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Letter to the Editor

Examining the effect of a mindfulness based program for the improvement of cognitive function in an early stage of schizophrenia. A random controlled trial

Dear Editor,

Mindfulness based interventions (MBIs) are standardized group programs used in clinical and health contexts. In psychosis three meta-analyses that considered only RCTs suggested that MBIs have an effect on psychotic symptoms as primary outcome, with a greater effect on negative rather than positive symptoms (Khoury et al., 2013; Jansen et al., 2020; Louise et al., 2018). However, their effect on a fundamental element of schizophrenia such as Cognitive Impairments (CI) has not been explored. CI has been described as a core element that evolves during and after the course of the illness (Kelleher et al., 2013). Several authors have found that people after a first psychotic episode exhibit worsened cognitive functioning compared to control groups (e.g. Aas et al., 2014). MBIs have shown promising effects on cognitive functions in the general population, such as improvements in working memory and attention (for a review, see Raffone and Srinivasan, 2017) and even in social cognition in outpatients with chronic schizophrenia (Mediavilla et al., 2019). In this study, we propose to test the effect of eight sessions of adapted MBIs for psychosis in patients with early onset schizophrenia. Specifically, we measured cognitive functions as primary outcome.

A single-blind, multicenter randomized controlled trial (registration number ISRCTN24327446) with pre post treatment and 3-month follow-up measures was designed. A parallel group randomized at 1:1 was selected. The study was approved by three ethical committees (e.g. Public Health Service in Valdivia).

All patients were diagnosed with early onset schizophrenia or its subtypes according to the DSM-IV-TR. The primary clinical diagnoses were schizophrenia (69.6%), schizoaffective disorder (7.1%), and schizotypal disorder (3.6%). For the inclusion and exclusion criteria see Langer et al. (2017). Sample size was originally calculated including two samples: at risk mental state (ARMS) and first episode of psychosis (FEP) (Langer et al., 2017); however, it was not possible to include the ARMS sample in this project. The MATRICS Consensus Cognitive Battery [MCCB] was used to test cognitive functions. In a simple randomization process participants were assigned to receive either mindfulness therapy (eight sessions, 1,5 h each, once a week), according to the standard training of Mindfulness Based Cognitive Therapy (MBCT; Segal et al., 2002) and adapted for patients with psychosis (Chadwick et al., 2005), alongside treatment as usual (MT + TAU) or TAU (TAU; i.e., pharmacological and psychosocial intervention).

First, multiple independent Welch *t*-tests were performed to evaluate possible differences between groups (MT and TAU) prior to the beginning of the intervention. Second, 2 × 2 mixed ANOVAs were conducted between subject variable Group (MT, TAU) and repeated measure variable Time (Pre, Post & Pre, Follow-up). Effect size is reported using Partial Eta Squared (η^2_P).

Participants were recruited through 4 clinical centers that participated in the study. This process yielded 70 candidates (see Fig. 1 for the consort diagram trial profile). Finally, 45 participants between 16 and 36 years of age met the inclusion criteria and the baseline assessments. No group differences were observed in the participants' age, sex or years of schooling (MT; M = 24.0, SD = 4.98, 62.5% male; TAU; M = 23.6, SD = 45.75, 95.2% male). The dropouts are detailed in Fig. 1.

Regarding the cognitive areas of interest in the study, we focused first on the Attention/Vigilance, Working Memory, and Social Cognition dimensions of the MATRICS. At Post-treatment, we found that neither Working Memory nor Social Cognition showed significant main effects or interactions. The Attention/Vigilance domain showed a significant Time main effect ($F(1,33) = 12.20$, $p < .01$, $\eta^2_P = 0.06$), without a significant Group main effect or Group × Time interaction. Similar results were found on the overall Composite Cognitive Score ($F(1,33) = 7.87$, $p < .01$, $\eta^2_P = 0.01$) and the Speed of Processing Domain ($F(1,33) = 4.40$, $p < .05$, $\eta^2_P = 0.02$) (for the rest of the dimensions see Supplementary data). At 3-month follow-up, the mixed ANOVA showed no significant main effects or interactions in the Attention/Vigilance and Working Memory domains, but we found a significant Group main effect in the Social Cognition domain ($F(1,24) = 5.00$, $p < .01$, $\eta^2_P = 0.01$), without significant interaction. However, after excluding cases due to missing data at follow-up, baseline Social Cognition differed between groups ($t = 2.45$, $df = 22.3$, $p = .02$). Furthermore, we found a significant Time main effect on the Speed of Processing domain ($F(1,24) = 6.78$, $p = .01$, $\eta^2_P = 0.01$).

Results show that MT and TAU produce the same positive effects on Attention/Vigilance, Speed of Processing and general cognitive functioning. At follow-up, the effect of MT and TAU on Speed of Processing was preserved. Given the novelty of this research, a direct comparison with previous studies was not possible. Nevertheless, a meta-analysis of the effect of Cognitive Remediation on cognitive functions in early schizophrenia found similar outcomes. Specifically, CR did not have a significant effect on global cognition and only the verbal learning domain of the MATRICS showed a significant improvement in comparison with the control groups (Revell et al., 2015). Relevant limitations should be noted and considered as part of the context of these findings. The sample size was small. The original recruitment target estimated was not achieved and this had a direct impact on the statistical power. We used simple randomization without stratification; thus, confounding variables in cognitive functions such as the prescription and dose of antipsychotic medications were not controlled.

In conclusion, eight MBIs sessions adapted for psychosis but not specific for cognitive impairments may not be enough to achieve significant effects on cognitive dimensions. Therefore, at least twelve sessions of MBIs tested in larger samples are recommended in order to confirm to what extent mindfulness does or does not have a differentiating effect on cognitive functions (Chien et al., 2019). Moreover, this is the first

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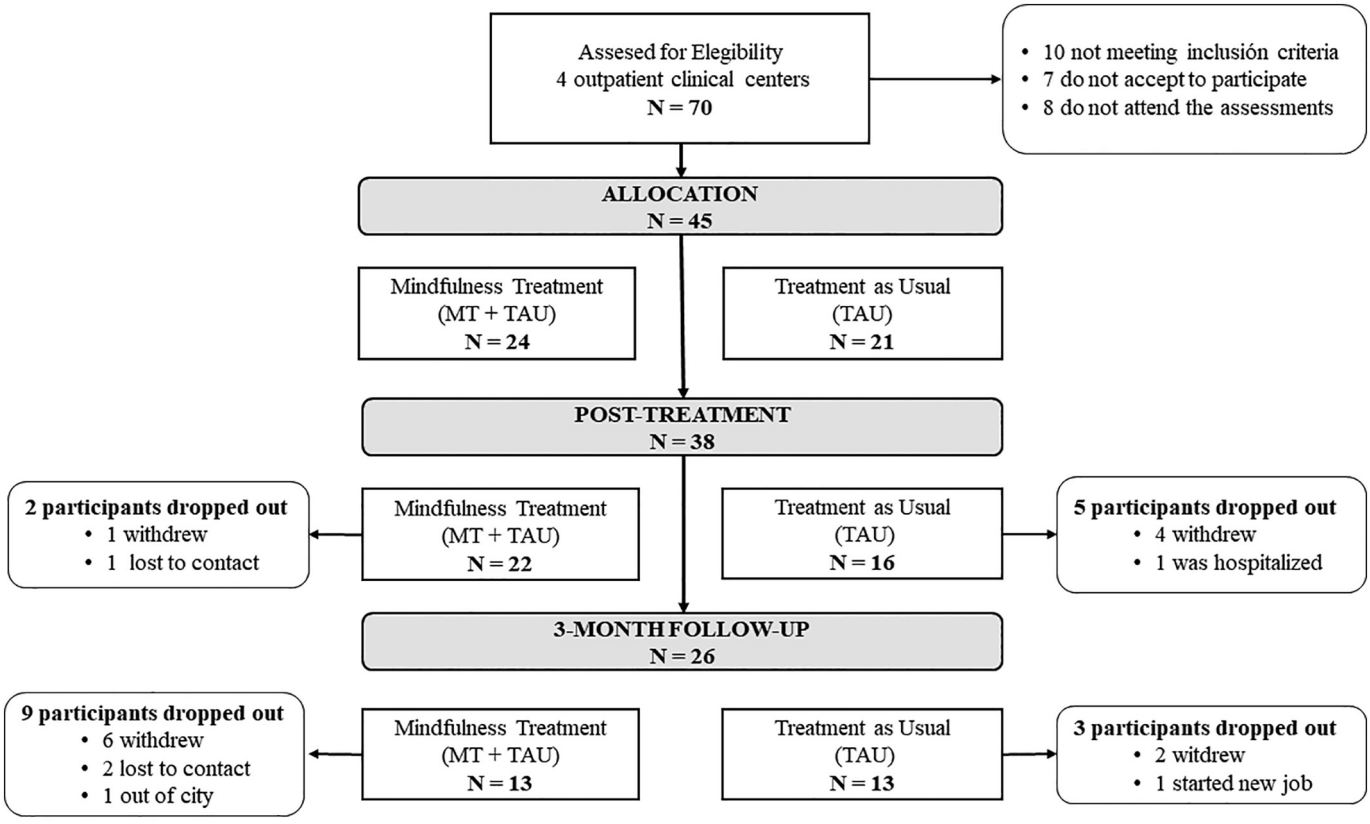

Fig.1. Flow Diagram random controlled trial

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study to apply mindfulness in schizophrenia in Latin America confirming its feasibility and acceptability, giving cross-cultural validity to mindfulness as a non-harmful intervention.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.schres.2020.07.012.

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