

The insular glutamatergic system in Alexithymia: A combined fMRI and MRS study.

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Introduction

Alexithymia (AL) is an **emotion dysfunction** mainly characterized by difficulties in describing and identifying your own emotions. A recent theory suggests that alexithymic features are the outcome of an **interoceptive failure**.



Interoception refers to the **sensation of internal bodily signals**, which is supported by the **insular cortex (IC)** and **guides emotional feeling states**.

Indeed, AL was found to show **aberrant insular activation**, in studies using functional magnetic resonance imaging (fMRI)^[1,2]. This finding was also corroborated by results of study using Magnetic Resonance Spectroscopy (MRS) showing an association between AL and **enhanced insular glutamatergic levels**^[3].

Objective: Investigating the relationship between neural correlates of Alexithymia and Interoception, using a combination of fMRI and MRS.

Methods

Participants & Procedure

11 male participants (Age: M=24.82; SD=4.45) filled in the Toronto Alexithymia Scale (TAS-20), afterwards they were asked to perform a task (Figure 1) during fMRI scanning. Finally, after the fMRI session, a MRS scan was done.

fMRI Task



Figure 1. Empathy for pain paradigm

Protocol and Preprocessing

Event-related design, including 64 pictures of hand in painful context and 64 pictures of hand in non painful context^[4]. ~900 volumes were obtained using a T2*-weighted multiband echo planar imaging (EPI) sequence; TR=1379ms, TE=42ms, flip angle 90°. All functional images were slice-time and motion corrected, unwrapped, coregistered to participants' individual structural volume, and spatially normalised. Contrast images were computed for the interaction for No Pain*TAS-20.

MRS

Protocol and Preprocessing

Spectrum was acquired with a Point Resolved Spectroscopy (PRESS) sequence; TR=2000ms, TE=40ms, flip angle 90°, FOV=16 cm. A volume of interest (VOI) and a shim box of 10x15x25 mm were placed in the right anterior insula using sagittal and a coronal T1 3D volumes (Figure 2). Spectra were analysed using Tarquin and concentration of Glutamate was obtained as ratio to water. The same scanner was used.

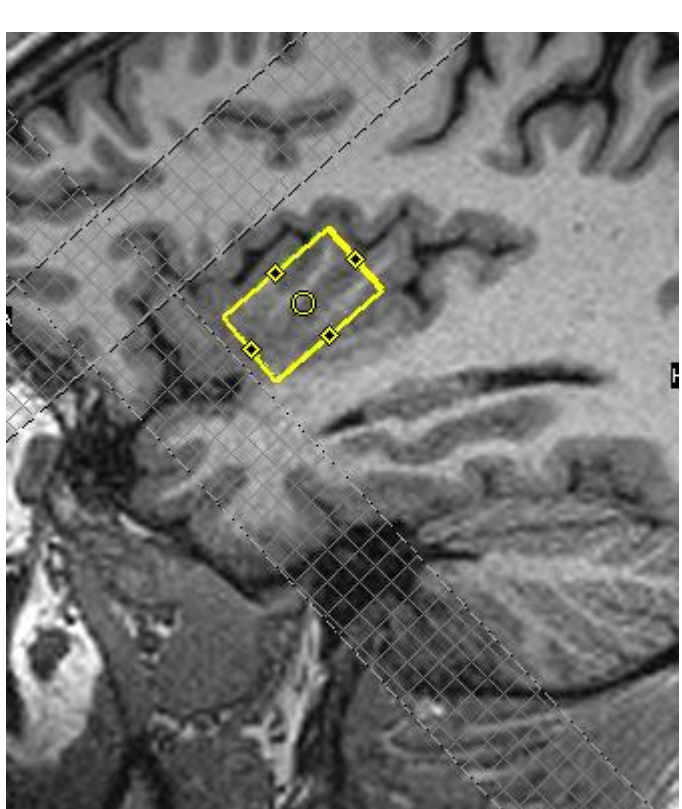


Figure 2. Sagittal view of the VOI position.

Statistical Analyses

Non-parametric two-tailed correlations between questionnaire scores, behavioural ratings, insular activations and glutamate concentrations were computed, using SPSS 22.

Results

Behavioral data

A **positive correlation** was observed between ratings of painful pictures and AL ($\tau=0.49$, $p<0.05$).

fMRI data

In No Pain condition, the activation of a cluster in the right IC was **positively correlated** with AL ($\tau=0.60$, $p=0.01$) and the factor 1 of the TAS-20 (difficulties describing emotions; $\tau=0.64$, $p<0.01$; Figure 3).

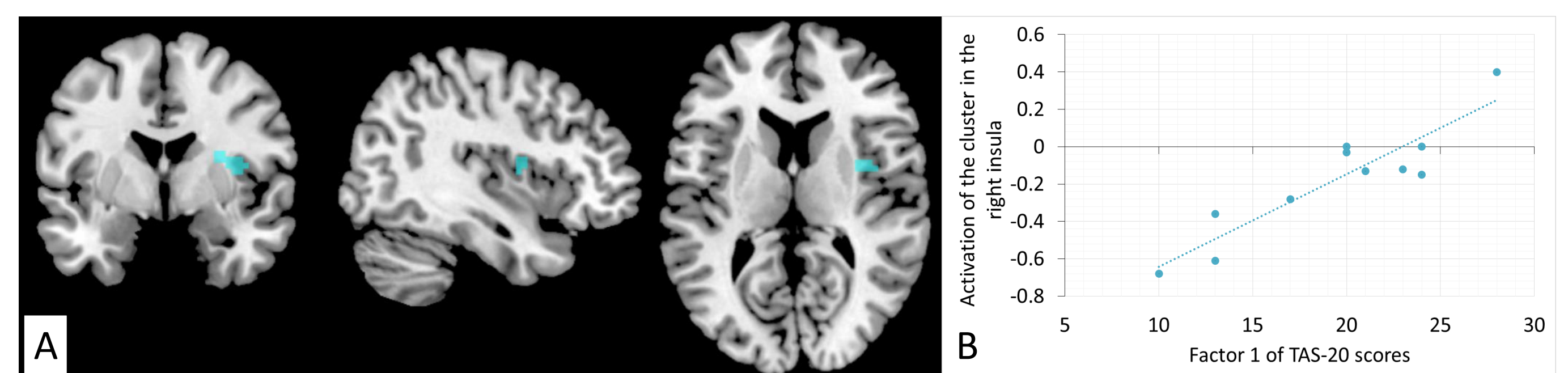


Figure 3. (A) A positive correlation was observed between the activation of cluster in the right IC and AL scores. [MNI 39 -1 11], Height threshold $T<3.21$, $p<0.001$ (unc.) (B) The extracted activation of this cluster was also positively correlated to the Factor 1 of the TAS-20.

MRS data

Glutamate concentrations of the right mid insula **were positively correlated** with scores of the factor 2 of the TAS-20 (difficulties identifying emotions; $\tau=0.57$, $p<0.05$; Figure 4).

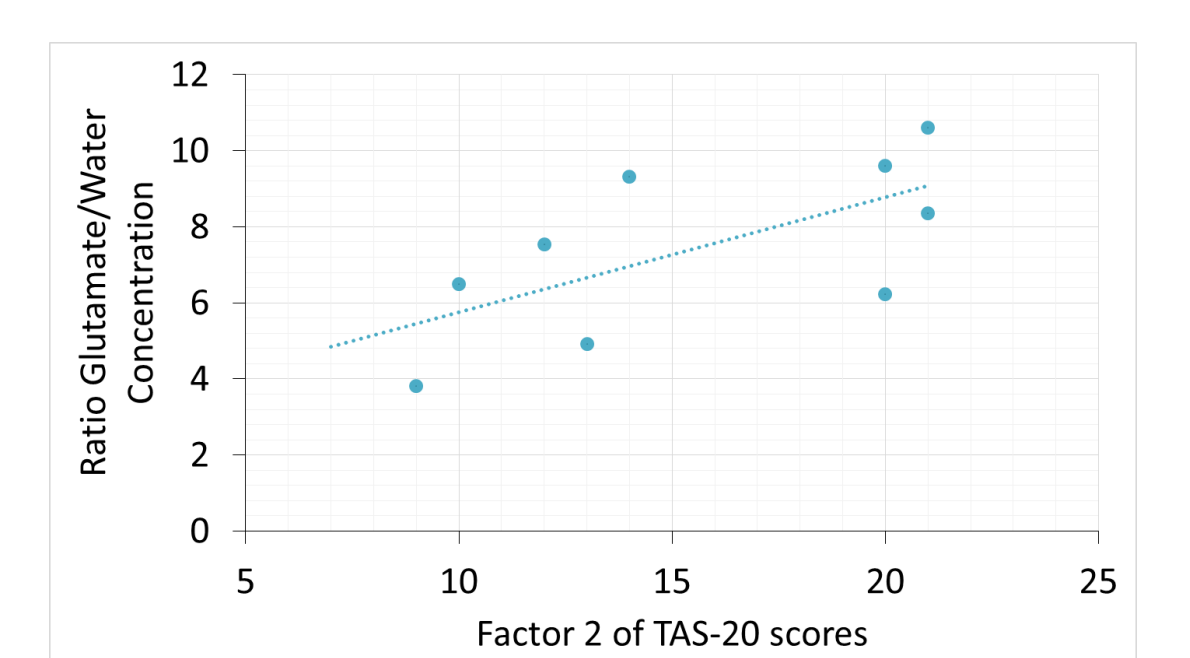
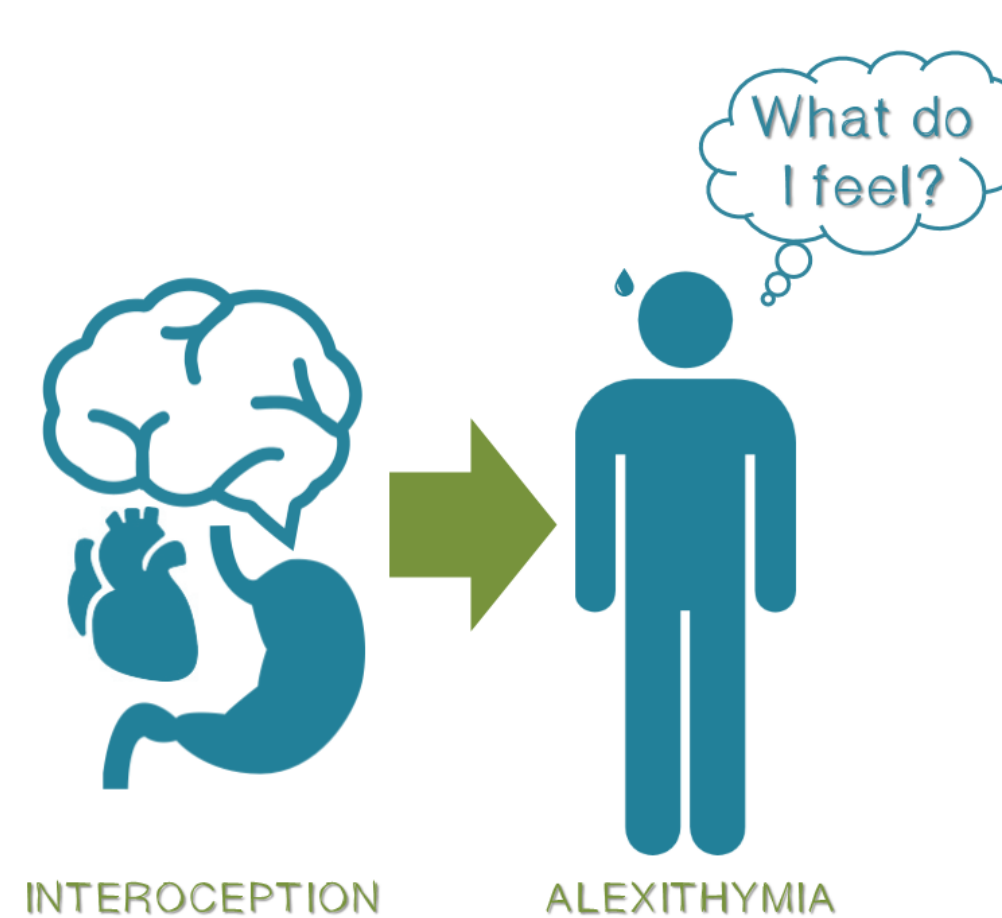


Figure 4. A positive correlation was observed between the ratio Glutamate/Water and the Factor 2 of the TAS-20.

Conclusion

- **Alexithymia** is related to a **hyper excitability of the insular cortex** at functional which seems subtended.
- This hyper excitability seems to be subtended by an **increased glutamate concentration**.
- This conclusion is in line with the emergent literature supporting **alexithymia as the outcome of an interoceptive failure**.
- **Interoception** seems to be disrupted in various clinical and subclinical psychiatric populations, and **should be subject of further studies**.
- **New therapies targeting interoceptive processes** should be developed.



References: ^[1] Moriguchi et al., (2007). *Cereb Cortex*.17, 2223-2234. ^[2] Bird et al., (2010). *Brain*.133, 1515-1525. ^[3] Ernst et al., (2014). *Soc Cogn Affect Neurosci*.9, 857-863. ^[4] Jackson et al., (2005). *Neuroimage*.24, 771-779.

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