

Elevated expression of *SLC6A4* encoding the serotonin transporter (SERT) in Gilles de la Tourette syndrome

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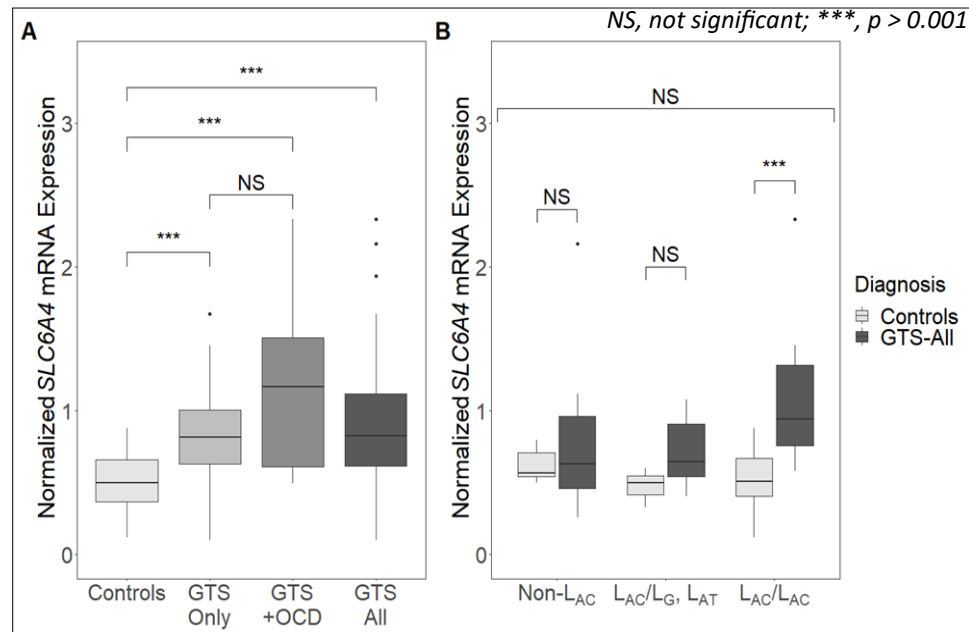
Introduction and Aim

Gilles de la Tourette syndrome (GTS) is a neurodevelopmental disorder with complex etiology. Serotonergic neurotransmission and the 5-HTTLPR polymorphism in the serotonin transporter (SERT) gene, *SLC6A4*, have been implicated in OCD and GTS pathology. The 5-HTTLPR and two linked SNPs are known to affect expression of SERT. Of the 5-HTTLPR/rs25531/rs25532 three-locus haplotype, the S and L_G alleles result in low expression and L_{AC} in high expression of SERT.

- ⇒ Is there an association between *SLC6A4* promoter variants and GTS(+OCD) diagnosis?
- ⇒ Does *SLC6A4* expression- and methylation levels differ between cases and control?
- ⇒ Does *SLC6A4* expression correlate with methylation patterns and/or 5-HTTLPR promoter variants?

Results

- ⇒ Elevated expression of *SLC6A4* in cases compared to controls (A), in particular in those with the L_{AC}/L_{AC} three-locus genotype (B).
- ⇒ No difference in mean methylation, genotype distribution or expression levels dependent on 5-HTTLPR genotype between cases and controls.

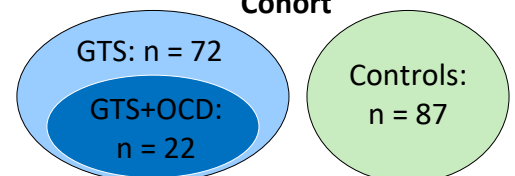


Conclusion

SLC6A4 is overexpressed in GTS individuals compared to controls and this appears to be driven by the L_{AC}/L_{AC} genotype, whereas controls with the same genotype have normal expression levels. *SLC6A4* expression does not appear regulated by DNA methylation at *SLC6A4* promoter region.

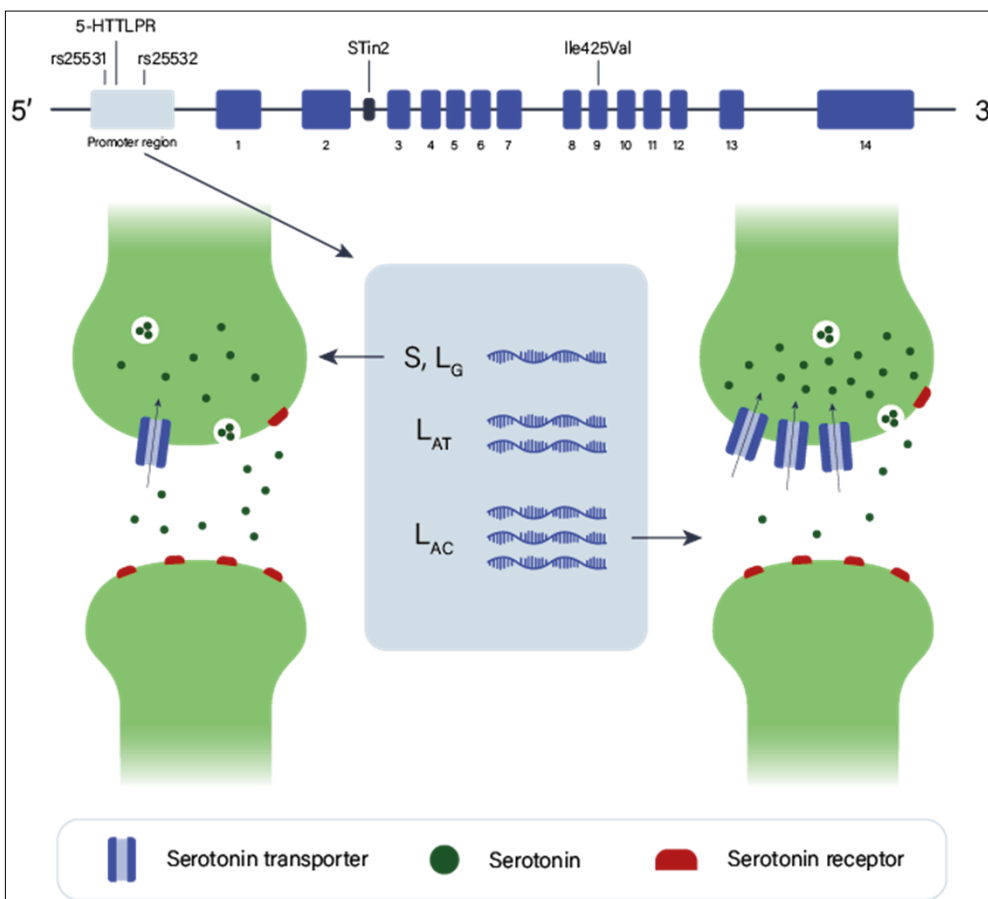
Methods

Cohort



SLC6A4 studied in DNA and RNA from peripheral blood.

- ⇒ Sanger sequencing of 5-HTTLPR, rs25531 and rs25532.
- ⇒ Bisulfite pyrosequencing of 8 CpG-sites in the promoter region.
- ⇒ Reverse-transcription quantitative PCR (RT-qPCR).



Modified from Levy et. al 2021