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Loneliness and susceptibility to social pain mediate the association between autistic traits and psychotic experiences in young non-clinical adults

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Understanding of the mechanisms involved in the occurrence of psychotic experiences (PEs) in highly autistic individuals is crucial for identifying appropriate prevention and intervention strategies. This study aimed to investigate the mediating role of susceptibility to social pain and loneliness in the relationship between autistic traits (ATs) and PEs in adults from the general population of 12 Arab countries. This cross-sectional study is part of a large-scale multi-country research project. A total of 7646 young adults (age range 18–35 years, mean age of 22.55 ± 4.00 years and 75.5% females) from twelve Arab countries (i.e., Algeria, Bahrain, Egypt, Iraq, Jordan, Kingdom of Saudi Arabia, Kuwait, Lebanon, Morocco, Oman, Palestine, and Tunisia) were included. Mediation analyses showed that, after adjusting over confounding variables, both loneliness (indirect effect: Beta = 0.18; Boot SE = 0.02; Boot CI 0.14; 0.21) and social pain (indirect effect: Beta = 0.03; Boot SE = 0.01; Boot CI 0.001; 0.05) partially mediated the association between ATs and PEs. Higher ATs were significantly associated with more loneliness and susceptibility to social pain, and directly associated with more severe PEs. Finally, higher loneliness and susceptibility to social pain were significantly associated with greater PEs scores. Findings indicated that individuals with higher ATs tend to experience greater loneliness and feel more pain from rejection, which can in turn be associated with higher levels of PEs. Interventions targeting susceptibility to social pain and loneliness as a means of mitigating PEs among highly autistic adults should be considered.

Keywords Autistic traits, Psychotic experiences, Loneliness, Social pain, Mediation, Adults, General population

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Autism and psychosis have been historically conceived as related disorders[1]. Over the following decades, autism spectrum disorder (ASD) was recognized as a separate diagnostic entity, characterized by the onset in early childhood of difficulties in communication and social interaction, coupled with restricted interests and repetitive behavior[2,3]. On the other hand, psychotic disorders are defined by the onset in early adulthood of positive (i.e., delusions and hallucinations), negative (i.e., diminished emotional expression or avolition), and cognitive symptoms[2]. Both groups of disorders may exist as a continuous phenotype in nature across the general population, with autistic traits (ATs)[4] and psychotic experiences (PEs)[5] being located at the mildest end. Although autism and psychosis have apparent differences in their defining characteristics, including developmental antecedents, clinical presentation and course, there is evidence that a symptom overlap exists between the two conditions along the continuum.

The relationship between autistic traits and psychotic experiences in the general population

Several systematic reviews of clinical studies pointed to the coexistence of autism and psychosis in patients' samples. For instance, a systematic review found estimated prevalence rates of up to 61% for ATs and up to 52% for ASD among patients with psychotic disorders[6]. Another systematic review reported a pooled prevalence rate of non-affective psychosis of 9.5% in patients diagnosed with ASD[7]. A meta-analysis encompassing thirteen studies and 1,958 individuals showed that individuals with schizophrenia spectrum disorders exhibited significantly higher ATs compared to controls, with a standardized mean difference of 1.39[8]. Similar findings were also demonstrated at the prodromal stage of psychosis, as a systematic review and metaanalysis by VaquerizoSerrano et al.[9] found that 11.6% of individuals fulfilling Clinical High-Risk for Psychosis criteria have an ASD diagnosis. Another systematic review observed higher levels of paranoia in individuals diagnosed with ASD compared to controls[10]. In particular, a systematic review and meta-analysis by Kiyono et al.[11] found a pooled prevalence of PEs in patients with ASD of 24%, with a calculated overall correlation between PEs and ATs of 0.34.

Apart from clinical research, some evidence supports the close connection between ATs and PEs in non-clinical populations. Several studies conducted among university students have, for example, found a significant link between specific autistic features (e.g., attention switching, attention to detail, communication difficulties) and positive schizotypal symptoms (e.g., ideas of reference, magical thinking, unusual perceptions)[12–16]. However, the use of students' samples could have impacted the generalizability of the findings to the broader population of adults[17]. Additionally, schizotypal traits, which reflect a putative liability for schizophrenia-spectrum disorders, are distinct from specific positive PEs such as paranoid delusions, thought insertion, or auditory hallucinations[18]. Less amount of research has been dedicated to the link between ATs and Pes—in particular—within the community, and even less in the non-clinical adult population. A large British birth cohort study reported that childhood ASD and ATs were associated with 2.8- and 1.15-fold increased risk of developing PEs in early adolescence, respectively[19]. Martinez et al.[20] were the first to address the overlapping symptoms and traits between autism and psychosis in an adult general population from an epidemiological approach in two large datasets (The Adult Psychiatric Morbidity Survey 2007, $N = 7353$; and 2014, $N = 7500$). Findings indicated that ATs were significantly linked to a range of psychotic experiences, and that highly autistic individuals were at increased risk for probable psychosis (odds ratio = 15.5 in 2007 and 22.5 in 2014) compared to those with lower ATs[20]. Thus, there appears a strong need for a further examination of how ATs relate to PEs in adult epidemiological samples. An examination of the nature and mechanisms underlying the association between these two spectrum conditions may facilitate the identification of common etiological factors, which may pave the way for new targeted preventive interventions and treatments for both autism and psychosis. Several theoretical and empirical perspectives attempted to explain the relationship between ATs and PEs, including shared neurobiological substrates (i.e., aberrancies in biological systems involved in synaptic development, plasticity, and function) of the two groups of conditions[21–23]. Besides, the autistic and psychotic phenotypes in the general population demonstrated a network of correlations with features of social relationships, including social withdrawal, perceived rejection, and difficulties in social interaction[24]. This study proposes to further explore the mechanisms underlying the relationship between ATs and PEs by examining the indirect effect of two potential mediators, i.e. susceptibility to social pain and loneliness, in the relationship in a large sample of non-clinical adults. Figure 1 illustrates the theoretically-driven conceptual framework proposed in this study.

Susceptibility to social pain and loneliness as potential mediators

Loneliness can be defined as a subjective distressing experience arising from a discrepancy between the desired/expected social relationships and those the person actually has. Social pain refers to "a specific emotional reaction to the perception that one is being excluded from desired relationships or being devalued by desired relationship partners or groups"[25], p. 202). In other words, social pain can be described as a distressing emotional state that results from perceptions of interpersonal loss or rejection (e.g., a relationship breakup, unrequited love, the death of a loved one), or from social injuries. Individuals describe negative experiences arising from social injury as "painful" and "hurting". Evidence from animal and human brain imaging studies gave support to the

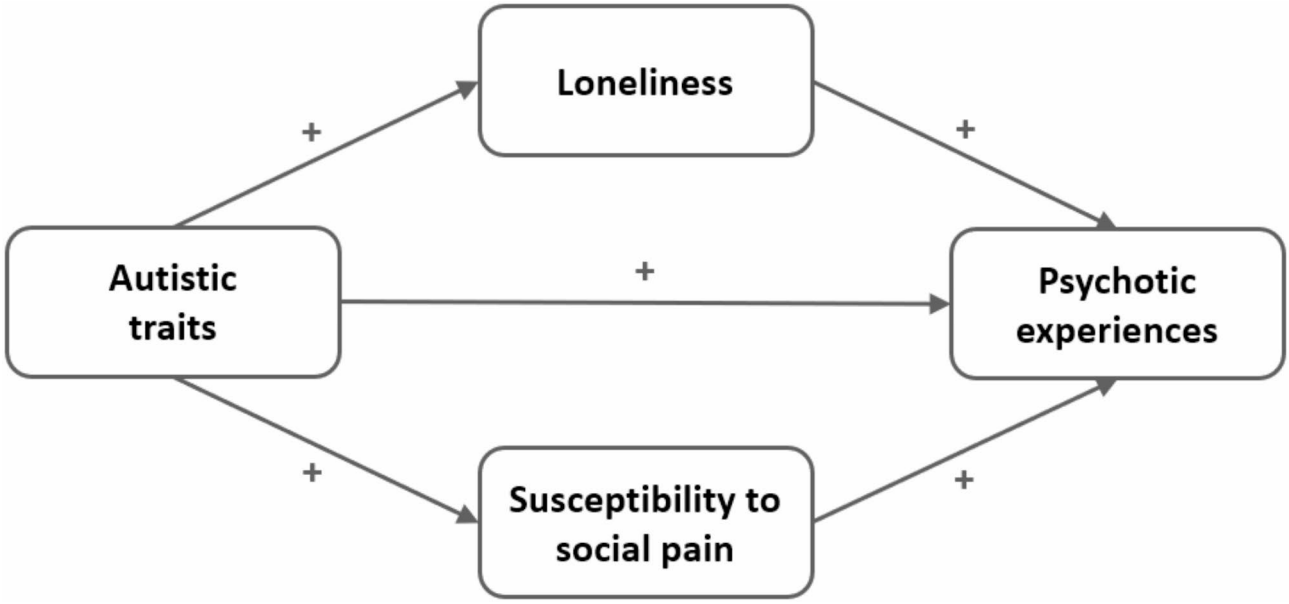

Fig. 1. Conceptual framework.

notion that social rejection hurts, and that this reference to "pain" is not simply metaphorical, but an expression of an overlap in neural and biological systems underlying physical and social pain[26–28]. Social pain can be assessed using either the cyberball experiment or self-report instruments. The cyberball game (i.e., a virtual online, interactive cyber ball-toss game, whereby the participant is made to believe he/she is being ignored and excluded from the game) covers emotional reactions to a specific situation rather than a consistent response tendency to perceive social pain in various situations[29,30]. Among standardized self-report measures, the Social Pain Questionnaire (SPQ) used in the present study refers to a general susceptibility to social pain, in which a social pain response is anticipated, but not actually experienced[31]. The serious negative consequences that both loneliness and susceptibility to social pain can have for health are increasingly recognized as an important emerging area of inquiry. Loneliness and susceptibility to social pain were both found to be strong risk factors for physical and mental health problems[32,33], as well as an elevated mortality[34,35].

More particularly, earlier research suggested that loneliness[36,37] and anticipated social rejection[38,39] could play a determinant role in the onset of psychotic symptoms. For example, a meta-analytic review revealed that loneliness is significantly associated with PEs (specifically and more robustly with paranoia); and that this association was stronger among non-clinical than clinical samples[40]. A systematic review and meta-analysis confirmed a significant positive loneliness-psychosis association, and indicated that higher loneliness scores were related to an increased likelihood of subclinical auditory hallucinations experiences (OR = 1.17)[41]. A quasi-experimental study observed that experiences of social pain was associated with a significant increase in paranoid beliefs[39]. On the other hand, people with high levels of ATs are also consistently found to experience more loneliness than controls, and to be frequently marginalized by social groups and rejected by peers[42,43]. Trimmer et al.[44] reported that individuals diagnosed with a high-functioning (IQ > 80) ASD displayed increased arousal than matched controls following exposure to social exclusion from the Cyberball game. More recently, experimental research has shown that subclinical ATs heightened rejection-induced social pain in nonclinical adults, both behaviorally (behavioral responses to the Social-Judgment Task) and in the brain (electroencephalographic oscillatory responses)[45].

Several explanations can be advanced to account for these relationships. As for the relationship between ATs and loneliness/susceptibility to social pain, research has shown that people with high ATs exhibit more communicative impairments, social withdrawal, atypical behaviors and decreased adaptive functioning; these social repercussions may lead, in turn, to subsequent distress and mental health problems[46,47]. Besides, increased levels of ATs may amplify experiences of perceiving oneself as a hopeless burden on others, difficulty maintaining reciprocal social relationships, and feelings of not belonging in the world, which may thereby increase the likelihood of psychopathology[48,49]. A possible mental health outcome of loneliness and susceptibility to social pain is the emergence of psychotic symptoms[38–41]. Regarding the relationship between loneliness/susceptibility to social pain and PEs, a plausible explanation is provided by the social defeat hypothesis of schizophrenia, which posits that long-term exposure to negative experiences of being excluded from the majority group may lead to dopaminergic hyperactivity, particularly in the mesolimbic dopaminergic neurotransmission system, thus causing an increased risk for developing psychosis[50]. Another explanation that can be advanced is the cognitive theory of psychosis[51], which stipulates that poor self-esteem and self-concept are possible pathways leading to psychosis. Feelings of loneliness play a role in strengthening negative self-concepts and poor self-esteem, which both are associated with negative contents of hallucinations and delusions[52]. Furthermore, there is some other evidence in adults from the general population supporting that loneliness, social isolation and perceived social

pain are significantly associated with systemic inflammation (e.g., higher Interleukin-6, C-reactive protein and fibrinogen)[53]. Such subclinical inflammation has been associated with psychosis in line with the inflammation hypothesis of schizophrenia[54,55]. Overall, these data suggest that susceptibility to social pain and loneliness experienced by highly autistic individuals in the general population may possibly be related to the emergence and severity of PEs.

Rationale of the current study

The need to conduct the present study was triggered by several considerations. First, up until now, there have been no studies worldwide that assess the mediating role of susceptibility to social pain and loneliness in the association between ATs and PEs to our knowledge. Exploring susceptibility to social pain and loneliness as possible mediators between ATs and PEs may aid in the detection, prevention and early intervention of psychosis that relate closely to these negative social experiences in young people at risk for ASD. Second, the vast majority of evidence available on the topic has been conducted in clinical populations. However, clinical studies of ASD and psychotic disorders cannot be substitutes for non-clinical studies of ATs and PEs. Given that individuals with high ATs and PEs have overlapping biological and genetic etiology[56,57] and tend to share similar psychological and behavioral features[58,59] with those with ASD and psychotic disorders, investigating individuals from the general population at the lowest severity of the phenotype expression of autism and psychosis may offer unique and valuable insights into the nature of the direct and indirect relationship between the two conditions. In addition, young adulthood represents the median age for the development of psychotic disorders[60], and is a common age of onset of PEs in the general population[61]. Young community adults represent thus a critical population for inquiry into the relationship between ATs and PEs. Elucidation of this relationship in a non-clinical sample at the mildest end of the autism-psychosis continuum should lead to a better understanding of the mechanisms involved in the occurrence of PEs in highly autistic individuals. This can offer significant implications for public health, prevention and early intervention, as the combined presence of subclinical autistic and psychotic traits was shown to be linked to depression, self-harm and suicidality[62]. Third, no published studies are yet available on ATs among adults in the Arab world. This represents a significant gap, bearing in mind that cultural differences may exert impact on the reporting and expression of ATs[63,64], PEs[65,66], loneliness[67] and sensitivity to social rejection[68]. The expression and interpretation of ATs can vary widely across cultures[69]. Indeed, there is evidence that social norms on how individuals process emotions and behave can vary between Western cultural backgrounds (from where most of the existing research originated) and other parts of the world[69,70]. However, no studies on ATs profile among community could be identified from Arab countries. In addition, the characteristics and prevalence of PEs seem to be largely dependent on culture[71,72], and to be over-represented in Arab contexts[73,74]; hence the high relevance of investigating the topic in Arab countries. Therefore, this study aimed to investigate the mediating role of susceptibility to social pain and loneliness in the relationship between ATs and PEs in adults from the general population of 12 Arab countries. It is hypothesized that: (1) the independent variable (ATs) would have a positively direct effect on PEs, regarded as a dependent variable, and (2) susceptibility to social pain and loneliness would serve as mediators of the relationship between the independent and dependent variables.

Methods

Participants and procedure

The *M*ultinational *A*utism *P*roject ("MAP") of the Arab world is a large-scale multi-country research project intended for offering, for the first time, an overview of the magnitude of ATs prevalence and correlates in the general adult population in Arab countries from an epidemiological perspective. To this end, a cross-sectional online research design was applied between February and April 2024. A total of twelve Arab countries were involved: Algeria, Bahrain, Egypt, Iraq, Jordan, Kingdom of Saudi Arabia, Kuwait, Lebanon, Morocco, Oman, Palestine, and Tunisia. Eligible participants were aged between 18 and 35 years (as the at-risk for psychosis population predominantly belongs to this age range[75]), originating from, and residing in one of the above-mentioned Arab countries, and consenting to take part in the study.

The questionnaire was available only in the Arabic language. The snowball sampling technique was used to recruit participants. Data were collected through a web-based anonymous questionnaire disseminated via Google Forms and multiple social media platforms. Once enrolled, participants were asked to complete the survey, then to identify other potential participants, contact them and encourage them to participate in our study. The first section of the questionnaire covered informed consent for participation in the study; participants were redirected to the rest of the survey only after ticking 'Yes' to the statement "I actively consent to take part in this study of my own free will". No financial rewards were offered. The protocol was approved by the home institutions of the study's principal investigators [SH and FFR], namely the Lebanese International University's School of Pharmacy ethics committee (2024ERC-025-LIUSOP) and the ethics committee of Razi Psychiatric Hospital, Manouba, Tunisia (ECRPH-2024-032). The present study was performed according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines[76].

Measures

Sociodemographic information

Data about age, sex (male, female), level of education (elementary, middle, secondary, university), tobacco use (Yes, No), alcohol drinking (Yes, No), lifetime cannabis use (Yes, No), household crowding index (i.e. the number of persons divided by the number of rooms in the house except the kitchen and bathrooms; with higher scores reflecting worse socioeconomic status), and perceived financial burden) were gathered from participants.

The autism-spectrum Quotient-28 (AQ-28)
The AQ-28 is a self-report measure that assesses ATs through a total of 28 items and the following five factors : Preference for routine (e.g., "New situations make me anxious"), Attention switching difficulties (e.g., "I find it easy to do more than one thing at once"), Difficulties with imagination (e.g., "I find it difficult to work out people's intentions"), Difficulties with social skills (e.g., "I find it hard to make new friends") and Fascination for numbers/patterns (e.g., "I notice patterns in things all the time")[77]. Each item is rated on a 4-point Likert scale, with "Definitely agree"/"Slightly agree" scoring 1 and "Definitely disagree"/"Slightly disagree" scoring 0. Fifteen items are reverse scored. Higher total scores (0–28) reflect greater levels of ATs. The Arabic validated version used in this study[78] showed a Cronbach α of 0.91 in the present sample.

The Social Pain Questionnaire (SPQ)
The SPQ is a self-administered scale that contains 10 items assessing perceived susceptibility to social pain (e.g., "It hurts my feelings if somebody denies a request of me"). Items are rated on a five-point Likert type scale ranging from 0 ("Applies not at all to me") to 4 ("Applies exactly to me")[31]. Higher total scores indicate higher perceived susceptibility to social pain. In the present study, the Arabic version of the SPQ was used[79], which had a Cronbach α of 0.94 in our sample.

The Jong-Gierveld loneliness scale (JGLS)
The JGLS is a self-report tool that measures feelings of loneliness through 5 items (e.g., "I experience a general sense of emptiness", "I miss having people around")[80]. Items are rated following a yes/no question format. Either 0 or 1 point is received for a negative or a positive answer, respectively. Greater total scores designate more pronounced loneliness experienced by respondents. The Arabic validated version of the scale was used[81], with a Cronbach α of 0.78 in the present sample.

The Prodromal questionnaire-brief (PQ-B)
The PQ-B is a self-report measure composed of 21 items rated as yes/no, serving to assess the severity of PEs[82,83]. A "yes" response to an item is followed by an item asking to rate the degree of distress experienced in relation to the statement. The Arabic validated version of the PQ-B was employed in this study {Fekih-Romdhane, 2023 #74}, which yielded a Cronbach α of 0.94.

Statistical analyses
Data analysis was performed using the SPSS software version 25. Reliability was checked using McDonald's omega values for the used scales. The PQ-B score had a normal distribution as shown by the skewness (= 0.652) and kurtosis (= − 0.040) values varying between ± 1[85]. The Student *t*-test was used to compare continuous variables between two groups, and Pearson correlation was used for linear correlation between continuous variables. The PROCESS SPSS Macro version 3.4, model 4 was used to calculate four pathways[86]; Pathway A determined the effect of ATs on the mediator (i.e., loneliness and susceptibility to social pain); Pathway B examined the association between the mediator (i.e., loneliness and susceptibility to social pain) and PEs, and Pathways C and C' estimated the total and direct effects of ATs on PEs. Significance was deemed present if the Bootstrapped confidence interval did not pass by zero[86]. The mediation analyses were adjusted over all variables that showed a $p < 0.25$ in the bivariate analysis. Significance was set at $p < 0.05$.

Results
A total of 7646 adults aged between 18 and 35 years met the inclusion criteria and were included in analysis. The mean age was 22.55 ± 4.00 years and 75.5% were females. Other descriptions of the sample can be found in Table 1.

Bivariate analysis
A significantly higher mean PQ-B score was found in Morocco compared to other countries, in females compared to males, in single compared to married people, in participants with a secondary level of education or less, in those who use tobacco (Table 2). Moreover, higher ATs, household crowding index, financial satisfaction, loneliness, and susceptibility to social pain were significantly associated with higher PQ-B scores, whereas older age was significantly associated with lower PQ-B scores (Table 3).

Mediation analysis
The results of the mediation analysis were adjusted over the following variables: sex, marital status, education, tobacco use, lifetime cannabis use, age, household crowding index, financial burden and country. Both loneliness (indirect effect: Beta = 0.18; Boot SE = 0.02; Boot CI 0.14; 0.21) and susceptibility to social pain (indirect effect: Beta = 0.03; Boot SE = 0.01; Boot CI 0.001; 0.05) partially mediated the association between ATs and PEs. Higher ATs were significantly associated with more loneliness and susceptibility to social pain, and directly associated with more severe PEs. Finally, higher loneliness and susceptibility to social pain were significantly associated with greater PEs scores (Figs. 2 and 3).

Discussion
The present study explored the mediating role of two important social factors, i.e. loneliness and susceptibility to social pain, in the relationship between ATs and PEs in a large sample ($N = 7646$) of young adults from the general population of twelve Arab countries. It was found that ATs exerted both direct and indirect effects on PEs through loneliness and susceptibility to social pain. These findings highlight the potential of the two factors

Sex	
Males	1876 (24.5%)
Females	5770 (75.5%)
Marital status	
Single	6658 (87.1%)
Married	988 (12.9%)
Country	
Oman	388 (5.1%)
Iraq	482 (6.3%)
KSA	285 (3.7%)
Jordan	388 (5.1%)
Palestine	435 (5.7%)
Egypt	1164 (15.2%)
Algeria	464 (6.7%)
Lebanon	878 (11.5%)
Morocco	434 (5.7%)
Bahrain	390 (5.1%)
Tunisia	1023 (13.4%)
Kuwait	1315 (17.2%)
Education	
Secondary or less	628 (8.2%)
University	7018 (91.8%)
Tobacco use	
No	6584 (86.1%)
Yes	1062 (13.9%)
Alcohol drinking	
No	6996 (91.5%)
Yes	650 (8.5%)
Lifetime cannabis use	
No	7137 (93.3%)
Yes	509 (6.7%)
Age (years)	22.55 ± 4.00
Household crowding index (person/room)	1.42 ± 0.90
Perceived financial burden	3.90 ± 2.82
Psychotic experiences	27.91 ± 20.88 [skewness = 0.652; kurtosis = − 0.040; minimum = 0; maximum = 105]
Autistic traits	11.50 ± 3.50 [skewness = − 0.076; kurtosis = 0.039; minimum = 0; maximum = 28]
Susceptibility to social pain	21.33 ± 9.94 [skewness = 0.035; kurtosis = − 0.689; minimum = 0; maximum = 40]
Loneliness	2.10 ± 1.72 [skewness = 0.284; kurtosis = − 1.186; minimum = 0; maximum = 5]

Table 1. Sociodemographic and other characteristics of the participants ($n = 7646$).

in explaining the relationship ATs-PEs in an under-represented non-clinical adult population from various Arab societies and cultural backgrounds.

ATs demonstrated a direct effect on PEs in our sample. This finding concurs with evidence from both clinical[6,8–11] and non-clinical studies[12–16] predominantly emerging from Western countries, and showing an overlap between autistic and psychotic traits and symptoms. This result is also consistent with the strong evidence from prospective studies showing that autistic traits significantly predict the subsequent development of PEs later in life[87–89]. This is also in line with birth cohort studies showing that parent-reported ATs in childhood significantly predict the development of PEs in early adolescence, suggesting that ATs can be an early precursor of psychosis[19,90,91]. These data preliminarily suggest that the existence of a significant relationship between autism and psychosis may be universal and independent of cultural context.

Another key finding was that ATs exerted significant indirect effects on PEs through higher levels of perceived loneliness and susceptibility to social pain. In other words, highly autistic adults could experience more severe susceptibility to social pain and loneliness; this, in turn, could be linked to more severe psychotic symptoms. This finding is in agreement with a previous experimental research demonstrating that individuals with high ATs showed more sensitivity to social disconnection[45], as well as with other prior research showing that these individuals are more prone to perceive themselves as a burden and to experience feelings that they do not belong[48]. Highly autistic people are found to often experience social rejection, which is mainly attributable to their poor social skills, and is regarded as a major contributing factor to their highly prevalent psychological distress (e.g[46,47]). , . Indeed, individuals with high levels ATs have a greater likelihood of experiencing poor social interactions and

	Mean ± SD	t/F	df/df1,df2	*p*
Country		8.55	11,7634	< **0.001**
Oman	28.32 ± 20.12			
Iraq	28.31 ± 21.23			
Saudi Arabia	27.19 ± 19.87			
Jordan	31.56 ± 21.54			
Palestine	30.27 ± 21.53			
Egypt	28.66 ± 21.14			
Algeria	27.25 ± 20.20			
Lebanon	26.31 ± 22.49			
Morocco	34.17 ± 22.17			
Bahrain	29.61 ± 19.64			
Tunisia	25.27 ± 20.75			
Kuwait	26.09 ± 18.92			
Sex		− 2.03	7644	**0.043**
Males	27.09 ± 20.12			
Females	28.18 ± 21.11			
Marital status		4.59	7644	< **0.001**
Single	28.32 ± 20.95			
Married	25.15 ± 20.15			
Education		2.22	7644	**0.026**
Secondary or less	29.69 ± 20.80			
University	27.76 ± 20.88			
Tobacco use		− 2.51	7644	**0.012**
No	27.67 ± 20.84			
Yes	29.40 ± 21.07			
Alcohol drinking		− 0.86	7644	0.390
No	27.85 ± 20.71			
Yes	28.64 ± 22.59			
Lifetime cannabis use		− 1.89	7644	0.059
No	27.79 ± 20.87			
Yes	29.60 ± 20.98			

Table 2. Factors associated with psychotic experiences. Numbers in bold indicate significant *p* values.

	1	2	3	4	5	7
1. Psychotic experiences	1					
2. Autistic traits	0.15***	1				
3. Age	− 0.10***	− 0.03**	1			
4. Household crowding index	0.05***	0.001	− 0.14***	1		
5. Financial burden	0.05***	0.04**	0.10***	0.07***	1	
7. Loneliness	0.18***	0.22***	− 0.11***	0.05***	0.10***	1
8. Susceptibility to social pain	0.06***	0.20***	− 0.05***	0.02	0.04***	0.36***

Table 3. Pearson correlation matrix. *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

interpersonal difficulties, as well as perceiving burdensomeness and feelings of non-belongingness, which may subsequently cause psychopathology[48,49]. Subsequently, a possible consequence to susceptibility to social pain and loneliness experienced by adults with high ATs is the development of psychotic symptoms[38–41]. A possible explaining theory is the social defeat hypothesis of schizophrenia[50], which stipulates that experiences of social rejection and exclusion lead to sensitization of the mesolimbic dopamine system, thereby contributing to the risk for psychotic symptoms and disorders. Interestingly, research has shown that when feelings of social rejection are coupled with subsequent environmental circumstances, such as social isolation and loneliness, the effects on the dopaminergic system are pronounced[92]. Other authors proposed that the relationship loneliness-psychosis can be explained by the cognitive model of psychosis[51], assuming that more feelings of loneliness may result in poorer self-esteem, which leads, in turn, to the development of psychosis[93]. Indeed, individuals who hold distorted beliefs about the world (e.g., the world is dangerous), others (e.g., others are hostile), and the self (e.g., one is different) would tend to more rigidly hold psychotic beliefs that are consistent with these cognitive

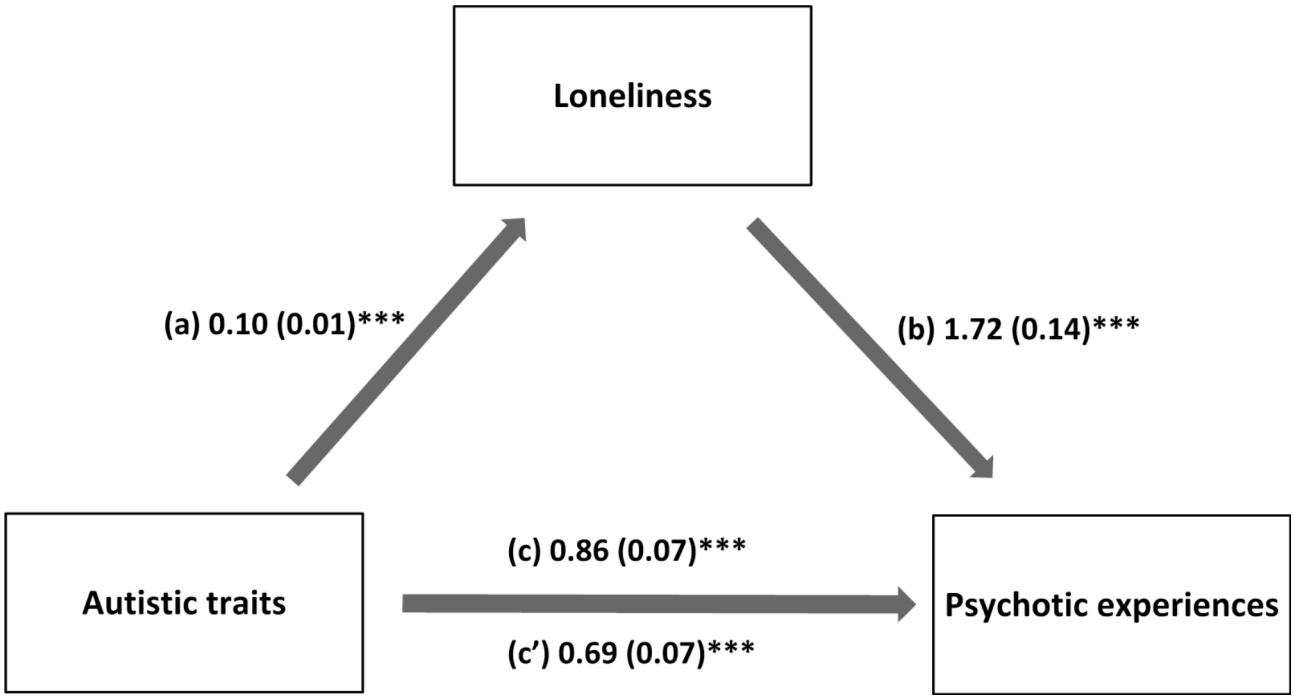

Fig. 2. (**a**) Relation between autistic traits and loneliness ($R^2 = 0.106$); (**b**) Relation between loneliness and psychotic experiences ($R^2 = 0.067$); (**c**) Total effect of autism on psychotic symptoms ($R^2 = 0.049$); (**c'**) Direct effect of autism on psychotic symptoms. Numbers are displayed as regression coefficients (standard error). $^{***}p < 0.001$.

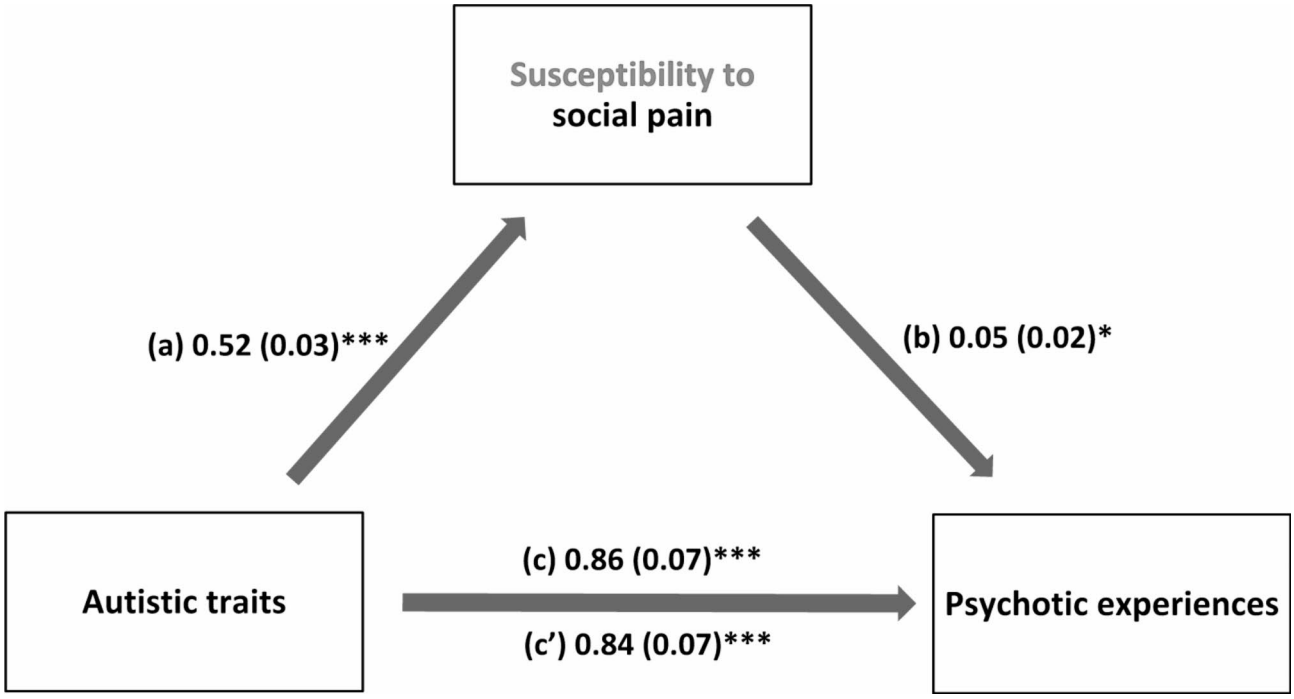

Fig. 3. (**a**) Relation between ATs and social pain ($R^2 = 0.072$); (**b**) Relation between social pain and PEs ($R^2 = 0.050$); (**c**) Total effect of ATs on PEs ($R^2 = 0.049$); (**c'**) Direct effect of ATs on PEs. Numbers are displayed as regression coefficients (standard error). $^{*}p < 0.05$; $^{***}p < 0.001$.

distortions[51]. This supports the idea that loneliness mediates the development and exacerbation of psychotic symptoms[37,94]. Furthermore, there is accumulating evidence to support that experiences of social pain may trigger the activation of the HPA axis along with increases in inflammatory markers, blood pressure and heart rate, and could therefore be assimilated to a social stressor[95]. Loneliness has also predicted atypical physiological reactivity to acute stress, including exaggerated inflammatory and immune responses, as well as elevated cortisol levels and blood pressure[96]. Taken together, earlier research suggests that chronic experiences of social pain and loneliness could be regarded as "social threats" that may activate the stress-responsive systems engaged in stress vulnerability following the vulnerability-stress model of psychosis[97,98]. Based on previous literature and current findings, people who score high on autism and psychosis risk measures seem to share similar difficulties in social relationships, characterized by susceptibility to social pain and extensive feelings of loneliness. The model hypothesized and tested in this study help understand the pathways between autistic/psychotic phenotypes and some aspects of the difficulties in social interactions. Because of the correlational nature of our results, the proposed model still needs to be tested using prospective data.

Study limitations

One limitation of this study is its cross-sectional design, which can only establish correlations and cannot determine causal inferences from the observed associations. Future studies are required to tease apart the causal pathways through which ATs may ultimately be linked to PEs in non-clinical adult populations. As our sample was exclusively composed of community individuals, findings still need to be confirmed in patients with ASD and psychotic disorders, before our conclusions can be translated and generalized to clinical populations. In addition, since only participants from Arab origin were included, future studies involving samples from Western countries are warranted to test whether the present results can be applicable to community adults in general, independently of the specific cultural contexts.

Implications of key findings and future directions

Being socially rejected and feeling lonely mark a threat to the fundamental human need of social belonging, and may contribute to reduced fundamental survival resources. In this regard, our study tested and supported the hypothesis that loneliness and susceptibility to social pain levels mediate the relationship ATs-PEs. Hence, findings provide additional evidence to the well-established theory that humans are a profoundly social creatures in nature, wired to connect with others and to form/maintain meaningful relationships[99]; which also implies the harmful consequences that can occur when such connections are threatened. Specifically, analyses indicated that individuals with higher ATs tend to experience greater loneliness and feel more pain from rejection in their interpersonal interactions, which can in turn be associated with higher levels of PEs. In light of these findings, social rejection and loneliness are proposed to be social stressful events that can be involved in the development of psychosis. This suggests that interventions targeting these two social factors as a means of mitigating PEs among highly autistic adults should be considered, such as oxytocin administration[100], improving social skills, providing opportunities for social contact, enhancing social support[101], as well as interventions addressing maladaptive social cognition[102]. Future experimental research can test whether such interventions are appropriate for individuals with high ATs and can be effective in reducing the risk of developing psychosis. In addition, future longitudinal studies should continue to elucidate the potentially unique impact that repeated or persistent experiences of loneliness and susceptibility to social pain occurring in many contexts can have on the relationship autism-psychosis in different clinical and non-clinical populations.

Conclusion

In sum, our data support the hypothesis that greater feelings of loneliness and pain from social rejection could be potential mechanisms explaining the relationship between ATs and PEs. These findings can be used to facilitate the development of strategies for preventing the emergence of PEs in individuals with high ATs. Nevertheless, the observed direct and indirect relationships were explored using a correlative approach. Therefore, further longitudinal and experimental studies are necessary to understand the extent to which loneliness and susceptibility to social pain may contribute to the etiology and maintenance of PEs in highly autistic individuals.

Data availability

Because of ethical committee constraints, none of the data collected or analyzed during this study are publicly available. However, the corresponding author (SH) may make the data available upon reasonable request.

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Author contributions
FFR and SH designed the study; FFR drafted the manuscript; SH carried out the analysis and interpreted the results; FS, AA, LSC, MH, HAMS, NEB, BZ, AYN, KJ, MLR, IN, NM, RA, BARH, AHM, SSF, OAA, and MD collected the data; MC, DM, AAL, and SO reviewed the paper for intellectual content; all authors reviewed the final manuscript and gave their consent.

Declarations

Ethics approval and consent to participate
The protocol was approved by the home institutions of the study's principal investigators (FFR and SH), namely the ethics committee of Razi Psychiatric Hospital, Manouba, Tunisia (ECRPH-2024-032) and the Lebanese International University's School of Pharmacy ethics committee (2024ERC-025-LIUSOP). When filling out the online form, each participant provided written informed consent. All methods were performed in accordance with the relevant guidelines and regulations (in accordance with the Declaration of Helsinki).

Competing interests
The authors declare no competing interests.

Additional information
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