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SPECIAL ISSUE

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Affective processes in the onset and persistence of psychosis

Abstract *Objectives* Cognitive models suggest that beliefs and appraisal processes are crucially important in the onset and persistence of psychosis. This study investigated whether (i) neuroticism increases the risk for development of psychotic symptoms, and (ii) a delusional interpretation and/or a depressed response to hallucinatory experiences predicts the onset of psychotic disorder. *Method* A general population sample with no lifetime evidence of any psychotic disorder was interviewed with the Composite International Diagnostic Interview Schedule (CIDI) at baseline and 1 and 3 years later. At year 3, individuals with CIDI evidence of psychotic symptoms were interviewed by clinicians to identify onset of psychotic disorder. *Results* Baseline level of neuroticism increases the risk for incident psychotic symptoms. Given the presence of hallucinatory experiences at baseline, the increase in risk of having the psychosis outcome was much higher in the group with delusional ideation or depressed mood at year 1 than in those without delusional ideation or depressed mood. *Conclusion* A cognitive style characterised by a tendency to worry increases the risk for newly developed psychotic symptoms. Individuals who report hallucinatory experiences and react to these with a delusional interpretation and/or negative emotional states have an increased risk for developing clinical psychosis.

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Introduction

Only a fraction of the individuals who report psychotic experiences, such as hallucinatory experiences and delusional ideation, will meet criteria for a clinical disorder (Claridge et al. 1996; Eaton et al. 1991; Johns et al. 2002; Peters et al. 1999; Tien 1991; Van Os et al. 2000). However, little is known about the mechanisms that mediate the relationship between non-clinical psychotic experiences and subsequent clinical disorder.

Current hypotheses on psychological mechanisms of psychosis have emphasised that the response to abnormal experiences is cognitively mediated by beliefs or appraisals (Bentall et al. 1994; Garety et al. 2001; Morrison 2001). According to these models, cognitive disturbances may lead to anomalous experiences, which in combination with maladaptive emotional and cognitive appraisal processes may lead to the formation of symptoms. Thus, the experience of a voice does not necessarily lead to a full-blown psychotic symptom. Only when an individual appraises this voice as coming from an external malevolent source and starts worrying about the experience, does a psychotic symptom develop. It is this interpretation that causes the associated distress and disability (Chadwick and Birchwood 1994; Morrison and Baker 2000) and thereby increases the risk of developing need for treatment.

In this article, we bring together data from three previously published papers, in order to investigate the following hypotheses: (i) high levels of neuroticism, or a tendency to worry, increase the risk for development of psychotic symptoms (Krabbendam et al. 2002) (Study 1); (ii) a delusional interpretation and/or a depressed response to hallucinatory experiences predicts the later onset of clinical psychotic disorder (Krabbendam et al. 2004, 2005) (Study 2).

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Study 1

Methods

Participants

The Netherlands Mental Health Survey and Incidence Study (NEMESIS) is a longitudinal cohort study of the prevalence, incidence, and course and consequences of psychiatric disorders in the Dutch general population. Subjects were contacted at three points in time, namely 1996 (baseline), 1997 (T_1) and 1999 (T_2) (Bijl et al. 1998a, b). The sampling procedure and response rate is described in detail in previous work (Van Os et al. 2000, 2001). A total of 7076 subjects aged 18–64 years were enlisted at baseline. At T_1, 5618 subjects participated for the second time; at T_2, 4848 subjects participated.

Procedure

The Composite International Diagnostic Interview (CIDI) version 1.1 was used (WHO 1990). The CIDI psychosis section (G-section) consists of 17 core psychosis items on delusions (13 items) and hallucinations (4 items): items G1-G13, G15, G16, G20 and G21. These items correspond to classic psychotic experiences like persecution, thought interference, auditory hallucinations and passivity phenomena. All these items can be rated in five ways: i) no experience; ii) experience present but not clinically relevant (not bothered by it and not seeking help for it); iii) experience is the result of drug use or somatic disease; iv) experience is not a real symptom because there appears to be some plausible explanation for it; v) true psychotic symptom. Categories ii-v will be denoted hereafter, respectively: NCR symptom (Not Clinically Relevant), secondary symptom, possible symptom and clinical symptom.

At T_2, clinical re-interviews were conducted by telephone by a psychiatrist using the two positive psychosis items from the Brief Psychiatric Rating Scale (BPRS) (Overall and Gorham 1962) for all individuals who had a rating of NCR, possible or clinical symptom on any CIDI psychosis item. Telephone re-interviews were completed on 74.4 % of the subjects eligible for re-interview. Two T_2 psychosis outcomes were defined, based on the BPRS interview at T_2 and clinical judgement of need for care: i) any psychotic experience at any level on either of the two BPRS items "unusual thought content" and "hallucinations" (score >1, hereafter: BPRS psychotic-like experiences), ii) a BPRS score on either of the two psychosis items that was greater than pathology level in terms of severity and functional impairment (i. e. BPRS score >3) and presence of clinical judgement of need for care (hereafter: needs-based diagnosis of psychosis).

At every measurement occasion, subjects also completed the 14-item Groningen Neuroticism Scale (Ormel 1980).

Analysis

In order to skew the sample at T_2 towards individuals with lifetime first-ever occurrence of symptoms, only individuals were included who at baseline and T_1 interview had a rating of lifetime absence on all the individual items in the CIDI psychosis section. Logistic regression was carried out to examine the associations between neuroticism at baseline and the two psychosis outcomes at T_2. Associations were expressed as odds ratios (ORs) with their 95 % confidence intervals (CIs). All associations were adjusted for the *a priori* selected possible confounding effects of age (10-year age-groups), sex, education (4 levels), and CIDI lifetime diagnosis of any DSM-III-R psychiatric disorder, as well as other possible confounding factors that are known to influence the risk for psychosis (Kendler et al. 1996; Van Os et al. 2000): single marital status, employment status (unemployed versus other), level of population density of area of residence (urbanicity, three levels), ethnic group (white versus other) and discrimination status (four levels).

Results

The risk set consisted of 3929 individuals. Neuroticism at baseline was positively associated with presence of BPRS psychotic-like experiences at T_2 (unadjusted OR 1.16, 95 % CI 1.09, 1.23; adjusted OR 1.20, 95 % CI 1.12, 1.30). The strength of the association increased with increasing levels of neuroticism (summary OR over three groups according to their tertile level of neuroticism: 2.21, 95 % CI 1.36, 3.60; middle scores, OR 1.80, 95 % CI 0.43, 7.54; high scores, OR 3.89, 95 % CI 1.03, 14.71; low scores used as reference category). Results were similar for the outcome of the needs-based diagnosis of psychosis.

Study 2

Methods

Procedure

The analyses were based on the three measurement points of the Dutch NEMESIS study (see above). Baseline Hallucinatory Experience (HE) was broadly defined as any CIDI rating of NCR, secondary, possible or clinical symptom on any of the 4 CIDI hallucination items, and Delusional Ideation (DE) at baseline and T_1 was broadly defined as any CIDI rating of NCR, secondary, possible or clinical symptom on any of the 13 CIDI delusion items. Baseline presence of Depressed Mood (DM) was assessed by item E2 of the CIDI depression section ("Have you ever felt depressed most of the time for a period of two years or longer?"). At T_1, the period between baseline and T_1 was assessed and this rating thus reflects onset of DM one year before baseline.

Analysis

All the analyses for this study were conducted in the group of individuals who i) had undergone both the baseline and the T_1 interviews and had received no lifetime diagnosis of any DSM-III-R affective or non-affective psychotic disorder at either interview, ii) had had a CIDI interview at T_2, and iii) at T_2 had not missed re-interview by clinicians about the presence of psychotic symptoms if they had been eligible for this clinical re-interview.

In order to test the hypothesis that, given the presence of hallucinatory experiences, the risk of developing the two psychosis outcomes (BPRS psychotic-like experiences, needs-based diagnosis) was greater in those who subsequently developed delusional ideation or depressed mood, an interaction was fitted between presence of HE at baseline (absence versus presence) and presence of DE or DM at T_1 (absence versus presence). The coefficient of this interaction reflects the difference in risk for the psychosis outcome between individuals with baseline HE who developed DE or DM at T_1 compared to individuals with baseline HE who did not develop DE or DM at T_1. In line with recent advances in the conceptualisation of interaction, we calculated the statistical additive interaction rather than the multiplicative interaction, as the former is more likely to yield information on the degree of synergism between causes, that is the extent to which both causes depend on each other or co-participate in disease causation (Darroch 1997). In order to calculate the statistical interaction under an additive model, the BINREG procedure in the STATA statistical programme (StataCorp 2001), which fits generalised linear models for the binomial family estimating risk differences, was used.

Results

The risk set consisted of 4672 individuals. The number of individuals with T_2 BPRS psychotic-like experiences was 85 (1.8 %) and 24 individuals (0.5 %) had a need for care in relation to psychotic symptoms. At baseline interview, 287 individuals (6.1 %) reported HE. Given the presence of HE at baseline, the increase in risk on the additive scale of having the psychosis outcome at T_2 was much higher in the group with DE at T_1 (n = 30) than in those without DE at T_1 (n = 257) (see Table 1). The difference in risks between the groups with and without DE at T_1 was statistically significant for each of the two psychosis outcomes (see Table 1). After adjustment for the effect of DE at baseline, the interactions between DE at T_1 and HE at baseline remained significant for both psychosis outcomes, indicating that the risk increasing effect of DE at T_1 reflected the emergence of DE between baseline and T_1. Similarly, given the presence of HE at baseline, the increase in risk on the additive scale of having the psychosis outcome at T_2 was higher in the group with DM at T_1 (n = 24) than in those without DM at T1 (n = 263) (see Table 1) and this effect remained after adjustment for baseline presence of DM.

In order to investigate whether the risk increasing effects of DE at T_1 and DM at T_1 overlapped, separate analyses were performed in which the interaction between DE and HE was adjusted for DM and the interaction between DM and HE was adjusted for DE. Adjustment for DM at T_1 did not change the interaction between DE at T_1 and HE at baseline (for all analyses, changes in risk difference coefficients were between 0.01 % and 0.5 %). In contrast, adjustment for the presence of DE at T_1 reduced but not nullified the risk increasing effect of DM at T_1 in those who reported hallucinatory experiences at baseline. After adjustment for DE, the risk difference between DM at T_1 and no DM at T1 was 13.54 % (95 % CI −4.34, 31.42; $\chi^2 = 2.20$, df = 1, p = 0.138) for the outcome of BPRS psychotic-like experiences, and 14.18 % (95 % CI −1.34, 29.71; $\chi^2 = 3.21$, df = 1, p = 0.073) for the needs-based diagnosis of psychosis.

Discussion

The findings of Study 1 suggest that neuroticism contributes to the risk of psychotic or psychosis-like symptoms at 3-year follow-up. These effects were present in individuals who were initially free of any lifetime level of psychotic or psychosis-like symptoms, or any lifetime

Table 1 Interactions between baseline hallucinatory experiences and delusion formation or depressed mood at T1 on the additive scale

		BPRS psychotic-like experiences (n = 85)	Needs-based diagnosis (n = 24)
Increase in risk[a] associated with baseline hallucinatory experiences	No delusion formation at T1 (n = 257)	9.69 % (5.93, 13.44)	3.04 % (0.92, 5.17)
	Delusion formation at T1 (n = 30)	29.22 % (10.68, 47.75)	21.76 % (5.39, 38.13)
Risk difference		19.53 % (0.61, 38.44)	18.72 % (2.22, 35.23)
Additive interaction[b]		$\chi^2 = 4.10$, df = 1, p = 0.043	$\chi^2 = 4.94$, df = 1, p = 0.026
Increase in risk associated with baseline hallucinatory experiences	No depressed mood at T1 (n = 263)	11.12 % (7.15, 15.08)	3.99 % (1.57, 6.41)
	Depressed mood at T1 (n = 24)	28.13 % (9.88, 46.37)	20.83 % (4.59, 37.08)
Risk difference		17.01 % (–1.66, 35.67)	16.84 % (0.41, 33.27)
Additive interaction[b]		$\chi^2 = 3.19$, df = 1, p = 0.074	$\chi^2 = 4.04$, df = 1, p = 0.045

[a] Risk of having the psychosis outcome at T2; [b] Tests whether increase in risk in group with delusion formation or depressed mood at T1 is significantly greater than increase in risk in group without delusion formation or depressed mood at T1

diagnosis of psychotic disorder. Previous research has indicated that neuroticism operates as a risk factor for onset of affective disorder (Boyce et al. 1991; Fergusson et al. 1989) and the present results provide support for the notion of a shared liability (Van Os et al. 1998; Van Os and Jones 2001). Cognitive processes traditionally associated with affective disorders may mediate the association between neuroticism and psychosis. Information-processing biases may serve to confirm psychotic beliefs, for example when attention is focused at external threats selectively (Freeman et al. 2000). Metacognitive beliefs, such as beliefs about uncontrollability of voices or delusion-related thoughts, will increase the risk of experiencing these symptoms (Baker and Morrison 1998) as well as the distress caused by them (Freeman and Garety 1999). Negative emotions may make hallucinatory experiences personally significant or more intrusive, and so trigger the individual to search for explanations of the experiences.

Study 2 shows that, 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, but this effect was partly mediated by the development of delusional ideation. Adjustment for lifetime presence of delusional ideation or depressed mood did not change the pattern of results, suggesting that the risk increasing effect reflects the effect of the emergence of delusional ideation or depressed mood between baseline and T_1. In sum, delusional ideation and depressed mood may arise as a secondary response to hallucinatory experiences in the development of clinical psychotic disorder. Our finding that the risk increasing effect of depressed mood was partly mediated by the presence of delusional ideation fits well with the view that delusional ideation may give rise to depressed feelings (Birchwood and Chadwick 1997). According to these authors, the sense of entrapment in the context of a threatening and powerful entity leads to feelings of powerlessness and depression.

The tendency to interpret anomalous perceptual experiences in a delusional way may be reinforced by cognitive mechanisms, particularly, a probabilistic reasoning bias or a "jumping to conclusions" data gathering style (Dudley et al. 1997; Garety et al. 1991), an abnormal attributional style, i. e. strong externalizing and personalizing bias (Fear et al. 1996; Kinderman and Bentall 1997), and poor ability to understand and conceptualize the mental processes of other people (theory of mind) (Corcoran et al. 1995; Frith and Corcoran 1996; Janssen et al. 2003b). The experience of social adversities may further increase the risk for development of psychotic symptoms. In the NEMESIS sample, experience of abuse before the age of 16 has been found to increase the risk of development of psychotic symptoms and disorder (Janssen et al. 2004). In the same sample, it was found that the experience of discrimination was associated with onset of delusional ideation (Janssen et al. 2003a).

The proposed role for secondary beliefs and appraisals in the onset and maintenance of psychotic disorder has implications for treatment. Cognitive therapy focuses on the modification of cognitive processes (Alford and Beck 1994; Beck 1976). Cognitive behavioural re-appraisal techniques could be instrumental in reducing the depression and fear generated by the voices and enhancing the perceived control over the experience. This may in some individuals prevent the formation of delusions and/or reduce the need for care (Chadwick and Birchwood 1994). Several studies have now evaluated the cognitive approach and have found that modification of beliefs can be successful in reducing the amount of time spent hallucinating as well as in the disruption caused by them (Gould et al. 2001; Haddock et al. 1998). Further elucidation of the cognitive processes involved in the onset and maintenance of clinical psychosis may contribute to the development of targeted psychological interventions.

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