

**Appendix 1** to Thiebes S, Leicht G, Curic S, et al. Glutamatergic deficit and schizophrenia-like negative symptoms: new evidence from ketamine-induced mismatch negativity alterations in healthy male humans. *J Psychiatry Neurosci* 2017.

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#### *Source analysis of MMN (LORETA)*

LORETA assumes that the smoothest of all activity distributions is most plausible ("smoothness assumption") and therefore, a particular current density distribution is found.<sup>1</sup> This fundamental assumption of LORETA directly relies on the neurophysiological observation of coherent firing of neighbouring cortical neurons during stimulus processing<sup>1-4</sup> and therefore can be seen as a physiologically based constraint. However, this coherent firing has been described on the level of cortical columns, which have a much smaller diameter than the voxels used in the LORETA software; the empirical basis for coherent firing in the millimetre range is not strong enough to fully accept this constraint as a physiological one, even if it might help to produce useful results. The characteristic feature of the resulting solution is its relatively low spatial resolution, which is a direct consequence of the smoothness constraint. Specifically, the solution produces a "blurred-localized" image of a point source, conserving the location of maximal activity, but with a certain degree of dispersion. It should be emphasized that this solution will typically produce a "blurred-localized" image of arbitrary distributions due to the principle of superposition. However, some distributions of point sources may superpose in such a way that they actually cancel out on the scalp and therefore cannot be correctly localized by any method. The version of LORETA used in the present study used the digitized Talairach atlas<sup>5</sup> available as digitized MRI from the Brain Imaging Center, Montreal Neurologic Institute, estimating the current source density (microAmperes/mm<sup>2</sup>) distribution for either single timepoints or epochs of brain electric activity on a dense grid of 6239 voxels at 5 mm spatial resolution.<sup>6</sup>

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*Table S1*

Means and standard deviations of the PANSS scores

PANSS scores	Baseline		Placebo		Ketamine	
	Mean	SD	Mean	SD	Mean	SD
<b>Total</b>	30.46	0.93	31.04	1.37	53.93	10.72
<b>Positive</b>	6.96	0.62	6.96	0.69	11.54	3.86
<b>Negative</b>	8.00	0.00	8.13	0.34	14.33	4.43
<b>Disorganization</b>	10.21	0.42	10.42	0.72	19.67	5.18
<b>Excitement</b>	8.31	0.45	8.38	0.58	11.58	2.59
<b>Distress</b>	8.31	0.45	8.38	0.65	12.63	3.15

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*Table S2*

Means and standard deviations of the 5D-ASC scores

5D-ASC scores	Placebo		Ketamine	
	Mean	SD	Mean	SD
<b>Total</b>	172.65	269.61	2764.80	1316.58
<b>Oceanic boundlessness (OBN)</b>	19.75	43.95	820.70	451.54
<b>Visionary restructuralization (VRS)</b>	26.27	59.11	606.36	371.51
<b>Dread of ego dissolution (DED)</b>	31.02	32.76	560.41	427.72
<b>Vigilance reduction (VIR)</b>	81.72	109.69	567.55	279.26
<b>Auditory alterations (AUA)</b>	14.99	55.67	202.04	252.23

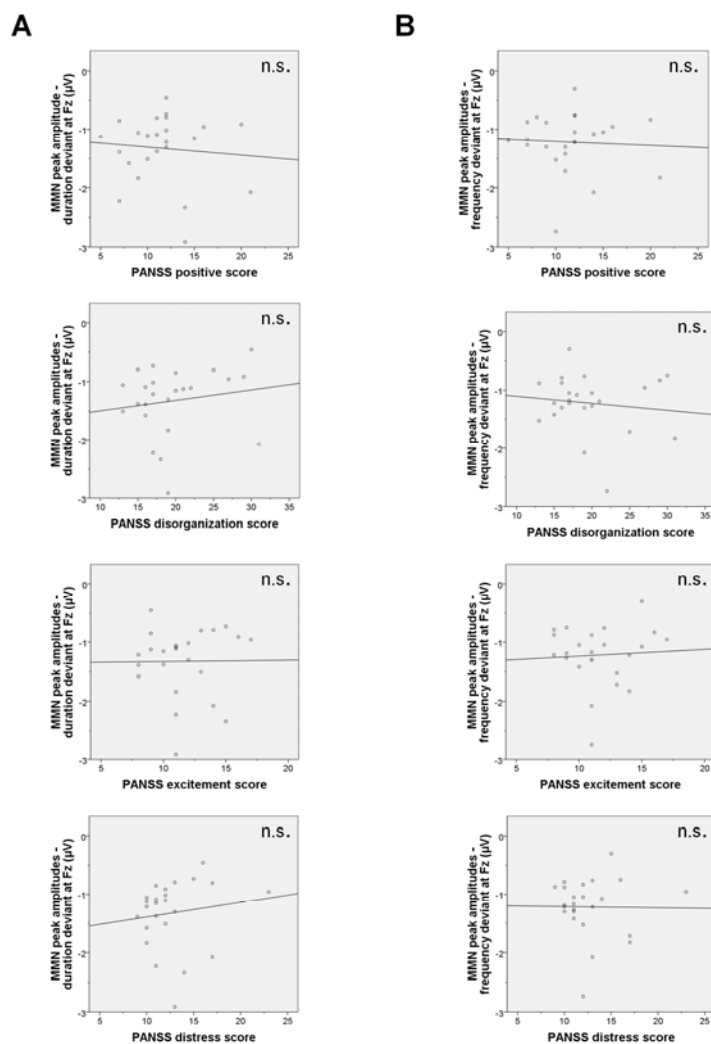
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Figure S1

Scatterplots illustrating the MANOVA results, with MMN amplitude of the duration deviant (A) and MMN amplitude of the frequency deviant (B) as dependent variables and the four PANSS factors: positive, disorganization, excitement and distress.



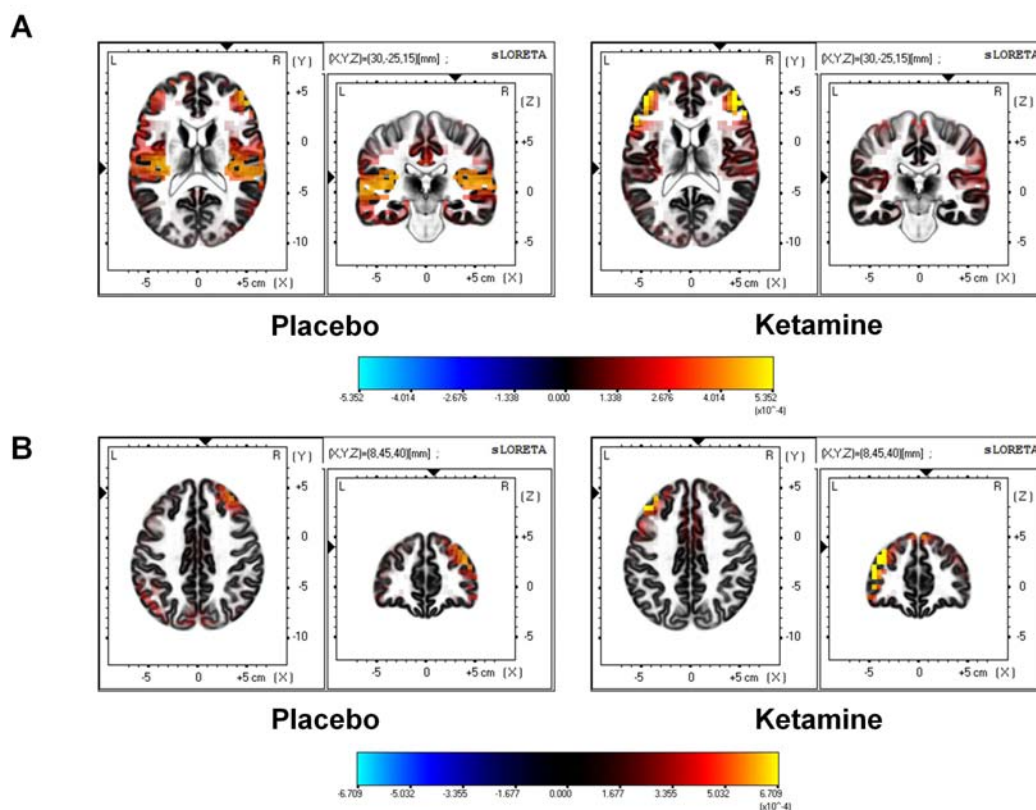
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**Figure S2**

LORETA CSD results for the placebo and the ketamine condition separately of the early MMN (A) and the late MMN (B) for the frequency deviant.



## References

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