Association between polymorphism of genes encoding for 5-HT1A and 5-HT2A receptors and response to selective serotonin reuptake inhibitors in Malaysian patients with major depressive disorder

ABSTRACT

Inter-racial variations in genotype frequency have been implicated as a probable cause of the inconsistencies in pharmacogenetic studies of major depressive disorder (MDD). The aim of this study was to determine whether the polymorphisms of the serotonin 1A (5HT1A) 1019C>G and serotonin 2A (5HT2A) 1438A>G are associated with response to SSRI treatment among Malaysian MDD patients. These polymorphic changes are shown to modulate the transcription of these genes and are associated with attenuation of the density of the encoded receptors. Modulation of these receptors is central to the activity of antidepressant medication. The study involved six weeks follow up of incidence and prevalence (diagnosed within 2 years to recruitment) MDD patients from a case-control hospital based study in Malaysia. Only Malaysians aged 18–65 years and diagnosed with MDD (other Axis 1 psychiatric diagnosis were excluded) on treatment with SSRIs were recruited. One hundred and ninety two patients (females - 71.4% and males – 28.6%) were recruited. A total of 77.7% of the patient showed response to treatment and the rest did not. The response rate was also highest among the females (81%) compared to males (67%). The frequencies of the genotypes 5HT1A1019C>G were GC (34.2%), CC (55.2%), GG (10%) and those of the 5HT2A 1438A>G were GA (45.3%), AA (33%), GG (21.9%). Association testing for response to SSRIs with the 5HT1A 1019C>G polymorphism and not the 5HT2A1438A>G polymorphism revealed a chi-square score of 3.911 with $P \leq 0.05$ ($P=0.048$) in a dominant model of inheritance. This study revealed that the dominant effect of the G-allele in both the GG and GC genotypes of the 5HT1A receptor gene was associated with treatment response in Malaysian MDD patients.