

## Altered neural processing during emotional faces in remitted Cushing's disease

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### Introduction

Patients with long-term remission of Cushing's disease (CD) demonstrate residual psychological complaints. At present, it is not known how previous exposure to hypercortisolism affects psychological functioning in the long-term. Previous Magnetic Resonance Imaging (MRI) studies demonstrated abnormalities of brain structure<sup>1,2</sup> and resting-state connectivity in patients with long-term remission of CD<sup>3</sup>, but no data are available on functional alterations in the brain during the performance of emotional or cognitive tasks in patients with long-term remission of CD.

### Objective

To examine brain activation during emotion processing in patients with long-term remission of CD.

### Methods

**Study design:** A cross-sectional, case-control study.

**Patients:** 21 CD patients in long-term remission (mean age 45±8 yr, 17 females) and 21 healthy controls matched for age, gender and education. Remission was achieved by transsphenoidal surgery (100%) and in some cases by additional radiotherapy (24%) and/or bilateral adrenalectomy (5%). The mean duration of remission was 10.8±7.9 years.

**Magnetic Resonance Imaging:** We examined activation of the amygdala and the medial prefrontal cortex (mPFC) using 3T MRI, during the processing of emotional faces (angry, fearful, happy, neutral, sad) versus scrambled faces.

**Validated questionnaires:** Questionnaires were used to assess depressive symptoms (MADRS, IDS), anxiety (BAI, FQ), apathy (AS), irritability (IS) and cognitive failure (CFQ). Clinical severity was assessed using the Cushing's syndrome Severity Index (CSI).

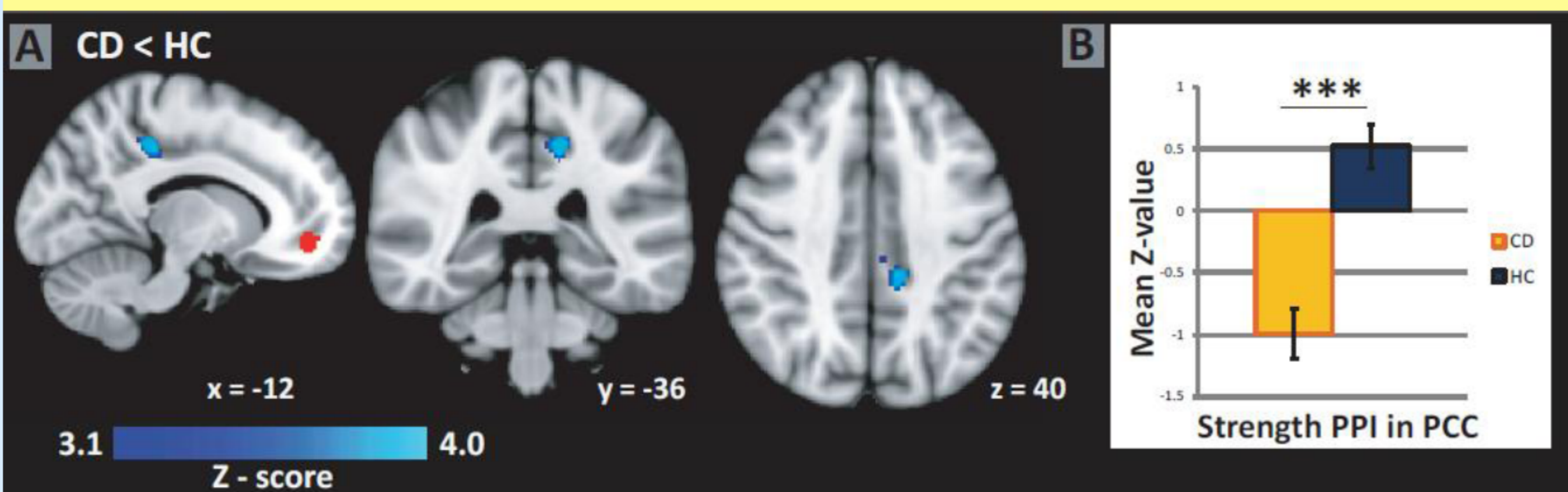


### Conclusions

Patients with a history of CD in present remission show alterations in brain function and task-related functional coupling in patients with long-term remission of CD relative to matched healthy controls. These alterations may, together with abnormalities in brain structure, be related to the persisting psychological morbidity in patients with CD after long-term remission.

#### Psychophysiological interaction analysis ↓

CD-patients showed a decreased positive functional coupling related to the task (emotional faces > scrambled faces) between the vmPFC cluster and the posterior cingulate cortex relative to controls ( $P = 0.049$ ).

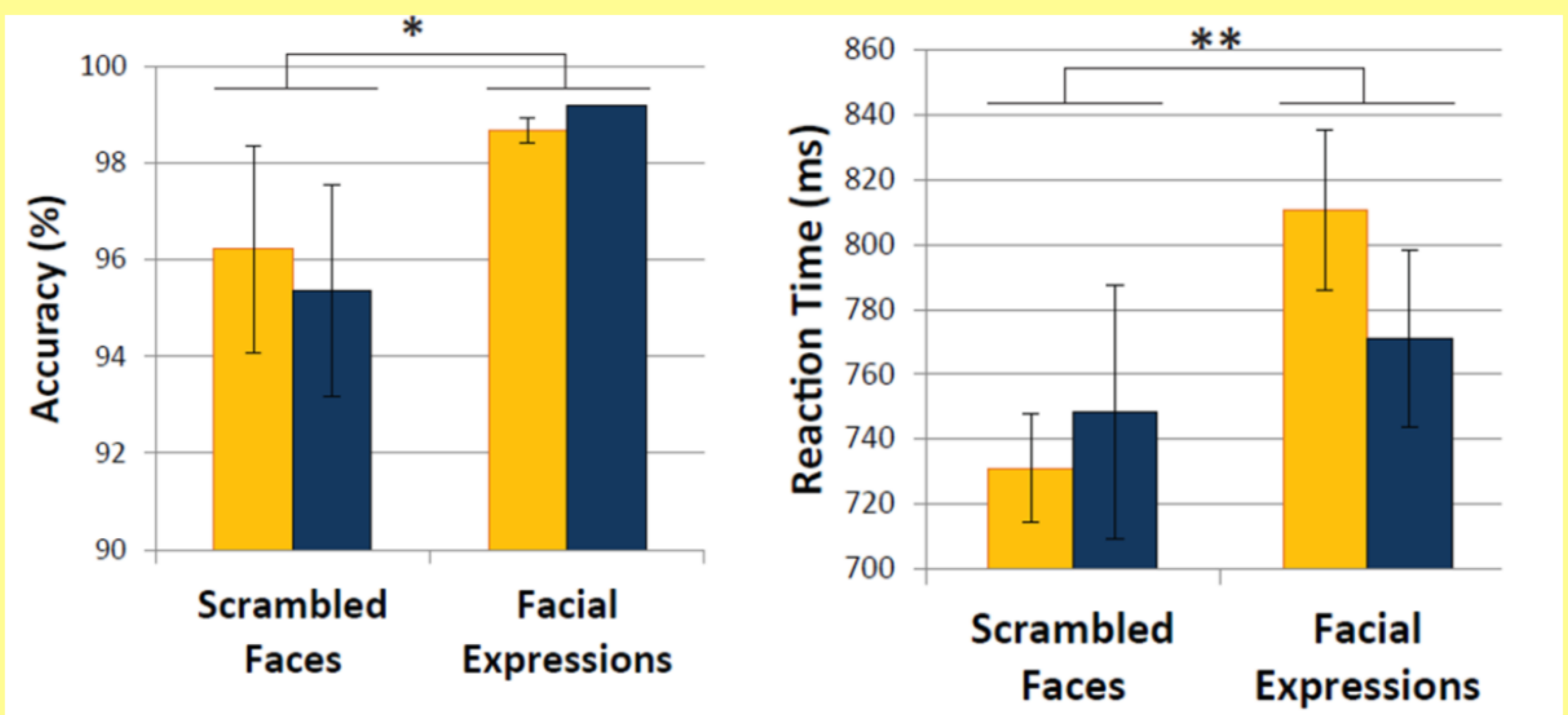


### Results

#### Behavioral data

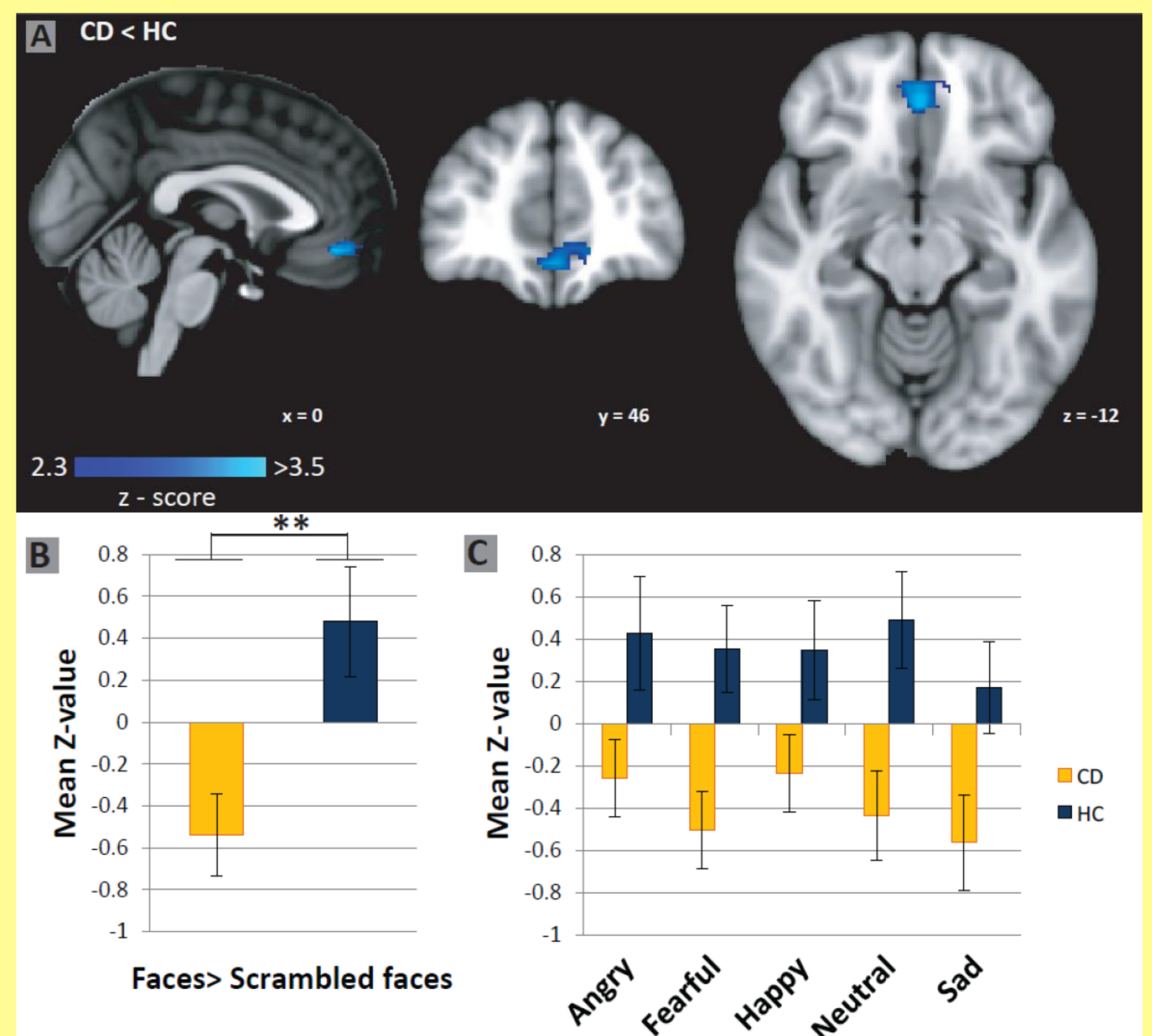
A significant effect of condition on both accuracy ( $P = 0.05$ ) and reaction time ( $P = 0.003$ ) was revealed. However, there was no effect of group on performance, nor an interaction between group and condition.

Furthermore, there were no differences between the separate emotions.



#### Psychopathology and cognitive failure

Comparisons on the psychometric data between patients with long-term remission of CD and the matched healthy controls showed significant differences on the MADRS ( $P < .001$ ). No further significant differences were found between patients and controls.



#### Regions of interest analyses ↑

Group-comparisons showed decreased activation of the ventromedial PFC (vmPFC) in CD-patients relative to controls ( $P = 0.021$ ). There were no differences in amygdala activation.

#### References

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