

Neuroimaging and Blood Biomarkers as Indicators of Ketamine Efficacy in Treatment Resistant Depression (NeuroMarket)

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Major Depressive Disorder (MDD) is highly chronic with treatment resistance in 30% of patients (TRD). Increasing use of the NMDA antagonist ketamine, an efficient antidepressant (AD), needs to be balanced by side effects particularly in the target group of severe depression. Here, clinical decisions lack estimation on patients' individual benefit.

We will validate a combination of AD response biomarkers focusing on peripheral and central mechanisms associated with glutamatergic plasticity. Ketamine was shown to rectify altered glutamate levels, dampened mTOR pathway, decreased BDNF and increased acetylated alpha-tubulin. Markers will thus assess these sources of disturbed brain networks which show a plastic modification early after successful treatment. Pretreatment biomarkers are monitored after ketamine to assess changes and their potential as active probes for individual improvement. Efficacy of the combination of peripheral BDNF, Tubulin and mTOR

regulated proteome with non-invasive MRI markers of glutamate and brain connectivity is compared to a newly established blood biomarker. Markers correspondence is tested across existing datasets and within a prospective trial. Animal and human studies align in timepoints, models and modalities. Focusing on a fundamental pathophysiological signature we will contribute to validated stratification and response monitoring and rely on established collaborations combining latest technological advances on proteomics and neuroimaging.