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GENETIC POLYMORPHISM OF DOPAMINE D2 RECEPTOR *(DRD2)* AND PERSONALITY RISK BEHAVIOUR ASSOCIATED WITH DRUG ADDICTION

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ABSTRACT

Objective: To investigate the types and frequencies of allelic variants of *DRD2*, drug injecting behaviours and personality traits among intravenous drug users (IVDUs) in Malaysia.

Methods: Ninety-three IVDUs that met the inclusion and exclusion criteria were assessed with Diagnostic and Statistical Manual (DSM) of American Psychiatric Association Version IV (DSM IV), Tridimensional Personality Questionnaire (TPQ) and WHO Drug Injecting Study Phase II Questionnaire. DNA were extracted from subjects' whole blood and then subjected to polymerase chain reaction (PCR) method to analyze the frequencies of *DRD2* allelic variants among IVDUs.

Results: A total of 88% of the 93 IVDUs fulfilled 6 to 7 criteria of an addict using DSM IV. Genotype analysis demonstrated a significant difference of the *TaqI*A polymorphism between IVDUs and control ($p<0.05$), where 69.9% were carriers of the *A1* allele, the allele which is highly associated with substance abuse. Comparatively, only 42.6% of the healthy controls were carriers of this allele. No significant differences were recorded for other variants screened (*Pro$_{310}$Ser, Ser$_{311}$Cys*, *-141C Ins/Del, A-241G, Val$_{96}$Ala, Val$_{154}$Ile* and *Leu$_{141}$Leu*). For the TPQ analysis, IVDU subjects scored high Novelty Seeking (NS) and Harm Avoidance (HA) traits; both significantly different from control, and low scores for Reward Dependence (RD). High NS is especially associated with dopaminergic pathways which could mediate the mechanism of drug seeking behaviour.

Conclusion: *TaqI*A polymorphism and high NS traits were found to be present at a higher percentage significantly among the IVDUs compared to controls; thus may have an implicated role for the increased vulnerability to addiction. Screening of this marker would be useful to identify individuals at risk of becoming an addict.

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CHAPTER 1

INTRODUCTION

1.1   Study Background

Drug abuse is a worldwide problem affecting both developed and developing countries. However, the detrimental effect on socioeconomic growth of a country would be more if the percentage of drug addicts is high among the youth, who would be the pillar of the country. A study conducted as early in 1978 showed 11% of 16,600 secondary school students in 2 different states in Malaysia have had experience of drug use (Spencer & Navaratnam, 1980). The numbers would have definitely increased over the years. Apart from the hindrance on socioeconomic development, drug abuse poses health hazards, especially HIV infection and AIDS associated with intravenous drug use as well as increase in crime rate (Low et al, 1996).

Realizing the enormous burden it causes, it is thus very important to curb drug addiction. The government of Malaysia has spent a huge amount of money and implemented many steps at all levels to reduce the incidence of drug addiction, but the number of addicts rises with a large number of them with complications including HIV/AIDS. Singh and Crofts (1993) pointed out that the rapid spread of HIV among Malaysian addicts were through sharing of needles for injections and sexual activities.

Many researchers are thus looking at the possible underlying factors that are involved in the mechanism of drug addiction. Understanding the pathogenesis of drug addiction is important to unravel the mechanisms by which drug of abuse results in dependence. Thus far, drug dependency is known to have caused by various factors including social, environmental, psychological, biochemical and genetic influences (Leshner, 1996; Low et al, 1996; Kuhar, 2002; Trujillo et al, 2006). There are