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The bi-directional associations between psychotic experiences and DSM-IV mental disorders

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Abstract

Objective—While it is now recognized that psychotic experiences (PEs) are associated with an increased risk of later mental disorders, we lack a detailed understanding of the reciprocal time-lagged relationships between first onsets of PEs and mental disorders.

Methods—The WHO World Mental Health (WMH) surveys assessed lifetime prevalence and age-of-onset of PEs and 21 common DSM-IV mental disorders among 31,261 adult respondents from 18 countries.

Results—Temporally primary PEs were significantly associated with subsequent first onset of 8 of the 21 mental disorders (major depressive disorder, bipolar disorder, generalized anxiety disorder, social phobia, post-traumatic stress disorder, adult separation anxiety disorder, bulimia nervosa, alcohol abuse), with ORs (95%CI) ranging from 1.3 (1.2–1.5; major depressive disorder) to 2.0 (1.5–2.6; bipolar disorder). In contrast, 18 of 21 primary mental disorders were significantly associated with subsequent first onset of PEs, with ORs (95% CI) ranging from 1.5 (1.0–2.1; childhood separation anxiety disorder) to 2.8 (1.0–7.8; anorexia nervosa).

Conclusions—While temporally primary PEs are associated with an elevated risk of several subsequent mental disorders, we found that most mental disorder are associated with an elevated risk of subsequent PEs. Further investigation of the underlying factors accounting for these time-order relationships might shed light on the etiology of PEs.

Introduction

A recent study based on data from 18 countries participating in the WHO World Mental Health Surveys (WMH) found that lifetime prevalence of any psychotic experience (PE) among adults was 5.8% (standard error [se] = 0.2) (1). These WMH estimates were broadly consistent with PE prevalence estimates in other population-based studies (2, 3). The relatively high lifetime prevalence of PEs is much higher than the 0.7% mean morbid risk for schizophrenia (4) and raises important questions about the clinical significance of PEs with respect to the risk of psychosis and mental disorders in general.

There is solid evidence from prospective studies that PEs are associated with an increased risk of later psychotic disorders (5–7). In addition, there is some evidence that PEs are associated with increased risk of subsequent non-psychotic mental disorders (8), but this field of research has for the most part examined associations between lifetime PEs and lifetime common mental disorders *regardless of temporal priority*. For example, there is evidence linking the lifetime prevalence of PE with high prevalence of depression and anxiety disorders (9–12), substance use disorders (13), and behavioural disorders (14). Despite these clues, there is a lack of empirical data on whether temporally primary common

mental disorders are associated with an increased risk of subsequent first onset of PEs, and conversely, which mental disorders are predicted by pre-existing PEs.

We had the opportunity to carry out a preliminary exploration of the bidirectional time-lagged associations between PEs and mental disorders using retrospective age-of-onset (AOO) reports within the WMH surveys. The aims of this study were to explore the associations of (a) temporally primary PEs with the subsequent onset of mental disorders and (b) temporally primary mental disorders with the subsequent onset of PEs.

METHOD

Samples

The WMH surveys are a coordinated set of community epidemiological surveys administered in probability samples of the household population in countries throughout the world (www.hcp.med.harvard.edu/WMH) (15). Eighteen of the 29 WMH surveys completed up to now included a Psychosis Module. These 18 countries are distributed across North and South America (Colombia, Mexico, Peru, Sao Paulo in Brazil, USA); Africa (Nigeria); the Middle East (Iraq, Lebanon); Asia (Shenzhen in the People's Republic of China); the South Pacific (New Zealand); and Europe (Belgium, France, Germany, Italy, the Netherlands, Portugal, Romania, Spain). All 18 surveys were based on multi-stage, clustered area probability household sampling designs (Supplementary Table S1). Individual country sample sizes ranged from 301 in France to 7 263 in New Zealand. The weighted average response rate across all 18 surveys was 72.1%.

In keeping with previous epidemiological studies of PEs (1, 13, 16, 17), we made the *a priori* decision to exclude individuals who had PEs but who also screened positive for possible schizophrenia/psychosis or manic-depression/mania (i.e. respondents who (a) reported (1) *schizophrenia/psychosis* or (2) *manic-depression/mania* in response to the question “*What did the doctor say was causing (this/these) experiences?*”; and/or (b) those who ever took any antipsychotic medications for these symptoms). This resulted in the exclusion of 140 respondents (0.4% of all respondents), leaving 31 261 respondents for this study (see Table S1).

Procedures

All surveys were conducted in respondents' homes by trained lay interviewers. Informed consent was obtained before beginning interviews in all countries. Procedures for obtaining informed consent, ethical approvals and protecting individuals were monitored for compliance by the institutional review boards of the collaborating organisations in each country (18). Standardised interviewer training and quality control procedures were used consistently in the surveys. Full details of these procedures are described elsewhere (18, 19).

All WMH interviews had two parts. Part I, administered to all respondents, contained assessments related to core mental disorders. Part II included additional information relevant to a wide range of survey aims, including assessment of PEs. All Part I respondents who met criteria for any DSM IV mental disorder as well as a probability sample of other respondents were administered Part II. Within the different sites, items related to PEs were either

administered to all respondents or a random sample of those administered Part II. Part II respondents were weighted by the inverse of their probability of selection for Part II to adjust for differential sampling. Additional weights were used to adjust for differential probabilities of selection within households, nonresponse, and to match the samples to population socio-demographic distributions. The weighted data are analysed here.

Data collection and Data items

The diagnostic instrument used in the WMH surveys was the WHO Composite International Diagnostic Interview (CIDI) (20), a validated fully-structured diagnostic interview (http://www.hcp.med.harvard.edu/wmh/cidi/instruments_download.php) designed to assess the prevalence and correlates of a wide range of mental disorders according to the definitions and criteria of both the DSM-IV and ICD-10 diagnostic systems. WHO translation, back-translation, and harmonisation protocols were used to adapt the CIDI for use in each participating country (21).

Psychotic experiences (PEs)—The CIDI Psychosis Module included questions about 6 PE types – 2 related to hallucinations (HEs: visual hallucinations, auditory hallucinations) and 4 related to delusions (DEs: thought insertion/withdrawal, mind control/passivity, ideas of reference, plot to harm/follow) (Supplementary Material Tables S2a and S2b). The module began by asking respondents if they ever experienced the PEs (e.g., “*Have you ever seen something that wasn’t there that other people could not see?*”; “*Have you ever heard any voices that other people said did not exist?*” etc). Positive responses were then probed to determine if the reported PEs ever occurred when the person was ‘*not dreaming, not half-asleep, or not under the influence of alcohol or drugs*’ (this probe question was included in the main question in European Study of the Epidemiology of Mental Disorders (ESEMEd) countries). Respondents who reported PEs were then asked a further probe question about the age-of-onset (AOO) of PEs (i.e., *How old were you the very first time (this/either of these things/any of these things) happened to you?*). In the 8.0% of cases where PE AOO was missing, we used imputation to assign predicted values based on a set of predictors that included all the variables in the substantive models (22). Key summary statistics (n, mean, SE, median, IQR) for the observed data (without imputation) and the entire dataset after imputation are shown in Supplementary Material Table S4.

DSM-IV Mental disorders—The WMH survey version of the CIDI assessed lifetime history of 21 mental disorders considered in this paper including *mood disorders* (major depressive disorder, bipolar disorders); *anxiety disorders* (panic disorder, generalized anxiety disorder, specific phobia, social phobia, agoraphobia without panic, post-traumatic stress disorder (PTSD), separation anxiety disorder further divided into childhood, and adult separation anxiety disorders); *impulse control disorders* (intermittent explosive disorder, attention deficit disorder, oppositional defiant disorder, conduct disorder); *eating disorder* (anorexia nervosa, bulimia nervosa, and binge eating disorder); and *substance use disorders* (alcohol abuse, alcohol dependence, drug abuse, and drug dependence). The disorders that require childhood onset (e.g., attention deficit disorder, oppositional defiant disorder, conduct disorder, separation anxiety disorder) were included in Part II and are limited to respondents in the age range 18–39/44 due to concerns about recall bias among older

respondents (23). All other disorders were assessed for the full sample age range. Clinical reappraisal studies indicate that lifetime diagnoses based on the CIDI have good concordance with diagnoses based on blinded clinical interviews (24).

In keeping with previous research, standardised diagnostic hierarchy rules among the disorders assessed were applied where appropriate (25). When applied, a person is excluded from a diagnosis, even though he/she has sufficient symptoms to meet criteria, because the person may have another disorder that is thought to account for those symptoms. For example, someone who has alcohol dependence cannot be diagnosed with alcohol abuse as dependence is a more severe diagnosis. Therefore, alcohol abuse with hierarchy means it cannot occur exclusively during episodes of alcohol dependence. However, given that the analysis was based on a person-year data array (see below), these diagnoses can change within persons over time. For example, a respondent with an onset of alcohol abuse at age 18 and alcohol dependence at 22 would be coded as having alcohol abuse over the years 18–21 and as having alcohol dependence beginning at age 22.

Statistical Analysis

Discrete-time survival analyses (26) with person-year as the unit of analysis and time-varying measures for prior onset of other mental disorders were used to examine the predictive associations of temporally prior disorders with the subsequent onset of each mental disorder considered in the analysis. A person-year dataset was created such that each year in the life of each respondent (up to and including the age of onset of the outcome disorder or their age at interview, whichever came first) was treated as a separate observational record. We estimated survival models that examined bivariate associations between PEs and only one common mental disorder at a time (with adjustment for age-cohorts, sex, person-year, education, marital and employment status, and country) as well as multivariate models that included information on all temporally primary common mental disorders to predict the outcome disorder. The latter models included measures for both type and number of prior mental disorders. In the case of multivariate models of the associations between temporally primary PEs and later disorders, we controlled for the association of other temporally primary disorders, again including measures for both type and number of these disorders, in order to determine if significant net associations existed between temporally primary PEs and subsequent onsets of the outcome disorders. Measures of number of temporally primary disorders (e.g., dummy predictors for exactly 2, exactly 3, and more than 3 such disorders) provide a coarse characterization of the non-additive associations among the predictor disorders. Previous research has shown that the coefficients associated with these predictors are for the most part negative and significant (27), indicating the presence of “sub-additive” interactions among comorbid disorders. The latter suggests that the predictive associations of having multiple temporally prior disorders increase at a decreasing rate as the number of such disorders increases. A more detailed discussion of the logic of these models is presented elsewhere (27).

All survival coefficients and standard errors were exponentiated to create odds-ratios with 95% confidence intervals. Because the WMH survey data were based on geographically clustered and weighted data, standard errors (SE) were estimated with the Taylor series

linearization method (28) using SUDAAN software (29) to adjust for weighting and clustering. Statistical significance was evaluated using F tests or Wald χ^2 tests based on design-corrected coefficient variance–covariance matrices. Statistical significance was evaluated consistently using two-tailed .05-level tests.

RESULTS

Lifetime prevalence of DSM-IV mental disorders among respondents with and without psychotic experiences

We first examined lifetime prevalence of mental disorders among respondents with and without PEs regardless of the temporal order of PE and mental disorders (Table 1). Compared to those with no PEs, those with PEs had significantly higher odds of having 20 of the 21 mental disorders examined (based on lifetime prevalence). Odds Ratios [OR] and 95% Confidence Intervals [95%CI] ranged from 1.6 (1.2–2.1) for Drug Abuse to 3.6 (2.6–5.0) for Bulimia nervosa.

Temporal priorities between onset ages of PEs and DSM-IV mental disorders

Table 2 examines the temporal sequence between ages of onset of PEs compared to mental disorders within the subset of respondents having both PEs and particular mental disorders. We show the proportion of respondents with (a) PE onset prior to particular mental disorder onset, (b) PE onset in the same year with the mental disorder, and (c) PE onset after the mental disorder onset, and then test if the proportions with PE onset before or after mental disorders significantly differ (i.e., those with onset in the same year were excluded from this comparison). While the overall findings indicate that most PEs have their onset after mental disorders, this pattern varies between diagnoses. For example, the proportion of respondents with PE onset prior to the onset of bipolar disorders was significantly higher (54%) than the proportion with PE onset after the onset of bipolar disorder (39%) ($\chi^2 = 6.0$, $p < .02$), while there was no difference of PE onset with respect to the onset of depressive disorders ($\chi^2 = 0.1$, $p = .767$). By contrast, for many disorders (e.g. 4 of 8 anxiety disorders, and all of the impulse control disorders), higher proportions of respondents reported PE onsets after the onset of the mental disorders of interest.

Time-lagged associations between lifetime PEs and subsequent onset of mental disorders

A limitation of the results in Table 2 is that they do not take into consideration differences in the age-of-onset distributions of the different disorders in relation to the age of onset distribution of PEs. This issue is addressed in Table 3 (a more detailed presentation of these analyses can be found in Supplementary material Table S4), where we show the results from bivariate and multivariate models of the associations between PEs and subsequent mental disorders (i.e. the temporal order requires the onset of PE to precede the onset of the mental disorder of interest). In the bivariate analysis, the associations are adjusted for age-cohort, gender, person-year, employment status and country as well as time-varying education and marital status (without mental disorder co-morbidity). In these models, preceding PEs were significantly associated with increased odds for 16 of the 21 mental disorders. It is noteworthy that 3 of the 5 remaining disorders have childhood onsets by definition (AHHD, conduct disorder, childhood separation anxiety disorder). These three disorders also had

elevated ORs with temporally prior PEs in the range 1.7–2.5, but none of these elevated ORs was statistically significant due to the rarity of PEs occurring prior to the onsets of these disorders. In the multivariate models, we further adjusted for temporally prior comorbid mental disorders (i.e. adjusting for comorbid mental disorders that had onsets prior to the onset of the mental disorder of interest, but not necessarily prior to the onset of PEs). Those with PEs were significantly more likely to subsequently experience 8 of 21 disorders (major depressive disorder, bipolar disorder, generalized anxiety disorder, social phobia, post-traumatic stress disorder, adult separation anxiety disorder, bulimia nervosa, alcohol abuse), with ORs (95%CI) ranging from 1.3 (1.2–1.5) for major depressive disorder to 2.0 (1.5–2.6) for bipolar disorder. In the multivariate models shown in Supplementary Table S4, the ORs associated with number of temporally prior disorders were for the most part lower than 1.0, indicating a general pattern of sub-additive interactions whereby the incremental association of each additional temporally primary disorder lessens in magnitude as the number of such disorders increases.

Time-lagged associations between lifetime mental disorders and subsequent onset of PEs

Next we examined the associations between preceding mental disorders and the subsequent onset of PEs (Table 4). In bivariate models, 20 of the 21 mental disorders were significantly associated elevated odds of subsequent PEs (drug abuse was the only disorder not associated with later PE onset – note that our study excluded PEs that were experienced under the influence of alcohol or drugs). In multivariate models, we found that 18 of the 21 mental disorders were significantly associated with the later onset of PEs, with ORs (95%CI) ranging from 1.5 (1.0–2.1) for associated with the later onset of PEs, with ORs (95%CI) ranging from 1.5 (1.0–2.1) for childhood separation anxiety disorder to 2.8 (1.0–7.8) for anorexia nervosa. As with the previous models predicting mental disorders after temporally primary PEs (Supplementary Table S4), the ORs (95% CIs) associated with number of temporally primary mental disorders (2, 3, 4, 5+) were for the most part less than 1, confirming the existence of sub-additive interactions among mental disorders in predicting first onset of temporally secondary PEs. The joint associations of all the number-of-disorder coefficients were significant ($\chi^2_4 = 31.1, p < .001$).

The key findings from Tables 3 and 4 are summarized in the Figure, which allows quick comparisons between; (a) the ORs for the onset of mental disorders after the onset of PEs, with (b) the ORs for the onset of PEs after the onset of mental disorders, when sorted by mental disorder type.

DISCUSSION

This large, cross-national study demonstrates that individuals with PEs are at increased risk of experiencing a wide range of mental disorders at some stage in their life compared to other people in the population. The mental disorders include mood, anxiety, impulse control, and eating and substance-use disorders. The lack of specificity in these associations even in multivariate models is consistent with the hypothesis that PEs may be non-specific markers of a wide range of mental disorders (30).

Our temporally-ordered analyses have provided new insights into the bidirectional relationship between PEs and mental disorders. We found a strikingly consistent increased risk of PE onset after nearly all of the mental disorders we examined. That is, *most mental disorders were associated with increased risk of subsequent PEs* even in multivariate models. Of the 21 disorders examined in this study, only three externalizing disorders did not significantly predict subsequent PEs in the multivariate model (i.e. conduct disorder, drug abuse, drug dependence).

We also found that the onset of PEs predicted significantly increased risk of subsequent major depressive disorder, bipolar disorder, generalized anxiety disorder, social phobia, post-traumatic stress disorder, adult separation anxiety disorder, bulimia nervosa, and alcohol abuse. Thus, in addition to risk of psychotic disorders (8), an increased risk of subsequent mood disorders, some anxiety disorders, eating disorders and substance use disorders are seen after PE onset. These findings call into the question the specificity of the association between PEs and psychotic disorders (31).

Curiously, in the analyses of PEs predicting subsequent onset of mental disorders, PEs predicted none of the four impulse control disorders and only one of the four substance-use disorders (alcohol abuse), while PEs did predict a number of the mood and anxiety disorders. These findings reveal that the temporal relationships between PEs and mental disorders are bidirectional for some disorders. Importantly, this is not due to the different age-of-onset distributions of these disorders, as pervasively significant time-lagged bivariate associations were found across disorders. The differential came only when we estimated multivariate models in which we can see unique incremental associations of a single temporally primary disorder with a temporally secondary disorder net of the additive effects of comorbid disorders. Taking into account the temporal order of the variables of interest, sub-additive associations between comorbid mental disorders and PEs were identified in both analyses (i.e. this feature is also bidirectional).

While the current study has many strengths (e.g. large sample size, range of countries, uniform methodology for data collection), it also has several important limitations. We relied on lay interviewers to administer the questionnaire. We excluded those who were screen-positive for possible psychotic disorders (based on self-report, use of antipsychotic medications to treat PEs). However, we did not have access to valid measures of clinical psychotic disorders, an important consideration for understanding the utility of PEs as predictors of later psychotic disorders. We relied on retrospective reports about age of onset, which might have led to a recall bias despite the use of special age of onset probes in the CIDI that have been shown to improve the accuracy of retrospective age of onset reporting (32). And we estimated models that assumed that predictive associations were additive and independent of age-of-onset, time-since-onset, and, in the models for temporally primary PEs predicting later disorders, interactions of PEs with disorders occurring prior to the onset of the outcome disorders. More complex models that relaxed these simplifying assumptions might well shed light on the asymmetries found here in the time-lagged multivariate associations between PEs and other disorders. Large prospective surveys would be needed to confirm the temporal order between the variables examined in this study. An additional caution is that even in the presence of unequivocal information on temporal ordering of

onsets, we cannot infer causality, as common unmeasured causes may influence associations between temporally primary and secondary disorders (see below).

Future directions

Our findings provide a heuristic framework for the generation of new hypotheses related to PEs, which we will explore in subsequent studies. For example, it will be of interest to see what proportion of early versus late onset PEs arise (a) de novo, or (b) following the onset of a mental disorder, as well as the extent to which early-onset PEs and PEs of different types (e.g., DEs vs. HEs) predict the subsequent first onset of different types of mental disorders and do so differentially as a complex function of age-of-onset, time-since-onset, and existence of complex comorbidities. It is also feasible that an underlying diathesis might lead to both an increased risk of PE and an increased risk of mental disorders (regardless of the temporal order of these variables). It is plausible that familial/genetic factors and/or adverse early life exposures (e.g. childhood adversities, cannabis use) could lead to both an increased risk of later mental disorders and an increased risk of PEs (33–35). The comprehensive nature of the WMH survey will allow us to explore these and other related hypotheses in future analyses, albeit within the context of the inherent limitations of cross-sectional data assessed with fully-structured diagnostic interviews.

CONCLUSIONS

Individuals with PEs were significantly more likely to have subsequent first onsets of 8 of 21 common mental disorders (major depressive disorder, bipolar disorder, generalized anxiety disorder, social phobia, post-traumatic stress disorder, separation anxiety disorder (adult), bulimia nervosa, alcohol abuse). Conversely, most temporally primary mental disorders were significantly associated with the subsequent first onset of PEs. Our findings have important implications for the understanding of how PEs fit into the structure of psychopathology and within psychiatric taxonomy. A better understanding of how PEs unfold across the lifespan and interact with mental disorder may provide clues to help guide clinical management.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1. Summary of the bidirectional association between psychotic experiences and mental disorders. The Odds ratios were extracted from Tables 3 and 4. Bars to the left (in orange if significant) represent the odds ratio of the onset of mental disorders after the onset of Psychotic Experiences. Bars to the right (in blue if significant) represent the Odds Ratio for the onset of mental disorders after the onset of Psychotic Experiences. Odds ratios for nonsignificant associations are shown in light gray.

Lifetime prevalence of DSM-IV mental disorders among those with and without psychotic experiences across WMH samples.

Table 1

Type of mental disorders	Among the total sample (n = 31,261)			Among those with lifetime psychotic experiences (n = 2,385)			Among those without lifetime psychotic experiences (n = 28,876)			Odds ratio between lifetime PE and lifetime mental disorder
	n ^a	% ^b	SE	n ^a	% ^b	SE	n ^a	% ^b	SE	
I. Mood disorders										
Major depressive disorder with hierarchy	6824	11.8	0.2	897	25.4	1.2	5927	10.9	0.2	2.3* (2.0–2.6)
Bipolar disorder (broad)	1212	2.3	0.1	196	6.5	0.6	1016	2.1	0.1	2.8* (2.2–3.5)
II. Anxiety disorders										
Panic disorder	1019	1.8	0.1	181	4.8	0.5	838	1.6	0.1	2.7* (2.2–3.4)
Generalized anxiety disorder with hierarchy	1832	3.4	0.1	276	8.0	0.6	1556	3.1	0.1	2.4* (2.0–3.0)
Social phobia	2495	4.7	0.1	382	12.1	0.8	2113	4.3	0.1	2.4* (2.0–2.8)
Specific phobia	4108	8.4	0.2	630	20.5	1.1	3478	7.6	0.2	2.6* (2.3–3.0)
Agoraphobia without panic	557	1.0	0.1	102	3.1	0.4	455	0.9	0.1	2.8* (2.0–3.9)
Post-traumatic stress disorder	1811	3.7	0.1	328	10.2	0.7	1483	3.3	0.1	3.0* (2.5–3.6)
Separation anxiety disorder (Child)	449	2.2	0.1	90	5.7	0.8	359	2.0	0.1	2.3* (1.6–3.1)
Separation anxiety disorder (Adult)	877	3.7	0.2	186	11.1	1.0	691	3.2	0.2	3.1* (2.4–4.0)
III. Impulse-control disorders										
Intermittent explosive disorder with hierarchy	1023	3.3	0.1	153	8.4	0.7	870	3.0	0.1	2.1* (1.7–2.6)
Attention deficit disorder	368	1.5	0.1	79	5.1	0.8	289	1.3	0.1	2.6* (1.8–3.9)
Oppositional defiant disorder with hierarchy	311	2.2	0.2	68	5.8	0.9	243	1.9	0.2	2.7* (1.8–4.1)
Conduct disorder	329	2.1	0.2	64	5.4	0.8	265	1.8	0.2	2.3* (1.6–3.4)
IV. Eating disorders										
Anorexia nervosa	69	0.4	0.1	13	0.7	0.3	56	0.3	0.1	1.8 (0.7–4.4)
Binge eating disorder with hierarchy	563	2.1	0.1	128	5.0	0.5	435	1.9	0.1	2.0* (1.5–2.6)
Bulimia nervosa with hierarchy	364	1.1	0.1	89	3.8	0.5	275	0.9	0.1	3.6* (2.6–5.0)
V. Substance-use disorders										
Alcohol abuse with hierarchy	1908	5.1	0.2	232	9.8	0.9	1676	4.8	0.2	1.7* (1.4–2.0)
Alcohol dependence	1170	2.4	0.1	205	6.3	0.6	965	2.1	0.1	2.3* (1.8–2.8)

Type of mental disorders	Among the total sample (n = 31,261)		Among those with lifetime psychotic experiences (n = 2,385)		Among those without lifetime psychotic experiences (n = 28,876)		Odds ratio between lifetime PE and lifetime mental disorder	
	n ^a	% ^b	n ^a	% ^b	n ^a	% ^b		OR ^c
Drug abuse with hierarchy	644	1.8	83	3.6	561	1.7	1.6*	(1.2-2.1)
Drug dependence	481	1.2	104	3.8	377	1.0	2.7*	(1.9-3.6)

^aUnweighted number of respondents in each disorder category;

^bEstimates were based on weighted data.

^cBased on a series of logistic regression, each one comparing respondents with psychotic experiences and respondents without psychotic experiences, adjusted for country.

*** Significant at the .05 level, two-sided test.

Table 2
Lifetime prevalence of psychotic experiences (PEs) onset before and after the onset of DSM-IV mental disorder.

Type of mental disorders	Number of respondents with PE and Dx	Respondents with both lifetime prevalence of mental disorder (Dx) of interest and lifetime PEs									
		% with PE onset prior to Dx onset	SE	% ^b	SE	% with PE onset and Dx onset in the same year	SE	% with PE onset after Dx onset	SE	Chi-square goodness of fit test for equal proportions ^a	P-value
I. Mood disorders											
Major depressive disorder with hierarchy	897	44.5	2.0	10.2	1.2	45.4	2.2	0.1		[0.767]	
Bipolar disorder (broad)	196	53.7	5.0	7.2	2.5	39.1	5.0	6.0**		[0.024]	
II. Anxiety disorders											
Panic disorder	181	42.2	5.3	10.9	3.9	46.9	5.3	1.0		[0.343]	
Generalized anxiety disorder with hierarchy	276	46.1	4.2	6.8	1.9	47.1	4.3	0.0		[0.839]	
Social phobia	382	22.6	2.8	6.7	2.2	70.7	3.3	113.0**		[<.001]	
Specific phobia	630	6.7	1.2	4.5	0.9	88.9	1.5	549.8**		[<.001]	
Agoraphobia without panic	102	28.4	5.8	3.7	1.9	68.0	5.9	38.2**		[<.001]	
Post-traumatic stress disorder	328	40.0	3.9	11.2	2.3	48.8	3.6	4.2**		[0.047]	
Separation anxiety disorder (Child)	90	9.1	2.8	3.8	2.0	87.1	3.4	163.5**		[<.001]	
Separation anxiety disorder (Adult)	186	46.7	5.0	7.5	1.9	45.8	5.0	0.0		[0.893]	
III. Impulse-control disorders											
Intermittent explosive disorder with hierarchy	153	25.4	3.3	5.3	2.3	69.4	3.9	105.0**		[<.001]	
Attention deficit disorder	79	9.4	4.9	2.9	2.7	87.6	6.1	3145.0**		[<.001]	
Oppositional defiant disorder with hierarchy	68	17.6	5.8	1.1	1.1	81.3	5.9	401.3**		[<.001]	
Conduct disorder	64	17.7	5.9	4.9	3.4	77.5	7.2	54.0**		[<.001]	
IV. Eating disorders											
Anorexia nervosa	13	23.6	13.6	-	-	76.4	13.6	-		-	
Binge eating disorder with hierarchy	128	44.7	5.9	6.9	2.9	48.3	5.9	0.2		[0.656]	
Bulimia nervosa with hierarchy	89	49.8	6.3	8.4	4.0	41.8	6.4	1.4		[0.266]	
V. Substance-use disorders											
Alcohol abuse with hierarchy	232	50.1	4.6	2.6	1.2	47.3	4.6	0.5		[0.494]	

Type of mental disorders	Number of respondents with PE and Dx	Respondents with both lifetime prevalence of mental disorder (Dx) of interest and lifetime PEs						Chi-square goodness of fit test for equal proportion ^a	P-value
		% with PE onset prior to Dx onset	SE	% ^b	% with PE onset and Dx onset in the same year	SE	% ^b		
Alcohol dependence	205	43.3	4.4	6.3	2.6	50.4	4.8	2.8	[0.109]
Drug abuse with hierarchy	83	55.0	6.9	3.2	2.0	41.8	6.8	36.6**	[0.026]
Drug dependence	104	48.2	6.3	7.6	3.8	44.2	6.2	2.5	[0.192]

^aChi-square goodness of fit tests were performed on a reduced subset of respondents comparing % with PE onset prior to Dx onset versus % with PE onset after Dx onset.

^bEstimates were based on weighted data.

"-" Goodness of fit test cannot be computed due to small expected counts (<5).

Table 3

Associations between lifetime psychotic experiences (PEs) and the subsequent onset of DSM-IV mental disorders.

Type of mental disorders	Bivariate models ^a		Multivariate models ^b	
	Odds of disorder		Odds of disorder	
	OR	(95% C.I.)	OR	(95% C.I.)
I. Mood disorders				
Major depressive disorder with hierarchy	1.6*	(1.4–1.9)	1.3*	(1.2–1.5)
Bipolar disorder (broad)	2.7*	(2.0–3.5)	2.0*	(1.5–2.6)
II. Anxiety disorders				
Panic disorder	2.0*	(1.5–2.8)	1.3	(0.9–1.8)
Generalized anxiety disorder with hierarchy	1.9*	(1.5–2.4)	1.4*	(1.1–1.8)
Social phobia	2.0*	(1.5–2.7)	1.4*	(1.0–1.8)
Specific phobia	1.0	(0.7–1.5)	0.9	(0.6–1.3)
Agoraphobia without panic	2.0*	(1.2–3.4)	1.2	(0.7–2.1)
Post-traumatic stress disorder	2.0*	(1.6–2.6)	1.3*	(1.1–1.7)
Separation anxiety disorder (Child)	1.7	(0.9–3.2)	1.2	(0.6–2.3)
Separation anxiety disorder (Adult)	2.7*	(1.9–3.6)	1.6*	(1.2–2.2)
III. Impulse-control disorders				
Intermittent explosive disorder with hierarchy	1.5*	(1.1–2.1)	1.2	(0.9–1.6)
Attention deficit disorder	2.5	(0.8–7.4)	1.8	(0.6–5.6)
Oppositional defiant disorder with hierarchy	2.6*	(1.2–5.7)	2.1	(0.9–5.0)
Conduct disorder	1.9	(0.9–4.1)	1.2	(0.5–3.0)
IV. Eating disorders				
Anorexia nervosa	0.9	(0.3–2.8)	0.7	(0.2–2.0)
Binge eating disorder with hierarchy	1.7*	(1.1–2.5)	1.0	(0.7–1.6)
Bulimia nervosa with hierarchy	3.2*	(2.2–4.8)	1.9*	(1.2–3.1)
V. Substance-use disorders				
Alcohol abuse with hierarchy	1.7*	(1.3–2.3)	1.4*	(1.1–1.9)
Alcohol dependence	1.9*	(1.4–2.7)	1.1	(0.8–1.7)
Drug abuse with hierarchy	1.9*	(1.2–2.8)	1.4	(0.9–2.1)
Drug dependence	2.3*	(1.5–3.4)	1.4	(0.9–2.0)

* Significant at the .05 level, 2-sided test.

^a Lifetime PEs was used as a predictor of mental disorder onset in separate discrete-time survival model controlling for age-cohorts, gender, person-years, country, time-varying education, time-varying marriage and employment status.

^b Lifetime PEs was used as a predictor of mental disorder onset in separate discrete-time survival model including the controls specified above, other temporally primary mental disorders and number of temporally primary mental disorders (2,3,4 5+ disorders). Full details of these models are shown in Supplementary material Table S4.

Table 4

Associations between DSM-IV mental disorders and the subsequent onset of psychotic experiences.

Type of mental disorders	Bivariate models ^a		Multivariate model ^b	
	OR	(95% C.I.)	OR	(95% C.I.)
I. Mood disorders				
Major depressive disorder with hierarchy	2.5 *	(2.1–3.0)	2.2 *	(1.8–2.7)
Bipolar disorder (broad)	2.6 *	(1.9–3.7)	1.9 *	(1.3–2.9)
II. Anxiety disorders				
Panic disorder	2.5 *	(1.8–3.4)	1.6 *	(1.2–2.3)
Generalized anxiety disorder with hierarchy	2.4 *	(1.8–3.1)	1.7 *	(1.2–2.3)
Social phobia	2.2 *	(1.8–2.6)	1.5 *	(1.2–2.0)
Specific phobia	2.6 *	(2.2–2.9)	2.2 *	(1.8–2.7)
Agoraphobia without panic	2.5 *	(1.8–3.6)	1.9 *	(1.3–2.7)
Post-traumatic stress disorder	2.5 *	(1.9–3.2)	1.8 *	(1.3–2.4)
Separation anxiety disorder (Child)	2.1 *	(1.5–3.0)	1.5 *	(1.0–2.1)
Separation anxiety disorder (Adult)	2.8 *	(2.1–3.9)	1.9 *	(1.3–2.8)
III. Impulse-control disorders				
Intermittent explosive disorder with hierarchy	2.4 *	(1.9–3.0)	1.9 *	(1.5–2.5)
Attention deficit disorder	2.7 *	(2.0–3.8)	1.7 *	(1.2–2.4)
Oppositional defiant disorder with hierarchy	3.0 *	(2.1–4.3)	2.0 *	(1.3–3.1)
Conduct disorder	2.5 *	(1.7–3.7)	1.4	(0.9–2.3)
IV. Eating disorders				
Anorexia nervosa	2.9 *	(1.1–8.1)	2.8 *	(1.0–7.8)
Binge eating disorder with hierarchy	2.2 *	(1.6–3.2)	1.8 *	(1.2–2.6)
Bulimia nervosa with hierarchy	2.7 *	(1.8–4.2)	1.8 *	(1.2–3.0)
V. Substance-use disorders				
Alcohol abuse with hierarchy	1.8 *	(1.4–2.5)	1.8 *	(1.3–2.5)
Alcohol dependence	2.4 *	(1.8–3.3)	2.0 *	(1.3–2.9)
Drug abuse with hierarchy	1.5	(1.0–2.3)	1.1	(0.7–1.8)
Drug dependence	2.6 *	(1.7–3.9)	1.3	(0.8–2.3)
Joint effect of all types of disorders, χ^2_{21}, [p-value]			130.4 **	[<.001]
Difference between types of disorders, χ^2_{20}, [p-value]			27.9	[0.111]
VI. Number of disorders				
2 disorders			1.0	(0.7–1.3)
3 disorders			0.5 *	(0.4–0.8)
4 disorders			0.4 *	(0.2–0.8)
5+ disorders			0.2 *	(0.1–0.4)

Type of mental disorders	Bivariate models ^a		Multivariate model ^b	
	OR	(95% C.I)	OR	(95% C.I)
Joint effect of all number of disorders, χ^2_4 , [p-value]			31.1 **	[<.001]

*** Significant at the .05 level, 2-sided test.

^aEach lifetime mental disorder type was used as a predictor of psychotic experiences onset in separate discrete-time survival model controlling for age-cohorts, gender, person-years, country, time-varying education, time-varying marriage and employment status.

^bThe model was estimated with dummy variables for all temporally primary mental disorders and number of temporally primary mental disorders entered simultaneously including the controls specified above.

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