Title

S.07.02 In vivo measurements of brain serotonergic markers and analysis of drug use profiles among recreational ecstasy and hallucinogen users

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S.07.01 Frontal cortex serotonin transporter binding is positively associated with the cortisol awakening response in healthy volunteers

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Stress vulnerability is linked to the serotonin transporter gene. Both stress and dysfunctional serotonergic neurotransmission are critical in the development and treatment of neuropsychiatric disorders. We studied associations between serotonergic markers and hypothalamic–pituitary–adrenal (HPA) axis activity in 32 healthy volunteers. Our results suggest that in mentally healthy individuals prefrontal serotonin transporter (SERT) binding is associated with basal HPA-axis reactivity. Thirty-two healthy volunteers (mean age 35 ±20, 7 women) underwent SERT imaging with 11C[DASB]-PET and performed saliva home-sampling of the cortisol awakening response. The cortisol awakening response (area under curve with respect to increase from baseline, AUCi) correlated positively with prefrontal SERT in a model adjusting for age and genotype ($p = 0.01$). The correlation was not accounted for by age, gender, BMI, personality, SERT promoter genotype, perceived stress, or seasonality (daylight minutes at scan). No significant correlation was demonstrated in midbrain ($p = 0.48$), pallidostriatum ($p = 0.17$), or occipital cortex ($p = 0.88$). However, a trend was observed in anterior cingulate ($p = 0.07$). Individuals carrying the s- or L_G "stress-vulnerable" alleles of the SERT promoter gene did not show a stronger coupling between frontal SERT binding and the cortisol awakening response as tested by an interaction analysis. Our results are consistent with the hypothesis that prefrontal serotonergic neurotransmission is coupled with basal stress reactivity in healthy individuals. This coupling might be established through early neurodevelopment and seems not to be modified by SERT promoter genotype in the adult brain of mentally healthy individuals.

S.07.02 In vivo measurements of brain serotonergic markers and analysis of drug use profiles among recreational ecstasy and hallucinogen users

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The aim of the current study was (1) to compare substance user profiles for MDMA (3,4-methylenedioxy-N-methamphetamine – ecstasy) preferring (MPU) and hallucinogen preferring users (HPU), and (2) in subgroup of these users to separate presynaptic (MDMA) from postsynaptic (MDMA and hallucinogens) drug effect on in-vivo serotonergic markers using PET (positron emission tomography) [1].

Ninety-eight young recreational Danish drug users (26±5 y.o., 85 males) reporting minimum 15 illicit drug experiences and use of MDMA/hallucinogens within the last year were included and divided in MPUs ($n = 50$) and HPUs ($n = 48$) based on the relative number of lifetime exposures. A subgroup of 14 MPUs and 10 HPUs and a group of 21 non-using control subjects underwent [F-18]altanserin-(5-HT_{2A})- and [11-C]DASB-(SERT)-PET.

Compared to HPUs, more MPUs reported drug use at parties, in binges, administration of MDMA as tablets rather than powder, and co-use of stimulants. When compared to non-users, significant decreases in SERT binding were seen in MPUs (neocortex: −59%, pallidostriatum: −19%) but not in HPUs. The SERT binding was negatively correlated to the number of lifetime MDMA exposures, and the time of abstinence from MDMA was positively correlated to subcortical but not to cortical SERT binding. A small decrease in neocortical 5-HT_{2A} binding in the total drug user group was also detected.

Since MDMA but not hallucinogen use was found to be associated with decreases in cerebral SERT binding, our data suggest that this effect is mediated through a direct presynaptic MDMA effect rather than by the 5-HT_{2A} agonistic effects of MDMA.

References

[1] Erritzoe D., Frokjaer V.G., Holst K. K., Christoffersen M., Johansen S.S., Svarer C., Madsen J., Rasmussen P.M., Ramsøy T., Jernigan T.L., Knudsen G.M., 2011. In vivo imaging of cerebral serotonin transporter and 5-HT2A receptor binding in MDMA and hallucinogen users. Manuscript accepted for publication in Archives of General Psychiatry.