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

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