Modulating effect of COMT genotype on the brain regions underlying inhibition

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INTRODUCTION

Catechol-O-Methyltransferase (COMT) is an important enzyme which degrades catecholamines, such as dopamine, notably in prefrontal cortex (Männistö & Kaakkola, 1999). The COMT gene is located in the chromosome 22q11. A transition of guanine to adenosine at codon 158 of this COMT gene results in a valine to methionine substitution (Lotta & al., 1995). This phenomenon leads to different COMT genotypes, each associated with different COMT enzymatic activity. Precisely, individuals homozygous for met allele (MM) exhibit the lowest enzymatic activity, while homozygous for val allele (VV) have the higher. Heterozygotes (VM) exhibit an intermediate level of activity (Weinshilboum & al., 1999). A large number of studies reported a behavioral effect of COMT on executive functioning. However, most of them used multi-determined executive tasks (Barnett & al., 2007).

In this context, given the established role of frontal area in executive functioning, notably in inhibition (Nee & al., 2007; Laird & al., 2005), we were interested to determine the effect of COMT Val158Met genotype on activity in these areas when a task assessing a specific inhibitory process was administered.

MATERIALS & METHODS

Forty-five right-handed native French speakers young adults, aged from 18 to 30, were recruited and separated into three groups according to their COMT genotype : 15 VV (6 males), 15 MM (7 males) and 15 VM (8 males).

A modified form of the Stroop task (Stroop, 1935) was administered in a fMRI session. The Stroop paradigm consists in the inhibition of a predominant response (WORD READING) to promote another one (COLOR NAMING).

BEHAVIORAL RESULTS

ANOVA 3 (group) x 2 (item) : Significant interference effect in the three groups; no group effect or interaction were observed.

Figure 1 : Mean reaction time (ms) in each group (VV – MM – VM) for interferent (II) and neutral (IN) items.

FMRI RESULTS

1. Main task effect : Classical fronto-parietal network associated with interference resolution in the Stroop task.

Figure 2 : Statistical Parametric Mapping associated with the interference effect (II – IN) in the three groups of subjects. Functional results are displayed at puncorr < 0.05, over the normalized structural image of a typical subject.

2. Group comparisons using t-test : Increased brain activity in the superior temporal gyrus (x = -60; y = -52; z = 14) in VV and VM by comparison with MM.

Figure 3 : Interference effect (II-IN): VV>MM (Puncorrected < 0.001).

Figure 4 : Interference effect (II-IN): VM>MM (Puncorrected < 0.001).

DISCUSSION

The fronto-parietal brain network associated with interference resolution observed in the three groups is consistent with prior reports (Nee & al., 2007; Laird & al., 2005).

Interestingly, similar interference effects are observed at a behavioral level in the three groups although as specific pattern of brain activity was found in the carriers of the val allele. Indeed, these subjects recruited supplementary areas in the superior temporal gyrus, an area previously observed in reading task and associated to phonological processes (Simos & al., 2000; Yagishita & al., 2008). This pattern of behavioral and brain imaging data seems to indicate that the reading process remains more activated in the VV and VM groups but not impede their inhibitory abilities in the Stroop task.

REFERENCE