Joint Meeting of the Austrian Neuroscience Association (13th ANA Meeting) and the Austrian Pharmacological Society (19th Scientific Symposium of APHAR)
Vienna, Austria, 16–19 September 2013

ABSTRACT

A4.4

Ketamine-induced time-dependent modulation of the thalamo-cortical network in healthy volunteers

Anna Höflich[1], Andreas Hahn[1], Georg S. Kranz[1], Thomas Vanicek[1], Christian Windischberger[2], Siegfried Kasper[1], Dietmar Winkler[1] and Rupert Lanzenberger[1,*]

[1]Department of Psychiatry and Psychotherapy, Medical University of Vienna, Austria; [2]MR Center of Excellence and Center of Medical Physics and Biomedical Engineering, Medical University of Vienna, Austria

Background: A number of studies have described disturbances of thalamic functioning in schizophrenia [1]. In the light of recent evidence suggesting a significant impact of the glutamatergic system on key symptoms of this disorder, we aimed to assess whether changes in thalamic functional connectivity are driven by alterations of the glutamatergic system. Using ketamine, a selective NMDA receptor antagonist, we assessed time-dependent changes of functional connectivity before, during and after intravenous application of a subanaesthetic dose of esketamine using long-term resting-state functional MRI (fMRI). We specifically aimed to analyse ketamine-induced effects on cortico-thalamic functional connections.

Methods: Thirty healthy volunteers (25 ± 4.6 years, 18 males) underwent two fMRI sessions in a double-blind, placebo-controlled study design. Subjects underwent a resting-state fMRI scan lasting for 55 minutes. During fMRI either esketamine hydrochloride (mean dose 15.5 ± 3.1 mg) or placebo (0.9% saline solution) was applied intravenously over a time period of 20 minutes using a fully automated MRI-compatible infusion system. Resting-state measurements were performed at 3 Tesla (Siemens Trio, Erlangen, Germany) using single-shot gradient-recalled EPI with TR / TE = 1800 / 38 ms, a matrix size of 128 × 128 voxel and a field-of-view of 190 × 190 mm. Preprocessing was performed as described previously [2] using SPM8 (www.fil.ion.ucl.ac.uk/spm). For the calculation of thalamo-cortical connectivity the cortex was divided in non-overlapping regions of interest (prefrontal cortex, motor cortex / supplementary motor area, somatosensory cortex, temporal lobe, posterior parietal cortex, occipital lobe—based on the automated anatomical labeling atlas (AAL)) and used as seed regions in a seed–voxel correlation analysis.

Results: Analysis revealed significant increase of cortico-thalamic connectivity of the somatosensory and temporal cortex. Immediately after the start of the ketamine infusion a significant increase in functional connectivity of the postcentral gyrus with the ventrolateral region of the thalamus was observed, with significant difference to the placebo condition ($p < 0.05$, FWE-corrected). The analysis of temporo-thalamic connections revealed a ketamine-associated increase of the temporal seed region with the medial dorsal nucleus. Again, differences between the ketamine scan and the placebo scan were present shortly after start of the ketamine application ($p < 0.05$, FWE-corrected). For both seed regions, effects of esketamine on cortico-thalamic connectivity were evident during the entire duration of the ketamine infusion and the following 2.5 minutes.

Discussion: Our results point toward the fact that changes of thalamic functioning as described for schizophrenia can be partly mimicked by NMDA receptor blockage. This adds substantial knowledge about the neurobiological mechanisms underlying the profound changes of perception and behaviour during the application of NMDA receptor antagonists.

Acknowledgements: This research was funded by Austrian National Bank (grant 14193).

References

1. Woodward ND, Karbasforoushan H, Heckers S: **Thalamocortical dysconnectivity in schizophrenia.** *Am J Psychiatry,* 2012; 169(10):1092–1099.
2. Hahn A, Wadsak W, Windischberger C, Baldinger P, Höflich AS, Losak J, Nics L, Philippe C, Kranz GS, Kraus C, Mitterhauser M, Karanikas G, Kasper S, Lanzenberger R: **Differential modulation of the default mode network via serotonin-1A receptors.** *Proc Natl Acad Sci USA,* 2012; 109(7):2619–2624.

Presenting author underlined,
*denotes corresponding author.