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ORIGINAL PAPER

Psychotic experiences and mood episodes predict each other bidirectionally: a 6-year follow-up study in a community-based population

Umut Kırlı[1,2] · Tolga Binbay[3] · Marjan Drukker[2] · Jim van Os[2,4,5] · Köksal Alptekin[3] · Bülent Kayahan[6] · Hayriye Elbi[6]

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Abstract

Background Psychotic experiences (PEs) are not exclusive to psychotic disorders and highly correlated with mood episodes. In this representative general population-based study, longitudinal bidirectional associations between the extended psychosis phenotype and mood episodes were investigated, accounting for other possible causes.

Methods Households were contacted in a multistage clustered probability sampling frame covering 11 districts and 302 neighbourhoods at baseline ($n=4011$) and at 6-year follow-up ($n=2185$). Participants were interviewed with the relevant sections of the composite international diagnostic interview both at baseline and at follow-up. Sociodemographic, familial and environmental risk factors associated with the extended psychosis phenotype and mood episodes were assessed. Logistic regression and cross-lagged panel correlation models were used for the associations between the extended psychosis phenotype and mood episodes.

Results PEs were associated with subsequent depressive and manic episodes. There was bidirectionality in that mood episodes were associated with subsequent PEs, and PEs were associated with subsequent mood episodes. The associations occurred in a sub-additive pattern. There were substantial synchronous and cross-lagged correlations between these psychopathology domains, with reciprocally similar cross-lagged correlations. Familial risk and adverse life events were associated with both psychopathology domains, whereas some sociodemographic risk factors and alcohol/cannabis use were associated with only one domain.

Conclusion The sub-additive bidirectional associations between PEs and mood episodes over time and the similarity of cross-lagged correlations are suggestive of mutually causal connections between affective and psychotic domains of psychopathology.

Keywords Psychotic experiences · Depression · Mania · Hypomania · Bidirectionality

✉ Tolga Binbay
tolgabinbay@deu.edu.tr

[1] Psychiatry Unit, Van Education and Research Hospital, Van, Turkey

[2] Department of Psychiatry and Neuropsychology, School for Mental Health and Neuroscience (MHeNS), European Graduate School of Neuroscience (EURON), Maastricht University Medical Centre, Maastricht, The Netherlands

[3] Department of Psychiatry, Faculty of Medicine, Dokuz Eylul University, 35340 Izmir, Turkey

[4] Department of Psychosis Studies, Institute of Psychiatry, King's Health Partners, King's College London, London, UK

[5] Department of Psychiatry, Brain Center Rudolf Magnus Institute, University Medical Center Utrecht, Utrecht, The Netherlands

[6] Department of Psychiatry, Faculty of Medicine, Ege University, Izmir, Turkey

Introduction

An extensive volume of literature suggests that psychotic experiences (PEs) are not exclusive to, and more common than psychotic disorders in the general population [1–4]. Cross-sectional studies have demonstrated high prevalence of PEs in individuals with mood disorders [5–8]. Conversely, mood disorders are prevalent in individuals with PEs [8, 9]. For example, among respondents with lifetime PEs, major depressive disorder was reported to be the most common disorder (25.4%) of the 21 DSM-IV mental disorders examined in the World Health Organization World Mental Health (WMH) Surveys [10]. Furthermore, research has shown that PEs and mood episodes may represent markers of severity of each other, bidirectionally driving poor outcome [8, 11–15]. Despite these clues, few studies have examined the longitudinal associations between PEs and mood episodes and these studies have produced conflicting results. PEs have been associated with subsequent mood episodes among both adolescent [16–19] and adult populations [20]. However, a study with an adult sample found no association between PEs and subsequent depression [21]. Furthermore, mood episodes have been associated with subsequent PEs among both adolescent [19] and adult populations [21]. However, another study with an adolescent sample found no association in this direction [18]. The majority of the above-mentioned studies did not take familial liability and social/environmental covariates into account and this can be the reason for the observed inconsistency in results.

It has been suggested that psychopathology may be represented by overlapping and reciprocally impacting dimensional liabilities (e.g. psychotic, affective) [22]. Phenomenologically, one of these dimensions might emerge, increasing the risk of the other. Given strong evidence linking the lifetime prevalence of PEs with high prevalence of mood episodes, we hypothesized that PEs and mood episodes would predict each other, bidirectionally over time. Furthermore, given evidence that co-occurrence of psychotic and affective domains may reflect general severity of multidimensional psychopathology, building up over time [14, 23], the risk of subsequent psychopathology after PEs or mood episodes may be additive. Finally, meta-analysis of risk factors identified age, sex, education, marital status, alcohol use, cannabis use, life events, childhood adversity and family history of mental illness as important predictors of PEs [1, 2]. We hypothesized that a substantial part of these risk factors would be shared between PEs and mood episodes.

The first aim of this paper was to analyse the bidirectional associations between PEs and mood episodes; over a 6-year period, in a general population sample. The second aim was to analyse if baseline PEs would combine synergistically (on an additive scale) with baseline mood episodes to increase odds of subsequent PEs and mood episodes. The third aim was to evaluate the differential effect of risk factors on PEs and mood episodes.

Methods

Sample and study design

The TürkSch, Izmir Mental Health Survey for Gene-Environment Interaction in Psychosis is a longitudinal, general population-based study covering a time frame of approximately 6 years. The main objective of the TürkSch is to assess prevalence, incidence, risk factors, comorbidity and course of mental disorders [24–26].

The baseline (T_1) sample was randomly selected from the wider Izmir metropolitan area using a multistage sampling procedure, stratified by urbanicity covering 11 districts and 302 neighbourhoods. Izmir is the third most urban area of Turkey with approximately 2.6 million residents in 2007 [27]. Addresses were provided by the Turkish Institute of Statistics (TurkStat) and the households were visited in person by trained lay interviewers between 2007 and 2009. One household member aged between 15 and 64 years was randomly selected using the Kish within-household sampling method [28]. A total of 4011 participants were interviewed at baseline. Full details on the Izmir metropolitan area, sampling, representativeness, instruments and procedures of this assessment (T_1) have been published previously [24]. At follow-up (T_2), addresses of all T_1 participants were re-visited in person 6 years after the baseline assessment in average (years 2013–2015). Several attempts were made to reduce the number of non-respondents from the baseline sample. The study team telephoned the T_1 participants to make appointments for interviews. Any contact information for T_1 participants who could not be reached was collected by asking neighbours in the area or the neighbourhood authorities. If additional information was obtained on the T_1 respondent, the person was contacted at the new contact address. At T_2, 954 individuals from the baseline sample could not be contacted (i.e. after at least three consecutive attempts to contact anyone at the address), and 386 individuals were lost due to residency in a remote area. Forty-four individuals were found to be deceased or imprisoned and 24 addresses were demolished. Furthermore, 418 individuals refused to participate in the follow-up assessment. As a result, a total of 2185 individuals were successfully re-interviewed at T_2. Baseline and follow-up TürkSch assessments were approved by the Ege University ethics committee and have therefore been performed in accordance with the ethical standards

laid down in the 1964 Declaration of Helsinki and its later amendments.

Interviewers, interviewer training and quality control

At T_1, lay interviewers had at least high school education, a health-related profession, and/or were experienced in doing field surveys. At T_2, lay interviewers were psychology graduates. In both assessments, lay interviewers had a 2-week formal training which included basic information on common mental disorders, symptom dimensions in psychosis, and ethical aspects of the project, as well as practical training on CIDI interviews. The field work was closely monitored by the study team (UK, TB, HE, BK, KA). Each interview at T_1 and T_2 was conducted according to a standard procedure, with recording and quality coding [24]. If the quality of the interview was considered low, a phone call (T_1 $n=234$; T_2 $n=156$) or a second visit (T_1 $n=392$; T_2 $n=560$) was planned by the study team [24].

Assessments

Both at baseline and at follow-up participants were screened using the Composite International Diagnostic Interview (CIDI) 2.1 [29]. The CIDI is a fully structured interview developed by the World Health Organization [30] and has been used in various surveys around the world including Turkey [31–33]. Primarily designed for use in epidemiological studies of mental disorders, the CIDI can be used by both clinicians and trained lay interviewers. CIDI was found to have excellent inter-rater reliability in general population-based samples in almost all sections with kappa values ranging from 0.67 to 0.97 [34].

CIDI-based screening of symptoms provides information on frequency, duration, help-seeking, severity of symptoms and psychosocial impairment. In both assessments of TürkSch, the CIDI assessment included screening sections on alcohol and substance-related disorders, depressive and dysthymic disorders, manic and bipolar affective disorders, schizophrenia and other psychotic disorders and two final sections with concluding questions, interviewer observations, and interviewer ratings [24].

Assessment of mood episodes

To assess depressive and hypo/manic episodes, the same case identification procedure was applied at baseline and follow-up. For depression (CIDI section E), participants were asked if they had experienced an episode lasting at least 2 weeks during which they felt depressed, or had a lack of interest. If endorsed, participants were asked if, during this period, they had experienced lack of energy, appetite change, sleep problems, being slow or restless, feelings of worthlessness or guilt, decreased self-esteem, trouble thinking or indecisiveness, and thoughts of death. For manic and hypomanic episodes (CIDI section F), participants were asked whether they had experienced elevated mood or irritability for a period of at least four consecutive days either noticed by others or causing problems. If this was the case, participants were asked if, during this period, they had experienced excessive goal-directed activity, psychomotor agitation, spending sprees, sexual indiscretions, increased talkativeness, flight of ideas, loss of normal social inhibitions, increased self-esteem or grandiosity, decreased need for sleep, and distractibility. For both depressive and manic episodes, the final assessment included questions on probable association of symptoms with substance use or physical illness, help-seeking due to symptoms, the route of help-seeking, clinician diagnosis, and treatment history. All responses were re-evaluated by a team of clinicians. *Depressive episode* and *hypomanic/manic episode* were coded positive in accordance with the definitions and criteria of DSM-IV. Furthermore, any *mood episode* variable was constructed and coded positive if there was either a depressive or a hypomanic/manic episode. Time frame was the past year at T_1 and the last 6 years at T_2 (since baseline).

Assessment of psychotic experiences

To assess PEs, the same case identification procedure was applied both at T_1 and T_2. PEs were rated using 14 CIDI delusions items (G1, G2, G3, G4, G5, G7, G8, G9, G10, G11, G12, G13, G13b and G14) and 5 CIDI hallucinations items (G17, G18, G20, G20C, and G21). All items were rated dichotomously indicating the presence or absence. Kappa for agreement between clinicians for delusions and hallucinations was found to be 0.85 and 0.87, respectively [35].

Rating of PE can be difficult because sometimes individuals can be describing a plausible event or a religious or superstitious belief that in the CIDI may be rated as a PE. Therefore, the following procedure was followed. First, during the interview, each time a participant endorsed a CIDI PE, the participant was asked to give an example, which was written down verbatim by the interviewer for later review with the mental health clinician on the team. All CIDI interviews were reviewed by the study team. When it was not clear whether the participant had truly endorsed a positive PE, the participant was re-contacted by a clinician over the telephone to confirm the PE ($n=156$). Thus, delusional and hallucinatory experiences were coded positive if the team clinician confirmed the PE at review.

Using CIDI items G25 (duration of the PE: between 1 day and 6 months or more), G26, G28, G29 and G29A (level of dysfunction), G16 and G23 (told doctor about psychotic

beliefs), a *measure of impairment associated with PEs* was defined [26, 36]. In addition, all individuals endorsing at least one CIDI psychosis item associated with help-seeking or, if there was no help-seeking, occurring with a frequency of at least once per week, were re-contacted by the study team and invited for a clinical evaluation with the Structured Clinical Interview for DSM-IV (SCID) by the team psychiatrist. Thus, 225 participants at T_1 and 263 participants at T_2 were clinically re-interviewed to identify participants with psychotic disorder. Using the *measure of impairment associated with PEs* and the SCID results, an *extended psychosis phenotype* variable was constructed including four categories. *The psychotic disorder group* included all individuals diagnosed with any DSM-IV disorder with psychotic features. The *clinical PE* group included individuals who had a CIDI PE leading to any of the 7 CIDI impairment items but who did not have a diagnosis of psychotic disorder. The *subclinical PE* group included individuals with a CIDI PE not leading to any distress, impairment or help-seeking. All other individuals were included in the '*no psychosis'* category. The time frame for PEs was lifetime at baseline assessment (T_1) and the last 6 years at follow-up assessment (T_2).

To analyse the longitudinal bidirectional associations between PEs and mood episodes, an independent variable combining baseline PEs and mood episodes was constructed (baseline mental status) (0: *no PE, no mood episodes*; 1: *PE, no mood episodes* 2: *no PE, mood episodes*; 3: *both PE and mood episodes*). This variable was used in logistic regression models of the dichotomous outcome variables "*any follow-up PE*", "*any follow-up mood episodes*", *"follow-up depressive episode*", "*follow-up hypomanic/manic episode*".

Other assessments

The baseline and follow-up assessments included a sociodemographic questionnaire and additional questions to define patterns of help-seeking (the route of help-seeking, diagnosis, prescribed medication and hospitalization). *Educational achievement* was defined based on last graduated school including five categories (University or higher, high school, secondary school, primary school, non-graduate). *Marital status* was recoded into (living as) married and non-married (single, divorced or widowed). *Socioeconomic status* was based on profession and recoded into 4 ordinal categories (1: I and II professional and IIIA non-manual high employees, 2: IIIB non manual low employee and V and VI skilled workers and technicians, 3: IVA, IVB, and IVC owners of small businesses, and 4: VIIA and B manual workers) [37]. *The status of psychotropic medication use at baseline and follow-up* was recoded into 4 categories (0: never 1: use at baseline, no use at follow-up 2: no use at baseline, use at follow-up 3: use at both assessments).

Using questions derived from the Family Interview for Genetic Studies [38], history of mental disorders in the father, mother, siblings, and offspring was assessed. Thus, guided by previous works [39] a *family history of mental disorders* variable was defined and coded as "0" no or undefined family history of mental disorders,"1" common mental disorder (non-psychotic disorders of depression/anxiety, conversion, somatoform etc. in at least one family member), and "2" severe mental illness (bipolar disorder/ psychotic disorder/hospitalization/completed suicide) in at least one family member [36].

Alcohol and cannabis use were assessed using screening questions on CIDI sections of alcohol and substance-related disorders. Conform previous CIDI-based research [36, 40] and using information from both T_1 and T_2, cannabis use of 5 times or more was defined as exposure status for cannabis. Regular alcohol use was defined as use of alcohol at least once a week. Using information from both T_1 and T_2, alcohol use was recoded into three variables: "0" *never used*, "1" *non-regular user* (history of alcohol use at any level but no regular use at follow-up assessment), and "2" *regular user* at follow-up assessment [41]. *Life events* were assessed using the List of Threatening Life Events [42]. The events were a serious illness, injury or an assault (suffering or happening to a close relative); death of a relative or a close friend, divorce, separation, serious problems with a relative/ neighbour/ close friend, being dismissed from the job, unemployment, major financial problems, police/ court appearance. Time frame was the last 6 years. The number of life events was a continuous variable with a minimum of 0 and maximum of 12. Childhood adversity between age 0–5 years and between age 6–15 years was death of any parent, divorce of parents and separation from parents for at least for 3 months and dichotomized to none or at least one [36].

Statistical analyses

All analyses were conducted using the software package STATA, version 13 (StataCorp, 2013). To evaluate the possibility of bias caused by differential attrition over time, we compared the participants at T_2 with the individuals who participated at T_1 and not at T_2 on sociodemographic characteristics using the chi-squared tests. Results were presented showing the p values and effect size measures *(Cramer's V)*.

To analyse the longitudinal bidirectional associations between PEs and mood episodes (first aim), crude associations were analysed between PEs at T_1 and mood episodes at T_2, and vice versa. Subsequently, results were adjusted for sociodemographics, familial and environmental risk factors. Furthermore, considering the possible influence on expression of both PEs and mood episodes, models additionally included *psychotropic medication use* (reference category: none at T_1 or at T_2).

Besides the model with the binary PEs variable, we modelled PEs as a continuum stratified by the severity (the extended psychosis phenotype variable). Using a cross-lagged panel design, polychoric correlations between the extended psychosis phenotype and mood episodes at both time points were computed.

For the second aim, interaction contrast ratios (ICRs) were used to test departure from additivity [43]. Using the odds ratios (OR) derived from the previous logistic regression models of the dichotomous outcome variables "*any follow-up PE*" and "*any follow-up mood episodes*", we calculated ICRs using the formula (i.e. $ICR = OR_{\text{both PE and mood episodes}} - OR_{\text{PE, no mood episodes}} - OR_{\text{no PE, mood episodes}} + 1$). Confidence intervals and *p* values for ICRs were generated using the nlcom procedure in Stata version 13.2 [44].

For the third aim, logistic regression was used to assess the associations between risk factors and the presence of mood episodes and PEs, separately. In all analyses, alpha was set at 0.05.

Results

Participant characteristics

The average age of the participants at T_1 was 44.7 years (range = 21–71; SD = 13.3). Details of the sociodemographic, clinical and diagnostic characteristics of participants at T_1 and T_2 were presented in Table 1. Attrition was slightly higher in males, and the difference between participants and non-participants was below the significance level (*males: non-participants 43.4% male vs. participants 40.6%;* $\chi^2 = 3.28$, *df* = 1, $p = 0.07$, *Cramer's V* = 0.02). Attrition was higher in the younger age group (*15–29 years: non participants 39.8% vs. participants 32.0%;* $\chi^2 = 35.16$, *df* = 2, $p < 0.01$, *Cramer's V* = 0.09); in non-married participants (*non-married: non-participants 34.2% vs. participants 25.0%;* $\chi^2 = 40.6$, *df* = 1, $p < 0.01$, *Cramer's V* = 0.10) and in participants with higher educational achievement (*at least high school: non-participants 43.8% vs. participants 39.3%;* $\chi^2 = 8.29$, *df* = 1, $p = 0.004$, *Cramer's V* = 0.04) with small effect sizes.

About one-fourth of the sample (*n*: 578; 26.4%) reported contact with a mental health service at least once in their lifetime. Furthermore, 541 participants (24.8%) reported psychotropic medication use (Table 1). The details of the dynamic transitions over time in the extended psychosis phenotype are presented in Fig. 1. About one-third of subclinical PEs persisted (29.1%) and a small proportion (1.5%) evolved into psychotic disorder expression at T_2. Of the clinical PEs, a higher proportion persisted (51.3%) and evolved into psychotic disorder expression (6.9%).

Main effects of sociodemographics, familial and environmental risk factors on the presence of psychotic experiences and mood episodes at follow-up assessments

Non-married marital status, family history of mental disorders (both common and severe), childhood adversity and number of life events exposed to for the last 6 years were significantly associated with both PEs and mood episodes at follow-up. Female sex was significantly associated with mood episodes but not with PEs. Younger age (≤45 years), lower educational achievement and alcohol/cannabis use were significantly associated with PEs but not with mood episodes. As expected, the status of psychotropic medication use was associated with both follow-up PEs and mood episodes (Table 2).

Longitudinal bidirectional associations between psychotic experiences and mood episodes

In comparison with the reference category of *no PE, no mood episodes*, the baseline group of *mood episodes in isolation was* significantly associated with the *follow-up PEs*. Bidirectionally, the baseline category of *PE in isolation was* significantly associated with *follow-up mood episodes* (Table 3). Furthermore, the association was significant with both follow-up depressive (*unadjusted* OR: *2.0, 95% confidence interval [CI]: 1.3–3.2; adjusted* OR: *1.5, 95% CI: 1.1–2.5*) and hypomanic/manic episodes (*unadjusted* OR: *4.8, 95% CI: 1.6–14.2; adjusted* OR: *3.2, 95% CI: 1.1–10.1*). The baseline category of *PE and mood episodes combined* was the strongest predictors of both *follow-up PE* and *mood episodes* (Table 3). However, there was no significant evidence that baseline PEs combined synergistically (on an additive scale) with baseline mood episodes to increase odds of subsequent PEs (ICR: 0.3, 95% CI − 2.0 to 2.5, $p = 0.82$) and mood episodes (ICR = 1.8, 95% CI − 1.3 to 4.8, $p = 0.26$). Finally, the bidirectional associations between PEs and mood episodes were attenuated, when adjusted for the status of psychotropic medication use (data not shown).

Polychoric correlations between mood episodes and the extended psychosis phenotype (stratified by severity) at T_1 and T_2 were demonstrated in Fig. 2. The synchronous correlations (*r*) between mood episodes and the extended psychosis phenotype were 0.48 at baseline and 0.51 at follow-up. The cross-lagged correlations (*r*) were 0.34 and 0.32.

Discussion

Findings

In this representative general population-based study, we mainly investigated the longitudinal bidirectional

Table 1 Sociodemographic and Clinical Characteristics of Participants at Baseline and Follow-up Assessments

	Baseline T_1 *n* (%)	Follow-up T_2 *n* (%)
Age categories		
15–30	699 (32.0)	354 (16.2)
31–45	750 (34.3)	844 (38.6)
46–71	736 (33.7)	987 (45.2)
Sex		
Male	887 (40.6)	887 (40.6)
Female	1298 (59.4)	1298 (59.4)
Education		
Non-graduate	155 (7.1)	106 (4.9)
Primary school	811 (37.1)	845 (38.7)
Secondary school	360 (16.5)	278 (12.7)
High school	539 (24.7)	499 (22.8)
University or higher	320 (14.6)	457 (20.9)
Marital status		
Married	1638 (75.0)	1741 (79.7)
Non-married	547 (25.0)	444 (20.3)
Socioeconomic status		
1	466 (21.3)	160 (7.3)
2	585 (26.8)	415 (19.0)
3	352 (16.1)	273 (12.5)
4	782 (35.8)	1337 (61.2)
Contact with a mental health service		
None	1872 (85.7)	1788 (81.8)
At least once	313 (14.3)	397 (18.2)
Use of psychotropic medication		
None	1899 (86.9)	1798 (82.3)
At least once	286 (13.1)	387 (17.7)
Extended psychosis phenotype		
No PE	1616 (73.9)	1729 (79.1)
Subclinical PE	334 (15.3)	193 (8.8)
Clinical PE	187 (8.6)	191 (8.7)
Psychotic disorder	48 (2.2)	72 (3.3)
Mood episodes		
None	1783 (81.6)	1984 (90.8)
Present	402 (18.4)	201 (9.2)
Total	2185 (100)	2185 (100)

associations between mood episodes and PEs. Mood episodes were associated with subsequent PEs, and bidirectionally, PEs were associated with subsequent mood episodes after accounting for other possible causes. Furthermore, in comparison with either PEs or mood episodes in isolation, the combined group had the higher odds for both subsequent PEs and mood episodes. However, no evidence was found that the latter associations are additive. Therefore, we assume that PEs and mood episodes had sub-additive bidirectional associations over the follow-up period. The bidirectional associations between PEs and mood episodes were attenuated, when adjusted for psychotropic medication use. Considering that the decision of either prescribing or using a psychotropic medication is likely associated with impairment and severity of the psychopathology, adjustment for these can be expected to result in attenuation of reciprocal associations of mood episodes and PEs, representing an adjustment for the severity driving the association itself. Finally, mood episodes were correlated with the severity of the extended psychosis phenotype. In light of these results, PEs may be conceptualised as a marker for the severity of affective psychopathology, as argued elsewhere [45]. Similarly, these results are in agreement with reports that affective dysregulation may be a marker for dysfunction associated with PE [13–15, 23].

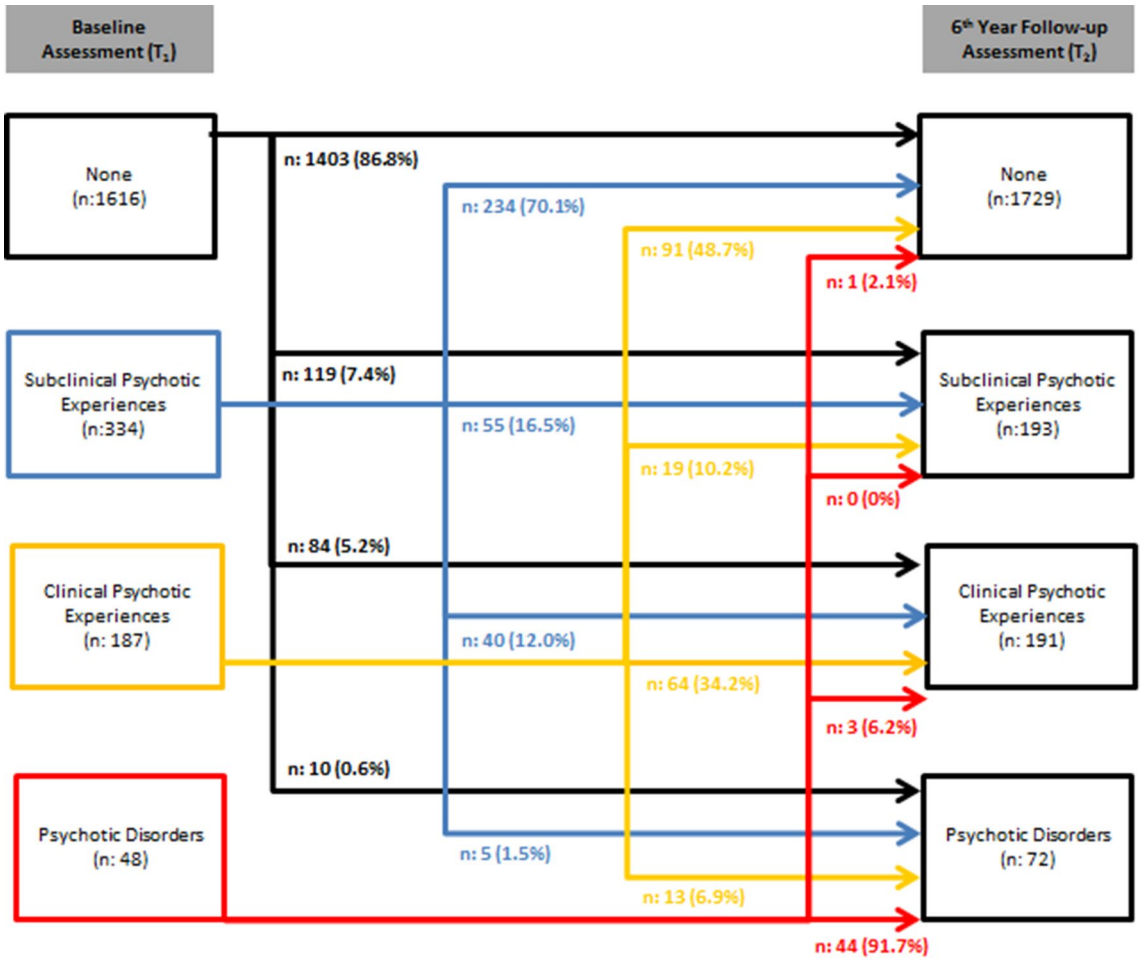

Fig. 1 The dynamic transitions over time in the extended psychosis phenotype. $N = 2185$ participants interviewed at 6-year follow-up (T_2)

The cross-lagged correlations between the extended psychosis phenotype and mood episodes were reciprocally similar (0.34 and 0.32), suggesting mutual causal connections between affective and psychotic domains of psychopathology [46]. While some sociodemographic risk factors such as non-married marital status were associated with both psychopathology domains, some other factors were associated with only one domain. In line with previous epidemiological results [2, 47], female sex was associated with mood episodes, whereas no significant sex differences were found for the extended psychosis phenotype. Conversely, younger age (≤45 years) was significantly associated with the extended psychosis phenotype but not with mood episodes, in agreement with previous findings [1, 47–50]. Furthermore, educational achievement was significantly associated with the extended psychosis phenotype, but not with mood episodes. Familial risks (both common mental disorders and severe mental illness) were associated with both psychopathology domains, in agreement with previous evidence [1, 2, 50]. Some environmental exposures such as life events over the last 6 years and childhood adversity were associated with both psychopathology domains at follow-up. However, alcohol and cannabis use were associated with the extended psychosis phenotype, but not with mood episodes.

Our results demonstrated substantial synchronous and cross-lagged correlations between mood episodes and the extended psychosis phenotype. There is growing evidence that affective and psychotic domains of psychopathology have strong overlap in terms of symptom dimensions [14, 51, 52]. Similar to the epidemiological results, there are grey areas between the boundaries of psychotic and affective disorders in the current classification systems [53]. A transdiagnostic approach based on the dimensional scores of both psychotic and affective domains (i.e. positive, negative, disorganisation, manic, depressive) may be useful to represent common 'psycho-affective' psychopathology more accurately [45]. Such an approach might be effective to determine the place of psychopathology in the psychosis spectrum (i.e. affective/non-affective; clinical/subclinical) [45]. Keeping in mind the proposed sub-additive bidirectional associations

Table 2 Differential effect of sociodemographic, familial and environmental factors on the presence of follow-up mood episodes and psychotic experiences

Sample		Psychotic experience present at T_2		Mood episode present at T_2	
Categories	*N* (%)	*N* (%)	OR (CI)	*N* (%)	OR (CI)
Age (at T_1)					
46–65	987 (45.2)	173 (37.9)	1 (ref)	83 (41.3)	1 (ref)
15–45	1198 (54.8)	283 (62.1)	1.5 (1.2–1.8)‡	118 (58.7)	1.2 (0.9–1.6)
Sex					
Male	887 (40.6)	192 (42.1)	1 (ref)	53 (26.4)	1 (ref)
Female	1298 (59.4)	264 (57.9)	0.9 (0.7–1.1)	148 (73.6)	2.0 (1.5–2.8)‡
Education					
University or higher	457 (20.9)	67 (14.7)	1 (ref)	34 (16.9)	1 (ref)
High school	499 (22.8)	107 (23.5)	1.6 (1.1–2.2)†	45 (22.4)	1.2 (0.8–2.0)
Secondary school	278 (12.7)	65 (14.2)	1.7 (1.2–2.6)†	24 (11.9)	1.2 (0.7–2.0)
Primary school	845 (38.7)	193 (42.3)	1.7 (1.3–2.3)‡	89 (44.3)	1.5 (1.0–2.2)
Non-graduate	106 (4.9)	24 (5.3)	1.7 (1.1–2.9)*	9 (4.5)	1.2 (0.5–2.5)
Marital status					
Married	1741 (79.7)	310 (68.0)	1 (ref)	147 (73.1)	1 (ref)
Non-married	444 (20.3)	146 (32.0)	2.3 (1.8–2.8)‡	54 (26.9)	1.5* (1.1–2.1)
Family history of mental disorder					
None/undefined	1789 (81.9)	331 (72.6)	1 (ref)	121 (60.2)	1 (ref)
Common mental disorder	336 (15.4)	102 (22.4)	1.9 (1.5–2.5)‡	68 (33.8)	3.4 (2.5–4.8)‡
Severe mental illness	60 (2.7)	23 (5.0)	2.7 (1.6–4.7)‡	12 (6.0)	3.4 (1.8–6.7)‡
Alcohol use					
Never used	1090 (49.9)	204 (44.8)	1 (ref)	98 (48.8)	1 (ref)
Non-regular user	723 (33.1)	157 (34.4)	1.2 (0.9–1.5)	71 (35.3)	1.1 (0.8–1.5)
Regular user	372 (17.0)	95 (20.8)	1.5 (1.3–2.0)†	32 (15.9)	0.9 (0.6–1.4)
Cannabis use					
None	2122 (97.1)	418 (91.7)	1 (ref)	192 (95.5)	1 (ref)
At least five times	63 (2.9)	38 (8.3)	6.2 (3.7–10.4)‡	9 (4.5)	1.7 (0.8–3.4)
Life events for the last 6 years					
None	482 (22.1)	53 (11.6)	1 (ref)	17 (8.5)	1 (ref)
At least one	1703 (77.9)	403 (88.4)	2.5 (1.8–3.4)‡	184 (91.5)	3.3 (2.0–5.5)‡
Childhood adversity					
None	1870 (85.6)	375 (82.2)	1 (ref)	162 (80.6)	1 (ref)
At least one	315 (14.4)	81 (17.8)	1.4 (1.1–1.8)*	39 (19.4)	1.5 (1.1–2.2)*
Psychotropic medication					
None	1644 (75.2)	244 (53.5)	1 (ref)	30 (14.9)	1 (ref)
T_1 (+) T_2 (−)	154 (7.1)	28 (6.2)	1.3 (0.8–2.0)	5 (2.5)	1.8 (0.7–4.7)
T_1 (−) T_2 (+)	255 (11.7)	110 (24.1)	4.4 (3.3–5.8)‡	108 (53.7)	39.5 (25.5–61.3)
T_1 (+) T_2 (+)	132 (6.0)	74 (16.2)	7.3 (5.1–10.6)‡	58 (28.9)	42.2 (25.6–69.4)
	Mean (SD)	Mean (SD)	OR (CI)	Mean (SD)	OR (CI)
Number of life events for the last 6 years	1.6 (1.5)	2.5 (1.9)	1.6 (1.5–1.7)‡	2.6 (1.8)	1.5 (1.4–1.6)‡

*$p < .05$, †$p < .01$, ‡$P < .001$

between the psychotic and affective dimensions, future research on the reciprocal influences of these dimensions, and the underlying factors moderating these, might provide a useful framework for the clinical delineation of the spectrum of affective and psychotic psychopathology.

Methodological issues

As far as we are aware, this is the first longitudinal study in a large community-based population that examines the bidirectional associations between PEs and mood episodes

Table 3 Longitudinal bidirectional associations between extended psychosis phenotype and mood episodes

Baseline mental status[a]		Extended psychosis phenotype present at T_2			Mood episode present at T_2		
Category	*N* (%)	*N* (%)	OR (CI)	OR[b] (CI)	*N* (%)	OR (CI)	OR[b] (CI)
PE (−) Mood (−)	1427 (65.3)	168 (36.8)	1 (ref)	1 (ref)	68 (33.8)	1 (ref)	1 (ref)
PE (−) Mood (+)	189 (8.6)	45 (9.9)	2.3‡ (1.6–3.4)	1.8† (1.2–2.7)	39 (19.4)	5.2‡ (3.4-8.0)	3.4‡ (2.2–5.4)
PE (+) Mood (−)	356 (16.3)	143 (31.4)	5.0‡ (3.9–6.6)	3.9‡ (3.0-5.2)	33 (16.4)	2.0† (1.3–3.1)	1.6* (1.1–2.4)
PE (+) Mood (+)	213 (9.8)	100 (21.9)	6.6‡ (4.8-9.0)	4.3‡ (3.1–6.1)	61 (30.4)	8.0‡ (5.5–11.8)	5.1‡ (3.4–7.7)

[a]*PE* presence of baseline extended psychosis phenotype *Mood* presence of baseline mood episode

[b]Adjusted for age, sex, marital status, educational level, family history of mental disorders, childhood adversity, number of life events for the last 6 years, alcohol and cannabis use

*$p < .05$, †$p < .01$, ‡$p < .001$

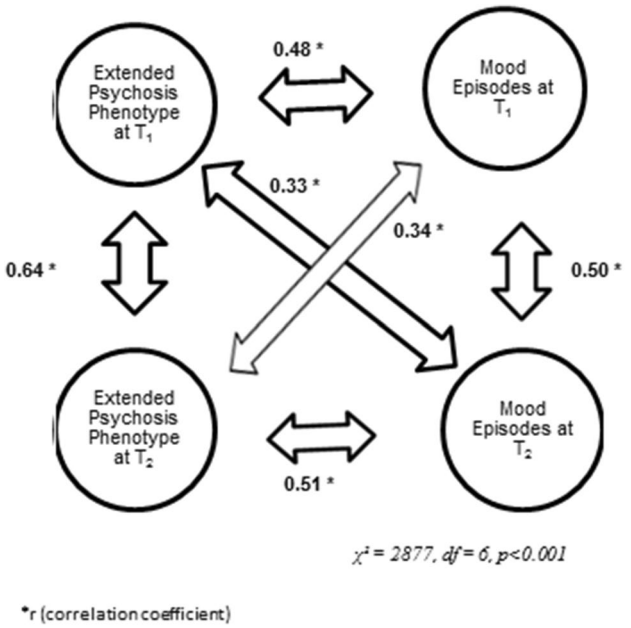

Fig. 2 Polychoric correlations between mood episodes and the extended psychosis phenotype

controlling for common risk factors. The longitudinal design enabled us to measure non-lifetime clinical features which were subject to change in time. Furthermore, adjustment addressed some other causes of psychopathology, such as sociodemographic features, familial risk, alcohol and substance use, and adverse life events.

In spite of the strengths, the results need to be considered in the light of the following limitations. First, as with most longitudinal studies, our initial sample size was reduced because of the attrition. The comparison of baseline characteristics between non-participants and participants showed that attrition was higher in younger, non-married and higher-educated individuals. However, differences between participants and non-participants were quite small (Cramer's $V \leq 0.1$). In addition, associations between PEs and mood episodes would only be confounded by non-response if this was differential with regard to the two dimensions in the association, and this is unlikely. However, the results of the study should be interpreted in the light of a degree of underlying selective drop-out. Second, despite the quality checks of the interviews using a standard procedure for formal consistency, appropriate recording and coding which was described above and in more detail elsewhere [24], the assessment of PEs and mood episodes in the general population inevitably is associated with a degree of misclassification (false positives and false negatives) [54]. However, there is little reason to assume that misclassification was differential with regard to PEs on the one hand and mood episodes on the other. Therefore, it is unlikely that findings are biased. Third, while clinical re-interviews were conducted to identify participants with psychotic disorders, the definitions of depressive and manic/hypomanic episodes were based on the CIDI results. Fourth, we only considered positive dimensions of PEs. However, negative and disorganized dimensions were also found to be predictive of later psychopathology [45]. Thus, these results cannot be generalized to negative and disorganised dimensions.

Sensitivity analyses in younger age group

It is well-known that the incidence of psychosis is higher in younger age groups [47, 55] and may be of different origin than psychotic syndromes observed in older age groups. Thus, the associations studied in the present paper may be different in the youngest age group with the highest incidence. A sensitivity analysis was performed including participants aged 45 years or younger. Correlations were similar or a little stronger in this age group. The synchronous

correlations (*r*) between mood episodes and the extended psychosis phenotype were 0.53 at baseline and 0.58 at follow-up. The cross-lagged correlations (*r*) were 0.34 and 0.36.

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