**Variants in Catechol-O-Methyltransferase gene are associated with impulsivity and executive function: relevance for major depression**

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**Introduction**

- COMT is important in PFC to eliminate DA from the synaptic cleft
- the Val to Met substitution in COMT results in different enzyme activity
- COMT activity related changes in dopaminergic neurotransmission are critical for modulating cognitive functions subserved by the PFC, such as working memory, executive functions, cognitive flexibility, impulsivity
- Impulsivity is a multidimensional personality trait that includes the inability to delay gratification and acting without regard to future consequences
- It is a characteristic of several psychiatric conditions, such as mood disorders, and it has a strong heritable component suggesting that it can be an intermediate phenotype, and an important risk factor for major depression
- our aim was to investigate the role of impulsivity and dopaminergic system in depression by analysing catechol-O-methyltransferase (COMT) gene

**Methods**

- all participants provided buccal cell DNA and filled out the NewMood booklet (sem and standard, validated psychiatric questionnaires)

**LEVEL 1:**
- big number of Caucasian participants from Manchester, UK (1267), and Budapest, Hungary (942)
- used questionnaires for LEVEL 1:
  - Impulsiveness-Venturesomeness-Empathy Scale (IVE) for impulsivity,
  - Big 5 neuroticism items for neuroticism,
  - Brief Symptom Inventory (BSI) for depressive symptoms
- Background questionnaire for reported lifetime depression

**LEVEL 2:**
- smaller interviewed Manchester population (207)
- used questionnaires, tasks for LEVEL 2:
  - NEO-PI-R for neuroticism
  - Stocking of Cambridge (SOC) spatial planning task for executive functions

**Results**

- Selected hSNP-s and their location on the COMT gene (all the SNPs were in Hardy-Weinberg equilibrium in both populations)
- **MODEL 1**
  - Reported depression
  - Depressive symptoms (BSI)
  - Neuroticism (BFI)
  - Impulsivity (IES)
  - COMT
  - TAA/1/1: 30.9%, -0.044; TAA/2/2: 31.6%, 0.042; TAA/3/3: 31.6%, 0.151
  - TGG/1/1: 17.1%, -0.327; TGG/2/2: 63.0%, 0.073; TGG/3/3: 20.0%, 0.002
  - CGA/1/1: 12.3%, 0.003; CGA/2/2: 46.0%, 0.154; CGA/3/3: 41.8%, 0.002
  - TTA/1/1: 11.2%, 0.514; TTA/2/2: 21.7%, 0.044; TTA/3/3: 67.0%, 0.047; TTA/4/4: 0.300
  - TAG/1/1: 5.2%; TAG/2/2: 0.05; TAG/3/3: 0.0; TAG/4/4: 0.0
  - r² (age and sex were covariables)

- **MODEL 2**
  - Depressive symptoms (BSI)
  - Neuroticism (NEO-PI-R)
  - Impulsivity (NEO-PI-R)
  - SOC ITT

**Conclusions**

- people with current or lifetime depression scored higher on impulsivity scales, and impulsivity is negatively associated with executive functions
- variations in the COMT gene are significantly associated with self reported impulsivity in two independent European populations
- according to our results self-reported impulsivity is a possible trait marker for depression
- the COMT haplotype association with impulsivity was in opposite direction to the COMT effect on cognitive function

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**References**