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Schizophrenia Research 61 (2003) 157–162
SCHIZOPHRENIA RESEARCH
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Age-dependence of Schneiderian psychotic symptoms in bipolar patients

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Received 22 October 2001; accepted 23 May 2002

Abstract

Psychotic symptoms frequently occur in bipolar disorder, especially in younger patients. However, whether the association with younger age also extends to psychotic symptoms that have traditionally been associated with schizophrenia, such as Schneiderian first-rank symptoms (FRSs), is unclear. This study examined FRSs in bipolar I patients and their relationship to age and gender. The sample comprised 103 consecutive inpatients who met DSM IV criteria for bipolar disorder, manic or mixed. FRSs were rated with the Scale for the Assessment of Positive Symptoms (SAPS). Interaction between FRSs and gender and FRSs and age was assessed using logistic regression. A high rate of FRSs in manic and mixed patients was found with a higher frequency in men (31%) than in women (14%; $P=0.038$). A monotonic increase in the association between FRSs and younger age was apparent (odds ratios (OR) over five levels: 1.42; 1.00–2.01). These results confirm previous findings that FRSs are not specific to schizophrenia and suggest in addition that a dimension of nuclear psychotic experiences of developmental origin extends across categorically defined psychotic disorders.

Keywords: Psychosis; Neurodevelopment, Age; Gender; First-rank symptoms; Bipolar

1. Introduction

There is a longstanding debate on the relationship between affective and nonaffective psychosis and the evidence regarding shared areas of psychopathology, outcome, treatment response and genetic risk has been discussed extensively elsewhere (Brockington et al., 1980a,b; Cloninger et al., 1985; Crow, 1981; Johnstone et al., 1988; Kendell, 1991; Kendell and Brockington, 1980; Maier et al., 1993; Murray and O'Callaghan, 1991; Taylor and Amir, 1994). It is safe to say that there is no conclusive and/or consistent evidence demonstrating complete psychopathological,

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doi:10.1016/S0920-9964(02)00320-1

prognostic, therapeutic or aetiological discontinuity between affective and nonaffective psychosis (van Os et al., 1998, 1999c). Several large-scale studies have now been conducted with the purpose of identifying the symptom dimensions of psychosis. These studies show convergence in demonstrating a four-factor (McGorry et al., 1998; van Os et al., 1999a) or possibly five-factor solution (Kitamura et al., 1995, 1998), despite having been conducted with different instruments in different countries and with samples with varying levels of chronicity. The best replicated dimensions are those of positive, manic, depressive and negative symptoms. The clinical validity of these dimensions is supported by their differential associations with outcome, treatment needs and treatment outcomes (van Os et al., 1996, 1999a,b).

In categorically defined bipolar disorder, the dimension of manic symptoms is accompanied frequently by the dimension of positive psychotic symptoms (González-Pinto et al., 1998) including those typically associated with schizophrenia, such as Schneider's first rank symptoms (FRSs; Schneider, 1959; Peralta and Cuesta, 1999). The presence of the positive symptom dimension in affective disorders is age-dependent, especially in bipolar patients (Ballenger et al., 1982; Verdoux and Bourgeois, 1993; González-Pinto et al., 1998; Carlson et al., 2000). Within the positive symptom dimension, mood incongruent psychotic symptoms are more frequent in people with an early onset of bipolar disorder (Rosen et al., 1983; Mc Glashan, 1988). However, the cause of the association between age and the positive psychotic symptom dimension in bipolar illness remains unclear, and this leads to frequent misdiagnosis during the first years of the disease (Ballenger et al., 1982; González-Pinto et al., 1998).

Among patients diagnosed with schizophrenia, FRSs are more common in the younger age groups, and it has been suggested that FRSs are associated with maturational processes during puberty, especially in boys (Galdos and van Os, 1995). Delusional ideas including FRS-type experiences are also associated with younger age in primary care patients (Verdoux et al., 1998; van Os et al., 2002), suggesting that the association is not specific to the clinical disorder of schizophrenia, and that a dimensional view may be more valid. According to this view, the age-dependent nuclear symptoms of psychosis dimensionally extend not only across the different categorically defined disorders, but also, in attenuated form, nonclinical populations. Although the association between age and psychosis in bipolar disorder has been examined before (Ballenger et al., 1982; González-Pinto et al., 1998; Carlson et al., 2000), it is not known whether this association extends to FRSs. In the current study, therefore, we examined whether FRSs are also associated with younger age in patients with a diagnosis of mania. In addition, we tested for possible gender differences.

2. Methods

2.1. Procedure

We gathered data on 103 subjects consecutively admitted between February 1997 and January 1999 to the only psychiatric ward in an area of 350 000 inhabitants. The psychiatric unit is located in a public general hospital. There are no private hospitals in the area, so the sample represents the whole manic population needing inpatient psychiatric treatment. A total of 1503 patients were hospitalized in this period. Patients were included in the study after informed consent to participate was obtained. Subjects with mental retardation, organic brain disorders or drug abuse as a primary diagnosis were excluded. All patients diagnosed with schizoaffective disorder by DSM IV criteria were excluded.

All subjects met DSM IV (American Psychiatric Association, 1994) criteria for bipolar disorder, manic or mixed. The DSM IV axis I diagnosis was made by using the Structured Clinical Interview for DSM IV (SCID-I, Spitzer et al., 1996). The day after admission, patients with prominent manic symptoms were assessed with a protocol that included SCID-I and Schneider's first-rank symptoms (FRSs) (Schneider, 1959). FRSs were rated using the Scale for the Assessment of Positive Symptoms (SAPS; Andreasen, 1984). The 11 items considered as true 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 and PH) who had reached good interrater reliability for SCID-I diagnosis (kappa = 0.88). The final diagnosis took into account the symptoms displayed by the patient during the entire duration of the hospitalization. Patients with psychotic symptoms in the absence of affective symptoms during periods of 3 days or more were excluded from the study, as were all patients without a definitive diagnosis of bipolar manic or mixed episode. This last group included a total of 59 patients who had manic symptoms with a duration shorter than that of the positive psychotic symptoms, or about whom no consensus could be reached between the assessors.

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. No patient was rated in more than one episode.

2.2. Statistical analysis

The mean age of those with and without FRS was compared. Logistic regression with presence of FRSs as the response variable and age as the exposure variable was conducted using STATA (STATA, 2001), yielding odds ratios (OR) and their 95% confidence intervals. To assess dose response in the association between age and FRSs, the age distribution was divided by its quintiles to create quintile groups. Interaction with gender was assessed by the likelihood ratio test. As we assessed the associations between FRS and calendar age in prevalent cases (i.e. people who had been ill for different periods of time), we adjusted for age at onset (quintile group variable) in order to examine to what degree any association with calendar age was dependent on age at onset.

3. Results

A total of 51 women (49.5%) and 52 males (50.5%) were included. There were 78 (75.7%) who met DSM IV criteria for bipolar disorder, manic, and 25 (24.2%) for bipolar disorder, mixed. The mean (± S.D.) age of the patients was 36.9 (± 12.4) (range, 16–74 years). Presence of one or more FRSs was documented for 23 (22.3%) patients diagnosed with manic episodes. Bipolar I diagnosed patients with FRSs had a mean age of 32.0 years, while the mean age of patients without FRSs was 38.3 years ($t = 2.16$, $df = 101$, $P = 0.033$). Males more frequently presented with FRSs (31%) than females (14%; $\chi^2 = 4.312$; $df = 1$; $P = 0.038$). There was a monotonic increase in the risk of presenting with FRSs with lower age (Table 1; OR linear trend 1.42, 95% CI: 1.00–2.01; $P = 0.050$). This association was only slightly reduced after adjustment for gender (adjusted OR = 1.36, 95% CI: 0.95–1.93), and there was no strong evidence that the effect of age on FRSs was modified by gender (LRS = 3.6, $df = 1$, $P = 0.16$). There was no evidence for an association between FRSs and age at onset (OR over quintile groups: 1.15, 95% CI: 0.83–1.59), and the association between calendar age and FRS increased rather than decreased after adjustment for age at onset (OR = 1.44, 95% CI: 0.96–2.17).

Table 1
Association between age and first rank symptoms

	Quintile group	% with FRS	% without FRS	OR (95% CI)
Highest age	5	10.53	89.47	1*
	4	15.79	84.21	1.59 (0.23, 10.82)
	3	21.74	78.26	2.36 (0.40, 13.84)
	2	27.78	72.22	3.27 (0.55, 19.61)
Lowest age	L	33.33	66.67	4.25 (0.78, 23.1)
OR linear trend#		1.42 (1.00, 2.01)		

* Reference category.
\# Overall increase in risk with one unit increase in age quintile group.

4. Discussion

Our study confirms previous reports of a high rate of FRSs in manic and mixed states. As many as 22.3% of the patients with a DSM IV diagnosis of bipolar disorder had these types of symptoms. The rate of FRSs is reported to vary from 15.3% to 41%, depending on the sample and the diagnostic criteria (Mellor, 1970; Brockington et al., 1978; Abrams and Taylor, 1981; Ballenger et al., 1982; Tohen et al., 1992; Peralta and Cuesta, 1999).

Although used universally to distinguish between schizophrenia and bipolar disorder, it is clear that FRSs are not always present in schizophrenia (Andreasen and Akiskal, 1983; Radhakrishnan et al., 1983; Marneros, 1984) and, more importantly, that they are not

restricted to schizophrenia (Crichton, 1996). Thus, FRSs vary dimensionally, i.e. they are more frequent in but not specific to schizophrenia, whereas FRSs are not rare in patients diagnosed with manic episodes (Peralta and Cuesta, 1999). Recent genetic studies of FRSs support this dimensional view (Loftus et al., 2000; Cardno et al., 2001, 2002).

In accordance with the dimensional view, the results suggest a negative association between age and FRSs in bipolar patients, similar to that reported in schizophrenia and nonclinical samples. There are no previous reports of a negative association between age and FRSs in patients with bipolar disorder, although the link between age and psychosis, in general, is well established in bipolar disorder (Rosen et al., 1983; González-Pinto et al., 1998; Carlson et al., 2000). In a previous study, Galdos and van Os (1995) found that cognitively complex FRSs did not appear before adolescence, and suggested that a certain degree of cognitive development is necessary to display such experiences. Traditionally, FRSs have been considered as the essence of the psychotic condition (Jaspers, 1963), with the term psychosis being considered as equivalent to schizophrenia. However, as proposed before, FRSs should be considered symptoms of psychosis rather than symptoms of schizophrenia (Peralta and Cuesta, 1999).

Interestingly, one factor that influences the clinical manifestations of any cerebral lesion is the age of the brain. Our finding that the association with calendar age was independent of age at onset of bipolar disorder supports this observation. In fact, as suggested before (Weinberger, 1995), the existence of a critical period of vulnerability for the expression of psychosis suggests that the neural systems mediating this behaviour reach a functional peak during the aforementioned critical period, regardless of the underlying brain disorder. In fact, the etiology of schizophrenia has focused on postpubertal brain changes that may be involved in triggering the expression of vulnerability for abnormal brain development (Walker and Bollini, 2002). Moreover, it has been proposed that as the CNS becomes older, there are a greater number of final adult synapses formed and more brain protective factors in place against the development of psychotic symptoms (De Lisi, 1997).

The differences related to gender are intriguing, as we found a higher presence of FRSs among men. Tanenberg-Karant et al. (1995) also found that males had more FRSs than females in a sample of patients with a diagnosis of schizophrenia in their first hospitalization. Differential maturational rate is a possible explanation of this lower prevalence of FRSs in these women (Galdos and van Os, 1995). Brain development during childhood and adolescence is characterized by progressive myelinisation (De Bellis et al., 2001). The myelinisation process is more rapid in females until their 40s, and after this age, there are no differences between the sexes (Benes et al., 1994). The pace of cerebral development in early life is slower in males than females (Castle and Murray, 1991). Thus, the male brain may be susceptible to environmental adversity for a longer period than the more rapidly maturing female one (Seeman, 1989). This could be related to the gender-related differences found in FRSs.

There is at least one other hypothesis that could explain a higher prevalence of FRSs in younger patients with a diagnosis of bipolar disorder. The proposal hypothesis is related to the activity of dopamine and dopamine receptors across the age. In fact, PET studies demonstrated that the number of D-2 dopamine receptors could be greater in patients with psychotic bipolar disorder and with schizophrenia than in patients diagnosed with bipolar disorder without psychotic symptoms or that in the control group. Therefore, the density of D-2 dopamine receptors are thought to be associated with psychosis and not with diagnosis (Pearlson et al., 1995). Also, it has been shown that the density of D-2 dopamine receptors declines with age in several brain areas and the decline in these receptors in males may be different from that in females (Wong et al., 1984). The dopamine hypothesis of schizophrenia, which postulates a dopaminergic dysfunction in this disorder, has now received more direct support by research using imaging techniques (Carlsson et al., 2000). In fact, an aberration of the turnover of dopamine in the brain has been demonstrated in drug-naive schizophrenic patients, compared to age-matched controls (Hietala et al., 1994). Moreover, SPECT and PET studies have shown that an amphetamine challenge enhances this release significantly more in drug-naive schizophrenic patients than in age-matched controls, and this elevation correlates with the induction of positive psychotic symptoms (Breier et al., 1997). It is noteworthy that mania can be induced by stimulant drugs like amphet-

amine that increase the amount of available dopamine (Seeman, 1987).

The result suggests that, as far as the dimension of FRSs is concerned, schizophrenia and bipolar disorder differ only quantitatively, the same age-dependent processes determining variation in nuclear experiences of psychosis.

There are some limitations to this study. The sample included patients diagnosed with mania, but not patients with bipolar depression which can also be accompanied by FRSs. Moreover, it consisted of inpatients and not outpatients, and although the majority of patients with a diagnosis of a manic episode need to be hospitalized, it would be interesting to study FRSs in a community sample diagnosed with mania. Also, all patients were treated as clinically required, so the rate of FRSs is probably underestimated. Nevertheless, the association between FRSs, younger age and male gender in bipolar patients suggests that a psychotic dimension of the schizophrenia type could be related to age-dependent developmental factors across the spectrum of psychotic disorders.

Acknowledgements

This research was supported by a grant from the Basque Government (2001021004) and by a grant from F.I.S (Fondo de Investigaciones Sanitarias. Ministerio de Sanidad y Consumo; 97/757/2000).

References

Abrams, R., Taylor, M.A., 1981. Importance of schizophrenic symptoms in the diagnosis of mania. Am. J. Psychiatry 138 (5), 658–661.

American Psychiatric Association, 1994. Diagnostic and Statistical Manual of Mental Disorders, 4th edn. APA, Washington, DC (DSM IV).

Andreasen, N.C., 1984. The Scale for the Assessment of Positive Symptoms (SAPS). University of Iowa, Iowa.

Andreasen, N.C., Akiskal, H.S., 1983. The specifity of Bleulerian and Schneiderian symptoms: a critical re-evaluation. Psychiatr. Clin. North Am. 6, 41–54.

Ballenger, J.C., Reus, V.I., Post, R.M., 1982. The "atypical" clinical picture of adolescent mania. Am. J. Psychiatry 139, 602–605.

Benes, F.M., Turtle, M., Khan, Y., Farol, P., 1994. Myelinisation of a key relay zone in the hippocampal formation occurs in the human brain during childhood, adolescence, and adulthood. Arch. Gen. Psychiatry 51, 477–484.

Breier, A., Su, T.P., Saunders, R., Carson, R.E., Kolachana, B.S., De Bartolomeis, A., et al., 1997. Schizophrenia is associated with elevated amphetamine-induced synaptic dopamine concentrations: evidence from a novel positron emission tomography method. Proc. Natl. Acad. Sci. U. S. A. 94, 2569–2574.

Brockington, I.F., Kendell, R.E., Leff, J.P., 1978. Definitions of schizophrenia: concordance and prediction of outcome. Psychol. Med. 8 (3), 387–398.

Brockington, I.F., Kendell, R.E., Wainwright, S., 1980a. Depressed patients with schizophrenic or paranoid symptoms. Psychol. Med. 10 (4), 665–675.

Brockington, I.F., Wainwright, S., Kendell, R.E., 1980b. Manic patients with schizophrenic or paranoid symptoms. Psychol. Med. 10 (1), 73–83.

Cardno, A.G., Sham, P.C., Murray, R.M., Mc Guffin, P., 2001. Twin study of symptoms dimensions in psychoses. Br. J. Psychiatry 179, 39–45.

Cardno, A.G., Sham, P.C., Farmer, A.E., Murray, R.M., Mc Guffin, P., 2002. Heritability of Schneider's first-rank symptoms. Br. J. Psychiatry 180, 35–38.

Carlson, G.A., Bromet, E.J., Sievers, S., 2000. Phenomenology and outcome of subjects with early and adult onset psychotic mania. Am. J. Psychiatry 157, 213–219.

Carlsson, A., Water, N., Waters, S., Carlsson, M., 2000. Network interaction in schizophrenia-therapeutic implications. Brain Res. Rev. 31, 342–349.

Castle, D.J., Murray, R.M., 1991. The neurodevelopmental basis of sex differences in schizophrenia. Psychol. Med. 21, 565–575.

Cloninger, C.R., Martin, R.L., Guze, S.B., Clayton, P.J., 1985. Diagnosis and prognosis in schizophrenia. Arch. Gen. Psychiatry 42 (1), 15–25.

Crichton, P., 1996. First-rank symptoms or rank-and-file symptoms? Br. J. Psychiatry 169, 537–540. discussion 541-550.

Crow, T.J., 1981. The failure of the Kraepelinian binary concept and the search for the psychosis gene. In: Kerr, A., McClelland, H. (Eds.), Concepts of Mental Disorder: A Continuing Debate. Gaskell, London, pp. 31–47.

De Bellis, M.D., Keshavan, M.S., Beers, S.R., Hall, J., Frustaci, K., Masalehdan, A., Noll, J., Boring, A.M., 2001. Sex differences in brain maturation during childhood and adolescence. Cereb. Cortex 11 (6), 552–557.

De Lisi, L.E., 1997. Is schizophrenia a lifetime disorder of brain plasticity, growth and aging? Schizophr. Res. 23, 119–129.

Galdos, P., van Os, J., 1995. Gender, psychopathology, and development: from puberty to early adulthood. Schizophr. Res. 14 (2), 105–112.

González-Pinto, A., Gutiérrez, M., Mosquera, F., Ballesteros, J., Lopez, P., Ezcurra, J., Figuerido, J.L., De León, J., 1998. First episode in bipolar disorder: misdiagnosis and psychotic symptoms. J. Affect Disord. 50 (1), 41–44.

Hietala, J., Syvalahti, E., Vuorio, K., Nagren, K., Lehikoinen, P., Ruotsalalainen, U., et al., 1994. Striatal D2-dopamine receptor characteristics in neuroleptic-naive schizophrenic patients studied with positron emission tomography. Arch. Gen. Psychiatry 51, 116–123.

Jaspers, K., 1963. General Psychopathology (translated by J. Hoening and M.W. Hamilton). University of Chicago, Chicago.

Johnstone, E.C., Crow, T.J., Frith, C.D., Owens, D.G., 1988. The Northwick Park "functional" psychosis study: diagnosis and treatment response. Lancet 2 (8603), 119–125.

Kendell, R.E., 1991. The major functional psychoses: are they independent entities or part of a continuum? In: Kerr, A., McClelland, H. (Eds.), Concepts of Mental Disorder: A Continuing Debate. Gaskell, London, pp. 1–16.

Kendell, R.E., Brockington, I.F., 1980. The identification of disease entities and the relationship between schizophrenic and affective psychoses. Br. J. Psychiatry 137, 324–331.

Kitamura, T., Okazaki, Y., Fujinawa, A., Yoshino, M., Kasahara, Y., 1995. Symptoms of psychoses. A factor-analytic study. Br. J. Psychiatry 166 (2), 236–240.

Kitamura, T., Okazaki, Y., Fujinawa, A., Takayanagi, I., Kasahara, Y., 1998. Dimensions of schizophrenic positive symptoms: an exploratory factor analysis investigation. Eur. Arch. Psychiatry Clin. Neurosci. 248 (3), 130–135.

Loftus, J., De Lisi, L.E., Crow, T.J., 2000. Factor structure and familiarity of first-rank symptoms in sibling pairs with schizophrenia and schizoaffective disorder. Br. J. Psychiatry 177, 15–19.

Maier, W., Lichtermann, D., Minges, J., Hallmayer, J., Heun, R., Benkert, O., Levinson, D.F., 1993. Continuity and discontinuity of affective disorders and schizophrenia. Results of a controlled family study. Arch. Gen. Psychiatry 50 (11), 871–883.

Marneros, A., 1984. Frequency of occurrence of Schneider's first rank symptoms in schizophrenia. Eur. Arch. Psychiatr. Neurol. Sci. 234 (1), 78–82.

Mc Glashan, T.H., 1988. Adolescent versus adult onset of mania. Am. J. Psychiatry 145, 221–223.

McGorry, P.D., Bell, R.C., Dudgeon, P.L., Jackson, H.J., 1998. The dimensional structure of first episode psychosis: an exploratory factor analysis. Psychol. Med. 28 (4), 935–947.

Mellor, C.S., 1970. First rank symptoms of schizophrenia: I. The frequency in schizophrenics on admission to hospital. Br. J. Psychiatry 117 (536), 15–23.

Murray, R.M., O'Callaghan, E., 1991. The congenital and adult-onset psychoses: Kraepelin lost, Kraeplin found. In: Kerr, A., McClelland, H. (Eds.), Concepts of Mental Disorder: A Continuing Debate. Gaskell, London, pp. 48–65.

Pearlson, G.D., Wong, D.F., Tune, L.E., Ross, C.A., Chase, G.A., Links, J.M., Dannals, R.F., Wilson, A.A., Ravert, H.T., Wagner, H.N., De Paulo, J.R., 1995. In Vivo D2 dopamine receptor density in psychotic and non-psychotic patients with bipolar disorder. Arch. Gen. Psychiatry 52 (6), 471–477.

Peralta, V., Cuesta, M.J., 1999. Diagnostic significance of Schneider's first-rank symptoms in schizophrenia. Br. J. Psychiatry 174, 243–248.

Radhakrishnan, J., Kuruvilla, M., Richard, J., Verghese, A., 1983. Schneider's first rank symptoms: prevalence, diagnostic use and prognostic implications. Br. J. Psychiatry 142, 557–559.

Rosen, L.N., Rosenthal, N.E., Van Dusen, P.H., Dunner, D.L., Fieve, R.R., 1983. Age at onset and number of psychotic symptoms in bipolar I and schizoaffective disorder. Am. J. Psychiatry 140, 1523–1524.

Schneider, K., 1959. Clinical Psychopathology (traslated by M.W. Hamilton). Grune and Straton, New York.

Seeman, P., 1987. Dopamine receptors in the dopamine hypothesis of schizophrenia. Synapse 1, 133–152.

Seeman, V.P., 1989. Prenatal gonadal hormones and schizophrenia in men and women. Psychiatr. J. Univ. Ott. 14, 473–475.

Spitzer, R.L., Williams, J.B.W., Gibbon, M., First, M.B., 1996. SCID-I: Version 2.0 for DSM IV. Lilly Research Laboratories, Indiana.

Tanenberg-Karant, M., Fenning, S., Ram, R., Krishna, J., Jandorf, L., Bromet, E.J., 1995. Bizarre delusions and first rank symptoms in a first-admission sample: a preliminary analysis of prevalence and correlates. Compr. Psychiatry 36 (6), 428–434.

Taylor, M.A., Amir, N., 1994. Are schizophrenia and affective disorder related?: the problem of schizoaffective disorder and the discrimination of the psychoses by signs and symptoms. Compr. Psychiatry 35 (6), 420–429.

Tohen, M., Tsuang, M.T., Goodwin, B.S., 1992. Prediction of outcome in mania by mood-congruent or mood-incongruent psychotic features. Am. J. Psychiatry 149, 1580–1584.

van Os, J., Fahy, T.A., Jones, P., Harvey, I., Sham, P., Lewis, S., Bebbington, P., Toone, B., Williams, M., Murray, R., 1996. Psychopathological syndromes in the functional psychoses: associations with course and outcome. Psychol. Med. 26 (1), 161–176.

van Os, J., Jones, P., Sham, P., Bebbington, P., Murray, R.M., 1998. Risk factors for onset and persistence of psychosis. Soc. Psychiatry Psychiatr. Epidemiol. 33 (12), 596–605.

van Os, J., Gilvarry, C., Bale, R., Van Horn, E., Tattan, T., White, I., Murray, R., 1999a. A comparison of the utility of dimensional and categorical representations of psychosis. UK700 Group [In Process Citation]. Psychol. Med. 29 (3), 595–606.

van Os, J., Gilvarry, C., Bale, R., Van Horn, E., Tattan, T., White, I., Murray, R., 1999b. To what extent does symptomatic improvement result in better outcome in psychotic illness? UK700 Group. Psychol. Med. 29 (5), 1183–1195.

van Os, J., Verdoux, H., Bijl, R., Ravelli, A., 1999c. Psychosis as a continuum of variation in dimensions of psychopathology. In: Häfner, H., Gattaz, W.F. (Eds.), Search for the Causes of Schizophrenia. Springer, Berlin, pp. 59–80.

van Os, J., Hanssen, M., Bijl, R.V., Ravelli, A., 2002. Strauss (1969) revisited: a psychosis continuum in the general population? Schizophr. Res. 45 (1–2), 11–20.

Verdoux, H., Bourgeois, M., 1993. A comparison of manic patients subgroups. J. Affect Disord. 27, 267–272.

Verdoux, H., Maurice-Tison, S., van Os, J., Salamon, R., Bourgeois, M.L., 1998. A survey of delusional ideation in primary-care patients. Psychol. Med. 28, 127–134.

Walker, E., Bollini, A.M., 2002. Pubertal neurodevelopment and the emergence of psychotic symptoms. Schizophr. Res. 54, 17–23.

Weinberger, D.R., 1995. From neuropathology to neurodevelopment. Lancet 346, 552–557.

Wong, D.F., Wagner, H.N., Dannals, R.F., Links, J.M., Frost, J.J., Ravert, H.T., Wilson, A.A., Rosenbaum, A.E., Folstein, M.F., Petronis, J.D., Douglas, K.H., Toung, J.K.T., Kuhar, M.J., 1984. Effects of age on dopamine and serotonin receptors mesured by positron tomography in the living human brain. Science 226, 1393–1396.