A 5-Choice Serial Reaction Time Task Screen of ENU-Mutagenised Zebrafish Identifies Lines Showing Heritable Impulsivity and Two Mutations Cosegregating with Impulsivity

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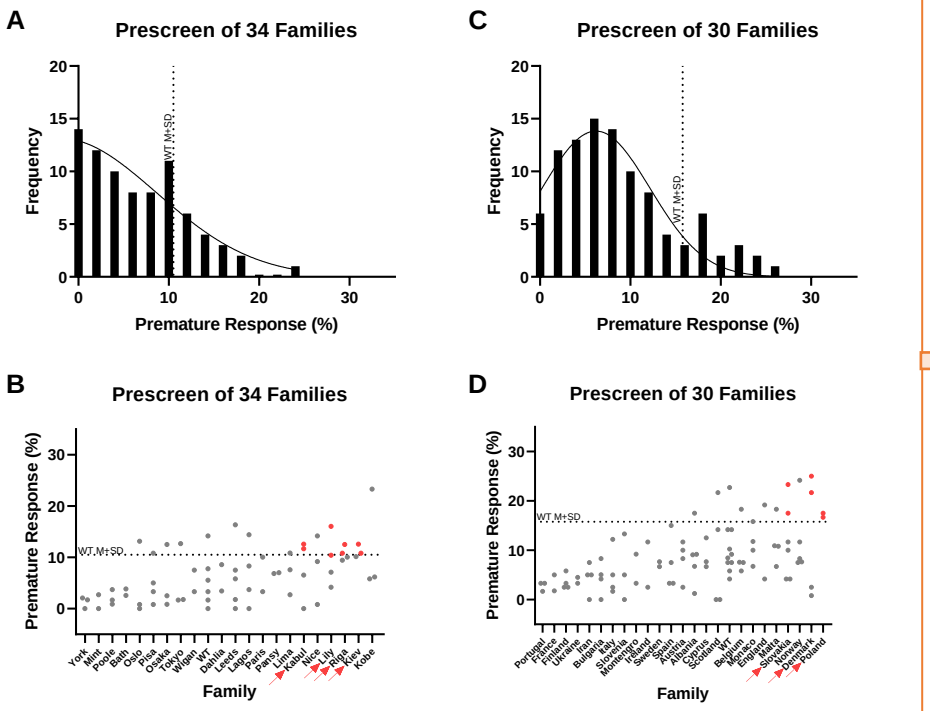
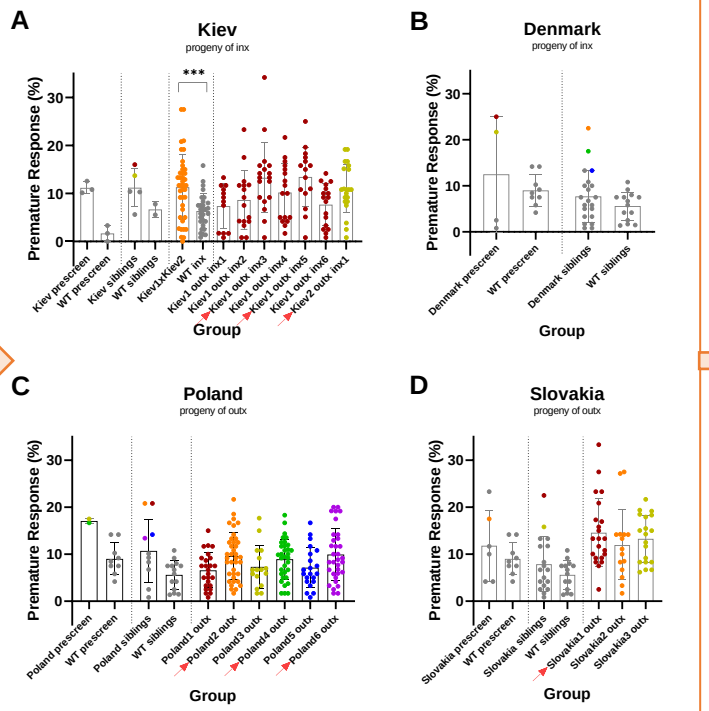


We aimed to identify genes and pathways underlying impulsivity as a risk factor for addiction.

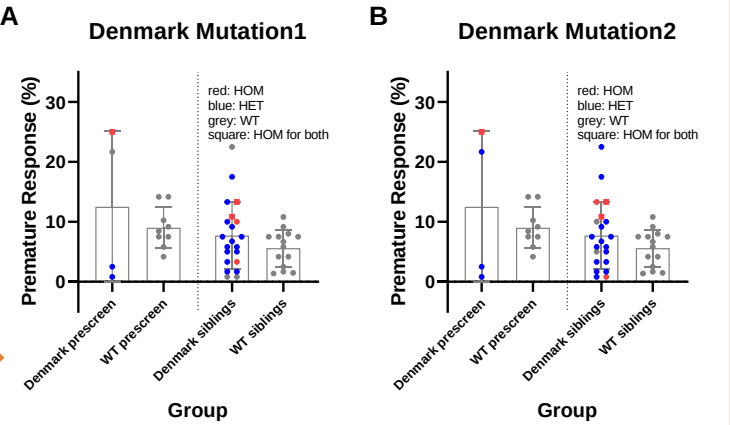
1) We generated 102 F3 ENU families covering 7926 dominant and 3554 recessive alleles.

2) Prescreen of 6 fish from 102 families identified 7 candidate families with at least 2 fish showing premature response higher than WT M+SD.



3) Siblings of 4 candidate families were screened and confirmed the phenotype.

4) Next generation of 3 candidate families were screened and confirmed the heritability of the phenotype.



5) Exome sequencing of F1 of 7 candidate families identified 113 candidate mutations of which 10 are associated with impulse control disorders in GWASs.

6) Competitive allele specific PCR of F3 of 3 candidate families identified 2 candidate mutations in a candidate family cosegregating with the phenotype.

7) Confirmation and characterisation of ENU and CRISPR-Cas9 lines are ongoing.

This is the first forward genetic screen for impulsivity showing potential success.

Queen Mary University of London
NIH National Institute on Drug Abuse Advancing Addiction Science
ZANTIKS behaviour, simply
I·B·A·N·G·S International Behavioural and Neural Genetics Society