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A new computerized cognitive and social cognition training specifically designed for patients with schizophrenia/schizoaffective disorder in early stages of illness: A pilot study

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ABSTRACT

People with schizophrenia/schizoaffective disorders at early stages of the illness present cognitive and social cognition deficits that have a great impact in functional outcomes. Cognitive Remediation Therapy (CRT) has demonstrated consistent effect in cognitive performance, symptoms and psychosocial functioning. However, any CRT intervention or social cognition training have been specifically designed for patients in the early stages of psychosis. The aim of this pilot study is to assess the efficacy of a new computerized cognitive and social cognition program for patients with schizophrenia/schizoaffective disorder with recent diagnosis. A comprehensive assessment of clinical, social and non-social cognitive and functional measures was carried out in 53 randomized participants before and after the 4-months treatment. Significant results were observed in Spatial Span Forwards, Immediate Logical Memory and Pictures of Facial Affect (POFA) total score. None of these results were explained by medication, premorbid social functioning or psychopathological symptoms. No impact of the intervention was observed in other cognitive and social cognition outcome neither in clinical and functional outcomes. This new computerized intervention may result effective ameliorating visual attention, logical memory and emotional processing in patients in the early stages of schizophrenia/schizoaffective disorder.
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1. Introduction

Cognitive impairments are considered a core feature in schizophrenia, being presented all over the course of the illness (Jahshan et al., 2010). Patients in the early phases of schizophrenia present a medium-to-large effect deficit across all neurocognitive functions, showing the greatest deficits in immediate verbal memory and speed processing (Mesholam-Gately et al., 2009). Impairments in different cognitive functions, such as attention, verbal memory, processing speed and executive functions (EEFF), seem to be associated to clinical and functional outcomes at early stages of the illness (Bodnar et al., 2008; Milev et al., 2005; Torgalsboen et al., 2014).

Social Cognition has been the last aspect included in the wide range of altered neurocognitive domains in schizophrenia. Social cognition refers to the mental operations underlying social behavior and it is understood as a multidimensional construct that comprises emotional processing, social perspective and knowledge, attributional bias and theory of mind (ToM) (Green et al., 2008; Penn et al., 2008)

As well as in chronic people with schizophrenia, impairments in emotional recognition (Amminger et al., 2012; Horan et al., 2012) and ToM (Bora and Pantelis 2012) have been described in patients with a recent diagnosis. Furthermore, although attributional biases have been less studied at early stages of the illness, they have been observed in early-stages psychosis subjects (Thompson et al., 2013).

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Evidence suggests that both cognitive and social cognition impairments influence the social functioning and daily life of patients at early phases of the illness (Allot et al., 2011; Vesterager et al., 2012) as well as in chronic patients (Hoertnagl and Hofer, 2014). These findings highlight the importance of considering neurocognitive deficits as targets for remediation with the final objective of enhancing the improvement of functional outcomes in these patients. Due to the limited effect pharmacological treatments have shown ameliorating cognitive and social cognition deficits, (Hill et al., 2010; Kucharska-Pietura and Mortimer, 2013) different non-pharmacological therapies have been long considered. Cognitive remediation therapy (CRT) is an evidence-based treatment that seems to positively impact on neurocognitive impairments. Functional improvement has been also related to CRT, although such gains are much more pronounced when CRT is offered along with other rehabilitative interventions (Wykes et al., 2011). CRT has resulted to be effective beyond gender, previous cognitive impairment of participants, type of CRT intervention, and duration of therapy. However, baseline symptoms and strategic approach seem to modulate the effect of CRT in neurocognitive gains (Wykes et al., 2011). Different authors have shown patients with an early onset of the illness may also benefit from CRT at a cognitive (Ueland and Rund, 2005; Wykes et al., 2007; Eack et al., 2009) and functional level (Wykes et al., 2007; Eack et al., 2010a; Lee et al., 2013). These benefits have been observed applying classical (Ueland and Rund, 2005; Wykes et al., 2007) or new technologies solutions CRT paradigms. In a recent study, Fisher et al. (2015) demonstrated that a Neuroplasticity-Based Auditory Training via laptop computer improved verbal memory in schizophrenia patients with recent onset. The effect of CRT on social cognition is also observed in patients in the early phases of schizophrenia. Applying the Cognitive Enhancement Therapy (CET), a CRT approach that includes computerized exercises of CRT and social-cognitive group sessions, Eack et al. (2007) found larger improvements in the ability to understand and manage emotions as well as in the ability to use emotions to facilitate thinking and decision-making in the CET group. Thus, after two years of treatment, the CET group showed improvements in neurocognition and social cognition (Eack et al., 2009), which were related with the improvement and maintenance of functional outcomes 1 year after the treatment (Eack et al., 2010a, 2011). Additionally, cognitive improvement was associated with preserved gray matter volume in different brain regions in CET group (Eack et al., 2010b). Although authors did not comprehensively explore the effect of CET in different social cognition abilities, they proved the impact of a CRT program that includes cognitive and social cognition abilities training in patients in the early stages of schizophrenia. Taking into account these finding, the administration of CRT at early stages has been suggested to play a “protective” role in neurocognitive and functional impairments of schizophrenia patients (Barlati et al., 2012).

In the last decade different specific social cognitive trainings (SCT) have been developed for patients with psychosis and positive results have been observed (Kurtz and Richardson, 2012; Henderson, 2013), although further research is needed. SCT seem to impact in ToM alterations (Wolwer and Frommann, 2011; Bechi et al., 2012), emotional processing deficits, attributional biases (Penn et al., 2007) as well as functional outcomes (Wolwer and Frommann, 2011; Tas et al., 2012). There are several studies using SCT in the early phases of schizophrenia, but no SCT programs specifically designed for patients at early stages of psychosis currently exist. Patients in the early phases of schizophrenia/schizoaffective disorder present specific characteristics such as younger age, lower level of cognitive dysfunction or emotional status related to the recent diagnosis. In fact, a recent study suggests that working memory and social cognition deficits could be more preserved at early stages of the illness (McCleery et al., 2014). Attending to the promising results of Eack et al. (2007, 2009, 2010a), developing a specific cognitive and social cognition training for psychosis patients of recent diagnosis may improve and even prevent cognitive, social cognition and functional alterations in schizophrenia patients.

The NeuroPersonalTrainer® is a neurocognitive rehabilitation platform, initially developed for acquired brain injury patients by the Guttmann Institute (Barcelona, Spain). This platform has been modified and adapted to treat neurocognitive needs of early-stages psychosis patients. New cognitive exercises and levels of complexity as well as a new Social Cognition Module based on multimedia content have been specifically created by experienced psychologists and neuropsychologists for this population. Thus, a new platform, the NeuroPersonalTrainer-Mental Health (NPT-MH), has been developed. All exercises present different levels of complexity, allowing the design of individualized and personalized cognitive rehabilitation sessions adapted to the patient's cognitive profile, making the NPT-MH a suitable cognitive rehabilitation tool to implement at the early stages of psychosis.

The main objective of this study was to explore the preliminary efficacy of this new computerized cognitive and social cognition program, i.e. NPT-MH, in terms of cognitive, social cognition, clinical and functional improvement in patients with schizophrenia/schizoaffective disorder in the early stages of the illness.

2. Method

2.1. Participants and procedure

Fifty-three participants were recruited from the outpatient service of the Mental Health Department of the Parc Taulí Hospital (Sabadell, Spain). Patients were included if they met the following inclusion criteria: (1) lifetime history of a single episode of schizophrenia/schizoaffective disorder according to the DSM-IV criteria, with less than 5 years of evolution; (2) No changes in antipsychotic medication during the month prior to the study recruitment; (3) Clinical stability defined as being an outpatient for at least the previous 4 weeks to the study, score less than 4 in the P1, P2 and P3 items of the Positive and Negative Syndrome Scale (PANSS) (Andreasen et al., 2005) and score less than 4 in the Calgary Depression Scale (Addington et al., 1990). Participants were excluded if they (1) had IQ $<$ than 70, (2) had history of brain damage or (3) were abusing substances (except nicotine or caffeine) for at least 12 months prior to study enrollment. All participants were informed about the characteristics of the study and all of them signed an informed consent prior to participation. The study was approved by the Ethical Committee of the Taulí hospital.

An expert psychiatrist interviewed each patient using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) (APA, 1994) for diagnosis, reviewed the medical records, confirmed the inclusion and exclusion criteria, administered clinical scales and controlled pharmacological treatment. Two expert neuropsychologists administered and corrected the neurocognitive assessment (neuropsychological tests and social cognition tasks). Mood, social functioning and quality of life scales were administered by a clinical psychologist.

Upon recruitment, participants were randomized into the NPT-MH group or the non-specific computer training group (control group), using a computer-generated permuted-block randomization scheme by an independent statistician. Clinical, cognitive, social cognition and functional measures were assessed at baseline (along the 4 weeks prior to treatment) and post-treatment (along the 4 weeks after treatment). The neurocognitive assessment was carried out by the same neuropsychologists that administered the interventions in both groups. Clinical and functional assessments were carried out by the same evaluators that assessed clinical and functional outcomes at baseline (a psychiatric and a clinical psychologist), both blinded to the treatment condition of participants.

2.2. Assessments

2.2.1. Neuropsychological measures

An extensive neuropsychological exploration was carried out in every patient. Attention was assessed by the Digits forward subtest from the WAIS-III (Wechsler, 1999), Spatial span forward of the Wechsler Memory Scale (WMS-III) (Wechsler, 2004) and the index of maintained attention from the Conners Continuous Performance Test-II (CPT-II) (Conners, 2000); the Rey Auditory Verbal Learning Test (RAVLT) (Rey, 1964), Logical Memory and Visual Reproduction subtests (VR) of the WMS-III were used respectively for the assessment of verbal learning and

memory and visual memory; processing speed was assessed by the index of reaction time from the CPT-II and Trail Making Test (TMT) part A (Reitan and Wolfson, 1985); Digits backward subtest of the WAIS-III and Spatial span backward subtest of the WMS-III were applied in order to explore working memory; EEFF (flexibility, inhibition, verbal fluency and planning and problem solving) were also assessed with the TMT part B, Stroop Word and Color Test (Golden, 2001), the PMR, Spanish version of the Verbal Fluency Test (Artiola et al., 1999), and the Total Move and Problem Solving Time indexes from the Tower of London (TOL) (Shallice, 1982) respectively. All neuropsychological data was collected in raw scores. In all tests increased scores meant better performance, except for TMT and Reaction Time of CPT-II.

2.2.2. Social cognition measures

Three different aspects of Social Cognition were assessed: emotional processing, ToM and attributional bias. Emotional processing was measured by the Pictures of Facial Affect (POFA) (Ekman and Friesen, 1976). In this task patient has to recognize six basic emotions (happiness, sadness, anger, fear, disgust, and surprise) in 60 male and female faces, scoring 0 (wrong answer) or 1 (correct answer) for each face.

Three different ToM tasks (two cognitive and one affective) were administered to all participants. The first ToM task consisted of 4 classic false belief/deception stories. The "Sally & Anne" (Baron-Cohen et al., 1985) and "The Box of Chocolate" stories (Happe, 1994) were applied to assess first order ToM abilities, and "The Burglar" (Happe, 1994) and "The Ice-Cream Van" (Baron-Cohen, 1989) for the second order ToM skills. Stories were read aloud by the examiner, and subjects were asked to listen and subsequently answer a ToM question and a control question. Both questions were scored 0 (wrong answer) or 1 (correct answer). So as to avoid a possible learning effect two homologous false belief/deception first order ToM stories ["The cigarettes" (Happe, 1994) and "The piggy bank" (Frith and Corcoran, 1996)] and second order ToM stories ["The train station" and "The Coke" (Frith and Corcoran, 1996)] were administered in the post-treatment assessment. The second cognitive ToM task was the Hinting Task (Corcoran et al., 1995). In this task patients needed to understand indirect speech and infer the mental state of one character to answer the ToM question. We selected and administered three of the ten stories of the Hinting task at baseline in order to reduce assessment duration. three homologous stories were selected for the post-treatment assessment to avoid learning effect. In both cases, total score of the task was 6. The Reading the Mind in the Eyes Test (RMET) (Baron-Cohen et al., 2001) was the third administered ToM task. This affective ToM task contains 36 male and female eyes pictures with 4 answers multiple choices for each item. Patients had to infer mental states through gaze choosing one of the four possible answers. Total score of the tasks is 36, giving 1 point to every correct answer and 0 to the fail.

Attributional biases were assessed using The Internal, Personal and Situational Attributions Questionnaire (IPSAQ) (Kinderman and Bentall, 1995). This questionnaire was designed to assess the extent to which individuals attribute negative and positive events to different attributional loci. The scale consists of 32 social items describing 16 positive and 16 negative events. Patients are asked to generate the most likely cause of each event and to state whether the cause is due to self, other people or circumstances. Six subscale scores are generated (number of positive events attributed to self, other people, and circumstances; and corresponding scores for negative events) and these are used to calculate two composite scores: externalizing bias (EB) and personalizing bias (PB).

2.2.3. Clinical and functional measures

Severity of clinical symptoms was rated with the *Positive and Negative Syndrome Scale (PANSS)*. Anxiety levels were measured with the state part of the State-trait Anxiety Inventory (STAI-trait) (Spielberger et al., 1983). In both scales decreased score meant a better clinical status. As functional measures instruments Social Functioning Scale (SFS) (Birchwook et al., 1990), and Quality of Life Interview (QoLI) (Lehman, 1988) were administered. In both scales increased scores meant better functioning and quality of life.

2.2.4. Other measures

Socio-demographic variables (age, gender and years of education) were also collected. Furthermore, important clinical and functional data were also registered: type of diagnosis, years of illness duration, type of medication, dose of antipsychotic medication (converted to chlorpromazine equivalents), intellectual functioning, as obtained through the abbreviated form of Wechsler Adult Intelligence Scale (WAIS-III) (Blyler et al., 2000), the Premorbid Adjustment Scale (PAS) (Cannon-Spoor et al., 1982) and the Global Assessment of Functioning (GAF) (Hall, 1995).

2.3. Training

To adapt the NeuroPersonalTrainer® to early-stages psychotic patients' needs, different levels of complexity in all cognitive exercises were developed, as well as new tasks of executive functions (specifically working memory). The Social Cognition Module was specifically designed for psychotic patients in early stages of the illness. Thus, pictures, stories and videos of the tasks represent common social situations where a young adult can find him/herself e.g.,at work, at the pub, with friends or relatives, and problems people in early stages of psychosis must face during such situations (social misunderstandings, "faux pas" situations, management of emotions in social context.) (see Fig. 1)

The NPT-MH includes two rehabilitation modules: the Cognition module that comprises attention, memory and executive functions tasks with different levels of complexity; and the Social Cognition module (Caballero-Hernández et al., 2014), which allows working different aspects of emotional processing, theory of mind and cognitive biases through 43 multimedia-based tasks. Social cognition tasks are organized by level of difficulty. A 'Tutorial' with information about the social cognition contents of tasks for a particular level and strategies to cope with related social situations is available. In addition, the module includes different 'Warnings' that appear on the screen when two consecutive errors are made. The purposes of these 'Warnings' are to maximize social skills learning reminding the strategies offered during the 'Tutorials', and to avoid the effect of cognitive deficits (e.g., attention alteration) on social skills acquisition.

All exercises of the NPT-MH offer an immediate success/failure feedback and a final summary of the results of performance.

Each rehabilitation session with NPT-MH was individualized and tailored to the cognitive needs of each patient. The selection of tasks and difficulty level in each treatment session was daily scheduled by an expert neuropsychologist based on the participant cognitive profile, obtained during the baseline neurocognitive

Fig. 1. Tutorials, warnings and exercises examples of the NeuropersonalTrainer- Mental Health.

assessment, and in his/her tasks performance in previous treatment sessions. All sessions included cognitive (first ~30min of the session) and social cognition exercises. Considering the influence of the CRT with strategic approach in neurocognitive improvements (Wykes et al., 2011), neuropsychologists adopted an active role during all treatment sessions. In this way neuropsychologist individually coached every patient to achieve the correct performance in the tasks. During social cognition exercises performance, neuropsychologist worked with every patient on the "Tutorial" information at the beginning of every level in order to assure the understanding of different social cognition aspects. At this moment, the patient was motivated to reflect on the common misunderstandings during social situations and understand how people handle them. Neuropsychologist constantly monitored participant performance, reminding the "Tutorial" information and/or administering errorless learning and scaffolding techniques when participant needed it.

To avoid the potential acquisition of cognitive abilities associated with using computers, non-specific computer training was developed for the control group. Computer tasks were divided in (a) an course focused in text editing, spreadsheet management and creation of dynamic presentations, (b) playing non-specific internet games previously selected by therapists, and (c) watching documentary videos about the functioning of the brain and the human body.

Both trainings were administered in 1-h sessions, twice per week during 4–5 months. A room was specifically set up for the study with six computers, allowing the administration of the trainings to six participants at the time. During every session each participant worked individually in his/her own computer. A neuropsychologist was always guiding sessions in both groups. In order to assure a therapeutic effect, a minimum of 15 h of training for each participant was established by clinical consensus for any of the two interventions.

2.4. Statistical analysis

Participants that did not achieve a minimum of 15h of training were excluded from the statistical analysis. All variables were analyzed using a General Linear Model (GLM) of repeated measures, with factors time (pre- and post-treatment) and group (NPT-MH and control). As differences in PAS were found between groups, baseline PAS as well as baseline psychotic symptoms (PANSS total score) and antipsychotic drugs doses were introduced as covariates in all models (ANCOVAS). Significant interactions ($p < 0.05$) or trend to significance (< 0.08) were further examined with post-hoc comparison. Effect sizes are reported with partial eta squared, where 0.009 corresponds to a small effect, 0.058 a medium effect and 0.137 a large effect (Cohen, 1988).

Since psychotic symptoms tend to wax and wane in the early phases of schizophrenia/schizoaffective during the first years of evolution, a PANSS change score (PANSS post-treatment –PANSS pre-treatment) was created in order to control its effect in relation to the intervention. Lineal regression models including the PANSS change score as an independent variable were performed for every cognitive, social cognition, clinical and functional change score in which an interaction was found.

3. Results

Main clinical and social characteristics of the sample are summarized in Table 1. Participants (NPT-MH group - Control group) were taking the following medication: Conventional antipsychotic (21.4–0%), atypical antipsychotic (96.4–100%), mood stabilizers (7.1–20%), SSRIs (18.8–8%), dual antidepressants (0–4%), tricyclic antidepressants (0–4%), other antidepressants (7.1–4%), anticholinergic drugs (3.6–8%), benzodiacepines (21.4–12%). Significant differences between groups were only found in conventional antipsychotic medication ($X^2 = 6.04$, $p = 0.01$). No significant differences in doses of antipsychotic medication converted to chlorpromazine equivalents were observed between the NPT-MH group (269.73 $\pm$ 195.23) and the Control group 244.07 $\pm$ 202.58).

In total, 40 participants completed the study. Mean training hours were 30.7 (8.8) in the NPT-MH group and 27.1 (9.8) for the control group. Dropout rates were similar in both groups (see Fig. 2).

3.1. Efficacy results in cognitive and social cognition outcomes

Means, main effects and interactions of cognitive and social cognition variables are shown in Table 2. There were no differences between groups in baseline cognitive measures except a difference at trend level in TMT-B ($p = 0.08$).

Main effects of time were observed in Spatial Span Backwards (Mean Rating Change= 0.8, S.D.= 1.69), Inmmediate Logical Memory (Mean Rating Change= 5.56, S.D.= 7.87), Delayed Logical Memory (Mean Rating Change= 4.42, S.D.= 5.56), Delayed Visual Retention (Mean Rating Change= 13.6, S.D.= 17.01), Stroop Word-Color (Mean Rating Change= 3.5, S.D.= 5.29), TMT-A (Mean Rating Change= −6.2, S.D.= 13.56), TMT-B (Mean Rating Change= −23.94, S.D.= 33.9), Fluency Test (FAS) (Mean Rating Change= 3.25, S.D.= 8.21), Hinting Task (Mean Rating Change= 1.15, S.D.= 1.54), POFA Total Score (Mean Rating Change= 3.25, S.D.= 3.68), POFA Disgust (Mean Rating Change= 1.05, S.D.= 1.96), POFA Anger (Mean Rating Change= 0.7, S.D.= 2.07) and POFA Surprise (Mean Rating Change= 0.37, S.D.= 1.05).

Significant time by group interactions were found in Spatial Span Forwards, Inmmediate Logical Memory, Delayed Logical Memory, TMT-B, POFA total score and POFA_Fear. Post hoc analyses revealed that NPT-MH group showed greater significant values than the Control group at post-treatment in Spatial Span Forwards ($p = 0.013$), Immediate Logical Memory ($p = 0.01$) and POFA Total Score ($p = 0.025$). In all cases partial eta squared showed a medium-large effect size for the interaction. Non-significant results were observed in the Control group at post hoc analyses.

Lineal regression analysis showed that PANSS change score was not associated to any of the following cognitive change scores: Spatial span forward ($B = -0.02$; $p = 0.6$), Immediate Logical Memory ($B = -0,2$; $p = 0.1$) or POFA Total Score ($B = -0.1$; $p = 0.4$.

3.2. Efficacy results in clinical and functional outcomes

There were no differences between groups in any clinical or functional measure at baseline. Means, main effects and interaction of clinical and functional variables are shown in Table 3.

There was a main effect of time in PANSS Total (Mean Rating Change= −6.87, S.D.= 9.78), PANSS Positive (Mean Rating Change= −1.78, S.D.= 2.21), Negative (Mean Rating Change= −2.85, S.D.= 4.07) and General Psychopathology (Mean Rating Change= −2.2, S.D.= 5.22) Subscales, STAI-state (Mean Rating Change= −4.68, S.D.= 9.23) and SFS (Mean Rating Change= 6.5, S.D.= 16.41). Both groups showed a decreased of all clinical variables and a small increase of the SFS score. No significant time by group interaction was observed in clinical or functional outcomes.

4. Discussion

This pilot study provides initial evidence for the preliminary efficacy of a new computerized cognitive and social cognition program for patients with schizophrenia/schizoaffective disorder at an early stage of the illness. After treatment, participants that received the NPT-MH training showed significant greater improvement in visual attention, logical memory, and emotional processing than those in the control group. However, some cognitive changes were also observed in the Control group, although none of them were related to the control training condition.

Administration of CRT to schizophrenia patients has been generally associated with enhancement of practically all cognitive domains (Wykes et al., 2011). Nevertheless, CRT efficacy in first-episode samples is a recent research field and results do not seem to be so generalized (Wykes et al., 2007). Yet, verbal learning and memory, specifically immediate verbal memory, have been reported to be sensitive to CRT in early-stages psychosis patients (Eack et al., 2009; Lee et al., 2013; Fisher et al., 2015). In this study significant improvement of the Immediate Logical Memory was related to the NPT-MH intervention. However, the NPT-MH group did not improve scores in immediate verbal, temporal lobe-related

Table 1
Clinical and social characteristics of the sample.

	NP-MH group	Control group	Differences between groups
N	28	25	
Age. M (S.D.)	30.9(5.9)	30.02(7.4)	$X^2=3.5$ ($p=0.07$)
Gender. *N* (%)			
Male	17(60.7)	17(68)	$X^2=0.3$ ($p=0.6$)
Female	11(39.3)	8(32)	
Intelectual and premorbid status. M (S.D.)			
Years of education	12.86(4.2)	11.3(2.4)	$F=2.2$ ($p=0.1$)
PAS [a]	0.3(0.12)	0.3(0.2)	$F=$ 6.7 ($p=0.01$)
IQ	85.5(12.8)	82.2(11.6)	$F=$ 0.4 ($p=0.5$)
Diagnosis. *N* (%)			
Paranoid schizophrenia	21(75)	21(84)	$X^2=5.5$ ($p=0.2$)
Disorganized schizophrenia	1(3.6)	0(0)	
Bipolar schizoaffective disorder	3(10.7)	4(16)	
Depressive schizoaffective disorder	3(10.7)	0(0)	
Clinical and Functional scores			
Years of illness duration. M (S.D.)	2.3(1.7)	3.01(1.8)	$F=0.4$ ($p=0.5$)
PANSS Total. M (S.D.)	54.8(10.9)	58.7(12.02)	$F=0.4$ ($p=0.5$)
PANSS positive. M (S.D.)	10.1(2.6)	10.8(3.4)	$F=0.2$ ($p=0.6$)
PANSS negative. M (S.D.)	17.4(5.2)	19.2(5.5)	$F=0.2$ ($p=0.7$)
PANSS general. M (S.D.)	27.2(5.2)	28.7(5.7)	$F=0.8$ ($p=0.4$)
GAF. M(S.D.)	59.1(8.4)	56.8(8.6)	$F=0.3$ ($p=0.6$)

M= Mean; S.D.= Standard deviation; PAS= Premorbid Adjustment Scale IQ= Intelligence Quotient; PANSS= Positive and Negative Syndrome Scale; GAF= Global Assessment of Functioning.

[a] Significant differences=0.001.

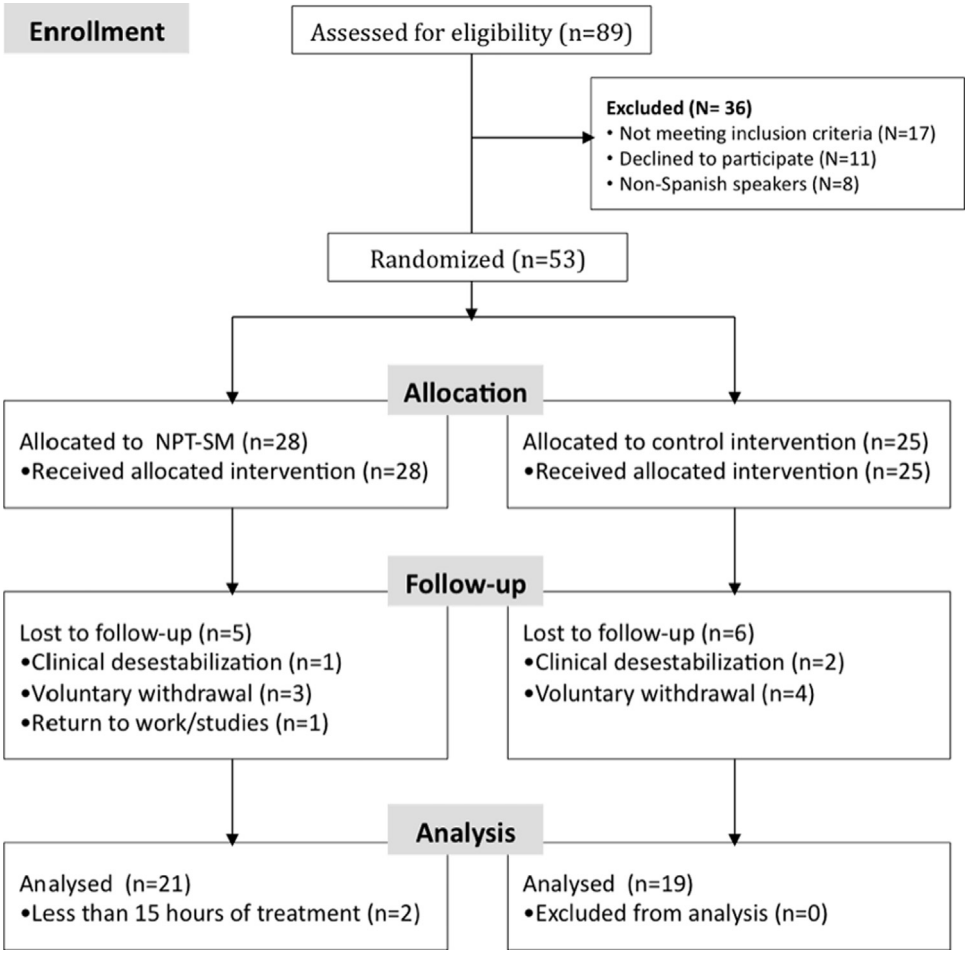

Fig. 2. Flow diagram of the sample.

memory measures. Immediate verbal memory can be influenced by attention, encoding and retrieval processes. In addition, logical memory requires a higher executive component, since information has to be well organized and contextualized to be properly stored. Thus, the NPT-MH training could not have a direct effect in learning and verbal memory per se, but could improve executive

Table 2
Change in cognition and social cognition performance.

Outcomes	NPT-MH		Control		Time		Group		interaction		
	Pre M (S.D.)	Post M (S.D.)	Pre M (S.D.)	Post M (S.D.)	*F*	*p*	*F*	*p*	*F*	*p*	ηp^2
Cognitive											
Digit Forwards	8.19 (2.1)	8.71 (1.9)	7.21 (1.5)	7.47 (2.0)	2.04	0.161	4.29	0.045	0.22	0.639	0.005
Digit Backwards	5.67 (2.0)	6.29 (1.8)[a]	5.05 (1.8)	4.79 (1.6)	0.61	0.439	4.02	0.052	3.75	0.060	0.089
Spatial Span Forwards*	8.24 (1.8)	9.33 (1.6)[a]	7.72 (2.2)	7.89 (1.9)	1.12	0.297	3.12	0.086	4.14	0.049	0.103
Spatial Span Backwards	7.05 (2.0)	8.05 (1.9)	6.26 (2.0)	6.84 (2.4)	8.54	0.006	2.69	0.109	0.61	0.441	0.016
CPT-II reaction time	432 (70)	415 (54)	406 (52)	420 (67)	0.03	0.858	0.27	0.610	3.95	0.056	0.116
CPT-II maintained attention	0.31 (0.1)	0.04 (0.1)	-0.04(0.1)	0.05 (0.1)	2.07	0.160	0.13	0.720	1.13	0.296	0.038
Immediate Logical Memory*	27.33 (9.1)	35.38 (10.2)[a]	24.00 (9.9)	26.79 (9.7)	20.8	< 0.001	4.39	0.043	4.89	0.033	0.114
Delayed Logical Memory	12.57 (5.9)	19.24 (8.6)	12.72 (5.4)	15.06 (5.8)	24.99	< 0.001	0.95	0.336	7.56	0.009	0.174
Learning AVLT	46.05 (10.3)	48.29 (8.1)	42.58 (10.5)	43.47 (11.6)	1.69	0.202	1.91	0.174	0.31	0.581	0.008
Delayed AVLT	7.90 (3.4)	7.95 (3.6)	7.84 (3.5)	7.37 (4.0)	0.28	0.600	0.09	0.765	0.42	0.521	0.011
Inmediated VR	87.43 (13.5)	92.00 (12.4)	84.68 (13.7)	85.47 (12.3)	2.99	0.092	1.48	0.231	1.49	0.229	0.038
Delayed VR	54.24 (24.8)	69.24 (20.8)	53.32 (29.4)	65.37 (21.6)	24.78	< 0.001	0.11	0.741	0.29	0.591	0.008
Stroop word-Color	40.57 (3.9)	43.24 (8.1)	35.74 (9.3)	40.16 (9.8)	17.91	< 0.001	2.72	0.107	1.09	0.301	0.028
Trail Making Test-A	43 (15)	39 (18)	48 (16)	40 (14)	8.68	0.005	0.51	0.478	1.17	0.287	0.029
Trail Making Test-B	106 (33)	96 (39)	133 (58)	94 (35)	25.24	< 0.001	1.01	0.324	8.49	0.006	0.187
Fluency Test (FAS)	33.33 (10.4)	35.95 (13.2)	28.68 (8.8)	32.63 (9.2)	6.26	0.017	1.66	0.205	0.26	0.616	0.007
Move ToL	37.76 (17.4)	35.38 (18.8)	38.84 (23.3)	32.58 (20.0)	1.58	0.215	0.03	0.872	0.32	0.575	0.008
Problem Solving Time ToL	332 (113)	313 (97)	390 (202)	325 (120)	3.21	0.081	0.91	0.346	0.99	0.327	0.025
Social cognition											
Reading the Mind in the Eyes	23.10 (4.5)	24.14 (5.2)	22.42 (4.7)	21.95 (4.9)	0.19	0.661	1.06	0.309	1.37	0.249	0.035
Hinting Task	4.57 (1.3)	5.57 (0.8)	4.16 (1.4)	5.47 (0.9)	22.07	< 0.001	1.01	0.323	0.41	0.526	0.011
ToM1 order	3.86 (0.5)	3.90 (0.3)	3.79 (0.6)	3.89 (0.3)	0.69	0.410	0.13	0.723	0.09	0.755	0.003
ToM2 order	3.09 (0.8)	3.09 (1.1)	3.05 (1.0)	2.63 (0.8)	1.38	0.247	1.14	0.293	1.38	0.247	0.035
IPSAQ Externalizing	0.20 (3.0)	3.60 (14.5)	0.00 (3.4)	−0.11(2.8)	0.90	0.348	1.06	0.310	1.03	0.317	0.027
IPSAQ Personalizing	1.11 (0.6)	1.03 (0.8)	1.15 (0.5)	1.07 (0.4)	0.87	0.357	0.06	0.810	0.01	0.975	< 0.001
POFA Total*	45.57 (6.0)	50.24 (5.0)[a]	45.16 (5.0)	46.84 (4.2)	34.68	< 0.001	1.56	0.219	7.65	0.009	0.167
POFA_Happiness	9.81 (0.5)	9.86 (0.4)	9.74 (0.8)	9.84 (0.5)	0.39	0.536	0.12	0.736	0.06	0.815	0.001
POFA_Sadness	7.81 (1.7)	8.29 (1.2)	7.47 (2.3)	7.74 (1.4)	2.63	0.113	0.81	0.376	0.22	0.643	0.006
POFA_Disgust	7.10 (1.8)	8.24 (1.5)	6.74 (1.9)	7.68 (1.5)	11.08	0.002	1.11	0.300	0.09	0.757	0.002
POFA_Anger	7.33 (1.9)	8.33 (1.8)	6.63 (2.1)	7.00 (1.8)	4.32	0.045	4.09	0.050	0.92	0.344	0.024
POFA_Surprise	8.62 (1.5)	9.19 (1.1)	9.16 (0.9)	9.32 (0.9)	4.84	0.034	1.07	0.307	1.56	0.220	0.039
POFA_Fear	4.90 (2.5)	6.33 (2.2)	5.42 (2.5)	5.26 (2.5)	3.41	0.073	0.15	0.699	5.31	0.027	0.123

X=Mean; S.D.=Standard deviation; CPT-II=Continous Performance Test II; AVLT=Auditory Verbal Learning Test; VR=Visual Reproduction; Tol=Tower of London; ToM=Theory of Mind; IPSAQ=Internal. Personal and Situational Attributions Questionnaire; POFA=Pictures of Facial Affect.
ηp^2 equivalences with Cohen's *d*: Small effect size: $d=0.2$; $\eta p^2=0.01$; Medium effect size: $d=0.5$; $\eta p^2=0.06$; Large effect size: $d=0.8$; $\eta p^2=0.14$.

[a] Significant differences GNPT-MH vs Control for post treatment.

* Variables with significant interaction effect and significant post-hoc analysis ($p<0.05$).

Table 3
Change in Clinical and Functional performance.

OUTCOMES	NT-MH		Control		Time		Group		Interaction		
	Pre M (S.D.)	Post M (S.D.)	Pre M (S.D.)	Post M (S.D.)	*F*	*p*	*F*	*p*	*F*	*p*	ηp^2
Clinical											
PANSS total	54.65 (11.6)	46.75 (10.5)	58.42 (12.0)	52.63 (10.0)	18.79	< 0.001	2.31	0.137	0.45	0.508	0.012
PANSS positive	9.90 (2.6)	7.90 (1.4)	10.42 (2.7)	8.89 (2.2)	24.97	< 0.001	1.43	0.238	0.45	0.506	0.012
PANSS negative	17.65 (5.8)	14.6 (5.3)	19.42 (5.5)	16.79 (5.3)	18.55	< 0.001	1.69	0.201	0.10	0.753	0.003
PANSS general	26.95 (5.4)	24.2 (5.2)	28.58 (5.9)	26.95 (5.7)	6.77	0.013	1.94	0.172	0.44	0.511	0.012
STAI-state	23.9 (8.8)	16.81 (10.7)	22.82 (10.1)	21.12 (12.4)	9.09	0.005	0.27	0.606	3.41	0.073	0.086
Functional											
SFS	132.14 (21.9)	138.52(18.6)	125.76(18.3)	132.41 (20.6)	5.76	0.022	1.11	0.298	0.01	0.961	< 0.001
QoLI	3.79 (1.6)	4.12 (1.4)	4.65 (1.3)	4.74 (1.5)	1.33	0.257	2.89	0.097	0.45	0.507	0.012

PANSS=Positive and Negative Syndrome Scale; STAI-State=State-trait Anxiety Inventory; SFS=Social Functioning Scale; QoLI=Quality of Life Interview.
ηp^2 equivalences with Cohen's d: Small effect size: $d=0.2$; $\eta p^2=0.01$; Medium effect size: $d=0.5$; $\eta p^2=0.06$; Large effect size: $d=0.8$; $\eta p^2=0.14$.

aspects related to memory. Additionally, CRT in first-episode psychotic patients has shown to be effective enhancing executive functions such as cognitive flexibility (Wykes et al., 2007; Eack et al., 2009) and planning (Eack et al., 2009). Lee et al., (2013) initially found a positive impact of CRT in attention and working memory in first-episode patients that disappeared after controlling for diagnosis and baseline attention/working memory. In the current study, even after controlling for baseline functional status, baseline psychotic symptoms and doses of antipsychotic, the NPT-MH participants significantly improved visual attention after the intervention when compared with the control group. In Lee et al., (2013) the lack of CRT efficacy in attention and working memory could be explained by the mixed psychiatric sample, which included first-episode major depression and first-episode psychosis. Differences in cognitive profile and disease progression could explain positive, but different, CRT effects in both disorders.

Altogether, results suggest that CRT in the early phases of psychosis could have an impact in cognitive alterations related to frontal lobe dysfunction such as attention and executive functions. Thus, NPT-MH training may induce some improvements in frontal-lobe-related cognitive functions such as attention and Immediate Logical Memory, although no evidence for executive functions gains were found. CRT effect in processing speed has been also observed in schizophrenia patients in early stages of the illness (Bowie et al., 2014). However, speed-processing measures in this study did not significantly change after treatment.

One of the main findings of this study was the impact of the NPT-MH program in emotional processing. NPT-MH participants significantly improved their general ability for recognizing facial expressions. A more detailed analysis by specific emotions showed that this improvement might be related to a greater performance in recognizing fear. Both, chronic and first-episode schizophrenia patients present difficulties identifying facial emotions (Kohler et al., 2010; Daros et al., 2014), specifically negative emotions (Goghari and Sponheim, 2013; Daros et al., 2014), which has been related with functionality (Fett et al., 2011). Although more evidence is needed to conclude that emotional recognition is amenable to change after social cognition training (Henderson, 2013), our results support previous findings (Eack et al., 2009; Gil-Sanz et al., 2014) suggesting that emotional processing could be modified by CRT, even at early stages of the illness. No other significant effect in social cognition measures were found with the NPT-MH training. ToM, and to a less degree attributional biases, have been found to improve after SCT in schizophrenia patients (Penn et al., 2007; Wolwer and Frommann, 2011; Bechi et al., 2012), but, to our knowledge, CRT or SCT effects in these social cognition domains in early-stages psychosis have not been studied yet.

Participants in both groups showed improvements in all clinical variables and in one functional outcome that were not associated with neither treatment nor control condition. These clinical gains could be explained by the normal evolution of pharmacological treated patients with schizophrenia or schizoaffective disorder of recent diagnosis. Moreover, both groups also showed changes in cognitive and social cognition outcomes at post-treatment assessment. This general cognitive and social cognition improvement could be related to the clinical amelioration observed in the sample. However, the regression analysis carried out with the variables that resulted significant in the time by group interactions did not show any relation between the psychiatric clinical improvement and the cognitive gains. Unexpectedly, the control group obtained a better improvement than the NPT-MH group in the TMT-B, an executive functions measure. This result could be influenced by the trend towards significance observed in this variable between groups at baseline, although practice effects at re-test could also account for the improvement. Nevertheless, it may be more adequate to consider that the active condition of the Control group could somehow impact the cognitive and social cognition performance of the patients. In fact, previous studies have observed that non-specific computerized games may have some impact in executive functions, such as working memory, and reaction time in first-episode schizophrenia patients (Dang et al., 2014). These results could also suggest that the effect of the NPT-MH intervention treating cognitive deficits in patients with psychosis in early phases of the illness is small or insignificant. However, taking into account that none significant time-by-group interactions were associated to the control training, a masking effect of some specific efficacy results, due to the active control condition, may be also considered. In spite of that, altogether these findings support the potential change in cognitive aspects at the early stages of the disease, suggesting as other authors (Eack et al., 2009; Fisher et al., 2015; Wykes et al., 2007) the importance of an early intervention in these patients.

Contrary to other studies (Ueland and Rund, 2005; Eack et al., 2009; Lee et al., 2013), the NPT-MH training did not show any direct impact in functional measures. Taking into account that functional improvement is the most important target in CRT intervention in psychosis (Wykes et al., 2011), these results have to be seriously considered in the assessment of program effectiveness. Functioning outcomes in the context of CRT seem to be best achieved when combined with other psychiatric rehabilitation (Wykes et al., 2011). Furthermore, longer follow-up may be required to observe a translation of cognitive and social cognition gains into real functional improvement in patients in early phases of the schizophrenia, as it has been suggested in chronic patients (Fisher et al., 2010). Related-CRT gains in executive functions (Wykes et al., 2007), memory (Lee et al., 2013) and social cognition (Eack et al., 2011) have been associated with functional outcome at early stages of the illness. Thus, a follow-up analysis of the functional sample outcomes, as well as the study of NPT-MH intervention combined with other psychiatric rehabilitation, could be valuable.

Several limitations in the present study should be considered. First, the sample size could have decreased the significance of some results. It must be considered that the current pilot study was carried out with half of the sample size that was estimated for a future efficacy study. Furthermore, the number of analyses carried out in the reduced sample could lead to Type I error. Thus, all findings in this study have to be cautiously understood in the context of an exploratory study. Second, both schizophrenia and schizoaffective disorder subjects were included in the study, which must be considered for data interpretation. Third, the lack of blinding on the neuropsychological assessment could be considered as another limitation of this study. However, although Tarrier and Wykes (2004) pointed that unblinded trials in Cognitive Behavioral Therapy showed greater treatment effects than those using blind raters, in a more recent meta-analysis Wykes et al. (2011) concluded that specific methodological biases, particularly masked assessment, had no effect on cognitive outcomes from CR studies. Forth, the drop out rates in the NPT-MH group (25%) were quite large. Althouth attrition rates were similar in Control group (24%) and in previous studies (Fisher et al., 2015; Wykes et al., 2007), increasing participation and adherence to treatment must be an essential target in futures NPT-MH research. Finally, although the inclusion of active control groups in CRT studies has been suggested (Wykes et al., 2011), a third control group with treatment as usual (TAU) could allow to understand the affective clinical improvement observed in both groups and to clarify some potential effects of the NPT-MH training in cognitive and social cognition measures.

In conclusion, this exploratory study supports the importance of an early intervention on psychosis patients with recent diagnosis and suggests that the NPT-MH may have a small effect in important aspects of cognition and social cognition in patients with schizophrenia/schizoaffective disorder in early phases of the illness. However, the results of this pilot study indicate that the NPT-MH had no impact in functional outcomes. Thus, futures studies including larger samples and long-term follow up should be carried out to further clarify the efficacy of NPT-MH training in early stages of psychosis.

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