# Do Specific Early-Life Adversities Lead to Specific Symptoms of Psychosis? A Study from the 2007 The Adult Psychiatric Morbidity Survey

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Previous studies have reported associations between childhood adversities, eg, loss of a parent, being raised in institutional care, sexual and other kinds of abuse by adults and bullying by peers, and psychosis in adulthood. However, the mechanisms by which these adversities lead to psychotic experiences are poorly understood. From models of the psychological processes involved in positive symptoms, it was predicted that childhood sexual abuse would be specifically associated with auditory hallucinations in adulthood, and that disruption of early attachment relations and more chronic forms of victimization such as bullving would be specifically associated with paranoid ideation. We therefore examined the associations between sexual trauma, physical abuse, bullying, and being brought up in institutional or local authority care and reports of auditory hallucinations and paranoid beliefs in the 2007 Adult Psychiatric Morbidity Survey. All simple associations between childhood adversities and the two symptom types were significant. Childhood rape was associated only with hallucinations (OR 8.9, CI = 1.86-42.44) once cooccurring paranoia was controlled for. Being brought up in institutional care (OR = 11.08, CI = 3.26-37.62) was specifically associated with paranoia once comorbid hallucinations had been controlled for. For each symptom, doseresponse relationships were observed between the number of childhood traumas and the risk of the symptom. The specific associations observed are consistent with current psychological theories about the origins of hallucinations and paranoia. Further research is required to study the psychological and biological mediators of these associations.

*Key words:* paranoia/hallucinations/childhood sexual abuse/victimization/disrupted attachment

Environmental stress, especially if experienced during childhood, plays an important role in conferring risk of psychosis. Children born into poverty<sup>1</sup> or exposed to an inner city environment<sup>2</sup> are at elevated risk of illness and this association also exists for "subclinical" psy-

chotic experiences.<sup>3</sup> Aspects of the family environment may also be important. In a prospective cohort study, risk of psychosis in adulthood was raised if the mother, during pregnancy, reported that the birth was unwanted.<sup>4</sup> It has also been reported that early separation from a parent is associated with increased psychosis risk.<sup>5</sup>

Epidemiological and prospective studies have reported that bullying at school is associated with an increased risk of later psychosis, <sup>6,7</sup> but more extreme forms of victimization may have a greater effect. Psychotic patients report very high rates of early psychological trauma prior to onset, but when this association was first discovered, there was concern about whether people with severe psychiatric problems could accurately report their early-life experiences. Recently, Fisher et al<sup>9</sup> have shown that patients' reports tend to be accurate when judged against the reports of siblings, are stable over long periods, are unaffected by current symptoms, and are therefore most likely valid. The association between childhood trauma and psychosis has now been replicated many times (eg, Bebbington et al<sup>10,11</sup> and Shevin et al<sup>12</sup>). The only recent study not to show an association between abuse and psychosis, using data from Australia<sup>13</sup> has recently been subjected to a re-analysis in which the association was found.<sup>14</sup>

In his seminal analysis of the kinds of inferences that may be warranted from epidemiological data, Austin Bradford Hill<sup>15</sup> argued that, in addition to the strength and consistency of associations, the presence of a doseresponse effect, the temporal sequence of events, the specificity of effects, and the existence of plausible mechanisms should be considered when judging whether effects are causal. The strength and consistency in the evidence on childhood adversity and psychosis has been established in a recent meta-analysis of epidemiological, prospective and case-control studies that found an overall odds ratio for the association of 2.78<sup>16</sup>; this review also found that 9 out of 10 studies that have looked for doseresponse effects have found them.<sup>16</sup> Temporal ordering is

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evident in the case of childhood adversity. However, although the specificity of associations may provide clues into the underlying mechanisms, these have not been given sufficient attention in research into severe psychiatric problems.

From evidence on the psychological mechanisms underlying hallucinations and paranoid ideation (persecutory beliefs), we have argued that some degree of specificity should be expected between different types of adversity and symptoms. <sup>17</sup> That is, while recognizing that the psychological impacts of different kinds of early trauma are likely to vary from individual to individual and that they are also likely to overlap to some extent. we have argued that different types of trauma are likely to have different potencies with respect to particular cognitive processes and are therefore likely to differ in the symptoms they are associated with. For example, paranoid delusions seem to be related to the over-anticipation of social threats<sup>18</sup> and a tendency to attribute negative experiences to the actions of others, <sup>19</sup> which were argued to be the likely consequence of disruption of early attachment relations and experiences of victimization. Indeed, there is evidence that paranoid beliefs arise in the context of insecure attachment, 20 discrimination 21 and experiences of powerlessness. 22 In the case of hallucinations, we 17 argued that severe trauma in early life, especially sexual abuse, would likely impair the source monitoring processes required to discriminate between thoughts and external stimuli. Consistent with this hypothesis, in an analysis of the National Comorbidity Study data, Shevlin et al<sup>23</sup> found a dose-response relationship between severity of sexual abuse in childhood and risk of hallucinations in adulthood. More recently, in a comparison between hallucinating, remitted hallucinated and nonhallucinating psychiatric patients, Varese et al<sup>24</sup> found that source monitoring deficits were equally evident in currently hallucinated and remitted hallucinated patients, but that dissociative experiences mediated the relationship between childhood trauma and hallucinations. This finding suggests that a combination of trait source monitoring deficits and trauma-linked dissociation might be an important pathway to hallucinations.

One limitation of the available evidence is that, by and large, it has not taken into account the co-occurrence of different kinds of psychotic symptoms. Hallucinations and paranoid delusions often occur together. The purpose of the present study is therefore to see whether specific associations between childhood sexual abuse and hallucinations on one hand, and attachment disrupting events, victimization experiences and paranoid beliefs on the other, hold up when this co-occurrence is considered. We used data from the 2007 Adult Psychiatric Morbidity Survey. In a previous analysis of these data, Bebbington et al<sup>11</sup> reported a strong association between childhood sexual abuse and psychosis, which was not mediated by cannabis use but was partially mediated by

depression. That analysis did not address the effects of non-sexual early adversity or examine relationships between adversity and specific symptoms.

# **Methods**

# Sample

The Adult Psychiatric Morbidity Survey 2007 (APMS 2007) was carried out between October 2006 and December 2007 by the National Centre for Social Research and the University of Leicester. The survey was commissioned by the NHS Information Centre for Health and Social Care and employed a multistage stratified probability sampling design. Individuals aged 16+ years living in private households were identified for interview in England using postcodes. From 13 171 eligible households, 7353 individuals completed phase one. 27 Researchers administered computer-assisted interviews and selfcompletion questionnaires using laptops to obtain data on topics including physical health, mental health, service use, religion, social capital, discrimination and sexual abuse. Although the survey implemented two phases, the present analysis used only phase one data. For more information, see McManus et al.<sup>2</sup>

# Measures

Paranoia and Hallucinations. The APMS2007 screened for possible psychosis using the Psychosis Screening Questionnaire (PSQ, Bebbington and Nayani<sup>28</sup> which has 5 sections to identify psychotic-like experiences that may have occurred within the past year: hypomania, thought control, paranoia, strange experiences, and hallucinations. Each section has an initial question followed by 1 or 2 follow-up questions to determine severity. For present purposes, only the paranoia and hallucination sections were of interest.

The highest severity of *paranoia* was assed using the question, "Have there been times that you felt that a group of people was plotting to cause you serious harm or injury?" The highest severity of *auditory-verbal hallucination* (AVH) was identified by respondents answering yes to the question: "Did you at any time hear voices saying quite a few words or sentences when there was no one around that might account for it?"

Sexual Abuse. Three items were selected from the 'domestic violence and abuse' section of the survey and were treated separately in the analyses. A "yes" or "no" response was required for the following: Sexual talk: "Before the age of 16, did anyone talk to you in a sexual way that made you feel uncomfortable?"; Sexual touch: "Before the age of 16, did anyone touch you, or get you to touch them, in a sexual way without your consent?"; Rape: "Before the age of 16, did anyone have sexual intercourse with you without your consent?"

As indices of victimization both within and outside the childhood home, we chose questions assessing physical abuse and bullying by peers. *Physical abuse*: One item required a "yes" or "no" response: "Before the age of 16, were you ever severely beaten by a parent, step-parent or carer?" *Bullying*: Respondents had to select "bullying" from a list of options on a card following the question; "Now looking at this card, could you tell me if you have ever experienced any of these problems or events, at any time in your life?" along with "more than 6 months ago, and before the age of 16" to the question "When did that happen?"

Separation Experiences. Two items taken from the 'parenting' section of the survey were selected to represent separation from parents, requiring "yes" or "no" responses to the questions: Institutional care: "Up to the age of 16 did you spend any time in any kind of institution such as a children's home, borstal, or young offenders unit?"; Local Authority care: "Where you ever taken into Local Authority care (ie, into a children's home or foster care) as a child up until the age of 16?"

Demographic Confounds. The following were considered as possible confounds: sex (1 Female, 0 Male), age (years), ethnicity (1 White British, 0 Other), highest educational qualifications (1 Degree, 2 Non-degree, 3 A-Level, 4 GCSE, 5 Other, 6 None), social class (1 Professionals, 2 Managerial and technical, 3 Skilled—nonmanual, 4 Skilled manual, 5 Partly skilled, 6 Unskilled, 7 Armed forces) and intellectual functioning as measured by the National Adult Reading Test.<sup>29</sup>

# Statistical Analyses

Descriptive statistics were produced using STATA 9.2 and logistic regression models were specified and estimated using Mplus6.1.<sup>30</sup> The logistic regression model was estimated three times with auditory-verbal hallucinations and paranoid ideation as dependent variables that were both regressed on all the independent variables. The residuals of the dependent variables were correlated, allowing all the effects on the two dependent variables to be estimated simultaneously in a single model, thereby enabling accurate estimation of the effects of the different kinds of adversity on each of the symptoms. Model parameters were estimated using robust maximum likelihood.

In the first model, the variables representing sexual abuse (Rape, Sexual touch Sexual talk), victimization (Physical abuse, Bullying), and separation experiences (Institutional care, Local authority care) were independent variables. In the second, control variables (age, sex, ethnicity, education, social class, and IQ) were added as additional independent variables; these were selected either because they might plausibly covary with adversity (ethnicity, education, social class) or because they are

important individual difference variables which might plausibly be related to psychosis risk (age, sex, IQ). Finally, in order to examine possible dose-response relationships, a total adversity score was calculated as the sum of the seven variables representing sexual abuse, victimization, and separation experiences. This was recoded into four dummy variables indicating experiencing one, two, three, or four or more adverse experiences. The reference category represented those who experienced no adversity. These variables were used in the model instead of the individual adversity variables and the model was estimated with and without the control variables.

#### Results

Simple bivariate associations between symptoms and types of adversity are summarized in table 1. All these associations were statistically significant (all p < .005). Only two associations did not survive Bonferroni correction (the relationships between AVHs and bullying and Local Authority care). The results of the logistic regression analyses are summarized in table 2.

# Associations with Childhood Sexual Abuse

In our logistic regression models, childhood sexual abuse (rape, not sexual touching, or sexual talk) was significantly and specifically associated with AVHs both before and after adjusting for demographic confounds and IQ. The association between rape and hallucinations was strong: respondents who reported being raped before the age of 16 were approximately 6 times more likely to have experienced AVHs in the 12 months preceding assessment after controlling for demographic confounds and IQ. Conversely, rape was not a significant predictor of paranoia, either before or after controlling for demographic confounds and IQ.

Association With Victimization Experiences (Physical Abuse and Bullying)

Experiences of physical abuse predicted paranoia and AVHs and this effect remained significant after controlling for demographic confounds and IQ. The effects of bullying on paranoia and AVHs were nonsignificant.

Associations With Separation Experiences (Institutionalization and Being Taken into Local Authority Care)

A significant relationship was observed between institutional care and paranoia indicating an increased risk both with and without controlling for the demographic confounds and IQ. This effect was substantial; an individual brought up in institutional care was approximately 11 times more likely to experience paranoia in the survey period compared with someone with a more benign life history. Being taken into Local Authority care was

Table 1. Bivariate Associations Between Hallucinations, Paranoia and Specific Childhood Adversities

		Hallucinations					Paranoia				
			Absent		Present			Absent		Present	
		N	$\overline{N}$	%	N	%	N	$\overline{N}$	%	$\overline{N}$	%
Rape	No	7123	7069	99.2	54	0.8	7046	6938	98.5	108	1.5
	Yes	143	131	91.6	12	8.4	140	127	90.7	13	9.3
	Total	7266	7200	99.1	66	0.9	7186	7065	98.3	121	1.7
Sexual touch	No	6632	6582	99.2	50	0.8	6565	6470	98.5	95	1.5
	Yes	635	619	97.5	16	2.5	622	596	95.8	26	4.2
	Total	7267	7201	99.1	66	0.9	7187	7066	98.3	121	1.7
Sexual talk	No	6502	6453	99.2	49	0.8	6441	6350	98.6	91	1.4
	Yes	758	741	97.8	17	2.2	739	709	95.9	30	4.1
	Total	7260	7194	99.1	66	0.9	7180	7059	98.3	121	1.7
Physical abuse	No	7111	7051	99.2	60	0.8	7033	6928	98.5	105	1.5
	Yes	212	206	97.2	6	2.7	207	189	91.3	18	8.7
	Total	7323	7257	99.1	66	0.9	7240	7117	98.3	123	1.7
Bullying	No	6301	6252	99.2	49	0.8	6240	6153	9.6	87	0.4
	Yes	1022	1005	98.3	17	1.7	1000	964	96.4	36	3.6
	Total	7323	7257	99.1	66	0.9	7240	7117	98.3	123	1.7
Institutional care	No	7117	7057	99.2	60	0.8	7037	6930	98.5	107	1.5
	Yes	210	204	97.1	6	2.9	206	191	92.7	15	7.3
	Total	7327	7261	99.1	66	0.9	7243	7121	98.3	122	1.7
LA care	No	7148	7087	99.1	61	0.9	7066	6952	98.4	114	1.6
	Yes	166	161	97.0	5	3.0	164	156	95.1	8	4.9
	Total	7314	7248	99.1	66	0.9	7230	7108	98.3	122	1.7

Note: LA, local authority.

a significant negative predictor of paranoid ideation and AVHs (ie, it seemed to be protective), but this effect became nonsignificant after controlling for demographic confounds and IQ.

#### Dose-Response Relationships

Most participants reported experiencing no adverse events (74.2%) with increasingly smaller numbers reporting 1 (18.1%), 2 (5.3%), 3 (1.3%), or 4 or more (.4%). For both paranoia and AVHs, there was a general increase in the odds ratios with and without controlling for demographic confounds and IQ. However, the increase was not linear with 2 adverse events producing a higher odds ratio than 3 events for paranoia. Similarly, 3 adverse events produced a higher odds ratio than 4 or more events for AVHs.

# Discussion

In light of the continuing debate about the best taxonomy of the psychotic disorders, <sup>31</sup> a pragmatic approach is to try and understand the mechanisms underlying particular psychotic experiences such as hallucinations and paranoid ideation. On the basis of the known psychological processes underlying these experiences, we made predictions about associations between specific kinds of adversity and each symptom. <sup>17</sup> Although examination of

simple bivariate relationships seemed to suggest that all the different adversities conferred a risk of both kinds of psychotic experience, as expected, controlling for the co-occurrence of hallucinations and paranoia revealed a more interesting pattern of specific associations. On the whole, our predictions were upheld. Childhood rape was associated with hallucinations and institutional care was associated with paranoid beliefs. Physical abuse was associated with both kinds of psychotic experience. Dose-response relationships were observed for both symptoms, with multiple traumas generally associated with increasing odds ratios, although the effects observed were nonlinear. This finding shows, not surprisingly, that individuals exposed to more than one type of adverse experience early in life are especially vulnerable to psychotic experiences. The nonlinear effects may suggest that there are particular combinations of traumas that are especially toxic with respect to each kind of experience. However, the confidence intervals for multiple traumas were very wide, so it is more likely that the apparent nonlinearity simply reflects the fact that some of the ORs were poorly estimated. An unexpected observation was that. on some analyses, local authority care (as opposed to institutional care) was protective. Speculating, the most likely explanation is that a substantial proportion of the individuals captured by this variable were subject to foster care arrangements designed to provide

**Table 2.** Odds Ratios and Their Associated 95% CI for the Effects of Childhood Sexual Abuse, Victimization, Separation Variables and Total Adversity on AVHs and Paranoid Ideation

			Demographics adjusted			
	Paranoia	AVHs	Paranoia	AVHs		
Gender			0.54* (0.30-0.98)	1.07 (0.58–1.97)		
Age			0.96* (0.94-0.98)	0.99 (0.97-1.01)		
Ethnicity			0.36* (0.17-0.75)	1.05 (0.31–3.54)		
Education			1.05 (0.84–1.32)	0.98 (0.78–1.23)		
Socioeconomic status			1.06 (0.87–1.31)	1.17 (0.91–1.53)		
IQ			0.96* (0.94-0.99)	0.95* (0.92-0.98)		
Rape	2.78 (0.93-8.28)	8.90* (1.86-42.44)	1.29 (0.38-4.41)	6.09* (1.38-26.89)		
Sexual touch	1.30 (0.45–3.71)	1.22 (0.34-4.37)	1.31 (0.43-4.01)	1.68 (0.47–6.06)		
Sexual talk	1.40 (0.54–3.61)	1.52 (0.58-4.01)	2.04 (0.72-5.80)	1.57 (0.50-4.95)		
Physical abuse	8.52* (3.55–20.43)	4.79* (1.49–15.34)	5.99* (2.39-15.07)	3.82* (1.01–14.41)		
Bullying	1.46 (0.81–2.63)	2.08 (0.99-4.37)	1.32 (0.71–2.46)	1.56 (0.71–3.43)		
Institutional care	11.08* (3.26–37.62)	3.45 (0.50-23.72)	12.68* (3.56-45.11)	4.04 (0.74–21.92)		
Local authority care	0.17* (0.03-0.80)	0.35* (0.04–3.45)	0.19 (0.04–1.00)	0.31 (0.03-3.02)		
Number of adverse events						
1	3.33* (1.80-6.16)	2.32* (1.05–5.09)	3.70* (1.89–7.27)	2.43* (1.05–5.59)		
2	7.49* (3.47–16.17)	10.80* (4.17–27.99)	7.33* (3.23–16.62)	9.14* (3.68–22.71)		
3	9.92* (3.14-31.33)	27.42* (6.26–119.97)	5.65* (1.48–21.61)	17.64* (4.30–72.23)		
4 or more	17.54* (2.93–104.89)	14.83* (2.80–78.55)	16.46* (2.71–99.77)	13.68* (2.33–80.27)		

Note: AVH, auditory-verbal hallucinations. Adjusted demographic variables include sex, age, ethnicity, education, social class, and IQ. \*p < .05.

nurturing parenting experiences. There is evidence that good quality foster care can repair disturbed attachment styles in children who have experienced adversity<sup>32</sup>.

It might be useful to consider the findings against Hill's 15 criteria for inferring causation from epidemiological data. Certainly in the case of exposure to multiple early traumas, the associations appear to be strong (most of the odds ratios reported here are within the range of those reported in a recent meta-analysis of data on smoking and lung cancer, although towards the lower end of that range<sup>33</sup>). The observed associations were specific and with dose-response effects. Given that the adversities considered were all experienced before adulthood, there is evidence of temporal ordering. Finally, as our predictions were made on the basis of our understanding of the psychology of hallucinations and paranoia, the mechanisms linking adversity to psychotic experiences are inherently plausible even though they require further investigation.

It might be objected that the specificities identified here raise problems about the positive syndrome identified in numerous statistical analyses of psychotic symptoms. <sup>25,26</sup> If different symptoms are associated with different kinds of adversity, why do hallucinations and paranoid beliefs often co-occur? In fact, there are many possible explanations for the positive syndrome within this context. First, there may be other causal factors, eg, dopamine dysregulation, <sup>34</sup> that increase the probability of both

kinds of psychotic experiences considered here. Second, some kinds of adversity (eg, being sexually abused and being in receipt of institutional care) almost certainly tend to co-occur. Third, adversities do not have "pure" psychological effects (eg, although we predicted that childhood sexual assault will impact on hallucinations, eg, via the mechanism of dissociation, <sup>24,35</sup> this kind of experience may also impact on attachment processes, especially if the perpetrator is a parent or if parents fail to respond to requests for protection). A final, explanation for the positive syndrome is that the occurrence of one symptom increases the likelihood of another; in these circumstances, symptom A may be said to mediate between adversity and symptom B. In fact, there is evidence supporting this kind of mediation for both hallucinations and paranoia. For example, it has been shown that beliefs can influence the source monitoring judgments of hallucinating patients<sup>36</sup> but also that anomalous hallucinatory experiences may sometime provoke delusional interpretations.<sup>37</sup> We think it likely that all these factors play some role in explaining the positive syndrome.

We acknowledge some important limitations to this study. Although it could be argued that different findings might have been obtained from clinical samples, epidemiological samples are less likely to be affected by selection biases that might impact on correlations between variables. Clearly, data from epidemiological surveys must be imperfect in terms of the precision with which different

kinds of early adversity are defined and reported. For example, the definition of childhood rape used in the APMS2007 was sexual intercourse before the age of 16 without consent, and it could be argued that even consensual intercourse before that age (which is illegal in most jurisdictions) could be harmful. It could be argued that the retrospective reporting of adverse events provides opportunities for bias, although studies of people with common psychiatric disorders<sup>38</sup> and people with psychosis<sup>9</sup> suggest that their recall of past trauma is usually accurate. A related limitation is that the APMS2007 questions about psychosis concerned experiences in the last year, rather than across the lifetime. It is possible that some people classified as not experiencing hallucinations or paranoia in our analyses in fact suffered from these experiences in the past. In future research, it would be preferable to use incident data collected from first-episode patients. However, it is worth noting that the most likely effect of misclassifying participants through under-recognition of past symptoms would be to reduce any observed associations.

Our definitions of childhood trauma were, by necessity, conservative, and may fail to reflect more subtle types of adverse experience which are difficult to capture epidemiologically. The predictions made about relationships between specific adversities and specific symptoms are based on current understandings of the cognitive and emotional mechanisms involved in hallucinations and paranoia and the likely impact of different kinds of events on those mechanisms; these understandings are incomplete and may be subject to revision. (For example, although in a separate study we have shown that dissociative experiences, measured using a standard instrument, mediate between childhood trauma and hallucinations.<sup>24</sup> the psychological mechanisms underlying dissociation are as yet poorly understood). As we have already noted, it is unlikely that adversities evoke "pure" psychological effects. A further consideration is that individuals vary in the way in which they react to adversity according to pre-existing resilience factors and circumstances that may be more or less supportive (eg, under some circumstances being admitted to foster care may lead to improved attachment security<sup>32</sup>). In all likelihood, there is no such thing as the cause of any psychiatric symptom, and each emerges as a consequence of complex interactions between psychosocial and biological factors. Under these circumstances, it might be thought remarkable that our predictions were mostly supported.

The apparently negative finding for bullying deserves further consideration as it is inconsistent with the results of previous studies.<sup>6,7</sup> The first-order associations between bullying and the different kinds of adversity were all statistically significant, and the association between bullying and paranoia survived Bonferroni correction (although, consistent with our hypotheses, the association with AVHs did not). The APMS2007

interviews required people to identifying bullying in a list of adverse experiences, essentially a yes/no response, which may have led to the under-reporting of this kind of experience. Hence, it would be premature to conclude from the present findings that bullying plays no role in the etiology of psychosis.

We believe that this is the first study to test for specific adversity-symptom relationships, as opposed to relationships either between adversities and psychosis broadly defined or between a specific adversity and a specific symptom without considering the problem of comorbidity. <sup>21,23</sup> It will be useful to replicate the findings in other samples, making use of whatever additional potential confounding data that may be available (eg, genetic risk as indicated by whether or not participants have a first-degree relative with psychosis). However, in order to properly understand the pathways between adversity and psychosis, it will be necessary to conduct studies in which highly detailed accounts of early experience are collected at the same time as potential biological and psychological mediators are assessed.

There are some clinical implications from this research. At the simplest level, the findings indicate that inquiries about early adversity should be routine during the assessment and treatment of psychosis, which may require appropriate training for staff.<sup>39</sup> It is important for clinicians to recognize that different kinds of trauma often co-occur and that the specific effects reported here do not preclude the presence of multiple kinds of adversity in the histories of individual patients. Clinical formulations and treatment plans should take into account the findings from these inquiries. Ultimately, research into the psychological and biological mechanisms linking adversity to psychosis may yield new targets for therapeutic intervention. For example, studies might focus on the role of attachment problems in paranoia, or dissociative processes in patients with hallucinations, and consider how psychological interventions that specifically target these processes might be delivered. The clinical implications of the present findings are not restricted to psychological therapies. As animal studies indicate that victimization leads to profound biological changes, including sensitization of the dopamine system, 40 the extent to which life experiences predict response to pharmacotherapy is worthy of investigation.

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