance levels compared to control.
Brooks et al., [102]; RCT, 10 wk in duration	Panic Disorder (DSM-III-R or ICD-10) with or without agoraphobia. *N* = 46; (Age *M* = 33.46 yr., *SD* = 8.63)	(1) AEX (running); (2) Clomi-pramine; or (3) Placebo pill (control group)	Hamilton Anxiety Rating Scale (HAM-A); CGI (observer rating), Panic and Agoraphobia Scale score (observer (PAS-O) and patient (PAS-P) ratings	Compared with placebo, drug and AEX groups resulted in significant improvements in symptoms. Clomipramine treated symptoms more effectively and more quickly than AEX.
Brooks et al., 2003 [103]; RCT, 10 wk	Panic Disorder (DSM-III-R) with or without agoraphobia; *N* = 28 (Age *M* = 32.7 yr., *SD* = 9.35).	1) AEX (walking/running 3x per week), including a weekly meeting with trainer; (2) Clomi-pramine (CLPM); or (3) Placebo pill (control group)	Changes in baseline response to ipsapirone challenge (a panic attack inducer): cortisol Acute Panic Inventory, NIMH Self-Rating Scale	Baseline cortisol was lower after 10 weeks in the CLPM group, but not AEX or placebo. Sig ↓ psych variables measured by NIMH scale for AEX & CLPM groups. CLPM treat-ment Sig ↓ hypothermic effect of ipsapirone

Abbreviations: AEX = Aerobic exercise; CBT = Cognitive behavioural therapy; CLPM = Clomipramine; DSM = Diagnostics and Statistical Manual of Mental Disorders; HAM-A = Hamilton Anxiety Rating Scale; ICD-10 = International Classification of Diseases 10; LSAS = Liebowitz Social Anxiety Scale; MAGT = Mindfulness and acceptance based group therapy; NIMH = National Institute of Mental Health; PAS = Panic and Agoraphobia Scale ; PEP = Post-event processing; RCT = Randomized-controlled trial; SAD = Social Anxiety Disorder; Sig = Significant/significantly; SPIN = Social Phobia Inventory; SSRI = Selective serotonin reuptake inhibitor;

Table III. Continued

Study	Diagnosis & Participant Data	Intervention(s)	Main Outcome Measure(s)	Significance
Oeland et al., [5]; RCT 20 wk; 32 wk follow-up	Panic disorder or Generalized Anxiety Disorder (ICD-10); *N* = 48; Median age: 1) Exercise Group 36 years (*n* = 27); 2) Control group 40 years	(1) Opportunity to participate in group structured AEX (65%-75% VO_2 max, 30 min) and RET (5 muscle groups, 60 min); 2 sessions x 20 wk (adjuvant to current treatment) (2) Already physically active non-intervention controls; treatment as usual	1. Achieving a level of physical activity equivalent to public health standards (150 min/wk & Δ VO_2max) 2. Quality of Life (EuroQoL 5D)	Sig increase in number of mins physically active at wk 20 and sig > than that of control group (exceeded Nordic public health standards). Sig increase in VO_2max compared to control at week 20. At wk 20 QoL > than control group, but was not retained at follow-up (correlated with a decrease in physical activity from wk 20 to wk 32)
Wedekind et al. [104]; Double-blind RCT; 10 wk	Panic Disorder with or without agoraphobia (DSM-IV & ICD-10); *N* = 60 (Age: *M* = 31.9 yr., *SD* = 8.1)	(1) AEX + paroxetine (an SSRI) 40 mg/day; (2) Relaxation + paroxetine; (3) Placebo pill + AEX; (4) Relaxation + placebo AEX was performed 3x per/w for 45 minutes as described in [105].	1. Within-subjects change in panic and agoraphobia severity (clinician rated) 2. Clinical Global Impression Scale (self report); 3. HAM-A	All groups showed sig improvements from baseline. AEX was not sig > relaxation training on any measure except PAS & HAM-A at week 4. Paroxetine was superior to both placebo conditions, but this was *not* dependent on being combined with AEX.

AEX = Aerobic Exercise; DSM-IV = Diagnostics and Statistical Manual of Mental Disorders 4th Ed; HAM-A = Hamilton Anxiety Rating Scale; ICD-10 = International Classification of Diseases 10; PAS = Panic and agoraphobia scale; QoL = Quality of Life; RET = Resistance training; Sig = Significant/significantly; SSRI = Selective serotonin reuptake inhibitor; VO = Volume of oxygen; Wk = Week

Glossary of Terms

**Definitons directly extracted from Merriam-Webste Medical Dictionary* [106]

***Adjuvant:** something (as a drug or method) that enhances the effectiveness of medical treatment <used chemotherapy as an adjuvant to surgery>

***Agoraphobia:** abnormal fear of being helpless in an embarrassing or unescapable situation that is characterized especially by the avoidance of open or public places

***Bipolar disorder:** any of several mood disorders characterized usually by alternating episodes of depression and mania or by episodes of depression alternating with mild nonpsychotic excitement

***Comorbid:** existing simultaneously with and usually independently of another medical condition

***Clomipramine:** a tricyclic antidepressant used in the form of its hydrochloride $C_{19}H_{23}ClN_2 \cdot HCl$ to treat obsessive-compulsive disorder and panic disorder

***Contraindication:** something (such as a symptom or condition) that is a medical reason for not doing or using something (such as a treatment, procedure, or activity)

Cross-sectional study: an observational study in which exposure and disease are determined at the same point in time in a given population

***Epidimiology:** a branch of medical science that deals with the incidence, distribution, and control of disease in a population

***Functional magnetic resonance imaging (fMRI):** magnetic resonance imaging used to demonstrate correlations between physical changes (as in blood flow) in the brain and mental functioning (as in performing cognitive tasks)

***Insulin resistance:** reduced sensitivity to insulin by the body's insulin-dependent processes (as glucose uptake, lipolysis, and inhibition of glucose production by the liver) that results in lowered activity of these processes or an increase in insulin production or both and that is typical of type 2 diabetes but often occurs in the absence of diabetes

Longitudinal study: a type of study design in which participants are followed over time with continuous or repeated monitoring of risk factors or health outcomes, or both

***Mania:** excitement manifested by mental and physical hyperactivity, disorganization of behavior, and elevation of mood; specifically : the manic phase of bipolar disorder

***Meta-analysis**: a quantitative statistical analysis of several separate but similar experiments or studies in order to test the pooled data for statistical significance

Paroxetine: an antidepressant of the selective serontonin reuptake inhibitor class

Randomized controlled trial: A clinical trial in which participants are randomly assigned to the experimental group (in which they are exposed to the actual variable of interst, e.g.. a drug) or a control group

***Selective serotonin reuptake inhibitor:** any of a class of antidepressants (as fluoxetine or sertraline) that inhibit the inactivation of serotonin by blocking its reuptake by presynaptic nerve cell endings

Self-efficacy: the belief that one is capable or competent of carrying out some task or action; degree to which one believes he or she can succesfully achieve a goal

Social anxiety disorder: a condition chracterized by the experience of extreme anxiety while one is in social situations, especially when they are around unfamiliar people or situations, or where they are worried they might be judged by others

Statistical significance (significant): When two or more variables are correlated or affect one another at probability that is unlikely due to chance alone.

Symptomatology: a group of symptoms occurring together and characterizing a particular disease

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