

Do Atomoxetine and Methylphenidate Differentially Impact Sustained Attention and Inhibitory Control in Individuals with ADHD?

Bedard, A.-C.¹; Halperin, J. M.^{1,2}; Stein, M. A.³; & Newcorn, J. H.¹

¹Mount Sinai School of Medicine; ²Queens College of the City University of New York; ³University of Illinois at Chicago



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Introduction

- Attention-Deficit/Hyperactivity Disorder (ADHD) is a common neurodevelopmental disorder defined by inattention and hyperactivity/impulsiveness and characterized by poor inhibitory control.
- Although stimulant medication improves aspects of sustained attention and inhibitory control, it is important to understand how the longer-acting stimulant Concerta (MPH) and nonstimulant atomoxetine (ATX) similarly and differentially influence aspects of sustained attention/vigilance in the same individual.
- No study to date has directly compared the effects of these drugs on inhibitory control and sustained attention in a large sample of youth with ADHD.

Objectives

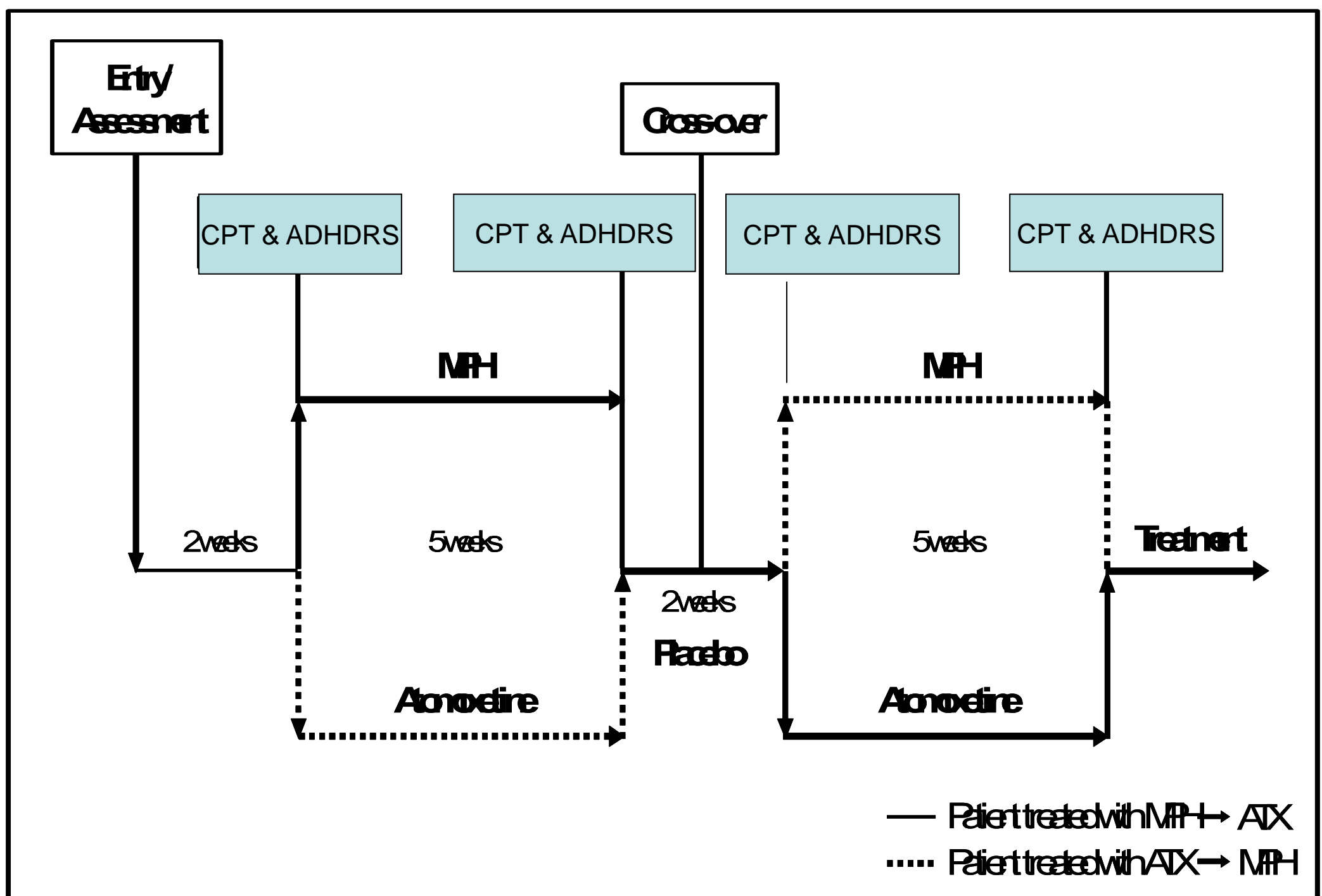
- To test whether ATX improves objective measures of attention and inhibitory control, given the uncertainty regarding the magnitude of clinical effects of ATX in relation to MPH.
- Hypothesis: performance will be improved by both treatments, but the magnitude of response may differ by drug because ATX and MPH work via different neurochemical mechanisms.

Sample

	Total Sample (n=102)	
Age, mean (SD)	10.5 (2.7)	
Gender (% male)	75%	
Full-Scale IQ, mean (SD)	96.5 (13.0)	
Ethnicity (%)	African American	32%
	Asian	1%
	Caucasian	18%
	Hispanic	36%
	Biracial/Other	13%
Baseline ADHD-RS, mean (SD)	Hyp./Imp.	15.5 (7.8)
	Inatt.	20.9 (5.3)
ATX Final Dose (%)	0.5 mg/kg	12%
	1.0 mg/kg	22%
	1.4 mg/kg	19%
	1.8 mg/kg	47%
MPH Final Dose (%)	18 mg	7%
	36 mg	27%
	54 mg	35%
	72 mg	31%
ATX Mean Final Dose, mean (SD)	1.4 (0.46)	
MPH Mean Final Dose, mean (SD)	52.4 (16.6)	

Procedure

- A randomized, double blind, crossover design.
- Medication was titrated in two 4-6 week treatment blocks separated by a 2-week placebo washout.
- Assessments occurred at baseline, following placebo washout, and at the end of each treatment.

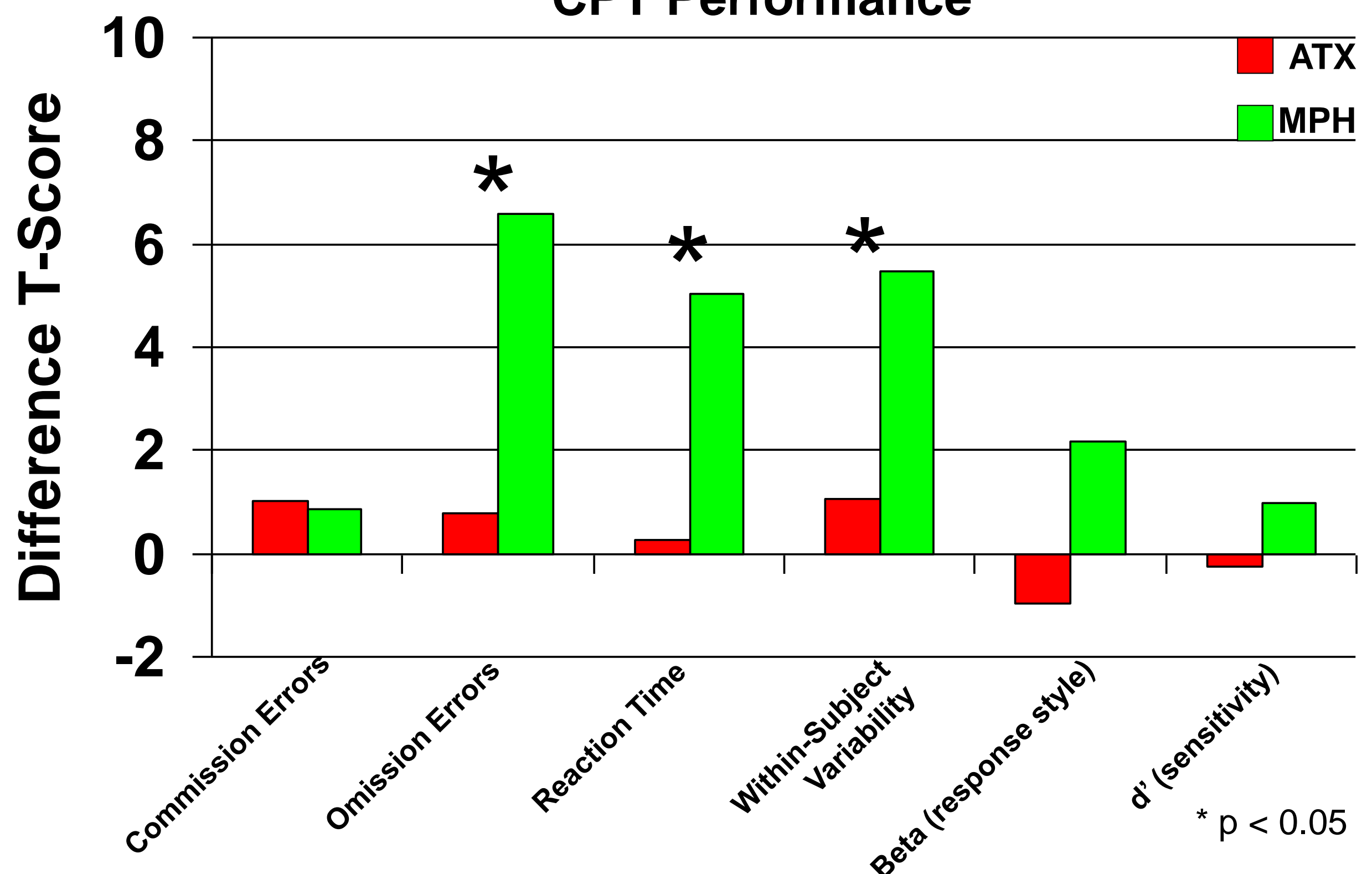


Measures & Analyses

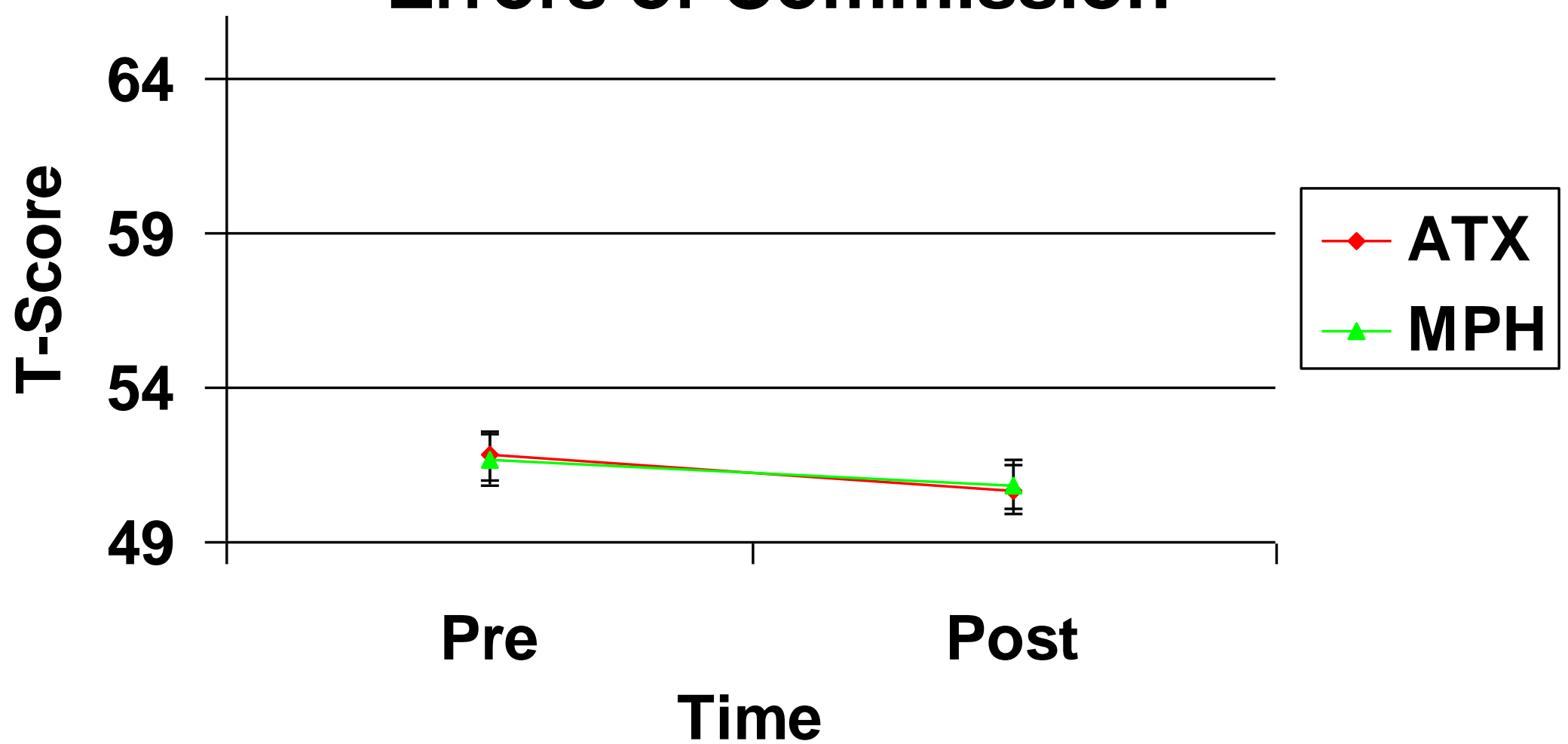
- Attention and inhibitory control: the Conners' CPT II provides age-adjusted scores of reaction time, response consistency, signal detection, and errors.
- Behavior: the ADHD-Rating Scale (ADHD-RS), screens for 18 DSM-IV-TR ADHD items, based on parent interview by a blind rater.
- Repeated measures analyses of variance (ANOVA) with Time (pre-med, post-med) and Drug (MPH, ATX) entered as within-subject factors.
- Correlations between changes in cognitive performance and changes in behavior were examined by drug.

Results

Summary of Differential Drug Effects on CPT Performance



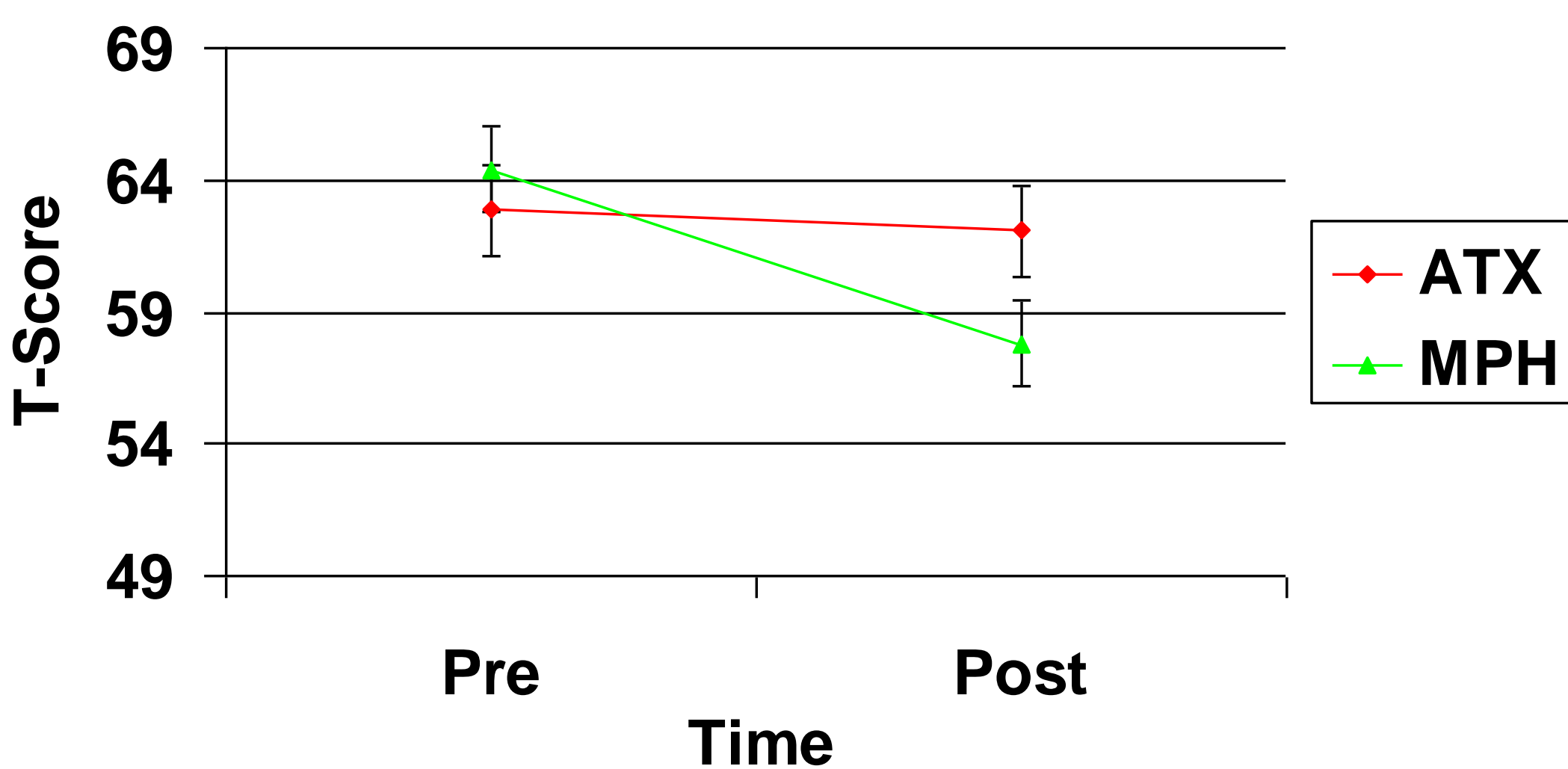
Errors of Commission



Time: $F(1, 101) = 2.32, p = .13, \eta_p^2 = 0.02$

Drug x Time: $F(1, 101) = 0.03, p = 0.86, \eta_p^2 < 0.001$

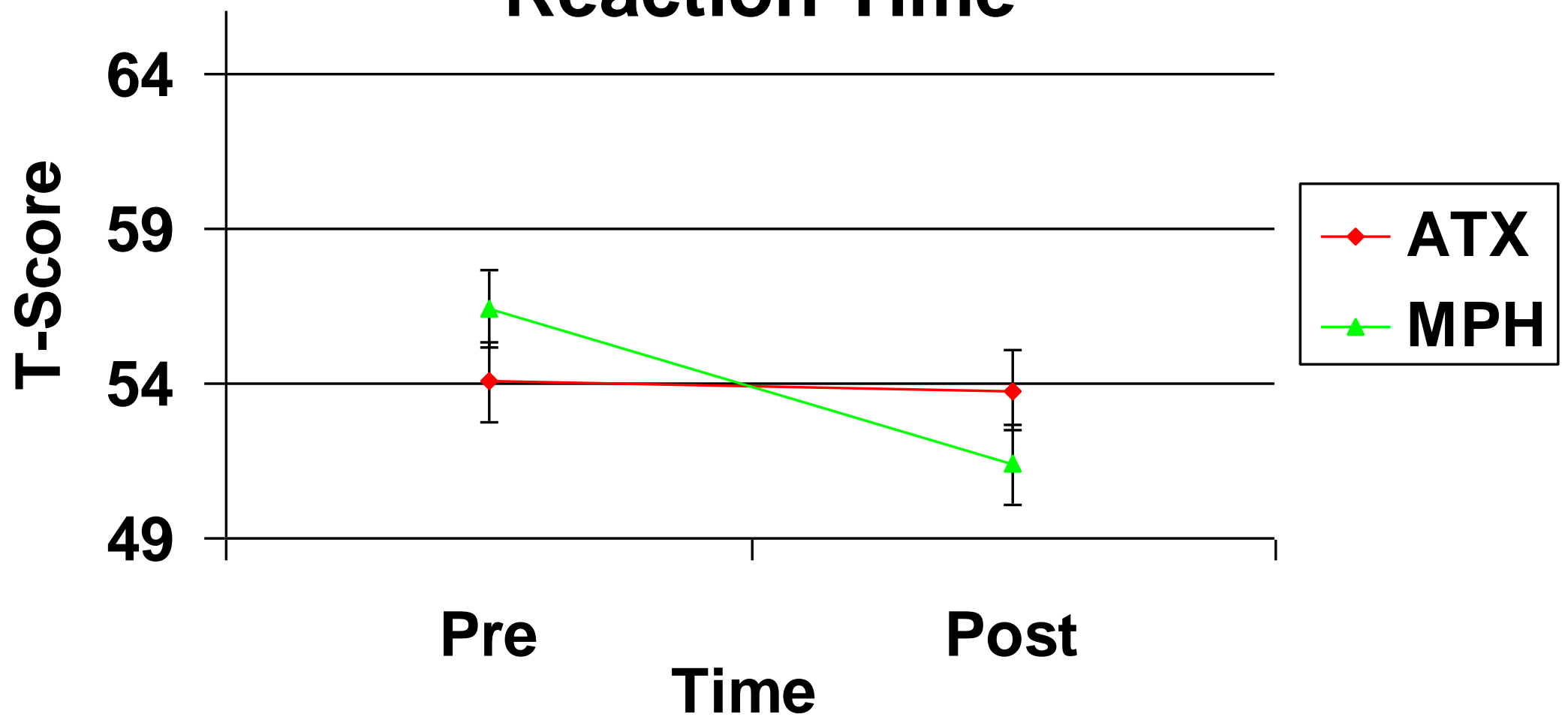
Errors of Omission



Time: $F(1, 101) = 6.35, p = .01, \eta_p^2 = 0.06$

Drug x Time: $F(1, 101) = 4.54, p = 0.04, \eta_p^2 = 0.04$

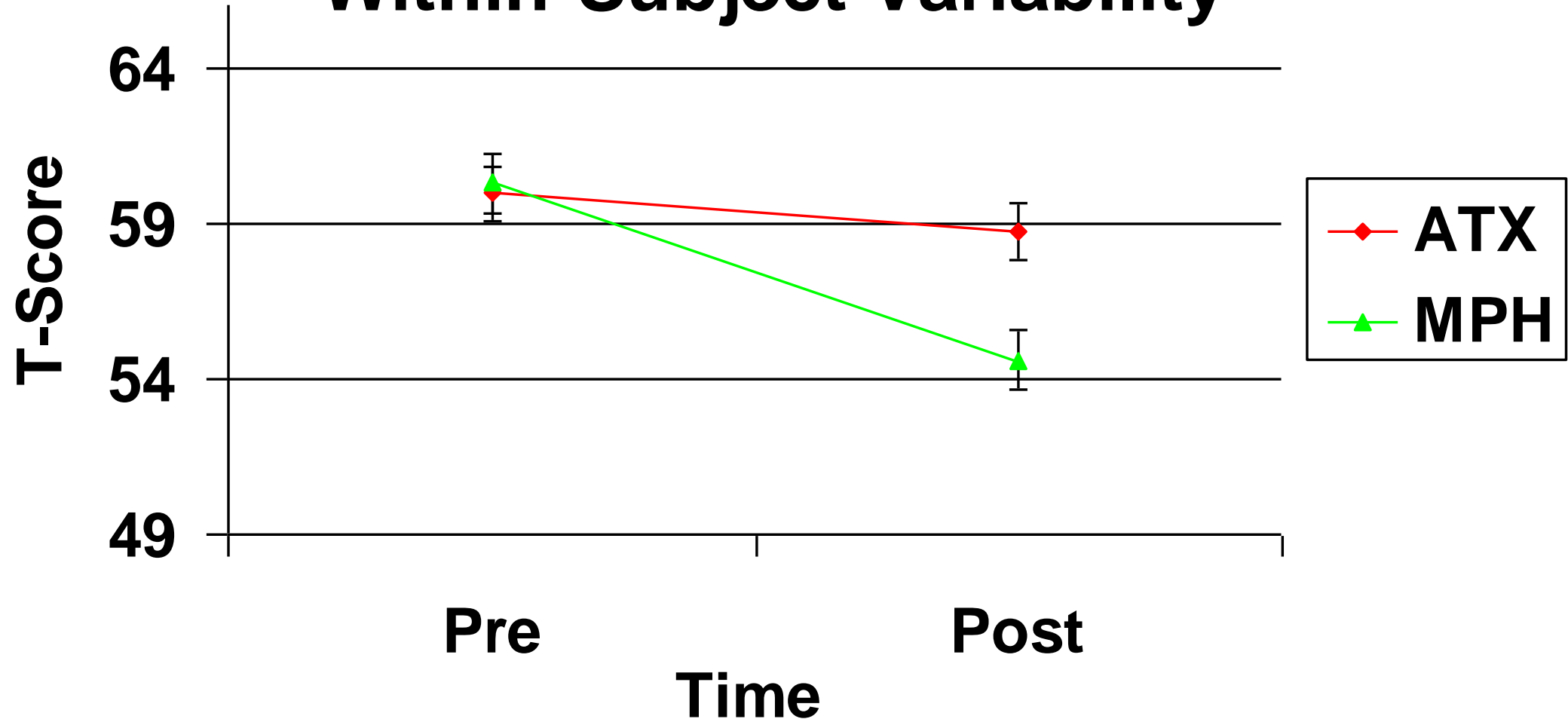
Reaction Time



Time: $F(1, 101) = 9.22, p = .003, \eta_p^2 = 0.08$

Drug x Time: $F(1, 101) = 8.45, p = 0.004, \eta_p^2 = 0.08$

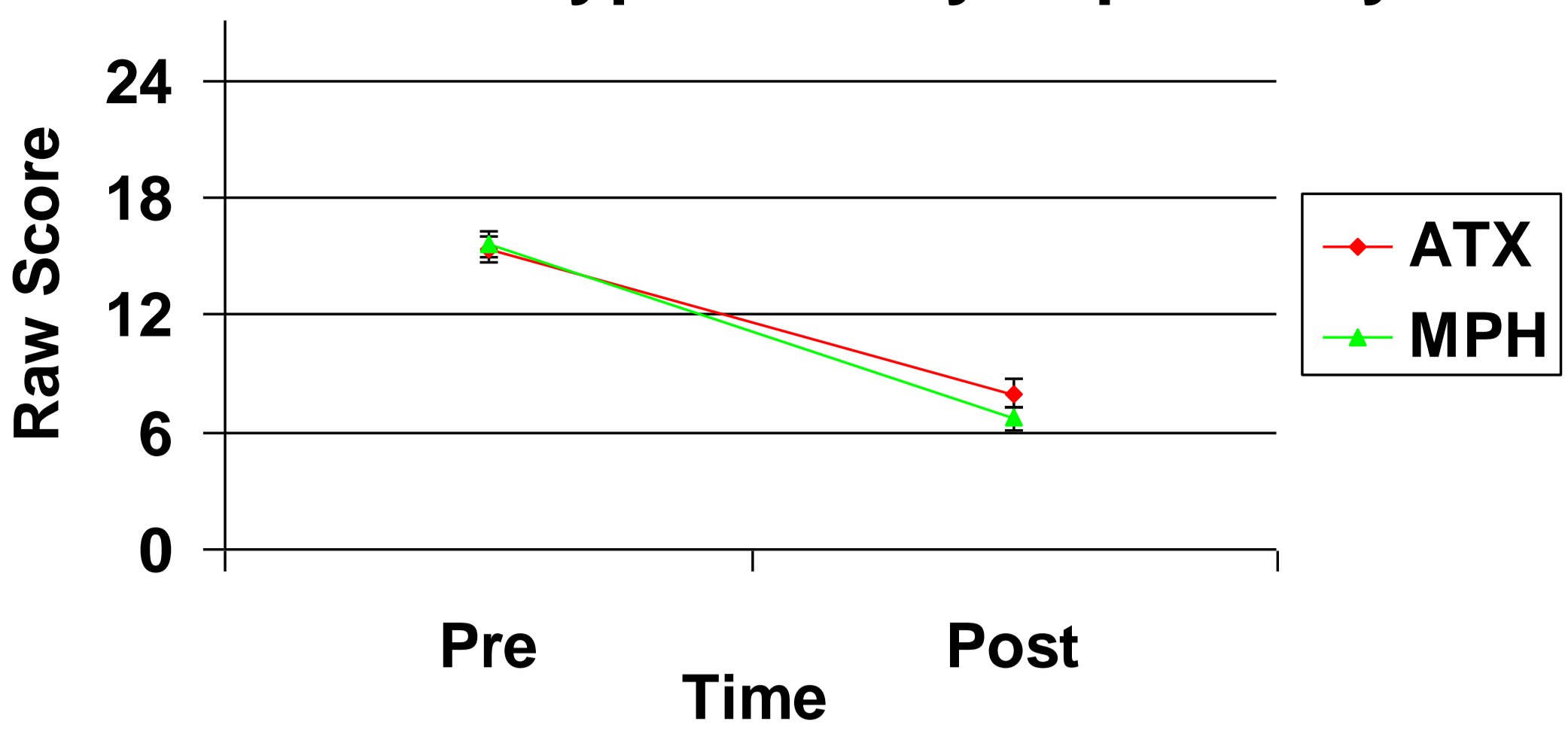
Within-Subject Variability



Time: $F(1, 101) = 17.74, p < .001, \eta_p^2 = 0.15$

Drug x Time: $F(1, 101) = 10.06, p = 0.002, \eta_p^2 = 0.09$

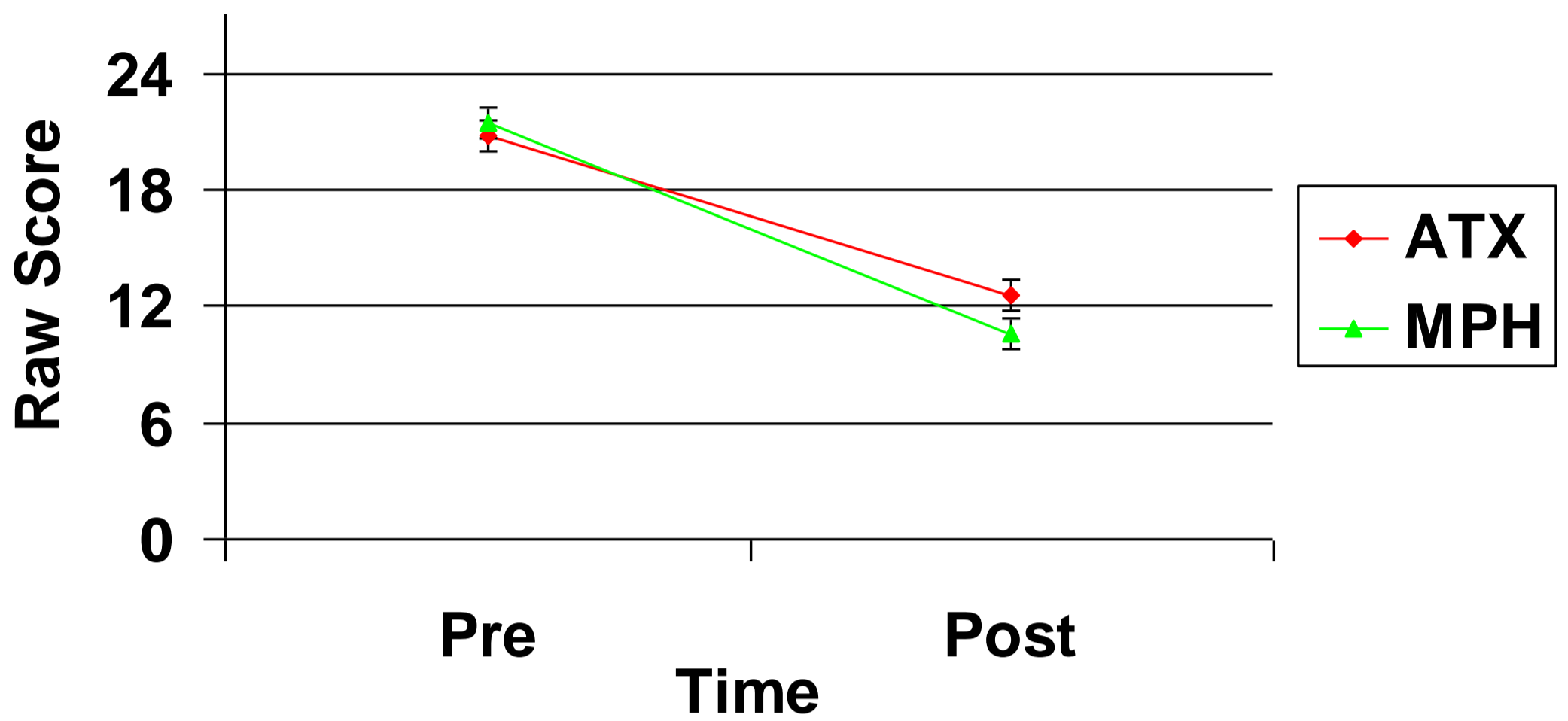
ADHD-RS Hyperactivity/Impulsivity



Time: $F(1, 101) = 220.19, p < .001, \eta_p^2 = 0.69$

Drug x Time: $F(1, 101) = 3.56, p = 0.06, \eta_p^2 = 0.03$

ADHD-RS Inattention



Time: $F(1, 101) = 401.20, p < 0.001, \eta_p^2 = 0.80$

Drug x Time: $F(1, 101) = 7.49, p = 0.007, \eta_p^2 = 0.07$

- No significant correlations between changes in cognitive performance and changes in behavior for either MPH or ATX ($p > 0.05$).

Conclusions & Implications

- These data suggest that MPH treatment produces improvements in both ratings of attention and CPT measures of attention and cognitive control. However, changes in these measures are not correlated, raising the question of whether the CPT findings represent empirical confirmation of the rating changes, or improvement in a different functional domain.
- Although ATX results in clinically-significant improvements in ADHD symptoms, changes are less evident on objective measures derived from CPT.
- MPH has a greater impact than ATX for improving response consistency, reaction time and errors of omission in youth with ADHD.
- Neither treatment significantly improved CPT measures of inhibitory control.
- Effect sizes for cognitive improvements are small ($\eta_p^2 = .02 - .15$) compared to behavioral improvements ($\eta_p^2 = .69 - .80$) for both treatments and may be a function of within-group heterogeneity.
- Future studies examining the profiles of cognitive responders versus nonresponders are planned.

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