

HOW KETAMINE CHANGES NEUROPHYSIOLOGY OF DEPRESSIVE PATIENTS BRAINS - RANDOMIZED CONTROLLED TRIAL

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OBJECTIVE

Administration of subanesthetic doses of non-competitive NMDA (N-methyl-D-aspartic acid) antagonist, ketamine hydrochloride, led in numerous studies to the rapid onset (hours), but relatively shortly detectable (days) antidepressant-like effect [1]. Maximum of mood improvement within the period from 2 hours to 3 days was significantly better on ketamine than on placebo. Functional imaging studies found out consistently abnormal type of metabolism or perfusion in dorsolateral prefrontal cortex and/or in anterior cingulate cortex in depressive depression. Both structures are functional and neuroanatomically linked. Theta activity (4-8 Hz) scanned in EEG from prefrontal regions reflects both dorsolateral prefrontal cortex activity and projection of rhythms generated in anterior cingulum. Increased glucose metabolism in rostral part of anterior cingulum (Brodmann area 24/32) before a treatment predicate the response and hyperactivity (higher current density in theta frequency band) in the same regions is connected with the response rate in depressive patients. These findings support also QEEG (quantitative electroencephalography) cordance, measuring a regional cerebral activity. QEEG cordance computing combines complementary information of absolute and relative EEG spectrum in algorithm that was developed in half nineties on UCLA (University of California, Los Angeles) by Leuchter and Cook. Cordance value correlates with regional cerebral perfusion and metabolism much better than the other QEEG indicators. Previous studies demonstrated predictive value of prefrontal QEEG cordance reduction in depressive patients treated with different antidepressants. Congruently with previous findings we hypothesized in our compressed model decrease of prefrontal QEEG theta cordance in 10 minutes of ketamine hydrochloride infusion as the prediction of antidepressant response in following day.

METHODS

14 depressive disorder patients (6 female and 8 male) diagnosed with a moderate to severe depressive episode without psychotic symptoms (F32.1, F32.2 according to ICD-10) on constant antidepressant medication were included [table 1]. All of the participants received single infusion with subanesthetic dose of ketamine hydrochloride solution (0.54mg/kg). Depressive symptoms and overall clinical state was assessed using MADRS (Montgomery-Åsberg Depression Rating Scale) and BDI (Beck Depression Inventory) [schema 1]. Response to treatment was defined as equal to or more than 50% reduction of MADRS scores. EEG measurements on the baseline, after 10 and 30 minutes of infusion were taken into account in computation of prefrontal QEEG theta cordance [schema 2].

RESULTS

There were 64.3% (9) of subjects who responded to single ketamine hydrochloride infusion following day [graph 1]. 88.9% (8) of responders decreased prefrontal QEEG theta cordance. No significance appeared in repeated measures ANOVA ($F_{2,36}$; $df=2,24$; $p<0.11$), nevertheless subsequent pair comparison found significant difference in cordance values between baseline and after 10 minutes of ketamine infusion in responders ($F=4.12$; $p<0.003$) without correction for repeated measures [graph 2].

CONCLUSIONS

Preliminary results have shown the higher tendency of prefrontal QEEG cordance to decrease in ketamine responders. These results imply predictive function of prefrontal QEEG theta cordance even in the compressed model. Combination of latest QEEG method and fast-acting antidepressant-like effect of ketamine in this trial is unexampled.

LIMITATIONS

Larger sample size is needed to increased precision in estimates of cordance sensitivity and specificity.

REFERENCES

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Table 1

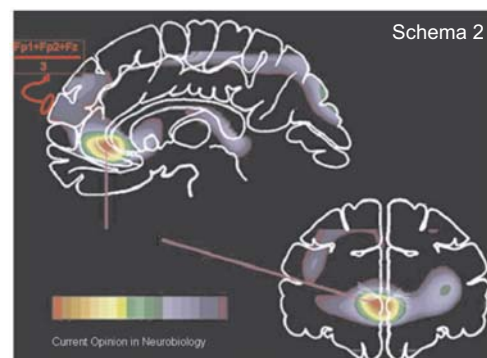
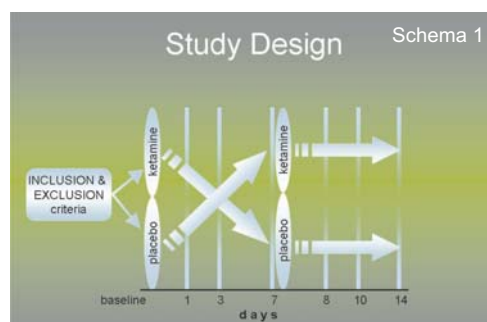
Demographic and clinical characteristics

	responders (N=9)	non-responders (N=5)
Age (years)	38.9 ± 7.1	36.3 ± 4.9
Sex (male/female)	6 / 3	3 / 2
Handedness (R/L)	9 / 0	5 / 0
MADRS (baseline)	26.5 ± 3.7	26.2 ± 4.3
MDD treatment (years)	10 ± 7.5	18 ± 6.0

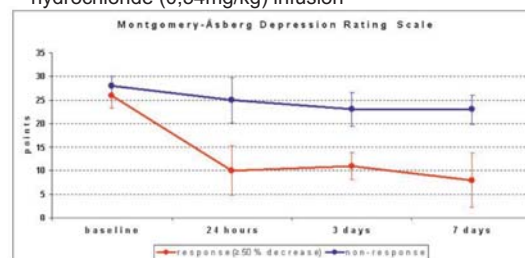
Results are reported as account or mean ± SD (standard deviation)

MADRS - Montgomery-Åsberg Depression Rating Scale

MDD - Major Depressive Disorder



Graph 1 Objective scale changes after single ketamine hydrochloride (0.54mg/kg) infusion



Graph 2 QEEG Cordance Values During Ketamine Infusion

