Statistical Analysis Plan & Power

Before any specific statistical techniques are applied, we will examine all variables at all time points for illegitimate values, outliers, and other inconsistencies. Distributions of demographic variables and other clinically important baseline variables will be examined and summarized by means, standard deviations, minima, and maxima for continuous measures and proportions for categorical measures. We will make every effort to obtain all data to reduce or eliminate missing data issues. Intent-to-treat analysis will be implemented for all estimation and testing. Tests will be two-sided and statistical significance determined by $p < 0.05$.

R61 Component. Summaries of clinical and demographic variables will be provided for each of the three cohorts (C1) D-serine 80mg/kg (n = 12) vs. placebo (n = 3), (C2) D-serine 100mg/kg (n = 12) vs. placebo (n = 3), and (C3) D-serine 120mg/kg (n = 12) vs. placebo (n = 3). As a precaution, any indication of imbalance on important baseline measures between treatment arms (despite randomization) will trigger investigation of whether differences in the primary outcome measures are attributable to these imbalances. For analyses described below, the placebo groups from each of the three cohorts will be combined to yield an effective placebo group of n = 9, unless descriptive analyses suggest systematic differences between the three placebo groups, in which case the groups will remain separate in subsequent analyses.

Aim 1 Analysis: Aim 1 hypothesizes that D-serine will lead to greater plasticity, MMN, and theta-ITC changes than placebo, with the largest effect being seen at the 120mg/kg dose. Plasticity improvement (defined as change from trials 20 – 30 to trials 70 – 80 at end of session) in the 3rd week of treatment will be examined by using Cohen's d effect size estimates. Within each D-serine group, Cohen's d for within-subject change will be computed by taking the mean change in plasticity divided by the pre-treatment standard deviation. Similar Cohen's d values will be computed for the combined placebo group. Corresponding 95% confidence intervals (based on standard theory or constructed via bootstrapping if assumptions for constructing the confidence intervals based on parametric methods are not satisfied) will be computed. Similar procedures will be followed for assessing within-subject changes in MMN and theta-ITC. For each D-serine dose level, Cohen's d for between-group differences will be computed as (mean change for the D-serine group minus mean change for the placebo group) divided by standard deviation of the change scores in the combined placebo group.