P130 ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) AND 5HT2C RECEPTOR:
A SLIGHT INCREASE IN THE TRANSMISSION OF Cys23 TO ADHD CASES

Nugent E, Hawi Z, Lowe N, Kirley A, Fitzgerald M, and Gill M
Dept. of Genetics, Trinity College, Lincoln Place Gate,
Dublin 2, Ireland, Phone: 353-1-6082444;
Fax: 353-31-6798558; E-mail: nugentea@tcd.ie

Recent evidence suggests that interaction with and balance
between serotonergic and dopaminergic neurotransmission
is important in the mediation of hyperactive behaviour.
Animal model studies have *rmly implicated the genes of the
serotonergic system in predisposing to ADHD. Serotonin
exerts its effects via a heterogenous family of receptors of
which there are at least 14 distinct subtypes.
The non-spec*c serotonin receptor agonist (m-chlorophenylpiperazine)
is known to suppress locomotion in normal
mice. However, when administered to mice bearing a
mutated 5-HTR2C gene, it induces hyperactivity in these
animals (Lora et al., 2000). This effect was blocked by pretreatment
with 5HT1B receptor antagonist, indicating that
the behavioural consequences of the mCPP-induced 5HT1B
receptor stimulation are unmasked in animals devoid of
5HT2C receptor function. A Cysteine to Serine substitution
at amino acid 23 of the 5HT2C has been identi*ed which
may in"uence the receptor folding thereby hindering the
formation of a normal hydrophobic pocket and subsequently
the binding of bulky ligands. In a family based association
study design, we analysed the Cys-Ser polymorphism at the
5HT2C receptor gene in 60 Irish ADHD trios using transmission
disequilibrium test (TDT). We observed a slight
increase in the transmission of the Cysteine allele to the
affected ADHD cases (Chi-square $\chi^2$ 1.8, P $\leq$ 0.26). This
may suggest the involvement of 5HT2C gene in predisposing
to ADHD.