P.3.026 Clinical and genetic predictors of antidepressant response and remission in treatment-resistant depression

R. Calati[1]*, I. Massat[2], S. Kasper[3], S. Montgomery[4], J. Zohar[5], J. Mendlewicz[6], A. Serretti[1]. *[1]University of Bologna, Institute of Psychiatry, Bologna, Italy; [2]Université Libre de Bruxelles, Fonds de la Recherche Scientifique (FNRS) Laboratoire de Neurologie Expérimentale, Brussels, Belgium; [3]Medical University Vienna, Department of Psychiatry and Psychotherapy, Vienna, Austria; [4]University of London, Imperial College, London, United Kingdom; [5]Chaim Sheba Medical Center, Chaim Sheba Medical Center, Tel-Hashomer, Israel; [6]Université Libre de Bruxelles, Université Libre de Bruxelles, Brussels, Belgium*

Purpose of the study: Few studies investigated clinical and genetic predictors of antidepressant response and remission in treatment-resistant depression (TRD). The present one has been performed in the context of the European multicenter project "Patterns of Treatment Resistance and Switching Strategies in Affective Disorder", carried out by the Group for the Study of Resistant Depression (GSRD). Its aim was to identify predictors of antidepressant response/remission in a sample of TRD prospectively assessed patients and to compare the results to ones previously obtained on another sample of TRD patients retrospectively assessed in the context of the same project [1].

Methods: Three hundred ninety-two patients who failed to respond to a previous antidepressant were firstly included in a 6-week treatment with venlafaxine; secondly, those who failed to respond were treated for a further 6-week treatment with escitalopram. Both treatments were continuously prescribed at their optimal dose. MINI was administered at baseline. HRSD, MADRS, CGI-S and CGI-I scales were administered from baseline to week 12. Other information has been collected at baseline, such as socio-demographic characteristics, psychiatric antecedents and previous treatments. The candidate genes considered for their possible role in the modulation of treatment response and remission phenotypes were: CYP1A2, CYP2C9, CYP2C19 CYP2D6, COMT, BDNF, HTR1A, HTR2A, CREB1, DTNBP1, GNB3, GRIK4, MAOA, PTGS1, PTGS2, COX2, OXTR, MAPK1, NACHRA7, HOMER1, ARC, CACNA1C and S100B genes. Statistical analyses on responders and remitters at the endpoints of the study were performed using Chi2, Student t test and stepwise regression.

Results: Non responders (N = 167) and non remitters (N = 234) to venlafaxine reported a higher rate of side effects, higher CGI-S and lower CGI-I scores, and higher treatment doses. Moreover, non remitters showed a higher rate of MDD first degree familial antecedents. Non responders (N = 63) to escitalopram reported a higher treatment dose at the end of the trial while non remitters (N = 107) reported a higher rate of current suicide risk, a higher rate of comorbid anxiety disorders (with the exclusion of OCD), in particular panic disorder and generalized anxiety disorder, a higher rate of side effects at baseline, higher CGI-S scores at baseline, and higher treatment doses at the end of the trial. No or only marginal relationships emerged between COMT polymorphisms and response/remission. Genetic analyses on the other genes are in progress.

Conclusions: Through the present investigation some clinical variables have been identified as associated with treatment response/remission in TRD. If we compare these findings with the ones previously reported by the same group (GSRD) in a retrospective investigation on an independent sample [1], we find some similarities: in particular, severity, current suicide risk, comorbid anxiety disorder and panic disorder seem to be predictors of treatment resistance/non response/non remission in two sample of TRD patients, prospectively and retrospectively followed. Further clarification of the role of other clinical and genetic variables should be explored.

Reference(s)

[1] Souery, D., Oswald, P., et al.. 2007 Clinical factors associated with treatment resistance in major depressive disorder. Results from a European multicenter study. J Clin Psychiatry 68, 1062–1070.

P.3.027 A single dose of the antidepressant fluoxetine modulates emotional processing in young adult volunteers

L. Capitao[1]*, S. Murphy[1], C. Harmer[1]. *[1]P1vital Limited, Dept. of Psychiatry, Oxford, United Kingdom*

Selective serotonin reuptake inhibitors (SSRIs) are effective in the treatment of both depression and anxiety. However, the downstream mechanisms through which they influence and improve mood throughout the treatment are not well understood.

There is growing evidence suggesting that SSRIs have subtle effects on emotional processing that are seen early in treatment, in the absence of any subjective changes in mood. For instance, it has been demonstrated that even though healthy adults report no subjective change in mood or anxiety following a single dose of the serotonergic antidepressant citalopram, sensitive behavioural measures such as the interpretation of facial expressions of emotion indicate that there are effects consistent with early