Role of distress in delusion formation*

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Background Contemporary cognitive psychological theories suggest that distress plays a mediating role in delusion formation.

Aims To study the amplifying role of distress from early perceptual intrusions to delusion formation.

Method A general population sample of 7076 individuals was interviewed with the Composite International Diagnostic Interview (CIDI) in 1996 (baseline), 1997 (TI) and 1999 (T2). At T2, clinicians also scored the Brief Psychiatric Rating Scale (BPRS) item 'unusual thought content'. Analyses compared hallucinatory experiences with and without subjective distress at baseline for risk of delusion formation at follow-up.

Results Individuals experiencing hallucinations with distress, compared with those without distress had a fourfold increased risk of subsequent delusion formation.

Conclusions This finding corroborates the hypothesis that distress associated with early perceptual intrusions serves as a catalyst in the development of delusions.

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Hallucinations and delusions tend to co-occur both in clinical and in non-clinical samples (Liddle & Barnes, 1990; Johnstone & Frith, 1996; van Os et al, 2000). One possible explanation for this association may be that the experience of hallucinations gives rise to secondary delusional interpretations (De Clérambault, 1942; Maher, 1988). Little is known, however, about the factors that mediate the transition from hallucinatory experience to delusional interpretation. Recent psychological hypotheses on delusion formation emphasise the role of attributional style, distress and worry in the aetiology and maintenance of delusions (Garety et al, 2001). Thus, the experience of voices or visions may lead to full-blown delusional ideation, when it is attributed to an external source or when it is given personal significance.

In an earlier study, for example, it was reported that delusion formation in adolescents hearing voices was mediated by, among other factors, attributions of externality, perceived power over the person and emotional appraisals (Escher et al, 2002). We wished to extend these results to a large general population sample that had no previous evidence of delusional ideation. It was hypothesised that people experiencing hallucinations with distress at baseline, compared with those without, would show a greater risk of developing delusions over the follow-up period.

METHOD

Procedure, instruments and sample

The Netherlands Mental Health Survey and Incidence Study (NEMESIS study) is a large general population study with three measurement points (hereafter: baseline, T1 and T2) in 1996, 1997 and 1999. At the three measurement points, respectively 7076, 5618 and 4848 individuals aged 18–64 years participated. Trained lay interviewers in all three measurements applied the Composite International Diagnostic Interview (CIDI; Smeets & Dingemans, 1993). The CIDI has 17 psychosis items (13 delusions, 4 hallucinations) with six possible ratings for each psychosis item: (1) no psychotic experience; (2) no clinically relevant psychotic experience; the individual is not experiencing distress and is not seeking help; (3) and (4) psychotic experience is the result of drug misuse or somatic disease; (5) true psychiatric symptom; individual experiences distress and/or seeks help; (6) what appears to be a true psychotic symptom may not be a real symptom because there appears to be some plausible explanation for it, i.e. it may actually exist.

At baseline, the lay interviewers enquired about lifetime presence of symptoms and at the two follow-up measurements the period between the measurements was assessed. For the current analysis, ratings of 2 and 5 on the four hallucination items at baseline, both indicative of the presence of a psychotic experience in the absence of doubt or secondary cause but crucially different in terms of subjective distress and help-seeking behaviour, were included in the analyses. The distinction between the ratings of 2 and 5 was validated in a previous study (van Os et al, 2001). The four hallucination items encompassed all possible hallucinatory modalities.

At baseline and T2, attempts were made to clinically validate the lay interviewer-administered CIDI interview. Each time, when at baseline (possible) psychotic symptoms (CIDI rating of 5 or 6) were detected in the NEMESIS study, a psychiatric clinician conducted clinical re-interviews over the telephone by using the Structured Clinical Interview for DSM–III–R (SCID; Spitzer et al, 1992). If a clinician did not agree with the psychosis rating of the trained lay interviewer, the psychosis rating was changed to the rating of the clinician. All DSM–III–R diagnoses in the NEMESIS study are based on these corrected ratings. At baseline, 47.2% of the eligible individuals were actually interviewed. The probability of a selection bias was assessed in a previous study and deemed unlikely (Hanssen et al, 2003). At T2, all individuals with a rating of 2, 5 or 6 on any CIDI psychosis item were administered a clinical re-interview over the telephone by an experienced clinician. The proportion of eligible individuals who were successfully

re-interviewed was 74.4%. At T2, the clinician also scored the 'unusual thought content' item of the Brief Psychiatric Rating Scale (BPRS; Lukoff *et al*, 1986). The BPRS symptom items are rated on a seven-point scale on the basis of frequency of the symptom and functional impairment. Ratings 2–3 represent a non-pathological form of the symptoms and ratings 4–7 represent a pathological form (Lukoff *et al*, 1986). For a more detailed description of the NEMESIS study see Bijl *et al* (1998) and van Os *et al* (2001).

Analyses: the development of delusions

The study sample at T2 was restricted to individuals who did not report delusions at baseline and again at T1 (i.e. had no ratings of 2 or 5 on any of the CIDI delusion items at baseline and T1) in order to skew the sample towards people with true incident delusions at T2 (original sample at T2: $n=4848$; sample restricted to those without delusions at baseline and T1, and non-missing data on the delusion variable at T2, hereafter referred to as 'risk set': $n=4236$; risk set and non-missing covariates: $n=4181$).

All analyses were carried out with Stata version 7 Special Edition (StataCorp, 2001). Logistic regression analysis was performed with the BPRS 'unusual thought content' item measured at T2 as a dependent variable (score 1 rated absent and score >1 rated present) and the baseline CIDI ratings on hallucinations with and without distress (entered as two dummy variables) as independent variables. To account for possible confounding variables, we controlled for the following *a priori* chosen covariates, guided by previous findings in this sample (van Os *et al*, 2000, 2001, 2002; Krabbendam *et al*, 2002; Janssen *et al*, 2003): age (5 categories), gender, urbanicity (3 levels), ethnic group (0: person and both parents born in the Netherlands and 1: other), neuroticism (Ormel, 1980), experience of discrimination (a 6-item questionnaire measuring experience of discrimination regarding the colour of skin or ethnicity, gender, age, appearance, handicap and sexual orientation), experience of abuse before the age of 16 years (a 4-item questionnaire), educational level (4 levels), unemployment and single marital status. The effect sizes of baseline hallucinations with and without distress on risk for delusion formation at T2 were

compared using the Wald test. In order to exclude misclassification at the lower end of the BPRS scoring range of the unusual thought content item, analyses were repeated with a more stringent definition of the BPRS 'unusual thought content' item as a dependent variable, i.e. a score >2. Finally, in an attempt to clinically validate any findings, analyses were repeated using the clinical definition of delusions, namely a score >3 on the BPRS item 'unusual thought content', which is indicative of the level of pathology in terms of functional impairment (Lukoff *et al*, 1986).

Sensitivity analyses

Sensitivity analyses were conducted to examine whether differential attrition in the sample as a whole (7076 at baseline, 4848 at T2) could have biased the findings. This was done by multiple imputation of missing values of delusional ideation at T2 ($n=1962$ missing, 31.4%) using the HOTDECK command in Stata. The HOTDECK procedure is used several times within a multiple imputation sequence as missing data are imputed stochastically rather than deterministically. A total of 1000 imputation sequences were run, yielding 1000 data-sets in which the regression coefficients were estimated within the HOTDECK procedure. Imputation of missing values was stratified by known risk factors of psychosis (van Os *et al*, 2000, 2001, 2002; Krabbendam *et al*, 2002; Janssen *et al*, 2003), namely age, gender, urbanicity, ethnic group, neuroticism, experience of discrimination, experience of abuse before the age of 16 years, educational level, unemployment and single marital status. The HOTDECK procedure replaces missing values in the relevant variables by values randomly sampled from complete lines in the same stratum. Individuals who had delusions at baseline and at T1 were again excluded from these analyses ($n=831$).

RESULTS

Data

At baseline and limited to the risk set ($n=4236$), 161 individuals (males: 34.8%) reported lifetime occurrence of hallucinations without distress, whereas 32 (males: 21.9%) reported hallucinations with distress. Five subjects reported both types of hallucinations.

In the risk set ($n=4236$), visual, auditory, olfactory and tactile hallucinations

without distress were reported by 79 (1.9%), 26 (0.6%), 34 (0.8%) and 60 (1.4%) individuals, respectively. Visual, auditory, olfactory and tactile hallucinations accompanied by distress were present in 19 (0.5%), 8 (0.2%), 5 (0.1%) and 8 (0.2%), respectively. In the group of 161 individuals who reported hallucinatory experiences without distress, the proportions of visual, auditory, olfactory and tactile hallucinations were 49.1% (79/161), 16.2% (26/161), 21.1% (34/161) and 37.3% (60/161), respectively. In the distress group ($n=32$) these proportions were 59.4% (19/32), 25.0% (8/32), 15.6% (5/32) and 25.0% (8/32), respectively.

Thirty-seven individuals in the risk set (males: 35%) had developed delusions (BPRS >1) at T2, 16 of these 37 (males: 56%) had developed delusions with a BPRS score >2, and 7 (males: 71%) of these 16 had developed clinical delusions according to the BPRS definition (BPRS >3).

Distress and delusion formation

The risk for delusion formation at T2 was five times greater in the individuals who at baseline were distressed by their hallucinations (6 out of 32 persons reporting hallucinations with distress developed delusions (BPRS >1: OR=25.0, 95% CI 9.3–67.8) than in the individuals who reported hallucinations without distress (7 out of 161 persons reporting hallucinations without distress developed delusions (BPRS >1: OR=4.9, 95% CI 2.0–11.9) (Table 1). This difference was statistically significant ($\chi^2=5.2$, d.f.=1, $P=0.02$). After adjustment for the covariates, the difference remained robust ($\chi^2=3.8$, d.f.=1, $P=0.05$) (Table 1).

Results were similar using the more stringent definition of delusions (BPRS >2), with again a highly significant difference in effect size ($\chi^2=8.7$, d.f.=1, $P=0.003$) (Table 1), also after adjustment of covariates. Similar results were apparent for the clinical definition of delusions: no individuals with hallucinations without distress developed clinically relevant delusional ideation, whereas the risk was very high in those whose hallucinatory experiences were accompanied by distress (Table 1).

Sensitivity analyses

Using 1000 imputation sequences in which missing values of the outcome of delusions at T2 were imputed stochastically, the estimated effect size for baseline hallucinations with distress was (OR=18.3, 95%

Table I Comparison between hallucinations with and without distress regarding the formation of delusions 3 years later

Covariates	Baseline Hallucination with distress (OR; 95% CI), frequency[1]	Baseline Hallucination without distress (OR; 95% CI), frequency[1]	χ^2	d.f.	P
Unadjusted					
T2: BPRS delusion >1	25.0 (9.3–67.8) 6/32	4.9 (2.0–11.9) 7/161	5.2	1	0.02
T2: BPRS delusion >2	50.4 (14.9–169.9) 4/32	0.9 (0.1–7.8) 1/161	8.7	1	0.003
T2: BPRS delusion >3	126.4 (26.8–595.3) 3/32	—[2] 0/161	—	—	—
Adjusted					
T2: BPRS delusion >1 +covariates	13.7 (4.4–42.4)	3.2 (1.2–8.4)	3.8	1	0.05
T2: BPRS delusion >2 +covariates	25.1 (4.8–131.3)	0.5 (0.04–4.9)	8.5	1	0.004
T2: BPRS delusion >3 +covariates	136.2 (13.1–1414.3)	—[2]	—	—	—

BPRS, Brief Psychiatric Rating Scale.
1. Frequency means the number of individuals with delusion formation given the number of individuals with lifetime hallucinations with or without distress.
2. Predicts failure perfectly.

CI 5.6–60.2) and for baseline hallucinations without distress (OR=5.4, 95% CI 2.1–14.3), indicating a similar pattern of results.

DISCUSSION

The results show that those who experience negative emotional states associated with anomalous perceptual intrusions have a much greater risk of developing delusional ideation, including experiences of clinical relevance, than individuals who report similar experiences without distress.

Individuals reporting distress associated with their hallucinations did show a much greater risk for developing clinical delusions than those reporting hallucinations without distress. Our findings support the amplifying role of distress in current cognitive models of delusion formation (Freeman & Garety, 1999; Birchwood et al, 2000; Morrison & Baker, 2000; Garety et al, 2001). According to these models, feelings of uncontrollability and hopelessness associated with negative emotional states may contribute to the onset of delusional interpretations. Emotions may also make hallucinatory experiences personally significant or more intrusive, which in turn may trigger the individual to search for explanations of the experiences. The distress caused by hallucinatory experiences may in turn be related to the interpretation of the experience (Morrison & Baker, 2000). The mechanism of delusion formation may depend on the initial interpretation individuals give to their unusual perceptual intrusions. If this initial interpretation leads to distress, the individual may be more prone to selective attentional processes and safety behaviours, diminishing the opportunity to test the accuracy of the psychotic experience (Garety et al, 2001), resulting in increased levels of delusional ideation.

The role of distress associated with unusual experiences may also be crucial to understand further transitions over the psychosis continuum. Peters et al (1999) measured delusional ideation in the general population as well as in those with delusions using the Peters et al Delusions Inventory (PDI). The PDI scores of the general population and the patients with delusions showed a large degree of overlap and nearly 10% of the general population scored above the mean of the group with delusions. However, compared with patients, the general population displayed significantly less distress, preoccupation and conviction regarding their unusual perceptual experiences and ideas.

The present study is limited to psychological factors, but biological factors may also be relevant in this regard. Hemsley's cognitive model hypothesises that the problem in schizophrenia encompasses the inability to integrate the moment-by-moment sensory input with stored memory (Hemsley, 1993, 1994). A neuronal circuit, including the limbic system, is proposed to be involved in this integration process. Distress can lead to an increased dopamine release that in turn may influence the functioning of these brain structures (Robinson & Becker, 1986). Thus, a stress-induced dopaminergic response in humans could result in a heightened risk for positive psychotic symptoms in vulnerable persons, with possible subsequent sensitisation of dopaminergic response and persistence of delusional ideation (Laruelle, 2000).

In summary, the present findings have implications for early intervention in psychosis or psychosis-like experiences, and underline the significance of cognitive–behavioural therapy in treating psychotic disorders (Kingdon & Turkington, 1994; Turkington & Kingdon, 2000). If distress associated with hallucinations is involved in the development of delusions, ameliorating the distress may prevent the formation of delusions in some individuals. Cognitive–behavioural, anxiety-reducing and reappraisal techniques could be instrumental in preventing the development of delusions in those with anomalous experiences (McGorry et al, 2002; Morrison et al, 2002).

However, this work should be interpreted in the light of several potential limitations. First, distress was operationalised as feeling disturbed by the hallucinations and/or displaying help-seeking behaviour. Thus, the mediating role of distress in the development of delusions is a general one, as we did not have any information linking distress to content of or beliefs about hallucinations and/or delusions. Second, differential attrition in this longitudinal design could have biased the results. However, sensitivity analyses generated essentially similar results. Third, the present study monitored only one of the many mediating and maintaining factors proposed by Garety et al (2001). However, it was not possible to examine the role of many other important variables in the formation of delusions (e.g. externalising attributional biases, problems with self-monitoring, dysfunctional schemas etc.), as we did not gather this information. Finally, the outcome 'unusual thought

content' was very rare, affecting the precision with which we could estimate effect sizes.

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CLINICAL IMPLICATIONS

■ Psychotic experiences are common and transitions to clinical disorder are in part determined by emotional factors.

■ Not only the presence of an unusual perceptual experience in itself but also the emotional appraisal by the subject is an important risk factor for subsequent delusion formation.

■ Cognitive–behavioural therapy, in the context of early hallucinatory experiences, may be more efficient when specifically targeting the distress generated by the experience.

LIMITATIONS

■ The distress measures used in the present study were limited to 'feeling disturbed or displaying help-seeking behaviour'.

■ The outcome under study was very rare, affecting the precision with which we could estimate effect sizes.

■ The present study examined only one of the proposed mediating and maintaining factors in the cognitive model of Garety *et al* (2001).

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