P.505 The potential role of BDNF and prolactin genotypes on antidepressant response in depressive patients

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volved in the precipitation of suicidal behaviour. Recently variation in *GABRA6* gene in interaction with stress showed an association with a constellation of phenotypes significantly increasing risk of suicide [1]. The CB1 endocannabinoid receptor, encoded by the *CNR1* gene involved in mediating the effects of stress has been a promising obesity drug target, however, rimonabant, a molecule acting on this receptor significantly increased suicide risk. While suicide is a complex phenomenon with distinct risk factors appearing in constellation patterns, different neurotransmitter systems and neural elements may contribute to the modulation of suicide risk via influencing distinct related phenotypes. In our study we compared effects of two genetic variants in distinct neurochemical systems in interaction with recent stress on suicide-related risk phenotypes.

Methods: Two-thousand-and-six subjects in a large general population sample participated in the study. The Brief Symptom Inventory [2] was used to evaluate symptoms related to suicide risk. Life events occurring in the past one year were measured by the List of Threatening Experiences [3]. Participants provided buccal mucosa cells and were genotyped for *GABRA6* rs3219151 and *CNR1* rs776602 by Sequenom's MassARRAY technology with IplexTM assay. Data were analysed using linear regression models testing gene-by-environment effects on each depression and anxiety symptom as the outcome variable with age and gender as covariates. FDR Q values were calculated to correct for multiple testing.

Results: In interaction with recent stress, *GABRA6* rs3219151 significantly influenced several depression-related suicide risk items in contrast to *CNR1* rs7766029 (e.g. thoughts of ending life $q=0.008$ vs $q=0.08$; feeling hopeless about the future $q=0.024$ vs $q=0.08$; feelings of worthlessness $q=0.008$ vs $q=0.08$; feelings of guilt $q=0.007$ vs $q=0.683$, p values shown for *GABRA6* rs3219151 and *CNR1* rs7766029 respectively). In case of thoughts of death or dying, however, *CNR1* rs7766029 had a more pronounced effect ($q=0.007$ vs $q<0.001$ for *GABRA6* rs3219151 and *CNR1* rs7766029 respectively). Only *GABRA6* rs3219151 had an effect on anxiety-related suicide risk factors including spells of panic ($q<0.0001$), extreme restlessness ($q<0.001$), or feeling tense or keyed up ($q=0.024$).

Discussion: Both *GABRA6* rs3219151 and *CNR1* rs7766029 had a strong effect on suicide risk-related phenotypes in interaction with recent stress, however with different symptom profiles. While *GABRA6* rs3219151 increased risk of several phenotypes including on thoughts of ending life, feelings of worthlessness, hopelessness and guilt, and, unlike *CNR1* rs7766029, also had a strong effect on intense restlessness and drive to act immediately, thoughts directly related to death or dying had a more marked association with *CNR1* rs7766029. Thus both *GABRA6* and *CNR1* are potential targets for pharmacological intervention in suicide risk. Future studies should focus on distinct suicide risk profiles which may be decreased by intervention via distinct neural targets.

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P.505 The potential role of BDNF and prolactin genotypes on antidepressant response in depressive patients

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Background: Two-thirds of patients with major depressive disorder (MDD) do not respond optimally to the antidepressant medication [1]. To improve the current situation it is necessary to identify the pathological mechanisms underlying the symptoms of a depressive episode [2,3], enabling tailored forms of antidepressant treatment. Brain-derived neurotrophic factor (BDNF) has been associated with the response to antidepressant drugs in mood and anxiety disorders. Prolactin (PRL) is a pituitary hormone with behavioural effects which may be involved in the antidepressant pharmacological response acting as a neurotrophic fac-

tor within the brain. With multiple factors associated with efficacy of antidepressants, investigation of the effect of genetic factors promises to limit sub-optimal treatments [4].

Aim: The aim of the study was to investigate the relationship of BDNF and PRL genotypes with short-term antidepressant drug response, comparing the first two weeks to the second two weeks of treatment in drug-naïve patients with a major depressive disorder.

Methods: In a prospective inception cohort design, we included 186 Russian participants (28 men and 158 women) of 18-70 years clinically diagnosed with depressive disorder who initiated antidepressant medication, including SSRIs and TCAs. These patients had not been treated with antidepressant drugs in the preceding three months with 54.5% never been treated with antidepressant drugs. DNA polymorphisms were genotyped for PRL rs1341239, BDNF rs6265 and rs7124442 in the Laboratory of Genetics of the University of Groningen with the MassARRAY® System (Agena Bioscience™) and in the Laboratory of Molecular Genetics and Biochemistry of the Mental Health Research Institute with "StepOnePlus" (Applied Biosystems).

We measured the primary clinical outcome by differences in scores using the Hamilton Depression Rating Scale ($\triangle$HAMD) between baseline and week two, and week two and week four for non-specific and specific antidepressant effects. Higher $\triangle$HAMD score denotes better clinical outcome.

Paired-sample t-tests determined the statistical significance between $\triangle$HAMD between the two time-points. Independent T-Test determined the statistical significance between polymorphisms and $\triangle$HAMD in baseline and week two, and week two and week four.

Results: Comparisons between genotypes did not reveal any significant differences in scores during the first two weeks of treatment (all p-values $>$ 0.05). For the latter two weeks, homozygous C BDNF rs7124442 responded significantly worse (5.60 $\pm$ 3.64) in comparison to homozygous T during this period (8.51 $\pm$ 4.26).

Further analysis of homozygous C BDNF rs7124442 revealed significance in all women (5.57 $\pm$ 3.77) and post-menopausal ($\geq$ 50 years of age) women (4.90 $\pm$ 4.06) but not in pre-menopausal ($<$ 50 years of age) women (7.00 $\pm$ 2.34) in comparison to homozygous T. With respect to PRL rs1341239, no association between antidepressant response and genotypes was established within the patients, including within pre-menopausal and post-menopausal women.

Conclusions: PRL rs1341239 genotype did not affect HAMD score differences in patients. Difference in HAMD scores for BDNF rs6265 genotypes were not found to be significant in most patients. Homozygous C BDNF rs712442 patients were found to respond significantly worse in the last two weeks of treatment, with the exception of pre-menopausal women.

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P.506 Effects of N-acetylcysteine in autistic disorders: a systematic review and a meta-analysis

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Background: Autism Spectrum disorder isa neurodevelopmental disorder characterized mainly by deficits in comunication, social interaction and repetitive behavior patterns, as well as stereotypic patterns. Recent publications have been highlighted clinical benefits of oral N-acetylcysteine in psychiatric and neurological disorders. through mechanisms such as oxidative stress and glutamate and dopamine neurotransmitter systems. Therefore, N-acetylcysteine has been used in autistic symptons, such as repetitive and ritualized behaviors, hiperactivity, irritability and stereotypy. Although the mechanisms the efficacy of the drug in ameliorate these symptons are not tottaly established, it can be explained by two pathways, glutamatergic modulation and antioxidative action.

Objective: The aim of the present study was to realize a systematic review followed by meta analisys of all available controled clinical trials of studies assessing the effects of N-acetylcysteine over autistic symptons following recommendations Cochrane group.

Methods: We searched MEDLINE and EMBASE databases using the key words "Autistic Disorder [Mesh]", "Autism Spectrum Disorder [Mesh]", "Autism", "Child Development Disorders, Pervasive [Mesh]", "Acetylcysteine [Mesh]" and "N-acetylcysteine".

We included randomized controlled trials assessing the efficacy of N-acetylcysteine for autistic symptons. It was included 4 eligible randomized clinical trials (n = 131) in the final analysis [1,2,3,4] and one study was excluded due to not contemplating a commom scale [5]. Each study was imputed five times each one, once we assessed the follow-