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Psychopharmacogenetics

5. Psychopharmacogenetics

© SPMM Course 5. Psychopharmacogenetics Psychopharmacogenetics focuses on how polymorphisms in genes affecting the mechanism of action of a drug's effect and/or metabolism (both peripheral and central) can influence an individual's clinical response to the drug, in terms of both therapeutic efficacy and adverse effects. Drug Effect Biological substrate Nicotine replacement Response to nicotine replacement (esp. in women) Dopamine receptor DRD2 variant Clozapine Drug response No association with DRD2 variants DRD3 Ser9Gly polymorphism - controversial DRD4 polymorphisms- no correlation 5HT2A receptor polymorphism - associated 5HT2C receptor polymorphism - associated 5HT transporter linked polymorphic region (5HTTLPR) - associated CYP2D6 variations - overall efficacy not affected Methylphenidate Poor response of ADHD symptoms. Homozygosity for the 10-repeat allele at DAT1 Clozapine Agranulocytosis HLA loci variants Typical antipsychotics

No association with DRD2 variants DRD3 Ser9Gly polymorphism - associated DRD4 polymorphisms- no correlation 5HT2A receptor polymorphism - associated Typical antipsychotics Extrapyramidal symptoms, postural hypotension & excess sedation Poor metabolizers of CYP2D6 Typical antipsychotics Acute akathisia Polymorphisms in DRD3 and DRD2 Typical antipsychotics Tardive dyskinesia DAT polymorphism, 5-HTTLPR and the tryptophan hydroxylase (TPH) polymorphism and to some extent CYP1A2 polymorphisms Typical antipsychotics Hyperprolactinaemia & NMS DRD2 polymorphism

© SPMM Course The serotonin transporter (5-HTT) protein acts as the primary mechanism for removing 5-HT from the synaptic cleft. Two polymorphisms have been identified within the human 5-HTT, an insertion/deletion polymorphism in the promoter region (5-HTTLPR) results in a short (s) and a long (l) variant, and a VNTR polymorphism in intron.

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