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1000. Aspects of Heritability of Altered Endocannabinoid Functioning in Schizophrenia and Bipolar Disorder

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Background: Based on translational findings, it has been hypothesized that the endocannabinoid anandamide is associated with an adaptive/protective function countering neurotransmitter abnormalities in psychosis. Therefore, the endocannabinoid system could also be linked to vulnerability, and possibly heritable risk, for schizophrenia.

Methods: We investigated levels of the eicosanoids anandamide, 2-arachidonoylglycerol, palmitoylethanolamide and oleoylethanolamide in plasma by LC/MS-MS in a total of 39 twin pairs, with 25 twin pairs discordant for schizophrenia, 6 twin pairs discordant for bipolar disorder as well as 8 healthy pairs of twins.

Results: In twin pairs discordant for schizophrenia we found significantly higher levels of anandamide and palmitoylethanolamide in plasma when compared to healthy twins ($p<0.002$). The same held true for twin pairs discordant for bipolar disorder. There was no significant difference of any investigated eicosanoid in either groups of discordant twins. However, 5 initially healthy, twins discordant for schizophrenia as well as 3 initially healthy discordant bipolar twins developed a psychotic disorder within five years after initial assessment. In discordant schizophrenia twins all initially healthy twins who later developed a psychotic disorder showed significantly lower levels of anandamide ($p=0.042$) as well as 2-arachidonoylglycerol ($p=0.049$) when compared to the discordant twins who remained healthy.

Conclusions: We found significant elevations of endocannabinoid system components in serum related to familial vulnerability, but not to clinical state. The directionality of the effect agrees with a model indicating a protective role of anandamide in schizophrenia. Our results suggest an investigation of abnormal endocannabinoid signaling as a potential intermediate phenotype of schizophrenia.

Keyword(s): Endocannabinoids, Anandamide, Schizophrenia, Bipolar disorders, Twin study

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1001. Auditory Verbal Hallucinations: A Product of Dysregulated Integration?

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Background: Auditory verbal hallucinations (AVH) are not only among the most common but also one of the most distressing symptoms of schizophrenia and other psychotic disorders. Despite elaborate research, the underlying brain mechanisms are as yet elusive. While it became evident, that no localized pathology seems to account for AVH, aberrant connectivity as a possible brain mechanisms predisposing to AVH remains likewise unresolved.

Methods: We obtained model-based resting state connectivity analysis in a 49 psychotic patients with chronic AVH (debriefed after scanning for acute AVH) and a matched sample of controls. As functional neuroimaging has associated the experience of AVH with activation of bilateral language-related areas, aberrant connectivity ($p<0.05$ corrected) was assessed by seeding functional connectivity analyses from these areas.

Results: We found both increased and decreased connections of language related cortical areas with medial temporal lobe structures, indicating aberrant interactions underlying predisposition and experience of AVH. Patients with AVH showed consistent hypo-connectivity between language areas, which correlated with symptom severity. In contrast, there was an increased connection between language areas and cortical regions associated with the brains "default mode system".

Conclusions: Functional connectivity analyses presented evidence for three traits underlying chronic auditory verbal hallucinations: dysbalance of connections between neocortical areas and medial temporal lobe structures, decreased connectivity within the bilateral cortical language network and increased interactions between language related and default mode areas.

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1002. Neural Response to Reward in Young Men with Nicotine Dependence

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Background: Nicotine is one of the most addicting and widely used drugs. Little is known about the effects of nicotine on reward-related brain function, especially in younger smokers. We tested the hypothesis that nicotine dependence would be associated with altered response to monetary reward.

Methods: Young men (*M* age=20 years; 47.5% European America, 47.5% African American and 5% Other) with current high nicotine dependence (n=17) or with no history of psychiatric disorders or nicotine use (n=42) participated in a functional magnetic resonance imaging study using a guessing task that includes anticipation and receipt of monetary reward. Factorial models examined group and condition effects, and regressions examined the association of nicotine dependence scores and age of initiation with neural response in the ventral striatum, a critical region of reward circuitry.

Results: Young men with nicotine dependence exhibited greater response to reward anticipation and outcome in the striatum than did comparison men (20 voxels, t=3.03, p_{uncorr}<0.01, Talairach coordinates: -6,-3,-3; 56 voxels, t=3.25, p_{uncorr}<0.01, Talairach coordinates: 14,5,12, respectively). Higher nicotine dependence level was associated with greater striatal activity during reward anticipation (105 voxels, t=4.75 p_{FWE}< .05, Talairach coordinates: 1,-18,12) and later onset of smoking was associated with greater striatal activity during reward outcome (31voxels, t=4.70, p_{FWE}< .05, Talairach coordinates: 6,-4,11). Additional analyses will consider frequency and quantity.

Conclusions: In young adults, nicotine dependence may be associated with greater neural responding in reward-related brain areas. Accordingly, these findings raise questions about the influence of development and nicotine exposure on neural reward function.

Keyword(s): Nicotine, Reward, fMRI, Adolescence, Ventral Striatum

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