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Meditation-based mind-body therapies for negative symptoms of schizophrenia: Systematic review of randomized controlled trials and meta-analysis

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ABSTRACT

Meditation-based mind-body therapies (yoga, tai-chi, qi-gong, mindfulness) have been suggested to have a potential therapeutic effect on negative symptoms.

We conducted a systematic review and meta-analysis of randomized controlled trials (RCTs) examining effectiveness of yoga, tai-chi, qi-gong and mindfulness on negative symptoms of schizophrenia, using different databases and trial registries. The primary outcome was effect of mind-body therapies on negative symptoms and the secondary outcome was effect on positive symptoms.

Fifteen RCTs were included in the meta-analysis ($N = 1081$ patients). Overall, we found a beneficial effect of mind-body interventions on negative symptoms at endpoint compared to treatment-as-usual or non-specific control interventions, but the effect was small and moderate to high heterogeneity was present. A subgroup analysis for different types of therapy revealed a significant effect of mindfulness-based and yoga interventions on negative symptoms, but heterogeneity within the yoga subgroup was high. Our results did not show an increase of positive symptoms ($N = 1051$).

Our results suggest a potential for meditation-based mind-body therapies in the treatment of negative symptoms, in particular for mindfulness based approaches and to a lesser extent yoga. Limitations in the available comparisons do not allow concluding on a specific effect of these interventions. Overall, the currently available evidence remains limited and does not yet allow one to recommend mind-body therapies for the reduction of negative symptoms. However, the present findings justify further research on mind-body therapies for the treatment of negative symptoms.

1. Introduction

Yoga, tai-chi, qi-gong, and mindfulness are different mind-body therapies used to promote general health and to reduce stress. These various forms of meditation practice share commons roots and are suggested to have comparable effects on mind and body, in particular with a small to moderate reduction in multiple negative dimensions of psychological stress (Goyal et al., 2014). In this systematic review we focus on techniques that include meditation as an essential component and do not address other mind-body interventions or psychotherapies. Yoga, tai-chi, qi-gong, and mindfulness include meditation for beginners that consists of basic training of internal concentration by focusing the body and/or breathing, and leads to an altered dynamic of consciousness. Meditation practice is essentially a practice of awareness and all the considered interventions share fundamental meditation exercises such as sited meditation or body-scans (Brown et al., 2015).

Over the last decade researchers have suggested that these group practices could have a therapeutic role for patients suffering from schizophrenia as add-on therapy to antipsychotic treatment (Behere et al., 2011; Helgason and Sarris, 2013; Louise et al., 2018; Vancampfort et al., 2012). Broderick and Vancampfort have provided a series of Cochrane reviews on yoga for schizophrenia (Broderick et al., 2015; Broderick and Vancampfort, 2019). They applied strict inclusion criteria and could only identify a very limited number of small studies that lacked many key outcomes, which precluded concluding on the efficacy of yoga interventions.

In this context the negative symptoms of schizophrenia are a therapeutic target of high interest, as effective treatment remains an unmet therapeutic challenge (Aleman et al., 2017). Several mechanisms of meditation-based mind-body therapies could potentially contribute to an amelioration of negative symptoms. First, empowerment of self-control over symptoms is a common mechanism of these therapies and could support a modification of

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defeatist beliefs associated with negative symptoms (Campellone et al., 2016). Second, meditation has been suggested to stimulate the reward system, which is dysfunctional in patients with negative symptoms, and to improve anhedonia (Kirk and Montague, 2015).

An interesting recent meta-analysis focusing on the broader effects of exercise on negative symptoms has also addressed mind-body exercise (Vogel et al., 2019). The authors included yoga and tai-chi but not mindfulness interventions, thus focusing on the exercise and not the meditation aspect of practice. They found a positive effect of mind-body exercise on negative symptoms, but it is not clear whether this result applies to all meditation-based practice. In addition, they did not perform subgroup analysis to compare different mind-body interventions.

We conducted a systematic review of all randomized clinical trials (RCTs) investigating the effect of meditation-based mind-body therapies as adjunctive treatment to antipsychotic treatment on negative symptoms. Our primary hypothesis was that practice of meditation-based mind-body therapies would lead to a lower negative symptom severity in comparison to treatment-as-usual or to a non-specific control intervention. We did not perform a comparison with specific interventions that have previously been associated with an improvement of negative symptoms (e.g. exercise, social skills training), because we wanted to detect an efficacy signal and not superiority over another form of specific treatment. Our secondary hypothesis was that addition of mind-body therapies would not lead to an increase in positive symptoms.

It has been suggested that longer mind-body interventions have stronger effects, but this question has so far not been addressed in patients with schizophrenia (Carmody and Baer, 2009; Fjorback et al., 2011). Therefore, we planned to explore if negative symptom severity at endpoint is associated with total hours of practice.

2. Methods

2.1. Registration

This work was prepared according to Preferred Reporting items for Systematic reviews and Meta-Analyses (PRISMA-P) guidelines (Moher et al., 2009). On 17th January 2019, the protocol entitled "Mind-body therapies as treatment of negative symptoms of schizophrenia: systematic review of randomized controlled trials and meta-analysis" was published in the International Prospective Register of Systematic Reviews (PROSPERO CRD42019120394); from that date forward it is available from: http://www.crd.york.ac.uk/PROSPERO/.

2.2. Search strategy

The literature was searched with no restriction regarding the date of publication, using Medline, EMBASE, PsychINFO, PsyARTICLES, ScienceDirect and Cochrane Database of Systematic Reviews, from the 2nd to the 30th of March 2019. Additionally, trial registries were also searched for relevant articles: ClinicalTrials.gov and clinicaltrialsregister.eu. The following keywords combinations were used: ("schizo*", psychosis or psychotic), and (yoga, qi-gong, "qi gong", "tai chi", tai-chi, "transcendental meditation", mindfulness, mindfulness-based, meditation, compassion, "loving kindness", or loving-kindness). We used a combination of free-text keywords and MeSH terms to identify a maximum of articles for screening (G.J. Ho et al., 2016). Only English, French and German languages articles were retained. The electronic search was supplemented by examining the reference lists of retrieved articles, and, when available, relevant abstracts for relevant studies. For mindfulness practice, only mindfulness-based programs focusing on mindfulness meditation were considered (e.g. mindfulness-based stress reduction or mindfulness-based cognitive therapies). Interventions that were not based on meditation practice were excluded. In particular, we excluded acceptance-based therapies, which share some elements with mindfulness-based approaches but do not employ formal practice of meditation (Hayes et al., 2006).

2.3. Inclusion criteria and study selection

To be included in the analyses, studies had to fulfill the following criteria: (a) be a rater-blind, controlled randomized trial, (b) report data of patients suffering from schizophrenia or schizoaffective disorder, (c) compare yoga, tai-chi, qi-gong, or mindfulness to a non-specific control intervention or treatment-as-usual, (d) with a duration of intervention of at least 30 min for a total of 8 h of practice over a minimum of 3 weeks; these criteria were selected because effects on negative symptoms need time to develop and these characteristics can be found in standard mindfulness-based program format which have the most empirical support for its efficacy among meditation-based interventions (Carmody and Baer, 2009); (e) report results in English, German or French language, (f) report results on negative symptoms as means and standard deviations or statistical values. Concerning the comparison conditions non-specific control interventions could include any form of intervention not previously associated with an improvement of negative symptoms (e.g. leisure therapy, occupational therapy). We excluded reviews, pilot/single dose studies, case reports, and case series (Fig. 1). Cross-over RCTs were excluded as carry-over effects of considered mind-body therapies are unknown.

2.4. Outcomes and data extraction

Our primary outcome was the effect of adjunctive mind-body therapies on negative symptoms, as assessed with the negative subscale of Positive and Negative Syndrome Scale (PANSS-N) (Kay et al., 1987), the Scale for Assessment of Negative Symptoms (SANS) (Andreasen, 1989) or another scale reporting negative symptoms. Secondary outcome was the effect of adjunctive mind-body therapy on positive symptoms as assessed by the positive subscale of the Positive and Negative Syndrome Scale (PANSS-P), the Scale for the Assessment of Positive Symptoms (SAPS) (Andreasen, 1984) or another scale reporting positive symptoms. Review authors (M.S. and S.K.) independently screened for eligibility titles, trials protocol and abstracts of papers identified in the electronic searches (Fig. 1). The reviewers then examined full-text of retained articles. When they disagreed a common full-text discussion of the paper was done.

For the final set of RCTs we conducted quality assessment of methodology following criteria described in Cochrane handbook for systematic reviews of interventions to assess risk of bias (Higgins et al., 2011). In addition to assessment of the different types of bias, we aggregated these categorizations into a summary bias score as described in the legend to Table 2. Discrepancies were resolved upon discussion between the two raters.

After qualitative analysis, one reviewer (M.S.) performed data extraction for meta-analysis, and one author checked data for accuracy (S.K.). In case of lacking data, the principal authors of studies were contacted by email. In case of trials evaluating multiple active interventions, only the mind-body therapy arm and the control arm were considered. For one study of interest endpoint scores for the primary outcome was not available (Visceglia and Lewis, 2011), but we were able to impute the PANSS negative endpoint scores based on the Ikai et al. (2014) study reporting baseline, change and endpoint scores for our primary and secondary outcome (Abrams et al., 2005). Additionally, for Ho et al. (2012), we imputed the SANS total score from the SANS domains scores, using the correlation matrix from a previously published dataset (Bischof et al., 2016).