# Affectively Salient Meaning in Random Noise: A Task Sensitive to Psychosis Liability

Mariana Galdos<sup>1,2,3</sup>, Claudia Simons<sup>1,4</sup>, Aranzazu Fernandez-Rivas<sup>2,3</sup>, Marieke Wichers<sup>1</sup>, Concepción Peralta<sup>5</sup>, Tineke Lataster<sup>1</sup>, Guillermo Amer<sup>6</sup>, Inez Myin-Germeys<sup>1</sup>, Judith Allardyce<sup>1</sup>, Miguel Angel Gonzalez-Torres<sup>2,3</sup>, and Jim van Os<sup>1,7,\*</sup>

<sup>1</sup>Department of Psychiatry and Neuropsychology, South Limburg Mental Health Research and Teaching Network, EURON, Maastricht University Medical Centre, PO Box 616 (DRT 10), 6200 MD Maastricht, the Netherlands; <sup>2</sup>Department of Neuroscience, University of the Basque Country, Basque Country, Spain; <sup>3</sup>Department of Psychiatry, Basurto Hospital, Bilbao, Spain; <sup>4</sup>GGz Eindhoven, Eindhoven, the Netherlands; <sup>5</sup>Zaldibar Psychiatric Hospital, Zaldibar, Spain; <sup>6</sup>Service of Neurology, Son Dureta Hospital, Palma de Mallorca, Spain; <sup>7</sup>Division of Psychological Medicine, Institute of Psychiatry, De Crespigny Park, Denmark Hill, London, UK

Stable differences in the tendency to attribute meaning and emotional value to experience may represent an indicator of liability to psychosis. A brief task was developed assessing variation in detecting affectively meaningful speech (speech illusion) in neutral random signals (white noise) and the degree to which this was associated with psychometric and familial vulnerability for psychosis. Thirty patients, 28 of their siblings, and 307 controls participated. The rate of speech illusion was compared between cases and controls. In controls, the association between speech illusion and interview-based positive schizotypy was assessed. The hypothesis of a dose-response increase in rate of speech illusion across increasing levels of familial vulnerability for psychosis (controls, siblings of patients, and patients) was examined. Patients were more likely to display speech illusions than controls (odds ratio [OR] = 4.0, 95% confidence interval [CI] = 1.4-11.7), also after controlling for neurocognitive variables (OR = 3.8,95% CI = 1.04–14.1). The case-control difference was more accentuated for speech illusion perceived as affectively salient (positively or negatively appraised) than for neutrally appraised speech illusions. Speech illusion in the controls was strongly associated with positive schizotypy but not with negative schizotypy. In addition, the rate of speech illusion increased with increasing level of familial risk for psychotic disorder. The data suggest that the white noise task may be sensitive to psychometric and familial vulnerability for psychosis associated with alterations in top-down processing and/or salience attribution.

*Key words:* psychotic disorders/experimental design/delusions/hallucinations/environment

#### Introduction

Epidemiological surveys have established that experiences resembling the delusions and hallucinations observed in psychotic disorders are prevalent in the general population and predominantly occur in a context of affective dysregulation. Subthreshold psychotic experiences share the same age-related developmental expression and also display etiological (sharing the same genetic and nongenetic risk factors) and temporal (increased risk of transition from subthreshold to clinical state) continuity with psychotic disorders.<sup>2,3</sup> The distribution of psychotic experiences in the general population thus is thought to reflect stable individual differences in psychosis liability, most of which is expressed transitorily, below the level of illness, during adolescence and young adulthood.<sup>4</sup> It has been proposed that these findings can be examined from the perspective that internal representations (thoughts or percepts) or external objects (environments) acquire altered meaning or emotional value, 5,6 possibly associated with alterations in top-down processing of information from the senses<sup>7,8</sup> or changes in dopamine signaling, <sup>5,6</sup> prompting the individual to develop a cognitive scheme to make sense<sup>9</sup> of these.

It may thus be hypothesized that stable differences in the tendency to attribute meaning and emotional value to experience—varying from aberrant to adaptive—are associated with the tendency to express psychotic experiences and thus represent an indicator of liability for psychotic disorder.

Several approaches toward experimental assessment of attribution of meaning or emotional value have been reported. Hoffman<sup>10</sup> described an experimental design

<sup>\*</sup>To whom correspondence should be addressed; tel: +31-43-3875443, fax: +31-43-3875444, e-mail: j.vanos@sp.unimaas.nl.

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measuring individual differences in picking up spurious messages (speech illusions) from multispeaker babble and showed that speech illusions predicted transition to schizophrenia-spectrum disorder in individuals with prodromal signs of psychosis.<sup>7</sup> A related approach involves detection of speech stimuli embedded in noise in the context of a speech recognition paradigm. 11 A further variant of the "false-positive meaning" approach is the experiment in which pure white noise is presented and individuals indicate whether or not they perceive spoken words. 12,13 Other approaches include experimental induction of salience in the form of the illusion of remembering a stimulus not presented before<sup>14</sup> and the use of a monetary reward training paradigm, training individuals to discriminate between reward-predictive (CS+) and random (CS-) stimuli, and using speed of response to CS+ and CS- as an indicator of adaptive (rapid response to CS+) or altered (rapid response to CS-) motivational salience. 15

In the current study, an extension of the "false-positive meaning" approach was used because it allows for testing in large samples, is not dependent on memory and motivation, makes no assumption about the universality of the rewarding property of money in mixed samples of patients and controls, and does not equate the "reward" aspect of salience, denoting incentive and pleasure, with the "importance" aspect. In addition, an attempt was made to increase the sensitivity of the task by combining a pure white noise paradigm with the paradigm of words embedded in white noise of variable intensity. Finally, the aberrant meaning paradigm was extended to allow for the inclusion of a dimension of affective salience because experimental work by Holt and colleagues 16 suggests that patients with a diagnosis of schizophrenia were more likely to assign affective meaning to neutral stimuli, compared with those without delusional ideation, a finding that is congruent with the epidemiological observation that affective dysregulation may contribute causally to the persistence and clinical relevance of reality distortion.

The aim of the current study, therefore, was to measure (1) variation in detecting affectively salient speech in neutral random signals (white noise), (2) neurocognition, and (3) the tendency to express positive psychotic experiences in patients, their healthy siblings, and controls, hypothesizing that affectively salient meaning attributed to white noise would be associated with (1) patient status, particularly in those with the highest levels of positive psychotic symptoms, (2) familial vulnerability status, assessing trend across low- (control), medium- (sibling of patient), and high- (patient with psychotic disorder) risk groups, and (3) psychometric vulnerability status in the form of positive psychotic experiences (schizotypy) in controls, independent of measures of neurocognition.<sup>17</sup> Given the wellknown age dependence of expression of psychosis liability in the general population, <sup>2,18</sup> a sample of adolescents and young adults was targeted.

#### Methods

#### Sample

Patients with psychotic disorder, their healthy siblings nearest in age, and healthy controls were recruited using consecutive admissions between January 2007 and September 2008 at the Psychiatric Hospitalization Unit of the Basurto, Zaldibar, and Zamudio Hospitals in Basque Country, Spain (patients), and schools serving these areas (controls). Patients were seen when the responsible medical officer judged them to be no longer in an acute psychotic state and recovered for the purpose of interview. Inclusion criteria were (all 3 groups) as follows: aged 16– 35 years, white ethnic group, native Spanish speaker, intelligence quotient (IQ) in excess of 75 according to the Wechsler Adult Intelligence Scale (WAIS), and (patients) meeting criteria for DSM-IV affective or nonaffective psychotic disorder. Exclusion criteria were as follows: patients in an acute psychotic phase or intoxicated with drugs of abuse, patients with comorbid autism, and patients with organic psychosis. Most of the healthy controls (n = 218) were 1 of a pair of sibs (the familial relationship in controls was required for another, genetically sensitive aspect of the study) meeting similar inclusion and exclusion criteria; they were recruited in the same catchment area as the cases, through educational institutes (vocational school, professional school, or university) and staff and relatives of these. The study was approved by the local Ethics Committee, and subjects provided written informed consent. In order to assess population reference values for white noise speech illusion, an additional control reference group of 97 subjects living in the same region and meeting similar inclusion and exclusion criteria was collected using an advertising procedure (hereafter: control reference group).

## Instruments

Interviewers were Spanish psychology graduates, who had been trained extensively at Maastricht University, the Netherlands. Follow-up training sessions in order to prevent interview "drift" were conducted regularly on site. The following tasks were administered.

White Noise Task. Subjects wore earphones and were presented 1 of 3 different types of stimuli: (1) white noise only, (2) white noise + clearly audible neutral speech, and (3) white noise + barely audible neutral speech. Stimuli 2 and 3 were not separate conditions; the intermixing of white noise stimuli with audible speech was presented in order to create a higher level of expectancy, thus occasioning higher levels of top-down processing. Participants were presented 25 fragments of each in random order and asked to respond to each by pressing 1 of 5 buttons hereafter referred to as 1: positive speech illusion (endorsed hearing positive voice), 2: negative speech illusion (endorsed hearing negative voice), 3: neutral speech

illusion (endorsed hearing neutral voice), 4: no speech heard, and 5: uncertain; this latter option was included in order to make the ratings of 1–3 more conservative. The recordings were delivered using stimulation software E-prime 1.1 (Psychology Software Tools, Pittsburgh, Pennsylvania), and stimuli were reproduced in random order. The length of the task was approximately 15 min. The rate of hearing a voice in the white noise—only condition (25 trials) was the variable of interest in the analyses.

Wechsler Adult Intelligence Scale. General cognitive abilities and achievement, expressed as a single IQ score, were assessed using Similarities, Arithmetic, Vocabulary, Block Design, and Object Assembly subtests of the WAIS-III. 19,20

Flanker. The Flanker Continuous Performance test (http://www.cogtest.com)<sup>21,22</sup> is a measure of executive control of attention. The task is to respond by pressing the right or left mouse button depending on whether the middle element in a display of 5 lines has an arrowhead pointing to the right or left. There are 3 trial types. In neutral trials, the flankers are just horizontal lines without arrowheads. In congruent trials, all flankers have arrowheads pointing in the same direction as the target. In incongruent trials, the flankers have arrowheads pointing in the direction opposite to that of the target. The incongruent condition involves more cognitive effort because the flankers are associated with a response that needs to be suppressed. One half of the trials of each trial type are presented with the stimuli above the fixation cross on the screen, and the other half are presented below fixation, in order to prevent subjects from keeping their gaze fixed in one position. The test consists of 144 trials of neutral, congruent, and incongruent flankers, which are presented randomly. Outcome measures were the proportion of correct trials for the neutral, congruent, and incongruent conditions.

The Rey Auditory-Verbal Learning test. A Spanish version of the Rey Auditory-Verbal Learning test (RAVLT)<sup>23</sup> was used to measure auditory verbal episodic memory and related executive function. The test was presented as described by Spreen and Strauss.<sup>24</sup> The responses were recorded on a database solution based on FileMakerPro<sup>®</sup> to automate recording and analysis.<sup>25</sup> The test consists of 2 learning lists of 15 words and a third with the 30 words of the 2 learning lists and 20 distractor words. The test assesses learning, interference, and delayed free recall and recognition. Several indexes can be obtained. Outcomes used were immediate recall index (total proportional acquisition), delayed recall index (proportion correct delayed recall), and the retention index (proportion words retained).

OPCRIT. The Operational Criteria Checklist for Psychotic Illness and associated OPCRIT computer pro-

gram<sup>26</sup> were used to establish DSM-IV diagnosis on the basis of current symptomatology, assessed with the Positive and Negative Syndrome Scale (PANSS),<sup>27</sup> as well as lifetime psychopathology, as recorded in the case notes.

Structured Interview for Schizotypy—Revised. The Structured Interview for Schizotypy—Revised<sup>28</sup> was used to determine a broad range of schizotypal symptoms and signs. Items can be scored on a 4-point scale from absent (0) to severe (3). Positive schizotypy covers the symptoms referential thinking (2 items), magical ideation, illusions, psychotic symptoms, and suspiciousness (6 items). Negative schizotypy covers the symptoms social isolation, introversion, restricted affect, and poverty of speech (4 items). Mean schizotypy scores for these dimensions were calculated resulting in a positive schizotypy and a negative schizotypy score. Because both scores consisted of 4 equidistant values, they were recoded 0 to 3, for ease of interpretation of odds ratios (ORs).

## Analyses

In order to have sample constancy in the comparison between adjusted and nonadjusted analyses, only participants with complete values for white noise task, age, sex, and all the neurocognitive variables used were included in the analyses.

As white noise speech illusion scores for positive, negative, and neutral voices were highly skewed, the 3 outcomes were analyzed as dichotomous variables. In addition, a variable "any speech illusion" was constructed denoting the presence of any positive, negative, or neutral voice perceived in white noise.

In order to assess whether the white noise task was sensitive particularly to affectively salient speech illusions rather then neutral speech illusions, a composite variable was constructed reflecting positive or negative speech illusions. Subsequently, it was examined whether case-control differences in neutral speech stimuli would be reducible to affectively salient speech stimuli but not the other way around.

Case-control status was the binary response variable and white noise speech illusion the binary exposure variable in logistic regression models, all adjusted for age, sex, and years in full-time education. As controls (consisting of sib-pairs) and cases and their siblings pertained to the same family, multilevel logistic regression using the XTGEE routine in the STATA statistical program, version 11.0,<sup>29</sup> was conducted in order to correct standard errors of all reported ORs for clustering at the level of family. In order to test whether case-control differences were contingent on level of psychotic symptoms in the patients, case-control analyses were repeated with the patient group stratified according to mean PANSS-positive symptom score.

In order to test whether any association with white noise speech illusion was confounded by neuropsychological

**Table 1.** Sample Demographics and Neurocognition (% [n] or Mean [SD])

	Patients $(N = 30)$	Controls ( $N = 307$ )	Siblings $(N = 28)$	
Male sex	67% (20)	49% (149)	57% (16)	
Age (years)	25.3 (4.5)	20.9 (3.5)	25.9 (5.5)	
Years of full-time education	12.2 (1.8)	13.9 (2.8)	13.1 (2.7)	
WAIS-IQ	96.2 (16.2)	106.3 (14.4)	98.7 (16.2)	
Flanker congruent	0.85 (0.17)	0.96 (0.06)	0.95(0.07)	
Flanker incongruent	0.78 (0.17)	0.90 (0.10)	0.88 (0.15)	
Flanker neutral	0.88 (0.14)	0.96 (0.06)	0.94 (0.10)	
RAVLT immediate recall index	0.63 (0.16)	0.75 (0.10)	0.69 (0.11)	
RAVLT delayed recall index	0.60 (0.24)	0.81 (0.15)	0.73 (0.19)	
RAVLT retention index	0.052 (0.01)	0.061 (0.01)	0.059 (0.01)	

Note: WAIS-IQ, Wechsler Adult Intelligence Scale intelligence quotient; RAVLT, the Rey Auditory-Verbal Learning test.

impairment, models were additionally adjusted for WAIS-IQ score; Flanker proportion of correct trials for the neutral, congruent, and incongruent conditions; and RAVLT immediate recall index, delayed recall index, and retention index.

In order to assess the association between white noise speech illusion and schizotypy in controls, multilevel logistic regression models of the binary response variable "any speech illusion" were assessed with 4-level schizotypy variables as exposure variables, adjusted for age, sex, and years in full-time education. The same analysis was conducted in the sibling group—although this latter analysis was underpowered, it was conducted to test for similarity of direction of effects.

In order to test the hypothesis that white noise responses systematically increased over the levels of the familial risk variable (a 3-level variable "group": 0 = controls, 1 = siblings of patients, and 2 = patients), as would be expected if white noise represented an intermediary cognitive phenotype, <sup>30–32</sup> the model with the linear effect of the group variable was compared, by likelihood ratio test, with the group variable entered as a set of dummy variables. A large or significant improvement of the latter over the former is evidence of deviation from linearity.

#### Results

#### Sample

Cases were older than controls, more frequently male, and had spent less time in full-time education (table 1). The majority of cases and controls were from social classes 3 and 4. Diagnoses in the cases were as follows: schizophrenia or schizophreniform disorder (n = 24), affective psychosis (n = 3), and psychotic disorder NOS (n = 3); mean GAF score was 43 (SD = 20.3); and mean age at first treatment for psychosis was 21.0 years (SD = 3.0). All patients were taking antipsychotic medication and had been receiving an antipsychotic for a mean of 4.8 years. Total PANSS score was 67.6 (SD = 15.0; neg-

ative subscore: 19.0, SD = 5.0; positive subscore: 16.3, SD = 6.6; general score: 32.3, SD = 7.5). Patients had lower scores on all neurocognitive variables (table 1; standardized effect sizes controlled for age, sex, and years of education; WAIS-IQ score: -0.13; Flanker neutral condition: -0.33, Flanker congruent condition: -0.38, and Flanker incongruent condition: -0.33; RAVLT immediate recall index: -0.30, RAVLT delayed recall index: -0.33, and RAVLT retention index: -0.22; all effect sizes P < .001, except WAIS-IQ P = .009).

#### Case-Control Speech Illusions

The rate of any speech illusion was 9% in controls and 30% in cases (OR = 4.0, 95% confidence interval [CI] = 1.1-14.2). Splitting the patient group around the median value of the PANSS-positive psychotic symptom score revealed a much higher OR in the case-control comparison for patients with the highest level of positive symptoms (OR = 5.3, 95% CI = 1.5-18.9) compared with those with the lowest level (OR = 2.0, 95% CI = 0.4-10.2). This contrast was not apparent when analyses were split according to level of PANSS general symptom score (ORs of 4.3 and 3.6, respectively).

In the combined sample of cases and controls and controlling for case-control status, age, sex, and years of education, no speech illusion was associated with any of the neurocognitive variables, with the exception of an association with lower WAIS-IQ (standardized effect size: -0.10, P = .038); effect sizes for speech illusions associated with case-control status were not reduced after adjustment for neurocognitive variables (table 2). ORs were higher for affectively appraised speech illusions (positive or negative) compared with affectively neutral speech illusions (table 2).

The adjusted OR for the composite variable reflecting positive or negative speech illusions was 11.2 (95% CI = 2.0–63.3) and 4.4 (95% CI = 1.1–16.8) for the neutral speech illusion. Entering both neutral and combined positive/negative speech illusions in the same model revealed

Table 2. White Noise Speech Illusion in Cases and Controls, Before and After Adjustment for Neurocognition

	Control ( $N = 307$ ) % ( $n$ )	Case $(N = 30) \% (n)$	OR <sup>a</sup> (95% CI)	Adjusted OR <sup>b</sup> (95% CI)	
Positive speech illusion	1 (4)	17 (5)	13.3 (2.3–76.3)	9.4 (1.02–85.9)	
Negative speech illusion	2 (7)	17 (5)	8.6 (1.8–40.9)	19.0 (2.4–150.0)	
Neutral speech illusion	7 (21)	27 (8)	4.2 (1.3–13.5)	4.4 (1.1–16.8)	
Any speech illusion	9 (27)	30 (9)	4.0 (1.4–11.7)	3.8 (1.04–14.1)	

Note: OR, odds ratio; CI, confidence interval.

that the effect size for the neutral condition was reducible to the positive/negative speech illusion but not the other way around (OR neutral speech illusion: 2.4, 95% CI = 0.5-11.3; OR positive/negative speech illusion: 7.4, 95% CI = 1.02-53.6).

Schizotypy and Speech Illusions in Controls and Siblings

In the controls, any speech illusion was strongly associated with positive schizotypy but not with negative schizotypy (table 3). Similar associations were apparent for the siblings (age-, sex-, and years of education-adjusted OR linear trend positive schizotypy: 3.9, 95% CI = 0.8–18.9; age-, sex-, and years of education-adjusted OR linear trend negative schizotypy: 1.2, 95% CI = 0.5–3.2).

## Reference Control Group

In the group of reference controls (n = 97; mean age 23.4 years, SD = 4.8; proportion males 49%), the rate of pos-

**Table 3.** Associations between white noise speech illusion and schizotypy in the controls

	N	n With Any Speech Illusion	% With Any Speech Illusion	OR <sup>a</sup> (95% CI)
Positive schizotypy				
Level 1	259	17	7	1
Level 2	38	7	18	3.7 (1.3–10.1)
Level 3	6	2	33	10.3 (1.6–68.5)
Level 4	4	1	25	4.3 (0.4–50.8)
Linear trend		_		2.4 (1.4–4.1)
Negative schizotypy				
Level 1	242	19	8	1
Level 2	44	6	14	2.2 (0.8–6.1)
Level 3	16	2	13	1.3 (0.3–6.4)
Level 4	5	0	0	_ ` ′
Linear trend				1.1 (0.6–2.0)

*Note*: Abbreviations are explained in the first footnote to table 2. <sup>a</sup>OR adjusted for age, sex, years of education, and familial clustering in controls; any speech illusion was response variable; 4-level schizotypy was exposure variable (level 1 reference category).

itive speech illusions (1%, n = 1), negative speech illusions (2%, n = 2), and neutral speech illusions (7%, n = 7) was the same as in the sib-pair control group (table 2), as was the rate of any speech illusion (10%, n = 10).

## Test for Trend Across Risk Groups

The test of trend for the ranks across ordered groups revealed a significant trend across controls (9% any speech illusion), siblings of patients (14%), and patients (30%), indicative of progressively higher rates of speech illusions with increasing familial vulnerability for psychotic disorder (table 4).

### Discussion

The tendency to detect affectively salient speech illusions in random noise was (1) more prevalent in patients with a psychotic disorder, (2) progressively greater across groups with increasing familial risk for psychotic disorder, and (3) associated with high levels of positive but not negative schizotypy in healthy controls and siblings of patients, independent of measures of neurocognition. The results therefore suggest that white noise speech illusion reflects individual differences in risk for psychotic symptoms and disorder.

Contrary to the findings reported by Roiser and colleagues, 15 evidence for altered salience attribution using the white noise task was present despite the prescription of antipsychotic medication in patients. This may not be considered surprising, however, because many patients continue to display positive symptoms despite antipsychotic medication, ie, continue to display mechanisms of ascribing altered meaning and emotional value to experience. The results indeed suggest greater effect sizes when patients with higher levels of positive symptoms were selected for analysis, again suggesting that the white noise task may be specific for the positive symptom domain. Although it could be argued that the larger effect size for patients with psychotic symptoms was caused by patients actually hallucinating during the task, this mechanism cannot explain the parallel finding of an association between speech illusion and schizotypy in controls.

<sup>&</sup>lt;sup>a</sup>OR adjusted for familial clustering in controls, age, sex, and years of education only.

<sup>&</sup>lt;sup>b</sup>OR adjusted for familial clustering in controls, age, sex, and education and additionally for Wechsler Adult Intelligence Scale intelligence quotient score; Flanker proportion of correct trials for the neutral, congruent, and incongruent conditions; and the Rey Auditory-Verbal Learning test immediate recall index, delayed recall index, and retention index.

Table 4. White Noise Speech Illusion Across Ordered Risk Groups

	Any Speech Illusion	OR <sup>a</sup> (95% CI)	Positive Speech Illusion	OR <sup>a</sup> (95% CI)	Negative Speech Illusion	OR <sup>a</sup> (95% CI)	Neutral Speech Illusion	OR <sup>a</sup> (95% CI)
Controls ( $n = 307$ )	9% (27)	1 <sup>b</sup>	1% (4)	1 <sup>b</sup>	2% (7)	1 <sup>b</sup>	7% (21)	1 <sup>b</sup>
Siblings $(n = 28)$	14% (4)	1.82 (0.54–6.14)	0% (0)	_	4% (1)	1.65 (0.17–16.50)	11% (3)	1.80 (0.46–7.06)
Patients $(n = 30)$	30% (9)	4.20 (1.52–11.59)	17% (5)	12.37 (2.16–70.70)	17% (5)	8.80 (1.98–39.10)	27% (8)	5.01 (1.69–14.85)
OR linear trend Test for deviation from linearity <sup>a</sup>	2.03 (1.23–3.35) $\chi^2 = 0.06, P = .81$		_				$2.21 (1.29 - \chi^2 = 0.13,$	,

Note: Abbreviations are explained in the first footnote to table 2.

The findings may have relevance for 2 mechanisms that have been proposed to mediate psychotic symptoms: altered top-down processing of sensory information and altered attribution of salience. It has been proposed that, to the degree that perception represents a reconstructive process resulting from the balance between top-down expectations and interpretations on the one hand and bottom-up sensory information on the other, hallucinations may result from a state of imbalance between top-down and bottom-up pathways of experience.<sup>7,8,10,11</sup> The finding that white noise was imbued with the meaning of human speech in the current study is in agreement with such a mechanism.

Another recent theory may be invoked to interpret the findings, particularly in relation to the finding of differential attribution of emotional value associated with speech illusion. Thus, it has been suggested that psychosis may arise when a neutral stimulus becomes imbued with an emotional quality, thus influencing behavior and commanding attention<sup>5,6</sup> and inducing the patient to develop a cognitive scheme (delusion) to explain this experience of altered emotional value. Although the difference in effect sizes between neutral and affective speech illusions were suggestive, the CIs overlapped so that it cannot be assumed that the white noise task is truly specific for affectively salient speech illusions. However, further analyses revealed that case-control differences for neutral speech illusions were reducible to affectively salient speech illusions but not the other way around. It cannot be excluded that patients displayed a greater tendency to display affectively salient speech illusions simply because they were in a greater state of emotional turmoil. However, this may not be likely because speech illusion effect sizes did not depend on the PANSS general symptom score to the same degree as was observed for the PANSS-positive symptom score.

Strengths of the study were the large sample of controls, the interview-based measures of schizotypy, the ex-

perimental design, the targeted younger age group, and adequate control for neurocognitive measures. To the degree that the controls were younger, and the rate of both psychotic experiences and speech illusions may be higher in younger age groups, unadjusted results may be considered conservative. Weak points were the relatively small sample size of patients and their siblings, resulting in wide CIs, and absence of technology allowing for quantification of task-related brain processing, as has been shown recently for exposure to white noise 33 and the reward aspect of salience.<sup>34</sup> The control group consisted of sibpairs and this, given that sibs resemble each other, may have impacted negatively on statistical power and also may have affected representativeness. However, it was shown, using a second reference control group, that rates of speech illusions were stable across control samples and thus likely reflect the population rate.

Clearly, the white noise task cannot be considered a diagnostic test, given the fact that 70% of patients did not display speech illusions. Instead, it may be considered as a risk factor, similar to findings that a third of patients with schizophrenia display ventricular volumes that are larger than 1 SD above the mean of controls, 35 or evidence that probabilistic reasoning bias can be demonstrated in a third of the patient population,<sup>32</sup> or, finally, that evidence of a family history of schizophrenia is present in 20% of patients. However, if sensitivity could be improved, the white noise task may be suitable to assess vulnerability in population samples, eg, for the purpose of etiological or high-risk studies. Thus, although these findings must be considered preliminary and await replication and extension, the use of a simple and brief task of altered top-down processing and/or altered attribution of meaning or emotional value to experience, without the need for lengthy conditioning procedures, may have advantages in research. For example, it would be possible to examine to what degree affectively salient speech illusions represent a state associated with active

<sup>&</sup>lt;sup>a</sup>Adjusted for age, sex, years of education, and familial clustering in control and case sibling pairs.

<sup>&</sup>lt;sup>b</sup>Reference value.

psychotic symptoms, which may change with treatment. Alternatively, affectively salient speech illusions may represent a trait indexing, at least to a degree, psychosis vulnerability. The current results suggest it may be both because patients with higher levels of symptoms displayed higher levels of speech illusions, whereas controls with stable trait psychometric vulnerability displayed similar alterations, as did siblings at higher than average genetic risk for psychotic disorder.

In conclusion, evidence was presented that random noise, presented in an experimental design, may be used to uncover the state-mediated trait to ascribe meaning and emotional value to experience, a process associated with psychotic symptoms and disorder, independent of measures of information processing. Further development of this paradigm may be helpful for research.

#### References

- Van Rossum I, Dominguez M, Lieb R, Wittchen H-U, van Os J. Affective dysregulation and reality distortion: a 10-year prospective study of their association and clinical relevance. Schizophr Bull. September 30, 2009; doi: 101093/ schbul/sbp101.
- Van Os J, Linscott RJ, Myin-Germeys I, Delespaul P, Krabbendam L. A systematic review and meta-analysis of the psychosis continuum: evidence for a psychosis proneness-persistence-impairment model of psychotic disorder. *Psychol Med.* 2009;39:179–195.
- 3. Polanczyk G, Moffitt TE, Arseneault L, et al. Childhood psychotic symptoms share etiological and clinical features with adult schizophrenia: results from a representative birth cohort. *Arch Gen Psychiatry*. In press.
- Collip D, Myin-Germeys I, Van Os J. Does the concept of "sensitization" provide a plausible mechanism for the putative link between the environment and schizophrenia? Schizophr Bull. 2008;34:220–225.
- Gray JA, Feldon J, Rawlins JNP, Hemsley D, Smith AD. The neuropsychology of schizophrenia. *Behav Brain Sci.* 1991; 14:1–84.
- Kapur S. Psychosis as a state of aberrant salience: a framework linking biology, phenomenology, and pharmacology in schizophrenia. Am J Psychiatry. 2003;160:13–23.
- 7. Hoffman RE, Woods SW, Hawkins KA, et al. Extracting spurious messages from noise and risk of schizophrenia-spectrum disorders in a prodromal population. *Br J Psychiatry*. 2007;191:355–356.
- Vercammen A, Aleman A. Semantic expectations can induce false perceptions in hallucination-prone individuals. *Schiz-ophr Bull.* 2010;36:151–156.
- Maher BA. Delusional thinking and perceptual disorder. J Individ Psychol. 1974;30:98–113.
- Hoffman RE. New methods for studying hallucinated 'voices' in schizophrenia. Acta Psychiatr Scand Suppl. 1999;395: 89–94.
- 11. Vercammen A, de Haan EH, Aleman A. Hearing a voice in the noise: auditory hallucinations and speech perception. *Psychol Med.* 2008;38:1177–1184.
- 12. Bentall RP. The illusion of reality: a review and integration of psychological research on hallucinations. *Psychol Bull*. 1990;107:82–95.

- 13. Merckelbach H, van de Ven V. Another White Christmas: fantasy proneness and reports of 'hallucinatory experiences' in undergraduate students. *J Behav Ther Exp Psychiatry*. 2001;32:137–144.
- Corlett PR, Simons JS, Pigott JS, et al. Illusions and delusions: relating experimentally-induced false memories to anomalous experiences and ideas. Front Behav Neurosci. 2009;3:53.
- 15. Roiser JP, Stephan KE, den Ouden HE, Barnes TR, Friston KJ, Joyce EM. Do patients with schizophrenia exhibit aberrant salience? *Psychol Med.* 2009;39:199–209.
- Holt DJ, Titone D, Long LS, et al. The misattribution of salience in delusional patients with schizophrenia. Schizophr Res. 2006;83:247–256.
- 17. Krabbendam L, Marcelis M, Delespaul P, Jolles J, Van Os J. Single or multiple familial cognitive risk factors in schizophrenia? *Am J Med Genet*. 2001;105:183–188.
- 18. Galdos PM, Van Os JJ, Murray RM. Puberty and the onset of psychosis. *Schizophr Res.* 1993;10:7–14.
- 19. Wechsler D. WAIS-III Administration and Scoring Manual. San Antonia, TX: The Psychological Corporation; 1997.
- Lopez JM, Santin C, Torrico E. Utilidad de las formas cortas de la Escala de Inteligencia de Wechler para adultos (WAIS). An Psicología. 2003;1:53–63.
- Eriksen BA, Eriksen CW. Effects of noise letters upon the identification of a target letter in a nonsearch task. *Percept Psychophys.* 1974;16:143–149.
- 22. Posner MI, Inhoff AW, Friedrich FJ, Cohen A. Isolating attentional systems: a cognitive-anatomical analysis. *Psychobiology*. 1987;15:107–121.
- Rey A. L'examen Clinique en Psychologie [Clinical Assessment in Psychology]. Paris: Presses Universitaires de France; 1964.
- 24. Spreen O, Strauss E. A Compendium of Neuropsychological Tests. Adminstration, Norms, and Commentary. 2nd ed. New York, NY: Oxford University Press; 1998.
- 25. Amer G, García Soriano MT, García A, Tarongí S, Barceló I. Registro Automatizado del test de aprendizaje auditivoverbal de Rey. Descripción e implementación en una consulta de Neurología Cognitiva y de la Conducta. *Neurologia*. 2001;16:456–457.
- McGuffin P, Farmer A, Harvey I. A polydiagnostic application of operational criteria in studies of psychotic illness. Development and reliability of the OPCRIT system. *Arch Gen Psychiatry*. 1991;48:764–770.
- 27. Kay SR, Fiszbein A, Opler LA. The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophr Bull*. 1987;13:261–276.
- 28. Vollema MG, Ormel J. The reliability of the structured interview for schizotypy-revised. *Schizophr Bull*. 2000;26:619–629.
- StataCorp. STATA Statistical Software: Release 11. College Station, TX: StataCorp; 2009.
- Fusar-Poli P, Perez J, Broome M, et al. Neurofunctional correlates of vulnerability to psychosis: a systematic review and meta-analysis. *Neurosci Biobehav Rev.* 2007;31:465–484.
- 31. Dickinson D, Ramsey ME, Gold JM. Overlooking the obvious: a meta-analytic comparison of digit symbol coding tasks and other cognitive measures in schizophrenia. *Arch Gen Psychiatry*. 2007;64:532–542.
- 32. Van Dael F, Versmissen D, Janssen I, Myin-Germeys I, van Os J, Krabbendam L. Data gathering: biased in psychosis? *Schizophr Bull*. 2006;32:341–351.
- 33. Tregellas JR, Ellis J, Shatti S, Du YP, Rojas DC. Increased hippocampal, thalamic, and prefrontal hemodynamic

- response to an urban noise stimulus in schizophrenia. Am J Psychiatry. 2009;166:354–360.
- 34. Murray GK, Corlett PR, Clark L, et al. Substantia nigra/ventral tegmental reward prediction error disruption in psychosis. *Mol Psychiatry*. 2008;13(239):267–276.
- 35. Andreasen NC, Swayze VW, Flaum M, Yates WR, Arndt S, McChesney C. Ventricular enlargement in schizophrenia evaluated with computed tomographic scanning. Effects of gender, age, and stage of illness. *Arch Gen Psychiatry*. 1990;47:1008–1015.