PS89. Influence of anxiety symptoms on improvement of neurocognitive functions in patients with major depressive disorder: A 12-week, multicenter, randomized trial of tianeptine versus escitalopram, the CAMPION study

leading to the conclusion that other neurotransmitter pathways, above and beyond serotoninergic ones, can play a role in emergence of this rare and unique phenomenon.

PS87

An update on prediction of treatment outcome in treatment resistant depression

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Abstract

Objectives: Although single clinical predictors have repeatedly been associated with TRD (treatment resistant depression), they have not proven sufficient for predicting treatment outcome[1]. Thus, attention shifted to interaction-based models but only few multivariate investigations have been performed in TRD so far[2]. Using the data pool of the Group for the Study of Treatment-Resistant-Depression (GSRD) and a machine learning algorithm we intended to draw new insights and back up previous results featuring a set of 66 clinical and demographical predictors for treatment outcome.

Methods: 415 patients recruited between 2011 and 2015 in 11 participating centers showed full availability for all 66 predictors. Treatment response was defined by MADRS-score below 22 and a reduction of 50% or more. A score higher than 21 after at least two antidepressant trials of adequat dosage and length was considered as treatment resistance. After generating importance values for all predictors the prediction algorithm was trained in a sample of 385 patients. Subsequently, prediction was performed in a sample of 30 new patients not featured in the model generation.

Results: The accuracy for predicting treatment outcome in TRD was at 0.75 using all 66 predictors. Importance measurement revealed chronicity, i.e. full or partial intraepisodic recovery or chronic MDD, number of depressive episodes, age of first and last lifetime depressive episode, total time of hospitalization, education and occupation status, suicidal risk, marital status and number of children and cigarettes smoked per day as the most useful predictors.

Conclusion: Exploiting a machine-learning algorithm, we scored an accuracy of 0.75 for treatment outcome using a sample of 415 patients. Reaching a probability of 83.4% for a correct prediction for treatment resistance and 66.6% for response we exceeded the predictive capabilities of clinicians. Thus, these results strengthen our previous data mining approaches and suggest keeping the focus on interaction-based statistical approaches[3].

References

1. Souery D, Oswald P, Massat I, et al. Clinical factors associated with treatment resistance in major depressive disorder: results from a European multicenter study. J Clin Psychiatry. 2007 Jul;68(7):1062–70.
2. Kautzky A, Baldinger-Melich P, Souery D, et al. The combined effect of genetic polymorphisms and clinical parameters on treatment outcome in treatment-resistant depression. Eur Neuropsychopharmacol. 2015 Apr;25(4):441–53.
3. Kautzky A, Baldinger-Melich P, Kranz G, et al. A new prediction model for evaluating treatment resistant depression. *In Review.*

PS88

Association between Alu insertion/deletion polymorphism on the tPA gene and mirtazapine response in Koreans with major depression

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Abstract

Objectives: There is considerable evidence that disturbances in neurotransmitter systems contribute to the pathophysiology of depression. Brain-derived neurotrophic factor (BDNF) is involved in the pathophysiology of depression, and in the mechanism of action of antidepressant medications. The mature form of BDNF is derived from proBDNF through tissue type plasminogen activator (tPA) and the plasminogen system in the brain. Therefore, tPA might be involved in the development of major depressive disorder (MDD) and its response to antidepressant treatment. Mirtazapine acts as an antagonist of the adrenergic alpha 1, 2 and serotonin receptors. The present study determined the relationship between the Alu insertion/deletion (I/D) polymorphism on the tPA gene and the clinical outcome of mirtazapine treatment in 422 Korean MDD patients.

Methods: 422 patients were enrolled in this study, and symptoms were evaluated by 21-item Hamilton Depression Rating scale. After 1, 2, 4, and 8 weeks of mirtazapine treatment, the association between Alu I/D polymorphism on tPA gene and remission/response outcomes were evaluated.

Results: The proportion of I/I homozygote in responders was higher than that in non-responders, whereas the proportion of D/D homozygote in responders was lower than that in non-responders at 8 weeks of treatment (P=0.032, OR=1.57). The percent decline of HAMD-21 score in I allele carriers was larger than that of D allele homozygotes at 2 and 8 weeks after mirtazapine treatment (P=0.035 and 0.007, respectively). I allele carriers were also significantly associated with remission at 8 weeks of treatment (P=0.047, OR=2.2).

Conclusions: These results show that treatment response and remission to mirtazapine were significantly associated with Alu insertion/deletion polymorphism of the tPA gene. This suggests that Alu insertion/deletion polymorphism affects the therapeutic action of mirtazapine in MDD, and may be a potential genetic marker for the prediction of therapeutic response to mirtazapine treatment in patients with MDD.

PS89

Influence of anxiety symptoms on improvement of neurocognitive functions in patients with major depressive disorder: A 12-week, multicenter, randomized trial of tianeptine versus escitalopram, the CAMPION study

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Abstract

Background: Previous research has reported evidence that patients with major depressive disorder (MDD) show anxiety symptoms and neurocognitive impairments. However, the influence of anxiety on neurocognitive function in MDD patients during antidepressant treatment is unclear.

Method: MDD patients (n=164) completed a 12-week, multicenter, randomized trial assigned in a 1:1 ratio to either tianeptine or escitalopram. Changes of anxiety symptoms were assessed by the Hamilton Anxiety Rating Scale (HAM-A), and the Hamilton Depression Rating Scale (HAM-D), self-rated subjective cognitive impairment on memory and concentration, the Mini-Mental Status Examination (MMSE), Continuous Performance Test (CPT), Verbal Learning Test (VLT), and Raven's Progressive Matrices (RPM) were assessed every 4 weeks.

Results: During 12 weeks of treatment, decrease in the HAM-A score was significantly associated with improvement of subjective cognitive impairments on memory (p<0.001) and concentration (p<0.001), and objective measures on delayed memory (p=0.006) and reasoning ability (p=0.002), after adjusting for covariates such as baseline HAM-A scores, time, sex, age, education years and assigned medication using the Mixed effects and Generalized Estimated Equation model analysis. However, the other cognitive outcome variables, immediate memory, commission error, and MMSE, which showed significant improvement through 12-week study period, showed no significant association with improvement of anxiety.

Conclusion: Improvement of anxiety symptoms was significantly associated with improvement in subjective and objective neurocognitive functions such as delayed memory and reasoning ability in elderly MDD patients during antidepressant treatment, but not significantly associated with improvement of immediate memory and commission error.

PS90

Differences in hypochondriasis between Korean and American outpatients with major depressive disorder

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Abstract

Prior cross-cultural studies have shown that Americans and East Asians differ with regards to the presentation of hypochondriasis symptoms. However, few studies have attempted to examine the prevalence and nature of hypochondriacal concerns among both American and East Asian patients with major depressive disorder (MDD). This study aimed to explore hypochondriasis and its correlates, using the Hamilton Depression Rating Scale (HAM-D), among American and Korean MDD outpatients of ages 18 and older. Consistent with previous cross-cultural findings, Korean MDD patients exhibited significantly higher scores for hypochondriasis than Americans after controlling for total HAM-D scores and demographic variables (p<0.0001), even though American patients had significantly higher total HAM-D scores (p<0.0001). Whereas hypochondriasis appeared to be common among Koreans regardless of age, years of education, and employment status, Americans showed an increased tendency for hypochondriasis with greater age, fewer years of education, and unemployment. Despite the cultural differences, multivariate logistic regression analyses revealed that hypochondriasis is significantly associated with somatic anxiety (Koreans AOR=2.14, 95%CI 1.31–3.52; Americans AOR=1.98, 95%CI 1.69–2.31), suicide (Koreans AOR=0.42, 95%CI 0.24–0.74; Americans AOR=0.81, 95%CI 0.67–0.98), middle insomnia (Koreans AOR=1.95, 95%CI 1.18–3.23; Americans AOR=1.19, 95%CI 1.01–1.41), and psychic anxiety (Koreans AOR=1.62, 95%CI 1.00–2.61; Americans AOR=1.44, 95%CI 1.23–1.70) for both Korean and American MDD patients. Taken together, although hypochondriasis is more prevalent among Koreans, both Korean and American MDD patients with hypochondriacal symptoms appear to display high levels of somatic anxiety regardless of whether they experience actual physical symptoms. These findings suggest that both cultural and personal factors play a role in the presentation of hypochondriasis symptoms among Korean and American patients with MDD.

PS91

The effects of fluvoxamine on the steady-state plasma concentrations of escitalopram and desmethylescitalopram in depressed Japanese patients.

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Abstract

Background: This aim of this study was to determine the impact of fluvoxamine, an inhibitor of CYP2C19, on the pharmacokinetics of escitalopram, a substrate of CYP2C19.

Methods: Thirteen depressed patients initially received a 20 mg/day dose of escitalopram alone. Subsequently, a 50 mg/day dose of fluvoxamine was administered due to the insufficient efficacy of escitalopram. Plasma concentrations of escitalopram and desmethylescitalopram were quantified using HPLC before and after fluvoxamine co-administration. The QT and corrected QT (QTc) intervals were measured before and after fluvoxamine co-administration.

Results: Fluvoxamine significantly increased the plasma concentrations of escitalopram (72.3 ± 36.9 ng/ml versus 135.2 ± 79.7 ng/ml, p<0.01) but not those of desmethylescitalopram (21.5 ± 7.0 ng/ml versus 24.9 ± 12.0 ng/ml, ns). The ratios of desmethylescitalopram to escitalopram were significantly increased during fluvoxamine co-administration (0.37 ± 0.21 ng/ml versus 0.21 ± 0.10, p<0.01). The CYP2C19 genotype did not fully explain the degree of the change. Fluvoxamine co-administration did not change the QT or QTc intervals.

Conclusions: The results of the present study suggest that adjunctive treatment with fluvoxamine increases the concentration of escitalopram. The QTc interval did not change in this condition.