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Symptomatic and Functional Recovery: Does Symptom Severity Affect the Recovery of Executive Functioning in People with Psychotic Disorders?

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ABSTRACT

Background: Recovery in psychotic disorder patients is a multidimensional concept that can include personal, symptomatic, societal and functional recovery. Here we define Functional Recovery (FR) as recovery or compensation after the loss or impairment of skills in different cognitive functions. Some of the most impaired cognitive functions in psychosis are the executive functions, whose impairment in people with a psychotic disorder can produce problems that are difficult to overcome, partly because treatment often focuses only on Symptomatic Recovery (SR). Although symptom severity may be a risk factor for longstanding impairments of executive functioning, the association is not always found. To date, there has been little research on the association between the 2.

Method: This study is part of the UP'S study, a longitudinal cohort study of patients with a psychotic disorder. The Behaviour Rating Inventory of Executive Functioning Adult version (BRIEF-A) was used to measure FR at baseline and after 1 year. SR was measured using the Positive and Negative Symptom Scale-Remission (PANSS-R), also at baseline and 1 year? At both time points, correlations were computed as cross-sectional analyses. For the longitudinal analysis, the difference scores were used to calculate generalized linear models. Model selection was based on the Wald-Chi square test.

Results: 323 people were included for the baseline assessment of the UP'S study, 163 of whom had completed the T1 follow-up measurement at the time of this study. We found a moderate association between PANSS-R baseline scores and BRIEF-A baseline scores (β=3.76). While there was also an association between the PANSS-R score at baseline and the BRIEF-A difference scores (β=1.67), we found no association between the PANSS-R difference scores and the BRIEF-A differences scores.

Conclusion: Our finding that less overall symptom severity was associated with 1 year improvement in executive functioning suggests that symptom severity could be a way of improving executive functioning over a year. However, as no link was found within the year between changes in symptoms and changes in executive functioning, it is possible that symptom severity does not have an immediate effect on executive functioning, but that its effect is delayed. This leaves scope for targeted interventions to improve executive functioning, and thus functional recovery.

Keywords: Functional recovery; Executive functioning; Symptomatic recovery; Symptoms

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INTRODUCTION

Treatment of psychotic disorders often focuses mainly on reducing the positive and negative symptoms of psychosis-a reflection of the fact that research on the treatment of psychotic disorders focuses primarily on symptomatic recovery [1-3]. This is understandable, as these symptoms can interfere drastically with daily life, and as worse symptoms are linked to poor functional outcomes [4,5]. Only 14% of people with a psychotic disorder are thought to show symptomatic recovery over time, i.e., to have no residual symptoms after 6 months [3]. But because symptoms fluctuate, decrease with age, and do not always interfere with daily activities, this is too strict [6,7]. More importantly, whether or not there are residual symptoms, other forms of recovery, such as personal or functional recovery, can occur [8-11]. Recovery from psychosis can therefore be defined as a multidimensional concept that comprises 4 domains of recovery: Personal, symptomatic, societal and functional [12-14]. For functional recovery, however, there is no consensus on a definition [15]. The American Psychological Association (APA) defines functional recovery, or the recovery of functions, as "partial or full restoration of an ability that has previously been impaired as a result of damage (through disease or trauma) to the central or peripheral nervous system or to an organ or body part" [16]. Other research describes it broadly as "the capacity to adapt to the personal, family, social and labour needs of a productive adult with the disease" [17]. Both these definitions entail improving functional outcomes in multiple aspects of one's life. Together with the lack of consensus, this broad definition makes it difficult to measure the concept [18]. One way to measure it is through cognition. As cognitive impairments are thought to be a core feature of psychotic disorders, their role in disease outcome has raised the possibility that cognitive impairments-and recovery from them-should be seen as a separate form of recovery [19-23]. This even led to a proposal that cognition should be viewed as a separate domain for evaluation in the DSM-5, which would be consistent with the APA's definition of functional recovery [24,25]. Treatment that aims to reduce functional impairments often targets the cognitive skills [26-28]. But the mixed results produced by a vast body of research on these cognitive remediation treatments show that neither cognitive training nor measurements always generalize to better functioning [29-33]. These difficulties can be resolved by combining treatments, for example by adding cognitive training to rehabilitation training to improve functioning [34].

Given the importance of the cognitive skills in treatment, functional recovery in this study was defined as recovery or compensation after cognitive functioning skills had been lost or impaired [13,14,35]. And since executive functions are one of the most impaired cognitive functions in psychosis, we used them as a limited means of operationalizing functional recovery [13,36-39]. To capture the ecologically valid, daily-life executive functions that are linked to better functioning, we used a self-report measure [33,40]. Executive functions are cognitive processes that help us to interact with the world around us, respond to novel and/or demanding situations, and adjust our behaviour according to external inputs [41,42]. Impairments in these functions are present before the onset of psychotic disorders [43-45]. During a 1st episode, executive function in patients with more severe premorbid symptoms is also more severely impaired [46-50]. After the 1st episode, however, these impairments seem to stabilize, even though their manifestation differs according to the diagnoses in the psychosis spectrum [51-55]. But although, in all cases, impairments in executive functions during the illness negatively affect daily functioning, career, education, social relationships, and community outcomes [42,56-63], all research here focusses on the influence of impairments of executive functioning. Using executive functioning as a form of recovery-in this case functional recovery-forces us to look at it from a different perspective, i.e., that of the influence of improvements, or the recovery of functions. Earlier research has given us reason to believe that if functional recovery can be improved, we will also be able to help clients improve their daily-life functioning, social relationships, and personal recovery. This is also the basis of the framework of van der Stel, who uses the framework as a way to research improvements in the different forms of recovery [64]. Regarding the association between executive functions and symptom severity, one study found that those with symptoms in remission have better executive functions than those who remain in active psychosis [65-67]. However, most studies either have a limited follow-up period, or have longitudinal data with only a limited amount of follow-ups, or focus on the daily-life consequences of executive functions and symptoms, without examining the association between the two[68-74]. Even though a few studies that used longitudinal data on symptomatology and executive functioning consistently showed small to no changes in executive functioning after the 1st episode psychosis; and also found small to no associations between symptomatology and executive functions, the results of each study were influenced by small group sizes [75-77]. It thus seems that the body of research on the relationship between executive functioning and symptomatic severity during the illness is incomplete, and that the relationship between the 2 over time remains unclear [78,79]. We therefore investigated the association between changes in symptomatic recovery and changes in executive functioning in people with a psychotic disorder cross-sectionally and over time. We hypothesized that, at any point in time, worse symptoms would be positively associated with worse executive functioning. We also expected changes in symptom severity over a year to have an effect on changes in executive functioning over a year.

MATERIALS AND METHODS

This study is part of the UP'S cohort study, an ongoing observational cohort study investigating processes of recovery in people with psychotic disorders over a 10-year period [13,35]. It is a collaboration between Erasmus University Medical Centre Rotterdam and 9 mental healthcare institutions in the southwestern Netherlands. Patients were recruited in Community Mental Health (CMH) teams and were eligible for participation if they had a primary diagnosis of a schizophrenia-spectrum disorder according to DSM 5 criteria (i.e., schizophrenia, schizophreniform disorder, schizoaffective disorder, brief psychotic disorder, substance-induced psychotic disorder, delusional disorder, schizotypal disorder and psychotic disorder not otherwise specified); at the time of inclusion, they were aged between 18 and 65. Insufficient proficiency in the Dutch language was an exclusion criterion. In principle, each participant would be fol-

lowed over a 10-year time-period, with measurements every year. Inclusion, interviews, and follow-up measurements were all handled by students and/or researchers at a participating CMH team or at Erasmus University Medical Centre. First, an anonymized list of all eligible clients per team was drawn up through the Electronic Patient Files (EPF). This was based on age and primary diagnosis, the latter having been determined in a clinical interview by the team psychiatrist. To ensure that a representative sample of all clients with a psychotic disorder could be included, 30 clients per team were randomly selected from this list and invited to participate in the cohort study. However, if a client was actively psychotic according to the treating psychiatrist, or was an inpatient or in judicial detention, participation was not possible at that time, and this client was not approached. Once all participants on the list had been approached, a new list could be made. Provided the team was willing to participate, had room for a student or researcher, and provided inclusion in the cohort was still ongoing, selection lists could be made for that team. Ultimately, many lists of randomly selected patients will therefore be made per team over an extended period. After they had received information on the study and after their questions on it had been answered, clients were given 2 weeks to consider participation. Those willing to participate were asked to sign the informed consent form, after which an interview was planned. At the time of this study, 335 participants had been included in the cohort study, 163 of whom had completed the T1 follow-up measurement. This study includes data on all participants who had finished the baseline interview by December 29, 2022. **Figure 1** shows the inclusion chart.

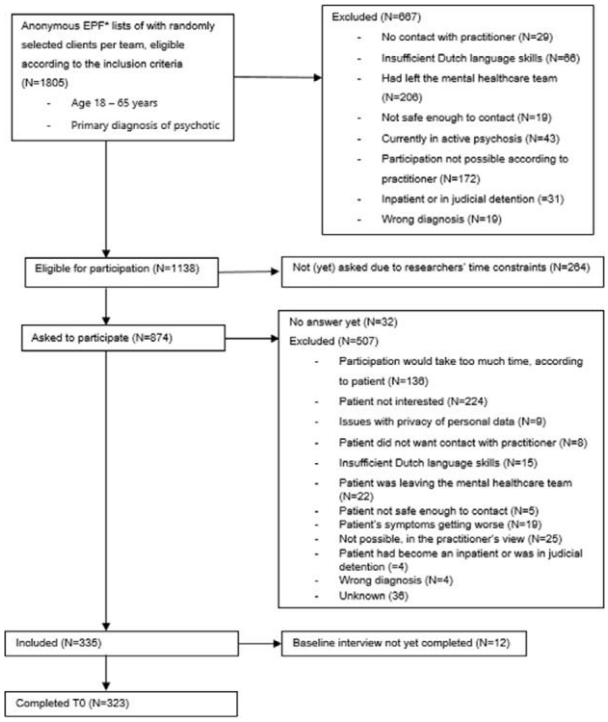

Figure 1: Inclusion flowchart for the up's study *EPF=Electronic Patient File

QUESTIONNAIRES

Functional Recovery

To operationalize functional recovery, we used the Behaviour Rating Inventory of Executive Functioning for Adults (BRIEF-A), a 76-item self-report questionnaire designed to assess executive functioning in real-world situations [80]. Each item is scored on a 3 level scale ranging from 1 (never) to 3 (always), and is part of 1 of 9 subscales. A higher score indicates poorer executive functioning. The 9 subscales are in turn part of 2 larger subscales, the Behaviour Regulation Index (BRI: 4 subscales), and the Metacognition Index (MI: 5 subscales). Together, these 2 indexes can be summarized as a Global Executive Functioning score (GEF), which was the score used in this study. For all indices, t-scores and percentiles must be calculated, which can then be used to compare scores with different population-based norm scores. Each scale has 2 cut-offs:

- T-scores above 65, or a percentile above 90, are considered clinical scores.
- T-scores between 60 and 65 are subclinical. T-scores below 60 are considered normal.

To test whether a score can be considered valid, the questionnaire also contains 3 validity scales: Negativity, improbability, and inconsistency. If a score is above cut-off on either of these scales, the results on the questionnaire for that participant are considered non-valid. In our study, all invalid scores were excluded from the analysis. The questionnaire has been evaluated for use in a schizophrenia sample [81]. Chronbach's α for the questionnaire ranges from 0.93 to 0.96 [82].

Symptomatic Recovery

Symptomatic recovery was operationalized through symptom severity using the Positive and Negative Symptom Scale-Remission (PANSS-R), a short version of the PANSS that is used to assess clinical remission, which is a 30-item inventory for assessing symptom severity. Before being able to score this questionnaire, it is mandatory for students and researchers to be trained. This shortened version contains 8 items of the original version across 3 subscales: 3 positive symptom items, 3 negative symptom items, and 2 general symptom items [4]. Each item is scored from 1 (absent) to 7 (extreme), and incorporates both the severity of the symptoms and the behavioural effect of the symptoms [83]. A mean score for each subscale and for the total scale is used in the analysis. Chronbach's α for the PANSS-R was found to be 0.80 [84].

Statistical Analysis

The dataset obtained from the study contained 323 participants on both the BRIEF-A and the PANSS-R at baseline, 163 of whom had completed the interview after 1 year. To indicate the representativeness of the sample, descriptive statistics were displayed for baseline and T1 (i.e., after 1 year). Pearson's correlation coefficients were calculated to explore the association between symptomatic recovery and functional recovery at baseline and after 1 year. Generalized linear models were used not only to examine the effect of PANSS-R baseline score on the BRIEF-A baseline score, but also to analyse the PANSS-R difference scores on the BRIEF-A difference scores. Difference scores were calculated as T1 minus baseline for both the PANSS-R and BRIEF-A. Correction for gender and age was applied in all models, and appropriate corrections for baseline scores on the BRIEF-A and PANSS-R were applied in the models with difference scores, where age, BRIEF-A and PANSS-R scores

were also centred. In all models, centred scores for age, BRIEF at baseline and PANSS at baseline were used. Model selection was based on the Wald-Chi square test. Sensitivity analysis was done to determine whether the effect of total scores on the PANSS-R differed from positive, negative, or generic scores of the PANSS-R on the BRIEF-A. All analyses were carried out using IBM SPSS statistics Version 27.1.1.

RESULTS

Patient Characteristics

At the time of this study, there was data of 323 participants after being included in the UP'S cohort study (**Table 1**). Their mean age was 41.5 years (SD=12.3, range 18-65); 64.4% were male; and 42.1% had a primary diagnosis of schizophrenia. Their average time in care was 12.3 years (SD=10.0). The average number of lifetime admissions to a psychiatric hospital was 3.2 (SD=3.5). 163 participants had completed both the baseline and 1 year follow-up measurements; their mean age was 41.9 (SD=11.7, range 19-66); 66.9% were male; and 41.1% of them had a primary diagnosis of schizophrenia. Their average time in care was 14.3 years (SD=10.7). Table 1 shows all descriptive statistics, including mean sample scores, for baseline and T1. The mean symptom score based on the PANSS-R, indicate a low symptomatology. The Screener for Intellectual Learning Disability (SCIL) was completed only at baseline; the mean score was 19.5 (SD=5.1), with 41.6% scoring below the cut-off of 19.

Although the mean executive function score was marginally better than in other samples of outpatients with psychotic disorders, it still lay far below that of a healthy population, both at baseline and after a year [85].

The mean difference score on the BRIEF-A was -1.23 (SD=7.87; range -25.00 to 31.00); on the PANSS-R, it was -0.18 (SD=0.78; range -2.62 to 1.88). **Table 2** shows correlations between all measures at baseline and T1.

Table 1: Descriptive statistics

Characteristics	Disorders	Baseline (T0) N=323			After 1 year (T1) N=136			
			Range	Mean (SD)	N (%)	Range	Mean (SD)	Difference score (T1-T0)
Age	-	-	18-65	41.5 (12.3)	-	19-66	41.9 (11.7)	-
Sex (male)	-	208 (64.4)	-	-	109 (66.9)	-	-	-
Time in treatment	-	-	0-37	12.3 (10.0)	-	-	14.3 (10.7)	-
Diagnosis	Schizophrenia	136 (42.1)	-	-	67 (41.1)	-	-	-
	Psychosis NOS	66 (20.4)	-	-	36 (22.1)	-	-	-
	Short-lived psychotic disorder	46 (14.2)	-	-	13 (8.0)	-	-	-
	Schizoaffective disorder	27 (8.4)	-	-	14 (8.6)	-	-	-
	Other psychotic disorders	48 (14.9)	-	-	33 (20.2)	-	-	-
Intelligence	SCIL score	-	4-28	19.5 (5.1)	-	NA	NA	-
Symptoms	PANSS-R Total	-	1-4.5	2.0 (0.8)	-	1-4	1.8 (0.74)	-0.18 (0.78)
Executive Functioning**	BRIEF-A	-	35-83	56.5 (10.3)	-	36-85	55.4 (10.8)	-1.23 (7.87)

*Number of admissions and number of involuntary admissions are "in the past" at baseline, and "for the last year" at T1
**BRIEF-A scores only apply to those having a valid score according to BRIEF-A guidelines.
PANSS-R=Positive and Negative Symptom Severity-Remission; BRIEF-A=Behavioural Rating Inventory of Executive Functioning-Adults

Table 2: Correlation matrix

	Age	PANSS-R T0	PANSS-R T1	BRIEF-A T0	BRIEF-A T1
Age	1	-	-	-	-
PANSS-R T0	-0.044	1	-	-	-
PANSS-R T1	0.055	0.466	1	-	-
BRIEF-A T0	0.045	0.28	0.266	1	-
BRIEF-A T1	-0.074	0.373	0.246	0.717	1

N for each item: Age N=314, PANSS-R T0 N=280, PANSS-R T1 N=155. BRIEF-A T0 N=267, BRIEF-A T1 N=151
PANSS-R=Positive and Negative Symptom Severity-Remission; BRIEF-A=Behavioural Rating Inventory of Executive Functioning-Adults.

Symptomatic Recovery and Functional Recovery

The regression model of the BRIEF-A at baseline showed a clear effect of the PANSS-R at baseline (β=3.76), and no effect for age (β=0.02) or sex (β=-1.161). **Table 3** shows the same model for changes on the BRIEF-A after 1 year. The regression analysis suggested no association between changes on the BRIEF-A and changes on the PANSS-R. As neither gender nor age were effect-modifiers, effects are not included in the model. However, the PANSS-R score at baseline showed a small effect on the BRIEF-A difference score (β=1.67). Sensitivity analysis showed no differences in effects on BRIEF-A scores for PANSS total or PANSS scores on the positive, negative, or general subscales.

Table 3: Regression model of symptomatic recovery on functional recovery

	BRIEF-A Difference score			
Parameter	**β**	**SE**	**Wald Chi-Square**	**p**
Intercept	14.08	3.98	12.5	<0.001
Sex (male)	-2.04	1.37	2.21	0.138
Age	-0.04	0.06	0.6	0.44
BRIEF-A T0	-0.3	0.07	19.56	<0.001
PANSS-R T0	1.67	0.93	3.22	0.073

PANSS-R T0=Positive and Negative Symptom Severity-Remission at Baseline; BRIEF-A T0=Behavioral Rating Inventory of Executive Functioning-Adults at Baseline; BRIEF-A Difference score=Behavioral Rating Inventory of Executive Functioning-Adults' scores after a year minus baseline scores.

DISCUSSION

This study investigated the association between changes in symptomatic recovery and changes in executive functioning over a year in people with a psychotic disorder. We had hypothesized that, at any point in time, worse symptoms would be associated with worse executive functioning. This hypothesis was confirmed, since we found associations between symptom severity at baseline and executive functioning at baseline, and correlations between the 2 after a year. We had also hypothesized that a decrease in symptom severity over a year would be associated with an increase in executive functioning recovery over that year. Our results are partly in line with this hypothesis, as we found associations between symptoms at baseline and changes in executive functioning after a year. However, we found no association between 1 year changes in symptom severity and 1 year changes in executive functioning. Our use of executive functioning was intended to provide a limited way of operationalizing functional recovery, which we defined as recovery or compensation after the loss or impairment of skills in cognitive functioning, such as executive functions [13,14,35,39]. Symptomatic recovery, on the other hand, was operationalized using symptom-severity scores [13]. As we found symptomatic recovery levels at baseline to be predictive of changes in functional recovery levels within a year, people with psychotic disorders have considerable scope for better functional recovery. Given the impact referred to above of these functions on career, social relationships and personal recovery, the improvement of these functions may be relevant to many clients who are currently in outpatient care, especially if they are combined with good symptomatic recovery levels. The association between symptomatic recovery at baseline and changes in functional recovery is partly consistent with earlier research showing a weak association between the two [75-77]. The question therefore remains whether improvements in functional recovery can be achieved even when symptoms are still present. Our finding that fewer symptoms at baseline were associated with a 1 year improvement in functional recovery suggests that symptom severity should be reduced before improvements in functional recovery can be expected. On the other hand, due to the lack of an association between changes in symptoms within the year and changes in functional recovery within the year, we still believe that functional recovery can improve regardless of whether a person's symptoms improve or not.

The importance of our study lies in the fact that earlier research has shown cognitive impairments-especially impairments in executive functioning to be critical both to the illness and to the multidimensional recovery process. Although these impairments have been shown to increase the risk of psychosis and suicide, they are also linked to important outcomes such as career, social relationships, and personal recovery [39,42,45,57-63,86]. These cognitive skills are often targeted by treatment to reduce impairments in work, school or other capacities [26,27]. Almost all of these studies investigated the effects of executive impairments, not the effects of improvements in executive function. They do, however, give us reason to believe that if these executive functions can be improved over time, we will also be able to help clients improve their daily-life functioning, social relationships, and personal recovery. This is why we chose to follow van der Stel's proposal and use executive functioning as a limited way of operationalizing functional recovery-a framework he saw as providing ways of improving all forms of recovery [12,64]. An important note in this discussion is that symptom severity in this cohort at baseline and after a year was low to moderate. This is consistent with earlier cohort studies involving people with psychotic disorders [87,88]. Furthermore, executive functioning levels at baseline and after a year were only marginally better than in other samples of outpatients with a psychotic disorder, and were still far below those in a healthy population [85]. This suggests that even when symptoms are improving, some difficulties persist with regard to achieving improvements in executive functioning. To disentangle this relationship, more research over a longer period is needed.

Strengths and Limitations

To our knowledge, this is the 1st study to examine the association between changes in symptomatic recovery and changes in executive functioning over a year in a large group of psychotic patients. It was conducted in a large ongoing cohort study with 323 participants at baseline, 163 had already completed 1 year follow-up measurement, who were in mental healthcare, and had an established diagnosis of a psychotic disorder. Demographic variables also showed that the cohort was representative of those currently in community mental healthcare in the Netherlands [89]. The study was set up with the help of a scientific board and a peer expert group, who viewed, dis-

cussed and approved all the measures for use in this cohort [13]. Our study also has a number of limitations. Firstly, executive functioning was used as an operationalization of functional recovery. Although, theoretically, such operationalization is limited, the definition and operationalization of functional recovery is known to vary widely [15,17,18], and could thus have been problematic. Furthermore, because treatment intended to reduce impairments in work, school or other capacities often target the cognitive skills [26,27]. This is why we chose to follow the proposal of van der Stel, and use self-reported executive functioning as a limited way to operationalize functional recovery. Another reason to choose it was because van der Stel saw that this framework offered ways of improving recovery [12,23,64]. Since the theoretical framework has not yet been universally acknowledged, further research is needed to establish whether recovery (including functional recovery) can indeed be improved through executive functions. Secondly, our study did not include several covariates. Although the direct relationship between symptoms and executive functioning had never previously been investigated properly, there are several variables that influence both. For example, both are known to have an association with antipsychotic medication, migration status and substance abuse [88-92]. For this reason, it is not possible to understand the complex relationship between the two by examining the association between them in the absence of any other variables. Nonetheless, such an approach does help us understand the basic association between them, and may provide the broader perspective we need to further understand how all the other variables influence the outcome of the illness.

Thirdly, we also need to consider the clients who are not willing to participate in this study. Although this cohort study has been shown to be representative of the current Dutch outpatient population, a group of clients is still unwilling or unable to participate. One group might change the outcome of this study: Those who are unable to participate due to their severe symptoms (such as in active psychosis). If we had been able to include them, mean symptomatology would not only have been higher, differentiation would also have been greater. These clients may also have had greater differences between baseline and 1 year, simply because their symptoms would have been treated after a year. This would have made them the perfect group to test what happens with functional recovery right after symptomatic recovery has been achieved. Unfortunately, however, even though it is still a future aim of the ongoing study to include them, active psychosis often makes it difficult for people in this group to provide valid answers to a questionnaire such as the BRIEF-A. It is therefore possible that we will never be able to include clients who are undergoing a severely psychotic episode. Finally, as discussed in our Introduction, executive functioning impairments can vary across psychotic disorder diagnoses [55]. It would therefore have been informative to see whether this was also the case here. Similarly, it would have been informative to see whether the influence of psychotic symptoms on executive functions would differ between diagnoses. Unfortunately, as the diagnoses were collected from the EPF (i.e., in line with the study protocol), they may not have been fully reliable, since clinical diagnoses in the Netherlands have been shown to agree only moderately with instrumentally set diagnoses [13,93]. It was therefore decided not to use the diagnoses as a factor in this study, but to analyse them as a single group. Further research is thus needed to further determine whether the different psychosis diagnoses may have influenced the results.

CONCLUSION

In conclusion, although we found an association between baseline symptomatic recovery and changes in executive functioning, no association was found between changes in psychotic symptomatology over time and changes in executive functioning. As functional recovery was operationalized through executive functioning, these results suggest either

- That changes in symptomatic recovery over a 1 year period are independent of changes in functional recovery.
- That the influence of symptomatic recovery on functional recovery delays a response by more than a year.

Either way, at one point, symptom severity does have an influence on possible functional recovery improvements within a year. Stability of symptoms is therefore important. Further research should determine whether such an influence applies across different psychotic diagnoses.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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