Schizophrenia Research 212 (2019) 140–149

Contents lists available at ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

Effectiveness of a mindfulness-based psychoeducation group programme for early-stage schizophrenia: An 18-month randomised controlled trial

Wai Tong Chien [a,*], Ho Yu Cheng [a], Terry W. McMaster [b], Annie L.K. Yip [c], JoJo C.L. Wong [a]

[a] The Nethersole School of Nursing, Faculty of Medicine, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong, China
[b] Department of Psychology, Concordia University, Montreal H4B 1R6, Quebec, Canada
[c] School of Nursing, The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong, China

ARTICLE INFO

Article history:
Received 8 October 2018
Received in revised form 17 April 2019
Accepted 28 July 2019
Available online 12 August 2019

Keywords:
Functioning
Mindfulness-based intervention
Psycho-education group
Psychotic symptoms
Schizophrenia

ABSTRACT

Current psychosocial interventions in schizophrenia are evidenced to improve patients' illness-related knowledge, mental status and relapse rate, but substantive benefits to patients, such as their functioning and insight into the illness, remain uncertain. This multi-centre randomised clinical trial aimed to examine the effects of mindfulness-based psycho-education group intervention for adult patients with early-stage schizophrenia over an 18-month follow-up. The controlled trial was conducted with a repeated-measure, three-arm design at two psychiatric outpatient clinics in Jilin (China) and Hong Kong. A stratified random sample of 180 outpatients with schizophrenia spectrum disorders (60/group) was randomly assigned to a mindfulness-based psycho-education group programme, psycho-education group and treatment-as-usual group. The primary outcomes on patients' psychosocial functioning and other patient outcomes, such as psychotic symptoms, in the three groups were compared over the 18-month follow-up (baseline and 1-week, 9-month and 18-month post-intervention). One hundred and sixty (89%) patients completed at least two post-tests. Their mean age and duration of illness were 25–28 years (SD = 6.1–7.8) and 2.1–2.5 years (SD = 1.3–2.0; range 4–54 months), respectively. Compared with the two other groups, the mindfulness-based group exhibited a significantly greater improvement with moderate to large effect sizes (Cohen's d = 0.49–0.98) in functioning ($p = 0.005$), duration of psychiatric re-hospitalisations ($p = 0.007$), psychotic symptoms ($p = 0.008$) and illness insight ($p = 0.001$) over the 18-month follow-up. Supplementary MRI findings indicated that the mindfulness-based intervention resulted in significant changes in gray matter volume and density in brain regions concerning attention and emotional regulation. Mindfulness-oriented psycho-education group intervention can be an effective intervention for adults with early-stage schizophrenia and exert long-term effects on patients' functioning and mental conditions.

1. Introduction

With the continuous reduction in psychiatric institutionalisations, most people with schizophrenia receive community-based rehabilitation services after a short acute inpatient treatment. In 2016, about 22 million individuals with this disorder worldwide were diagnosed with a wide range of psychological, volitional and behavioural abnormalities (Owen et al., 2016; World Health Organisation, 2016). Despite the increased development of new anti-psychotic medication to reduce psychotic symptoms, people with schizophrenia still experience disabling residual symptoms, poor functioning and high risks of relapses (Bellack, 2006; Chien and Yip, 2013).

Recent systematic reviews have suggested that psycho-education groups and cognitive-behavioural therapy for schizophrenia can enhance patients' knowledge of and coping with this illness, medication adherence and relapse prevention (Xia et al., 2011; Zhao et al., 2015). Psycho-education is recommended as an integral part of a comprehensive treatment programme for early-stage schizophrenia (National Collaborating Centre for Mental Health, 2014). However, the engagement and long-term compliance with community-based psychosocial intervention of schizophrenic patients remain a challenge for healthcare professionals (Bellack, 2006; Chien et al., 2017). The low illness acceptance and insight, distress over psychotic symptoms, inadequate self-empowerment for illness management, poor volition and concentration and/or lack of interest in lengthy psychosocial intervention of schizophrenic patients are attributed to their sub-optimal treatment engagement and compliance and lead to poor mental and psychosocial conditions (Chien and Chan, 2013; Lee et al., 2006; Zhao et al., 2015). However, these factors in

* Corresponding author.
E-mail address: wtchien@cuhk.edu.hk (W.T. Chien).

https://doi.org/10.1016/j.schres.2019.07.053
0920-9964/

schizophrenia care have received limited research attention (Bäuml et al., 2006). In addition, emotional regulation plays an important role in the psychosocial functioning of these patients, but impairment in emotional regulation and control is common amongst psychotic patients (Moran et al., 2018). Thus, an insight-enhancing, patient-empowering approach must be developed for schizophrenia intervention, and its effects on improving patients' illness insight and functioning need to be tested.

Mindfulness-based stress reduction (MBSR) programmes are amongst the very few interventions that focus on enhancing an individual's self-awareness and acceptance and modifying his/her negative thoughts, emotions and feelings towards an illness and related distress (Chiesa and Serretti, 2011; Kabat-Zinn et al., 1992). Recent studies have revealed the promising performance of standardised eight-session MBSR programmes in stress reduction, self-acceptance and illness management in depression and anxiety disorders (Chiesa and Serretti, 2011; Moritz et al., 2015). The positive psychological effects of mindfulness training are believed to be mediated or attributed by reductions in over-general memory and ruminative thinking, improvements in meta-awareness and specificity of describing depressive/anxiety symptoms and enhancement of individuals' ability to reflect on their current crises in a decentred manner and thus relate differently to the distressed experience(s) (Hölzel et al., 2011b). A growing body of evidence has demonstrated that neural structures in adults are modifiable upon training (Hölzel et al., 2011a). The practice of mediation and MBSR has been found to increase brain gray matter density, particularly in the hippocampus and insular regions; these regions have been postulated to play a key role in the modulation of emotional regulation and awareness (Gotink et al., 2016; Hölzel et al., 2011a). Although several studies have shown that mindfulness practices can potentially exacerbate psychotic symptoms (Hölzel et al., 2011b), two pilot studies on mindfulness training alone or mindfulness integrated with cognitive–behavioural therapy for psychotic patients with distressing voices and/or paranoia reported statistically significant pre- and post-test improvements on these patients' insight, psychological distress and disability (Chadwick et al., 2009; Dannahy et al., 2011). The findings of a qualitative grounded theory analysis of 16 psychotic patients revealed that learning to respond mindfully to distressing symptoms leads to feelings of reclaimed power and acceptance of the illness experience (Abba et al., 2008). The focused awareness of sensation and thoughts, enhanced acceptance, holding and letting be of illness experiences and enhanced self-empowerment and emotional regulation regarding illness management provided by the mindfulness-based intervention approach (N. Khoury et al., 2013; B. Khoury et al., 2013) may also be helpful for patients with early-stage schizophrenia who need to cope with their active psychotic symptoms and related emotional distress. Recent systematic reviews have indicated that psycho-education programmes can improve not only the knowledge and treatment adherence of schizophrenic patients but also their stress coping and problem-solving abilities, thus enhancing their social and occupational functioning (Bäuml et al., 2006; Xia et al., 2011; Zhao et al., 2015). Integration of psycho-education into mindfulness intervention may produce complementary and synergic effects that could enhance the cognitive, informational and behavioural readiness of patients to be aware of or accept their illness condition and then to learn, select and adopt effective strategies in controlling their psychotic symptoms by relating differently and insightfully to the symptoms (Chien et al., 2017).

Asian psychotic patient populations have less self-affirmation and openness to experience attitudes than Western patients (Lam and Chien, 2016; Strauss et al., 2015), but mindfulness-based interventions were developed/tested in Western populations (Baer, 2003; Chiesa and Serretti, 2011). Therefore, a three-arm randomised controlled trial of a mindfulness-based psycho-education group programme (MPGP) for early-stage schizophrenia spectrum disorders (≤5 years of illness) was conducted in Chinese populations in this study. The outcomes on schizophrenic patients under the programme, patients receiving usual psychiatric care with a psycho-education group programme (CPGP) and patients with treatment-as-usual (TAU) were compared over 18 months of follow-up. We hypothesised that the MPGP participants would show significantly greater improvements in their psychosocial functioning (primary outcome) and illness insight and larger reductions in psychotic symptoms and re-hospitalisation rates than the participants in CPGP or TAU over the 18-month follow-up.

2. Methods

An 18-month assessor-blind multi-site RCT with repeated measures and a three-group design (ClinicalTrials.gov NCT01667601; Ethical approvals: HSEARS20140218003/KCE-13-0148/ER for Hong Kong; JMC-12-3404RCT61 for China) was implemented at four psychiatric outpatient clinics (two in Hong Kong and two in Jilin, China). Around 2200 patients with schizophrenia and its subtypes were attending the two study clinics in each city ($N = 4400$) during the study period.

2.1. Participants and randomisation

Amongst the 600 (27%) outpatients accessible for screening by ALKY in each city, 308 (51%) in Hong Kong and 285 (48%) in Jilin were found to be eligible and agreed to participate. All eligible patients were Chinese residents, aged 18–60, diagnosed with schizophrenia or its subtypes according to DSM-IV-TR (American Psychiatric Association, 2000) via the Structured Clinical Interview (First et al., 2001), have had the illness for ≤5 years and were able to read and communicate in Chinese. Patients who were diagnosed as co-morbid with organic brain syndrome, had a learning disability, were mentally unstable/unfit for research as recommended by a psychiatrist or received (receiving) any psychosocial intervention(s) within the past six months were excluded. Twenty-eight and 31 (about 5%) eligible patients in the two cities refused to participate mainly due to the lack of interest/time and feeling of being stigmatised.

Sample size estimation was based on the effect sizes of patients' psychosocial functioning, mental state and re-hospitalisation rates ranging from 0.46 to 0.70 at 6-month and 12-month post-interventions in two controlled trials (Chien et al., 2012; Chien and Thompson, 2014) and systematic reviews (Chiesa and Serretti, 2011; Lam and Chien, 2016) of psycho-education and/or mindfulness-based programmes for psychotic disorders. Another pilot trial of mindfulness-based intervention for schizophrenia indicated that the effect sizes on symptom severity and average hospital days at post-test are 0.52 and 0.46, respectively, compared with a psycho-education group (Wang et al., 2016). Considering a 15% attrition rate (Chien and Bressington, 2015; Wang et al., 2016), 180 participants in the three groups (60 per group) showed statistical differences in psychosocial functioning and re-hospitalisation rates at a moderate effect size of 0.46 and study power of 0.80 (two-tailed, $p < 0.05$).

Ninety participants were randomly selected in each city (29% and 32%) by using two independent sets of computerised random numbers generated by an independent statistician, as recommended by the National Health and Medical Research Council Clinical Trials Centre. Informed written consent was obtained, followed by a baseline measurement conducted by a trained research assistant. The participants were stratified by gender and symptom severity (using the Positive and Negative Syndrome Scale; Bell et al., 1992) and randomly assigned into one of the three study groups based on two new sets of computerised random numbers generated by the statistician. The group allocation lists were concealed to the researchers, clinical staff and outcome assessors.

2.2. Interventions

2.2.1. MPGP

The participants received a six-month MPGP (12 two-hour sessions biweekly; 14–16 subjects/group) that was modified from Kabat-Zinn's MBSR and integrated into a psycho-education programme tested in Chinese psychotic patients (Chien and Bressington, 2015; Chien and Thompson, 2014; Wang et al., 2016). Two trained psychiatric nurse specialists (with >5 years of clinical and >3 years of mindfulness training experiences; one for the two clinics in each city) led/facilitated six MPGP groups. The programme comprised seven parts (see details in *Supplementary Information Table A*), such as guided body scan for awareness, mindful exercises, homework practice and education workshop on schizophrenia management and problem solving. During the early stages/sessions, each participant was encouraged to perform regular practice (at least once daily; 20–30 min per practice session) of focused/intentional attention of body sensations, thoughts and feelings. In later sessions, they were encouraged to establish self-constructive views and self-empowerment to work on their negative thoughts and emotions and thus enhance their positive thoughts to resolve illness-related problems in their minds, life situations, thoughts and emotions, particularly those relating to traditional Chinese culture (beliefs/attitudes and behaviours). Examples included the following:

- Sessions 1–3: Understanding participants' strong interdependence, encouraging mutual support, practicing the expression of feelings openly and exploring different views on life situations in groups;
- Sessions 4–8: Cultivating an open and accepting attitude, positive thinking and responses to life problems and developing a 'decentred' (passing events in mind) attitude on thoughts and feelings (Ma and Teasdale, 2004; Chien and Thompson, 2014); education workshops on schizophrenia and its treatment and care, coping and problem-solving training for illness/symptom management;
- Sessions 9–12: Reconstructing role perception and identity by putting aside strong self-centeredness, which is traditionally common amongst Chinese people.

2.2.2. CPGP

Conventional CPGP was implemented similar to MPGP (12 two-hour sessions biweekly; 13–16 subjects/group). The group psycho-education manual established in Lehman et al.'s (2004) PORT programme and modified by Chan et al. (2009) was adopted. The group participants received education and psychological support from a trained psychiatric nurse specialist who was experienced in psychiatric rehabilitation and education groups (5–7 years). The CPGP consisted of four phases: (a) overview, engaging and goal setting (two sessions); (b) mental health education, survival and stress management skills training (four sessions); (c) relapse prevention and resilience promotion through problem-solving and interpersonal and living skills training (four sessions); and (d) evaluating the knowledge and skills learned and future plans (two sessions).

2.2.3. TAU

The patients in TAU received only routine community psychiatric and mental healthcare services, which were similar across the clinics attended by all of the study groups. These services could involve psychiatrist consultations, treatments and referrals for specialised care (every 4–6 weeks); mental health education and advice on community services by mental health nurses; advice/referrals on social welfare and finance by social workers; and home visits by community nurses (every 3–5 weeks).

2.3. Training of nurse therapists and intervention fidelity

A three-day training workshop was provided by the researchers to the two psychiatric nurse specialists conducting the MPGP or CPGP (see *Supplementary Information Table B*). The nurses then delivered a similar group programme to five inpatients with schizophrenia for supervised practice and evaluation before study implementation.

An expert panel (psychiatrists, nurse specialists, occupational therapists, clinical psychologists and ex-patients with schizophrenia) validated the MPGP and CPGP manuals. Most of the topics/items in these manuals were independently rated as very satisfactory in terms of their relevance (92%–99%) and appropriateness (90%–91%); only a few items were modified in terms of their expressions/format to enhance clarity. All MPGP and CPGP sessions were audio-recorded (with participants' consent) and reviewed by the researchers and interventionists to monitor treatment fidelity in-between sessions. Fidelity levels (adherence to items/topics) were examined with a checklist (Bellg et al., 2004) by the first author, and the scores ranged from 91%–98% for MPGP (average of 93.5%) and 90%–96% for CPGP (average of 91.8%), indicating a very satisfactory intervention compliance and consistency amongst the interventionists.

2.4. Data collection and outcomes

After obtaining the patients' consent, a research assistant assessed their characteristics and study/outcome variables at the baseline in a quiet interview room before randomisation. Another research assistant who was blinded to the intervention allocation measured the study outcomes via three post-tests (1-week and 9- and 18-month post-intervention).

The participants' outcomes on psychosocial functioning (primary outcome), insight into the illness/treatment and psychotic symptoms were measured with validated instruments in Chinese administered by the research assistants. Table 1 summarises the psychometric properties of the instruments, including the Specific Level of Functioning Scale (SLOF; Schneider and Struening, 1983) and its three subscales (self-maintenance, social functioning and community living skills), Insight and Treatment Attitudes Questionnaire (ITAQ; McEvoy et al., 1989), Positive and Negative Symptoms Scale (PANSS; Bell et al., 1992) and its two subscales (Positive Symptoms and Negative Symptoms) and Five Facet Mindfulness Questionnaire (FFMQ; Baer et al., 2006). SLOF was reported by one family carer of each patient. The participants' numbers and durations (days/month) of re-hospitalisation in the past six months, the total participants per group being hospitalised and the types/dosages of antipsychotics used were retrieved from patient records. All medication dosages were transformed into haloperidol equivalents (Bezchlibnyk-Butler et al., 2013), and other psychological therapies received during the study period were checked and compared between groups.

2.5. Statistical analyses

The intention-to-treat principle was adopted for data analysis using SPSS (IBM) for Windows (version 22.0). The participants' characteristics and baseline outcome variable scores with significant between-group differences were set as co-variate(s) in the outcome analyses. The mixed-model multivariate analysis of variance (MANOVA) test was performed to examine the interaction (Group × Time) treatment effects within- and between-group on all outcomes across four measurements. Missing data, which were found to be minimal, were replaced by the group mean values of the respective outcomes. With significant MANOVA results, a repeated-measure ANOVA test was used to compare between-

Table 1
Outcome measurements used in this study.

Study outcomes	Measurements	Number of items and rating	Psychometric properties		
			Cronbach's alpha	Test-retest reliability	Validities
Primary outcome					
Psychosocial functioning	Specific Level of Functioning Scale (SLOF) (Schneider and Struening, 1983; Chien et al., 2006; Chan et al., 2009)	43 items (1-'fully dependent' to 5-'fully self-sufficient') ↑ score: ↑psychosocial functioning	0.90–0.95	0.84–0.88	Content
Secondary outcomes					
Insight into illness/ treatment	Insight and Treatment Attitudes Questionnaire (ITAQ) (McEvoy et al., 1989; Wang et al., 2016)	22 items (0-'no insight' to 2-'good insight') ↑ score: ↑insight into illness/treatment	0.82	0.82	Content
Psychotic symptoms	Positive and Negative Symptoms Scale (PANSS) (Bell et al., 1992; Chien et al., 2012)	30 items (0-'absent' to 7-'extreme') ↑ score: ↑ psychotic symptoms	0.87–0.92	0.85–0.90	Concurrent
Level of performance of mindfulness skills	Five Facet Mindfulness Questionnaire (FFMQ) (Baer et al., 2006)	39 items (1-'never/very rarely true' to 5-'very often/always true') ↑ score: ↑ level of performance/practice of the five mindfulness skills, namely observing, describing, performing with awareness, non-judgmental to inner experience, and not over-reacting to these experiences.	0.76–0.92		Predictive
MRI data	Signa 3-T MRI system (CV/I hardware, LX9.0 software) with a standard head coil; image analysis was performed by using a voxel-based morphometry tool	Three-dimensional magnetisation-based rapid gradient echo pulse sequence was acquired to collect a T1-weighed MPRAGE-sequence (i.e., 1.0 × 1.0 × 1.3 mm, T1 = 1000 ms, Repetition Time (TR) = 2500, Echo Time (TE) = 3.00 ms, matrix = 256 × 192, FOV = 256 × 256, sagittal slices = 128, and total time = 7 min)		Normalisation parameters at different time-points ensured regional differences between images could be captured (Driemeyer et al., 2008)	Calibration and normalisation parameters estimated at pre-scan and different time-points

group differences on individual outcomes (SLOF, re-hospitalisation rates, ITAQ and PANSS) and dosage of antipsychotics across measurements.

For outcomes with significant between-group differences, Helmert's contrast tests were used to compare the between-group mean score differences on individual outcomes at each post-test (Tabachnick and Fidell, 2001). Differences in participant outcomes in MPGP indicating significant treatment effects were examined between the four clinics and two cities under study and between low (<6 sessions) and high (≥10 sessions) attendees by using ANOVA or Kruskal–Wallis H tests. The total number of patients hospitalised (in the last six months) between groups and the total score of FFMQ amongst the MPGP participants were also compared across measurements by using the Kruskal–Wallis test (followed by the Mann–Whitney *U* test, if found significant). The level of statistical significance was set at $p = 0.05$.

3. Results

The study commenced in January 2014 and ended in February 2016, with the recruitment ending in May 2014. As shown in the study diagram (Fig. 1), 160 participants (89%) completed at least two of the three post-tests. One to two participants in each of the three study groups withdrew from the study ($n = 5$) or lost contact ($n = 4$ during intervention and $n = 3$ at 1-week post-intervention); their data were not analysed. Eight participants ($n = 2$ in MPGP and CPGP, $n = 4$ in TAU) also lost contact in the 18-month follow-up. Three participants (5%) in MPGP and CPGP failed to complete more than six intervention sessions. The reasons for study withdrawal and incompletion of interventions were similar between groups, and they included time inconvenience for programme attendance ($n = 4$), lack of interest in participation ($n = 4$) and poor mental state ($n = 4$) and inadequate family/social support ($n = 3$).

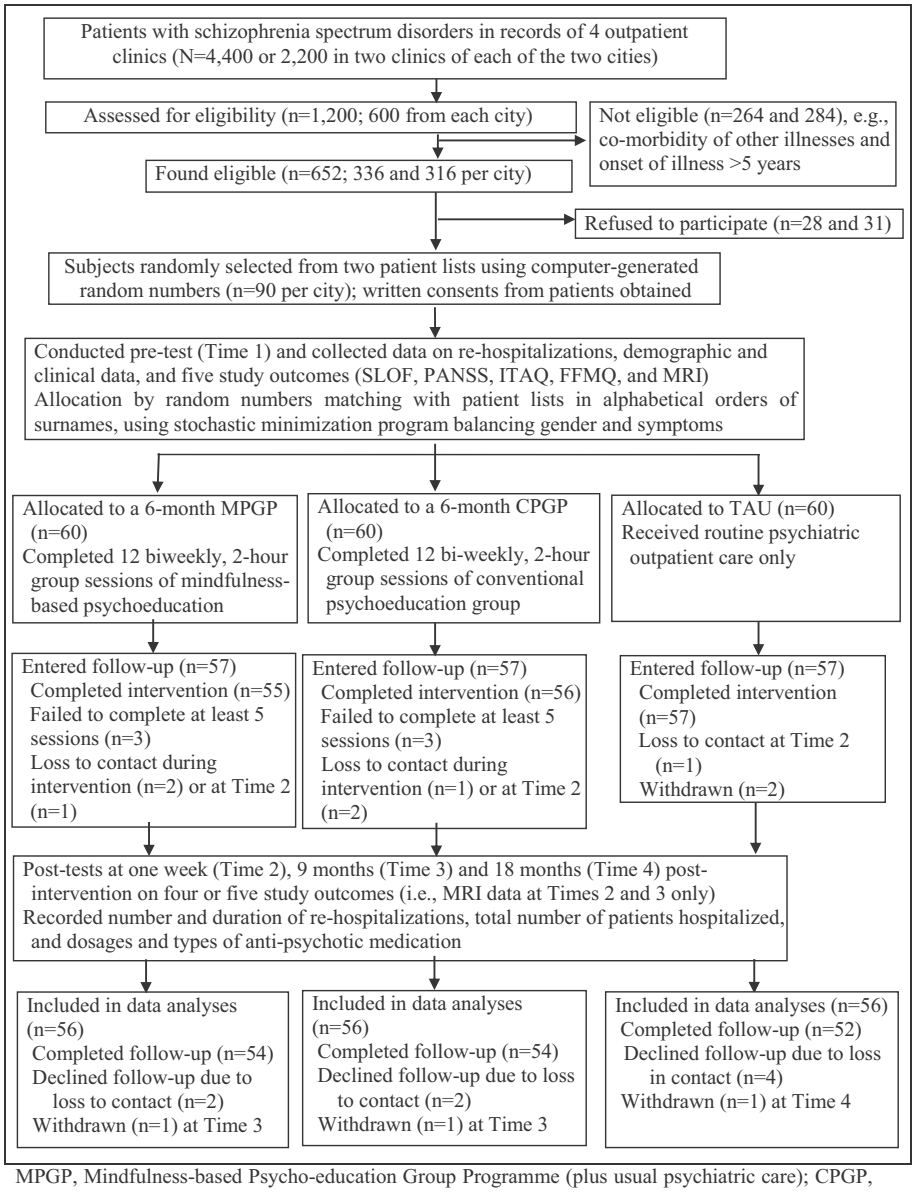
3.1. Participant characteristics

The socio-demographic and clinical characteristics of the participants are summarised in Table 2. Their mean ages were 24–26 ± 6.7–7.2 years (range: 18–38 years), and more than half were male (53%–57%) and clinically diagnosed with schizophrenia (50%–57%). More than half of the participants were prescribed with first-generation antipsychotics, and 78%–83% of them were in a low/medium dosage (haloperidol equivalents of 5.0–10.3 mg/day; Bezchlibnyk-Butler et al., 2013)

No significant differences were found in all participant characteristics in the three groups ($p > 0.18$) and two studied cities ($p > 0.15$). No significant between-group differences in baseline outcome scores were also observed (Table 3). Only very minimal missing data (<2%) were found in two outcomes of eight participants in the different study groups, and these data were filled by using the individuals' previous data (Tabachnick and Fidell, 2001).

3.2. Treatment effects

The effects of MPGP, CPGP and TAU on participant outcomes across the three post-tests are summarised in Table 3. The results showed significant combined interactive (Group × Time) treatment effects on the five outcomes amongst the three groups [$F(5,166) = 9.02$, $p = 0.001$, Wilks' $\lambda = 0.98$ and partial $\eta^2 = 0.44$], showing a large effect size. For between-group effects on individual outcomes considered independently, MPGP indicated significantly greater improvements than CPGP or TAU in the primary outcome, namely, psychosocial functioning [$F(2,165) = 8.10$, $p = 0.005$] (Fig. 2), and in three other outcomes, namely, duration of re-hospitalisation [$F(2,166) = 6.82$, $p = 0.007$], psychotic symptoms [PANSS total score, $F(2,166) = 6.31$, $p = 0.008$] and insight into the illness/treatment [$F(2,166) = 9.25$, $p = 0.001$]. MPGP also showed



MPGP, Mindfulness-based Psycho-education Group Programme (plus usual psychiatric care); CPGP, Conventional Psychoeducation Group Programme (plus usual psychiatric care); TAU, Treatment-as-usual only.
FFMQ, Five Facet Mindfulness Questionnaire; ITAQ, Insight and Treatment Attitudes Questionnaire; PANSS, Positive and Negative Syndrome Scale; SLOF, Specific Level of Functioning scale.

Fig. 1. Flow diagram of the controlled trial procedure.

significant improvements in three functioning (SLOF) subscales ($p < 0.05$) and in positive and negative symptoms (PANSS subscale scores; $p = 0.004$ and 0.008, respectively) compared with the CPGP and TAU groups over the 18-month follow-up. MPGP also had significantly fewer patients re-hospitalised over past six months than CPGP or TAU at 9-month and 18-month follow-ups ($n = 6$ vs. 13–21; $p = 0.08$–0.006).

The contrast tests results indicated that MPGP had significantly greater improvements in the mean score differences of four outcomes in the three post-tests than CPGP and/or TAU.

(a) Psychosocial functioning (SLOF) increased in all three post-tests (between-group mean difference = 18.8–43.3, $p = 0.008$–0.001) compared with TAU and in post-tests 2–3 (mean difference = 15.7 and 12.8, $p = 0.01$ and 0.03) compared with CPGP.
(b) Average hospital stay (days) decreased in post-tests 2–3 compared with TAU (mean difference = 9.8 and 11.5, $p = 0.008$ and 0.002) and CPGP (mean difference = 3.0 and 8.3, $p = 0.05$ and 0.009).
(c) Psychotic symptoms (PANSS total score) decreased in all three post-tests (mean difference = 26.4–41.8, $p = 0.01$–0.001) compared with TAU.
(d) Insight into the illness/treatment (ITAQ) improved in 9- and 18-month follow-ups (mean difference = 4.2 and 6.9, $p = 0.008$ and 0.005) compared with TAU.

Regarding the subgroup analyses of the participants in MBPG, no significant differences were observed in the significant outcomes, dosages/types of antipsychotics and other family/individual psychotherapies between the two cities ($p = 0.20$–0.38) or the four clinics ($p = 0.10$–0.26) and in subgroups of MPGP with low (<6)

Table 2
Baseline socio-demographic and clinical characteristics of participants.

Characteristics	MPGP (n = 60) n, %	CPGP (n = 60) n, %	TAU (n = 60) n, %	*F* or *H* value[a]	P
Gender				1.13	0.30
Male	34, 56.7	32, 53.3	34, 56.7		
Female	26, 43.3	28, 46.7	26, 43.3		
Age (years) (mean, SD)	(24.2, 7.2)	(25.8, 6.7)	(25.4, 6.8)	1.20	0.27
18–25	27, 45.0	25, 41.7	27, 45.0		
26–30	21, 35.0	21, 35.0	23, 38.3		
31–38	12, 20.0	14, 23.3	10, 16.7		
Primary clinical diagnosis				1.60	0.20
Schizophrenia	34, 56.7	32, 53.3	30, 50.0		
Schizophreniform disorder	12, 20.0	11, 18.3	13, 21.7		
Schizoaffective disorder	9, 15.0	10, 16.7	9, 15.0		
Other psychotic disorders	5, 8.3	7, 11.7	8, 13.3		
Monthly household income (HKD)[b] (mean, SD)	(16,013, 3812)	(15,904, 3980)	(15,365, 4020)	1.42	0.26
10,000 or below	10, 16.7	9, 15.0	8, 13.3		
10,001–15,000	21, 35.0	22, 36.7	22, 36.7		
15,001–25,000	22, 36.7	20, 33.3	24, 40.0		
25,001–35,000	7, 11.6	9, 15.0	6, 10.0		
Duration of illness (years) (mean, SD)	(2.0, 1.6), range = 0.5–3.9	(1.9, 1.4), range = 0.5–4.1	(2.1, 1.4), range = 0.3–4.5	1.80	0.18
<1	21, 35.0	20, 33.3	20, 33.3		
1–2	20, 33.3	20, 33.3	21, 35.0		
2–3	12, 20.0	12, 20.0	13, 21.7		
3–5	7, 11.7	8, 13.4	6, 10.0		
Use of psychiatric services				1.50	0.25
Medical consultation and treatment planning	60, 100.0	58, 96.7	60, 100.0		
Nursing advice on services and brief education	54, 90.0	55, 91.7	53, 88.3		
Social welfare and financial advice	46, 76.7	47, 78.3	50, 83.3		
Individual/family counselling	22, 36.7	20, 33.3	18, 30.0		
Type of medication				1.98	0.15
Conventional antipsychotics	32, 53.3	31, 51.7	30, 50.0		
Atypical antipsychotics	17, 28.3	16, 26.7	18, 30.0		
Anti-depressants	4, 6.7	5, 8.3	5, 8.3		
Blended mode[c]	7, 11.7	8, 13.3	7, 11.7		
Dosage of medication[d]				1.82	0.18
High	12, 20.0	10, 16.7	13, 21.7		
Medium	34, 56.7	32, 53.3	30, 50.0		
Low	14, 23.3	18, 30.0	17, 28.3		

CPGP, Mindfulness-based Psychoeducation Group Programme (plus usual psychiatric care); CPGP, Conventional Psychoeducation Group Program (plus usual psychiatric care); TAU, Treatment-as-usual only.
[a] Analysis of variance (F-test, df = 148) or Kruskal-Wallis test by ranks (H statistic, df = 3) values.
[b] US$1 = HK$7.83.
[c] Patients were taking more than one type of psychotropic medication such as both the conventional and atypical antipsychotics.
[d] Dosages of neuroleptic/antipsychotic medications in terms of haloperidol-equivalent mean values (Bezchlibnyk-Butler et al., 2013).

and high (≥10 sessions) attendance (p = 0.13–0.21). Mindfulness performance (FFMQ score; Table 3) in MPGP was significantly enhanced over the 18-month follow-up.

3.3. MRI analysis as supplementary data to support the effects of MBPG

To support the effects of MBPG on the brain structural change of interoceptive awareness/attention and emotional regulation, a priori MRI analysis of the selected region of interest (ROI: bilateral insulae and hippocampi) was performed to supplement the neurophysiological changes induced by the intervention (Gotink et al., 2016). A radiologist who was blinded to the group allocation collected and analysed the MRI data a week before and 9 and 18 months after intervention. ROI was examined with high-resolution MRI data (Signa 3-T MRI system) at the Biomedical Imaging Centre of the study hospitals. Image analysis was performed using a voxel-based morphometry tool/software with default settings (MATLAB 7.0, Mathworks Inc., Natick, USA), thus allowing automatic statistical comparisons of all scanned data on ROI (within the left hippocampus, posterior cingulate cortex, left temporo-parietal junction and cerebellum). Volumetric changes in the brain images were processed and measured by Ana Navarrete using the freeware MiPAV 7.0.1 (http://mipav.cit.nih.gov/). A repeated-measure ANCOVA test using age and gender as covariants was implemented to compare the MRI data on ROI between groups at the baseline and 9- and 18-month post-intervention to support the changes in cerebral connectivity (volume and density) or neuroplasticity in association with the MPGP effects.

The results indicated that compared with CPGP and TAU, MPGP had significantly greater increments in gray matter concentration in all four brain regions (corrected for multiple comparisons across the brain regions), namely, left hippocampus [F(2,160) = 10.97, p = 0.005; large effect], posterior cingulate cortex [F(2,135) = 13.12, p = 0.001; large effect], dorsal anterior insula [F(2,159) = 9.13, p = 0.007; moderate effect] and cerebellar vermis/brainstem [F(2,160) = 8.25, p = 0.01; moderate effect] over 18 months of follow-up (see *Supplementary Information Table C*).

4. Discussion

This multi-centre RCT provided evidence on the benefits of MPGP together with routine psychiatric care in early-stage schizophrenia spectrum disorders with a long-term (18 months) follow-up. In line with progressively elevating mindfulness performance (FFMQ score), the MPGP participants' outcomes, including those in psychosocial functioning, psychotic symptoms,

Table 3
Outcome measure scores at pre- and post-tests and results of MANOVA (group × time) test ($N = 168$).

Outcome/instrument	MPGP (n = 56)								CPGP (n = 56)								TAU (n = 56)								F(2,166), Cohen's d
	Baseline (Time 1)		1-week (Time 2)		9-month (Time 3)		18-month (Time 4)		Baseline (Time 1)		1-week (Time 2)		9-month (Time 3)		18-month (Time 4)		Baseline (Time 1)		1-week (Time 2)		9-month (Time 3)		18-month (Time 4)		
	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	
Psychosocial function/SLOF (43-215)[a]	102.3	16.4	128.8	17.1	147.9	18.8	156.1	16.8	110.1	17.8	122.2	15.8	132.2	14.3	143.4	16.1	102.8	14.0	110.1	19.8	117.1	22.5	112.8	12.5	8.10***, 0.70
Self-maintenance	35.1	11.8	42.3	13.9	49.6	10.1	53.6	10.1	36.6	9.8	40.1	10.1	43.0	9.1	47.8	9.8	33.8	9.1	35.6	8.5	38.5	10.0	37.0	8.9	7.83**, 0.65
Social functioning	32.4	9.3	40.1	11.3	46.1	10.8	47.2	10.8	35.3	7.9	38.8	10.0	41.4	8.8	46.3	10.2	33.5	8.5	35.5	8.9	37.2	10.2	35.2	8.2	7.12**, 0.60
Community living skills	34.8	10.9	46.4	15.2	52.2	15.0	55.3	14.0	38.2	11.5	43.3	11.5	47.8	10.9	49.3	11.9	35.5	10.0	39.0	9.2	41.4	11.9	40.6	11.8	8.60***, 0.78
Re-hospitalisations																									
Average number[b]	2.1	1.2	2.0	1.9	1.8	1.5	1.8	1.0	2.0	1.2	2.0	1.5	2.0	1.6	2.2	1.4	2.2	1.5	2.1	1.6	2.4	2.0	2.3	2.0	3.80, 0.26
Duration[c]	19.8	6.8	15.0	8.1	13.0	6.2	10.5	4.8	19.5	8.9	16.5	9.2	15.9	9.0	18.8	9.8	19.3	9.6	19.7	9.0	22.8	11.0	22.0	10.8	6.82**, 0.49
Number of patients being hospitalised	(16)[e]		(12)		(6)		(6)		(17)		(15)		(13)		(14)		(15)		(17)		(20)		(21)		9.23[d],**, 0.88
Psychotic symptoms/PANSS (30-210)	98.2	10.5	72.1	9.0	67.6	9.8	63.2	9.0	96.0	7.9	89.1	9.0	86.1	9.8	88.1	11.3	90.0	10.5	98.5	11.7	102.8	11.7	105.0	14.8	6.31**, 0.54
Positive symptoms	27.3	7.8	24.1	7.9	20.8	6.3	16.0	6.9	28.8	6.0	25.9	8.8	24.0	7.9	24.5	9.3	26.9	9.2	27.8	9.8	29.9	9.0	32.7	10.1	7.50**, 0.64
Negative symptoms	24.2	7.5	20.0	8.1	19.2	5.9	18.5	5.2	23.6	7.3	23.0	8.2	22.8	6.9	22.0	10.0	23.0	9.1	23.9	8.6	24.2	9.1	24.9	10.0	4.12*, 0.39
Insight/ITAQ (0–22)	9.2	2.8	11.9	4.2	14.2	5.3	15.9	6.8	9.5	2.8	10.5	4.2	12.2	5.9	13.9	6.9	9.2	2.0	10.3	4.2	10.0	6.0	9.1	5.5	9.25***, 0.98
Performance of mindfulness skill/FFMQ (5-25)	9.8	3.9	13.8	5.4	15.3	4.2	18.9	6.8																	8.12[d],**, 0.70

MPGP, Mindfulness-based Psycho-education Group Programme (plus usual psychiatric care); CPGP, Conventional Psychoeducation Group Programme (plus usual psychiatric care); TAU, Treatment-as-usual only.
FFMQ, Five Facet Mindfulness Questionnaire; ITAQ, Insight and Treatment Attitudes Questionnaire; PANSS, Positive and Negative Syndrome Scale; SLOF, Specific Level of Functioning scale.
Baseline (Time 1), 1st measurement at the start of intervention; 1-week (Time 2), 2nd measurement at 1-week post-intervention; 9-month (Time 3), 3rd measurement at 9-month post-intervention; 18-month (Time 4), 4th measurement at 18-month post-intervention.

[a] Possible range of scores of each scale indicated in parenthesis.
[b] Average number of readmissions to a psychiatric hospital or inpatient unit over the previous 6 months at the four measurements (Times 1 to 4).
[c] Duration/length of readmissions to a psychiatric inpatient ward/unit in terms of average number of days of hospital-stay over the previous 6 months at Times 1 to 4.
[d] Kruskal-Wallis test values showing the statistical differences on the total number of patients being hospitalised over the past six months measured between groups, or on the mindfulness practice scores using FFMQ in the MPGP, across four measurements.
[e] Total number of patients in each group being hospitalised over the previous six months at times 1–4 indicated in parenthesis.

* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.005$.

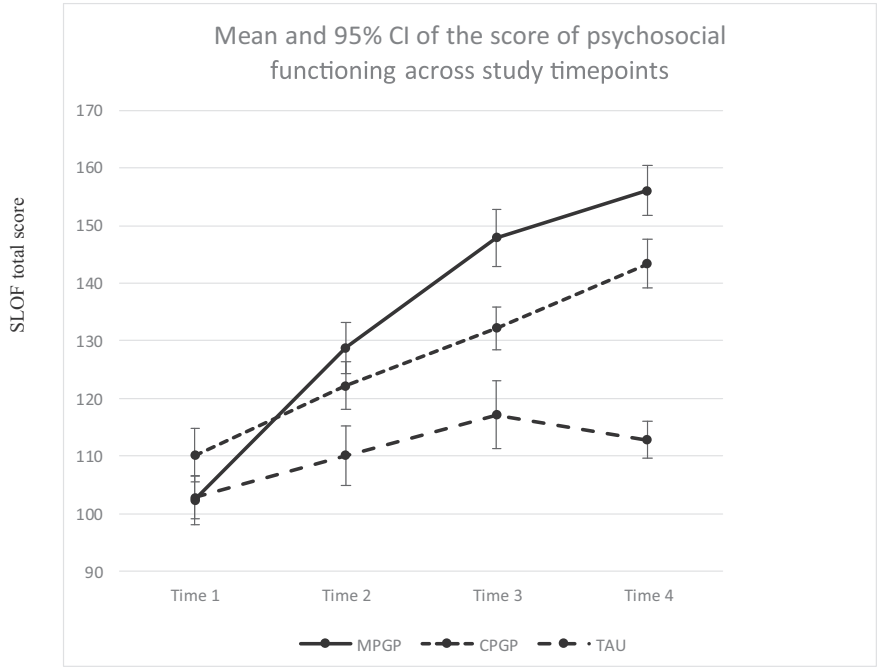


Fig. 2. Time-changing trend profile plots of psychosocial functioning (SLOF total score) of participants across three study groups.

length of re-hospitalisation and insight into the illness, in the two Chinese communities (Hong Kong and Jilin, China) were much more positive/improved when compared with those of the conventional psycho-education groups and usual care only. The short- and long-term outcomes, particularly in psychosocial functioning, insight into the illness and symptom severity, produced by MPGP demonstrated even larger effect sizes than those reported in systematic reviews (Aust and Bradshaw, 2017; Hölzel et al., 2011b; N. Khoury et al., 2013; B. Khoury et al., 2013). As suggested in two recent systematic reviews (N. Khoury et al., 2013; B. Khoury et al., 2013; Aust and Bradshaw, 2017), mindfulness-based intervention can also exert moderate–large effects on negative symptoms, which have rarely been found in most psychiatric treatments and psychosocial interventions for schizophrenia.

In addition, the total number of patients being re-hospitalised in MPGP was significantly lower than that in the two other groups across the follow-ups. MPGP with combined mindfulness and psycho-education group training provided sustainable and considerable benefits (with moderately large effect sizes) to the psychotic patients over the 18-month follow-up. Nevertheless, without examining the benefits of the individual core components, further research is recommended to explore the individual benefits of MPGP to the participants.

Moreover, MPGP can improve various domains of patients' psychosocial functioning (e.g. social functioning and self-maintenance) in early-stage schizophrenia, which is important for these patients to be successfully integrated into the community and live independently in their social environment (Bäuml et al., 2006; Lee et al., 2006). Unlike in the psycho-education groups, MPGP demonstrated a significant effect on enhancing patients' insight into their illness/treatments. These findings support the claim that mindfulness-based intervention is an effective strategy in assisting and facilitating the early recovery (symptom alleviation and functioning improvement) of psychotic patients in community-based rehabilitation (Chiesa and Serretti, 2011). These findings also dispute the common cautions and myths in recent literature about the potential of mindfulness or meditation practices in exacerbating psychotic symptoms and therefore do not support their usage in treating psychosis (Baer, 2003; Coelho et al., 2007; Leykin and DeRubeis, 2009).

The supplementary data of MRI on the significantly increased cerebral gray matter density after MPGP may be related to the patients' insight into their illness/its treatment and improved control of their psychotic symptoms and functioning. The enhanced neural connectivity and activations in the left hippocampus, dorsal anterior insula, posterior cingulate cortex and cerebellar vermis/brain stem after mindfulness practices could facilitate the modulation of cortical arousal and responsiveness and functional activities for emotional, consciousness and attentional responses (Luders et al., 2009), thus relating to enhanced emotion regulation and attentional/consciousness responses to stressors (Milad et al., 2007). The enhanced neural connections/activities in the hippocampus and cerebellum might also have contributed to the increased self-projection and introspective observations of situational experiences encountered (Buckner and Carroll, 2007), thus increasing one's thought/memory process, cognitive/emotional regulation and perceptions of self and others' viewpoints (Carmody et al., 2009). However, the neuroplasticity that occurred in the cerebral cortex amongst the MPGP participants might be due to the effects of other treatments, such as medication and psychosocial skills training. Further research is recommended to investigate the changes in cerebral structure, functions and mechanism of actions induced by mindfulness practices.

This study obtained exceptionally low attrition and high intervention completion rates, especially in MPGP, which are more desirable than those in other psychosocial intervention studies in psychosis. Although the anticipated benefits induced by the 12-session mindfulness training with face-to-face education, review and skills learning could have motivated the participants to complete the programme, other reasons could explain the low attrition rates. The voluntary participants could be highly motivated to improve their illness condition and intensively involved in their community-based rehabilitation. The participants were also young, highly educated and adequately supported by their families; moreover, a culture of respect and trust for professionals/therapists prevails amongst Chinese patients (Chien and Bressington, 2015),

resulting in strong enthusiasm towards illness management and very high intervention completion rates.

However, this work has a few limitations. Firstly, the participants were not blinded to the intervention allocation, which could produce a desirable response bias and likely inflate the treatment effects (Boutron et al., 2017). Secondly, the participants had early-stage (<5 years) schizophrenia only and low to moderate levels of anti-psychotic medication, which is not representative of the wider Chinese psychotic patient populations. Thirdly, although the levels of performance in mindfulness practice in the MPGP participants were assessed by FFMQ, the patients' adherence and regularity of mindfulness practices were difficult to be standardised or addressed by interventions using manual-driven psychosocial or psycho-education programmes (Xia et al., 2011). Lastly, the individual/combined benefits of the individual components of the mindfulness/psycho-education in MPGP are unknown in this study. Therefore, future research is recommended on the therapeutic components and mechanism of actions of MPGP and identifying the relationships amongst patient outcomes, therapeutic components and potential moderators (e.g. symptom severity and illness duration/insight) and mediators (e.g. acceptance and psychological flexibility). In addition, participants' feedback and satisfaction with MPGP and therapist performance can be obtained to understand the acceptability and usefulness of the integrative mindfulness and psycho-education strategies in MPGP. Moreover, patients who had participated in other psychosocial interventions over the past six months or were co-morbid with learning and cognitive problems and mentally unstable were excluded from the study. This exclusion might reduce the generalisability and clinical efficacy of the findings.

Overall, the findings of this study support the use of MPGP in relapse prevention, improvement of psychosocial health and functioning, and thus, community-based rehabilitation in early-stage schizophrenia. Further research is recommended to investigate the effects of mindfulness-based programmes on patients with psychotic disorders by using wider socio-demographic and clinical characteristics in Asian populations and different settings.

Funding

This study was funded by the General Research Fund of The University Grant Council, Hong Kong S.A.R., China (Grant number: 15603815).

Contributors

WTC led all aspects of the study, including study design, writing of the article, data analyses, and writing of the article. ALKY coordinated intervention training, led subject recruitments, and provided inputs to the manuscript. TWM helped the study coordination, assisted the intervention fidelity monitoring and provided statistical support and edits for the article. HYC provided inputs to the writing and final edit on the article. All authors contributed to and have approved the final manuscript. JCLW provided inputs to study design, data analysis and final edits on the article.

Ethical approvals and consents

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consents were obtained from all individual participants (patients) in the study.

Declaration of competing interest

All authors declare that they have no conflict of interest regarding the conduct of this study.

Acknowledgements

The study was supported by the General Research Fund (Ref.: 15603815) of The University Grant Council, Hong Kong S.A.R., China. We expressed our gratitude to the participants and clinicians whose time, effort and willingness to support this study made this clinical trial possible. We also showed our sincere thanks to the outpatient clinics in Jilin, China and Hong Kong provided access and assistance for the implementation and data collection of this study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.schres.2019.07.053.

References

Abba, N., Chadwick, P.D.J., Stevenson, C., 2008. Responding mindfully to distressing psychosis: a grounded theory analysis. Psychother. Res. 18 (1), 77–87.
American Psychiatric Association, 2000. Diagnostic and Statistical Manual of Mental Disorders, fourth text-revised ed. American Psychiatric Association, Washington, DC. DSM IV-TR.
Aust, J., Bradshaw, T., 2017. Mindfulness interventions for psychosis: a systematic review of the literature. J. Psychiatr. Ment. Health Nurs. 24 (1), 69–83.
Baer, R., 2003. Mindfulness training as a clinical intervention: a conceptual and empirical review. Clin. Psychol. Sci. Pract. 10, 125–143.
Baer, R.A., Smith, G.T., Hopkins, J., Krietemeyer, J., Toney, L., 2006. Using self-report assessment methods to explore facets of mindfulness. Assessment 13 (1), 27–45.
Bäuml, J., Froböse, T., Kraemer, S., Rentrop, M., Pitschel-Walz, G., 2006. Psychoeducation: a basic psychotherapeutic intervention for patients with schizophrenia and their families. Schizophr. Bull. 32 (Suppl.1), S1–S9.
Bell, M., Milstein, R., Beam-Goulet, J., Lysaker, P., Cicchetti, D., 1992. The positive and negative syndrome scale and brief psychiatric rating scale: reliability, comparability, and predictive validity. J. Nerv. Ment. Dis. 180 (11), 723–728.
Bellack, A.S., 2006. Scientific and consumer models of recovery in schizophrenia: concordance, contrasts, and implications. Schizophr. Bull. 32 (3), 432–442.
Bellg, A.J., Borrelli, B., Resnick, B., Hecht, J., Minicucci, D., Ory, M., Ogedegbe, G., Orwig, D., Ernst, D., Czajkowski, S., 2004. Enhancing treatment fidelity in health behaviour change studies: best practices and recommendations from the NIH behavior change consortium. Health Psychol. 23 (5), 443–451.
Bezchlibnyk-Butler, K.Z., Jeffries, J.J., Procyshyn, R.M., Virani, A.S., 2013. Clinical Handbook of Psychotropic Drugs, Twentieth ed. Hogrefe and Huber, Boston.
Boutron, I., Altman, D.G., Moher, D., Schulz, K.F., Ravaud, P., CONSORT NPT Group, 2017. CONSORT statement for randomized trials of non-pharmacologic treatments: a 2017 update and a CONSORT extension for non-pharmacologic trial abstracts. Ann. Intern. Med. 167 (1), 40–47.
Buckner, R.L., Carroll, D.C., 2007. Self-projection and the brain. Trends Cogn. Sci. 11, 49–57.
Carmody, J., Baer, R.A., Lykins, E.L., Olendzki, N., 2009. An empirical study of the mechanisms of mindfulness in a mindfulness-based stress reduction program. J. Clin. Psychol. 65 (6), 613–626.
Chadwick, P., Hughes, S., Russell, D., Russell, I., Daqnan, D., 2009. Mindfulness groups for distressing voices and paranoia: a replication and randomized feasibility trial. Behav. Cogn. Psychother. 37 (4), 403–412.
Chan, S.W., Yip, B., Tso, S., Cheng, B.S., Tam, W., 2009. Evaluation of a psychoeducation program for Chinese patients with schizophrenia and their family caregivers. Patient Educ. Couns. 75 (1), 67–76.
Chien, W.T., Chan, W.C.S., Thompson, D.R., 2006. Effects of a mutual support group for families of Chinese people with schizophrenia: 18-month follow-up. Br. J. Psychiatry 189, 41–49.
Chien, W.T., Bressington, D., 2015. A randomized controlled trial of a nurse-led structured psychosocial intervention program for people with first-onset mental illness in psychiatric outpatient clinics. Psychiatry Res. 229 (1–2), 277–286.
Chien, W.T., Chan, W.C.S., 2013. The effectiveness of mutual support group intervention for Chinese families of people with schizophrenia: a randomised controlled trial with 24-month follow-up. Int. J. Nurs. Stud. 50 (10), 1326–1340.
Chien, W.T., Thompson, D.R., 2014. Effects of a mindfulness-based psycho-education programme for Chinese patients with schizophrenia: two-year follow-up. Br. J. Psychiatry 205, 52–59.
Chien, W.T., Yip, A.L.K., 2013. Current approaches to treatments for schizophrenia spectrum disorders, part I: an overview and medical treatments. Neuropsychiatr. Dis. Treat. 9, 1311–1332.

Chien, W.T., Leung, S.F., Chu, C.S.K., 2012. A nurse-led, needs-based psycho-education intervention for Chinese patients with first-onset mental illness. Contemp. Nurse 40 (2), 194–209.
Chien, W.T., Bressington, D., Yip, A., Karatzias, T., 2017. An international multi-site, randomized controlled trial of a mindfulness-based psychoeducation program for people with schizophrenia. Psychol. Med. 47, 2081–2096.
Chiesa, A., Serretti, A., 2011. Mindfulness based cognitive therapy for psychiatric disorders: a systematic review and meta-analysis. Psychiatry Res. 187 (3), 441–453.
Coelho, H.F., Canter, P.H., Ernst, E., 2007. Mindfulness-based cognitive therapy: evaluating current evidence and informing future research. J. Consult. Clin. Psychol. 75 (6), 1000–1005.
Dannahy, L., Hayward, M., Strauss, C., Turton, W., Harding, E., Chadwick, P., 2011. Group person-based cognitive therapy for distressing voices: pilot data from nine groups. J. Behav. Ther. Exp. Psychiatry 42 (1), 111–116.
Driemeyer, J., Boyke, J., Gaser, C., Buchel, C., May, A., 2008. Changes in gray matter induced by learning - revisited. PLoS One 3 (7), e2669. http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0002669.
First, M.B., Spitzer, R.L., Gibbon, M., Williams, J.B.W., 2001. User's guide for the structured clinical interview for DSM-IV Axis-I disorders – research version. In: Biometrics Research. The New York State Psychiatric Institute, New York.
Gotink, R.A., Meijboom, R., Vernooij, M.W., Smits, M., Hunink, M., 2016. 8-Week mindfulness based stress reduction induces brain changes similar to traditional long-term meditation practice: a systematic review. Brain Cogn. 108, 32–41.
Hölzel, B.K., Carmody, J., Vangel, M., Congleton, C., Yerramsetti, S.M., Gard, T., Lazar, S.W., 2011. Mindfulness practice leads to increases in regional brain gray matter density. Psychiatry Res. 191 (1), 36–43.
Hölzel, B.K., Lazar, S.W., Gard, T., Schuman-Olivier, Z., Vago, D.R., Ott, U., 2011. How does mindfulness meditation work? Proposing mechanisms of action from a conceptual and neural perspective. Perspect. Psychol. Sci. 6 (6), 537–559.
Kabat-Zinn, J., Massion, A.O., Peterson, L.G., Fletcher, K.E., Pbert, L., Lenderking, E.R., Santorelli, S.F., 1992. Effectiveness of a meditation-based stress reduction program in the treatment of anxiety disorders. Am. J. Psychiatry 149, 936–943.
Khoury, N., Lecomte, T., Fortin, G., Masses, M., Therien, P., Bouchard, P., Chapleau, M.A., Paquin, K., Hofmann, S.G., 2013. Mindfulness-based therapy: a comprehensive meta-analysis. Clin. Psychol. Rev. 33 (6), 763–771.
Khoury, B., Lecomte, T., Gaudiano, B.A., Paquin, K., 2013. Mindfulness interventions for psychosis: a meta-analysis. Schizophr. Res. 150, 176–184.
Lam, A.H.Y., Chien, W.T., 2016. The effectiveness of mindfulness-based intervention for people with schizophrenia: a systematic review. Neuropsychiatry 6 (5), 208–222.
Lee, S., Chiu, M.Y.L., Tsang, A., Chui, H., Kleinman, A., 2006. Stigmatizing experience and structural discrimination associated with the treatment of schizophrenia in Hong Kong. Soc. Sci. Med. 62 (7), 1685–1696.
Lehman, A.F., Lieberman, J.A., Dixon, L.B., McGlashan, T.H., Miller, A.L., Perkins, D.O., Kreyenbyhl, J., American Psychiatric Association, Steering Committee on Practice Guideline, 2004. Practice guideline for the treatment of patients with schizophrenia, second edition. Am. J. Psychiatry 161 (Suppl. 2), 1–56.
Leykin, Y., DeRubeis, R.J., 2009. Allegiance in psychotherapy outcome research: separating association from bias. Clin. Psychol. Sci. Pract. 16 (1), 54–65.
Luders, E., Toga, A.W., Lepore, N., Gaser, C., 2009. The underlying anatomical correlates of long-term meditation: larger hippocampal and frontal volumes of gray matter. Neuroimage 45, 672–678.
Ma, S.H., Teasdale, J.D., 2004. Mindfulness-based cognitive therapy for depression: replication and exploration of differential relapse prevention effects. J. Consult. Clin Psychol. 72 (1), 31–40.
McEvoy, J.P., Apperson, L.J., Appelbaum, P.S., Ortlip, P., Brecosky, J., Hammill, K., Geller, J.L., Roth, L., 1989. Insight in schizophrenia: its relationship to acute psychopathology. J. Nerv. Ment. Dis. 177 (1), 43–47.
Milad, M.R., Wright, C.I., Orr, S.P., Pitman, R.K., Quirk, G.J., Rauch, S.L., 2007. Recall of fear extinction in humans activates the ventromedial prefrontal cortex and hippocampus in concert. Biol. Psychiatry 62, 446–454.
Moran, E.K., Culbreth, A.J., Barch, D.M., 2018. Emotion regulation predicts everyday emotional experience and social functioning in schizophrenia. Clin. Psychol. Sci. 6, 271–279.
Moritz, S., Cludius, B., Hottenrott, B., Schneider, B.C., Saathoff, K., Kuelz, A.K., Gallinat, J., 2015. Mindfulness and relaxation treatment reduce depressive symptoms in individuals with psychosis. Eur. Psychiatry 30 (6), 709–714.
National Collaborating Centre for Mental Health, 2014. Psychosis and Schizophrenia in Adults: Treatment and Management, National Clinical Guideline No. 178 (Updated ed. 2014). The National Institute for Clinical Excellence, London, UK.
Owen, M.J., Sawa, A., Mortensen, P.B., 2016. Schizophrenia. Lancet 388 (10039), 86–97.
Schneider, L.C., Struening, E.L., 1983. SLOF: a behavioural rating scale for assessing the mentally ill. Soc. Work Res. Abstr. 19 (3), 9–21.
Strauss, C., Thomas, N., Hayward, M., 2015. Can we respond mindfully to distressing voices? A systematic review of evidence for engagement, acceptability, effectiveness and mechanisms of change for mindfulness-based interventions for people distressed by hearing voices. Front. Psychol. 6, 1154. https://doi.org/10.3389/fpsyg.2015.01154.
Tabachnick, B.G., Fidell, L.S., 2001. Using Multivariate Statistics, third ed. Allyn and Bacon, Boston.
Wang, L.Q., Chien, W.T., Yip, L.K., Karatzias, T., 2016. A randomized controlled trial of a mindfulness-based intervention program for people with schizophrenia: 6-month follow-up. Neuropsychiatr. Dis. Treat. 12, 3097–3110.
World Health Organisation, 2016. Fact Sheet – Schizophrenia (Rev. April 2016). Online document. WHO. http://www.who.int/mediacentre/factsheets/fs397/en/. (Accessed 2 January 2018).
Xia, J., Merinder, L.B., Belgamwar, M.R., 2011. Psychoeducation for schizophrenia. Cochrane Database Syst. Rev. 6, CD002831 https://doi.org/10.1002/14651858.CD002831.pub2.
Zhao, S., Sampson, S., Jayaram, M.B., 2015. Psychoeducation (brief) for people with serious mental illness. Cochrane Database Syst. Rev. (4), CD010823 https://doi.org/10.1002/14651858.CD010823.pub2.