The Expanding Psychosis Phenotype

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ABSTRACT

The psychosis phenotype is traditionally thought of as a dichotomous entity with symptoms that can be clearly distinguished from the normal state. An alternative, dimensional approach assumes that psychotic symptoms are continuous with normal experiences and are not necessarily associated with disability. Evidence for a continuum of psychosis comes from studies showing that the core symptoms of psychosis, delusions and hallucinations, are much more prevalent in the general population than their clinical counterparts. These milder forms of expression of psychosis show similar patterns of associations with demographic and environmental risk factors as the clinical disorder, providing further support for the notion of continuity. Although the majority of individuals experiencing these lesser psychotic “symptoms” are not in need of care, they may nevertheless have an increased risk of developing a clinical disorder. Transitions over the psychosis continuum may in part be driven by the cognitive and emotional response to the psychotic or psychosis-like experiences.

Key words: Psychosis; General Population; Risk Factors.

RESUMEN

El expandible fenotipo de la psicosis. El fenotipo de la psicosis es tradicionalmente considerado como una entidad dicotómica con síntomas que pueden ser claramente distinguidos del estado normal. Una aproximación alternativa dimensional asume que los síntomas psicóticos están en continuidad con la experiencia normal y no se relacionan necesariamente con una alteración. Evidencias del continuo de la psicosis provienen de los estudios que muestran que la sintomatología fundamental de la psicosis, delirios y alucinaciones, es más prevalente en la población general que en la clínica. Estas formas atenuadas de expresión de la psicosis muestra un patrón similar, en factores de riesgo demográficos y ambientales, que los trastornos clínicos, proveyendo un mayor soporte a la noción de continuidad. Aunque la mayoría de las personas experimentan esos “síntomas” psicóticos menores sin necesidad de cuidados pueden, sin embargo, tener un mayor riesgo de desarrollar un trastorno clínico. Transiciones sobre el continuo psicótico pueden en parte ser manejadas por la respuesta cognitiva y emocional de la experiencia psicótica o con tendencia a la psicosis.

Palabras clave: psicosis, población general, factores de riesgo.

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The hypothesis that psychosis exists in nature as a distribution of symptoms is not so bold as it may seem (Hafner, 1989). For example, in the case of depression, both genetic and community studies suggest that the phenotype is more likely to exist as a continuous distribution of symptoms rather than a true disease dichotomy (Anderson, Huppert, & Rose, 1993; Henderson, Korten, & Medway, 2001; Kendler & Gardner, 1998). Given the substantial degree of overlap in terms of psychopathology, outcome, risk factors and treatment between depression and psychosis (Van Os, Jones, Sham, Bebbington, & Murray, 1998), it is unlikely that psychosis, contrary to depression, would have a completely non-continuous, dichotomous distribution. Although possibly more skewed because of their lower prevalence, a degree of continuity in the distribution of symptoms would be expected.

**Are there findings supporting a psychosis continuum?**

Many studies have shown that delusional ideation is prevalent in the general population (Eaton, Romanoski, Anthony, & Nestadt, 1991; Peters, Joseph, & Garety, 1999; Verdoux et al., 1998). Similarly, hallucinations occur in up to around 5%-10% of the general population (Johns, Nazroo, Bebbington, & Kuipers, 2002; Romme, Honig, Noorthoorn, & Escher, 1992; Tien, 1991). In the National Comorbidity Study, 28.4% of all individuals from the general population reported one or more psychosis-like experience (Kendler, Gallagher, Abelson, & Kessler, 1996). Olsson and colleagues reported that 20.9% of the clients in a large, urban, general medicine practice reported one or more psychotic symptoms (Olsson et al., 2002).

Data on psychotic symptoms collected as part of the Dutch NEMESIS study (Bijl, van Zessen, Ravelli, de Rijk, & Langendooen, 1998) also suggest a psychosis continuum in the general population (Van Os, Hanssen, Bijl, & Ravelli, 2000; Van Os, Hanssen, Bijl, & Vollebergh, 2001). In this study, a representative general population sample of 7076 men and women was interviewed using the Composite International Diagnostic Interview (CIDI). For the 17 CIDI core positive psychosis items, the authors studied the four possible ratings on each of these items: (i) a rating of “true”, psychiatrist verified, presence of hallucinations and/or delusions (ii) a rating indicating that the symptom was present but the respondent did not appear to be bothered by it, (iii) a rating indicating that the symptom was the result of drugs or physical disorder, (iv) a rating indicating that the symptom appeared to be present but the interviewer was uncertain because there could have been a plausible explanation. Although all symptom ratings were strongly associated with the presence of DSM-III-R psychotic disorder in terms of relative risk, the authors found that of the 1237 individuals with any type of positive psychosis rating (17.5%), only 26 (2.1%) had a DSM-III-R diagnosis of non-affective psychosis. In addition, all four positive symptom ratings were elevated in both cases and non-cases of any DSM-III-R psychiatric disorder, although more so in the former (odds ratio (OR) 3.2, 95% CI 2.8, 3.7). Although psychotic symptoms in this sample were much more common than psychotic disorders, the distribution of individual total psychotic symptom scores in the sample was very skewed. These findings...
therefore suggest that both symptoms and underlying psychological mechanisms of psychosis occur as part of a continuous, albeit very skewed, distribution that shows only very partial overlap with clinical disorder.

ASSOCIATIONS WITH DEMOGRAPHIC FACTORS

One way to further test the hypothesis of a psychosis continuum would be to investigate to what degree non-clinical, or attenuated, psychotic phenomena show a similar pattern of correlation with risk factors as their equivalents do in clinical psychotic disorders such as schizophrenia. Continuity between the lesser psychotic states and clinical disorder would imply that risk factors that have been associated with the clinical disorder are also associated with the community level of psychotic symptoms.

Samples of patients who receive a diagnosis of schizophrenia for the first time (incident cases) show, as a group, a characteristic pattern of associations with a range of demographic variables (Galdos, van Os, & Murray, 1993; Hafner et al., 1994). Thus, incident patients are more likely to be young, single and unemployed. The characteristic age-related variation in the incidence of schizophrenia is mirrored in a similar age-related expression of variably defined schizotypy (Claridge et al., 1999), delusional ideation measured with the PDI (Peters et al., 1999), and delusions and hallucinations in the absence of a clinical psychotic disorder (Van Os et al., 2000). In addition, the expression of schizophrenia has been reported to differ between the sexes (Crow, 1999). A number of studies have found men to display more negative symptoms than women (Roy, Maziade, Labbe, & Merette, 2001; Schultz et al., 1997; Shtasel, Gur, Gallacher, Heimberg, & Gur, 1992), while women may have a higher prevalence of positive symptoms (Sharma, Dowd, & Janicak, 1999). These sex differences in psychotic expression were also reported in the wider range of psychotic experiences in the general population (Maric, Krabbendam, Vollebergh, de Graaf, & van Os, 2003).

A key epidemiological finding is that schizophrenia appears in boys at an earlier age than girls, causing the prevalence of the disorder to be higher in boys than in girls during adolescence (Konnecke, Hafner, Maurer, Loffler, & an der Heiden, 2000). We have recently investigated whether similar age-related sex differences exist in the expression of associated, sub-clinical psychosis-like experiences (see Figure 1) (Spauwen, Krabbendam, Lieb, Wittchen, & van Os, 2003). If the non-clinical psychotic experiences increase differentially with age in boys and girls in the same fashion as the clinical disorder schizophrenia (Fig. 1B), a likely explanation would be that a normal, sex-related maturational event after puberty causes expression of psychosis along a continuum of severity. However, if the sex differences in age of onset of schizophrenia are not reflected in similar sex differences in the age of onset of non-clinical psychotic experiences (Fig 1A), it is unlikely that these normal maturational events themselves play a causal role in the expression. The Early Developmental Stages of Psychopathology (EDSP) study (Lieb, Isensee, von Sydow, & Wittchen, 2000) is a longitudinal study of 2548 adolescents and young adults aged 17-28, who were assessed by trained psychologists with the core psychosis sections on delusions and hallucinations of the Munich-Composite International Diagnostic Interview. In this sample, the cumulative incidence of positive
The risk of sub-clinical psychotic experiences was significantly higher for males in the younger half of the cohort (17-21yrs) (OR=0.70, 95% CI 0.52, 0.95, but similar in the older half (22-28yrs) (OR=1.18, 95% CI 0.89, 1.58). Thus, the non-clinical psychotic experiences increase differentially with age in boys and girls in the same fashion as the clinical disorder schizophrenia, suggesting that normal maturational changes in adolescence with differential age of onset in boys and girls cause the expression of psychosis, the extreme of which is schizophrenia.

ASSOCIATIONS WITH SOCIAL AND ENVIRONMENTAL RISK FACTORS

Similar to the argument for the demographic variables, the social and environmental risk factors for psychotic illness should also contribute to a larger pool of preclinical psychotic experiences, which exist in the general population. If this were true, populations who report higher levels of disorder due to more exposure to certain social and environmental risk factors should show a similar increase in the level of psychosis-like symptoms.
The effect of the urban environment

In the Dutch NEMESIS Study, we examined to what degree the increase in risk for psychotic disorder, associated with urban life is reflected in similar increases in the mean number of psychotic and psychosis-like symptoms (Van Os et al., 2001). Lifetime level of psychotic and psychosis-like symptoms independently increased with level of urbanicity in the same manner as did DSM-III-R-psychotic disorder (summary OR over five levels of urbanicity for DSM-III-R psychotic disorder 1.44, 95% CI 1.24, 1.68; for clinically relevant psychotic symptoms OR=1.28, 95% CI 1.17, 1.40; for any psychotic or psychosis-like experience OR=1.19, 95% CI 1.14, 1.25). At all levels of urbanicity, psychotic and psychosis-like symptoms were strongly associated with psychotic disorder. These findings suggest that the increased prevalence of psychotic disorder should be interpreted in light of increased levels of “psychosis proneness” in urban populations. Since the association between symptoms and disorder did not differ as a function of urbanicity, the implication is, first, that susceptibility to psychotic disorder varies between populations and can be demonstrated by comparing rates of psychosis-like experiences, and second, that the psychosis-like experiences are on a quantitative continuum with the disorder.

The effect of childhood trauma

An association between trauma and psychosis has been suggested by studies showing a high incidence of trauma in the lifetimes of patients with psychosis (Read, Perry, Moskowitz, & Connolly, 2001). A history of trauma has particularly been related to positive symptoms of psychosis (Ellason & Ross, 1997; Heins, Gray, & Tennant, 1990). We analysed data from the NEMESIS follow-up study in order to investigate the hypothesis that individuals from the general population who report childhood abuse are at increased risk of developing psychotic disorder as well as psychotic symptoms (Janssen et al., 2004). The risk set was restricted to those individuals with no previous lifetime presence of psychotic or psychosis-like symptoms in order to exclude the possibility that current psychotic beliefs would bias the way the abuse questionnaire was answered, and to be sure that the experience of abuse preceded the experience of psychotic symptoms. At baseline, subjects were asked using a semi-structured interview whether they had experienced any kind of emotional, physical, psychological or sexual abuse before age 16 years. The psychosis outcome was specified at three levels, two involving severity of positive symptoms of psychosis and one using additional clinical judgement of need for care: i) any rating >1 on either BPRS item “unusual thought content” or “hallucinations” (BPRS psychotic-like experiences); ii) any rating >3 on either “unusual thought content” or “hallucinations” (BPRS pathology-level psychosis); iii) need for care in relation to symptoms of psychosis was assessed by clinicians according to the Camberwell Assessment of Need (Slade, Phelan, Thornicroft, & Parkman, 1996); those who met criteria for BPRS pathology-level psychosis and clinician consensus on need for care, were defined as a case for treatment, hereafter referred to as “need for care status”. The rates of BPRS psychotic-like experiences were 0.7% (n= 27) in those non-
exposed and 2.6% (n = 11) in those exposed to childhood abuse. For BPRS pathology-level psychosis, the rates were 0.1% (n = 4) in those non-exposed and 1.4% (n = 6) in those who were exposed to childhood abuse. For those with need for care status, the rates were 0.1% (n = 3) for the non-exposed and 0.9% (n = 4) for those exposed to childhood abuse. Childhood abuse was significantly associated with BPRS psychotic-like experiences (exact p = 0.001; OR = 3.6, 95% CI 1.8, 7.2), with BPRS pathology-level psychosis (exact p = 0.000; OR = 13.0, 95% CI 3.7, 46.3) and with need for care status (exact p = 0.003; OR = 11.5, 95% CI 2.6, 51.6). The results suggest that reported childhood abuse predicts psychotic disorder, but also psychotic and psychosis-like symptoms at lower levels of the continuum. In sum, the similarity of the pattern of associations between psychotic disorder and mental states that occupy a lower position on the distribution is again suggestive of a continuum of psychotic experiences.

**What factors drive variation along the continuum?**

The majority of the individuals experiencing lesser forms of psychosis are not in need of care. However, longitudinal studies indicate that they may nevertheless have an increased risk of developing a clinical disorder (Chapman, Chapman, Kwapisl, Eckblad, & Zinser, 1994; Kwapisl, Miller, Zinser, Chapman, & Chapman, 1997; Poulton et al., 2000; Yung et al., 1998). It is crucial to understand the psychological mechanisms that mediate transition from having one or two psychotic symptoms to becoming a patient with a psychotic disorder. The study of these mechanisms would be particularly important in view of the interest in preventing individuals from making transitions from non-clinical to clinical psychotic states. In addition, it would further our understanding of the continuities and discontinuities between the expression of psychosis at the level of the general population and clinical psychotic disorder (Johns & van Os, 2001).

Current hypotheses on psychological mechanisms of psychosis have emphasised that response to abnormal experiences is cognitively mediated by beliefs or appraisals (Bentall, Kinderman, & Kaney, 1994; Garety, Kuipers, Fowler, Freeman, & Bebbington, 2001; Morrison, 2001). Thus, the mere experience of voices itself may not lead to full-blown psychotic symptoms, but attributing the voice to an external malevolent source and giving it personal significance does. It is this interpretation that causes the associated distress and disability (Chadwick & Birchwood, 1994; Morrison & Baker, 2000 and thereby increases the risk of developing need for treatment. In order to investigate these psychological mechanisms data from the NEMESIS follow-up study were analysed. We hypothesised that a delusional interpretation and/or a depressed response to hallucinatory experiences would predict the later onset of clinical psychotic disorder (Krabbendam, Myin-Germeys, Hanssen, Bijl et al., 2004; Krabbendam, Myin-Germeys, Hanssen, de Graaf et al., 2004).

The analyses were based on the three measurement points, baseline, T1 (assessing the period between baseline and one year later) and T2 (assessing the period between T1 and 2 years later). The risk set was limited to the individuals who had received no lifetime diagnosis of any DSM-III-R affective or non-affective psychotic disorder at the baseline and T1 measurement and consisted of 4672 individuals. The number of individuals
with BPRS psychotic-like experiences at T2 was 85 (1.8%), the number of individuals with BPRS pathology-level psychosis was 39 (0.8%) and 24 individuals (0.5%) had a need for care in relation to psychotic symptoms. At baseline interview, 287 individuals (6.1%) reported hallucinatory experiences. Given the presence of hallucinatory experiences at baseline, the increase in risk on the additive scale of having the psychosis outcome at T2 was much higher in the group with delusional ideation at T1 (n= 30) than in those without delusional ideation at T1 (n= 257) (see Table 1). The difference in risks between the groups with and without delusional ideation at T1 was statistically significant for each of the three psychosis outcomes (see Table 1). After adjustment for the effect of delusional ideation at baseline, the interactions between delusional ideation at T1 and hallucinatory experiences at baseline remained significant for all three psychosis outcomes, indicating that the risk increasing effect of delusional ideation at T1 reflected the

| Table 1. Interactions between baseline hallucinatory experiences and delusion at T1 on the additive scale (risk differences). |
|---------------------------------------------------------------|---------------------------------------------------------------|---------------------------------------------------------------|
| BPRS psychotic-like experiences ((n=85)) | BPRS pathology-level psychosis ((n=39)) | Needs-based diagnosis ((n=24)) |
| Increase in risk associated with baseline hallucinatory experiences | | |
| | No delusion formation at T1 | Delusion formation at T1 |
| (n=257) | 9.98% (5.93, 13.44) | 29.22% (10.68, 47.75) |
| | 6.04% (3.08, 8.99) | 28.43% (11.05, 45.81) |
| | 3.04% (0.92, 5.17) | 21.76% (5.39, 38.13) |
| Risk difference | 19.53% (0.61, 38.44) | 22.39% (4.76, 40.02) |
| Additive Interaction<sup>a</sup> | X<sup>2</sup> = 4.10, df=1, p=0.043 | X<sup>2</sup> = 6.20, df=1, p=0.013 |
| | X<sup>2</sup> = 4.94, df=1, p=0.026 |
| Increase in risk associated with baseline hallucinatory experiences | | |
| | No depressed mood at T1 | Depressed mood at T1 (n=24) |
| (n=263) | 11.12% (7.15, 15.08) | 28.13% (9.88, 46.37) |
| | 6.94% (3.80, 10.07) | 28.65% (10.43, 46.86) |
| | 3.99% (1.57, 6.41) | 20.83% (4.59, 37.08) |
| Risk difference | 17.01% (-1.66, 35.67) | 21.71% (3.22, 40.19) |
| Additive Interaction<sup>b</sup> | X<sup>2</sup> = 3.19, df=1, p=0.074 | X<sup>2</sup> = 5.30, df=1, p=0.021 |
| | X<sup>2</sup> = 4.04, df=1, p=0.046 |

<sup>a</sup> Risk of having the psychosis outcome at T2.

<sup>b</sup> Tests whether increase in risk in group with delusion formation or depressed at T1 is significantly greater than increase in risk in group without delusion formation or depressed mood at T1.
emergence of delusional ideation between baseline and T1. Similarly, given the presence of hallucinatory experiences at baseline, the increase in risk on the additive scale of having the psychosis outcome at T2 was higher in the group with depressed mood at T1 (n= 24) than in those without depressed mood at T1 (n= 263) (see Table 1) and this effect remained after adjustment for baseline presence of depressed mood.

Thus, in the general population, the risk of developing clinical psychotic disorder in individuals with baseline self-reported hallucinatory experiences was much higher in those who developed delusional ideation than in those who did not. Similarly, the development of depressed mood in those with baseline self-reported hallucinatory experiences increased the risk for onset of clinical disorder. These findings suggest that delusional ideation and depressed mood may arise as a secondary response to hallucinatory experiences in the development of clinical psychotic disorder. Transitions over the psychosis continuum may, at least in part, be driven by the emotional and cognitive responses to anomalous perceptual intrusions.

**Conclusion**

Many studies suggest that psychosis can be seen as a distribution of experiences that are not necessarily associated with disability, analogous to recent findings in affective disorder. Established demographic and social and environmental risk factors for schizophrenia such as age, urbanicity, and childhood trauma affect the occurrence of non-clinical psychosis-like experiences in addition to occurrence of full-blown schizophrenic disorders. The view that there may be a psychosis continuum is compatible with increasing evidence that a range of psychological and psychosocial factors drive variation in the continuum.

**References**


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