ABSTRACT

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Missing short-term influence from ketamine on gray matter
Sebastian Ganger1, Anna Höflich1, Andreas Hahn1, Natalia Lipskaia1, Christian Windischberger1 and Rupert Lanzenberger1,*
1Department of Psychiatry and Psychotherapy, Medical University of Vienna, Austria; 2Center for Medical Physics and Biomedical Engineering, Medical University of Vienna, Austria

Background: Voxel-based morphometry (VBM) of structural MRI data has become a useful tool to investigate pathological alterations and longitudinal changes of gray matter volume. A recent pharmacological challenge demonstrated reversible short-term effects even within a few hours [1]. In this work, we investigated the effect of ketamine-infusion on VBM estimates of the gray matter.

Methods: In this study 28 subjects (15 female) aged 24.8 ± 4.6 years, underwent MRI in a Siemens Trio 3 Tesla scanner. T1-weighted structural images were acquired using a MPRAGE sequence, with a resolution of 1.1 mm × 1 mm × 1 mm (matrix = 160 × 240 × 256 voxel). All subjects underwent a placebo-controlled cross-over trial, comprising two measurement sessions (verum and placebo), each consisting of two runs (before and after infusion). The first run of each session was acquired before, and the second run after intravenous administration of either ketamine (esketamine hydrochloride, mean dose 15.0 ± 3.0 mg) or placebo (0.9% saline solution). The delay between the two structural scans was about 95 min, during which additional functional scans were acquired. T1-weighted images were segmented using VBM8's DARTEL algorithm. Statistical inference was made using repeated-measures ANOVA, correcting for multiple comparisons with the family-wise error rate at p < 0.05.

Results: There was no significant interaction of drug administration with time, indicating no direct effect before versus after ketamine infusion as compared to placebo, yet there was a significant effect of time (i.e. pre- vs. post-injection) independent of ketamine or placebo administration. Here, decreases in gray matter volume were observed within the superior frontal cortex (t = 7.62) and bilaterally in the inferior temporal lobe (t = 7.11).

Discussion: It has been shown previously that VBM can reveal gray matter differences after pharmacological challenge with a dopamine D2 antagonist [1]. However, we were not able to reproduce similar short-term effects of ketamine although this drug has been shown to elicit neuroplasticity effects via the NMDA receptor [2]. The missing validation of previously reported short-term changes in gray matter volume may in part relate to the different study drugs used. However, taking into account that both ketamine and placebo infusion induced gray matter decreases, one needs to consider that such short-term differences in VBM metrics could also be explained by the infusion effect per se. Similarly, it remains to be investigated whether the effects observed here are caused by physiological and/or scanner-specific artefacts, as the MRI signal in brain areas close to air cavities is sensitive to signal loss.

References