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SPOTLIGHT

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The neurostructural and neurocognitive effects of physical activity: A potential benefit to promote eating disorder recovery

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Abstract

Accumulating evidence suggests that supervised and adapted physical activity provides cognitive benefits for individuals with eating disorders (EDs). The mechanisms underlying the benefits of physical activity are poorly understood. Addressing this knowledge gap may inform the appropriate integration of structured physical activity into eating disorders treatment and recovery. We draw attention to recent findings in the study of the impact of physical activity on the brain, and we describe the neurostructural and neurocognitive changes associated with physical activity observed in various clinical and nonclinical populations. Considering the identified impairment in brain volume- and/or neurocognitive function in various EDs, we propose that positive effects of physical activity may play a meaningful role in successful ED treatment. Accordingly, we outline research steps for closing the knowledge gap on how physical activity may aid in ED recovery, and emphasize the need to combine measures of cognitive and behavioral responses to physical activity, with technology capable of measuring changes in brain structure and/or function.

KEYWORDS
anorexia nervosa, BDNF, binge-eating disorder, bulimia nervosa, exercise, lactate, myokines, physical activity, VEGF

1 | SPOTLIGHT PAPER

Solid evidence demonstrates the acute response and long-term effects of regular physical activity on brain neurostructures and neurocognitive functioning in both the general population and in several clinical populations (Lang et al., 2010; Lippi, Mattiuzzi, & Sanchis-Gomar, 2020; Mehren et al., 2020). Inclusion of structured physical activity in eating disorder (ED) treatment has been approached with caution given the propensity for individuals with EDs to (mis)use physical activity and exercise as a compensatory, weight loss, and affect regulating behavior. As reports of positive neurostructural and neurocognitive effects of physical activity in many clinical populations increase, we find it timely to ask whether similar beneficial effects of physical activity can be seen in individuals with various EDs and play a meaningful role in ED treatment and recovery.

1.1 | Physical activity to induce neurostructural changes and plasticity

Accumulating evidence identifies active muscle mass as an important communicating organ, producing a plenitude of myokines, many of which

bring important signals to the brain and other organs and influence factors including cognition, nutrient metabolism, and inflammatory processes (Delezie & Handschin, 2018; Severinsen & Pedersen, 2020). Whether the observed effects depend on increased volume of muscle mass, or simply *using* the muscle mass with reasonable strain, remains to be clarified, and is important when evaluating the role of physical activity in the treatment of some EDs. The myokines produced are assumed to either cross the blood–brain barrier and/or to connect to specific receptors at the blood–brain barrier and stimulate responses within brain tissue. Brain-derived neurotrophic factor (BDNF) and vascular endothelial growth factor (VEGF) are some of the signaling substances produced by muscle mass, and increased serum-concentration of these factors is associated with increases within the brain. These substances stimulate neural survival, promote growth and differentiation of new neurons and synapses, and stimulate synaptic plasticity and increased vascularization (Delezie & Handschin, 2018; Severinsen & Pedersen, 2020). Importantly, *intensive* muscle activity leads to increased lactate production, and lactate causes increases in brain vascularization, presumably by causing a rise in VEGF (Morland et al., 2017). Lactate also stimulates neuronal activity, calcium signaling, myelination, and memory formation (Delezie & Handschin, 2018). The effects of these signaling substances are identified within structures in the limbic system, in brain white matter, and overall, in frontal, temporal, and parietal regions (Haeger, Costa, Schulz, & Reetz, 2019).

Brain areas that are able to induce neuronal growth include the lining of the subventricular zone and the hippocampus (Kumar, Pareek, Faiq, Ghosh, & Kumari, 2019; Severinsen & Pedersen, 2020). The hippocampus is also responsive in functional matters to myokines, which is notable, as this area is particularly important in regulation of memory and cognitive function, and for resilience to stress and anxiety (Kumar et al., 2019; Severinsen & Pedersen, 2020). Integrated in the limbic system, hippocampal functioning also affects reward sensations, emotions, and mood. Impairment of neurotrophic signaling (here: BDNF specifically), discontinuation of hippocampal neurogenesis, or reduction in hippocampal volume are associated with cognitive disorders including Alzheimer's disease and major depressive disorder (Kumar et al., 2019; Lippi et al., 2020). Importantly, controlled physical activity of moderate to vigorous intensity has been shown to improve neurocognitive functioning in people with schizophrenia, autism spectrum disorder, and ADHD; reduced mild and moderate depression; and prevented age-related volume decrease of the hippocampus associated with cognitive decline (Ashdown-Franks et al., 2019; Lang et al., 2010; Lippi et al., 2020; Mehren et al., 2020).

The neurological and cognitive consequences of various EDs have been widely reported, especially in individuals with severe AN in whom reduced brain mass and impaired cognitive function are of considerable clinical concern (King, Frank, Thompson, & Ehrlich, 2018). Studies have also reported altered brain structures in individuals with bulimia nervosa (BN) (Wang et al., 2019), and individuals with binge-eating disorder (BED) have been shown to respond differently to dopamine than BMI-matched controls (Wang et al., 2011), which may indicate aberrant neurostructural or neurofunctional responses to stimuli. Specifically, MRI studies of patients within the bulimic spectrum disorders have reported decreased cortical volume and/or diminished activity within the frontostriatal circuits—areas essential in self-regulation (Donnelly et al., 2018). Whether the integration of structured physical activity in ED treatment can have positive impact on neurological and cognitive consequences of EDs, as observed in other psychiatric disorders, is worthy of cautious investigation.

1.2 | Neurocognitive and functional effects of physical activity

Among the many beneficial psychological effects associated with physical activity in both healthy individuals and clinical populations are improved executive function, self-efficacy, self-esteem, self-regulation, and impulse control (Ashdown-Franks et al., 2019; Lubans et al., 2016; Oaten & Cheng, 2006; Rosenbaum, Tiedemann, Sherrington, Curtis, & Ward, 2014; Rosenbaum, Tiedemann, Ward, Curtis, & Sherrington, 2015). All of these changes are desirable outcomes in the treatment of various EDs. Several studies have shown that adapted and supervised physical activity in ED treatment can reduce eating pathology, improve health parameters in patients with overweight, facilitate increases in energy intake and body weight in undernourished patients, reduce levels of depression, and improve quality of life (Vancampfort et al., 2014). In women with BN, physical activity as therapy had superior long-term effects in reduction of drive for thinness, bulimic cognitions, and bulimic behavior compared with cognitive-behavior therapy (Sundgot-Borgen, Rosenvinge, Bahr, & Schneider, 2002). We have also found comparable remission rates with long-term effects in women with BN and BED treated with supervised physical exercise and dietary therapy (PED-t) compared with cognitive behavior therapy (Mathisen et al., 2020).

We acknowledge both the historical hesitancy to include physical activity in ED treatment given the potential for compulsive exercise as well as the inconsistencies in terminology that complicate the literature (Gorrell, Flatt, Bulik, & Le Grange, 2021). Reports are emerging, however, that encourage revisiting the inclusion of physical activity or exercise in ED treatment (Quesnel et al., 2017). Moreover, positive genetic correlations between AN and measured physical activity suggest that some of the same gene variants that increase risk for developing AN are also associated with high physical activity levels (Watson et al., 2019). One interpretation of these findings is that the tendency for high activity may be in part caused by biology rather than psychological factors driving weight loss. The goal of including physical activity in the treatment of AN or BN would then be geared toward changing the function of the physical activity—as an arena for social interaction and enjoyment of movement with less rigidity and intensity than experienced by the compulsive maladaptive physical activity seen many of these patients (Davis et al., 1997; Gorrell et al., 2021). Physical activity is more frequently included in the treatment of BED; however, the focus is often on weight regulation as in behavioral weight loss treatments (Palavras, Hay, Filho, & Claudino, 2017) or integrated treatments such as Healthy Approach to Weight Management and Food in Eating Disorders (HAP-IFED) (Palavras et al., 2021). We encourage the exploration of incorporation of structured physical activity

as a therapeutic component of treatment for all EDs. We pose the question: "If therapeutically prescribed physical activity (in a manner that ensures less rigidity and compulsivity) can induce increased neuronal growth and plasticity while providing benefits to mood regulation and impulse control, might it support and enhance the effects of specific psychotherapy provided in ED treatment?"

1.3 | Closing the knowledge gap between positive effects of physical activity and recovery from EDs

In order to answer this question, several essential points need to be addressed to close the knowledge gap. Although patient safety is paramount—especially in low-weight AN and BN and purging disorder with high frequencies of purging—we encourage empirical evaluation of whether neurostructural and functional changes resulting from prescribed and supervised physical activity might be an overlooked benefit and an important contributor to recovery. Importantly, it is unresolved whether neurogenesis still occurs in *adult* humans, and whether the psychological and cognitive effects of physical activity are caused by neuronal growth associated with plasticity (Kumar et al., 2019; Lubans et al., 2016). Most studies on neurostructural changes induced by neurotrophic factors have been conducted in animals, or are based on postmortem or postsurgery human tissue sampling (Kumar et al., 2019). Such study designs have been criticized for inconsistent methodology and for not controlling for underlying mental or cognitive disorders (i.e., conditions that could have caused reduced neurogenesis or even loss of neurons) (Kumar et al., 2019). Nonetheless, we are unable to evaluate neurostructural changes without the use of invasive methods, precluding study in living humans. Accordingly, we are limited to controlled studies of regional brain function, and observation of changes in circulating levels of- and local release and/or uptake of neurotrophins after physical activity interventions as indices of brain-related change.

A systematic approach could address both fundamental research questions and clinical need. In the first instance, any prescribed physical activity interventions for EDs must address the optimal progression, frequency, duration, and intensity of physical activity and in all cases, ensure safety and do no harm (Cook et al., 2016; Dobinson, Cooper, & Quesnel, 2017; Mountjoy et al., 2015; Noetel, Dawson, Hay, & Touyz, 2017; Quesnel et al., 2017). This also necessitates accommodation of the level of physical activity shown to result in the optimal neurotrophic stimuli, that is, currently advised as approximately minimum 3 months of moderate–intensity aerobic exercise, with 2–3 sessions/week of minimum 30 min/session in duration (Lippi et al., 2020). Second, we need to continue to evaluate cognitive effects of physical activity via standardized questionnaires and sophisticated ecological momentary assessment with digital assessment tools. More nuanced monitoring could inform how and when affective benefits from physical activity emerge, which could involve different and changing responses in early versus late intervention. In order to document the neurobiological impact of physical activity interventions in EDs, we need to include biomarker and neuroimaging methods that provide a window into neurochemical as well as structural/volumetric and functional changes in the brain that occur in response to physical activity interventions as compared to healthy control individuals. Such technology may aid in detecting newly formed cells in neurogenic niches and their integration within specific neural circuitry (Kumar et al., 2019). These approaches call for collaboration with experts in neuroimaging to ensure best practices within their domain (King et al., 2018). Advances in imaging techniques, such as metabolic imaging, have the potential to further advance the field (Haeger et al., 2019).

BDNF is one of the major contributors to healthy cognitive effects in humans (Lippi et al., 2020), and physical activity is widely documented to increase its serum concentration (Delezie & Handschin, 2018). BDNF is reduced in AN, but our current understanding of how BDNF interacts with hypophagia and exercise behavior in AN is inconclusive (Ho, Klenotich, McMurray, & Dulawa, 2016). Hypothetically, to achieve any beneficial effect from central BDNF, the individual needs to be in optimal energy balance. This may suggest that individuals who are underweight may benefit from physical activity, but only under conditions of matched energy intake (i.e., intake equal to or exceeding expenditure), to avoid a state of negative energy balance induced by the prescribed physical activity. Nevertheless, the first area of knowledge that needs to be addressed with regard to ED treatment is whether the aforementioned myokine production from active muscle mass also occurs in individuals with various EDs, including low-weight AN. Further, by combining measures of neurobiological change with cognitive changes, we will be better equipped to understand any cause–effect from physical activity interventions on specific psychopathology in EDs. Acute neuroimaging and metabolic imaging studies, comparing ED patients with healthy controls, may increase our understanding of any aberrant neurofunctioning in EDs. Current knowledge of psychopathology, for example, impairment in self-regulation or aberrant reward seeking behavior and sensation, may guide us in choosing which brain circuits or domains to focus on. Long-term studies using the suggested combined methodology, following patients across treatment and short- and long-term follow-up with patients randomized to treatment with and without structured physical activity, would allow us to identify any favorable effects of physical activity on ED outcomes.

If neurostructural or functional changes within the brain cause or maintain eating disorders (Treasure, Duarte, & Schmidt, 2020), interventions that address such aberrations have the potential to improve outcomes of specialized psychotherapies for eating disorders. The healthy incorporation of non-maladaptive physical activity may also allow patients with EDs to develop more normative and healthy emotion-regulation strategies (i.e., noncompulsive physical activity), reduce the individual burden of disease, and support long-lasting recovery. With appropriate empirical foundation and justification, structured, prescribed physical activity may represent a promising, acceptable, noninvasive adjunct intervention to be thoroughly explored in the treatment of all EDs.

CONFLICT OF INTEREST

CMB reports: Shire (grant recipient, Scientific Advisory Board member); Idorsia (consultant); Lundbeckfonden (grant recipient); Pearson

(author, royalty recipient). The other authors have no conflict to declare.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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