

The relationship between childhood trauma and aberrant salience: a preliminary study in patients with Schizophrenia

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SUMMARY

Objectives

Aberrant salience represents one of the main pathogenetic mechanisms of psychotic symptoms. Exposure to childhood trauma constitutes a relevant environmental risk factor for subsequent development of Schizophrenia, but the possible influence of trauma on aberrant salience is poorly studied in literature. The primary objective of this study was to verify the association between childhood trauma and aberrant salience and secondly to evaluate the impact of clinical variables on aberrant salience.

Methods

Overall 53 outpatients (39 diagnosed with Schizophrenia and 14 with Schizoaffective Disorder) were recruited. The Childhood Trauma Questionnaire Short-Form (CTQ-SF), the Aberrant Salience Inventory (ASI) and the Positive and Negative Schizophrenic Symptoms (PANSS) were administered. Psychopathological differences according to ASI scores were evaluated and independent predictors of aberrant salience were assessed through linear regression analysis.

Results

Consistent with ASI scores, aberrant salience was present among 57% of patients. Aberrant salience was associated with higher severity of delusions, hallucinatory behavior, mannerisms and unusual thought content (PANSS) and emotional abuse/neglect (CTQ). According to linear regression analysis, emotional abuse during childhood and previous psychiatric hospitalizations are associated with higher aberrant salience.

Conclusions

The most striking results of this preliminary study was that patients with psychosis who had experienced an emotional abuse during childhood can be associated with a higher level of aberrant salience. Further studies are needed to understand the mechanisms through which childhood trauma influences the creation of salience, including the possible presence of both adaptive and aberrant alterations in the mechanism of salience processing.

Key words: Schizophrenia, aberrant salience, childhood trauma, emotional abuse, psychosis, trauma

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Conflict of interest

The Authors declare no conflict of interest

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Introduction

Over the past decade, several evidences have shown how exposure to childhood trauma represents an important environmental risk factor for subsequent development of Schizophrenia^{1,2}. Childhood trauma is defined as a set of negative experiences faced by the individual before the age of 16 including emotional abuse, physical abuse, sexual abuse, emotional neglect, physical neglect³.

Several models have been proposed to explain the association between childhood traumatic events and psychotic symptoms, including

the presence of dysfunctional cognitive patterns, affective dysregulation, insecure attachment style and dissociative mechanisms⁴.

Individuals with a personal history of childhood trauma have a threefold increased risk of developing Schizophrenia and tackling child abuse could result in a reduction of approximately 33% of cases of psychosis⁵. Exposure to childhood trauma has a significant impact on the clinical presentation of the disorder, relating with an early onset of illness, more frequent and prolonged hospitalizations, more serious global psychotic symptoms, suicidal ideation⁶ and the need for more intensive treatment⁷. Literature supports a correlation between specific traumatic experiences in childhood and clinical manifestations in psychosis. Patients with Schizophrenia who experienced abuse and neglect in childhood show more clinical severity than those who have undergone other types of traumatic experiences⁸. Affected individuals with a history of physical abuse, sexual abuse and neglect also manifest prominent cognitive deficits, a reduced speed of information processing and alterations in working memory^{9,10}. Repeated childhood traumas, in fact, cause structural and functional abnormalities on cerebral functioning. Stress can increase the release of dopamine in the mesolimbic areas, proportionally related to the increase of cortisol levels¹¹. Several studies have demonstrated a negative impact of childhood trauma on higher cognitive functions, both in patients with psychosis and in high-risk probands⁹. Childhood adversities can induce long-term effects on neuronal growth and plasticity and on cognitive functions, through epigenetic modifications¹². The cognitive processes underlying delusions and hallucinations include both attributing responsibility for negative events to other people, and interpreting internal thoughts or memories as events external to the subject¹³. Salience constitutes a physiological process of cognitive integration thanks to which objects and stimuli from the external environment and from internal representations reach attention, thus acquiring relevance and becoming able to influence thoughts and behaviors. The salient process has the purpose of directing attention to stimuli relevant to the individual (i.e. attractive, aversive, or supportive) and to the detriment of neutral or irrelevant stimuli¹⁴. The central processing of environmental stimuli also depends on the subject's life experiences, personal beliefs, as well as the socio-economic level in which the subject lives and has lived. The phenomenon of attributing meaning to stimuli is therefore not a static but rather dynamic mechanism, influenced by the needs of the individual in a precise moment of time¹⁵. Aberrant salience, or the assignment of salience or meaning to otherwise neutral or harmless stimuli, represents one of the main pathogenetic mechanisms of

psychotic symptoms. Dopamine, which in physiological conditions mediates the salience of contextually relevant stimuli, during a psychotic state, determines the *de novo* creation of salience, which becomes remarkably aberrant¹⁶. The individual perceives these experiences as altered, not physiological, and tends to give them an organization or meaning, which ultimately leads to the pathological condition, primary to structure and concrete delusion. Hallucinations will likewise build around an aberrant meaning of internal representations of perceptions and related memories¹⁷. Moreover, the recent emerging field of computational psychiatry approach may offer useful models for salience integration^{18,19}. In particular, according to Miyata²⁰, two kinds of computational models seem to be appropriate for the integration of salience: one is the neural network model that seems to be suitable for describing the relationship between different salience domains; the other type of model is the Bayesian inference model, in fact, several studies suggest that some domains of salience follow the same computational model of Bayesian surprise^{21,22}.

The pathogenetic hypothesis of aberrant salience allows to explain how neurobiology and subjective experiences intersect each other, promoting the onset of psychosis and the development of positive psychotic symptoms as a clinical entity¹⁶. At the same time, evidence supports the role of childhood traumatic experiences in the alteration of corticostriatal connections and the salience process²³. A recent study has shown a significant relationship between exposure to childhood trauma and self-disturbances, or alterations in self-perception, the substrate on which abnormal experiences develop; the authors hypothesized that aberrant salience and alterations in self-perception constitute two fundamental elements of connection between history of childhood trauma and psychotic experience²⁴.

Based on the above, the main hypothesis was that a history of childhood trauma is associated with a greater level of aberrant salience. In the literature there are consistent data with the starting hypothesis of our work, however deriving from a single study conducted on the general population²⁴. Accordingly, the primary objective of the study was to investigate the association between childhood trauma and aberrant salience in patients with Schizophrenia and Schizoaffective Disorder. The secondary objective was to evaluate the impact of clinical variables on aberrant salience and any correlation with a higher level of aberrant salience.

Materials and methods

Participants and procedures

In this observational cross-sectional study, participants

were consecutively recruited at the Outpatients Unit of Psychiatry of the University Hospital "Mater Domini" of Catanzaro.

The inclusion criteria were: patients aged between 18 and 65 with a diagnosis of Schizophrenia or Schizoaffective Disorder according to DSM-5²⁵ formulated through the Structured Clinical Interview for DSM-5 (SCID-5-CV)²⁶. The exclusion criteria were: 1) diagnosis of dementia, intellectual disability or other medical conditions associated with psychiatric symptoms; 2) substance abuse; 3) conditions that did not allow the completion of the assessment, such as language problems, dyslexia or poor knowledge of Italian.

For this preliminary study, the sample consists of 53 patients: N = 39 patients with Schizophrenia and N = 14 patients with Schizoaffective Disorder.

The study was conducted in accordance with the latest version of the Helsinki Declaration and was approved by the local ethics committee. All participants provided written informed consent, in accordance with the ethics committee guidelines.

Assessment

Clinical and socio-demographics characteristics

The information collected includes: socio-demographics, psychiatric familiarity, age at onset of the disorder, duration of untreated psychosis (DUP), presence of psychiatric comorbidity, number of previous hospitalizations and antipsychotic therapy.

The daily dose of antipsychotic drugs took by each patient was expressed as the equivalent daily dose of chlorpromazine, based on the international consensus study by Gardner et al.²⁷.

Childhood Trauma

Childhood Trauma Questionnaire Short-Form (CTQ-SF)³: is a self-administered test of 28 items Likert type from 1 (never) to 5 (very often), that account for 5 subscales: emotional abuse, physical abuse, sexual abuse, emotional neglect, physical neglect. The risk of childhood trauma is based on the cut-off scores of each of the subscales: emotional abuse (none = 5-8; mild = 9-12; moderate = 13-15; severe \geq 16), physical abuse (none = 5-7; mild = 8-9; moderate = 10-12; severe \geq 13), sexual abuse (none = 5; mild = 6-7; moderate = 8-12; severe \geq 13), emotional neglect (none = 5-9; mild = 10-14; moderate = 15-17; severe \geq 18), physical neglect (none = 5-7; mild = 8-9; moderate = 10-12; severe \geq 13). CTQ reliability is good with high internal consistency scores. Sexual abuse, emotional neglect, emotional abuse, physical abuse, reported coefficients of 0.93-0.95, 0.88-0.92, 0.84-0.89 and 0.81-0.86, respectively. The test-retest coefficient was close to 0.80.

Aberrant Saliience

Aberrant Saliience Inventory (ASI)²⁸: this self-administered questionnaire of 29 items with dichotomous response (yes/no), assesses the presence and level of aberrant saliience and the vulnerability to psychosis. It assesses 5 factors in line with Kapur's conceptualization¹⁶: the increase in meaning, the quality/intensity of sensory perceptions, the alteration of understanding, the increase in emotionality and the acuity of the functions cognitive; it also assesses the presence of magical thinking, a psychotic-like experience that plays a key role and a close correlation with psychotic symptoms. ASI \geq 14 indicates psychotic vulnerability to aberrant saliience²⁸.

Clinical assessment

Positive and Negative Schizophrenic Symptoms (PANSS)²⁹: is a clinician-administered tool of 30 items to evaluate the presence and severity of positive and negative symptoms and general psychopathology in Schizophrenia patients. In our study, the PANSS remission scale criteria were used according to the definition of remission developed by Andreasen et al.³⁰. The 8 items considered include Delusions (P1), Conceptual disorganization (P2), Hallucinatory behavior (P3), Affective flattening (N1), Passive / apathetic social withdrawal (N4), Lack of spontaneity and fluidity in the interview (N6), Mannerisms postural (G5) and Contents of unusual thinking (G9); symptomatic remission is defined as a score of 3 ("mild") or less, on all items considered.

Statistical analysis

The data analysis was performed with the Statistical Package for the Social Science 22.0 (SPSS Inc., Chicago Illinois) and the data presented as averages, standard deviations, frequencies and percentages. The univariate analysis was applied to the comparison of means through the t-test for continuous variables and the chi-square test for categorical ones.

A stepwise linear regression model was used to identify independent predictors of aberrant saliience. Variables that differed $p < 0.01$ at t-test entered into the multivariate linear regression model. The entry and exit criteria from the model were 0.2 and 0.4 respectively. The statistical significance level was set at $p < 0.05$.

Results

The socio-demographic and clinical characteristics are summarized in Table I. The average age of the sample is 39.3 ± 11.5 ; male, unmarried, unemployed and living with the family of origin prevail. Most patients, approximately 43%, report no familiarity with Schizophrenia spectrum disorders and related disorders. The age at onset of the

TABLE I. Sample description.

		N = 53	
		n	%
Mean age in years^a		39.3	(11.5)
Gender	Male	34	(64.2)
	Female	19	(35.8)
Civil status	Married	10	(18.9)
	Divorced	2	(3.8)
	Single	41	(77.4)
Education (years)^a		12.3	(3.1)
Employment	Employed	12	(22.6)
	Unemployed	24	(45.3)
	On pension	5	(9.4)
	Unpaid activity	4	(7.5)
	Invalid/retired	8	(15.1)
Living status	Alone	2	(3.8)
	Parents	34	(64.2)
	Partner	9	(17.0)
	Other	8	(15.0)
Diagnosis	Schizophrenia	39	(73.6)
	Schizoaffective Disorder	14	(26.4)
Familiarity for psychosis	Yes	10	(18.9)
	No	43	(81.1)
Age at onset (years)^a		24.1	(6.8)
Duration of untreated psychosis (years)^a		1.38	(2.1)
Previous psychiatric hospitalizations^a		2.42	(3.3)
Daily equivalent dose of chlorpromazine (mg)^a		440	(178)

^a: data are expressed as means and (SD).

psychosis is on average 24.3 ± 6.8 , while the duration of untreated psychosis (DUP) is 1.4 ± 2.1 years. The average dose of antipsychotics is 440 ± 178 mg/day in chlorpromazine equivalents.

The average values obtained with CTQ and ASI and the proportion of patients in remission to PANSS according to Andreasen³⁰ criteria are summarized in Table II.

The sample was divided according to the ASI scores and groups were subsequently compared. Thirty patients (57%) scored over the threshold of ASI. Significant differences emerged as patients who scored $ASI \geq 14$ had an earlier onset of illness ($p = 0.51$), more previous psychiatric hospitalizations ($p = 0.003$) and took higher average doses of antipsychotic drugs ($p = 0.02$). Furthermore, patients with a higher aberrant salience also exhibited higher means in items P1 ($p < 0.001$), P3

($p = 0.046$), G5 ($p = 0.004$), G9 ($p = 0.017$) of PANSS and in the CTQ subscales emotional abuse ($p < 0.001$), emotional neglect ($p = 0.046$) and total score ($p = 0.003$) (Tab. III).

Finally, Table IV shows the results of the linear regression analysis. Those variables with significant differences ($p < 0.01$) at the previous t-test entered into the analysis as independent variables and ASI total score was considered the dependent variable. A background of emotional abuse and the number of previous psychiatric hospitalizations resulted to be predictors of higher aberrant salience ($R^2 = 0.240$; $F = 9.202$; $p < 0.001$).

Discussion

The present study aimed at evaluating the association between childhood trauma and aberrant salience

TABLE II. Results of clinical assessment.

		Mean	SD
PANSS-R^a	Yes	13	(24.5)
	No	40	(75.5)
CTQ	Emotional abuse	8.7	(4.7)
	Physical abuse	7.0	(4.0)
	Sexual abuse	6.8	(4.1)
	Emotional neglect	11.8	(5.2)
	Physical neglect	8.1	(3.5)
	Total score	43.4	(15.5)
	ASI	Increased significance	4.1
Sharpening of senses		2.4	(1.5)
Impending understanding		2.5	(1.6)
Heightened emotionality		3.2	(2.0)
Heightened cognition		2.8	(2.0)
Total score		14.9	(7.7)

PANSS-R: Positive and Negative Schizophrenic Symptoms - Remission Criteria; CTQ: Childhood Trauma Questionnaire; ASI: Aberrant Saliency Inventory; Symptomatic remission is defined as a score of 3 ("mild") or less on all of eight items (P1, P2, P3, N1, N4, N6, G5, G9). Emotional abuse (cut-off > 8); physical abuse (cut-off > 7); sexual abuse (cut-off > 5); emotional neglect (cut-off > 9); physical neglect (cut-off > 7). ASI (cut-off \geq 14). ^a: data are expressed as frequencies and (%).

in patients with Schizophrenia and Schizoaffective Disorder. The secondary objective was to evaluate the impact of clinical variables on aberrant salience. Despite the small sample size and the observational cross-sectional approach of present investigation, these results seems to highlight that a history of emotional abuse during childhood and the number of lifetime psychiatric hospitalizations are associated with a higher level of aberrant salience.

Our research suggests an innovative aspect on identifying a specific correlation between distinct types of early traumatic experiences that could act as predictors directly related to the development and pervasiveness of the aberrant salience in patients with psychosis.

Various evidences support the relationship between exposure to psychosocial stress and alterations the development of salience. A study has shown that individuals exposed to childhood trauma report a reduction of reward response and increased psychotic experiences, suggesting the possible presence of both adaptive and aberrant alterations in the mechanism of processing the salience³¹. Considering the central role of dopamine in the processing of salience, the finding of an alteration of presynaptic function of dopamine in individuals who have experienced early traumatic

TABLE III. Comparison of PANSS and CTQ scores according to ASI score.

		ASI \geq 14 N = 30		ASI < 14 N = 23		t	p
		Mean	SD	Mean	SD		
PANSS	Delusions (P1)	3.3	(1.2)	2.0	(1.1)	4.252	< 0.001
	Conceptual disorganization (P2)	3.3	(0.9)	2.7	(1.3)	1.920	0.060
	Hallucinatory behavior (P3)	2.4	(1.0)	1.8	(1.0)	2.041	0.046
	Blunted affect (N1)	3.5	(1.1)	3.0	(1.1)	1.624	0.111
	Social withdrawal passive/apathetic (N4)	3.6	(1.4)	3.0	(1.5)	1.578	0.121
	Lack of spontaneity of conversation (N6)	3.1	(1.3)	2.5	(1.4)	1.567	0.123
	Mannerisms and posturing(G5)	2.9	(1.2)	1.9	(1.1)	2.995	0.004
	Unusual thought content (G9)	3.5	(1.3)	2.6	(1.2)	2.457	0.017
CTQ	Emotional abuse	10.5	(4.8)	6.4	(3.4)	3.427	< 0.001
	Physical abuse	7.8	(4.2)	6.0	(3.4)	1.585	0.119
	Sexual abuse	7.8	(5.2)	5.6	(1.4)	1.968	0.055
	Emotional neglect	13.1	(5.6)	10.2	(4.3)	2.049	0.046
	Physical neglect	8.7	(4.1)	7.4	(2.4)	1.363	0.179
	Total CTQ	48.7	(17.0)	36.4	(10.0)	3.086	0.003

PANSS: Positive and Negative Schizophrenic Symptoms; CTQ: Childhood Trauma Questionnaire; ASI: Aberrant Saliency Inventory. Significant results are in bold.

TABLE IV. Linear Regression analysis.

Dependent variable	Independent variables	B	t	p
ASI total score	(Constant)	-	4.539	0.001
	Previous psychiatric hospitalizations	0.308	2.191	0.033
	Emotional abuse	0.288	2.051	0.046

ASI: Aberrant Salience Inventory. Significant results are in **bold**.

experiences suggests that this may be a possible mechanism of mediation between childhood trauma and an increased risk of mental illness³². Further, the exposure to chronic psychosocial stressors is associated with functional alterations in brain regions responsible for processing salience and corticostriatal functional connectivity. These data suggest that exposure to psychosocial stress could lead to corticostriatal dysfunction and consequently to development of aberrant salience³³.

In our study, it also emerged that a history of emotional abuse in childhood is predictive of a higher aberrant salience in individuals with psychosis. Evidence of a casual association between childhood trauma and aberrant salience is limited in the literature: a single study in the general population revealed a significant relationship between childhood abuse (emotional, physical and sexual) and the presence of psychotic-like experiences, demonstrating only an indirect mediation of aberrant salience in this association²⁴. To date, to the best of our knowledge, there is no study in the literature that has investigated the relationship between childhood trauma and aberrant salience in a clinical population of patients with Schizophrenia.

Exposure to early trauma, in particular to interpersonal violence (emotional abuse, physical abuse or sexual abuse), can cause cognitive distortions in the processing of information in the individual (i.e. “people should not be trusted”; “people could be dangerous”). Studies have shown that child abuse is related to a decrease in Theory of Mind – ToM, or the ability to attribute mental states, beliefs, intentions, desires, emotions, knowledge – to oneself and to others, and the ability to understand that others have different mental states than their own³⁴. The connection between ToM and exposure to childhood trauma has also emerged in patients with Schizophrenia and has been associated with alterations of the brain networks involved in the elaboration of mental states³⁵.

By extending the results of previous studies, where mediation of cognitive biases in processing information related to the content of beliefs was demonstrated (i.e. a pattern of negative beliefs or attention to the threat)²⁴, present data indicate that childhood traumas

are also linked to the content of specific components of the aberrant salience, which lead to the assignment of an inadequate meaning to the stimuli. This result is consistent with a group of upcoming studies linking the experience of aberrant salience to the psychotic state and the risk of psychosis³⁶.

Moreover, it seems that interpersonal emotional violence in early age subjects has a stronger influence on aberrant salience than emotional or physical neglect. However, further studies are needed to replicate this association in clinical sample.

Lifetime psychiatric hospitalizations also were associated with aberrant salience; noteworthy, aberrant salience represents one of the main pathogenetic mechanisms underlying the production of florid positive psychotic symptoms (delusions, hallucinations and thought modifications)¹⁶ and it is already present in the prodromal phase of psychosis, during which the individual experiences increased cognitive and sensory skills, associated with a sense of increased awareness of things. Common feelings at this stage include increased emotions difficult to manage, a sense of internal confusion, perception of important upcoming revelations³⁷.

A study pointed out that patients with schizophrenia with more florid production symptoms showed increased hemodynamic responses in the left insula, corresponding to a higher level of aberrant salience, compared to patients with less severe positive symptoms³⁸. The presence of positive florid symptoms, especially the co-presence of hallucinations and delusions, compared to the presence of isolated symptoms, has been associated with a higher persistence of psychotic experiences with consequent worse clinical outcome and higher number of psychiatric hospitalizations. A specific hallucinatory-delusional state may represent an exacerbation of aberrant salience attribution, increasing the risk of an unfavorable clinical outcome³⁹.

Classical European psychopathology defines the following as the crucial elements in developing a more articulated delusional experience, starting from a pre-delusional phase, and its maintenance: the increase in meaning, the quality/intensity of sensory perceptions, the alteration of understanding, the increase in emotion

and the acuity of cognitive functions, or the dimensions of aberrant salience³⁷. In our study, patients with a higher level of aberrant salience reported a higher score in the symptomatic dimensions of PANSS “Delusions”, “Hallucinatory behavior”, “Postural mannerisms” and “Unusual contents of thought”, as well as a higher number of past psychiatric hospitalizations and a higher average dose of antipsychotic taken daily.

The abnormal transmission of dopamine is a crucial element among the theories that aim to explain how neurobiology correlates with the productive symptoms in psychosis; similarly, evidence supports a direct relationship between the presynaptic synthesis capacity of dopamine and the creation of aberrant salience in individuals at risk of psychosis⁴⁰. Since antipsychotics tend to block D2 receptors, therapy could reduce positive symptoms by mitigating the creation of dopamine-mediated aberrant salience¹⁶. In fact, it has been shown that patients with Schizophrenia under treatment show reduced adaptive salience compared to healthy controls and therefore a higher level of aberrant salience⁴⁰. This could support the result of our study, namely that a higher level of aberrant salience corresponded to a higher average dose of antipsychotic taken daily.

Conclusions

To conclude, the most striking result of our preliminary study is addressing the relationship between a psychosis-specific mechanism like aberrant salience and a transdiagnostic risk factor such as childhood trauma; specifically, our findings support the main hypothesis according which having experienced an emotional abuse in childhood can be associated with a higher level of aberrant salience in patients with psychosis.

Although our study did not examine neurobiological alterations (e.g. excessive dopamine release), our results could be interpreted as in line with predictions made by previous studies on the relationship between childhood adversity and behavioral expression of an excessive release of dopamine and therefore creation of aberrant salience³³.

In clinical practice, the results of this study increasingly strengthen the hypothesis that early traumatic experiences can be used as an indicator of disease progression, useful in identifying those patients with high risk of graver clinical manifestations and unfavorable course³³. An accurate anamnestic investigation aimed at detecting childhood trauma during the psychiatric evaluation of a patient suffering from psychosis, can be fundamental for an adequate diagnostic-therapeutic path.

Numerous evidences underline how the prevention of childhood trauma should be one of the objectives within programs driving to promote mental health and that early detection could be important to implement the possible interventions targeted at improving the outcome on long term in disadvantaged children⁴¹. Our study suggests, on the other hand, that aberrant salience could be an important mediator between the experience of trauma and the development and maintenance of psychotic symptoms; the early detection of aberrant salience in disadvantaged children/adolescents could be also an important target in the prevention of the onset of psychosis⁴². Further studies are needed to increase understanding of the mechanisms through which childhood trauma influences the creation of salience, including the possible presence of both adaptive and aberrant alterations in the mechanism of salience processing.

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