Statistical Analysis Plan

Modulation of GABA-A Receptors in Parkinson Disease-Transdermal Flumazenil Arm

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In this proposal, the investigators present data suggesting that continuous administration of transdermal flumazenil treatment leads to a decrease in axial motor symptoms of Parkinson's disease (PD). Our first outcome measure was general motor impairment related to PD, which was operationalized as the total Motor Disorder Society Unified Parkinson's Disease Rating Scale (MDS UPDRS) motor rating. Our second outcome measure was axial motor impairment, which was operationalized as MiniBEST dynamic balance sensory sub-score.

Our a-prior hypothesis for both outcome measures was that the effect of visit (1st day, 7th day, 14th day) on motor outcome would depend on treatment group (placebo vs. flumazenil). To test this hypothesis with our within-subject dataset, a pair of random-intercept mixed linear models was fitted, a visit model and an interaction model. Visit model included a fixed effect of visit and a random intercept by participant to account for baseline differences in motor outcome. Interaction model added a treatment by visit interaction term on top of the visit model. Null hypothesis was that the added visit by treatment interaction does not explain significant additional variance in motor outcome scores. Likelihood ratio test comparing the interaction model to the visit model was used to derive a p-value.