

## Structural abnormalities in cluster-headache, a VBM study

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### Introduction

Cluster headache (CH) is one of the most severe pain syndromes in humans and is characterised by frequent attacks of unilateral pain. CH was originally thought of as of vascular origin: marked dilatation of the ophthalmic artery during attacks have been reported (trigeminal nerve involvement).<sup>1</sup> Inflammatory changes of the cavernous sinus and, more recently, activation of the trigeminovascular system are suggested to explain the clinical picture<sup>2,3</sup>. Recent quantitative neuroimaging studies reported co-localization of anatomical and functional changes in CH individuals (increased hypothalamic grey matter volume corresponding with increased regional cerebral blood flow (rCBF) during CH attacks).<sup>4</sup> Although these results suggested a difference in CH neurobiology, they have not yet been replicated. The pathophysiological background of CH remains unclear. Furthermore, it is unknown whether brain changes are related to the side of the headaches.

The aim of the current study was to replicate prior findings, hence, identify whether individuals with CH show (i) anatomical differences compared to a control population and (ii) if these were significantly different in relation to the side of headache (pain-) focus.

### Methods

49 individuals with episodic- and chronic-CH (9 female) and 25 control subjects (14 female) aged between 18 and 65 years, were investigated using Voxel Based Morphometry (VBM, SPM99) based on T1 weighted 3D FFE images (gradient echo, axial orientation; 160 slices; slice-thickness, 1 mm; matrix 256 x 256, TE:3.3/TR 7ms, FOV: 220mm). All CH cases fulfilled International Headache Society criteria, and were identified by self-assessment as either having a right or left sided pain-focus during CH attacks. CH cases were examined outside attacks.

### Results

- (i) Individuals with episodic and chronic CH have significantly ( $p < 0.001$ ) decreased grey matter volume in the right putamen, and the superior temporal gyrus (STG), bilaterally (figure 1) and increased white matter volume in the uncinate fasciculus, bilaterally and the right optical radius (RO) (figure 2), compared to control subjects.
- (ii) Individuals with left sided headache ( $n=23$ ) showed significantly ( $p < 0.001$ ) decreased grey matter volume in the right globus pallidus and putamen and the pre- and postcentral gyri, bilaterally, and increased white matter volume in the left occipitofrontal fasciculus, the cingulum, the inferior longitudinal and the uncinate fasciculus, bilaterally.
- (iii) In contrast, individuals with right sided headache ( $n=26$ ) showed significantly ( $p < 0.001$ ) decreased grey matter volume in the left superior temporal gyrus, and increased white matter in the left optical radius (medial occipital gyrus), and superior frontal gyrus and the right medial and inferior frontal gyrus, compared to control subjects.

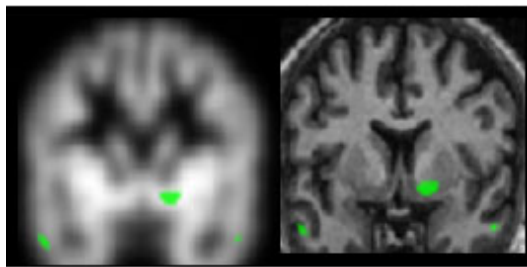


Figure 1: **decreased grey matter volume**  
(grey matter segment and anatomical image: right putamen and STG, bilaterally)

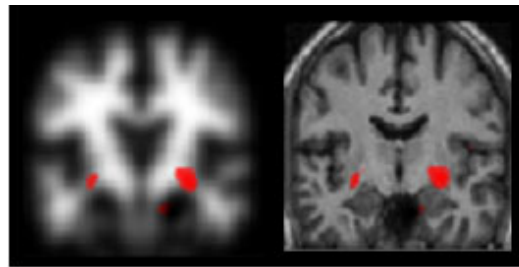


Figure 2: **increased white matter volume**  
(white matter segment and anatomical image: uncinate fasciculus, bilaterally)

### Conclusion

Structural brain abnormalities observed in individuals with CH, compared to control subjects are correlated with the perceived side of headache (pain-) focus during attacks. Individuals with left and right sided headache focus show structural differences in both grey and white matter volume. These morphological differences in CH may be the underlying cause for, or result of attacks. Further research is necessary to assess a shared pathophysiological background of CH attacks and anatomical abnormalities.

### References

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3. Sjaastad et al., 1990, Headache:30, 350-351.
4. May et al., 1999, Nature Medicine: 5, 836-838.