



Towards an improved access to psychiatric rehabilitation: availability and effectiveness at 1-year follow-up of psychoeducation, cognitive remediation therapy, cognitive behaviour therapy and social skills training in the FondaMental Advanced Centers of Expertise-Schizophrenia (FACE-SZ) national cohort

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Abstract

Psychosocial Interventions (PIs) have shown positive effects on clinical and functional outcomes of schizophrenia (SZ) in randomized controlled trials. However their effectiveness and accessibility remain unclear to date in “real world” schizophrenia. The objectives of the present study were (i) to assess the proportion of SZ outpatients who benefited from PIs between 2010 and 2015 in France after an Expert Center Intervention in a national multicentric non-selected community-dwelling sample; (ii) to assess PIs’ effectiveness at 1-year follow-up. 183 SZ outpatients were recruited from FondaMental Advanced Centers of Expertise for Schizophrenia cohort. Baseline and 1-year evaluations included sociodemographic data, current treatments, illness characteristics and standardized scales for clinical severity, adherence to treatment, quality of life, a large cognitive battery, and daily functioning assessment. Only 7 (3.8%) received a PI before the evaluation, and 64 (35%) have received at least one PI during the 1-year follow-up. Having had at least one PI during the follow-up has been associated in multivariate analyses with significantly higher improvement in positive and negative symptoms (respectively $p = 0.031$; $p = 0.011$), mental flexibility (TMT B, $p = 0.029$; C-VF, $p = 0.02$) and global functioning ($p = 0.042$). CBT and SST were associated with higher cognitive improvements, while CRT was associated with clinical improvement. These results have not been demonstrated before and suggest that the effect of each PI is larger than its initial target. The present study has confirmed the PIs’ effectiveness in a large sample of community-dwelling SZ outpatients at 1 year follow-up. Efforts to improve access to PI should be reinforced in public health policies.

Keywords Schizophrenia · Rehabilitation · Psychosocial interventions · Effectiveness · Functioning

Introduction

The concept of recovery has begun to transform practices and mental health systems throughout the world, switching from symptom-reduction to improved functioning and quality of life outcomes [1]. Recovery may be defined either

from a clinical perspective (i.e. clinical and functional remission) or from a consumer-oriented one, as a self-broadening process aiming at living a meaningful life beyond mental illness [2]. In a recent meta-analysis, only 13.5% of the persons with schizophrenia (SZ) met the criteria for clinical recovery [3].

A growing bundle of evidence suggests that this proportion could be deeply improved by psychosocial interventions (PIs) including psychoeducation (PSE), cognitive remediation therapy (CRT), cognitive behaviour therapy (CBT) and social skills training (SST). PSE has shown effectiveness in

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reducing psychotic relapse rates [4] and medication non-adherence [4]. CRT has shown effectiveness in improving cognitive and psychosocial functioning [5, 6]. CBT has shown effectiveness in positive and negative symptoms and psychosocial functioning [7]. SST has shown improvement on social and daily living skills [8], community functioning [8], negative symptoms and relapses [8]. All PIs appear to remain effective at 1-year follow-up [4–7], except for SST where it is less clear due to a lack of follow-up data [8]. In summary, each PI has shown some effectiveness in specific domains, but no longitudinal study has evaluated their global effectiveness in real-world conditions [9]. Moreover, PIs remain poorly available to service users with SZ in Western Countries: in 2010, only 15% of the 6007 participants with SZ in the French cohort ESPASS [10] and 36.5% of the 1825 persons with SZ in the 2nd Australian National Survey [11] were engaged in any form of psychosocial rehabilitation (including PIs, family interventions and sheltered or competitive employment).

The objectives of the present study were: (1) to assess the proportion of service users who received PIs between 2010 and 2015 in France after an Expert Center Intervention in a national multicentric non-selected community-dwelling SZ sample; (2) to assess PIs effectiveness at 1-year follow-up.

Materials and Methods

Study population

The FACE-SZ cohort is based on an ongoing French national network of schizophrenia Expert Centers that has been extensively described in a previous article [12]. Service users are referred to Expert Centers by their general practitioner or psychiatrist, who remains in charge of routine care and treatment. Patients are yearly followed up at the Expert Center and at the end of each evaluation a detailed evaluation report is sent to the patient and the referrer along with a personalized care program multifaceted and including the rationale for PI recommendation. The appraisal protocol was approved by the relevant Ethical Review Board (CPP-Ile de France IX) on January 18, 2010. All participants gave their written informed consent.

Data collected

General information on education, marital status, economic status, illness onset and trajectory and comorbidities, was recorded. Illness severity was assessed using the Positive and Negative Syndrome (PANSS [13]) and the Clinical Global Impression (CGI [14]) scales. Current depressive symptoms were evaluated using the Calgary Depression Rating Scale for Schizophrenia (CDSS [15]). Insight was

measured both with a self-reported measure (Birchwood Insight Scale; BIS [16]) and with the clinician-rated Scale to assess Unawareness of illness in Mental Disorders (SUMD [17]). Adherence into treatment was self-reported with the Medication Adherence Rating Scale (MARS [18]) and therapeutic observance was evaluated by clinicians with the Brief Adherence Rating Scale (BARS [19]). Quality of Life was evaluated with the self-reported Subjective Quality of Life scale (S-QoL [20]). General functioning was measured with the Global Assessment of Functioning scale (GAF [21]). Neuropsychological baseline and 1 year cognitive assessments included verbal fluency (L-VF; C-VF [22]) for spontaneous mental flexibility, Trail Making Test A and B (TMT-A or B) [22], respectively, for speed of processing and reactive mental flexibility, Continuous Performance Test-Identical Pair version (CPT-IP) [23] for sustained attention implying working memory mechanisms and premorbid IQ with the French-National Adult Reading Test (f-NART) [24]. To avoid test–retest effects, Intelligence Quotient (IQ) was assessed only at baseline with Wechsler Adult Intelligence Scale-4th edition (WAIS-IV) [25].

Site selection and training

Site selection and training have been described extensively in a previous article [12]. The ten sites opened in France were already actively involved in the treatment of patients with schizophrenia (pharmacological and non pharmacological), as well as in research on schizophrenia or psychiatric rehabilitation. Each Expert Centre has agreed and been trained to use the same package of assessment tools for the initial visit and for the follow-up. Clinical team members have monthly group meetings to monitor quality control, to ensure a good inter-rater reliability and to provide training in new therapeutic interventions.

Psychosocial intervention definition

The “PI+” group was defined as service users following at least one PI during the 1-year follow-up among manualized and standardized group psychoeducation (PSE), group cognitive behaviour therapy (CBT), group social skills training (SST) and individual and group cognitive remediation therapy (CRT) [26–32]. Beginning and ending dates of interventions were systematically recorded and only participants who completed at least 75% of the sessions were considered as PI+. PIs are part of the multifaceted individual care plan proposed to each service user at the end of the evaluation, in accordance with his needs and goals. There is no restriction in the access to interventions or in the number of interventions offered to one participant. The clinical profile of the service users attending to one or more interventions was studied in the analysis.

Statistical analysis

Clinical and functional outcomes were compared at baseline (“V0” visit) and after 1 year of follow-up (“V1”). For each outcome variable, improvement was defined as the difference between the values at V0 and V1, oriented so that a positive difference should correspond to an improvement of the patient’s condition. Each difference was adjusted by a linear regression over its confounding value at V0. Seventeen variables of interest were chosen: positive, negative, general psychopathology subscale scores and total score for PANSS, scores of the CDSS, CGI, GAF, S-QoL, BIS, and MARS, awareness and attribution scores of SUMD, number of words in the two verbal fluency tests, time at the TMT A and B, and d prime score in the fourth condition of the CPT-IP.

In the univariate analysis, the seventeen adjusted differences were compared to having had or not CBT, CRT, PSE, SST; having had or not at least one PI; having had or not at least one, two, or three PIs; the one-sided Student’s T test was used. The one-sided correlation test between the seventeen adjusted improvement variables and the number of PIs was also computed. Results are shown in Table 2 for the four types of PIs, and in Table 3 for the number of PIs.

In the multivariate analysis, the same 17 adjusted improvements were considered as responses. Having had or not at least one PI was retained as a predictor. The values at V0 of the 17 variables of interest were considered as covariates. 15 factors were added: (age at V0, age at first episode, level of education, memory score, IQ, gender, housing (independent or not), professional status (unemployed or not), diagnosis (schizophrenia vs. schizo-affective disorder), psychotic episodes, suicide attempts and full time hospitalizations during past year, alcohol and cannabis consumptions, treatment type (second generation vs. first generation antipsychotics)). Thus, improvement for each variable of interest was tested against a set of 33 potentially explanatory factors, including the predictor. Univariate significance *p* values were computed, and covariates significant at the 10% level were included in a regression model. Exhaustive variable selection determined the best model in the sense of adjusted *R*-squared. Results are shown on Table 4.

Data were analysed using the R software, version 3.2.3 [33]. The psych package version 1.5.8, was used [33]. Effect Size (Cohen’s *d*) was calculated using package effsize [34]. Size effects inferior to 0.20 were considered as negligible, from 0.20 to 0.40 as small, from 0.40 to 0.60 as moderate and superior to 0.60 as strong [34]. For variable selection, the leaps package version 2.9 was used [35]. The level of confidence intervals was set at 0.95, and the significance level of tests was set at 0.05. The initial data set had 9.23% missing data on average, over 54 variables of interest. The multivariate imputation method described in [36] was

applied, using the package mice [37]. Statistical treatments were first conducted using the standard pairwise deletion method and then repeated over 100 imputed datasets. The tables report *p* values from the pairwise deletion method; only conclusions remaining consistent through most imputed datasets were considered as significant.

Results

515 stabilized SZ outpatients (i.e. apart from an acute episode, meaning no hospitalization and no treatment change during the 4 weeks before evaluation) consulting were included in the 10 centers of the FACE-SZ national cohort between 2010 and 2015. Among the 431 patients with enough back up to be seen at V1, 183 were actually seen. There were no significant differences between patients seen and those lost to follow-up regarding our variable of interests (positive and negative symptoms severity, depressive symptoms, insight into illness, adherence into treatment, cognitive and psychosocial function, data not shown). The 183 included patients were mostly men (144, 78.7%), with a mean age of 33.9 (SD = 10.26) years, mean illness duration of 11.1 (SD = 9.19) years and a mean baseline PANSS total score of 69.9 (SD = 17.38). Baseline sample characteristics are shown in Table 1. At inclusion, 7 (3.8%) patients had received at least one PI (CRT *N* = 4, CBT *N* = 2, SST *N* = 1). Removing these patients did not change the results (data not shown).

64 (35%) had received at least one PI during the follow-up period: CRT (*N* = 36, 19.7%), CBT (*N* = 29, 15.8%), PSE (*N* = 31, 16.9%) and SST (*N* = 18, 9.8%). Overall, those with higher baseline insight scores (*p* = 0.007), better cognitive function and higher depressive symptoms (*p* = 0.017) accessed more to at least one PI during the 1-year follow-up. No clinical variable at baseline was associated with a specific PI except for higher depression level that was associated with CBT (*p* = 0.017) (Table 1).

In the univariate analyses, having had at least one PI during the 1-year follow-up has been significantly associated with improvement in negative symptoms (PANSS negative; *d* = 0.44; *p* = 0.003), insight (BIS; *d* = 0.42; *p* = 0.004), sustained attention/working memory (CPT-IP; *d* = 0.48; *p* = 0.023) and spontaneous and reactive mental flexibility (C-VF; *d* = 0.57; *p* < 0.001; TMT B; *d* = 0.58; *p* = 0.001) (Table 2). It was also correlated to mild improvements in positive symptoms (PANSS positive score; *d* = 0.31; *p* = 0.021), adhesion to treatment (MARS; *d* = 0.35; *p* = 0.024) speed of processing (TMT A; *d* = 0.30; *p* = 0.044) and global functioning (GAF score; *d* = 0.37; *p* = 0.012).

PSE was associated with a moderate improvement of adherence into treatment (MARS score; *d* = 0.53,

Table 1 Baseline characteristics and profile of service users having had PIs

Covariate	N or mean	% or SD	Type of PI				Number of PI's 1 or more
			CBT	CRT	PSE	SST	
Having had at least one PI at V1	64	35					
Gender (female)	39	21.31	1.000	1.000	1.000	0.371	1.000
Age	33.91	10.26	0.331	0.933	0.837	0.864	0.912
Housing	96	54.86	0.058	0.450	0.307	0.802	0.339
Profession	42	23.73	1.000	0.185	1.000	0.241	1.000
Diagnosis	148	80.87	0.019	0.638	0.618	1.000	0.697
Age first episode	22.84	6.29	0.507	0.926	0.858	0.440	0.193
Psychotic episodes on year before V0	85	50.3	0.684	0.705	0.427	0.212	0.873
Hospitalizations on year before V0	60	33.71	0.199	0.552	0.148	1.000	0.869
Suicide attempts on year before V0	13	7.3	0.231	0.468	1.000	0.625	1.000
Alcohol	8	5.63	0.610	1.000	1.000	0.574	1.000
Cannabis	7	4.93	1.000	0.350	0.350	1.000	0.423
Antipsychotic	114	90.48	0.035	1.000	0.711	0.623	0.062
Education	12.31	2.83	0.107	0.349	0.058	0.005	0.233
Memory score	22.56	6.79	0.321	0.038	0.066	0.001	0.188
f-NART IQ	84.97	14.59	0.074	0.049	0.295	0.001	0.132
PANSS total	69.85	17.38	0.828	0.968	0.713	0.398	0.700
PANSS positive	14.54	4.92	0.657	0.732	0.365	0.606	0.996
PANSS negative	21.03	7.22	0.673	0.824	0.626	0.912	0.824
PANSS general	34.27	9.54	0.712	0.908	0.653	0.190	0.411
CGI	4.48	1.04	0.189	0.788	0.730	0.633	0.299
GAF	48.52	12.45	0.942	0.316	0.984	0.986	0.850
CDSS	3.44	3.83	0.017	0.517	0.204	0.133	0.017
S-QoL	52.55	19.05	0.399	0.575	0.621	0.586	0.428
BIS	7.85	2.02	0.003	0.126	0.216	<0.001	0.007
MARS	6.68	2.29	0.626	0.907	0.354	0.004	0.669
SUMD attribution	1.81	0.76	<0.001	0.394	0.192	<0.001	0.018
SUMD awareness	1.6	0.6	0.001	0.449	0.710	0.059	0.083
TMTA time	46.24	25.81	0.021	0.504	0.318	0.006	0.715
TMTB time	111.85	69.39	0.390	0.804	0.375	0.002	0.712
CPT-IP	1.35	0.76	0.153	0.033	0.254	0.063	0.070
L-VF	17.01	6.38	0.036	0.107	0.124	0.042	0.017
C-VF	24.06	7.23	0.147	0.216	0.272	0.204	0.281

Having had CBT, CRT, PSE, SST, or having had at least 1, 2, or 3 PIs, was tested against 32 covariates. One-sided *p* values from Student *t* test or Fisher's exact test are reported. Results that remained significant after the multiple imputation procedure were retained (boldfaced *p* values)

The 33 Covariates were the following: gender; age; age at first episode; Type: schizophrenia against schizo-affective disorder; level of education; housing status (independent); professional status (student/employee); Premorbid intelligence: f-Nart; working memory score (WAIS-IV); having had or not a psychotic episode during past year; having had or not a full-time hospitalization during past year; suicide attempts during past year; treatment: antipsychotic or not; cannabis consumption at V0; alcohol consumption at V0; Positive and Negative Symptoms Scale (PANSS) total score and its 3 subscales: PANSS positive symptom score; PANSS negative symptom score; PANSS general: PANSS general psychopathology score; Clinical Global Impression: CGI score

GAF Global assessment of functioning, S-QoL subjective quality of life, CDSS score Calgary Depression Scale for Schizophrenia, Scale to Assess Unawareness of Mental Disorders (SUMD) with 2 scores: attribution score; awareness score, TMTA trail making test A, time, TMTB trail making test B, time, CPT-IP CPT-IP, d prime 4th condition, L-VF literal verbal fluency, number of words, C-VF categorical verbal fluency, number of words, Birchwood Insight Scale: self-rated insight

$p = 0.006$) and improvement in psychotic symptomatology (PANSS total score, $d = 0.47$, $p = 0.008$).

CBT has been associated with moderate improvement in global functioning (GAF score, $d = 0.59$, $p = 0.001$), spontaneous mental flexibility (C-VF, $d = 0.58$, $p = 0.003$) clinical global severity (CGI, $d = 0.46$, $p = 0.010$) and to mild improvement in positive symptoms ($d = 0.34$, $p = 0.026$) and speed of processing (TMT A, $d = 0.34$, $p = 0.012$).

CRT has been associated with high improvement in reactive mental flexibility (TMT-B, $d = 0.77$, $p < 0.001$) and with moderate improvement of other cognitive processes (sustained attention/working memory CPT-IP; $d = 0.45$, $p = 0.019$; spontaneous mental flexibility C-VF; $d = 0.49$, $p = 0.006$) and both positive ($d = 0.42$, $p = 0.007$) and negative ($d = 0.47$, $p = 0.005$) symptoms. CRT was also found to have a mild effect on clinical global severity (CGI score $d = 0.36$, $p = 0.022$) and on the level of insight into illness (SUMD awareness score $d = 0.38$, $p = 0.023$; SUMD attribution score $d = 0.42$, $p = 0.011$).

SST has been associated with moderate improvements in clinical severity (CGI score, $d = 0.44$, $p = 0.015$), spontaneous and reactive mental flexibility (C-VF; $d = 0.55$, $p = 0.015$; TMT B $d = 0.47$, $p = 0.006$) and global functioning (GAF; $d = 0.46$, $p = 0.005$). Mild improvements have also been found on negative symptoms ($d = 0.25$, $p = 0.044$) and speed of processing (TMT A; $d = 0.38$, $p = 0.024$) (Table 2).

Having had at least two PIs has been associated with small to moderate improvements on positive and negative symptoms ($d = 0.35$; $p = 0.020$; $d = 0.32$; $p = 0.037$), clinical severity ($d = 0.44$; $p = 0.007$), adherence to treatment ($d = 0.63$; $p = 0.004$) and reactive mental flexibility ($d = 0.51$; $p < 0.001$). Having had at least three PIs has a significant effect on clinical severity, psychosocial function ($d = 0.57$; $p = 0.005$ and $d = 0.46$; $p = 0.003$), adherence into treatment ($d = 0.49$; $p = 0.031$), and reactive mental flexibility ($d = 0.28$; $p = 0.050$). The total number of PIs has been positively correlated with improvement in positive and negative symptoms ($d = 0.15$; $p = 0.027$ and $d = 0.17$; $p = 0.014$), clinical severity ($d = 0.22$; $p = 0.002$), adherence into treatment ($d = 0.20$; $p = 0.009$), spontaneous and reactive mental flexibility ($d = 0.19$; $p = 0.014$; $d = 0.21$; $p = 0.005$;) and psychosocial function $d = 0.16$; $p = 0.018$) (Table 3).

In the multivariate analysis, having had or not at least one PI was retained as the main explanatory factor for the improvement of positive ($p = 0.031$) and negative ($p = 0.011$) symptoms PANSS scores, clinical global severity CGI score ($p = 0.003$), spontaneous and reactive mental flexibility (C-VF; $p = 0.002$; TMT B, $p = 0.029$) and global functioning GAF score ($p = 0.042$) (Table 4).

Discussion

Altogether, the findings of the present study may be summarized as follows:

1. Compared to the very low rates of service users with SZ benefiting from PIs outside of the Expert Centers network (12% of the 6007 participants in the 2010 ESPASS study [10]; 3.8% during the 12 months before evaluation in the present study), PIs were more frequently offered and delivered in the FACE network between 2010 and 2015 (35%).
2. In a large sample of non-selected community-dwelling SZ service users followed-up during 1 year, those who received one of the 4 PIs improved significantly more on clinical symptomatology, mental flexibility and functioning at 1 year compared to those who did not. Moreover, CBT and SST have been associated with higher cognitive improvements (in speed of processing and mental flexibility), while CRT was associated with clinical improvement, beyond cognitive symptoms. These results have not been demonstrated before and suggest that the effect of each PI is larger than its initial target (i.e. positive/negative symptoms for CBT, cognition for CRT). Furthermore, receiving more than one PI has been associated with higher improvements in clinical symptomatology, mental flexibility and psychosocial function. This suggests that improvements could be a function of the number of interventions, which has not been demonstrated before.

As mentioned in the rationale, the access to PIs was extremely low in France before the development of the FACE-SZ network in 2009. Only 15% of the 6007 participants with SZ included in the ESPASS cohort [10] were engaged in any form of psychosocial rehabilitation (including the 4 PIs, family interventions and sheltered or competitive employment) during the 6-months follow-up period; only 2% received CBT; 1% CRT; 2% SST and 7% PSE. Similarly, only 3.8% of the participants included in the FACE cohort had received from at least one PI on the year before evaluation. Several barriers to the implementation of evidence-based interventions in routine clinical practice have been identified in the literature including lack of available resource [38] lack of specific training [38, 39], lack of dedicated time to perform interventions [39], excessive caseloads for a limited workforce capacity [38], staff members' lack of knowledge about PIs and their efficacy [38, 39], negative management and team attitude towards PIs [39], lack of service users sharing the same diagnosis for structured psychoeducation [40] and difficulties to identify those who would need an intervention for CBT [38]. Wide spreading

Table 2 Univariate effects of psychosocial interventions per type

Improvement variable	I PI or more		CBT		CRT		PSE		SST	
	Cohen's <i>d</i> (95% CI)	<i>p</i> value								
PANSS total	0.29 (−0.04, 0.61)	0.029	0.38 (−0.04, 0.80)	0.015*	0.30 (−0.08, 0.69)	0.036*	0.13 (−0.29, 0.54)	0.227	0.24 (−0.28, 0.76)	0.072
PANSS positive	0.31 (−0.02, 0.63)	0.021	0.34 (−0.08, 0.76)	0.026	0.42 (0.04, 0.81)	0.007	0.21 (−0.20, 0.63)	0.083	0.02 (−0.50, 0.55)	0.458
PANSS negative	0.44 (0.11, 0.76)	0.003	0.31 (−0.11, 0.73)	0.045*	0.47 (0.08, 0.86)	0.005	0.20 (−0.21, 0.61)	0.142	0.25 (−0.27, 0.78)	0.044
PANSS psychopathology	0.05 (−0.27, 0.37)	0.372	0.27 (−0.15, 0.69)	0.083	0.01 (−0.37, 0.40)	0.466	0.01 (−0.41, 0.42)	0.487	0.27 (−0.25, 0.79)	0.078
CGI	0.44 (0.12, 0.76)	0.003	0.46 (0.05, 0.87)	0.010	0.36 (−0.02, 0.74)	0.022	0.47 (0.06, 0.87)	0.008	0.44 (−0.07, 0.95)	0.015
GAF	0.37 (0.04, 0.69)	0.012	0.59 (0.16, 1.02)	0.001	0.21 (−0.16, 0.59)	0.152	0.07 (−0.34, 0.47)	0.345	0.46 (−0.05, 0.97)	0.005
CDSS	−0.04 (−0.36, 0.28)	0.597	0.21 (−0.21, 0.63)	0.126	−0.27 (−0.65, 0.12)	0.920	0.05 (−0.36, 0.45)	0.407	−0.16 (−0.68, 0.36)	0.723
S-QoL	−0.07 (−0.42, 0.27)	0.668	−0.39 (−0.86, 0.08)	0.973	0.16 (−0.27, 0.59)	0.217	0.09 (−0.37, 0.56)	0.338	−0.31 (−0.92, 0.29)	0.856
BIS	0.42 (0.07, 0.77)	0.004	0.32 (−0.14, 0.77)	0.008*	0.45 (0.01, 0.89)	0.011*	0.09 (−0.36, 0.54)	0.324	0.31 (−0.27, 0.89)	0.016*
MARS	0.35 (−0.01, 0.70)	0.024	0.34 (−0.13, 0.82)	0.068	0.33 (−0.13, 0.79)	0.077	0.53 (0.06, 1.01)	0.006	0.43 (−0.18, 1.03)	0.063
SUMD attribution	0.24 (−0.09, 0.57)	0.071	−0.02 (−0.46, 0.42)	0.551	0.38 (−0.01, 0.77)	0.023	0.07 (−0.36, 0.50)	0.361	−0.20 (−0.71, 0.32)	0.876
SUMD awareness	0.39 (0.06, 0.72)	0.007	0.18 (−0.25, 0.61)	0.098	0.42 (0.03, 0.81)	0.011	0.25 (−0.17, 0.68)	0.104	−0.02 (−0.53, 0.49)	0.551
TMTA time	0.30 (−0.05, 0.65)	0.044	0.34 (−0.12, 0.81)	0.012	0.24 (−0.17, 0.66)	0.161	0.12 (−0.33, 0.58)	0.260	0.38 (−0.20, 0.96)	0.024
TMTB time	0.58 (0.22, 0.93)	0.001	0.20 (−0.27, 0.67)	0.115	0.77 (0.35, 1.20)	< 0.001	0.28 (−0.18, 0.73)	0.090	0.47 (−0.11, 1.06)	0.006
CPT-IP	0.48 (0.04, 0.92)	0.023	0.29 (−0.27, 0.84)	0.247	0.45 (−0.05, 0.95)	0.019	0.23 (−0.33, 0.78)	0.170	−0.18 (−0.88, 0.53)	0.697
L-VF	0.30 (−0.05, 0.65)	0.047*	0.25 (−0.22, 0.72)	0.158	0.08 (−0.34, 0.50)	0.359	0.00 (−0.47, 0.47)	0.504	0.40 (−0.18, 0.98)	0.119
C-VF	0.57 (0.21, 0.93)	< 0.001	0.58 (0.11, 1.06)	0.003	0.49 (0.07, 0.92)	0.006	−0.04 (−0.51, 0.43)	0.594	0.55 (−0.04, 1.13)	0.015

Effect of psychosocial interventions on 1-year improvements in 17 outcomes. Improvement in *p* values were calculated by a one-sided Student's *t* test. Results that remained significant after the multiple imputation procedure were retained (boldfaced without stars *p* values). Improvement variables were the following: Positive and Negative Symptoms Scale (PANSS) total score and its three subscales: PANSS positive; PANSS positive symptom score; PANSS negative; PANSS negative symptom score; PANSS psychopathology; PANSS general psychopathology score; Clinical Global Impression: CGI score; Global Assessment of Functioning: GAF; Subjective Quality of Life: S-QoL, Calgary Depression Scale for Schizophrenia: CDS score; Scale to Assess Unawareness of Mental Disorders (SUMD) with 2 scores: attribution score; awareness score; TMTA: Trail Making Test A, time; TMTB: Trail Making Test B, time; CPT-IP: CPT-IP, d prime 4th condition; L-VF: literal verbal fluency, number of words; C-VF: categorical verbal fluency, number of words, Birchwood Insight Scale: self-rated insight

Improvement variables were the following: Positive and Negative Symptoms Scale (PANSS) total score and its 3 subscales: PANSS positive PANSS positive symptom score, PANSS negative PANSS negative symptom score, PANSS psychopathology PANSS general psychopathology score, CGI score clinical global impression, GAF global assessment of functioning, S-QoL subjective quality of life, CDSS Calgary Depression Scale for Schizophrenia, Scale to Assess Unawareness of Mental Disorders (SUMD) with 2 scores: attribution score; awareness score; TMTA trail making test A, time, TMTB trail making test B, time, CPT-IP CPT-IP, d prime 4th condition, L-VF literal verbal fluency, number of words, C-VF categorical verbal fluency, number of words, Birchwood Insight Scale: self-rated insight

**p* values significant (< 0.05) after multiple imputation, that were therefore not retained for analysis

Table 3 Univariate effects of psychosocial interventions per number

Improvement variable	1 PI or more		2 PIs or more		3 PIs or more		Number of PIs	
	Cohen's <i>d</i> (95% CI)	<i>p</i> value	Cohen's <i>d</i> (95% CI)	<i>p</i> value	Cohen's <i>d</i> (95% CI)	<i>p</i> value	Correlation (95% CI)	<i>p</i> value
PANSS total	0.29 (−0.04, 0.61)	0.029	0.26 (−0.15, 0.66)	0.054	0.36 (−0.23, 0.96)	0.020*	0.15 (−0.01, 0.30)	0.030*
PANSS positive	0.31 (−0.02, 0.63)	0.021	0.35 (−0.05, 0.75)	0.020	0.25 (−0.34, 0.85)	0.092	0.15 (0.00, 0.30)	0.027
PANSS negative	0.44 (0.11, 0.76)	0.003	0.32 (−0.08, 0.72)	0.037*	0.29 (−0.31, 0.89)	0.073	0.17 (0.02, 0.32)	0.014
PANSS psychopathology	0.05 (−0.27, 0.37)	0.372	0.08 (−0.33, 0.48)	0.331	0.39 (−0.21, 0.99)	0.030*	0.08 (−0.08, 0.23)	0.169
CGI	0.44 (0.12, 0.76)	0.003	0.44 (0.04, 0.84)	0.007	0.57 (−0.01, 1.15)	0.005	0.22 (0.07, 0.36)	0.002
GAF	0.37 (0.04, 0.69)	0.012	0.23 (−0.17, 0.63)	0.093	0.46 (−0.12, 1.03)	0.003	0.16 (0.01, 0.31)	0.018
CDSS	−0.04 (−0.36, 0.28)	0.597	−0.15 (−0.55, 0.25)	0.776	0.00 (−0.59, 0.60)	0.497	−0.02 (−0.17, 0.14)	0.589
S-QoL	−0.07 (−0.42, 0.27)	0.668	−0.12 (−0.57, 0.33)	0.715	−0.33 (−1.10, 0.45)	0.767	−0.05 (−0.21, 0.12)	0.710
BIS	0.42 (0.07, 0.77)	0.004	0.26 (−0.19, 0.70)	0.075	0.22 (−0.50, 0.95)	0.019*	0.15 (−0.02, 0.30)	0.041*
MARS	0.35 (−0.01, 0.70)	0.024	0.63 (0.16, 1.09)	0.004	0.49 (−0.29, 1.26)	0.031	0.20 (0.03, 0.36)	0.009
SUMD attribution	0.24 (−0.09, 0.57)	0.071	−0.04 (−0.46, 0.37)	0.594	−0.07 (−0.67, 0.53)	0.664	0.04 (−0.12, 0.19)	0.315
SUMD awareness	0.39 (0.06, 0.72)	0.007	0.25 (−0.16, 0.66)	0.046*	0.00 (−0.60, 0.59)	0.507	0.11 (−0.04, 0.26)	0.079
TMTA time	0.30 (−0.05, 0.65)	0.044	0.23 (−0.22, 0.69)	0.086	0.33 (−0.36, 1.01)	0.072	0.12 (−0.04, 0.28)	0.075
TMTB time	0.58 (0.22, 0.93)	0.001	0.51 (0.05, 0.97)	<0.001	0.28 (−0.40, 0.97)	0.050	0.21 (0.05, 0.37)	0.005
CPT-IP	0.48 (0.04, 0.92)	0.023	0.13 (−0.41, 0.67)	0.301	−0.29 (−1.04, 0.45)	0.766	0.10 (−0.11, 0.30)	0.183
L-VF	0.30 (−0.05, 0.65)	0.047*	0.12 (−0.34, 0.58)	0.299	−0.04 (−0.73, 0.64)	0.546	0.06 (−0.10, 0.23)	0.221
C-VF	0.57 (0.21, 0.93)	<0.001	0.26 (−0.20, 0.72)	0.083	0.17 (−0.52, 0.85)	0.313	0.19 (0.02, 0.34)	0.014

Effect of psychosocial interventions on 1-year improvements in 17 outcomes. Improvement in *p* values were calculated by a one-sided Student's *t* test for having had 1, 2, 3 PIs or more, by a one-sided correlation test for the total number of PIs. Results that remained significant after the multiple imputation procedure were retained (boldfaced *p* values without star). Improvement variables were the following: Positive and Negative Symptoms Scale (PANSS) total score and its 3 subscales: *PANSS positive* PANSS positive symptom score, *PANSS negative* PANSS negative symptom score, *PANSS psychopathology* PANSS general psychopathology score, *CGI score* clinical global impression, *GAF* global assessment of functioning, *S-QoL* subjective quality of life, *CDSS Score* Calgary Depression Scale for Schizophrenia, Scale to Assess Unawareness of Mental Disorders (SUMD) with 2 scores: attribution score; awareness score; *TMTA* trail making test A, time, *TMTB* trail making test B, time, *CPT-IP* CPT-IP, d prime 4th condition, *L-VF* literal verbal fluency, number of words, *C-VF* categorical verbal fluency, number of words, Birchwood Insight Scale: self-rated insight

**p* values significant (< 0.05) after multiple imputation, that were therefore not retained for analysis

psychosocial interventions is one of the aims of the FACE-SZ expert center network. The present results suggest that expert center network is effective in increasing the rate of PIs delivery.

More specifically, 15.8% of the 183 participants included in the present sample received CBT during the follow-up period. This is higher than the proportion found in UK in 2014 (5.3% of 187 participants [41]) but it remains less developed compared to Australia (22.3% of 1825 participants [11]). The development of a large Australian PI network since the 2000s beyond the national public health system in this country may explain this difference [11]. Access to PSE (16.9% in the present sample) was higher compared to the 2010 ESPASS study (7%) [10] but PSE is still less available than in German-speaking countries (21% of 338 participants in 2003 [42]). In these countries, PSE has been included in the national mental health policy. The proportion of service users who have received CRT and SST in the present study was much higher compared to the ESPASS 2010

study [10] (respectively, 19.1% vs. 1% for CRT and 9.8% vs 2% for SST). To the best of our knowledge, no comparative data have been published for other countries.

CBT is the most documented intervention regarding its effectiveness, access rates and implementation in national policies [9, 38, 39, 43]. CBT has been associated in the present sample with improvements in positive symptoms but not negative symptoms, consistently with the findings of a previous study ($d=0.37$ [7] vs. $d=0.34$ in the present study). Moreover, CBT has been independently associated with improvements in speed of processing and mental flexibility in the present results, which has not been demonstrated before. Improvements in speed of processing have been previously associated in recent studies with functional change during psychosocial rehabilitation [44] and to participation in community activities [45]. Improved mental flexibility has been associated with better functional outcomes [45]. Future studies should determine whether improvement in cognitive functions mediates the relationship between CBT and the

Table 4 Multivariate analysis of six improvement variables against covariates

Explanatory covariates	Slope (95% CI)	<i>p</i> value
PANSS positive improvement		
1 PI or more	1.41 (0.13, 2.69)	0.031
Hospitalizations	1.41 (0.11, 2.72)	0.034
GAF	0.04 (−0.01, 0.09)	0.079
PANSS negative improvement		
1 PI or more	2.27 (0.53, 4.02)	0.011
Diagnosis	−1.75 (−3.93, 0.44)	0.116
SUMD awareness	−1.18 (−2.64, 0.27)	0.110
CGI improvement		
1 PI or more	0.49 (0.17, 0.82)	0.003
Psychotic episodes	0.27 (−0.14, 0.67)	0.195
PANSS total	0.02 (−0.01, 0.05)	0.166
PANSS positive	−0.04 (−0.08, 0.01)	0.090
PANSS psychopathology	−0.03 (−0.08, 0.01)	0.162
GAF	0.01 (0.00, 0.03)	0.133
TMTB time	−0.22 (−0.44, −0.01)	0.044
GAF improvement		
1 PI or more	3.69 (0.13, 7.24)	0.042
Education	0.46 (−0.20, 1.12)	0.173
TMTB time	−0.87 (−2.67, 0.93)	0.343
C-VF	0.16 (−0.10, 0.41)	0.223
TMTB time improvement		
1 PI or more	17.34 (1.85, 32.83)	0.029
Age	−0.58 (−1.50, 0.34)	0.211
f-NART IQ	0.62 (−0.17, 1.41)	0.120
PANSS psychopathology	−1.02 (−3.06, 1.02)	0.323
CPT-IP	9.40 (−2.45, 21.26)	0.118
C-VF improvement		
1 PI or more	3.54 (1.34, 5.74)	0.002
Hospitalizations	3.06 (0.66, 5.45)	0.013
Suicide attempts	2.49 (−1.70, 6.68)	0.242
TMTB time	−0.94 (−2.00, 0.11)	0.080
L-VF	0.10 (−0.07, 0.28)	0.239

For each improvement variable, the table displays the ANOVA table of the best-selected model out of covariates significant at threshold 10%. In all six cases, having had at least one PI is the main explanatory factor. The 33 covariates were the following: gender; age; age at first episode; Type: schizophrenia against schizo-affective disorder; level of education; housing status; professional status; Premorbid intelligence: f-Nart; working memory score (WAIS-IV); having had or not a psychotic episode during past year; having had or not a full-time hospitalization during past year; suicide attempts during past year; treatment: antipsychotic or not; cannabis consumption at V0; alcohol consumption at V0; Positive and Negative Symptoms Scale (PANSS) total score and its 3 subscales: PANSS positive symptom score; PANSS negative symptom score; PANSS psychopathology: PANSS general psychopathology score; Clinical Global Impression: CGI score Bold values indicate significant *p* values (*p* < 0.05)

GAF global assessment of functioning, *S-QoL* subjective quality of life, *CDSS score* Calgary Depression Scale for Schizophrenia, Scale to Assess Unawareness of Mental Disorders (SUMD) with 2 scores: attribution score; awareness score, *TMTA* trail making test A, time, *TMTB* trail making test B, time, *CPT-IP* CPT-IP, d prime 4th condition, *L-VF* literal verbal fluency, number of words, *C-VF* categorical verbal fluency, number of words, Birchwood Insight Scale: self-rated insight

improvement in global functioning. The effect size of the improvement of global functioning associated with CBT was larger in the present study compared with previous studies ($d=0.59$ in the present study vs. 0.38 [7]). The factors associated with effectiveness of CBT on global functioning in service users with SZ should be explored in future studies.

The present results suggest that PSE is associated with the improvement in adherence into treatment and clinical severity at 1 year, consistently with a previous study [4]. SST has shown moderate effects on global functioning in the present study, which is consistent with the results of a previous study [8], ($d=0.52$ [8] vs. $d=0.46$ in the present sample); however, the effect size on negative symptoms was smaller in the present study ($d=0.25$ vs. $d=0.40$ [8]). SST was also associated with mild improvements in speed of processing and moderate improvements in mental flexibility in the present study. Speed of processing has been recently described as a mediator of social competence, interpersonal relationships and community functioning [44, 45]; mental flexibility has also been associated with social functioning and problem solving [45]. Further studies should determine if the effect of SST on global functioning is mediated by the improvement in negative symptoms, speed of processing and/or mental flexibility.

Consistently with some studies [5, 6], CRT has shown a moderate positive effect on cognitive functioning in the present study ($d=0.42$ – 0.77 vs. $d=0.36$ [5]; $d=0.42$ [6]). CRT has been also associated in the present sample with moderate improvements in negative symptoms ($d=0.47$). This is consistent with the literature, although reported effects sizes were smaller in a recent meta-analysis (Hedge's $g=0.30$ [46]). Future studies should determine whether improving executive functions might mediate the association between CRT and negative symptoms reduction, as suggested in a previous study [47]. This effect may be mediated by specific CRT modules or by non-specific ones (e.g. contact with a therapist or attendance to sessions [48]). In contrast with other studies [5, 6], CRT has, however, not been associated with improvement in global functioning in the present sample ($p > 0.05$). Future studies should determine the parameters associated with the CRT effectiveness.

The total number of PIs delivered was associated in the present sample with symptom reduction and improvements in adherence to treatment and in cognitive and psychosocial functioning. This might support results from recent studies [49, 50] where combining several interventions was associated with better treatment outcomes. Future research should address this issue.

Unexpectedly, PIs were not associated with improvements in subjective quality of life (QoL). Studies on the associations between PIs and subjective QoL have, however, yielded conflicting findings, with some studies finding no association between changes in cognitive function or symptom

intensity and subjective QoL [26, 29, 51] and others reporting improvements in subjective QoL after CRT [31, 52]. Improvements in insight into illness in our sample might have led to a decreased subjective quality of life by increasing awareness of psychiatric symptoms and cognitive deficits [52]. It could also be related to self-stigma of schizophrenia that could moderate the association between improvements in insight and low subjective QoL [53]. The effects of psychiatric rehabilitation on subjective QoL should be further investigated.

Limits

Although the network of FondaMental Experts Center for Schizophrenia covers the whole French territory, it cannot be definitely asserted that the FACE-SZ database contains a representative sample of the French population of schizophrenic patients. However, some sample characteristics (including sex ratio, age at illness onset, comorbidities) suggest that the present sample may be compared to general stabilized community-dwelling SZ population. Institutionalized or very disabled patients are not able to receive a 2-day long comprehensive evaluation and were, therefore, not represented in the present sample, which limits the extrapolation of the present results to this population, as well as to patients younger than 16 years. As there was no control group, it was not possible to determine the exact impact of the FACE evaluation to improve access to PIs and to differentiate PI's specific effects on clinical and functional outcomes from non-specific effects related to psychotherapies in general. It can only be asserted that the proportion of patients who received PIs was 10 times higher after the baseline evaluation and recommendations (35% during the 12 months follow-up vs. 3.8% during the 12 months before evaluation). Furthermore as longitudinal studies may be more complicated in patients with SZ, a high rate of participants was lost to follow-up (50%). There were, however, no significant differences regarding our variables of interest between participants who completed the study and those who did not attend the follow-up.

Strengths

Compared to the previous studies mentioned in the rationale, the present study exhibits clear strengths: a large non-selected sample of community-dwelling SZ outpatients, the use of a large bundle of standardized evaluation scales, and the inclusion of a large number of potential confounding factors in the multivariate analysis.

Conclusion

Psychosocial interventions have been associated with a large bundle of improvements in the present sample of SZ community-dwelling service users. Each therapy has shown effectiveness on its primary target (e.g. cognition for CRT, psychotic symptomatology for CBT) but also effectiveness on other dimensions (e.g. cognition for CBT, negative symptoms for CRT). The largest global effects of PIs were found for negative symptoms, sustained attention / working memory and mental flexibility. Future health policies should determine which PI should be systematically proposed to each patient in a personalized/precision medicine approach to optimize accessibility, patient's adherence and effectiveness.

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Author contribution statement The authors had full access to the data in the study and take the responsibility for the integrity of the data and the accuracy of the data analysis. Dr Julien Dubreucq drafted the article and made the literature review. Pr Bernard Ycart and Mrs Agnès Hamon performed the statistical analysis. Dr Guillaume Fond, Pr Pierre Michel Llorca, M. Franck Gabayet and Mrs Claire Cécile Périer contributed to the interpretation of data and critically revised the article. All the authors were involved in the collection and analysis of the data. All authors contributed to and have approved the final manuscript.

Compliance with ethical standards

Conflict of interest All authors declare that they have no conflict of interest.

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