Acta Neuropsychiatrica 2017

DOI: 10.1017/neu.2016.64
First published online December 6, 2016

Letter to the Editor

Exercise and depression: where do we go from here? A rebuttal to Schuch et al.

Given the critical importance of studies exploring the effects of physical activity on depression, and the recent disconcerting report by Cooney et al. about exercise's (lack of) benefits (1), we read with great interest the article by Schuch et al. 'A critical review of exercise as a treatment for clinically depressed adults: time to get pragmatic', published last May in your journal (2).

The authors should be congratulated for their concise yet very thorough coverage of the methodological and clinical issues affecting the interpretation of past trials and/or meta-analytic findings. Focussing their analysis on issues related to Participants, Interventions, Comparison groups, Outcomes and Study design (the so-called 'PICOS' criteria), they have highlighted several key areas of concern which may have caused the benefits of exercise to be underestimated.

Although we agree with some of the views expressed by Schuch et al., we resist some of their suggestions because of our differing assumptions about the appropriate goals and current needs of scientific inquiry in this area.

Putting it briefly, Schuch et al. first discuss the use of study participants with heterogeneous symptoms and argued that such a diversity may be linked to distinct biopsychosocial profiles (e.g. somatic symptoms with lesser or higher severity, low or high levels of rumination), which is suspected to moderate the antidepressant impact of physical activity. The review by Schuch, Dunn, Kanitz, Delevatti and Fleck (3) was cited in support of this view. Accordingly, they recommend the development of 'a typology that would allow matching a depression type to the most appropriate exercise prescription' (p. 2). The fact that depressed individuals with a similar diagnosis of mood disorder (or with comparable scores on a standardised depression scale) differ in the extent to which the various constitutive symptoms of depression are visible is indisputable. However, one first reservation we'd like to express is about the statement that such differences would modulate the antidepressant effects of exercise. The reference used to legitimate this statement (3) is presented as a review article about the 'moderators of response in exercise treatment or depression', but it actually included a very small number of studies ($n = 11$), and some of the presented conclusions have been drawn on the basis of one single study [e.g. the moderating influence of baseline brain-derived neurotrophic factor (BDNF) levels]. If, as mentioned in its title, this review aimed at reporting on the dispersion of the antidepressant effects of exercise as a function of selected covariates, then it should have included the relevant studies (i.e. at least two) and the analysis should have compared the differences in effects.

In the following section (interventions), Schuch et al. elaborate on the approaches used for the quantification of exercise exposure in intervention studies with depressed participants. It is proposed that the energy-expenditure approach (i.e. amount of exercise prescribed in terms of kilocalories/week) may not be the 'optimal method of deciphering potential biological mechanisms driving the antidepressant effects of exercise', and that 'exercise prescriptions designed to specifically target putative mechanisms of the antidepressant effects of exercise could potentially achieve greater benefits' (p. 3). This idea is reiterated in the last paragraph of this section: 'Gaining better understanding on the neurobiological processes underlying the antidepressant effects of exercise will be crucial in designing more effective exercise interventions' (p. 3). We make three comments on this. First, the majority of trials that used exercise (aerobic or anaerobic) in the management of clinical depression *did not* quantify physical activity in terms of energy expenditure (expressed in kilocalories/week) but rather in terms of time spent at various relative intensities (4). Second, we don't think that any method employed in quantifying the prescribed 'dose' of physical activity will help in identifying the biological mechanisms through which exercise decreases depression. The one and only way to determine the biological processes at work and to establish the biological plausibility of exercise affecting depression

is to explore the biological adaptations that occur with physical activity, and to determine whether these are consistent with what is known about the etiology of depression. Finally, it is doubtful that an exercise prescription can be shaped to target a specific 'putative mechanism of the antidepressant effects of exercise'. Actually, research in exercise physiology has identified a multitude of nonspecific neurobiological adaptations to exercise training. For instance, it has been established recently that short (20 min) or long (40 min) duration aerobic exercise of either moderate (60 percent of heart rate reserve) or vigorous (80 percent of heart rate reserve) intensity increased serum BDNF levels in a comparable proportion (30–40%); whereas sitting for the same time caused a 10–15% decrease in BDNF (5).

Our last comment refers to Schuch et al.'s point about 'study design' in which researchers are encouraged to conduct pragmatic rather than traditional randomised-controlled trials (RCT). This recommendation is based on the rationale that pragmatic RCTs have 'high external validity by virtue of methodological features that are more closely aligned with real life practice norms such as interventions delivered in routine practice and non-restrictive eligibility criteria' (p. 5). Although we do not dispute the fact that minimising exclusion criteria or being more flexible in the application of compliance requirements more realistically reflects real-world situations, we do believe that this way of conducting research seriously limits internal validity (i.e. the degree to which the study is confound-free). As an illustration, the pragmatic RCT cited by Schuch et al. (6) compared a 4-week long exercise intervention of preferred intensity (3 weekly training sessions) with a prescribed-intensity exercise programme of same length and training frequency. Participation was voluntary and there were no attendance requirements. Preferred-intensity exercise (coupled with motivational education) decreased depression more than did prescribed-intensity exercise. But, it also appeared that participants who received the preferred-intensity intervention had a 16% higher attendance rate than participants in the prescribed-intensity group. In consequence, reduced depression could be the result of the independent variable manipulated by the researchers (i.e. preferred-intensity versus prescribed-intensity exercise), the different exercise doses in each group, or some combination of both. There is no clear way to decide between the different interpretations. Which type of validity (external versus internal) is more important depends largely on the purpose of the research. But if an investigator is conducting research that requires a high degree of control, internal validity is critical and external validity is not. On the contrary, when it is desirable to generalise research findings to other conditions or settings, external validity is more important. In light of (1) the current controversy as to the efficacy of exercise for the treatment of major depression (1,7), and (2) the limited understanding of the mechanisms (especially the neurobiological mechanisms) whereby exercise reduces depression, what seems mostly needed is to develop RCTs conducted with a high degree of internal validity.

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https://doi.org/10.1017/neu.2016.64 Published online by Cambridge University Press