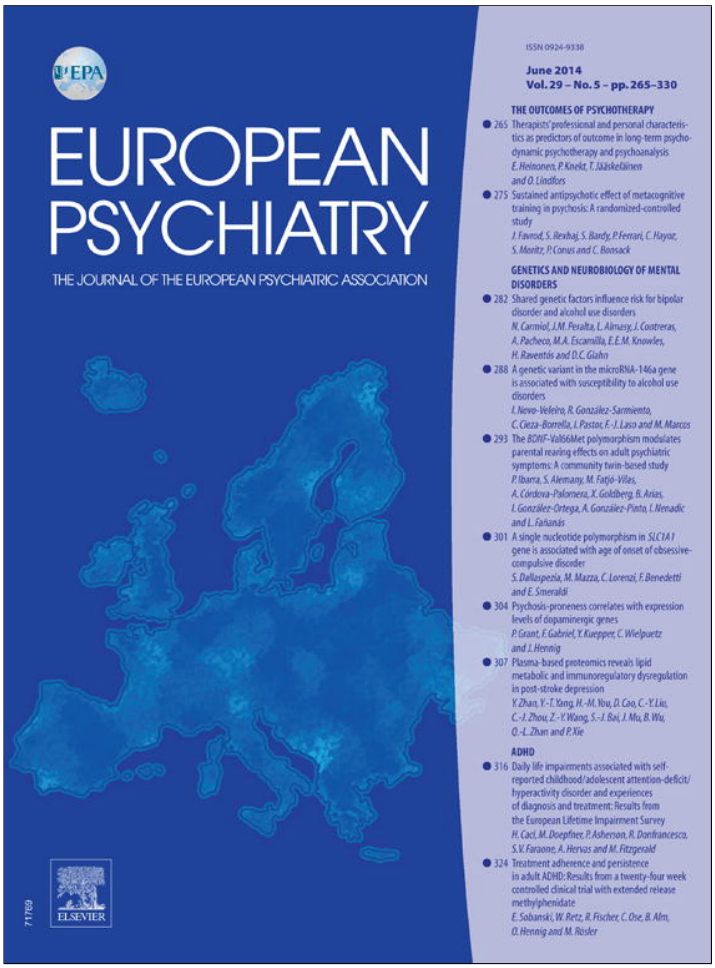

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Original article

Sustained antipsychotic effect of metacognitive training in psychosis: A randomized-controlled study

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ABSTRACT

Persistent psychotic symptoms represent a major challenge for psychiatric care. Basic research has shown that psychotic symptoms are associated with cognitive biases. Metacognitive training (MCT) aims at helping patients to become aware of these biases and to improve problem-solving. Fifty-two participants fulfilling diagnostic criteria of schizophrenia or schizoaffective disorders and persistent delusions and stabilized antipsychotic medication were enrolled in this study. Following baseline assessment patients were randomized either to treatment as usual (TAU) conditions or TAU + MCT. The intervention consisted of eight weekly 1-hour sessions (maximum: 8 hours). Participants were assessed at 8 weeks and 6-months later by blind assessors. Participants were assessed with the Psychotic Symptoms Rating Scales (PSYRATS) and the positive subscale of the PANSS. Between-group differences in post- and pre-test values were significant at a medium effect size in favor of the MCT for the PSYRATS delusion scale and the positive scale of the PANSS both at post and follow-up. The results of this study indicate that MCT training has a surplus antipsychotic effect for patients suffering from schizophrenia-related disorders who demonstrate only a partial response to antipsychotic treatment and that the effect of the intervention persists for at least 6 months after the intervention.

1. Introduction

While antipsychotics agents are undisputedly effective in the treatment of schizophrenia [48], a significant percentage (30 to 40%) of patients experience only a partial response [57]. In addition, antipsychotics strongly reduce the reactions to psychotic symptoms and lead to emotional detachment, but often have limited impact on other aspects such as the contents of delusions and convictions herein as well as level of insight [28,29,52]. Persistent psychotic symptoms represent a major challenge in psychiatry as they are associated with an increased risk of hospitalization [20,49], and interfere with social [11,16] as well as with role functioning [19].

Accordingly, medication treatment is increasingly complemented by psychological treatment, whereby cognitive-behavioral therapy (CBT; [54,56] and cognitive remediation treatment (CRT, [55]) are to date most promising complementary strategies. A new trend in cognitive psychology which has evolved from these two traditions has highlighted the importance of cognitive biases for the understanding of schizophrenia positive symptoms [36]. Cognitive biases are preferences or responses tendencies in the processing of information which operate as triggers for delusional experience [46]. These will be summarized in the following as they are picked up by metacognitive training which lies at the core of the present study. Different definitions of metacognition exist. From a cognitive experimental viewpoint, metacognition refers to the general capacity to think about thinking which generally includes awareness of one's own mental processes, the fallibility of one's own thought, the ability to infer emotions from others faces and prosody, and the cognitive understanding of ideas, beliefs and intentions of other people [26].

A plethora of studies [14] found that 40 to 70% of individuals with schizophrenia arrive at strong conclusions relying on a small amount of information (i.e., jumping to conclusions). Interestingly, patients do not seem to be conscious of their hasty judgment and instead perceive themselves as rather indecisive and hesitant [15] speaking for problems with metacognitive awareness. Individuals

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with schizophrenia can also exhibit memory disturbance, manifested as a reduction of distinct autobiographical memories [44], increased confidence in false memories and reduced confidence in real memories [30,31]. This phenomenon of increased confidence coupled with vague memories is liable to lead an individual to an altered apprehension of reality. Incorrigibility is a main criterion of delusional ideas, but has also been shown to exist beyond delusional content. This cognitive distortion has been termed bias against disconfirmatory evidence is also linked with acute symptoms [10,53]. Numerous studies have demonstrated that psychosis involves severe deficits in social cognition [6,47] which includes theory of mind and attributional biases. Theory of mind is the ability to interpret an individual's speech and actions in terms of his or her intentions, knowledge, and beliefs. While alterations of theory of mind are generally accepted, their specific contribution to delusional ideas is not yet well understood. Individuals with schizophrenia have a tendency to externalize personal experiences, particularly for negative events, which may increase feelings of powerlessness or give rise to feelings of being controlled [25,34]. More recently, a study showed that in addition to a tendency to externalize attributions, there is an excess of monocausal inferences in patients with schizophrenia [42]. The underlying mechanisms of this style of external cognitive attribution have not yet been fully unveiled. Moreover, many patients suffer from poor self-esteem which is observed in 50 to 75% of all patients [5,37]. In essence, half of all individuals with schizophrenia experience concomitant affective troubles [7].

1.1. Metacognitive training in schizophrenia

In order to target the aforementioned biases, Moritz et al. [35] developed a program of metacognitive training which has been validated through various studies showing its safety, feasibility and partial effectiveness, particularly for jumping to conclusions and delusions [1,12,17,23,32,38,39]. In a pilot study based of the French version of the program, we showed that metacognitive training is easy to apply and that it contributes to a reduction of delusional ideas in a francophone context [12]. Therefore, it was predicted that 8 sessions of metacognitive training will reduce significantly delusional ideation compared to treatment as usual and maintain at 6 months follow-up.

2. Subjects and methods

This RCT compares metacognitive training (MCT) to treatment as usual (TAU). Participants were evaluated at baseline (T0), and then randomized either to TAU or TAU + MCT. Randomization was completed by groups of six, eight or ten participants depending on the number of available candidates as we aimed to keep the time period between the first evaluation and the start of the intervention short. The intervention consisted of eight weekly 1-hour sessions, for a maximum of 8 hours of metacognitive training. At the end of the intervention (i.e., 8 weeks later), participants were again assessed (T1) by raters who were unaware of group allocation. A third assessment (T2) was performed 6 months later in order to measure the stability of improvement.

2.1. Identification of patients and recruitment

Outpatients were recruited, in two centers, either in the foundation HorizonSud in the canton of Fribourg and at the General Psychiatry Service and the Community Psychiatry Service of the Department of Psychiatry at the University Hospital Centre in Lausanne (Switzerland). HorizonSud is a social institution offering sheltered accommodation and work to psychiatric patients from the Gruyère area of the Fribourg canton. The foundation takes care of persons diagnosed with schizophrenia spectrum disorders. The General Psychiatry Service of the Department of Psychiatry is divided in specialized sections treating patients aged from 18 to 65 years according to specific diagnostic subgroups. Patients likely to fulfill diagnostic criteria for recruitment are treated in the E. Minkowski section (schizophrenia spectrum disorders) and in the rehabilitation unit of the Community Psychiatry Service. Potential participants were identified through systematic screening by the clinical teams. For newly admitted patients, the research coordinator attended weekly clinical meetings in each of these sections to identify patients fulfilling inclusion criteria (from case presentation of newly admitted patients or by reviewing the current cases with each treating clinical case manager). Inclusion criteria were a schizophrenia spectrum disorder (ICD diagnoses F20, F22, F25). The diagnosis was verified by an experienced clinician. Further criteria were: fluent command of the French language, age between 18 and 65 and partial response to antipsychotic medication. Partial response to antipsychotic medication was defined as a score higher than 2 on the P1 delusion item of the Positive and Negative Syndrome Scale (PANSS) and no increase in antipsychotic dosage or switch to clozapine during the 3 months prior to the study. The largest effect of antipsychotic agents is expected during the first 2 months of treatment [2].

For potential participants, an appointment was organized between patient, clinical case manager and research coordinator in order to explain the study. Each patient included was informed of the following: the aims of the study, the extent and the nature of their participation, including randomization, a description of the control and experimental interventions as well as the three evaluations (pre, post and follow-up). The patients included were also informed about the confidentiality of the data and their right to withdraw from participation at any time. They received a written description of the study.

Once the participant gave his/her consent, the understanding of the protocol of the study was verified with the university of California, San Diego Brief Assessment of Capacity to Consent (UBACC) a decisional capacity instrument [21]. In case of failure to clearly understand the study, patients were excluded. The study received approval by the ethics committee at the University of Lausanne with all participants signing an informed consent form.

Fig. 1 presents the CONSORT table indicating that 86 participants were interviewed to determine their eligibility for the trial. Twenty-three participants did not meet inclusion criteria. Five declined participation and six failed the *San Diego Brief Assessment of Capacity to Consent*.

Fifty-two participants were randomized into the two groups (i.e., TAU or TAU + MCT; screening-to-inclusion ratio: 60%), 26 in each group. Four participants later declined their participation. One participant in the TAU group left the region and could not then be evaluated at T2. This resulted in a drop-out rate of 9.6% for both groups. In the TAU + MCT group, 16 participants followed eight sessions, four followed seven sessions, three followed six sessions, one followed three sessions and one participant did not follow any sessions. On average, participant participated 87% of the sessions. The participant who followed three sessions and the participant who did not follow any session both left the study before T1.

2.2. Evaluation scales

At each time-point, participants were assessed using the Client Socio-Demographic and Service Receipt Inventory [8] which evaluates socio-demographic variables, prior contacts with mental health care services and medical treatments. Participants were assessed using the following instruments:

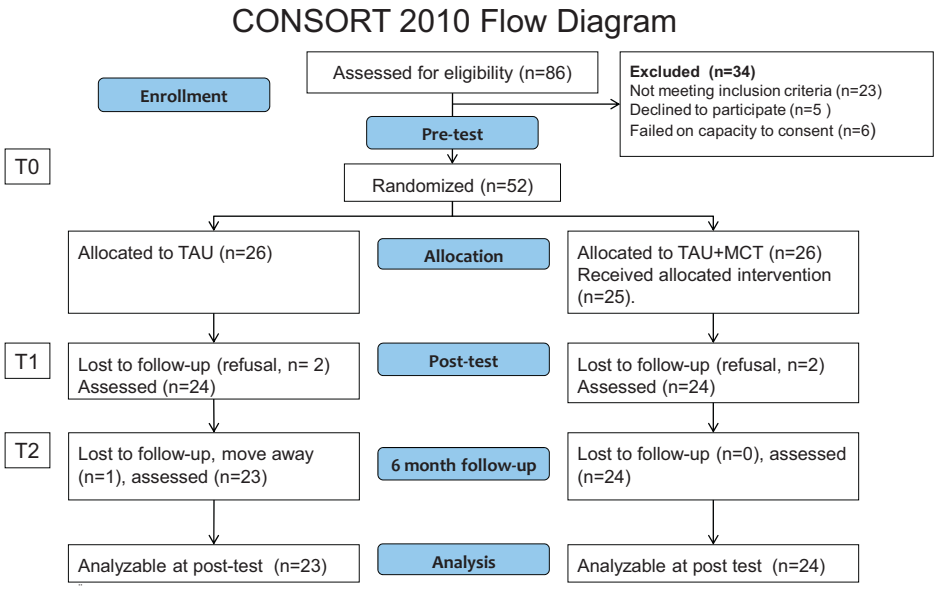

Fig. 1. CONSORT Flow Diagram.

- Psychotic Symptom Rating Scales (PSYRATS) – French version [13,18]. The PSYRATS is a 17-item multidimensional measure of delusions and auditory hallucinations. Symptoms are rated over the past 2 weeks. Two scales exist for auditory hallucinations (11 items) and delusions (6 items);
- Positive and Negative Syndrome Scale (PANSS) – French version [22,24]. The PANSS is a 30-item, seven point (1–7) rating instrument developed for the assessment of phenomena associated with schizophrenia. Symptoms are rated according to their presence in the past 2 weeks. We determined the positive syndrome scale (P1 to P7) and also assessed anxiety (G2), depression (G6);
- The Scale to Assess Unawareness of Mental Disorder (SUMD) – French version. The SUMD evaluates insight into various dimensions of the disease across the following independent dimensions:
  - presence of mental disorders,
  - need for treatment,
  - presence of signs and symptoms. The SUMD [3,41] is a standardized scale that relies on a direct interview with the patient. For our study, we choose to ask participants on their current insight to answer the three general items evaluating insight with regard to mental disorders, and the items on awareness and attribution of hallucinations and delusions.

2.3. Inter-rater reliability and raters independence checks

The independence of the raters was confirmed as follows: At T0, participants were randomized following the initial evaluation. Participants were instructed at the time of consent and again once appointments were scheduled for T1 and T2 that it was extremely important not to reveal their group allocation (MCT or TAU + MCT) to the assessors. The working hours of the judges were outside the times of group sessions to avoid encounters with the participants. At the HorizonSud Foundation, raters were only present at assessment times. Raters did not participate in clinical meetings or group therapist supervision. Meetings with the raters were organized by the therapists or research collaborators who were not involved in the evaluation. At the end of the T1 and T2 evaluation, raters had to guess the group of the participant and provide any clues that had been obtained during, for example, the interview. A comparison between the randomization and the attribution of the judges to one group showed that rater blindness was essentially secured: At T1, the rate of correct attribution was 58% ($\chi^2 = 1.4$, df(1), $P = 0.24$). At T1, five participants gave clues, four made references to their group and one misled the judge by saying that he was a part of the experimental group when in fact he was in the control group. At T2, the rate of correct attribution was 55% ($\chi^2 = 51$, df(1), $P = 0.47$). At T2, the judges did not receive any indication from the participants.

2.4. Inter-rater reliability

For all patients, symptom rating assessments were performed by clinicians trained to reliably administer these measurements. Regular random tests of inter-rater reliability were conducted. Intraclass correlations for the positive symptom items of the PANSS were good to excellent. ICC were 0.88 for delusions, 0.79 for conceptual disorganization, 0.95 for hallucinations, 0.82 for hyperactivity, 0.95 for grandiosity, 0.87 for suspiciousness/persecution and 0.78 for hostility. For the delusion scale of the PSYRATS, ICCs were excellent (range: 0.92 to 1.00). For the hallucination scale, the ICC were also excellent between 0.90 to 1.00. For both scales, the lowest ICC was obtained for the item disruption to life. For the SUMD items, the ICC ranged between 0.88 and 0.95

2.5. Treatment as usual (TAU)

Treatment as usual (TAU) was used as a control condition for different reasons. First, TAU in the Lausanne or Gruyère areas is multi-facetted and thus assures ethicality of our procedure. TAU consists of psychiatric management by a clinical team composed of at least one psychiatrist, a social worker and/or a psychiatric nurse, with additional access to community treatment or hospital admission. Treatment involves antipsychotic medication, regular office-based or community contacts with the clinical team for treatment monitoring, and socialization groups, therapy and psycho-educational groups. No attempts have been made to standardize this treatment as TAU was tailored to the patient's specific needs. Control participants did not undergo the MCT treatment program.

2.6. Metacognitive training (MCT)

The metacognitive training program, developed by Moritz et al. [32,33] is a new way of approaching the psychological treatment of psychotic symptoms. The principal goal of MCT is to make patients aware of and reduce cognitive biases (see introduction). At the core are attributional biases, jumping to conclusions, incorrigibility, theory of mind, overconfidence in memory errors and negative cognitive schematas. The program consists of two cycles of eight modules. Each module is administered during a 1-hour session to a group of three to ten patients. The program is composed of a manual [35] and slides. MCT is currently available in thirty languages and can been downloaded via the following web address: http://www.uke.de/mct. The program is described in details elsewhere [33]. Participants were invited to participate 8 sessions of 1 hour duration and received homework assignments between sessions.

2.7. Statistical analysis

All analyses were conducted using IBM SPSS Statistics package version 20. All statistical tests were two-tailed and significance was set at the 0.05 level. Assessment of group differences on nominal variables was undertaken through cross-table statistics, performing χ^2 tests of independence, and Fisher's exact tests when appropriate. From the pilot study [12], we estimated that 30 participants were required with an α of 0.05 and a β set at 0.80 for a decrease of the PSYRATS delusion subscale from 13 (SD 6) to 7.6 (SD 7.4). The raters in this pilot study were not blind. As trials in which raters are aware of group allocation have an inflated effect size [54] the sample size was increased to 52. Between-group differences in post- and pre-test values were examined using an analysis of covariance (ANCOVA) for each outcome variable. Differences between pre-test and post-test as well as pre-test and 6-month follow-up scores were treated as dependent variables, treatment condition as a fixed factor, and pre-treatment scores as covariates. Cohen's d effect sizes were calculated for between subjects at T1 and T2 [9]. For within-subjects Cohen's d were calculated between T0 and T1 and T0 and T2 in correcting for dependence among means in order to make direct comparisons with effect sizes from other studies. The formula 8 of Morris and DeShon [40] has been used. Friedman's two-way analysis of variance by ranks were used to compare chlorpromazine equivalents, in TAU and MCT + TAU conditions at the three different point of measure.

3. Results

Table 1 compares the main baseline variables after randomization. Results indicate that the participants of both groups were not different with respect to socio-demographic variables, treatment (i.e., chlorpromazine equivalents [4]; length of antipsychotic treatment or treatment with clozapine) as well baseline psychopathology.

3.1. Primary outcome

Between-group differences in post- and pre-test ANCOVA for PSYRATS delusion scale showed statistically significant at a medium effect size in favour of the MCT + TAU condition ($F = 5.07$, df(1), $P = 0.03$, Cohen's $d = 0.56$) (Table 2). Between-group differences in 6-month follow-up and pre-test ANCOVA for PSYRATS delusion scale showed statistically significant at a medium effect size in favour of the MCT + TAU condition ($F = 4.70$, df(1), $P = 0.04$, Cohen's $d = 0.64$) (Table 3). The positive syndrome scale of the PANSS was also improved in the MCT group relative to controls at post-test ($F = 9.87$, df(1), $P = 0.003$, Cohen's $d = 0.49$) and 6-month follow-up tests ($F = 4.95$, df(1), $P = 0.03$, Cohen's $d = 0.48$).

Table 1
Baseline characteristics: comparison between treatment as usual (TAU) and metacognitive training (MCT) + TAU groups.

	TAU	TAU + MCT	*P*
	n = 26 Mean (SD) *n* (%)	*n* = 26 Mean (SD) *n* (%)	
Socio-demographic characteristics			
Sex female/male	9/17	9/17	$\chi^2 = 0.0$; df(1); $P > 0.90$
Age	36.58 (SD 9.76)	36.85 (SD 10.38)	t = 0.10; df(50); $P = 0.92$
Marital status: never married	20 (76.9%)	22 (84.6%)	$\chi^2 = 0.5$; df(1); $P = 0.48$
First language: French	24 (92.3%)	21 (80.8%)	Fischer exact test $P = 0.42$
Country of origin: Switzerland	23 (88.4%)	20 (76.9%)	Fischer exact test $P = 0.47$
Educational level: post-secondary	2 (7.7%)	4 (15.4%)	Fischer exact test $P = 0.67$
Main source of income: State aid	23 (88.5%)	24 (92.0%)	Fischer exact test $P = 1.0$
Living condition: independent living	15 (57.6%)	11 (42.3%)	$\chi^2 = 1.23$; df(1); $P = 0.27$
ICD-10 diagnosis			
Schizophrenia	22	21	Fischer exact test $P > 0.90$
Schizoaffective disorders	4	5	
Substance use			
Cannabis use	4 (15.4%)	4 (15.4%)	Fischer exact test $P > 0.90$
Alcohol use	10 (38.5%)	11 (42.3%)	$\chi^2 = 0.08$: df(1); $P = 0.78$
Actual treatment			
Equivalents CPZ	379 (SD 163)	422 (SD 218)	t = −0.80; df(50); $P = 0.43$
Duration in year of actual antipsychotic treatment	3.88 (SD 4.94)	4.53 (SD 4.83)	t = −0.48; df(50); $P = 0.63$
Number of participants treated with			
Typical antipsychotic	6 (23.1%)	4 (15.3%)	$\chi^2 = 0.49$; df(1); $P = 0.48$
Atypical antipsychotic	25 (96.2%)	25 (96.2%)	Fischer exact test $P > 0.90$
Clozapine	7 (26.9%)	6 (23.1%)	$\chi^2 = 0.10$; df(1); $P = 0.75$
PANSS, item P1	4.46 (SD 0.86)	4.50 (SD 0.91)	t = −0.16; df(50); $P = 0.88$
PSYRATS delusion	15.31 (SD 3.50)	14.96 (SD 3.01)	t = 0.38; df(50); $P = 0.70$

Table 2
Between-group differences in post-test (T1) and pre-test (T0) ANCOVA.

	TAU ($n = 24$)		TAU + MCT ($n = 24$)		Differences T0-T1		F-test	Cohen's d		
	T0 Mean (SD)	T1 Mean (SD)	T0 Mean (SD)	T1 Mean (SD)	TAU Mean (SD)	TAU + MCT Mean (SD)	Group effect	Between group	Within-TAU	Within-MCT
PSYRATS delusion	14.96 (3.38)	13.46 (3.44)	15.04 (2.90)	11.08 (5.05)	1.50 (3.39)	3.96 (4.21)	5.07*	0.56	0.44	1.06
Amount of preoccupation	2.21 (0.88)	2.00 (0.93)	2.33 (0.96)	1.91 (1.02)	0.21 (1.06)	0.42 (1.25)	0.18	0.08	0.20	0.33
Duration of preoccupation	2.54 (0.88)	2.38 (0.77)	2.58 (0.88)	1.95 (1.00)	0.17 (0.89)	0.63 (1.22)	2.91	0.48	0.19	0.50
Conviction	3.04 (1.08)	2.92 (1.10)	3.13 (0.80)	2.21 (1.22)	0.13 (0.80)	0.92 (1.01)	8.84**	0.61	0.15	0.97
Amount of distress	3.09 (1.14)	2.63 (1.06)	2.84 (1.09)	1.96 (1.16)	0.46 (0.83)	0.88 (1.26)	3.76	0.61	0.54	0.69
Intensity of distress	2.58 (1.06)	2.25 (0.94)	2.50 (1.02)	1.83 (1.27)	0.33 (1.01)	0.67 (1.15)	1.64	0.38	0.33	0.53
Disruption to life	1.50 (0.66)	1.29 (0.69)	1.67 (0.64)	1.21 (0.78)	0.21 (0.83)	0.46 (0.78)	0.50	0.11	0.25	0.60
PANSS positive	18.75 (4.89)	17.89 (5.55)	19.79 (5.27)	15.25 (5.14)	0.86 (4.48)	4.54 (3.22)	9.87**	0.49	0.20	1.41
SUMD awareness of delusion	3.29 (1.49)	3.46 (1.62)	3.21 (1.50)	2.67 (1.49)	−0.17 (0.92)	0.54 (1.28)	5.56*	0.51	−0.19	0.42
SUMD attribution of delusion	3.46 (1.56)	3.59 (1.64)	3.09 (1.59)	2.88 (1.33)	−0.13 (1.68)	0.21 (1.06)	2.97	0.47	−0.07	0.19

*$P < 0.05$; **$P < 0.01$. PSYRATS: Psychotic Symptom Rating Scales; PANSS: Positive and Negative Syndrome Scale; SUMD: Scale to Assess Unawareness of Mental Disorder.

Table 3
Between-group differences in 6-month follow-up (T2) and pre-test (T0) ANCOVA.

	TAU ($n = 23$)		TAU + MCT ($n = 24$)		Differences T0-T2		F-test	Cohen's d		
	T0 Mean (SD)	T2 Mean (SD)	T0 Mean (SD)	T2 Mean (SD)	TAU Mean (SD)	TAU + MCT Mean (SD)	Group effect	Between group	Within-TAU	Within-MCT
PSYRATS delusion	15.26 (3.11)	11.65 (5.75)	15.04 (2.90)	8.00 (5.63)	3.61 (5.84)	7.04 (5.95)	4.70*	0.64	0.66	1.26
Amount of preoccupation	2.26 (0.86)	1.9 (1.24)	2.33 (0.96)	1.37 (1.31)	0.27 (0.96)	0.96 (1.33)	3.42	0.52	0.19	0.72
Duration of preoccupation	2.61 (0.84)	2.17 (1.34)	2.59 (0.88)	1.63 (1.21)	0.43 (1.34)	0.96 (1.60)	2.13	0.42	0.34	0.60
Conviction	3.13 (1.01)	2.78 (1.35)	3.13 (0.80)	1.63 (1.31)	0.35 (1.40)	1.50 (1.38)	9.36**	0.90	0.25	1.19
Amount of distress	3.12 (1.14)	1.91 (1.16)	2.83 (1.09)	1.50 (1.35)	1.21 (1.5)	1.33 (1.74)	1.08	0.33	0.81	1.09
Intensity of distress	2.61 (1.08)	1.74 (1.14)	2.50 (1.02)	1.08 (0.97)	0.87 (1.42)	1.42 (1.28)	4.28*	0.70	0.61	1.11
Disruption to life	1.52 (0.67)	1.04 (0.93)	1.66 (0.64)	0.79 (0.72)	0.48 (0.85)	0.87 (1.03)	1.43	0.30	0.59	0.85
PANSS positive	19.00 (4.84)	17.26 (5.55)	19.79 (5.27)	14.79 (4.78)	1.74 (5.29)	5.00 (4.65)	4.95*	0.48	0.33	1.08
SUMD awareness of delusion	3.35 (1.50)	3.22 (1.83)	3.21 (1.50)	2.25 (1.62)	0.13 (1.14)	0.96 (1.63)	4.74*	0.56	0.12	0.59
SUMD attribution of delusion	3.52 (1.56)	3.13 (1.77)	3.08 (1.59)	2.29 (1.65)	0.39 (1.56)	0.79 (1.56)	1.84	0.49	0.25	0.51

*$P < 0.05$; **$P < 0.01$. PSYRATS: Psychotic Symptom Rating Scales; PANSS: Positive and Negative Syndrome Scale; SUMD: Scale to Assess Unawareness of Mental Disorder.

Analyses of the PSYRATS conviction item exhibited the most marked change between baseline and post-test (F = 8.84, df(1), $P = 0.005$, Cohen's $d = 0.61$) as well as between baseline and the 6-month follow-up (F = 9.36, df(1), $P = 0.004$, Cohen's $d = 0.90$).

3.2. Secondary outcomes

In terms of secondary variables, The item on the awareness of developing delusional ideas of the SUMD was statistically improved for the MCT versus the TAU group between baseline and post-test (F = 5.56, df(1), $P = 0.02$, Cohen's $d = 0.51$), as well as between baseline and 6-month follow-up (F = 4.74, df(1), $P = 0.04$, Cohen's $d = 0.56$). The item on the attribution of delusional ideas to the illness on the SUMD were improved, but not in a statistically significant way ($P > 0.05$). The PANSS items of depression and anxiety were also not statistically different between groups ($P > 0.05$). Only 33 of the patients had persistent verbal auditory hallucinations, 15 in TAU and 18 in TAU + MCT, we observed a statistically significant improvement on the auditory hallucination subscale of the PSYRATS between baseline and post (F = 8.48, df(1), $P = 0.007$, Cohen's $d = 0.88$) and between baseline and 6-month follow-up (F = 4.46, df(1), $P = 0.04$, Cohen's $d = 0.61$). Chlorpromazine equivalents were not changed in the MCT condition but increased significantly in the TAU group (Friedman's two way analysis of variance by ranks = 6.42, df(2), $P = 04$).

4. Discussion

The psychological treatment of psychotic symptoms is often difficult and can lead to resistance from the patient if psychotic symptoms are challenged too bluntly. Recent treatment approaches thus usually adopt gentle ways to address psychopathological symptoms in patients.

This study shows that a metacognitive training program encompassing 8 sessions has an added value effect to standard treatment including antipsychotic medication, and that this effect is maintained at the 6-month follow-up. This additional antipsychotic effect seems to be exerted primarily through an amelioration of delusion conviction, a dimension of psychosis on which pharmacological treatment has a very limited impact [29].

The predicted improvement on the primary outcome (*delusional ideas* scale of the PSYRATS) was confirmed. Symptom decrease also emerged on the positive scale of the PANSS which is one of the most frequently used scales to measure psychotic symptoms. Nevertheless, we recommend utilization of the PSYRATS when positive symptoms are the primary target, as it is more specific and takes greater consideration of the different dimensions of the psychotic experience than the PANSS which pools distinct aspects into a single score [13].

An overarching of metacognitive training is to increase participants' awareness of the cognitive biases associated with psychotic symptoms and to reduce their impact on interpersonal relationships. Additionally, metacognition appears to be an important predictor of learning in schizophrenia and has been recently recommended to be incorporated in psychosocial interventions to increase learning [50]. Improvement of psychotic symptoms may be the results of the combined effects of becoming aware of the cognitive biases and learning improvement. Work by Lysaker et al. [27] suggests that metacognition is associated with cognitive flexibility and is an important predictor of outcome. Taken together, our results are in line with previous studies on the MCT [23,38,39] as well as other novel social cognition programs

like the Social Cognition and Interaction Training [45] indicating that bias modification exerts an add-on effect beyond treatment as usual.

It is also possible that this method helps patients to better distinguish what is part of the illness from what is being part of their personality. In essence, while delusional ideas or auditory verbal hallucinations are phenomena associated with the illness, the content of these symptoms is strongly related to the biography and the identity of the individual. These two core aspects of psychotic symptoms, form and content that are often highly intermingled. Therefore, this approach could reduce a patient's resistance towards treatment simply because the method does not directly challenge the content of the participant's delusional ideas or auditory hallucinations directly but is focused on the mechanisms associated with the construction of psychotic symptoms (''backdoor approach'') [33]. With MCT, the content of the psychotic symptoms will be addressed at some point during the intervention in a non-insulting way that allows the patient to integrate the psychotic experience into his/her personality.

The high rate of adherence and the low drop-out rate compared to other studies [51], lower than predicted on the basis of the pilot study [12], may be partly explained by utilization of the UBACC [21] which was not used for the pilot study. This tool allows verifying participant understanding of the study, excluding from the study those who do not have understood the protocol. It is also possible that the pedagogical nature of the tool increases the participant engagement in the study.

The fact that the participants of the TAU group demonstrated an improvement between T1 and T2 on the PSYRATS delusion scale requires further explanation. This improvement, which is significantly smaller than that in the experimental group, could partly be explained by contamination and crossover effects. This study involved numerous exchanges with clinicians, during which the metacognitive training technique was presented several times; this kind of program enables, in essence, a better understanding of the cognitive biases associated with the psychosis. The program's concrete examples probably helped the professionals involved to better comprehend what psychosis is, thus normalizing or demystifying the illness for them. It is possible that this new understanding led to changes in attitudes toward patients, an evolution producing less specific effects such as a decrease of distress on the PSYRATS delusional ideas items for patients of both groups [43]. The areas which exhibited the most improvement in the control group were, in fact, a decrease of the dimensions measuring distress. The improvement in the TAU condition only can also be explained by the fact that the ingredients of TAU intervention were active.

The limitations of this study were primarily linked to the absence of an active control group. In essence, even if the participants of the TAU group received a series of psychosocial interventions, the participants of the TAU-MCT group received a greater amount of therapeutic attention. Nevertheless, the improvements observed speak against this. Any effect linked to more treatment should have been just as observed with respect to other less specific symptoms like anxiety or depression, something which was not the case in this study. Another limitation of the study was that the persistence of delusional ideas during the last 3 months prior to the study was measured retrospectively. The validity of our results would be improved by a prospective evaluation with at least two evaluations prior to inclusion. Finally, this study did not measure how MCT affects subjective elements of recovery as well as functional improvements in life beyond reductions of delusion severity.

5. Conclusion

The results of this study indicate that metacognitive training has a surplus antipsychotic effect for patients diagnosed schizophrenia-related disorders who demonstrate only a partial response to antipsychotic treatment and that the effect of the intervention persists for at least 6 months after the intervention.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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