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ORIGINAL ARTICLE

Impact of distress related to attenuated psychotic symptoms in individuals at ultra high risk of psychosis: Findings from the Longitudinal Youth at Risk Study

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Aim: Recent studies have highlighted that attenuated psychotic symptoms (APS) are an important source of distress in ultra high risk (UHR) individuals and that this distress is related to transition to psychosis (TTP). This study examined distress associated with APS in UHR individuals and investigated its association with TTP.

Methods: The Comprehensive Assessment of At-Risk Mental State (CAARMS) was used to identify 173 UHR individuals, who were included as participants in the study. Distress related to APS was self-reported. Functioning was assessed on the Social and Occupational Functioning Assessment Scale. Associations between each of the 4 APS subscales in the CAARMS—non-bizarre ideas (NBI), perceptual abnormalities (PA), unusual thought content (UTC) and disorganized speech (DS)—with its distress level were examined.

Results: Of the 173 UHR participants, 154 (89%) reported distress related to one or more APS. NBI was rated to be the most distressing out of the 4 APS by the highest number of participants (32.9%) compared to UTC (12.1%), PA (24.9%) and DS (2.9%). Mean distress scores were significantly associated with CAARMS composite scores ($P < .001$). However, there was no significant relationship between distress scores and functioning. Both mean distress scores (OR = 1.034, $P = .029$) and functioning (OR = 0.892, $P = .022$) were significant predictors of transition to psychosis at 1 year of follow-up.

Conclusions: This study provides additional evidence to link subjective distress experienced by UHR individuals to APS and to their subsequent clinical outcomes and has significant clinical implications.

KEYWORDS

attenuated psychotic symptoms, distress, functioning, transition to psychosis, ultra high risk

1 | INTRODUCTION

In the past decade, there has been extensive research on at-risk mental state (ARMS) and ultra high risk (UHR) of psychosis (Fusar-Poli et al., 2013; Yung & McGorry, 1996). Although transition rates to psychosis have declined over the last few years (Yung et al., 2007; Ziermans, Schothorst, Sprong, & van Engeland, 2011), a significant proportion of UHR individuals has been reported to have a high prevalence of psychiatric comorbidities (Fusar-Poli, Nelson, Valmaggia, Yung, & McGuire, 2014; Hui et al., 2013; Lim et al., 2015) and experience significant impairment in functioning (Addington, Penn, Woods,

Addington, & Perkins, 2008; Hui et al., 2013), which in turn causes significant distress in this population (Lim et al., 2015; Rapado-Castro, McGorry, Yung, Calvo, & Nelson, 2015; Yung & McGorry, 1996).

Some recent studies have highlighted that attenuated psychotic symptoms (APS) are also an important source of distress in UHR individuals. In their study at the Personal Assessment and Crisis Evaluation clinic, Rapado-Castro et al. (2015) found that APS were the main source of distress (as rated by the case managers of the study subjects) for more than half of their UHR study population as compared to anxiety, trauma, personality disorder traits and autism spectrum disorder, with hallucinations and paranoia being more distressing than

thought disorder. In another study at the same clinic Power, Polari, Yung, McGorry, and Nelson (2015) reported that perceptual abnormalities (PA) were the most distressing amongst the APS, distress being self-rated on the Comprehensive Assessment of At-Risk Mental State (CAARMS; Yung et al., 2005) distress scale. Previously, Kelleher et al. (2012) found that 89% of community adolescents who fulfilled criteria for APS prodromal syndrome reported distress related to these symptoms.

These studies also tried to uncover the relationship between distress due to APS and risk of transition to psychosis (TTP). Power et al. (2015) found no association between TTP and levels of distress related to APS reported by the study participants. Conversely, Rapado-Castro et al. (2015) found that distress related to APS was associated with TTP, controlling for other sources of distress.

Additionally, studies on individuals with psychotic-like experiences (PLEs) have also looked into distress associated with these experiences. Yung et al. (2006) found that in a sample of non-psychotic, help-seeking youth, the frequency of bizarre ideation and persecutory ideas was associated with distress and disability. A more recent study on help-seeking adolescents reported that for those having a clinical high-risk status amongst these, a higher number of PLEs predicted higher average distress (Kline et al., 2014). Both these studies used different tools to measure PLEs and their associated distress.

Overall, more research on distress related to APS in UHR individuals need to be done. Recently, Attenuated Psychosis Syndrome was included in the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5), and one of the proposed criteria for the Attenuated Psychosis Syndrome includes "Symptom(s) is sufficiently distressing and disabling to the individual to warrant clinical attention" (Association AP, 2013). Therefore, identifying and understanding the clinical impact of distress related to APS is important.

Our aim in this study was to examine distress in relation to APS in UHR individuals. We also investigated whether distress levels in UHR were associated with TTP. We hypothesized that a high proportion of UHR individuals in our sample would have distress related to their APS and that the intensity and frequency of APS would be associated with the distress experienced. We also hypothesized that distress levels would be associated with poorer functioning and a higher likelihood of TTP within 1 year of follow-up.

2 | METHODS

2.1 | Setting and study participants

The Longitudinal Youth at Risk Study (LYRIKS) is a prospective, observational study conducted in Singapore on youths at UHR for psychosis. A total of 173 UHR participants were recruited. The study details and recruitment strategy have been reported previously (Lee et al., 2013; Mitter, Nah, Bong, Lee, & Chong, 2014). In brief, participants were referred from psychiatric services within the Institute of Mental Health in Singapore, community mental health and social agencies and health-care providers in public and private service. Participants were recruited if they were aged from 14 to 29 and

assessed to be UHR on the CAARMS (Yung et al., 2005). Participants were excluded if they (1) had a past or current history of psychosis or known intellectual disability (IQ < 70), (2) were currently using illicit substances, (3) were taking mood stabilizers (Berger et al., 2012) (4) had previous cumulative antipsychotic exposure of more than 5 mg haloperidol per day for 3 weeks (or equivalent; Larsen, McGlashan, & Moe, 1996; Phillips et al., 2009) or were on an antipsychotic at the point of recruitment or (5) had medical causes associated with their APS.

The follow-up period for all participants was 24 months, and assessments were done at 6-monthly intervals. Data collected at baseline and 1 year was used for this study. Regular contact with the participants at every 2 months was made by means of phone call or email, with the intent of minimizing attrition rate and monitoring for any deterioration in their symptoms and functioning.

Ethics approval for this study was provided by the National Healthcare Group's Domain Specific Review Board. Written informed consent or assent was obtained from all participants.

2.2 | Assessments

The CAARMS is a semistructured interview used to assess if an individual meets the UHR criteria. The positive symptom subscale of CAARMS was used in LYRIKS. It assesses 4 APS domains: unusual thought content (UTC), Non-bizarre ideas (NBI), PA and disorganized speech (DS). Each symptom was rated on a scale of 0–6 for the maximum intensity (I) and frequency and duration (F) over the last 1 year. CAARMS composite score was calculated according to the formula: $(I_{utc} * F_{utc}) + (I_{nbi} * F_{nbi}) + (I_{pa} * F_{pa}) + (I_{ds} * F_{ds})$ (Lim et al., 2015; Morrison et al., 2012).

UHR participants were classified into one or more of these 3 groups: (1) Vulnerability (Schizotypal personality disorder or having a first-degree relative with psychosis), (2) Attenuated Psychosis (AP; having symptoms that do not reach the threshold levels for psychosis) and (3) Brief Limited Intermittent Psychotic Symptoms (BLIPS; had a recent history of frank psychotic symptoms that resolved spontaneously within a week). Additionally, participants should have a drop in functioning as measured by the Social and Occupational Functioning Assessment Scale (SOFAS; Goldman, Skodol, & Lave, 1992) and sustained for a month over the last year. Therefore, for each participant, we rated $SOFAS_{best}$ and $SOFAS_{worst}$ over the last year.

Distress related to each of the 4 APS rated on the CAARMS was obtained by asking the participants the following: "Please state the level of distress related to the symptom experienced." This level was rated on a Likert scale from 0 (not at all distressed) to 100 (extremely distressed) for all the 4 CAARMS subscales, namely D_{utc}, D_{nbi}, D_{pa} and D_{ds}. Mean distress (D_{mean}) for each subject was calculated by the formula ($D_{utc} + D_{nbi} + D_{pa} + D_{ds}$)/the number of APS reported.

The Structured Clinical Interview for DSM IV Axis I Disorders (SCID-I; First, Spitzer, Gibbon, & Williams, 2002) was used to assess the presence of any comorbid psychiatric disorders at baseline and at conversion or at the end of follow-up period. All the assessments were performed by trained psychometricians. Supervision was provided by a research clinician and at monthly rater meetings.

2.3 | Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics 23. Descriptive statistics was used for sociodemographic data and to calculate mean distress for each of the CAARMS subscales. Multiple linear regressions were run separately for each of the UTC, NBI, PA and DS subscales to examine the association between intensity, frequency and duration of the APS reported with its distress. Effects of age and gender were adjusted for all these analyses. Association of distress with functioning (SOFAS$_{worst}$) was evaluated using Spearman's correlation for all the 4 subscales separately. Participants who did not report any symptom on that subscale were excluded for the subscale analyses. Additionally, associations between D_{mean} and CAARMS composite score and D_{mean} and SOFAS$_{worst}$ were also examined, with age and gender as covariates. Binary logistic regression was used to find the association between D_{mean} and TTP at 1 year of follow-up, with age, gender, SOAFS$_{worst}$, CAARMS composite score, presence of depression and treatment with antidepressants as covariates based on previous literature (Cannon et al., 2008; Fusar-Poli et al., 2012; Yung et al., 2003). Participants who did not complete 1 year of follow-up in the study were excluded from the last analysis. Statistical significance was established at $P < .05$.

3 | RESULTS

Table 1 shows the demographic characteristics of the study sample. Most of the UHR participants were males. A total of 167 (96.5%) out of the 173 UHR participants reported having at least 1 APS. As shown in Table 2, almost half of the UHR participants reported having UTC symptoms in the year prior to assessment. NBI symptoms were reported by the highest number of participants, whereas only about one-fourth of the UHR participants experienced DS symptoms. Intensity of symptoms was found to be the highest for NBI symptoms, followed by PA, UTC and DS symptoms. The frequency and duration of reported symptoms was the highest for NBI, followed by $F_{ds} > F_{utc} > F_{pa}$. Distress levels were found to be the highest for NBI symptoms, followed by $D_{pa} > D_{utc} > D_{ds}$.

A total of 39 (22.5%) UHR participants were assessed to have a current diagnosis of major depressive disorder, and 96 (56.5%) of them were receiving antidepressants.

TABLE 1 Sociodemographic characteristics of the study sample

	n = 173	
	Mean	SD
Age	21.27	3.52
	n	(%)
Gender		
Male	117	67.6
Female	56	32.4
Ethnicity		
Chinese	125	72.3
Malay	27	15.6
Indian	16	9.2
Others	5	2.9

TABLE 2 Clinical characteristics of the study sample

	n	(%)	Mean	SD
Unusual thought content				
Intensity	90	52.0	2.70	1.29
Frequency and duration			3.47	1.42
SOFAS$_{worst}$			48.97	9.15
Distress score			45.67	34.59
Non-bizarre ideas	137	79.2		
Intensity			3.26	1.16
Frequency and duration			3.64	1.13
SOFAS$_{worst}$			49.17	8.71
Distress score			62.01	29.24
Perceptual abnormalities	132	76.3		
Intensity			3.20	1.29
Frequency and duration			2.95	1.30
SOFAS$_{worst}$			49.57	8.69
Distress score			48.45	35.18
Disorganized speech	46	26.6		
Intensity			2.19	1.01
Frequency and duration			3.55	1.60
SOFAS$_{worst}$			46.79	7.70
Distress score			34.24	34.94
All subscales	173	100.0		
CAARMS composite score			24.46	15.10
SOFAS$_{worst}$			49.58	8.87
Distress score			48.39	26.97

CAARMS, Comprehensive Assessment of At-Risk Mental State; SOFAS, Social and Occupational Functioning Assessment Scale.

Distress from one or more APS was reported by 89% (154) of the UHR participants. The most frequently reported distressing APS was NBI (71.1%), whereas DS was the least frequently reported as distressing by UHR participants (15.6%). UTC and PA were found to be distressing by 39.9% and 56.6% of UHR participants, respectively. NBI was rated to be the most distressing out of the 4 APS on the CAARMS by the highest number of participants (32.9%) compared to UTC (12.1%), PA (24.9%) and DS (2.9%).

I_{nbi} was significantly associated with the D_{nbi} ($P < .05$), whereas both I_{pa} and F_{pa} were associated with D_{pa} ($P = .001$ and $P < .05$, respectively). Neither the intensity nor the frequency and duration of UTC and DS were associated with the distress related to these APS. D_{mean} was significantly associated with the CAARMS composite scores for the UHR participants ($P < .001$) (see Table 3).

There were no significant associations between distress from individual APS or D_{mean} with SOFAS$_{worst}$ (all $P > .05$) (see Table 4). D_{mean} was also not found to be significantly different between those who had current depression as assessed by SCID vs those who did not (51.7 vs 48.5; $t = 0.550$, $P = .583$).

A total of 20 (11.6%) out of the 173 UHR participants had withdrawn from the study by 1 year of follow-up, whereas 11 (6.4%) had developed psychosis. D_{mean} (OR = 1.034, $P = .029$) and SOFAS$_{worst}$ (OR = 0.892, $P = .022$) were significant predictors of TTP at 1 year of follow-up. Both predictors remained significant after adjusting for CAARMS composite scores in the model (see Table 5).

TABLE 3 Multiple linear regressions with distress as the dependent variable

	Unusual thought content				Non-bizarre ideas				Perceptual abnormalities				Disorganized speech				CAARMS composite			
		95% C.I. for B				95% C.I. for B				95% C.I. for B				95% C.I. for B				95% C.I. for B		
	ß	Lower	Upper	P	ß	Lower	Upper	P	ß	Lower	Upper	P	ß	Lower	Upper	P	ß	Lower	Upper	P
Age	0.118	-0.927	3.407	0.259	0.090	-0.650	2.145	0.292	0.153	-3.122	0.094	0.065	0.266	0.247	0.153	0.116	-0.018	-1.275	0.997	0.809
Gender	-0.010	-17.282	15.706	0.925	0.045	-7.889	13.567	0.602	0.082	-6.107	18.832	0.315	0.177	0.018	0.999	0.230	0.000	-8.482	8.432	0.995
Intensity	0.189	-0.509	10.686	0.074	0.211	0.964	9.704	0.017	0.219	2.901	11.798	0.001	0.134	0.192	0.453	0.419	0.291	0.256	0.785	<0.001[1]
Frequency and duration	0.195	-0.301	9.764	0.065	0.100	-1.844	6.996	0.251	0.270	1.483	10.434	0.009	-0.064	0.267	0.186	0.720				

CAARMS, Comprehensive Assessment of At-Risk Mental State.

R^2 values for models: Unusual thought content = 0.101; Non-bizarre ideas = 0.075; Perceptual abnormalities = 0.163; Disorganized speech = 0.147; CAARMS composite = 0.083.

[1] Association between CAARMS composite score and mean distress.

4 | DISCUSSION

This study is one of the first few studies to provide evidence to link subjective distress experienced by UHR individuals to APS and to the development of psychosis. We found that most of our study participants experienced distress related to one or more APS. Among the APS, NBI symptoms were associated with the highest level of distress, followed by PA, UTC and then DS. Participants with higher symptom burden, as assessed on the CAARMS composite score, were more likely to report higher distress levels. In addition, we also found that the UHR participants with higher distress levels were more likely to TTP at 1 year of follow-up.

As hypothesized, we found that a high proportion of UHR individuals in our study experienced distress in relation to their APS, which is consistent with reports from previous studies (Kelleher et al., 2012; Power et al., 2015; Rapado-Castro et al., 2015). This might be due to various factors. First, depressive and anxiety symptoms/disorders commonly coexist with APS in the UHR population (Lim et al., 2015; Meyer et al., 2005) and the vice versa is also true in patients with primary depressive or anxiety disorders (Wigman et al., 2012). This affective component might have intensified the emotional response of the UHR individuals to their APS, which could have led to higher levels of perceived distress. Additionally, twin studies have shown that stress reactivity and subclinical psychotic symptoms are linked genetically (Lataster et al., 2009), which might also explain this finding. Another possibility is that distressed UHR individuals were more likely to seek help, leading to higher chances of their referral for our study.

We found that NBI symptoms were related to the highest level of distress as compared to the remaining 3 APS assessed in our study. This is congruent with the findings from the study by Power et al. (2015) that reported highest mean distress scores for the NBI subscale of CAARMS. However, the majority of their study participants reported PA to be the most distressing APS, but in our study, NBI was reported to be the most distressing by the highest proportion of UHR participants. Rapado-Castro et al. (2015) had also reported hallucinations to be the main source of distress among the APS they studied. Cultural differences between the 2 societies could be one of the reasons for the differences in the emotional response to the same symptoms. Culture plays a crucial role in shaping the psychopathology of psychotic disorders (Katz et al., 1988; Suhail & Cochrane, 2002) and strategies to cope with symptoms (Viswanath & Chaturvedi, 2012; Wahass & Kent, 1997) as well as their outcomes (Viswanath & Chaturvedi, 2012). Cultural factors have also been reported to influence the understanding and causation of distress and help-seeking behaviours (Sheikh & Furnham, 2000).

Furthermore, we found that UHR individuals experiencing more intense and more frequent PA symptoms were more likely to report higher distress levels. Similarly, those with more intense NBI symptoms were more likely to have higher distress levels. This is again consistent with the reports by Power et al. (2015) on the correlation between higher frequency of PA symptoms and higher distress. It could be that the higher symptom burden led to the higher distress levels; however, we cannot exclude the possibility that higher distress might have led to more intense or more frequent APS. UHR

TABLE 4 Association between distress and functioning (SOFAS$_{worst}$)

	rho value	P
Unusual thought content	−0.018	0.864
Non-bizarre ideas	−0.074	0.391
Perceptual abnormalities	0.032	0.716
Disorganized speech	−0.160	0.288
CAARMS composite	−0.078	0.306

CAARMS, Comprehensive Assessment of At-Risk Mental State; SOFAS, Social and Occupational Functioning Assessment Scale.

individuals have been reported to be more sensitive to everyday stressors, and this stress is related to the intensity of their psychotic symptoms (Myin-Germeys, van Os, Schwartz, Stone, & Delespaul, 2001; Palmier-Claus, Dunn, & Lewis, 2012). Along similar lines, it can also be hypothesized that higher distress due to APS could have led to worsening of the symptoms themselves.

Contrary to our hypothesis and previous literature (Rapado-Castro et al., 2015) we did not find any significant association between the functioning of the study participants and the distress related to APS reported by them. Since the participants were interviewed and asked to rate their functioning and distress in the preceding 1 year, the possibility of recall bias affecting the reliability of this result cannot be excluded. However, it is possible that other socioenvironmental factors might have mitigated the effect of subjective distress on level of functioning.

Notably, we found that UHR individuals experiencing higher distress due to APS and lower functioning had a higher risk of TTP within 1 year of follow-up. This is consistent with the reported finding by Rapado-Castro et al. (2015) that distress related to APS is a significant factor associated with TTP in UHR individuals. Previous literature suggests that the clinical outcome of a psychotic experience is associated with how the person interacts with the experience and that cognitive and emotional appraisal of psychotic experiences interplays with their severity and other factors towards the development of a clinical outcome (Hanssen, Bak, Bijl, Vollebergh, & van Os, 2005; Krabbendam, Myin-Germeys, Bak, & van Os, 2005; Krabbendam et al., 2005). This could explain why UHR participants in our study with higher distress were more likely to develop a psychotic disorder during follow-up.

Our study has significant clinical implications. It highlights that the majority of UHR individuals experience distress in relation to

TABLE 5 Logistic regression results for association between transition to psychosis at 1-year follow-up and distress

	O.R.	95% C.I. for O.R.		P
		Lower	Upper	
Age	0.908	0.727	1.135	0.397
Gender	0.356	0.060	2.111	0.255
Use of antidepressants	0.489	0.107	2.230	0.356
Current depression	2.677	0.453	15.829	0.278
SOFAS$_{worst}$	0.892	0.809	0.983	0.022
CAARMS composite score	0.988	0.928	1.052	0.710
Mean distress	1.034	1.004	1.066	0.029

CAARMS, Comprehensive Assessment of At-Risk Mental State; SOFAS, Social and Occupational Functioning Assessment Scale.

their APS and need appropriate clinical help to deal with it. Those with higher levels of distress related to APS might require more intensive monitoring and care as they could be at a higher risk of developing full-blown psychotic disorders. Stress management strategies, including psycho-education; stress monitoring; and techniques like relaxation, meditation and distraction as well as cognitive behavioural therapy, have been tried and suggested as potentially beneficial to improve symptoms and their associated distress and reduce TTP in UHR individuals (Addington, Marshall, & French, 2012; Gleeson & McGorry, 2004; McGlashan et al., 2007).

The main limitation of our study is that some of the APS subgroups in the analyses had small sample sizes (eg, DS with $n = 46$), which limits the power of our study to perform subgroup analyses. Our conversion rates are also low, although this is in line with recent reported trends (Fusar-Poli et al., 2012; Yung et al., 2007). Next, distress levels in relation to the APS were self-reported and based on participants' recollection of the period being rated. Moreover, due to scarcity of other similar studies, we had to compare our study results mainly with those reported by Power et al. (2015) and Rapado-Castro et al. (2015), although our exclusion criteria were more restrictive than those used for their studies, and the latter study did not use the CAARMS to rate the distress.

In conclusion, we found that APS were distressing for UHR individuals and increased their likelihood of TTP. Functioning did not affect the distress experienced. Our study highlights the importance of management of APS in UHR individuals to alleviate the distress experienced by them and decrease their risk for TTP. More research is needed in future to understand the phenomenon of subjective distress related to APS in UHR individuals and its impact on the progression of the at-risk state.

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