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The role of psychotic-like experiences in the association between aberrant salience and anxiety: A psychopathological proposal based on a case-control study

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Abstract

Aim: Aberrant salience (AS) and psychotic-like experiences (PLEs) have been proven to be linked. Moreover, anxiety is a key symptom in psychosis-prone subjects and most psychotic patients. We propose a model that attempts to interpret the role of PLEs in the association between AS and anxiety among healthy controls and psychotic patients.

Methods: Demographic and psychometric data (Aberrant Salience Inventory, Community Assessment of Psychic Experiences, Symptom Check List-90-revised) from 163 controls and 44 psychotic patients was collected. Descriptive statistics, correlations, a linear regression model and a mediation analysis with covariates were subsequently performed.

Results: AS correlated with more frequent positive PLEs and higher anxiety levels in both patients and controls. However, positive PLEs' frequency mediated the relationship between AS and anxiety only among controls.

Conclusions: PLEs linked to AS appear to induce anxiety among the control group but not among psychotic patients. The progressive loss of both novelty and insight, which may, respectively, impair the somatic emotional reactivity to PLEs and the ability to recognize some bodily phenomena as the embodied correlates of anxiety, is seen as the most probable theoretical explanation.

KEYWORDS

aberrant salience, anxiety, psychopathology, psychosis, psychotic-like experiences

1 | INTRODUCTION

1.1 | Background

Psychotic-like experiences (PLEs) are widespread episodes among the general population (Rössler et al., 2007). They are particularly common

in children and adolescents and are characterized by subclinical, temporary psychotic symptoms such as dissociation, hallucinations and delusions. PLEs are usually described as stressful and terrifying episodes, both among patients and healthy populations (Heriot-Maitland et al., 2012). Even though PLEs are not themselves categorized in a DSM-5 diagnosis, their frequency in the individual has been proved to be a risk factor for more serious conditions such as psychosis (Hanssen et al., 2003) and is increased in subjects at ultra high risk for psychosis (UHR) (Nelson & Yung, 2009).

Acronyms: ASI, Aberrant Salience Inventory; CAPE, Community Assessment of Psychic Experience; PLEs, Psychotic-like experiences; SCL-90-R, Symptom Check List-90-revised.

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Another construct capable of predicting psychosis is aberrant salience (AS) (Cicero et al., 2010). Salience could be described as the “relevance” that a perceived (internal or external) object acquires for the subject who perceives it. We interpret salience as an anthropological device (Stanghellini, 1997), an inherent phenomenon of human existence which usually maintains a balance between commonness (adaptive salience) and eccentricity (AS), shaping the subjective way to experience the self, the objects of the world and the others. By that, we are inclined to see AS as an anomalous world experience (Sass et al., 2017) which may act as a point of departure for different trajectories, both clinical (anxious trajectory, psychotic trajectory, autistic trajectory, etc.) and non-clinical (artistic trajectory), directed by one’s subjective characteristics and life experiences. One of the most detailed models for the genesis of psychosis involves an alteration of such mechanisms, with the individual’s salience attribution being “aberrant” and being assigned to otherwise irrelevant stimuli (Kapur, 2003). While PLEs can be described as state-like transitory subclinical psychotic episodes (Fonseca Pedrero & Debbané, 2017), AS appears to be a transdiagnostic trait-like feature of general vulnerability to psychosis which usually remains stable over time (Li et al., 2020). However, increased scores on the “Aberrant Salience Inventory” (ASI) (Cicero et al., 2010), a useful tool to measure AS, tend to lead to more frequent and intense PLEs (Fonseca Pedrero & Debbané, 2017) and psychotic symptoms, but they did not differ in patients with any specific psychiatric diagnosis (Ballerini et al., 2022), thus confirming the transdiagnostic validity of AS. From our perspective, not only psychosis but also anxiety may represent one of the forms the vulnerability expressed by AS may take when confronted with particular experiences.

Recent data (Prochwicz & Gawęda, 2016) suggests the existence of a causal link between temperament, anxiety/depression and PLEs through mediation analysis. In fact, multiple studies highlight the connection between anxiety and psychosis (Hartley et al., 2013; Michail & Birchwood, 2009; Wilson et al., 2020); Anxiety and depressive symptoms during adolescence and early adulthood have long been recognized as one of the features of the prodromal period of psychosis (Howes & Murray, 2014), which may last up to 5 years and may be associated with progressive psychosocial impairment and disability (Yung et al., 2003).

Moreover, anxiety is a complex psychic state with cognitive, bodily, emotional and behavioural features. Abnormal bodily experiences or “cenesthopaties” have been proposed to be a disorder of background emotions (Graux et al., 2011), a detachment of the bodily features of emotions from their cognitive, emotional and behavioural correlates. Abnormal bodily phenomena are known to occur in UHR subjects (Madeira et al., 2016) and patients with psychosis (Stanghellini et al., 2020).

UHR subjects are now known to be individuals with non-psychotic mental disorders (mainly anxiety, depression, substance use disorders), low-grade psychotic symptoms (Michail & Birchwood, 2009) and abnormal bodily phenomena (Madeira

et al., 2016), some of which may be interpreted as somatic features of emotions such as anxiety. Moreover, people with anxiety disorders appear to have worse AS compared to controls, albeit still lower on average than subjects with psychosis (Neumann et al., 2021).

Since PLEs, particularly persecutory ideation, correlate with psychosis proneness, depression and anxiety (Cowan & Mittal, 2021) and since individuals with high-psychosis proneness display more pronounced anxiety compared with individuals with low-psychosis proneness (Szily & Kéri, 2013), we can hypothesize that anxiety in psychosis-prone subjects may be an index of the emotional reaction determined by the presence of distressing ego-dystonic PLEs, and of the partial preservation of the individual’s insight into illness, as insight preservation among psychotic patients is reported to be associated with more depressive and anxious mood (Bota et al., 2006). AS, as an index of psychosis proneness, is predominantly involved in the development of positive PLEs (Cicero et al., 2013) and positive psychotic symptoms (Kapur, 2003). As far as we know, psychosis proneness appears to be linked both to the development of PLEs (Cicero et al., 2013) and anxiety symptoms (Szily & Kéri, 2013), and anxiety appears to involve the AS of emotionally relevant stimuli (Nuss, 2015) so that we can hypothesize that the effect of AS on the somatic features of anxiety in psychosis prone subjects may be due to the presence of positive PLEs, as the bodily correlates of an anxious emotional reaction to new uncanny events. However, impaired insight into illness is a prevalent feature of psychosis which seems to be severe during the first episodes of psychosis, modestly improve over midlife, and decline again in late life (Gerretsen, Plitman, et al., 2014), so we can hypothesize that, among psychotic patients, the somatic features of anxiety may be totally or partially independent from PLEs due to the progressive loss of both novelty and insight, which may respectively impair the somatic emotional reactivity to PLEs and the ability to recognize some bodily phenomena as the embodied correlates of anxiety.

1.2 | Aims

The aim of this observational study is to examine the connections between AS, PLEs frequency and intensity and anxiety levels among both clinical populations and psychotic patients.

We intentionally targeted our study on young adults (aged 18–40 yo), both in the control group and in the psychotic sample. For what concerns the control group, this decision was made on the basis that anxiety during early adulthood is considered one of the features of the prodromal period of psychosis among not yet psychotic individuals (Howes & Murray, 2014). For what concerns the psychotic group, this decision was made on the basis that impaired insight into illness, which is known to affect anxiety levels, is particularly severe during the first episodes of psychosis (Gerretsen, Plitman, et al., 2014), and to avoid confounding factors such as the impact of chronicity and/or dampened salience (Kapur et al., 2005) on the relationship between

AS, PLEs and anxiety. Since AS appears to be a transdiagnostic feature of vulnerability to psychosis (Ballerini et al., 2022), in the psychotic sample no distinction was made regarding affective and non-affective psychosis.

The following hypotheses were tested:

1. presence of a correlation between positive PLEs and AS, both in the control group and in the psychotic group, based on the evidence that positive PLEs correlate with psychosis proneness (Cicero et al., 2013; Cowan & Mittal, 2021);
2. presence of a correlation between anxiety and AS, both in the control group and in the psychotic group, based on the observation that anxiety may involve the altered salience of emotionally relevant stimuli (Nuss, 2015) and that psychosis-prone subjects usually display high level of anxiety (Szily & Kéri, 2013; van Os & Guloksuz, 2017);

Since we interpret AS as a potential point of departure of different trajectories, in this study we intentionally focused on the intertwinement between the anxious and the psychotic trajectories predicted by AS. Although it is not a unanimously approved method (O'Laughlin et al., 2018), a mediation model was used to assess the following hypotheses:

3. presence, in the control group, of a mediated effect of AS on somatic anxiety via positive PLEs, based on the observation that UHR subjects usually present with anxious-depressive symptomatology together with PLEs (Michail & Birchwood, 2009) and on our assumption that anxiety may be an index of the emotional reaction determined by positive PLEs and of the partial preservation of insight;
4. absence, in the psychotic group, of a mediated effect of AS on anxiety via positive PLEs, based on the progressive loss of PLEs' distressing character of novelty among recurrent psychotic patients and on the observation that insight impairment is frequent in early psychosis (Gerretsen, Plitman, et al., 2014), and may affect anxiety levels (Graux et al., 2011), thus reducing the ability to recognize the bodily correlates of anxiety as a part of the emotion.

We are inclined to interpret AS as a basal anthropo-biological predisposition to encounter particular experiences or walk peculiar psycho(patho)logical paths, therefore, we chose AS as a predictor variable. However, some may argue about the possible mediating role of AS, so competing models were addressed and tested in the Supplementary Materials. The possibility of AS being an outcome variable was rejected a priori.

Since UHR subjects, which are individuals at the threshold of the psychotic trajectory, usually present to the General Practitioner complaining about anxiety, we chose this dimension as the outcome variable instead of PLEs. However, it is reasonable to assume that the relationship between PLEs and anxiety may also be bidirectional, with anxiety increasing the risk of developing more frequent or intense positive PLEs, so a competing model with anxiety as a mediator was addressed and tested in the Supplementary Materials.

2 | MATERIALS AND METHODS

2.1 | Participants

Individuals from the control group were recruited using convenience and snowball sampling methods, provided they met the following inclusion criteria: age between 18 and 40 years, Italian speakers, collection of online written informed consent. Exclusion criteria were the following: illiteracy or inability to provide the consent or to complete the survey online, lifetime diagnosis of a psychiatric disorder or substance use disorder. Based on the methodology adopted, a set of 45 participants was initially selected to reduce selection bias associated with the non-probabilistic sampling method. The first subjects were selected by sharing the research protocol in the University of Florence's social spaces. Each participant was then asked to choose five individuals and to send them the questionnaire. This recruitment procedure was carried out until the saturation of data. A questionnaire constituted by three different psychometric scales (discussed in the Section 2.2) was administered to each of the participants. The questionnaire was distributed through the use of a link developed with the "Google Forms" platform to be filled in anonymously online from a mobile phone, tablet or computer. The procedure was explained to respondents, and online written informed consent was collected before enrolment. The anonymity of participants was always ensured. The self-report was followed by a face-to-face clinical interview for subjects reporting a history of psychiatric problems, or an SCL-90-R (Derogatis, 1992) Global Severity Index score (GSI) >2, to explore undiagnosed conditions.

In total, 219 Italian adults were recruited after providing online informed consent. Of the 219 individuals who were contacted, 26 refused to participate. Of the 193 respondents, 16 participants were excluded because they reported a current or past psychiatric disorder, 10 were excluded because they reported a current or past substance use; 4 additional subjects with SCL-90-R GSI >2 were excluded after a clinical interview because of an undiagnosed psychiatric condition. Therefore, the final sample consisted of 163 subjects.

The psychiatric outpatient sample was recruited after a clinical interview held by medical specialists in Psychiatry at the Adult Psychiatry Unit of Florence University Hospital. All the patients received an information leaflet explaining exhaustively the protocol and its implications. Further explanations were given by the research team as needed. The inclusion criteria were the following: age between 18 and 40 years, diagnosis of a psychiatric disorder with lifetime presence of psychotic symptoms (Major Depression with psychotic features, Bipolar Disorder with psychotic features, Schizophrenia Spectrum and other psychotic disorders) according to DSM-5, Italian speakers, high-school degree or above scholarship, collection of written informed consent. The exclusion criteria were: illiteracy or inability to provide the consent or to complete the questionnaires, lifetime diagnosis of a substance use disorder, acute psychotic episode (according to clinical evaluation), cognitive impairment due to psychiatric or medical conditions, diagnosis of a neurological condition. Diagnosis, clinical status and level of clinical insight were assessed by

expert psychiatrists (authors A. B. and V. R.). Only the main diagnosis was included in the database. The anonymity of participants was always ensured.

In total, 79 Italian outpatients were recruited after providing informed consent. Of the 79 individuals who were selected, 17 refused to participate. Of the 62 responders, 14 were excluded because they reported a current or past substance use and 4 were excluded because they were having an acute psychotic episode. Therefore, the final sample consisted of 44 outpatients.

Overall, a total of 207 individuals participated in the study from September 2021 to July 2023. The procedure was approved by the Ethics Committee of the Local Institution (CEAVC, Comitato Etico Area Vasta Centro, approval code CEAVC_14709).

2.2 | Measures

Self-reported data were the following: socio-demographic information (age, gender, marital status, education, profession), presence of a current or past psychiatric diagnosis, use of psychopharmacological drugs.

Psychosis proneness was assessed by means of the ASI, a 29-item self-reported scale with dichotomous answers (“Yes”/“No”); scores range from 0 to 29; higher scores identify a higher vulnerability.

PLEs were measured via the Community Assessment of Psychic Experiences (CAPE), a 42 items self-reported scale (Konings et al., 2006) which covers three domains: positive (20 items), negative (14 items), and depressive (8 items) symptoms. Each symptom has two 4-point Likert scales: “Frequency” and “Distress.” The “Frequency” and “Distress” domain scores (each ranging from 1 to 4) result from the mean scores of the corresponding items. Since the AS hypothesis was developed to account for the psychopathogenesis of positive psychotic symptoms, the present study was intentionally focused on the positive symptoms frequency (CAPEposF) and distress (CAPEposD) subscales.

Multidimensional psychopathology was assessed using the Symptom Check List-90-revised (SCL-90-R), a 90-item self-report scale with items rated on a 5-point Likert scale (from 0 “not at all” to 4 “extremely”). For what concerns the control group, the self-report was followed by a face-to-face clinical interview for subjects reporting a GSI > 2 (to explore undiagnosed conditions). Since the present study was targeted at the difference in anxiety symptoms' psychopathogenesis between psychosis-prone subjects and psychotic patients, we intentionally chose to focus on the anxiety subscale (SCL-90-R-ANX), which mostly evaluates the somatic features of anxiety.

Insight impairment was assessed as mild, moderate or severe by two senior psychiatrists (authors A. B. and V. R.) through a face-to-face psychiatric evaluation based on an Italian adaptation of the VAGUS insight into psychosis scale–Clinician-Rated version (VAGUS-CR) (Gerretsen, Remington, et al., 2014), a new and very brief semi-structured interview which has not been officially validated into Italian yet.

Internal consistency reliability was estimated through Cronbach's alpha.

2.3 | Statistical analyses

A power analysis was conducted through the use of the software G*Power 3.1 (Faul et al., 2009). The settings: “Linear multiple regression: Fixed model, single regression coefficient” was employed, with standard values: two tails, $\alpha = .05$, $1-\beta = .80$ (as common practice (Serdar et al., 2021), expected effect size $f^2 = 0.20$ and 7 predictors. A minimum sample size of 42 was thus calculated.

An independent-samples *t*-test was performed on questionnaire scores to compare controls and patients (significance threshold equal to .05, two tails).

First, a linear regression model with the SCL-90-R-ANX as outcome including age, gender, years of education, and, only in patients, antipsychotic treatment status as covariates was tested to calculate the predictive power of ASI, CAPEposD and CAPEposF scores. Additionally, a correlation analysis was performed through the Pearson coefficient (significance threshold equal to .05, two tails).

The theorized mediation models involved X (ASI scores) having an effect on Y (SCL-90-R) anxiety scores both directly and through M1 and M2 (CAPEposF and CAPEposD).

Total, direct and indirect associations between ASI scores and SCL-90-R anxiety scores were computed using the PROCESS 4.1 tool for mediation analysis (model 4) in SPSS v.25 (Hayes, 2013). Bootstrapped samples (5000), with 95% confidence intervals were used. The same covariates that were employed in the linear regression were also utilized in this mediation analysis.

3 | RESULTS

3.1 | Descriptive statistics

A total of 207 subjects were recruited, 163 within the control group and 44 in the patient group. Overall, 51.5% of the sample was female (50.3% and 56% among controls and patients respectively). All the subjects were of caucasian ethnicity. The average age was 29.64, SD: 10.18 (controls 28.73, SD: 9.49; patients 32.74, SD: 12.78). Years in school averaged 16.81, SD: 2.84 (controls 17.61, SD: 2.71; patients 13.84, SD: 3.34). 70% (31) of the subjects in the lifetime psychotic group were under antipsychotic treatment. Among patients, 24 were diagnosed with Schizophrenia Spectrum Disorder, 19 with Bipolar Disorder with psychotic features and 1 with Major Depression with psychotic features. From a clinical point of view, the majority of patients presented with recurrent psychotic episodes and a mild-to-moderate impairment of clinical insight at the moment of the psychiatric evaluation and test administration.

Mean scores and T-test results on ASI, CAPE and SCL-90-R are shown in Table 1. Patients scored significantly higher than controls on ASI, CAPEposF and all subscales of SCL-90-R except for the domains

TABLE 1 Descriptive statistics for the analysed sample, and comparison of subjects.

Scales	df	Mean ± std. deviation		t	p	Cohen's d
		Control group (N = 163)	Psychotic group (N = 44)			
ASI	205	11.690 ± 6.098	14.360 ± 7.163	2.480	.014	0.421
CAPEposF	205	1.391 ± 0.340	1.617 ± 0.488	3.539	.000	0.601
CAPEposD	205	1.792 ± 0.615	1.941 ± 0.694	1.387	.167	0.236
SCL-90-R-SOM	205	0.605 ± 0.541	0.714 ± 0.678	1.121	.264	0.190
SCL-90-R-OC	205	0.940 ± 0.664	1.216 ± 0.763	2.368	.019	0.402
SCL-90-R-INT	205	0.785 ± 0.704	0.989 ± 0.801	1.655	.099	0.281
SCL-90-R-DEP	205	0.893 ± 0.743	1.029 ± 0.801	1.059	.291	0.180
SCL-90-R-ANX	205	0.678 ± 0.600	0.905 ± 0.643	2.193	.029	0.373
SCL-90-R-HOS	205	0.588 ± 0.609	0.701 ± 0.736	1.043	.298	0.177
SCL-90-R-PHOB	205	0.285 ± 0.512	0.747 ± 0.696	4.894	.000	0.831
SCL-90-R-PAR	205	0.801 ± 0.712	0.917 ± 0.723	0.956	.340	0.162
SCL-90-R-PSY	205	0.465 ± 0.513	0.836 ± 0.652	4.006	.000	0.681
SCL-90-R-SLEEP	205	0.824 ± 0.870	0.833 ± 0.645	0.064	.949	0.011
SCL-90-R-GSI	205	0.699 ± 0.534	1.919 ± 2.198	6.452	.000	1.096
SCL-90-R-PST	205	37.670 ± 20.147	47.680 ± 17.374	3.006	.003	0.511
SCL-90-R-PSD	205	1.525 ± 0.451	1.958 ± 1.022	4.135	.000	0.703

Note: p values < 0.05 are in bold.

Abbreviations: ANX, Anxiety; ASI, Aberrant Salience Inventory; CAPEposF, Community Assessment of Psychic Experiences–positive dimension–Frequency; CAPEposD, Community Assessment of Psychic Experiences–positive dimension–Distress; DEP, Depression; GSI, Global Severity Index; HOS, Hostility; INT, Interpersonal Sensitivity; OC, Obsessive-Compulsive; PHOB, Phobic Anxiety; PAR, Paranoid Ideation; PSD, Positive Symptom Distress; PST, Positive Symptom Total; PSY, Psychoticism; SCL-90-R, Symptom Check List-90-revised; SLEEP, Sleep; SOM, Somatization.

of Somatization (SCL-90-R-SOM), Interpersonal Sensitivity (SCL-90-R-INT), Depression (SCL-90-R-DEP), Hostility (SCL-90-R-HOS), Paranoid Ideation (SCL-90-R-PAR) and Sleep (SCL-90-R-SLEEP).

Internal consistency reliability was high among both cases and controls on all questionnaires: ASI (cases $\alpha = .871$, controls $\alpha = .885$), SCL90 (cases $\alpha = .963$, controls $\alpha = .970$), CAPE (cases $\alpha = .831$, controls $\alpha = .825$).

3.2 | Linear regression model

The results from the linear regression model (with SCL90-R-ANX as output) are shown in Table 2. Both the patient's and control's models were statistically significant (see Table 2).

Among controls, the following were statistically significant predictors for SCL90-R-ANX: Sex, Age, Years of Education, CAPEposF, ASI.

On the other hand, among patients, ASI was the only statistically significant predictor.

Hypothesis 1. Correlation between ASI and CAPE scores.

A correlation analysis between ASI and CAPE scores was performed for both patients and controls (Table 3). Among controls, ASI scores had a significant correlation with CAPEposF and CAPEposD scores (Pearson's r equal to 0.505 and 0.201, respectively). In the patient group, ASI was positively and significantly correlated with

CAPEposF ($r = 0.54$) and with CAPEposD ($r = 0.33$). Notably, among both groups, the strongest ($r > 0.4$) and significant ($p < .01$) correlation was found between ASI and positive PLEs frequency (CAPEposF).

Hypothesis 2. Correlation between ASI and SCL-90-R subscales scores.

Bivariate correlations between ASI and SCL-90-R scores were performed on both the control group and the psychotic group. The findings are shown in detail in Table 3. Among controls, ASI scores correlated significantly with every SCL-90-R subscale: the strongest correlations ($r > 0.4$) were found between ASI and SCL-90-R subscale of Interpersonal Sensitivity (SCL-90-R-INT), Depression (SCL-90-R-DEP), Anxiety (SCL-90-R-ANX), Paranoid Ideation (SCL-90-R-PAR), Psychoticism (SCL-90-R-PSY), Global Severity (SCL-90-R-GSI) and Positive Symptom Total (SCL-90-R-PST). Notably, among patients the strongest correlation ($r > 0.4$) was found between ASI and Anxiety (SCL-90-R-ANX).

3.3 | Mediation analysis

Mediation analysis was performed, with ASI as X, CAPEposF and CAPEposD as M1 and M2 and SCL-90-R anxiety score as Y (see Figures 1 and 2). Age, sex, years spent in education and antipsychotic

TABLE 2 Linear regressions with SCL-90-R-ANX as outcome.

	Regression analysis							
	Control group (N = 163)				Psychotic group (N = 44)			
	Coefficient	Std. error	t	p	Coefficient	Std. error	t	p
Intercept	-12.313**	3.185	-3.867	.000	10.995	7.096	1.549	.133
Sex	-1.835**	0.719	-2.552	.012	-2.937	2.366	-1.241	.225
Age	-0.018	0.037	-0.484	.629	-0.012	0.088	-0.143	.887
Years of education	0.264*	0.128	2.067	.040	-0.598	0.317	-1.884	.071
Antipsychotic treatment	-	-	-	-	-2.605	2.385	-1.092	.284
CAPEposD	0.95	0.614	1.547	.124	-0.399	0.240	-1.660	.109
CAPEposF	8.432**	1.210	6.966	.000	1.318	2.876	0.458	.651
ASI	0.208**	0.064	3.238	.001	0.772**	0.196	3.949	.001

Note: Control group summary—Multiple R-squared: 0.469, Adjusted R-squared: 0.449; F-statistic: 23.57, *p*-value: < 2.2e-16. Psychotic group summary—Multiple R-squared: 0.487, Adjusted R-squared: 0.349; F-statistic: 3.525, *p*-value: = .008565. *p* values < 0.05 are in bold.

Abbreviations: ASI, Aberrant Salience Inventory; CAPEposF, Community Assessment of Psychic Experiences—positive dimension—Frequency; CAPEposD, Community Assessment of Psychic Experiences—positive dimension—Distress.

*Correlation is significant at the .05 level (2-tailed).

**Correlation is significant at the .01 level (2-tailed).

TABLE 3 Pearson's correlations between Aberrant Salience Inventory (ASI) total score, Symptom Check List-90-revised (SCL-90-R) domains and Community Assessment of Psychic Experience (CAPE), positive dimension.

	ASI total score			
	Control group (N = 163)		Psychotic group (N = 44)	
	r	p	r	p
SCL-90-R-SOM	0.399**	.000	0.188	.365
SCL-90-R-OC	0.505**	.000	0.356	.087
SCL-90-R-INT	0.440**	.000	0.241	.219
SCL-90-R-DEP	0.427**	.000	0.157	.311
SCL-90-R-ANX	0.491**	.000	0.486**	.011
SCL-90-R-HOS	0.367**	.000	0.244	.165
SCL-90-R-PHOB	0.273**	.000	0.274	.213
SCL-90-R-PAR	0.419**	.000	0.392*	.041
SCL-90-R-PSY	0.409**	.000	0.136	.527
SCL-90-R-SLEEP	0.373**	.000	0.245	.318
SCL-90-R-GSI	0.498**	.000	0.318	.097
SCL-90-R-PST	0.551**	.000	0.286	.164
SCL-90-R-PSD	0.325**	.000	0.313	.147
CAPEposF	0.505**	.000	0.544**	.000
CAPEposD	0.221**	.004	0.335*	.034

Note: *p* values < 0.05 are in bold.

Abbreviations: ANX, Anxiety; DEP, Depression; GSI, Global Severity Index; HOS, Hostility; INT, Interpersonal Sensitivity; OC, Obsessive-Compulsive; PAR, Paranoid Ideation; PHOB, Phobic Anxiety; PSD, Positive Symptom Distress; PST, Positive Symptom Total; PSY, Psychoticism; posF, positive dimension—Frequency; posD, positive dimension—Distress; SLEEP, Sleep; SOM, Somatization.

*Correlation is significant at the .05 level (2-tailed).

**Correlation is significant at the .01 level (2-tailed).

treatment status were all included as covariates. Results are shown in Table 4.

Hypothesis 3. Mediation analysis, control group.

The analysis detected a significant total effect of ASI scores on SCL-90-R anxiety scores (see Table 4 for more details). Also, the direct effect and indirect effect were found to be significant. When examining the indirect path in more detail, CAPEposD was found not

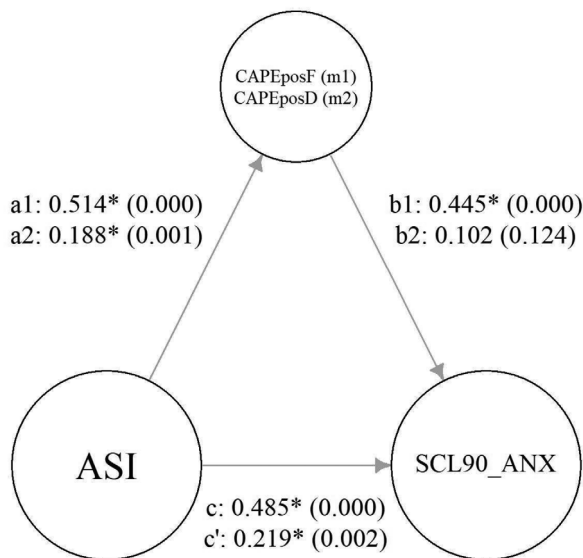


FIGURE 1 Control group. Mediation model testing the hypothesis that the effect of Aberrant Salience Inventory (ASI, X) total score on self-reported anxiety (SCL-90-R-ANX, Y) is mediated by positive PLEs frequency and distress measured by the Community Assessment of Psychic Experiences (CAPEposF and CAPEposD, M). Standardized regression coefficient is shown: a1 and b1 refer to CAPEposF, a2 and b2 refer to CAPEposD. a1 (ASI → CAPEposF); a2 (ASI → CAPEposD); b1 (CAPEposF → SCL-90-R-ANX); b2 (CAPEposD → SCL-90-R-ANX); c (ASI → SCL-90-R-ANX total); c' (ASI → SCL-90-R-ANX direct). ASI, Aberrant Salience Inventory; CAPEposF, Community Assessment of Psychic Experiences–positive dimension–Frequency; CAPEposD, Community Assessment of Psychic Experiences–positive dimension–Distress; SCL-90-R-ANX, Symptom Check List-90-revised, Anxiety. *Correlation is significant at the 0.05 level (2-tailed).

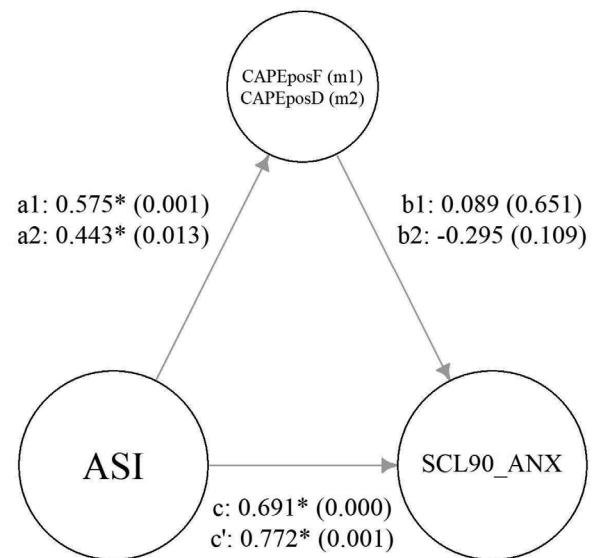


FIGURE 2 Psychotic group. Mediation model testing the hypothesis that the effect of Aberrant Salience Inventory (ASI, X) total score on self-reported anxiety (SCL-90-R-ANX, Y) is mediated by positive PLEs frequency and distress measured by the Community Assessment of Psychic Experiences (CAPEposF and CAPEposD, M). Standardized regression coefficient is shown: a1 and b1 refer to CAPEposF, a2 and b2 refer to CAPEposD. a1 (ASI → CAPEposF); a2 (ASI → CAPEposD); b1 (CAPEposF → SCL-90-R-ANX); b2 (CAPEposD → SCL-90-R-ANX); c (ASI → SCL-90-R-ANX total); c' (ASI → SCL-90-R-ANX direct). ASI, Aberrant Salience Inventory; CAPEposF, Community Assessment of Psychic Experiences–positive dimension–Frequency; CAPEposD, Community Assessment of Psychic Experiences–positive dimension–Distress; SCL-90-R-ANX, Symptom Check List-90-revised, Anxiety. *Correlation is significant at the 0.05 level (2-tailed).

significant, while CAPEposF achieved a significant mediation effect on SCL-90-R anxiety scores.

Sex and years spent in education reached significance in the direct path, while the only covariate that was significant in the indirect path was sex.

Standardized regression coefficients were also computed, as shown in Figure 1: a1 (ASI → CAPEposF); a2 (ASI → CAPEposD); b1 (CAPEposF → SCL-90-R-ANX); b2 (CAPEposD → SCL-90-R-ANX); c (ASI → SCL-90-R-ANX total) and c' (ASI → SCL-90-R-ANX direct). The only significant results were a1 (ASI → CAPEposF), a2 (ASI → CAPEposD), b1 (CAPEposF → SCL-90-R-ANX), c (ASI → SCL-90-R-ANX total) and c' (ASI → SCL-90-R-ANX direct).

Hypothesis 4. Mediation analysis, psychotic group.

The analysis showed a significant total effect of ASI scores on SCL-90-R anxiety scores. The direct effect was also found significant, while the indirect effect did not reach significance.

No covariates met the statistical significance threshold.

Standardized regression coefficients were also computed, as shown in Figure 2: a1 (ASI → CAPEposF); a2 (ASI → CAPEposD); b1

(CAPEposF → SCL-90-R-ANX); b2 (CAPEposD → SCL-90-R-ANX); c (ASI → SCL-90-R-ANX total) and c' (ASI → SCL-90-R-ANX direct). The only significant results were a1 (ASI → CAPEposF), a2 (ASI → CAPEposD), c (ASI → SCL-90-R-ANX total) and c' (ASI → SCL-90-R-ANX).

4 | DISCUSSION

Our study proposes a model to interpret the role of positive PLEs in the association between AS and anxiety between healthy controls and psychotic patients.

Our linear regression analysis showed that, while among controls the more significant predictors of anxiety were sex, positive PLEs frequency and AS, in the psychotic group only AS was a significant predictor of anxiety.

In the control group, AS seems to be an index of general subjective psychopathology, since strong ($r > 0.4$) and significant ($p < .01$) correlations were found between ASI and many SCL-90-R dimensions such as Interpersonal Sensitivity, Depression, Anxiety, Paranoid Ideation, Psychoticism and Global Severity and CAPE dimensions of

TABLE 4 Mediation model summary.

	Mediation analysis									
	Control group (N = 163)					Psychotic group (N = 44)				
	Coefficient	t	p	LLCI	ULCI	Coefficient	t	p	LLCI	ULCI
ASI to CAPEposF a1	0.514**	7.602	.000	0.022	0.039	0.575**	3.752	.001	0.0177	0.061
ASI to CAPEposD a2	0.188**	2.509	.001	0.048	0.247	0.443**	2.656	.013	0.076	0.582
CAPEposF to SCL90_ANX b1	0.445**	6.966	.000	5.091	9.301	0.089	0.458	.651	-4.596	7.232
CAPEposD to SCL90_ANX b2	0.102	1.547	.124	-0.026	0.319	-0.295	-1.659	.109	-0.895	0.095
c (total)	0.485**	7.195	.000	0.333	0.586	0.691**	4.439	.000	0.372	1.011
c' (direct)	0.219**	3.238	.002	0.086	0.345	0.772**	3.949	.001	0.370	1.174
Age	0.018	0.484	.629	-0.101	0.047	0.034	0.227	.822	-0.159	0.199
Sex	-0.154**	2.551	.012	-3.256	-0.444	-0.195	-1.271	.214	-7.255	1.697
Years of education	0.121*	2.067	.040	0.006	0.520	-0.264	-1.722	.096	-1.199	0.104
Antipsychotics treatment	-	-	-	-	-	-0.090	-0.599	.554	-5.829	3.191

Note: *p* values < 0.05 are in bold.

Abbreviations: ANX, Anxiety; ASI, Aberrant Salience Inventory; DEP, Depression; GSI, Global Severity Index; HOS, Hostility; INT, Interpersonal Sensitivity; OC, Obsessive-Compulsive; PAR, Paranoid Ideation; PHOB, Phobic Anxiety; PSD, Positive Symptom Distress; PST, Positive Symptom Total; PSY, Psychoticism; posF, positive dimension-Frequency; posD, positive dimension-Distress; SCL-90-R, Symptom Check List-90-revised; SLEEP, Sleep; SOM, Somatization.

*Correlation is significant at the .05 level (2-tailed).

**Correlation is significant at the .01 level (2-tailed).

positive PLEs frequency. This finding is not new, since ASI is a measure of psychosis proneness and since UHR subjects usually show a combination of PLEs together with a wide range of non-psychotic symptoms (especially anxious-depressive symptoms) (van Os & Guloksuz, 2017). Moreover, this is congruent with our view that salience alterations may be seen as a potential point of departure of different trajectories, both clinical and non-clinical. Notably, many of the aforementioned correlations lose both strength and significance in the psychotic group, where only correlations between AS, anxiety and positive PLEs frequency remain strong and significant. Anyway, since anxiety and positive PLEs seem to be the only strong and significant correlations shared between the control group and the psychotic sample, we can say that our Hypotheses 1 and 2 seem to be satisfied; however, regarding the positive PLEs dimension, it must be said that the psychotic group shows correlations only between AS and positive PLEs frequency, not distress. In other words, in the continuum from healthy subjects to psychosis-prone individuals to psychotic patients, the anthropological polymorphic vulnerability related to AS seems to be progressively oriented toward embodied anxiety and (sub)clinical psychotic symptoms frequency.

The results of our positive correlation between positive PLEs, anxiety and AS, both in the control group and in the psychotic group, are in line with the recent literature (Cicero et al., 2013; Cowan & Mittal, 2021; Nuss, 2015; Szily & Kéri, 2013; van Os & Guloksuz, 2017). Among the chosen variables, psychotic patients presented with worse AS, PLEs frequency and distress, and anxiety than the control group, as expected.

Moreover, even though inferences drawn upon mediation analyses on cross-sectional data are known to have inherent limitations (O'Laughlin et al., 2018), our analysis suggests that anxious

symptomatology may be subtended by different psychopathogenic pathways among psychosis-prone subjects and psychotic patients.

In fact, in the control group, positive PLEs frequency mediated the effect of AS on anxiety, whereas this was not observed in the psychotic group, consistently with our Hypotheses 3 and 4. However, we did not find any effect of positive PLEs distress in the development of anxious symptoms linked to AS in any group.

With regard to the control group, this result is in line with the observation that UHR subjects usually display anxious-depressive symptoms together with PLEs and may be interpreted assuming that embodied anxious symptoms may be an emotional reaction to frequent positive PLEs and an index of the partial preservation of insight. Although direct causality cannot be demonstrated, we may assume that healthy subjects may recognize the uncanny character of their PLEs and may react by developing somatic symptoms of anxiety. In fact, PLEs frequency being correlated with distress among the general population is not a new finding; instead, it is a well-replicated result (Armando et al., 2010; Wüsten et al., 2018; Yung et al., 2006; Yung et al., 2009). The nature of the specific PLEs is likely also relevant. Persecutory PLEs have been associated with higher anxiety in UHR populations (Cowan & Mittal, 2021) as compared to other kinds of PLEs. Interestingly, another study (Yung et al., 2009) showed that while persecutory PLEs were associated with higher distress levels, "magical thinking" PLEs were not significantly associated with distress. However, in this study, we did not perform a qualitative differentiation of PLEs, so more research is needed to shed light onto this point. Anyway, it is reasonable to assume that the relationship between PLEs and anxiety may also be bidirectional, with anxiety increasing the risk of developing more frequent or intense positive PLEs; however, UHR subjects usually

complain more about their anxious-depressive symptomatology rather than about their PLEs.

Since AS appears to be a transdiagnostic trait-like feature of anthropological vulnerability to particular experiences such as psychosis, in the psychotic sample no distinction was made regarding affective and non-affective psychosis (Ballerini et al., 2022). With regard to the psychotic group, we may assume that psychotic patients, while maintaining both high AS and anxiety, may lose PLEs' distressing character of novelty and may present with varying degrees of insight impairment onto their PLEs, therefore nullifying any mediation effect. From a speculative point of view, we can hypothesize that lack of novelty may reduce the somatic emotional reactivity to PLEs, while lack of insight may impair the ability to recognize some bodily phenomena as the somatic features of anxiety. In other words, anxiety among psychotic patients seems to depend more on their anthropological vulnerability subtended by AS, rather than on PLEs frequency. However, we cannot exclude that other factors such as social impairment or full-blown psychotic symptoms could hypothetically mediate the relationship between AS and anxiety in psychotic patients, so more research on this topic is needed.

Since the psychotic population in our sample was largely treated, it can be argued that antipsychotics could induce a decrease in anxiety levels, whereas controls do not benefit from such protection. Some literature seems to also point out this fact (Hershenberg et al., 2014). The covariate analysis of our data, though, seems to disprove such a hypothesis: among the psychotic group, treatment status was not a significant covariate in the mediation analysis; also, the T-test highlighted how patients presented with higher levels of anxiety compared to the control group. While this cannot definitely rule out the hypothesis that this difference in PLEs perception might be due to the effect of antipsychotics, it makes it less compelling as an explanation.

Another possibility is that psychotic subjects are, in a way, "used" to PLEs and thus might feel as less distressful. This could potentially happen through rationalization (Boldrini et al., 2020) ("it is just another voice in my head"). As further indirect evidence pointing toward this idea, a previous study argued that illness insight might be correlated to less severe psychotic symptoms (Bota et al., 2006); moreover, insight is at its lowest point during the first psychotic episodes (Gerretsen, Plitman, et al., 2014) and this was one of the reasons that made us target our study on young adults (aged 18–40 yo).

The clinical model assumes that lack of insight is a stable trait, whereas other models define insight as a dynamic mental state that varies over time and in intensity, depending upon internal and external changes (Thirioux et al., 2019). It is known that insight is negatively related to the severity of symptoms (global, positive, negative) of schizophrenia (Thirioux et al., 2019), and with the severity of manic or depressive symptoms in bipolar disorder and unipolar major depressive disorders (Ghaemi et al., 2000), although the correlation size appears to be smaller than for manic episodes (Thirioux et al., 2019). Overall, lack of insight appears to be a transdiagnostic feature which is prevalent in psychotic depression and mania (Peralta & Cuesta, 1998) and in severe schizophrenia.

Clinical insight is associated with cognitive and affective empathy; in other words, low-empathic capacities appear to be linked with a reduction of insight (Atoui et al., 2018).

Our sample of patients showed higher ASI total scores and higher SCL-90-R scores in the domains of Obsessive-Compulsive symptoms, Anxiety, Phobic Anxiety, Psychoticism, GSI, Positive Symptom Total, Positive Symptom Distress as compared to our control group.

AS seems to affect empathic capacities in healthy controls (Patti et al., 2023) and also Obsessive-Compulsive symptoms, Anxiety, Phobic Anxiety, Psychoticism, GSI, Positive Symptom Total, Positive Symptom Distress as measured by the SCL-90-R appear to affect empathy in patients with a personality disorder (Flasbeck & Brüne, 2021).

Although subjective empathy and insight were not directly quantified with self-reported scales, our psychiatric evaluation of clinical insight together with the comparison of the gathered data and the available literature may help us to describe our sample of patients as overall presenting with a mild-to-moderate insight impairment, congruently with the fact that deficits of insight are usually more severe during the first episodes of psychosis (Gerretsen, Plitman, et al., 2014). However, further research on the role of insight impairment in the relationship between anxiety and abnormal bodily phenomena is needed.

Surprisingly, as mentioned before, positive PLEs distress did not show any mediation effect in any group. The *p*-value (.25, see Section 3) was well above the threshold for significance; moreover, this finding concerns the control sample, which, due to its relative numerosity, is not prone to false negatives. This result, thus, deserves an attempt at an explanation. The CAPEposD subscale focuses on the general subjective distress that the individual consciously recognizes as directly linked to his/her positive PLEs, a discomfort which may take different symptomatic forms other than anxiety. Unlike that, the SCL-90-R-ANX subscale specifically targets the anxious symptomatology, mostly in its somatic features, regardless of whether the subject is aware of the connection with other experiences such as his/her positive PLEs or not. In other words, polymorphic conscious distress derived from PLEs seems not to affect the somatic features of anxiety, while PLEs frequency appears to increase embodied anxiety levels in psychosis-prone subjects, but not in psychotic patients.

5 | LIMITATIONS

Some limitations of the present study must be acknowledged. First, despite the sample being adequate as numerosity concerning both controls and patients, it is indeed imbalanced with fewer patients than controls (see Section 2). Despite the likelihood of false negative results among the patient's sample is small, it cannot thus be ruled out. Second, the use of self-reported instruments may be associated with a risk of under- or overreporting of subjective experiences: for example, the risk of underreporting may be particularly relevant in patients with poor insight. Third, our patient

group is composed by individuals with lifetime presence of psychotic symptoms among different DSM-5 diagnosis (Major Depression with psychotic features, Bipolar Disorder with psychotic features, Schizophrenia Spectrum and other psychotic disorders): even if psychosis and insight are reported to be transdiagnostic features (van Os & Guloksuz, 2017), we cannot exclude that both anxious symptomatology and psychopathogenesis may vary within each nosographic category. Fourth, our psychiatric evaluation of insight impairment relied on a clinical interview based on a semi-structured instrument that, despite being widely used in different countries with good reliability, has not been officially validated in Italian yet. Fifth, our study intentionally focuses on the role of positive PLEs in the association between AS and anxiety, but we cannot exclude that factors other than AS and PLEs may increase anxiety levels. Sixth, our sample is limited mostly to Italian people of caucasian ethnicity, somewhat limiting the cross-cultural value of our data. Additionally, categorical variables such as sex and antipsychotic treatment status were employed in the statistical analysis; even though such variables can be employed effectively in linear models (Lunt, 2015), such statistical tests are often more suited for dealing with continuous variables. Finally, inferences drawn upon mediation analyses on cross-sectional data have inherent limitations (O'Laughlin et al., 2018).

6 | CONCLUSIONS AND CLINICAL IMPLICATIONS

To conclude, AS seems to be an anthropological polymorphic trait of vulnerability linked to the development of both PLEs and anxiety, among both healthy controls and psychotic patients. Moreover, our study highlights at least two putative psychopathogenic pathways of anxiety development which differ nonpsychotic individuals from psychotic subjects. In fact, although direct causality cannot be demonstrated, the relationship between psychosis proneness and anxious symptomatology in the general population appears to be mediated by positive PLEs frequency, whereas the same cannot be said for psychotic patients, whose anxiety levels, albeit worse, seem not to depend on PLEs anymore.

This finding may imply important clinical implications. When a young subject with no prior psychiatric history reports anxiety symptoms and presents with high levels of AS, clinicians must suspect the presence of frequent positive PLEs. Therefore, General Practitioners may refer the patient for a psychiatric evaluation, whereas Psychiatrists may carefully prefer the off-label use of atypical antipsychotics rather than antidepressants (if needed), and in any case refer the patient for a targeted psychotherapeutic intervention before the occurrence of insight impairment or transition from PLEs to full-blown psychotic symptoms.

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflict of interest.

DATA AVAILABILITY STATEMENT

The database of the studies, with the extracted data items, can be shared upon reasonable request to the corresponding author.

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SUPPORTING INFORMATION

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