

P.1.g.005 Psilocybin-induced decrease in amygdala-putamen coupling during an event-related face discrimination task

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Background: Psilocybin is a modulator of amygdala activity presumably via its 5HT1A/2A agonistic properties. We have recently shown that reduced amygdala activity during threat processing might underlie psilocybin's effect on emotional processing in a block-design paradigm [1]. In this study, we investigated psilocybin's effects in an event-related face discrimination task in n=18 healthy volunteers who received psilocybin and placebo in a cross-over design. Face discrimination of emotional faces relies on both prefrontal as well as subcortical structures, namely the amygdala. We hypothesized that the amygdala activity alone or as part of a network is altered during psilocybin application. This could manifest in altered salience of emotional face-processing in task activity or in task-related connectivity of the amygdala.

Methods: Using a randomized, double-blind, placebo-controlled, cross-over design, subjects received either placebo or 0.16 mg/kg oral psilocybin in two separate imaging sessions at least 14 days apart (as reported in [1]). We used functional magnetic resonance imaging, beta-series connectivity and graph-theory network analysis to characterize effective connectivity during categorization of angry, fearful or happy affective faces in contrast to affective neutral faces in the brain. As the amygdala is a key target for psilocybin's effect during emotion processing, we used the left and right amygdala as a-priori region-of-interest seed masks for the connectivity analysis.

Results: Psilocybin (in contrast to placebo) increased reaction time for all three categories of affective stimuli in comparison to neutral stimuli. The rate of correctly recognized hits did not differ between face categories and between placebo and psilocybin. The face discrimination task demonstrated in the placebo condition a robust signal of visual cortex, fusiform cortex, limbic system namely the amygdala, prefrontal and motor cortices. During the face categorization task, there was a tendency for a stronger striatal activation during the angry face condition under psilocybin, but no difference for fearful or happy faces. During psilocybin, a beta-series connectivity analysis of the left-amygdala seed ROI showed a decrease in the connectivity with the striatum (mainly left putamen, cluster-corrected pFDR<0.03). This was not found during the happy or fearful face condition. On a behavioural level, the rate of correct classified angry faces correlated with the coupling between amygdala and putamen. The coupling correlated negatively with the sum score of altered states (TAS: $r=0.57$, $p=0.015$) and with anxiety ($r=0.51$, $p=0.03$) during psilocybin intake.

Conclusion: In summary, psilocybin alters subcortical limbic networks during processing of angry faces in comparison to neutral faces. During psilocybin, the coupling between amygdala and putamen is decreased. This points to a change in salience-evaluation of angry faces, which is partly supported by the behavioral effect. The stronger coupling between amygdala and putamen during angry face discrimination, the lower the anxiety rating during psilocybin. Therefore, our results support further that

psilocybin not only alters amygdala activity but exerts downward effects in the striatum.

References

- [1] Kraehenmann, R., Preller, K.H., Scheidegger, M., Pokorny, T., Bosch, O.G., Seifritz, E., Vollenweider, F.X., 2015. Psilocybin-Induced Decrease in Amygdala Reactivity Correlates with Enhanced Positive Mood in Healthy Volunteers. *Biol Psychiatry*. Oct 15; 78(8): 572–81. doi:10.1016/j.biopsych.2014.04.010. Epub 2014 Apr 26.

P.1.g.006 Comparison of lipid levels in acutely admitted psychiatric patients using different psychotropic drugs

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Introduction: Recent investigation has focused on the negative impact of psychotropic drugs on the somatic health for psychiatric patients, such as increased risk of diabetes 2, cardiovascular diseases, over-weight and metabolic syndrome [1]. Especially patients with psychotic disorders have been addressed. Changes in lipid values, primarily high triglycerides (TG) and low high density lipoprotein (HDL) have been reported to be associated with such adverse somatic conditions.

Aim of this study was to investigate whether there were differences in serum lipid levels measured at admittance between drug-free patients and patients on medication, based on which drug the patients were using.

Method: The study was conducted in the emergency psychiatric ward at Ålesund Hospital which is located at the west coast of Norway and with a catchment area of 125 000 inhabitants [2]. All acutely admitted patients (n=489) during one year (2006–07) were invited to participate, and about half of the patients (n=254, 52%) gave written consent and were included.

Current medication and current substance or drug abuse was recorded at admission, and the consenting patients gave a fasting blood sample within the first three days after admission. Patients using statins (n=9) were excluded from the study. Total cholesterol (TC), HDL and TG were analyzed in serum in mmol/litre.

Patients were divided into groups on the basis of the current medication at admission; one group for each drug. Reference group was patients without medication or drugs at admission. If one patient used more than one psychotropic drug, his serum lipid levels were included in the analyses for each of the drugs he used. Student's t-test was used to compare lipid values. All analyses were two-tailed with unequal variances.

Results (preliminary): Mean age was 43 years, 54% were men and 46% women. Lipid levels of patients without medication at admittance in mmol/litre (reference group, n=89) were: TC = 4.94, HDL = 1.26 and TG = 1.28. Compared with the reference group, lipid measures for all patients on psychotropic drugs (n=160) were 5.43 (P=0.005), 1.37 (ns) and 1.42 (ns), respectively.

The following single drugs had significantly different lipid levels compared with the reference group: Escitalopram (n=30) higher TC = 5.60 (P=0.011) and higher HDL = 1.61 (P=0.035); mirtazapine (n=25) higher TC = 5.91 (P=0.003); and risperidone (n=10) lower HDL = 1.02 (P=0.024). No other drug groups (including olanzapine (n=18) and quetiapine (n=17)) differed significantly from the reference group.

Conclusion: Except for a few drugs, we found no associations between each of the drugs and deviant lipid values. However,