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Original Article

Bridging the gap: aberrant salience, depressive symptoms and their role in psychosis prodrome

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SUMMARY

Objective

Aberrant salience (AS) is the unusual or incorrect assignment of salience, significance, or importance to otherwise innocuous stimuli and it is considered a key psychopathological feature of schizophrenia. Recent studies suggest AS can help identify individuals who are at risk of developing psychosis. Depressive symptoms (DS) are one of the major causes for help-seeking behaviors and might even predate the emergence of attenuated psychotic symptoms. The aim of this study is to investigate the relationship between AS and DS among young help-seekers.

Methods

A cross-sectional analytical study was conducted. 261 students (69% female, median age 23 years) accessing our counseling service were administered the Aberrant Salience Inventory (ASI), the Beck Depression Inventory-II (BDI-II) and the 16-item version of the Prodromal Questionnaire (PQ-16). Associations of age, sex, AS, DS, and psychotic-like experiences (PLE) were assessed using linear regression models.

Results

The median self-report scores were respectively BDI-II = 16 (IQR = 14), ASI = 13 (IQR = 9), and PQ-16 = 4 (IQR = 5). 90 students (37.2%) obtained a PQ-16 score ≥ 6, which is suggestive of a prodromal condition. Linear regression analysis showed that higher BDI and ASI scores predict higher PQ-16 scores and, thus, a higher PLE. Moreover, a second linear regression showed that three ASI subscales were significant predictors.

Conclusions

Since people with a high risk for the development of psychosis have much higher ASI scores than people without risk, our preliminary results suggest that the relationship between salience alterations and depressive symptomatology might provide helpful tools for identifying prodromal conditions.

Key words: aberrant salience, depressive symptoms, university students, help seekers, psychosis proneness

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Background

Aberrant salience (AS) is the unusual or incorrect assignment of salience, significance, or relevance to otherwise innocuous stimuli [1]. Kapur theorized psychosis as a state of AS linking biology, phenomenology, and psychopharmacology into a unitary framework in schizophrenia. On a psychopathological level, AS has been considered as a crucial "catalyst" in the development of psychotic experiences [2].

According to empirical evidence, individuals with Clinical-high Risk for psychosis (CHR) tend to attribute more significance to irrelevant stimuli compared to healthy controls [3]. This tendency is similar to what has been

observed in firs episode psychosis (FEP). As a result, the concept of AS has gained increased attention as a key psychopathological feature that can help identify individuals who are at risk of developing psychosis. Mapping AS could enrich the clinical characterization of the risk continuum of psychotic disorders (i.e., from psychosis proneness and CHR mental states to full-blown FEP) [4]. This feature is especially relevant for screening young adults and adolescents seeking help and should be included in a 'multiple-gate screening strategy' [5].

Despite the primary role played by positive symptoms in the definition of CHR since its first operationalizations [6,7], it is common for CHR subjects to exhibit comorbid psychiatric conditions [8], with mood and anxiety disorders being the most frequent [9,10]. These conditions are often associated with increased distress and poorer global and psychosocial functioning [11] and have been described as the primary cause for help-seeking in CHR individuals [12]. According to reports, a significant number of patients experiencing their first episode of psychosis (FEP) have reported enduring mental issues and increasing psycho-social impairment for an average period of 5 years prior to the onset of psychosis [13]. To effectively implement secondary prevention, it is crucial to thoroughly investigate and detect the most subtle and earliest subclinical syndromic manifestations, preceding the onset of attenuated positive psychotic symptoms.

The role of depression as prognostic factors for conversion is debated: meta-analysis found that affective symptoms show no effect on the risk of transition [11,14,15], while recent studies suggest that actual or past depressive or anxiety disorders might be a relevant risk factor for an unfavourable course of attenuated psychosis syndrome (APS) in CHR and increase the risk of transition to psychosis [9]. Moreover, there is evidence that affective comorbidity might increase the persistence of paranoid symptoms [16], decrease the likelihood of remission from the CHR state [17] and predict poorer global functional outcomes [18].

Therefore, exploring the relationship between AS and depressive symptoms (DS) might be crucial in early detecting psychosis prodrome among young help-seekers.

The aim of this study is to investigate the occurrence of AS among a group of young University students accessing our counseling psychological service and to analyze its association with both DS and psychotic-like experiences.

Methods

Setting and data collection

In December 2019, our Psychiatry and Clinical Psychology Unit launched a free counseling service for students enrolled at Tor Vergata University of Rome [19]. This service has a dual purpose: providing psychological support to students and identifying individuals at a higher risk of developing severe mental disorders.

All students accessing our counseling service were administered a battery of self-report questionnaires, including the Aberrant Salience Inventory (ASI), the Beck Depression Inventory-II (BDI-II) and the 16-item version of the Prodromal Questionnaire (PQ-16) before undergoing the first clinical assessment. International students who did not speak Italian were administered the English version of the same questionnaires, and the assessments were carried out in English.

All participants provided informed consent, and the Ethical Committee Board approved the study.

We conducted a cross-sectional study analyzing data collected from students (n = 261) seeking psychological help between December 2019 and November 2022. Inclusion criteria were:

1. mental health help-seeking request;
2. age 18-35 years;
3. no past or current substance dependence as defined in DSM-5 criteria.

Measurements

The Aberrant Salience Inventory (ASI)

The Aberrant Salience Inventory (ASI) is the only self-report instrument specifically developed for the assessment of AS [1]. It consists of 29 yes/no items and has five subscales measuring different aspects of the AS experience 20: feelings of increased significance (items: 1, 5, 10, 14, 15, 20 and 27), sense sharpening (items: 3, 9, 12, 17 and 21), impending understanding (items: 2, 6, 11, 16 and 29), heightened emotionality (items: 8, 13, 19, 23, 26 and 28) and heightened cognition (items: 4, 7, 18, 22, 24 and 25).

Cronbach's alpha for the ASI was .89 and ranged from .71 to .87 for the 5 subscales in the original validation study [1]. The Italian version of the ASI showed excellent reliability (internal consistency = .91; test-retest stability = .94 [95% confidence interval, CI: .92-.95]), and good factorial, convergent, divergent and discriminant validity was found in young people [21].

Beck's Depression Inventory (BDI-II)

The Beck's Depression Inventory (BDI-II) 22 is a 21-item self-report inventory measuring the severity of DS in adults and adolescents. For each item, participants are required to choose which sentence (rated on a Likert scale from 0 to 3) best describes how they have been feeling in the last two weeks. The BDI-II overall score ranges from 0 to 63, with higher scores reflecting higher levels of depression.

The Prodromal Questionnaire - 16 (PQ-16)

The Prodromal Questionnaire - 16 (PQ-16) is a 16-item questionnaire investigating perceptual abnormalities/hallucinations, unusual thought content/delusional ideas/paranoia and negative symptoms [23]. It was developed as a shorter version of the 92- item Prodromal Questionnaire [24]. The PQ-16 can be scored by the sum of the symptoms described in the questionnaire (0-16) or the additions of distress scores (range 0-48). When using the symptom total score, a cut-off of ≥ 6 seems fitting in general mental health settings, while a threshold of ≥ 8 is recommended when evaluating the distress score [23, 25].

Data analysis

All data were analysed using Jamovi (version 2.3.21.0). Sample characteristics were analysed by calculating descriptive statistics, including the means and standard deviations (SDs), frequencies and percentages for continuous variables. Counts and percentages are reported for categorical variables. First, a correlation matrix has been employed to analyse and establish relationships between the measured variables, providing valuable insights into their interdependence and associations. Then, a multivariable regression linear model, adjusted for age and gender, was performed to establish the effect of the independent variables (ASI and BDI-II score) on the outcomes (PQ-16 total score). In order to attain a more detailed analysis of the effect of AS on PQ-16 score, we performed a second regression model taking into consideration ASI subscales.

Results

The study involved 261 students who sought psychological counseling, spanning from December 2019 to November 2022. The sample was predominantly female, with 69% of respondents identifying as such. The age of participants ranged from 18 to 35 years, with median age being 23 years old (IQR = 4).

Sociodemographic characteristics of the sample are summarized in Table I.

A total of 249 students completed the ASI. 248 students completed the BDI-II. 99 (39.9%) scored less than 13, showing absence of depressive symptoms; 61 (24.6%) got a score between 14 and 19, indicative of mild depressive symptoms; 55 (22.2%) scored between 20 and 28, suggesting moderate depressive symptoms and the last 33 (13.3%) students obtained scores ≥ 29 suggestive of severe depressive symptoms. Finally, 242 students completed the PQ-16, resulting in 90 students (37.2%) with a PQ-16 score ≥ 6 and 97 (40.1%) with a score higher or equal than 8 at Likert distress scale.

The median self-report scores were respectively

TABLE I. *Sociodemographic and clinical characteristics of the sample*

(N = 261)	n	%	Median (IQR)
Age			23 (4)
Gender			
f	180	69.0%	
m	81	31.0%	
Foreign students			
Yes	31	11.9%	
No	230	88.1%	
Family history of mental illness			
Yes	28	10.7%	
No	233	89.3%	
Previous psychopharmacological therapy			
Yes	9	3.4%	
No	252	96.6%	
Substance use			
Yes	21	8.0%	
No	240	92.0%	

TABLE II. *Self-report questionnaires scores.*

	n	%	Median (IQR)
ASI	249		13 (9)
BDI-II	248		16 (14)
Negative (0-13)	99	39.9%	
Mild DS (14-19)	61	24.6%	
Moderate DS (20-28)	55	22.2%	
Severe DS (>29)	33	13.3%	
PQ-16	242		4 (5)
PQ-16 total score ≥ 6	90	37.2%	
PQ-16 distress score ≥ 8	97	40.1%	

ASI = 13 (IQR = 9), BDI-II = 16 (IQR = 14) and PQ-16 = 4 (IQR = 5).

Descriptive analyses of test variables are summarized in Table II.

Correlational analysis showed a significant relationship between ASI total scores and PQ-16 total symptoms score ($r = 0.555$, $p < 0.001$). At the same time, we found that DS correlated with AS ($r = 0.328$, $p < 0.001$) and PLE ($r = 0.507$, $p < 0.001$).

Our first multiple linear regression analysis revealed that both ASI score and BDI score significantly predicted PLE levels, while age and gender did not show a significant effect. This model explained 41.8% of variance of the explored outcome.

The second regression analysis performed showed that three ASI subscales ("sharpening of senses", "height-

TABLE III. *Linear regression – ASI total score.*

				Overall model test			
Model	R	R^2	Adjusted R^2	F	df1	df2	p
1	0.647	0.418	0.408	40.6	4	226	< .001

Model Coefficients – PQ-16 score				
Predictor	Estimate	SE	t	p
Intercept[a]	-1.6066	-1.6323	-0.984	0.326
Gender: m-f	-0.4524	0.3946	-1.146	0.253
Age	0.0582	0.0640	0.909	0.364
ASI score	0.2413	0.0300	8.045	< .001
BDI-II score	0.1305	0.0196	6.646	< .001

TABLE IV. *Linear regression ASI subscales.*

				Overall model test			
Model	R	R2	Adjusted R2	F	df1	df2	p
2	0.675	0.456	0.436	23.2	8	222	< .001

Model Coefficients – PQ-16 score				
Predictor	Estimate	SE	t	p
Intercept[a]	-0.6676	-1.6512	-0.404	0.686
Gender: m-f	-0.5377	0.3921	-1.371	0.172
Age	0.0511	0.0629	0.813	0.417
Increased significance	-01423	0.0300	8.045	0.279
Sharpening of senses	0.3525	0.1538	2.291	0.023
Impending understanding	0.0992	0.1796	0.552	0.581
Heightened emotionality	0.5281	0.1416	3.730	< .001
Heightened cognition	0.5477	0.1903	2.878	0.004
BDI-II score	0.1197	0.0198	6.051	< .001

ened emotionality" and "heightened cognition") were significant predictors of higher PQ-16 total scores. BDI-II total score remained a significant positive predictive factor in this model ($p < 0.001$). This time, linear regression model explained 45.6% of the variance ($R2 = 0.456$).
Linear regression models are summarized in Table III and IV.

Discussion

In the present study, we conducted a cross-sectional examination of the prevalence of AS, DS and PLE in a sample of help-seeking students and explored their correlation. The results of our research are in line with previous studies and indicate that AS scores in help-seeking individuals are correlated with measures of psychosis proneness (PQ-16).
The presence of AS is a frequently encountered phenomenon among Italian students: in our study, the ASI mean score was 12.8 (SD = 6.38) and the median score was 13, indicating that participants endorsed about a half of the items of the ASI. These results are strictly consistent with previous studies [21].
DS are relatively common in psychotic prodromal stage, representing one of the earliest and most frequent symptoms of psychosis [26], and they are associated with more severe positive symptoms in FEP [27]. Moreover, DS exhibits a stronger association with both help-seeking behaviors and distress in comparison to psychotic symptoms [28-30]. Consequently, DS are often the first symptoms identified when individuals initially seek psychiatric or psychological services [11]. Levels of DS tend to increase during the prodromal stage preceding psychosis onset [31] and decrease along with the remission of psychotic symptoms. Higher levels of DS have been reported in individuals that converted to psychosis [32] and depressed mood is significantly associated with poorer prognosis [33, 34]. In our study, higher BDI scores were significant predictive factors of more severe psychotic-like experiences, as measured by the PQ-16. This finding substantially confirms that DS represent a significant psychopathological dimension in young people suffering from an at-risk mental state [35]. Recent network analysis [36] states that affective symptomatology plays a central role in psychosis and may determine a heightened state of vulnerability; thus, worsening of DS may lead to global worsening of psychotic symptoms.
Since the ASI and the BDI-II measure deeply different constructs, correlational analysis suggests that their association might depend on some overlap in the pathogenetic pattern of psychosis prodrome. Higher level of AS has been associated with various psychopathological symptoms, especially anxious/depressive symptoms, somatic complaints and thought disorders [37]. However, several studies report high prevalence of psychiatric comorbidities in patients with clinical-high risk for psychosis [10,11,38]. These findings prompt us to contemplate the interconnection between AS and other expressions of psychopathology. We are more prone to adopt a dimensional perspective, rather than viewing the coexistence of AS and DS as a categorical comorbidity of two distinct disorders.
Birchwood et al. [39] proposed that DS may arise in early psychosis primarily due to the inherent disease process and/or negative cognitive interpretations of the significance and nature of psychotic symptoms. The disruption of early psychosis impacts individuals' interpersonal relationships and identity formation, especially during the critical developmental phase of youth. This observation aligns partially with the intrinsic hypothesis of depression in psychosis, which suggests that DS may occur following the development of positive symptoms [40].
Nevertheless, as we have seen, DS occurs as primary help-seeking behavior preceding not only the onset of full-blown psychosis, but also the emergence of APS [41]. Consequently, DS might be a result of primary subjective distress. Considering the link between AS and DS, Lisi and colleagues [37] suggest that it is plausible to hypothesize that elevated levels of AS can hinder adaptive responses to the environment and social interactions, thus increasing vulnerability to anxiety and depression.
With the expansion of the "at-risk mental state" concept into the realm of transdiagnostic psychiatry, demonstrating the relevance of ultra-high risk (UHR) criteria for persistent or incident non-psychotic disorders [42], the relationship between AS and DS in the prodromal condition may assume even greater importance. Our results align with the hypothesis put forth by Azzali and colleagues [5], highlighting the role of AS as a pluripotential factor in the pathogenesis of other mental conditions and its function as a state indicator of psychotic distress manifested as depressive symptomatology. However, since our data were collected at a single time point, we are unable to test the direction of causality in the links between AS and DS and the risk of transitioning to psychosis. This limitation represents the main constraint of our study.
In our study, around 13.33% of the sample obtain a score equal or higher than 21 at the ASI, with particularly elevated scores on the "increased significance", the "impending understanding" and the "heightened emotionality" subscales.
The sequence of "increased significance," "impending understanding," and, lastly, "heightened emotionality" has been interpreted as the delusional progression from a pre-delusional state of mind to fully developed psychotic experiences [21]. In this perspective, the statistically significant predictive value of the ASI dominions of "heightened emotionality" and "heightened cognition"

observed in our linear regression model may be interpreted as an indication that these dimensions carry a closer psychopathological relationship with the development of the delusional experience.
The fact that the exploration of PLEs as an indicator of increased risk for psychosis has not been extensively investigated through comprehensive clinical risk stratification interviews, such as SIPS/SOPS [43], represents the second main limitation of our research. However, our study examined AS in a sample of university students within an age range associated with an increased risk of developing psychosis who spontaneously sought help, indicating a higher risk compared to the general population.

Conclusion

The findings of this study carry significant clinical implications for the detection and secondary preventive intervention in at risk mental state. The early assessment of depressive episodes could be valuable in predicting an unfavorable course psychosis prodrome. Gaining insights into the role played by different symptoms in developing psychopathology could facilitate the identification of novel treatment targets and enhance overall outcomes [36,44,45].
However, empirical validation is needed for the prognostic validity of this approach. Alternatively, incorporating prediction models based on individual patient data could enhance stratification or personalized predictions within CHR samples.
Furthermore, the study of DS may help in identify distinct trajectories and potential varying clinical intervention needs in psychosis prodrome. Since false positive rates in transition to psychosis are still high, accurate detection may allow to optimize the efficiency of preventive approaches and plan specific interventions in order to reduce the severity of subclinical psychotic symptoms.
The data we have gathered confirms the effectiveness of ASI as a screening tool for identifying at-risk youth prone to psychosis [5,46]. Additionally, our findings support the importance of early detection and prompt intervention program for individuals showing signs of psychosis. Hence, it is imperative to prioritize the implementation of timely clinical strategies to improve prognosis in patients at risk [47].
Further longitudinal studies are required to enhance our understanding of the relationship between AS and DS, as well as to identify crucial clinical and psychopathological factors in CHR individuals that can potentially serve as predictors of transition to full psychosis [48-50].

Conflict of interest statement

The authors declare no conflict of interest.

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Authors' contributions

FFN, MP, AC, GA: data collection and curation; MR and GDL: conceptualization, investigation, methodology, supervision of the manuscript; FFN wrote the first draft of the manuscript; CN, EF, AS project administration, supervision, writing-review & editing; all the Authors reviewed and approved the final version of the manuscript.

Ethical consideration

The research was conducted ethically, with all study procedures being performed in accordance with the requirements of the 2013 World Medical Association's Declaration of Helsinki.

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