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The role of age in the development of Schneiderian symptoms in patients with a first psychotic episode

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Objective: The likelihood of developing psychotic symptoms greatly increases after puberty. In acute psychotic disorders, first rank symptoms (FRS) are prevalent and considered useful for the diagnostic process. The aim of this study was to test for a linear association between age and the probability of occurrence of FRS in patients with a first psychotic episode (FPE).
Method: A total of 112 patients, consecutively admitted with an FPE, were included at baseline and evaluated yearly over a 3-year period using SCID-I and a checklist of 11 items of FRS.
Results: FRS were documented for 65.2% patients at baseline. There was a dose–response relationship in the association between age and FRS. There was no interaction with sex or with final diagnostic category.
Conclusion: Variation in the expression of the core positive symptoms of psychosis is subject to the influence of underlying age-dependent maturational processes both in terms of occurrence and level of severity.

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Introduction

The likelihood of developing delusional thinking greatly increases after puberty and peaks in early adulthood (1–4). It is therefore no surprise that psychotic disorders such as schizophrenia mostly affect young individuals (5). The age-related expression of positive psychotic experiences is not confined to the group of patients with a diagnosis of non-affective psychosis, but also occurs in samples diagnosed with bipolar disorder, those with organic psychiatric disorder and samples of non-patients in the general population (6–9).

In the current study, we wished to extend the finding of age-related expression of positive psychotic experiences in a sample of patients with a first episode of psychotic symptoms followed for a period of 3 years. Such an extension is relevant, as the use of first-onset patients precludes any bias due to factors that are dependent on length of illness, such as age at examination (in contrast to age at onset), treatment effects, chronic effects and effects of onset of co-morbid negative symptoms over the course of the illness (10–14). To our knowledge, no previous studies have examined this issue in a follow-up sample of strictly incident cases of psychosis. In addition, we tested not only for a dose–response relationship in the association between age and probability of occurrence of first rank symptoms (FRS), but also for a linear relationship between age and number of FRS in those with at least one FRS. These dose–response analyses were included in order to support the notion of an underlying developmental process causally contributing to the experience of positive psychotic symptoms (15). In addition, we hypothesized that these associations would be the same regardless of gender or diagnostic category.

Aims of the study

To investigate the association between age and the occurrence of FRS in patients with a first psychotic episode (FPE) and to look for a linear relationship between age and number of FRS.

Material and methods

Procedure

Data were gathered on 112 subjects consecutively admitted between February 1997 and January 1999 to the only general hospital psychiatric ward in an area of 350 000 inhabitants. There are no private hospitals in the area, so the sample represents the whole psychotic population with an FPE needing in-patient psychiatric treatment. FPE was defined as the first time a patient displayed positive psychotic symptoms of delusions or hallucinations. Patients aged 15–65 years were included in the study after informed consent. Subjects with mental retardation, organic brain disorders or drug abuse as a primary diagnosis were excluded.

All subjects met DSM-IV (16) criteria for schizophreniform disorder, schizoaffective disorder, schizophrenia, delusional disorder, brief psychotic disorder, atypical psychosis, bipolar I, II disorder or major depressive disorder with psychotic symptoms. Three diagnostic groups were considered for the interaction between FRS and diagnosis: 'schizophrenia', 'bipolar disorder' (I or II) and 'other diagnosis', where this last group includes schizophreniform disorder, schizoaffective disorder, delusional disorder, brief psychotic disorder, atypical psychosis, or major depressive disorder with psychotic symptoms (with no history of manic or hypomanic episode).

The DSM-IV axis I diagnosis was made using the Structured Clinical Interview for DSM IV, SCID-I (17). The day after admission, patients with first-onset psychotic symptoms were assessed with a protocol that included SCID-I and FRS (18). FRS were rated using a checklist of 11 items (19). The 11 items considered as first-rank symptoms were: audible thoughts, voices arguing, voices commenting, delusional perception, somatic passivity, made thoughts, made impulses, made volition, made feelings, thought withdrawal and thought broadcasting. The evaluations were performed during a clinical interview lasting about 90 min and pertaining to the previous week. The interview was carried out by two psychiatrists (GP, PH) who had reached good inter-rater reliability for SCID-I diagnoses (kappa = 0.88).

Patients were evaluated by direct interview, with the same methodology, once a year over a period of 3 years. In order to have accurate diagnoses, those made at year 3 were considered as the definitive diagnosis for the analyses. When follow-up was not possible, the last diagnosis received by the patient was used.

Additional information from clinical records, family informants and staff observations were incorporated into the rating process. The patients were treated with medications as clinically appropriate.

Given the fact that patients presented with an FPE, age of FRS was defined as age at admission, i.e. the age at which incident psychotic symptoms gave rise to the need for admission.

Statistical analysis

The mean age at baseline of those with and without FRS was compared. Logistic regression with presence of FRS as the response variable and age as the exposure variable was conducted using STATA (20), yielding odds ratios (OR) and their 95% confidence intervals. In order to assess dose–response in the association between age and FRS, the age distribution was divided by its quintiles to create quintile groups. In order to assess dose–response within the group with at least one FRS, we regressed age on FRS (expressed as presence of 1, 2 or 3 or more FRS). Interaction with diagnosis (three categories of schizophrenia, bipolar and other) was assessed by the likelihood ratio test.

Results

A total of 112 patients with an FPE were included. Thirty-seven were women (33%). The mean (± SD) age of the patients was 28.86 ± 10.27 years (range: 16–61). The diagnostic distribution is shown in Table 1. Presence of one or more FRS was documented for 73 patients (65.2%): 22 of them had one FRS, 16 had two FRS, and 35 had three or more FRS.

Table 1. Last diagnosis received grouped by FRS

	Schneiderian symptoms		
	Without	With	Total
Last diagnosis received			
Schizophrenia	6	21	27
Bipolar	22	18	40
Other diagnosis	11	34	45
Total	39	73	112

Table 2. Association between age and first rank symptoms

	Quintile group	*n*	With FRS (%)	Without FRS (%)	OR (95% CI)
Highest age	> 36	20	50.0	50.0	1*
*largeuparrow*10*mm*	29–36	21	61.9	38.1	1.63 (0.47–5.63)
	25–28	29	62.1	37.9	1.64 (0.52–5.19)
	21–24	20	70.0	30.0	2.34 (0.64–8.54)
Lowest age	<21	22	81.8	18.2	4.5 (1.12–18.13)
OR linear trend					1.04 (1–1.08)

* Reference category.

Table 3. Association between age and number of first rank symptoms

Age	*n*	*B*	*t*	*P*	95% CI
Group with one FRS	22	0*			
Group with two FRS	16	−2.76	−0.87	0.388	−9.08–3.57
Group with three or more FRS	35	−4.55	−1.73	0.088	−9.79–0.69
Linear trend**		−2.25	−1.73	0.087	−4.84–0.34

* Reference category.

** Summary decrease in age with one FRS.

Analyses were conducted to compare patients with and without FRS. The mean age was different between the groups; patients with FRS had a median age of 26 (IQR: 21–30, mean = 27.5) while the median age of patients without FRS was 38 (IQR: 22–39, mean = 31.3). Patients with FRS were significantly younger than those without (Mann–Whitney U-test = 1098; $P = 0.046$).

There was a dose–response relationship between age and the presence of at least one FRS: the lower the age, the higher the likelihood of having an FRS (Table 2). Similarly, within the group of 73 subjects, the lower the age, the greater the number of FRS, although this effect was imprecise statistically (Table 3). There was no interaction with sex ($\chi^2 = 0.02$; d.f. = 1; $P = 0.88$) or with diagnostic category ($\chi^2 = 1.48$; d.f. = 2; $P = 0.48$).

Discussion

Our study confirms previous reports of a high rate of FRS in psychosis. Two-thirds of the patients with an FPE had at least one FRS, and in those with FRS, 70% had at least two symptoms. FRS are also frequent in other studies of psychosis with different inclusion criteria (21, 22). The high frequency and the relative ease with which they can be recognized have resulted in their universal use as the core symptoms of psychosis. However, although FRS have greatly influenced research in schizophrenia, and as 'non-understandable symptoms' have been used as a diagnostic criterion, in particular to distinguish between schizophrenia and other psychotic disorders, their significance is far from clear (22–27). It has been proposed that FRS represent a truly distinct dimension, partially independent from the pure paranoid dimension (22). In addition, recent genetic studies of FRS support the dimensional view, and point to a specific heritability of the vulnerability to develop these types of symptoms (28–30). The current results suggest that, in addition, their incidence is associated with underlying age-related developmental processes.

We did not find any evidence that there was an interaction between age and diagnosis with regard to prevalence of FRS, suggesting that the age-dependence of FRS occurs independent of diagnostic boundaries.

The absence of diagnostic specificity for age-dependence of FRS suggests that the description of discrete disease entities within the functional psychoses may not be the correct phenotypic representation (31). Schizophrenia, bipolar disorder and other psychoses may at least in part be expressions of the same underlying vulnerability (32, 33).

Other studies of FRS as diagnostic discriminators and as predictors of outcome have not found them to be useful to differentiate diagnostic categories, although they are always, as in the present study (Table 1), more frequent in patients with schizophrenia than in those with bipolar disorder (22). The results indicate a negative association between age and FRS in patients with an FPE, similar to that reported in bipolar disorder (9) and non-clinical samples (2). Moreover, although the results on the number of FRS in relation to age are imprecise statistically, it seems that the level of expression of FRS in individuals with FRS is negatively associated with age.

There have been no previous reports of a negative association between age and FRS in patients with an FPE. A previous study (1), found that cognitively complex FRS did not appear before adolescence, and suggested that a certain degree of cognitive development is necessary to display such experiences. On the contrary, after adolescence or early adulthood, age becomes a protective factor for FRS. This could be related to the development of the brain (34–39). Enhancement of neuronal connections between the cortex and limbic regions may increase the emotional stability and control observed in adult development (40, 41), something not present in patients with a psychotic episode. It has also been suggested that brain development could be delayed or impaired in schizophrenia, and to a lesser extent, in affective psychosis (42–45).

Dopamine (DA) acts as an essential neurotransmitter in the maturation of the brain. Laruelle (46)

has suggested that the neurodevelopmental abnormalities presented in schizophrenia are related with the prefrontal dopaminergic systems, which give rise to a state of enhanced vulnerability to develop 'sensitization' of DA pathways during late adolescence and early adulthood. In this sense, age-dependence of FRS expression may be related to the maturation of the dopaminergic system in the brain.

Feinberg proposed that schizophrenia and other psychoses might be caused by errors in the late maturational process of the brain (47). Closely related with this hypothesis is the suggestion that a fixed brain lesion could interact with certain normal maturational events that occur much later (7, 48). Both hypotheses could be true. However, the fact that FRS are related to age in clinical and non-clinical samples strongly suggests that normal maturation is an important developmental factor in the expression of the positive psychotic experiences that are considered the core of schizophrenia.

There are some limitations to the present study. The sample consisted of in-patients and not out-patients, and although most patients with mainly positive symptoms need to be hospitalized, it remains necessary to study FRS in a community sample diagnosed with an FPE. Furthermore, all patients were treated as clinically required, so the rate of FRS may have been lower than it would have been in an untreated sample.

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