Persistent Childhood and Adolescent Anxiety and Risk for Psychosis: A Longitudinal Birth Cohort Study

Morales-Muñoz, I, Palmer, E.R, Marwaha, S, Mallikarjun, P.K & Upthergrove, R

Institute for Mental Health, School of Psychology, University of Birmingham, Birmingham, UK

Background & Aims

Background

- Psychotic disorders are among the **leading causes of disability**,[1] with an incidence of 31.7 per 100,000 people in England.[2]
- Anxiety & Psychosis – **high rates of anxiety** after onset of psychosis are seen in 42%-74% of patients [3,4] as well as being a **prominent symptom** pre-psychosis, during prodrome, clinical high risk (CHR).
- No established link between **persistent** anxiety and psychosis

Objectives: To establish if…

1. There is a group of children and adolescents that experience persistently raised levels of anxiety.
2. There is an association between persistent anxiety across childhood and psychosis in early adulthood.
3. This association is mediated by peripheral markers of inflammation.

Methods

We used data from the **Avon Longitudinal Study of Parents and Children** (ALSPAC) study. Data were available in 8242 children at age 8 years, 7658 at age 10 years, 6906 at age 13 years, and 3889 at age 24 years.

Measures

- **Anxiety scores** - The Development and Well-Being Assessment (DAWBA) was used to capture child and adolescent anxiety. We created a **composite score** from the generalized anxiety scores and generalized anxieties symptoms score at **ages 8, 10, and 13.**
- **Anxiety classes** - We used **latent class growth analysis** (LCGA) using Mplus to identify differing levels of anxiety symptoms **across childhood and adolescence**.
- **Psychotic episodes** (PE) and **psychotic diagnosis** (PD) were assessed at age 24, derived from the Psychosis-like Symptoms Interview.

Regression Analysis

- We investigated the **prospective associations** between persistent high levels of anxiety, identified by LCGA, and **psychosis outcomes at age 24** using logistic regressions analyses.
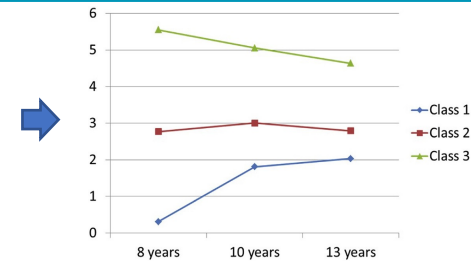
Path Analysis

- We conducted **path analysis** to investigate the mean of **C-reactive protein** (CRP) at ages 9 and 15 years a mediator.

Results

Anxiety classes

- We identified 3 classes of anxiety across childhood and adolescence: persistently low (70%), persistently moderate (20%) and persistently high levels (5%).


Regression analysis

- Individuals with persistent high levels of anxiety were twice as likely to develop PEs (odds ratio 2.02, 95% CI 1.26–3.23, p = .003) and over four times as likely to develop PD at age 24 (odds ratio 4.23, 95% CI 2.27–7.88, p, .001).
- A similar association was seen in generalised anxiety disorder and depression at age 24, but not in other mental health problem such as Hypomania, phobias and substance misuse.
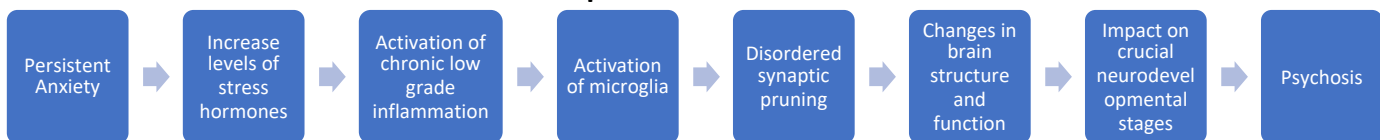
Path Analysis

- Path analysis model fit indices indicated good model fit (X2 = 3.26, p = 0.66, RMSEA= 0, CFI= 1.00).
- The mean of CRP at ages 9 and 15 mediated the associations of persistent anxiety with PEs (bias-corrected estimate 20.001, p = .013) and PD (bias-corrected estimate 0.001, p = .003).
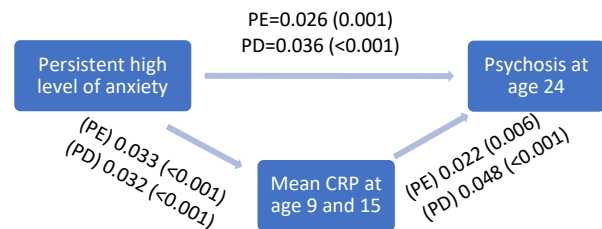
Discussion

- Persistent high levels of anxiety through childhood and adolescence could be a **risk factor for psychosis**.
- Persistent anxiety is potentially related to subsequent psychosis via **activation of stress hormones and inflammation**.
- These results contribute to the potential for **preventive interventions** in psychosis, with the novel target of early anxiety.

Proposed Mechanism

Persistent Anxiety → Increase levels of stress hormones → Activation of chronic low grade inflammation → Activation of microglia → Disordered synaptic pruning → Changes in brain structure and function → Impact on crucial neurodevelopmental stages → Psychosis

References

Full paper reference: Morales-Muñoz I, Palmer ER, Marwaha S, Mallikarjun PK, Upthergrove R. Persistent Childhood and Adolescent Anxiety and Risk for Psychosis: A Longitudinal Birth Cohort Study. Biol Psychiatry. 2021 Dec 13:S0006-3223(21)01836-9. doi: 10.1016/j.biopsych.2021.12.003. Epub ahead of print. PMID: 35151465.

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