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

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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-speci®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 □ 1.8, P □ 0.26). This may suggest the involvement of 5HT2C gene in predisposing to ADHD.