Neurological Predictors of Symptom Trajectories During and Following Treatment of Adolescents With a Primary Diagnosis of Major Depression

Sian Davies<sup>1</sup>, Sharon Neufeld<sup>1</sup>, Eleonore van Sprang<sup>2</sup>, Lizanne Schweren<sup>3</sup>, Rogier Keivit<sup>1</sup>, Peter Fonagy<sup>4</sup>, Bernadka Dubicka<sup>5</sup>, Raphael Kelvin<sup>6</sup>, Nicolas Midgley<sup>4</sup>, Shirley Reynolds<sup>7</sup>, Mary Target<sup>4</sup>, Paul Wilkinson<sup>8</sup>, Anne-Laura van Harmelen<sup>1</sup>, John Suckling<sup>8</sup>, Ian Goodyer<sup>8</sup>

## Keywords

Adolescent depression, cortical thickness, cortical surface area, treatment response, growth mixture modelling

<sup>&</sup>lt;sup>1</sup> University of Cambridge

<sup>&</sup>lt;sup>2</sup> VU University Medical Centre, Amsterdam

<sup>&</sup>lt;sup>3</sup> University Medical Centre, Groningen

<sup>&</sup>lt;sup>4</sup> University College London

<sup>&</sup>lt;sup>5</sup> University of Manchester

<sup>&</sup>lt;sup>6</sup> University of Cambridge and the Cambridge and Peterborough Foundation Trust

<sup>&</sup>lt;sup>7</sup> University of Reading

<sup>&</sup>lt;sup>8</sup> University of Cambridge; Cambridgeshire and Peterborough National Health Service Foundation Trust

## **Background**

Structural abnormalities in the anterior cingulate, orbitofrontal, prefrontal and insula regions are associated with treatment non-response. These observations are not consistent in depressed adolescents. Definitions of treatment non-response are non-standardised and arbitrary, contributing to variations across studies. We aimed to classify depressed adolescents into different trajectories of symptomatic change using a data-driven approach; and conduct a preliminary investigation of structural brain predictors of class membership.

#### **Methods**

465 depressed adolescents received psychological therapies in the IMPACT trial. Structural magnetic resonance imaging was conducted on 109 patients. Growth mixture modelling (GMM) was used to plot the trajectories of depressive symptoms measured over 86 weeks from randomisation. We used FreeSurfer to extract cortical thickness (CT) and surface area (SA) measures of 4 regions-of-interest (ROI). Logistic regressions were used to investigate their ability to predict class membership.

#### **Results**

Piecewise GMM of the total cohort revealed two classes. Continued-improvers (84% of sample) reported a persisting decrease in their depressive symptoms. Halted-improvers (16%) showed improvement up to 18 weeks, but no further improvement thereafter. Neither CT nor SA of any ROI significantly predicted class membership.

## **Conclusions**

Capitalising on repeated symptom assessments with longitudinal data-driven modelling may improve the precision of revealing patient groups with differential responses to treatment.

Differences in response trajectory for adolescent depression may not be apparent until after 18 weeks of treatment. CT/SA however, was not associated with subsequent symptom trajectory. This may be due to developmental issues or small effect sizes. A greater sample size is needed in future work.

# **Supported By**

National Institute for Health Research (NIHR) Health Technology Assessment (HTA) programme (project number 06/05/01).

SED was funded by a doctoral studentship awarded by the Neuroscience in Psychiatry (NSPN.Org) Consortium itself was funded by a strategic award from the Wellcome Trust (095844/Z/11/Z) awarded to IG and PF.