Interhemispheric Connectivity in Schizophrenia and Bipolar I disorder: a probabilistic tractography study

C. A. Chaddock[1], G. J. Barker[2], R. M. Murray[1], and C. McDonald[3]

[1]Department of Psychiatry, Institute of Psychiatry, London, United Kingdom, [2]Centre for Neuroimaging Sciences, Institute of Psychiatry, London, United Kingdom, [3]Department of Psychiatry, National University of Ireland, Galway, Ireland

Aims: To assess interhemispheric connectivity in schizophrenia and bipolar disorder using probabilistic tractography.

Background: A single cortical area has not been identified that can explain the wide range in symptoms identified in psychotic disorders (Honea et al, 2005). Therefore a hodological approach, which investigates the pathways that link major cortical and subcortical structures may prove more beneficial. Connectivity abnormalities, as measured by diffusion tensor imaging (DTI) or effective connectivity from functional MRI, have been identified in both schizophrenia and bipolar disorder; and could propose a link explaining the overlap in epidemiological (Cardno et al, 2002) and genetic studies (Craddock et al, 2005). Here, we use diffusion tensor imaging (DTI) to assess structural connectivity abnormalities across diagnostic boundaries in the psychosis spectrum, using a probabilistic tractography algorithm to reconstruct the major interhemispheric tracts.

Methods: DTI images were obtained (Jones et al, 1999) on 21 patients with schizophrenia, 20 patients with psychotic bipolar disorder and 38 controls. The diffusion tensor was estimated for each voxel (Basser et al, 1994) and Fractional Anisotropy (FA) calculated. Data were preprocessed for tractography using Camino (http://www.cs.ucl.ac.uk/research/medic/camino/). Diffusion within each voxel was classified as (i) isotropic, (ii) anisotropic with a single principal diffusion direction, or (iii) anisotropic with more than one direction of diffusion (Alexander et al, 2002). A single tensor model of diffusion was used for (i) and (ii), whilst a two tensor model was used for (iii) (Parker and Alexander, 2003). A probabilistic tractography algorithm (PICo) was used to estimate an index of connectivity from a (3x3 voxel) seed region placed in the genu or splenium of the corpus callosum.
Probability density functions (PDF) were calculated for each subject, and stream-line based tracking was repeated 10,000 times in a Monte Carlo fashion, to produce tract maps that indicated the probability of connection of every voxel in the brain to the seed region (Parker and Alexander, 2005). The tract maps were thresholded (at 0.001, 0.002, 0.006, 0.013 and 0.3) (Price et al, 2007) allowing varying degrees of certainty of tract reconstruction and data transferred to SPSS v13. Multivariate regression was used to assess group differences across all thresholds, with age, and gender entered as covariates.

Results: Groups did not differ in mean age (Scz = 40.0 yr; BP = 43.4; Controls 43.5; $F(2,81)=0.872$, $p=0.422$) but did differ in Gender ($\chi^2=9.475$, $p=0.009$)., with the schizophrenic sample containing more males.

There was no group difference in the volume of the reconstructed tracts in the genu ($F(2,74)$, $p=0.498$, $p=0.610$) or the splenium ($F(2,74)=1.891$, $p=0.158$).

Figure 1. displays the mean FA value (adjusted marginal value) extracted over tracts incorporating the genu and splenium of the corpus callosum, plotted against a varying threshold of connection probability. There was no main effect of group in mean FA where all thresholds and both regions of the corpus callosum were entered in to the analysis ($F(2,74)=1.314$, $p=0.275$). However, visual inspection shows that despite not reaching statistical significance in the overall model, there are lower FA values in bipolar disorder patients over all thresholds within both the genu and splenium.

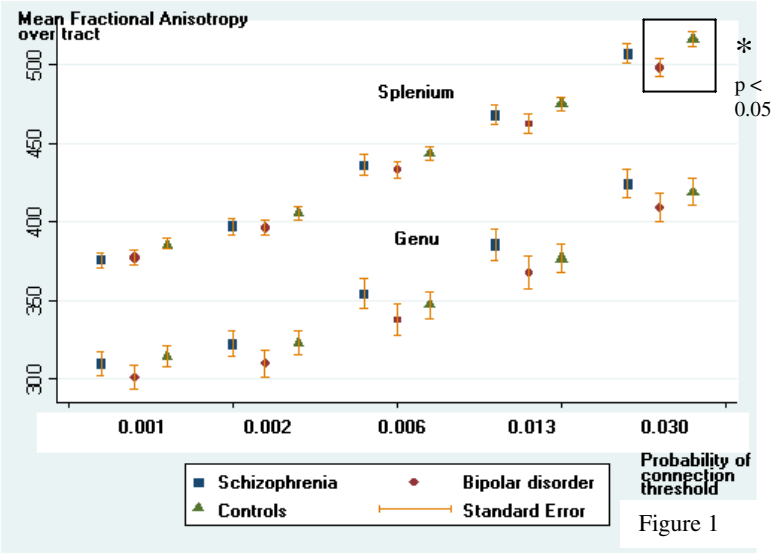

Figure 1

When group differences were separately assessed for bipolar disorder and schizophrenia at the level of individual thresholds, bipolar disorder patients were seen to show significantly lower FA (whilst controlling for multiple comparisons) when compared to controls at the highest threshold (0.03) in the splenium ($F(1,58)=4.826$, $p=0.032$). There were no significant FA differences in schizophrenics when compared to controls over any of the thresholds. A main effect of age was identified in the genu at the two highest thresholds in schizophrenics and controls which was not evident in bipolar disorder patients, whose FA did not decline as expected with age.

Discussion: This study provides preliminary evidence of a reduction in FA in bipolar disorder, which may be more likely to be based in the splenium than the genu. This is in support of previous voxel based analyses of a smaller subset of subjects (Chaddock et al, 2006). Non significant reductions of FA were evident at all thresholds in bipolar disorder in both the genu and splenium. The expected reductions of FA were not evident in schizophrenia, not replicating previous findings in schizophrenia. This study adds to the growing literature indicating changes to the white matter in bipolar disorder.

References:

Honea et al (2005), Am J Psychiatry, 162, 2233-2245
Cardno et al (2002), Am J Psychiatry, 159, 539-545
Craddock et al (2005) J Med Genet, 42, 193-204
Basser et al (1994) J Magn Reson B, 103, 247-254
Alexander (2002): Magn. Reson. Med. 48, 331-340
Parker and Alexander (2003), Inf. Process. Med. Imag. 18, 684-695
Parker and Alexander (2005), Philos. Trans. R. Soc. Lond, B, 360, 893-902
Price et al (2007) Neuroimage, 35, 458-466
Chaddock et al (2006) ISMRM Berlin, Poster presentation , Abstract ~ 886