Target-based biomarker selection - Mineralocorticoid receptor-related biomarkers and treatment outcome in major depression.

Abstract:
Aldosterone and mineralocorticoid receptor (MR)-function have been related to depression. We examined central and peripheral parameters of MR-function in order to characterize their relationship to clinical treatment outcome after six weeks in patients with acute depression. 30 patients with a diagnosis of major depression were examined 3 times over a 6 week period. Aldosterone and cortisol saliva samples were taken at 7.00 a.m. before patients got out of bed. Easy to use e-devices were used to measure markers of central MR function, i.e. slow wave sleep (SWS) and heart-rate variability (HRV). Salt-taste intensity (STI) and salt pleasantness (SP) of a 0.9% salt solution were determined by a newly developed scale. In addition, systolic blood pressure (SBP) and plasma electrolytes were determined as markers for peripheral MR activity. The relationship between the levels of these biomarkers at baseline and the change in clinical outcome parameters (Hamilton depression rating scale (HDRS)-21, anxiety, QIDS and BDI) after 6 weeks of treatment was investigated. A higher aldosterone/cortisol ratio (Aldo/Cort) (n = 17 due to missing values; p<0.05) and lower SBP (n = 24; p< 0.05) at baseline predicted poor outcome, as measured with the HDRS, independent of gender. Only in male patients higher STI, lower SP, lower SWS (all n = 13) and higher HRV (n = 11) at baseline predicted good
Likewise, in male patients low baseline sodium appears to be predictive for a poor outcome (n = 12; p = 0.05; based on HDRS-6). In conclusion, correlates of higher central MR-activation are associated with poorer clinical improvement, particularly in men. This contrasts with the finding of a peripheral MR-desensitization in more refractory patients. As one potential mechanism to consider, sodium loss on the basis of dysfunctional peripheral MR function and additional environmental factors may trigger increased aldosterone secretion and consequently worse outcome. These markers deserve further study as potential biological correlates for therapy refractory depression.