# Parcellating disconnectivity: understanding the microstructural abnormalities associated with neurocognitive deficits in traumatic brain injury

**V. F. Newcombe[1,2], J. G. Outtrim[1], D. A. Chatfield[1], A. Manktelow[1], P. J. Hutchinson[3], J. P. Coles[1,2], G. B. Williams[2], B. Sahakian[4], and D. K. Menon[1,2]**

[1]Division of Anaesthesia, University of Cambridge, Cambridge, Cambridgeshire, United Kingdom, [2]Wolfson Brain Imaging Centre, University of Cambridge, Cambridge, Cambridgeshire, United Kingdom, [3]Academic Department of Neurosurgery, University of Cambridge, Cambridge, United Kingdom, [4]Department of Psychiatry, University of Cambridge, Cambridge, United Kingdom

**Introduction:** Impulsivity and decision making are common cognitive processes impaired following traumatic brain injury (TBI). This neurocognitive dysfunction correlates imperfectly with lesion distribution, and may result from subtle insults to integrated neural systems, rather than overt lesions at focal injury sites. We hypothesized that the burden of microstructural injury, as defined by diffusion tensor imaging (DTI), would correlate with neurocognitive performance in a decision making task (Cambridge Gambling Task; CGT), a task thought to be subserved by dopaminergic networks.[1] The CGT task has been designed to allow decision-making and risk-taking behavior to be assessed outside a learning context, therefore, allowing the neurocognitive deficits in decision making to assessed in isolation (see www.camcog.com for details).

**Methods:** 42 patients underwent MR imaging at a minimum of six months post injury using a 3 Tesla Siemens Magnetom Total Imaging Matrix (TIM) Trio system. Comprehensive neuropsychological testing including the CGT was performed in all patients on the day of imaging. Informed consent was obtained in all cases. Ethical approval was obtained from the Local Research Ethics Committee. 18 age matched controls underwent the same neuropsychological testing and 38 age matched controls underwent an identical imaging protocol which included a 3D T1 weighted structural sequence (MPRAGE), and diffusion tensor imaging. The DTI parameters were as follows; 12 non-collinear directions, 5 b values ranging from 329 to 1590 s/mm$^2$, 4 b=0 images, Field of view, 100 x 100 matrix size, 63 axial slices, 2mm slice thickness, TR = 6000ms, TE = 100ms, diffusion sensitizing duration 23.5ms (δ), with 60 ms separation (Δ) (leading edge to leading edge). ADC maps were created using FDT in FSL.[2] The diffusion weighted data were normalized using a two step approach. First, all patient and control MPRAGE images were coregistered to the MNI152 template using the vtkCISG normalized mutual information algorithm.[3] The b=0 image was subsequently coregistered to the subject's own MPRAGE image. The transformation matrix normalizing the MPRAGE image was then applied to the b=0 image. Regions of interest (ROIs) were manually drawn using Analyze 7.0[4] in MNI125 space using Colin27[5] as a high resolution, high signal-to-noise template. The CGT provides a variety of behavioral measures, each of which corresponds to different aspects of the impulsive phenotype: impulsivity index, risk adjustment, rational choice, amount bet and deliberation time; each of which are known to map to specific brain areas.[1,6,7] ROIs that reflected neural processing associated with each of these were chosen based on previous PET[1,6] and fMRI[7] studies in healthy populations. The ROIs included the medial prefrontal cortex, ventrolateral prefrontal cortex, dorsolateral prefrontal cortex, superior frontal gyrus, orbitofrontal gyrus, frontal white matter, hippocampus, thalamus, striatum (dorsal and ventral) and the caudate. All coregistered images were visually inspected to ensure that ROIs corresponded to the regions specified. Mean ADC for the different ROIs were calculated and values correlated with the CGT results.

**Results:** Patients who had sustained TBI had average group metrics similar to control subjects for risk adjustment (p=0.63), probability judgment (p=0.48) and in the amount bet (p=0.24), indicating a similar level of risk adjustment to controls. TBI patients showed a preference for consistently early bets indicated a higher level of impulsiveness (p=0.01). However, within the TBI group, there were wide variations in metrics derived from the CGT, reflecting varying levels of impulsivity in the cohort. Scores on various task components of the CGT correlated significantly with ADC in ROIs that included brain regions known to subserve a given cognitive domain; such correlations were absent in areas not known to be involved in the target cognitive process underlying the behavioural metric. This double dissociation was consistent across all elements of the CGT (Figure 1).

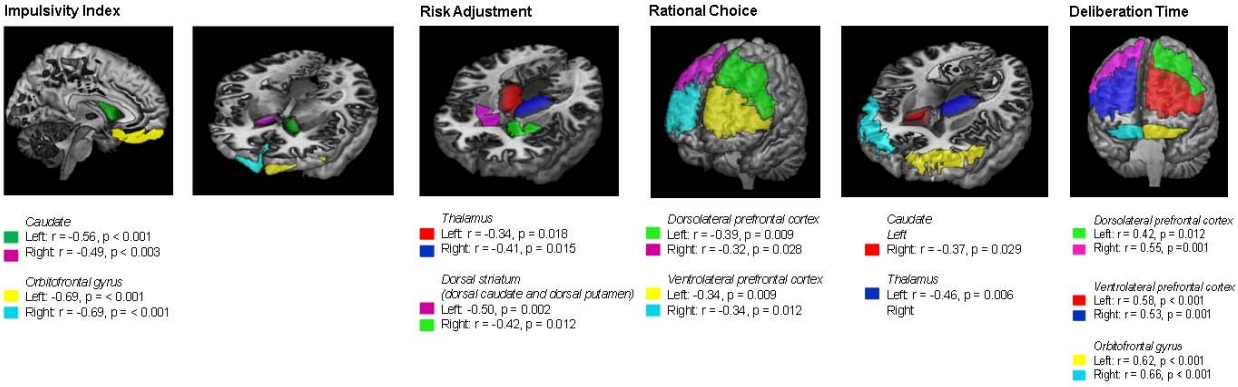


**Figure 1:** Correlations found with various aspects of the Cambridge Gamble Task. Colored regions show regions of interest with areas of corelation with ADC. There was no correlation with amount bet.

**Discussion:** Despite normal structural MRI appearances in some subjects, cognitive performance on neuropsychological testing correlated significantly with diffusivity parameters in cognate brain regions, identified on the basis of prior knowledge of the brain regions involved in these tasks. Our data add to the evidence that loss of microstructural integrity, as detected by DTI, is an important determinant of function following TBI, and confirm the involvement of key neurochemical networks in these complex neurocognitive tasks. DTI may be a useful research and clinical tool in this setting.

**References:**

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