

SHORT REPORT

A structural MRI study of motor conversion disorder: evidence of reduction in thalamic volume

T R Nicholson,¹ S Aybek,¹ M J Kempton,² E M Daly,³ D G Murphy,³ A S David,¹ R A Kanaan⁴¹Section of Cognitive Neuropsychiatry, Institute of Psychiatry, King's College London, London, UK²Department of Neuroimaging, Institute of Psychiatry, King's College London, London, UK³Department of Forensic and Neurodevelopmental Science, Institute of Psychiatry, King's College London, London, UK⁴Department of Psychiatry, University of Melbourne, Austin Hospital, Melbourne, Australia**Correspondence to**Dr Tim Nicholson,
Section Cognitive
Neuropsychiatry, PO Box 68,
Institute of Psychiatry, Denmark
Hill, London SE5 8AF, UK;
timothy.nicholson@kcl.ac.ukTRN and SA contributed
equally to this work.

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ABSTRACT**Objective** To investigate potential abnormalities in subcortical brain structures in conversion disorder (CD) compared with controls using a region of interest (ROI) approach.**Methods** Fourteen patients with motor CD were compared with 31 healthy controls using high-resolution MRI scans with an ROI approach focusing on the basal ganglia, thalamus and amygdala. Brain volumes were measured using Freesurfer, a validated segmentation algorithm.**Results** Significantly smaller left thalamic volumes were found in patients compared with controls when corrected for intracranial volume. These reductions did not vary with handedness, laterality, duration or severity of symptoms.**Conclusions** These differences may reflect a primary disease process in this area or be secondary effects of the disorder, for example, resulting from limb disuse. Larger, longitudinal structural imaging studies will be required to confirm the findings and explore whether they are primary or secondary to CD.**METHODS**

Fifteen patients with Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV diagnoses (by consultant neuropsychiatrists) of motor CD and 31 healthy controls were recruited. Subjects with major mental health disorder (any DSM axis 1 disorder in controls; psychosis, bipolar disorder or major depression in patients) or neurological illness were excluded. Groups were matched for gender (patients 67%, controls 61% women), age (patients mean 37 years, controls mean 32 years), handedness (patients 92%, controls 96% right-handed) and IQ (patients mean 108, controls mean 112). The patients all had motor weakness as their primary (most disabling) symptom at the time of scanning and were in the first episode of their disorder, that is, had not recovered from their initial symptoms (although motor symptoms did often progress during these episodes). Twelve patients initially had predominantly asymmetrical symptoms (eight had both arm and leg weakness (hemiparesis), three had leg only and one arm only) and three patients had predominantly symmetrical symptoms affecting legs only (paraparesis). All of the patients with initial asymmetrical leg weakness later developed symmetrical paraparesis and the patient with asymmetrical arm weakness later developed a mild tetraparesis. The mean duration of symptoms at the time of scanning was just over a year (14 months) with a range of 3 months to 3 years. At the time of scanning, all patients were still symptomatic: for four patients, symptoms were minor (little impairment of function); for seven, they were moderate (significant impairment of function); and for four, they were major (major impairment of function and little or no improvement from their peak disability). The median impairment was moderate. Subjects gave informed written consent and the study was approved by the local Research Ethics Committee (ref 07/H0805/33).

MRIs were acquired on all subjects using a General Electric three Tesla Signa HDX scanner, using a T1-weighted, steady-state, gradient-spoiled, gradient recalled echo acquisition. Images were acquired in the coronal plane with TE=2.8 ms, TR=7.1 ms, TI=450 ms, flip angle 20°, bandwidth 31.25 KHz and a 256×256×200 image matrix. The field of view and slice thickness were 280 mm and 1.4 mm respectively, yielding a final image resolution of 1.1×1.1×1.4 mm.

A ROI approach was taken and eight subcortical anatomical structures were chosen on the basis of previous findings as detailed above. Our selected

INTRODUCTION

Conversion disorder (CD) describes the presence of neurological symptoms that are not due to neurological disease and are thought to be psychological in origin. It is assumed that patients have normal brain anatomy and the disorder is one of 'function'; structural brain abnormalities of potential aetiological relevance would generally preclude the diagnosis. However, it is possible there are subtle neuroanatomical abnormalities that are only discernable at the group level rather than in individual patients. There has, to date, been one study of subcortical brain structures in motor CD, reporting reduced thalamic, caudate and lentiform nuclei volume in 12 patients with unilateral limb weakness compared with 12 controls using manual anatomical labelling methods.¹ We aimed to confirm these volume differences using a region-of-interest (ROI) approach on the thalamus and basal ganglia of high-resolution MRI scans of patients with motor CD and healthy controls. We also investigated the amygdala as an additional ROI, given that multiple functional imaging studies suggest a role for this structure in the aetiology of CD including suggestions of links between its role in emotion processing and the motor system.²⁻⁴

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regions were, bilaterally, the caudate and lentiform nuclei and the thalamus and the amygdala. FreeSurfer software V5.00 (<http://www.surfer.nmr.mgh.harvard.edu/fswiki>) was used to identify and measure subcortical structures. This is an automated procedure validated against non-automated and other automated methods.^{5 6} Unblinded visual inspection was conducted to exclude obvious segmentation errors; this occurred in only one subject (a patient) who was excluded, leading to a final total of 14 patients for analysis. An analysis of covariance design was used to covary for intracranial volume with handedness entered as a fixed factor. Correlations between clinical features and brain volumes were explored in patients.

RESULTS

There were significant reductions in thalamic volume bilaterally in patients compared with controls (left thalamus $t_{(44)}=3.80$, $p=0.001$, right thalamus $t_{(44)}=3.43$, $p=0.002$). Intracranial volume was also significantly reduced in patients, however ($t_{(44)}=2.70$, $p=0.012$), and when this was entered as a covariate, the thalamic reductions remained significant for the left thalamus ($F_{(1,43)}=5.44$, $p=0.024$) and was borderline significant for the right thalamus ($F_{(1,43)}=4.01$, $p=0.052$). After correction for intracranial volume, there was a significant ($F_{(1,43)}=4.14$, $p=0.048$) reduction in the volume of the left, but not the right, lentiform nucleus. There were no other ROI differences. Details of these comparisons are given in table 1. Covarying for handedness did not significantly alter these results. Within patients, there were no significant correlations between thalamic volumes and laterality, duration or severity of symptoms.

DISCUSSION

The finding of a smaller volume of the thalamus in CD compared with controls could either be evidence of a primary disease process in this area or could represent a secondary effect of the disorder. Support for a primary process comes from a

functional imaging study that found reduced activation of the thalamus (and other basal ganglia regions) in CD patients when in a symptomatic state compared with after recovery of function.⁷ This would be compatible with the thalamus' known function in relaying and integrating motor output and the proposed role of striathalamocortical premotor loops in intentional movement generation⁸ and subjective sensations of effort and volition.⁹ A primary process would have significant implications for the potential aetiology and conceptualisation of CD and challenge the easy distinction between functional and structural as commonly understood in this condition.¹⁰

However, the differences are also explicable by the secondary effects of chronic limb immobility as there is some evidence of similar thalamic volume losses after limb amputation (although the authors of that study focus on deafferentation rather than a lack of motor activity as the possible mechanism influencing neuronal plasticity and therefore changes in thalamic volume).¹¹ If the differences were secondary, this would be a strong indicator of the severity of motor CD in terms of the level of immobility. This would counter a widely held belief that CD patients are often significantly less symptomatic when not in the presence of others, especially assessing or treating clinicians. That belief finds support from recent evidence from CD with tremor, where patient diary records of symptoms were significantly higher than those recorded by 24 h monitoring (actigraphy) when compared with 'organic' tremor patients who also overestimate symptom levels but by less than half as much.¹² Therefore, at least for motor CD patients, our study could indicate that the level of dysfunction was sufficient to result in the same order of plastic change to the subcortical motor system as seen in amputation. However, the lack of correlation between thalamic volume loss and the clinical variables of symptom duration and severity in our study does not support the differences being secondary to immobility (though as we only had 13% power to detect the strongest correlation ($r=0.22$), this could be a type 2 error).

There have been two other volumetric studies of differences in CD, both focussed on the cortical motor system. One found evidence for increased thickness of the premotor cortex,¹³ another found decreased thickness of the motor cortex.¹⁴ While we note the consistency of these with the premotor activation and motor deactivation of our functional MRI study,² the primary or secondary nature of these differences is equally unclear.

Larger longitudinal studies could address this, ideally involving rescanning postrecovery, along with detailed correlations of volume changes with symptom levels and other potential confounders, such as pain, depression and anxiety, which have been associated with structural brain changes. Functional imaging at the same time periods could also help disentangle whether such changes were secondary to the disorder or potentially of more aetiological relevance.

Contributors TRN conceived the study, acquired the data, performed the ROI analysis and wrote the manuscript. SA, EMD and DGM conceived the study, acquired the data and reviewed the manuscript. MJK supervised the FreeSurfer analysis and reviewed the manuscript. ASD and RAK conceived the study and reviewed the manuscript.

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Ethics approval Local Research Ethics Committee (ref 07/H0805/33).

Table 1 Volumes of regions of interest (ROI) for patients and controls

ROI	Subject	Mean vol (mm ³)	SD	t test (p value)	ANCOVA covarying for ICV (p value)
Left thalamus	Control	8370	971	0.001**	0.024*
	Patient	7180	1040		
Right thalamus	Control	7900	817	0.002**	0.052
	Patient	6970	893		
Left lentiform nucleus	Control	7390	958	0.26	0.048*
	Patient	7060	899		
Right lentiform nucleus	Control	6830	848	0.08	0.39
	Patient	6340	859		
Left caudate nucleus	Control	3560	578	0.19	0.41
	Patient	3350	456		
Right caudate nucleus	Control	3370	605	0.53	0.09
	Patient	3260	479		
Left amygdala	Control	1640	236	0.20	0.67
	Patient	1540	239		
Right amygdala	Control	1710	223	0.10	0.76
	Patient	1610	200		
Intracranial volume (ICV)	Control	1 610 000	187 000	0.01*	N/A
	Patient	1 440 000	210 000		

* $p<0.05$, ** $p<0.01$.
ANCOVA, analysis of covariance.

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