

Statistical Analysis Plan

Memantine Effects on Sensorimotor Gating and Neurocognition in Schizophrenia

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The primary statistical considerations for these data are those required to test the primary hypothesis that memantine (MEM) would enhance sensorimotor gating and related measures of auditory information processing in schizophrenia (SZ) patients. The operational measure of sensorimotor gating was prepulse inhibition of startle (PPI). The primary hypothesis was tested by a 2-way repeated-measure ANOVA of PPI with MEM dose and prepulse interval (10, 20, 30, 60 or 120 ms) as within subject factors. The key dependent measure was %PPI, calculated according to common practices in the literature. The hypothesis that MEM will increase PPI in SZ patients was to be confirmed by a significant main effect of drug (active > PBO) or significant interaction among the variables of drug, dose (10 or 20 mg), diagnosis (healthy subject (HS) or SZ) or prepulse interval, and informative post-hoc comparisons. The assumptions behind these analyses range from the standard assumptions underlying the use of parametric analyses, to those specific to prepulse inhibition, e.g. related to the potential confounding effects of drug or diagnosis effects on startle magnitude. Data were demonstrated to be normally distributed and drug effects on PPI were shown to be independent of changes in startle magnitude. Analyses confirmed the hypothesis for the 20 mg dose of MEM in SZ patients.

The operational measure of mismatch negativity (MMN) is mean amplitude in response to oddball stimuli over the 135-205 ms range. The primary hypothesis was tested by an ANOVA of MMN with MEM dose as a within subject factor. The hypothesis that MEM will increase MMN in SZ patients was to be confirmed by a significant main effect of drug (active > PBO) or significant interaction among the variables of drug, dose (10 or 20 mg), diagnosis (healthy subject (HS) or SZ), and informative post-hoc comparisons. The assumptions behind these analyses range from the standard assumptions underlying the use of parametric analyses. Data were demonstrated to be normally distributed. Analyses confirmed the hypothesis for the 20 mg dose of MEM in SZ patients.

The operational measure of the auditory steady-state response (ASSR) is 40-Hz evoked power. The primary hypothesis was tested by an ANOVA of ASSR with MEM dose as a within subject factor. The hypothesis that MEM will increase ASSR in SZ patients was to be confirmed by a significant main effect of drug (active > PBO) or significant interaction among the variables of drug, dose (10 or 20 mg), diagnosis (healthy subject (HS) or SZ), and informative post-hoc comparisons. The assumptions behind these analyses range from the standard assumptions underlying the use of parametric analyses. Data were demonstrated to be normally distributed. Analyses confirmed the hypothesis for the 20 mg dose of MEM in SZ patients.