M35. IDENTIFICATION OF GENETIC LOCI FOR TREATMENT RESPONSE OF SELECTIVE SEROTONIN REUPTAKE INHIBITORS ON EMPIRICALLY DEFINED DEPRESSION SYNDROMAL FACTORS

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**Background** Major depressive disorder (MDD) is a complex and multifactorial disorder with heterogeneous syndromal presentations. Patients’ response to commonly prescribed selective serotonin reuptake inhibitors (SSRIs) varies across individuals and symptoms. Certain genetic variants may modify the effects of SSRIs treatment on different symptoms.

**Methods** We recruited patients with a diagnosis of MDD from two central hospitals in Taiwan, who were treated with escitalopram (38.5%), paroxetine (38.5%), fluoxetine (18.3%), and citalopram (4.8%). Depression severity was rated using the 21-item Hamilton Rating Scale for Depression (HRSD) in all participants, with a minimum score of 14 at baseline for inclusion. Patients were assessed repeatedly at week 2, 4, and 8. All participants were genotyped using Illumina HumanOmniExpressExome BeadChips in the International SSRI Pharmacogenomics Consortium. After quality controls, 421 patients (mean age of 43.7 years and 71% of females) with 4,241,701 genotyped and well-imputed SNPs were retained for analysis. We first performed exploratory factor analysis to identify latent syndromal factors for baseline HRSD. Treatment response was defined for two variables: score change (score difference between baseline and week 4, divided by the total score in each factor – scaling to range between 0-1), and binary response (≥50% score reduction from baseline to week 4). Linear and logistic regression models were used for association testing while adjusted for age and sex.

**Results** We obtained six empirically derived factors for HRSD, namely sleep, core, anxiety, somatization, psychomotor, and energy. The degree of improvement in syndromal severity at week 4 was ranged from 33% (energy) to 70% (psychomotor). No markers reached genome-wide significance level. Nevertheless, several loci showed suggestive signals with p-value<5×10^-6, 43 for score change and 12 for response. The most significant marker was rs2938029 (P=6.4×10^-7) in NRXN3 for anxiety score change. A number of known genes were mapped for their associations with syndrome improvement in different factors, such as IL7R and MORN3 (core), RARB and SLC5A8 (psychomotor), KCNIP4 (energy) for score change, and SUCLG2 (anxiety), C8A and POC1B (psychomotor) for binary response. Interestingly, loci in or near (15kb away) an enhancer (ENSR00002058236) were associated with sleep factor in both score change and response outcome variables.

**Discussion** We found several genes that might affect treatment response of different empirically defined syndromal factors among SSRIs treated depression patients. Further replication studies are needed to confirm our findings in other populations.

**Disclosure:** Nothing to Disclose.