

CBT significantly decreased GP appointments at 6 months follow-up compared with PPT with a large effect size ( $\eta^2 = 0.5$ ,  $p < 0.05$ ). A similar trend was seen for total cost ( $\eta^2 = 0.5$ ,  $p < 0.06$ ) with each PPT patient costing £790 more on average than their CBT counterparts during the 6 months after therapy.

**Conclusion.** Whilst CBT appears to be efficacious in the short-term, PPT caused significantly increased healthcare utilisation compared with CBT in the 6 months after therapy. This aligns with similar studies that demonstrate a ‘ sleeper effect ’ in which patients who receive PPT, but not CBT, deteriorate before improving over long-term follow-up.

Additional research is needed to correlate this data with symptoms and capture the long-term benefits of these psychotherapies for MUS.

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### The Effects of Developmental Stress on Dopaminergic Function in Adulthood: A Systematic Review and Meta-Analysis

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**Aims.** Exposure to traumatic experiences during childhood and adolescence is a significant risk factor for the development of psychiatric disorders in adulthood. An estimated 50% of the worldwide incidence of depression and anxiety can be attributed to childhood maltreatment (Li et al., 2016). In addition, approximately one-third of psychotic experiences are attributable to a history of developmental trauma (McGrath et al., 2017). It is thought that long-lasting, trauma-induced adaptive changes in neurobiological function may lead to a predisposition towards pathophysiology (McCrorry and Viding, 2015). However, the precise mechanisms through which developmental trauma exposure alters brain function on cellular and circuit levels remain poorly elucidated.

**Methods.** A systematic literature search and meta-analysis was performed to establish how dopaminergic functioning in adulthood is affected by developmental stress in rodents. Three databases, Medline®, Embase®, and PsycINFO®, were systematically searched initially on 2nd December 2023. Terms for three superordinate concepts (‘ childhood ’ terms, ‘ trauma ’ terms, and ‘ dopamine ’ terms) were combined. Cohen’s *d* statistic was used for effect sizes. This protocol is pre-registered on PROSPERO® (ID: CRD42018106382).

**Results.** A total of 104 studies met our inclusion criteria. Meta-analysis indicated that developmental stress exposure leads to complex and long-lasting effects in basal and post-amphetamine extracellular dopamine concentrations in the medial prefrontal cortex, amygdala, and nucleus accumbens. In addition, there is a significant downregulation of D1 receptors and upregulation of D2 receptors in prefrontal and striatal regions involved in threat and reward processing. Effect sizes ranged from 0.36 to 1.55.

**Conclusion.** These findings strongly suggest that dopaminergic dysfunction is a mechanistic link between developmental trauma and vulnerability towards mental illness in adulthood.

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### White Matter Microstructure Abnormalities in Individuals at High Risk for Psychosis: A Meta-Analysis of Fractional Anisotropic Changes Associated With Transition to Psychosis

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**Aims.** Recent studies have focussed on detecting white matter abnormalities in subjects who transition to psychosis (UHR-T). Research suggests that fractional anisotropy (FA), may be decreased in UHR-T. However, global and regional findings have been inconsistent. By objectively combining data in a meta-analysis, we have investigated white matter alterations associated with transition, by comparing FA in UHR-T with subjects that do not transition (UHR-NT) and healthy volunteers.

**Methods.** The meta-analysis was registered on PROSPERO (ID: CRD42021265348) and followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses PRISMA guidance. A systematic database search of PUBMED and EMBASE identified reports, which were screened by 2 independent researchers (CN and DD) for inclusion, from inception to 20 July 2021. Discrepancies were decided on consensus with a third researcher (KM). Reference lists of eligible studies were also screened. Authors of screened reports were contacted to provide parametric maps. Coordinate-based meta-analysis was conducted using Seed-based *d*-Mapping software to combine parametric map and coordinate data from reports, using a random-effects model. Quality and risk of bias analysis were conducted using the Newcastle-Ottawa Scale. Heterogeneity and sensitivity analyses were also conducted.

**Results.** The search strategy identified 889 potential studies, from which 6 met eligibility criteria. A total of 71 UHR-T, 142 UHR-NT and 148 healthy volunteers were included. Weighted-mean decreases in FA were observed in UHR-T compared with: UHR-NT ( $d = -0.99$ ;  $p < 0.0001$ ; 95% CI  $-1.43$  to  $-0.55$ ); and healthy volunteers ( $d = -0.91$ ;  $p = 0.04$ ; 95% CI  $-1.78$  to  $-0.05$ ). The level of heterogeneity for the former was not significant. For UHR-T, regional FA decreases were observed in areas including the left genu of the corpus callosum ( $Z$ -score =  $-1.76$ , 204 voxels,  $p < 0.0001$ ) compared with UHR-NT, while FA increases were most observed in the white matter region adjacent to the left postcentral gyrus ( $Z$ -score = 1.64, voxels = 16,  $p < 0.0001$ ). These findings persisted despite sensitivity analyses.

**Conclusion.** The findings suggest that white matter alterations, specifically in left frontotemporal tracts, are associated with an increased risk of transition to psychosis. The neurobiological implications of these findings, and their contribution to UHR-T prediction efforts, are explored, as are avenues for further research.

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