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# 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)<sup>[1,2]</sup>. This finding was also corroborated by results of study using Magnetic Resonance Spectroscopy (MRS) showing an association between AL and **enhanced insular glutamatergic levels**<sup>[3]</sup>.

**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<sup>[4]</sup>. ~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.

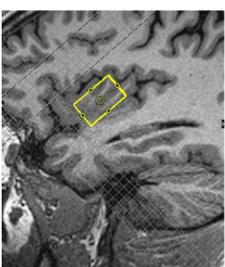


Figure 2. Sagittal view of the VOI position.

### 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.

### 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).

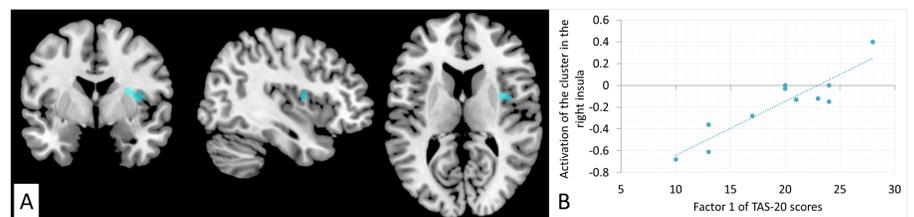


Figure 3. (A) A positive correlation was observed between the activation of cluster in the right IC and AL scores. [MNI 39 -1 11], Height threshold  $T<3.21$ ,  $p<0.001$  (unc.) (B) The extracted activation of this cluster was also positively correlated to the Factor 1 of the TAS-20.

### 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).

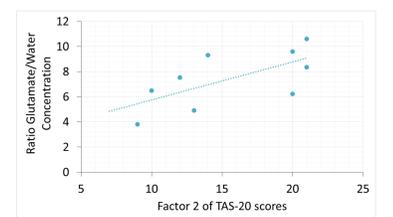
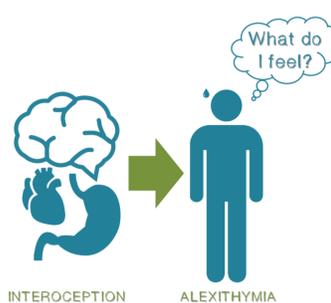


Figure 4. A positive correlation was observed between the ratio Glutamate/Water and the Factor 2 of the TAS-20.

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

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