

# Genetic Components in Dental Fear and Anxiety – Preliminary GWAS Results



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## Introduction:

The results of a recent genome-wide association study (GWAS) showed 3 significant associations between dental fear and anxiety and genetic loci, nearby genes *NTSR1*, *DMRTA1*, and *FAM84A* (Zhou et al. 2022). *NTSR1* mediates the functions of neurotensin, *NTSR1*-deficient mice may have emotional disorders involving fear memory (Yamauchi et al. 2007). *DMRTA1* is a candidate gene located within a known quantitative trait locus for contextual fear memory in mice (Carhuatanta et al. 2014). *FAM84A* encodes neurologic sensory protein 1, a candidate gene for schizophrenia (Sundararajan et al. 2018).

Also, genes *SLC6A4 (5-HTTLPR)* and *MC1R* have been associated with dental fear and anxiety. 5-HTTLPR is a polymorphism of the serotonin transporter encoding gene. Disturbed function of serotone may result in the development of various anxious symptoms (Francéski et al. 2018). *MC1R* variant alleles have predicted higher levels of dental fear and fear of pain (Randall et al. 2016).

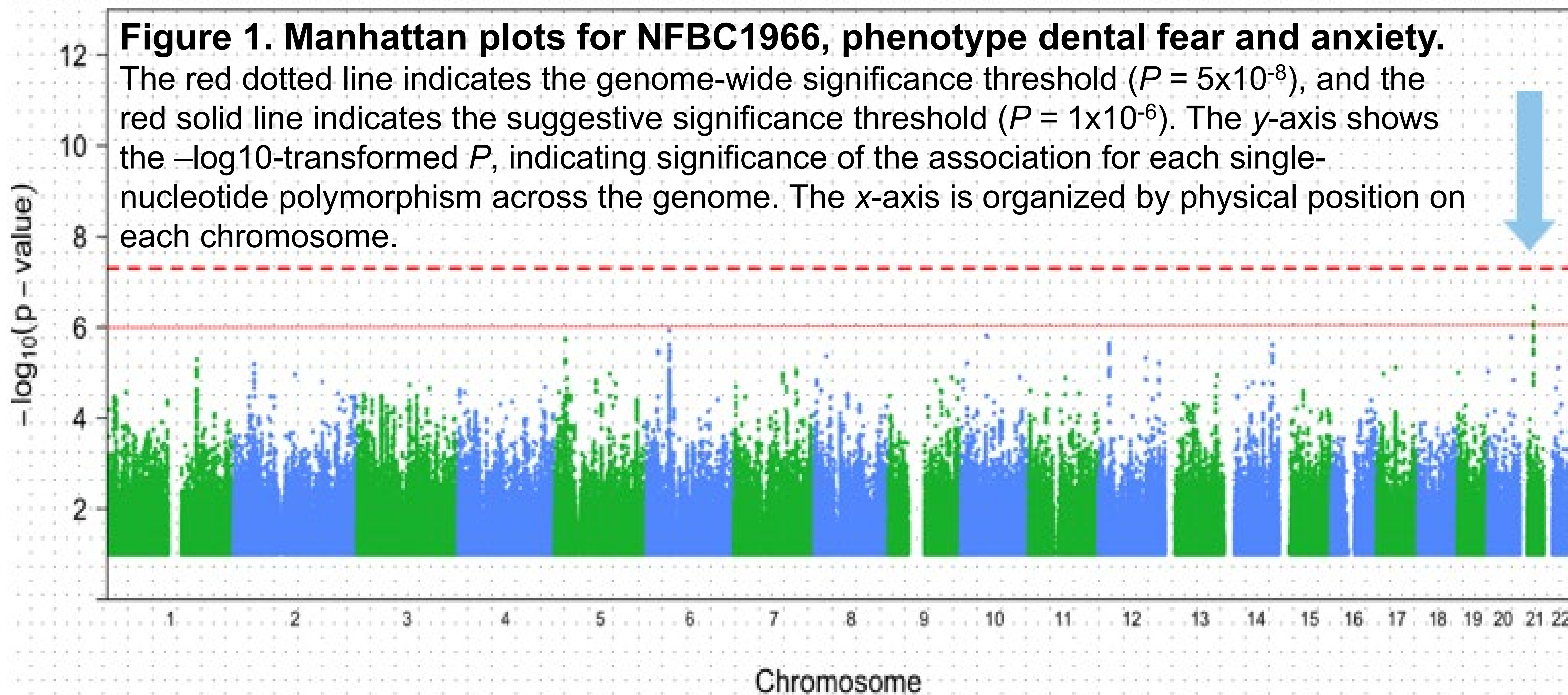
## Objectives:

The aim was to identify genes associated with dental fear and anxiety in Northern Finland Birth Cohort1966 (NFBC1966).

## Materials and methods:

- The study population was the NFBC1966, which consisted of 95.6% of the children born in the two northernmost provinces of Finland in 1966 (N=12,058).
- Dental fear and anxiety was measured with Modified Dental Anxiety Scale (MDAS) when the participants were 46-year-olds.
- The phenotype used in a genome-wide association study was dental fear and anxiety.
- MDAS was used as natural logarithmic conversion for sum of MDAS, where higher values indicated higher anxiety.
- The GWAS (n=1,440) was performed with the additive models using SNP test v2.5.1 and the frequentist association models.
- Associations at p-value  $<1 \times 10^{-6}$  were considered suggestive and those at p-value  $<5 \times 10^{-8}$  genome-wide significant.

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## Conclusion:

**Genes associated with dental fear and anxiety are poorly known. The results of this genome-wide association study suggest a possible connection between dental fear and anxiety and the neurotransmitter or neuroendocrine system. This result needs to be replicated in other study populations.**

## Results:

- The analysis revealed one suggestive association for dental fear and anxiety situated in chromosome 21, lead SNP rs58988229,  $p=3.6 \times 10^{-7}$ .
- This SNP is intergenic and situated near genes *ADAMTS1* (ADAM Metallopeptidase with Thrombospondin Type 1) and *CYYR1* (Cysteine and Tyrosine Rich 1).
- The *ADAMTS1* gene has been suggested in mice to connect with inhibitory neurotransmitter system (GABA), leading to altered brain function related to anxiety in the hippocampus (Kurumaji & Nishikawa 2012).
- The *CYYR1* gene has been predicted to encode a membrane protein that is an integral component of membranes ([www.genecards.org](http://www.genecards.org)) and relate to neuroendocrine system (Vitale et al.2007).
- Both *ADAMTS1* and *CYYR1* represent biologically plausible candidate genes for dental fear and anxiety.
- In this relatively small population, we were unable to confirm the previously found GWAS results between genetic loci and dental fear and anxiety.

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