Noradrenergic and serotonergic modulation of the processing of emotional pictures

A. Brühl[1], T. Kaffenberger[2], L. Jäncke[3], U. Herwig[1]

[1]Clinic for General and Social Psychiatry, Psychiatric University Hospital Zürich, Switzerland
[2]Department of Neurology, University Hospital Zürich, Switzerland
[3]Department of Neuropsychology, University of Zürich, Switzerland

Psychiatrische Universitätsklinik Zürich

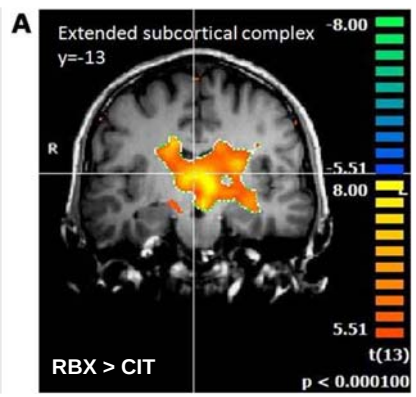
Aims

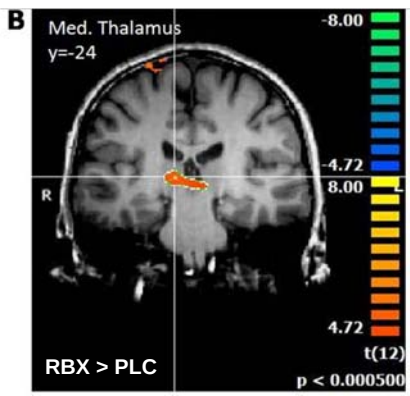
- to uncover brain regions modulated by noradrenergic and serotonergic antidepressants
- to differentiate noradrenergic and serotonergic influences onto brain activity during the perception of emotional pictures
- previous study [1] during the anticipation of emotional pictures: noradrenergic modulation in primarily thalamic, serotonergic effects prominent in prefrontal and insular regions; parieto-occipital areas modulated by both neurotransmitter systems

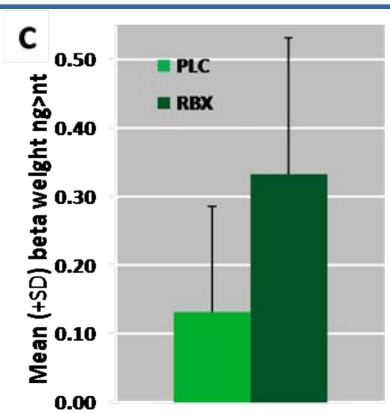
→ Final goal: to find markers potentially predictive of response to noradrenergic or serotonergic antidepressants

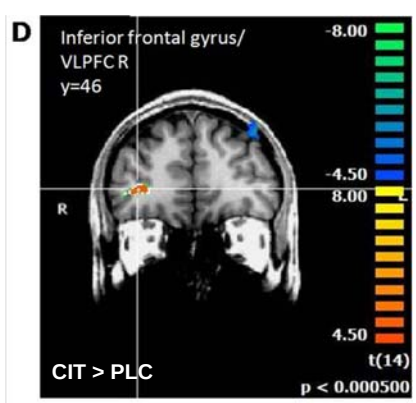
Methods

- Design: single-blind, pseudo-randomized, placebo-controlled, cross-over, functional magnetic resonance imaging (fMRI).
- Subjects: 21 subjects (16 analyzable).
- Treatment: single doses of either 40 mg citalopram (CIT, selective serotonergic reuptake inhibitor (SSRI)), 8 mg reboxetine (RBX, selective noradrenaline reuptake inhibitor (SNARI)) or placebo (PLC) 2-3 h before fMRI (at peak plasma level)
- Task: 56 trials, cued anticipation and perception of negative (ng), positive and neutral (nt) pictures from the International Affective Pictures System (IAPS)
- FMRI-analysis: Repeated measures ANOVA with the factors 'treatment' (CIT/RBX/PLC) and 'task' (contrasts ng>nt and ps>nt for emotional specificity).
- Main contrasts: CIT>PLC, RBX>PLC, RBX>CIT. Statistical level p<0.0005 versus PLC, p<0.0001 in the comparison RBX>CIT.









Results

1) RBX versus CIT:
activity ↑: prefrontal, occipital, cerebellar regions, extended subcortical region including midbrain, amygdala, caudate, thalamus and striatum (fig. A).

2) RBX versus PLC:
activity ↑: medial prefrontal, occipital regions, caudate, medial thalamus (fig. B + C, Cohen's d: 1.63).

3) CIT versus PLC:
activity ↓: left DLPFC, left precuneus, occipital regions.
activity ↑: bilateral ventrolateral prefrontal cortex (fig. D).

Conclusion

- differential modulation of the processing of emotional information by pretreatment with Citalopram (SSRI) and Reboxetine (SNARI)
- strong effect of noradrenergic modulation on emotion processing brain areas as thalamus, amygdala and prefrontal cortex
- serotonergic effects only in prefrontal regions
- previous studies: decreased amygdalar activity after acute application of Citalopram [2], increases after Reboxetine [3]
- anticipation of emotional pictures [1]: effect of Citalopram on prefrontal and insular regions, Reboxetine modulated thalamus, amygdala and midbrain regions

→ first study directly comparing the effects of acute serotonergic and noradrenergic modulation in the whole brain
→ identification of differential targets of these antidepressant mechanisms, could provide a basis for neurobiological reasons for differential treatment of depression

[1] Brühl A.B., Kaffenberger T., Herwig U. (2010). *Neuropsychopharmacology* 35, 521-533
[2] Murphy S.E., Norbury R., O'Sullivan U., Cowen P.J., Harmer C.J. (2009). *British Journal of Psychiatry* 194, 535-540
[3] Onur O.A., Walter H., Schlaepfer T.E., Rehme A.K., Schmidt C., Keysers C., Maier W., Hurlemann R. (2009). *Social Cognitive and Affective Neuroscience* 4, 119-126;

Contact: Dr. A. Brühl, Psychiatric University Hospital Zürich, Militärstrasse 8, CH-8021 Zürich, Switzerland, E-Mail: annette.bruehl@puk.zh.ch
This study was funded by a grant from the Swiss National Funds granted to U. Herwig (SNF-No. 3200B0-112 631).