

Guidance of treatment with the biomarker prefrontal theta cordance in rapid eye movement sleep improved response rates in Major Depression

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BACKGROUND

- Antidepressant treatment (AD) of Major Depression (MDD) is associated with delayed treatment effects and unsatisfactory response rates.
- About 50% of the patients with MDD are non-responders to the initial treatment trial.
- There is a need for biomarkers to predict the risk of non-response as early as possible, in order to intensify treatment immediately to increase final response rates.
- One of the most accurate biomarkers to determine treatment response as early as at week one is the prefrontal Theta-Cordance in rapid eye movement (REM) sleep (R-pfTC).
- The R-pfTC is a quantitative EEG measure computed from prefrontal absolute and relative theta power in tonic REM-sleep, correlating with frontocingulate brain activity.

AIM: Examine, if providing the prediction of R-pfTC prospectively and as early as at week 1 and changing the antidepressant medication in case of predicted non-response would (1) rescue predicted non-responder from non-response at week 5, and (2) increase the overall response rate at week 5.

METHODS

- 37 adult male and female in-patients with major depressive disorders randomly assigned either to the intervention condition (IG, N = 22, mean age: 39.5 years; 45.5 % females) or the control condition (CG, N = 15, mean age: 45.4 years; 46.7 % females).
- IG and CG were matched for gender, age and severity of depression.
- Depressive symptoms were first assessed at baseline before beginning of the AD medication with Hamilton Depression Rating Scale (HDRS).
- The R-pfTC was assessed from a polysomnogram as early as at week 1.
- Only in the IG, the cordance was provided prospectively to the psychiatrist in charge for guidance of treatment: In case of predicted non-response, AD treatment strategy was immediately adapted, whereas in case of predicted response treatment strategy was maintained.
- Response to treatment at week five was defined as a $\geq 50\%$ reduction of baseline HDRS score.

RESULTS

- IG did not differ from CG in gender distribution ($p = .94$), mean age ($p = .15$) or baseline HDRS scores (21.1 ± 5.9 vs. 22.3 ± 7.7 , $p = .93$).
- In cases in which R-pfTC predicted non-response at week 1, and physicians modified antidepressant treatment immediately, there was a 85.7% chance of response at week 5 instead of 20% in the CG, where the prediction of non-response by cordance was only retrospectively available (ANOVA for R-pfTC predicted non-responders: time x group: $F = 4.18$, $p = .03$, $\eta = .29$ [L]).
- In contrast, in cases in which R-pfTC predicted response and medication was continued without change, the response rate did not differ from that of cases with positive R-pfTC in CG (ANOVA for R-pfTC predicted responders: time x group: $F = .26$, $p = .77$).

- Overall treatment response rates were 16/22 (72.7 %) in the IG vs. 9/15 (60 %) in the CG (OR = 1.77, 95% CI: 0.44-7.17, $p = .48$). Due to the limited power of the study, the descriptive trend for higher overall response rate in the IG did not reach the significance level.

CONCLUSIONS

- Prefrontal theta cordance in REM sleep seems to be a promising biomarker for response prediction in a naturalistic in-patient setting.
- The preliminary results suggested that R-pfTC has the capability to increase treatment response by helping to avoid non-response through early change of treatment strategy.
- The power of these preliminary results of this on-going study is still insufficient to prove that overall response rates would increase by application of R-pfTC treatment guidance.

