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Affectively salient signal to random noise might be used to identify psychosis vulnerability in severe mental disorders

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ABSTRACT

Background: Subclinical psychotic symptoms are present in the general population. Furthermore, they are quite common in diagnostic categories beyond psychosis, such as BPD patients.
Methods: We want to assess the differences between 3 groups: BPD (n = 68), FEP (n = 83) and controls (n = 203) in an experimental paradigm measuring the presence of speech illusions in white noise. The Positive and Negative Syndrome Scale was administered in the patient group, the Structured Interview for Schizotypy-Revised, and the Community Assessment of Psychic Experiences in the control and BPD group. The white noise task was also analysed within a signal detection theory (SDT) framework. Logistic regression analyses and the general linear models were used to analyse the adjusted differences between groups.
Results: Differences were more prevalent in signals that were perceived as affectively salient in patients groups (9.6% in FEP vs 5.9% in BPD and 1% in controls; OR: 10.7; 95%CI: 2.2–51.6, p = 0.003 in FEP; OR: 6.3; 95%CI: 1.1–35.0, p = 0.036 in BPD). Besides, we found a worse general performance and more false alarms in the task for FEP group using SDT framework.
Conclusions: Experimental paradigms indexing the tendency to detect affectively salient signals in noise may be used to identify liability to psychosis in people with vulnerability. Its predictable value in other diagnostic categories and general population requires further research.

1. Introduction

Aberrant salience is the incorrect assignment of importance to neutral stimuli [1]. Contemporary models of psychosis [2] propose that the inappropriate processing of stimuli that would normally be considered irrelevant, due to “aberrant salience”, drives the development of psychotic symptoms, such as delusions and hallucinations. In the context of this model, “salience” refers to the motivational properties of a stimulus, which can cause it to attract attention and drive behaviour [3]. This aberrant salience is thought to generate a distorted model of the environment founded on erroneous inference [4]. Data from experimental animals suggest that aberrant motivational salience attribution results from out-of-context dopamine signalling in the ventral striatum [5], which may in turn be driven by abnormal regulation of subcortical dopamine transmission by the prefrontal cortex [4] and hippocampus [6].

First rank psychotic symptoms may be more common in schizophrenia than in other categories but their diagnostic value is too low to be of diagnostic importance [7]. Indeed, psychotic-like experiences are also common in the general population and in severe mental disorders such as, borderline personality disorder (BPD) [8,9]. Recent studies support the idea that the difference in psychotic experiences between BPD and schizophrenia are unclear and these experiences are quite similar in both groups of patients [10,11].

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These "subtle expressions of psychotic experiences" (common in clinical and non-clinical populations) offer clinicians a new way of understanding psychotic experience [12]. A recent study has found that hallucinations in healthy controls (HC) and patients only differ in the fact that patients have them with increased frequency, distress, negative content and less control perceived over them [13]. In trying to explain the underpinning mechanism of auditory hallucinations from a cognitive point of view, several mechanisms have been suggested, such as monitoring deficits and misattributions [14]. A dysregulation in top-down processing has been proposed to explain this mechanism [15,16].

Two recent studies have found that the tendency to identify affectively salient speech illusions in random noise was more prevalent in patients with a psychotic disorder than in HC independent of measures of neurocognition [17,18]. These results therefore suggest that white noise speech illusion could reflect individual differences in the risk of developing psychotic symptoms.

Several approaches toward experimental assessment of speech illusions have been reported [15,19]. It may 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.

In the current investigation, an extension of the 'false-positive meaning' approach was used as described in a previous paper introducing the 'white noise test' [17]. We wanted to evaluate the relation between psychotic-like experiences (speech illusions) in patients with first episode psychosis (FEP), patients at risk of developing psychosis (BPD) and HC.

The aim of the current study, therefore, was to measure (1) the variation in detecting affectively salient speech in neutral random signals (white noise) in three groups (BPD, FEP and controls), hypothesizing that affectively salient meaning attributed to white noise would be associated with mainly FEP patient status, and (2) the relation between speech illusion and psychometric vulnerability status in the form of positive psychotic experiences (schizotypy) in controls and BPD, and with positive symptoms in FEP.

2. Material and methods

2.1. Sample

Data were collected in a convenience sample of patients with a diagnosis of FEP and BPD, admitted consecutively to the inpatient unit of Basurto University Hospital (HUB) from January 2011 to December 2016. BPD patients were also collected from Day Hospital Units of HUB and AMSA clinic. Controls were recruited from the general population in the same catchment area as the patients, through advertisements and announcements. Controls did not report psychotic first-degree relatives. Patients were examined when the psychiatrist in charge considered that they were stable and were able to provide written informed consent. Inclusion criteria were the following (for the three groups): age between 18 and 65 years, sufficient mastery of the Spanish language, IQ >70; for FEP patients: exposure to antipsychotic medication <1 year. The psychotic episode fulfilled DSM-IV-TR criteria for affective or non-affective psychotic disorder; for BPD patients fulfilled DSM-IV-TR criteria for BPD, in the absence of any current psychotic disorder comorbidity. Exclusion criteria for FEP patients were: psychotic episode was the consequence of a somatic disorder and for all three groups: unwillingness to participate.

Two of the BPD had a history of psychotic symptoms. Sociodemographic variables were collected including age, sex, employment status, marital status and living arrangements. In the patient group, clinical scales such as the PANSS (Positive and Negative Syndrome Scale) [20] and GAF (Global Assessment of Functioning) [21] were used to assess functional impact of psychopathology. The Operational Criteria Checklist for Psychosis [22] was completed, based on clinical instruments and relevant data in the medical history, and used to establish the diagnosis of the patients using the associated OPCRIT computer programme [23].

2.2. Instruments

2.2.1. White noise

This task has been described previously [17,18]. 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. Participants were presented 25 fragments of each, in random order, and were 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: heard speech but uncertain whether voice was positive, negative or neutral. The rate of hearing a voice in the white noise–only condition (25 trials) was the variable of interest in the analyses. A dichotomous variable was created (speech illusion present versus not present) in which a speech illusion was considered a positive result. When a participant gave affective value to the speech illusion (negative or positive speech illusion), affectively salient speech illusion was considered. Two or more conditions were necessary for a positive result when the answer in the white noise task was 5.

2.2.2. SIS-R

The Structured Interview for Schizotypy–Revised [24] was used to determine a broad range of schizotypal symptoms and signs. Items can be scored on a 4-point scale from absent to severe (0–3). Positive schizotypy covers the symptoms referential thinking (2 items), magical ideation, illusions, psychotic symptoms, and suspiciousness (6 items). Negative schizotypy covers the symptoms of 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. In the analyses, SIS-R positive symptom score was used, divided by its median value, creating median groups.

2.2.3. CAPE

Community Assessment of Psychic Experiences [25] was used to assess the lifetime prevalence of positive and negative and depressive symptoms. This self-reporting scale measures positive and negative and depressive symptoms on both a frequency scale (0 = never to 4 = nearly always) and a distress scale (1 = not distressed to 4 = very distressed). In the analyses, CAPE positive symptom score was used, divided by its median value, creating median groups.

2.2.4. IQ

The short form of the Wechsler Adult Intelligence Scale – III [26] was assessed for an indication of intellectual functioning (IQ)

2.3. Signal detection theory (SDT)

The white noise task was also analysed within a signal detection theory (SDT) framework. SDT describes the probabilistic processes of decision-making under conditions of uncertainty [27,28]. In a SDT-based task, subjects are required to detect the presence of a

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target stimulus under conditions of relative uncertainty. To apply the SDT to the white noise task, we considered the "white noise with neutral speech" as target, and the "white noise only" as non-target, and the following four parameters were calculated:

a Target identification accuracy (Hits), being the proportion of trials correctly identified as targets (that is, the subject responds to hear a neutral voice).
b Non-target identification accuracy, being the proportion of trials correctly identified as non-targets (that is, the subject responds no speech heard).
c Target identification median reaction time (Hits RT).
d Non-target identification median reaction time (nonT RT).

Then, the following performance indices derivable from SDT were chosen to analyse: hits, false alarms (FA), Hits RT, nonT RT, the discriminability index *d'* as a global measure of performance, and response bias *c*, defined as the amount of certainty needed to make a decision on the response (a low value of *c* means that less information is needed to detect the target) [27]. *FA* is defined as:

FA = 1–(non target identification accuracy)

For the analyses, standardized scores for Hits (z-Hits), FA (z-FA), Hits RT (z-Hits RT) and nonT RT (z-nonT RT) were calculated. To calculate *d'* and *c* the formulas describes by Stanislaw and Todorov [29] were used.

2.4. Analyses

Socio-demographic differences between groups were assessed. A Kolmogorov-Smirnov test was used to test for deviation from normality. ANOVA was used to examine differences in continuous variables, and Kruskal-Wallis test was used for non-normally distributed variables. In the case of categorical variables, chi-square tests, and Fisher's exact test, when indicated, were performed.

Group differences in percentage of speech illusions and affectively salient illusions were assessed with Fisher 's exact test. As white noise speech illusion scores for positive, negative, and neutral voices were highly skewed, the 3 outcomes were analysed as dichotomous variables, consistent with previous works [17,18]. An "any speech illusion" variable was constructed denoting the presence of at least one instance 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 than neutral speech illusions, a composite variable was constructed reflecting any positive or negative speech illusions.

Affectively salient speech illusion was the binary response variable in logistic regression models, all adjusted for age, sex, cannabis abuse and IQ. In the group comparison of affectively salient speech illusions, non-affectively salient speech illusions were excluded from the analysis. In order to test whether differences were reducible to cognitive alterations, models were additionally adjusted for WAIS-IQ score. Adjusted ORs were obtained by adding the confounders to the logistic regression model.

In order to assess, in the patient group, whether speech illusions were associated with the binary PANSS positive symptom variable, logistic regression analyses were run with any speech illusions as the dependent variable and PANSS-positive symptom variable as independent variable.

In order to assess, in the control and BPD group, the association between white noise speech illusion on the one hand, and binary schizotypy and binary CAPE positive symptoms and SIS-R positive on the other, logistic regression models of "any speech illusion" and "affectively salient speech illusion" were run, adjusted for age and sex.

The SDT measures were compared between the three groups by means of ANOVA with Scheffe's test for multiple comparisons or the non-parametric Kruskal-Wallis test. These analyses were also performed adjusting for age, sex, cannabis abuse and IQ, by means of the general linear model (GLM). The SDT measures were considered as dependent variable, and the group and adjusting variables as independent. In the final models only significant adjusting variables were considered (IQ).

The statistical analyses were carried out using the Stata software programme, version 12 [30].

Table 1
Socio-demographic variables.

		FEP (*n* = 83)	BPD (*n* = 68)	Controls (*n* = 203)
		N (%) Mean (SD)	*N (%) Mean (SD)*	*N (%) Mean (SD)*
Sex*	Male	49 (59%)	22 (32%)	112 (55%)
	Female	34 (41%)	46 (68%)	91 (45%)
Age (years)*		36.2 (12.9)	35.4 (11.5)	31.3 (11.6)
Education (years)*		15.7 (3.0)	16.2 (2.9)	17.6 (2.4)
Employment*	Unemployed	36 (43.4%)	36 (53%)	36 (18%)
	Active	35 (42.2%)	16 (23.5%)	96 (47.8%)
	Student	8 (9.6%)	9 (13.2%)	63 (31.3%)
	Retired	3 (3.6%)	2 (3%)	3 (1.5%)
	Others	5 (7.3%)	1 (1.2%)	3 (1.5%)
Socio-economic level*	Upper class	0	4 (5.9%)	0
	Upper middle class	12 (14.5%)	8 (11.8%)	30 (14.8%)
	Middle class	53 (63.9%)	44 (64.7%)	160 (78.8%)
	Low middle class	17 (20.5%)	11 (16.2%)	13 (6.4%)
	Low	1 (1.2%)	1 (1.5%)	0
Marital status*	Single	51 (61.4%)	34 (50%)	120 (59.1%)
	Married/Partner	22 (26.5%)	24 (35.3%)	79 (39%)
	Divorced	7 (8.4%)	10 (14.7%)	4 (2%)
	Widowed	3 (3.6%)	0	0
Housing*	Parents	45 (54.2%)	32 (47%)	102 (50.2%)
	Partner/Family	23 (27.7%)	24 (35.3%)	85 (41.9%)
	Alone	15 (18%)	12 (17.6%)	16 (7.9%)
WAIS-IQ*		96.7 (15.2)	97 (13)	110.1 (15.4)

*Differences are statistically significant.

Table 2
Relation between psychotic symptoms and speech illusions.

	FEP			*BPD*			*HC*		
	X (SD)		p	X (SD)		p	X (SD)		p
Speech illusion 2	Yes	No		Yes	No		Yes	No	
PANSS positive (N = 83)	31.0 (8.1)	29.1 (9.9)	0.4						
PANSS negative	14.4 (9.3)	10.4 (6.9)	**0.03**						
PANSS general	42.0 (10.7)	42.0 (10.8)	0.9						
SIS-R positive (N = 181 HC)							2.0 (2.1)	1.5 (1.6)	0.2
SIS-R negative							1.7 (1.5)	1.5 (1.3)	0.4
CAPE positive (N = 65 BPD) (N = 194 HC)				11.2 (8.4)	11.0 (6.4)	0.9	4.9 (3.6)	4.1 (2.7)	0.1
CAPE negative				14.0 (6.5)	15.3 (8.2)	0.6	7.3 (4.4)	6.8 (4.1)	0.5
CAPE depressive				12.6 (5.6)	12.0 (4.8)	0.1	6.0 (3.3)	4.5 (2.5)	**0.003**

3. Results

3.1. Sample characteristics

83 FEP, 68 BPD and 203 controls were assessed at baseline. FEP, BPD and control subjects showed statistically significant differences in sex, age, level of education, marital status, socioeconomic status, housing and IQ (Table 1). Diagnoses in the FEP group were: schizophrenia or schizophreniform disorder (n = 44), affective psychoses (n = 21), brief psychotic episode (n = 3), delusional disorder (n = 9) and psychosis not otherwise specified (n = 6). All FEP and BPD patients were taking medication at the time of the assessment.

3.2. Affectively salient speech in neutral random signals

FEP patients had a much higher rate of speech illusions than BPD and controls (15.8% of controls, 17.6% of BPD and 39.8% of FEP, p < .001), differences between FEP and controls; and between FEP and BPD reached statistical significance (p = 0.003). However, there were no differences between BPD and controls.

FEP and BPD patients and had a much higher rate of affectively salient speech illusions than controls (9.6% versus 1.0% and 5.9%, respectively, p = 0.02). In general terms, the possibility of having an affectively salient speech illusion was much higher in the patient group (OR: 10.7; 95%CI: 12.2–51.6, p = 0.003 in FEP; OR: 6.3; 95%CI: 1.1–35.0, p = 0.036 in BPD). When we adjusted the model by sex, age, cannabis abuse and IQ, this result was only maintained in the FEP group (p = 0.03).

3.3. Speech illusion and positive psychotic dimension

Interestingly, speech illusions in the 3 groups were not associated with positive symptomatology. We found an association with negative dimension in the FEP group and with depressive dimension in the control group (Table 2).

3.4. Speech illusion and IQ

There was a relation with affectively salient speech illusions and IQ (p = 0.028). Subjects with low IQ had more possibilities of suffering speech illusions. Nevertheless, the relation between the FEP group and affectively salient speech illusion remained statistically significant when the model was adjusted for IQ (OR: 8.4, CI95%: 1.6–43.6, p = 0.01) or other variables such as sex, age, and cannabis abuse. The difference in BPD group did not reach statistical difference when IQ was taken into account, however, we could identify a tendency (OR: 4.9, CI95%: 0.8–29.1).

3.5. SDT frame-work

The main results of SDT analyses are shown in Table 3. We lost some data for the analyses with SDT method (FEP = 73, BPD = 67, HC = 201). After performing SDT, we found in the adjusted model by IQ, that FEP group had worse general performance (*d'*) and more FA answers. Besides, they had larger time of reaction time than controls and BPD group. There were no differences in hits index or in response bias *c*.

Table 3
SDT analyses, unadjusted and adjusted analyses.

SDT variables	Unadjusted analyses				*Adjusted analyses**			
	FEP[a]	BPD[b]	HC[c]		BPD vs FEP		HC vs FEP	
	X (SD)	X (SD)	X (SD)	p-value	β	p-value	β	p-value
z-Hits	−0.20 (1.10)	−0.02 (0.96)	0.07 (0.97)	0.1452	0.13	0.4197	0.07	0.6104
z-FA	0.30 (1.46)[c]	0.04 (1.33)	−0.12 (0.56)[a]	**0.0018**	-0.25	0.1339	−0.33	**0.0233**
z-Hits RT	0.66 (1.46)[b,c]	−0.12 (0.93)[a]	−0.20 (0.67)[a]	<**0.0001**	-0.68	<**0.0001**	−0.78	<**0.0001**
z-nonT RT	0.76 (1.43)[b,c]	−0.09 (0.86)[a]	−0.25 (0.67)[a]	<**0.0001**	-0.83	<**0.0001**	−0.92	<**0.0001**
Index *d'*	0.78 (0.95)[c]	1.06 (0.83)	1.21 (0.58)[a]	**0.0038**	0.24	**0.0447**	0.23	**0.0272**
Response bias *c*	1.20 (0.44)	1.25 (0.44)	1.26 (0.26)	0.7524	0.05	0.3752	0.06	0.1812

* Comparison of the SDT variables between groups adjusting for WAIS by means of the general linear models.
SD: standard deviation; β: beta parameter estimated from the general linear model, considering the FEP group as reference group; Ref: Reference group.
a,b,c Superscript letters indicate significant differences among groups by Scheffe test for multiple comparisons.

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4. Discussion

FEP patients demonstrated higher rates of speech illusions than the BPD group and control subjects, particularly speech illusions perceived as affectively salient. Moreover, BPD patients presented a higher proportion of affectively salient speech illusion compared to controls, but these differences did not maintain after adjusting for confounding factors. These results agree with those described in other papers. Interestingly, speech illusions were not associated with positive symptomatology in any group contrary to previous studies [17,18]. Up to our knowledge, this is the first time SDT frame-work was applied to white noise task. The discriminability index for the task was significantly worse in FEP group, and the number of FA detected was higher. However, no differences were found in response bias or in detected hits.

The higher proportion of affectively salient speech illusions in BPD and FEP patients may indicate a common pathway in the formation of positive symptoms such as hallucinations. This predisposition may contribute to the misinterpretation of the external/internal stimuli facilitating social problems in these groups. In our study, this vulnerability is independent of positive symptoms, in agreement with a recent paper that not described relation between speech illusion and positive schizotypy score in the general population [31]. This suggests that affectively salient speech illusion could be more a trait of psychosis than a state. In fact, we found an association with negative domain in FEP patients and with depressive domain in healthy controls, suggesting that psychosis–prone subjects could present more psychotic symptoms in general. However, other authors have described a relation between affectively speech illusions in the white noise task and experience of hallucinations and negative affect in healthy children [32]. These contradictory results require further research.

The most commonly reported difference between healthy and clinical voice hearers is the emotional valence of the voice, a negative emotional appraisal of the voice having a predictive value of 88% for the presence of a psychotic disorder [13]. The formation of delusions may be due to aberrant salience, or attributed importance to speech illusions. We cannot determine to what degree the mechanisms underpinning speech illusions in healthy participants are the same as those demonstrated in patients. But it seems that if speech illusion has associated an emotional value, the clinical diagnosis of psychosis is more common.

Contrary to the findings reported by Roiser and colleagues [33], evidence for altered salience attribution using the white noise task was present despite the prescription of antipsychotic medication in patients. This should not be considered surprising, however, because many patients continue to display mechanisms of ascribing altered meaning and emotional value to experience. This is supported by a high rate of speech illusions described in BPD. Patients prone to develop psychotic symptoms, such as BPD patients, could also present this aberrant tendency.

The results of SDT frame-work indicated a clear relation with a worse performance in FEP group, without significant differences between HC and BPD patients. FEP performed worse than other groups in the task and furthermore, they identified more FA and had longer reaction times in the task independently of IQ. This could be attributed to the greater genetic vulnerability to psychosis of this group. In our study, the FA and the global measure of performance showed the strongest association with FEP group, suggesting that the performance on this task is being influenced by poor accuracy in detecting non-targets rather than poor accuracy in detecting targets. Other studies had described an association between increased false recognitions and psychotic phenomena [27], although they found also a response bias in psychotic patients. Taken together, these findings suggest that diminished discriminability is a general characteristics underlying impaired reality-testing in psychotic patients.

Although it could be argued that patients actually hallucinating during the task caused the larger effect size for patients with psychotic symptoms, this mechanism cannot explain the parallel finding of an association between speech illusion and BPD patients. Furthermore, the tendency to develop affectively salient speech illusion is not related to a positive psychotic dimension.

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 [19,34]. The finding that white noise was imbued with the meaning of human speech in this study is in agreement with such a mechanism.

In our study, FEP patients maintained their tendency to develop affectively salient speech illusion independent of IQ. In the group of BPD patients this tendency did not remain statistically different but we could observe a tendency. Maybe a higher number of patients is necessary to retain this difference. As expected, FEP and BPD displayed lower IQ than controls at statistical significance. However, part of the association between speech illusions and these mental disorders thus may be mediated by cognitive alterations associated with psychosis.

FEP patients may represent an especially important population for exploring and testing hypotheses regarding psychosis liability because they are less likely to be affected by the potential consequences of psychotic illness over time [35]. This is more difficult to control in BPD patients as they are often prescribed long-term medication for several problems. In this study, the presence of medication was not taken into consideration.

The presence of affectively salient speech illusion would be a trait of psychosis, which contributes to the formation of the illness, and be part of the vulnerability underlying psychotic disorder. Studying people with subclinical psychotic experiences as part of a stable personality trait, such as patients with BPD, may shed further light on this issue. As far as we are aware, this is the first study that compares speech illusions in FEP, BPD and controls.

5. Conclusions

Our results demonstrate that a higher rate of affectively salient speech illusions is associated with psychotic patients. Furthermore, the detection of more FA in this group supports this idea. Nevertheless, the lack of differences between BPD patients and HC requires further research.

The white noise task is easy to administer, differentiates between psychotic patients and controls, and is independent from positive psychotic domain. Whether or not it indexes psychosis proneness in healthy participants and BPD patients remains uncertain [31,32]. More studies are required in order to understand its predictive value in the general population and in other diagnostic categories.

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