

**Kim Y-H, Ko M-H et al. Effects of single-dose methylphenidate on cognitive performance in patients with traumatic brain injury: a double-blind placebo-controlled study. Clinical Rehabilitation 2006;20:24-30.**

Design: Randomized clinical trial

Population/sample size/setting:

- 18 patients (16 men, 2 women, mean age 34) treated for sequelae of TBI at a university physical medicine department in Seoul
- Inclusion criteria were mild cognitive impairment (defined as a score of 20-29 on the MMSE-- ini Mental Status Examination) and having at least 6 months since the injury that caused TBI
- Exclusion criteria were severe motor weakness and psychiatric/psychological problems

Main outcome measures:

- Randomized to 20 mg methylphenidate (MP, n=9) or placebo (P, n=9)
- MP was administered as a single dose of 20 mg two days after completing a baseline assessment of cognitive function at time T1
  - o One cognitive task was for working memory and one was for visuospatial attention
  - o Both tasks were done at a computer and required the participant to press the spacebar when specified conditions were met
  - o For both tasks, both reaction time and accuracy were recorded as measures of test performance
- Two hours after administration of MP or P, at time T2, the participants again performed the test tasks which they had completed two days earlier at T1
- Two days after T2, a follow-up assessment of the same tasks was done at time T3, following complete washout of the test drug
- The main outcome was the improvement ratio, calculated as the percent of change of T2 from T1 and also from T3 to T1; the group improvement ratios were compared with the nonparametric Mann-Whitney U test
- For the visuospatial attention task there were no significant differences between the MP and P groups on either reaction time or accuracy
- For the working memory reaction times, the MP group improved 13.74% between T1 and T2, compared with 8.71% for P; this was significant at the  $p < .05$  level
- For the follow-up measure of working memory reaction times, the improvement ratio from T1 to T3 was 4% in the MP group and 3.85% in the P group; there was no difference between groups
- For working memory accuracy, the group difference between MP and P was not significant at the 0.05 level, but “approached” significance at the .07 level in favor of the MP group

Authors' conclusions:

- Administration of methylphenidate leads to improved cognitive function in patients with TBI, and appears to have most effect on working memory
- The study is limited by the small number of participants, and functional status was not investigated

Comments:

- The study is, as the authors acknowledge, too small to support conclusions about the effectiveness of methylphenidate in the setting of chronic TBI
- The inclusion criterion of mild cognitive impairment on the MMSE was defined as a score from 20 to 29
  - o The maximum score on the MMSE is 30; scores under 24 are generally considered consistent with dementia
  - o The baseline scores are not reported; if MMSE is related to test performance, it should have been reported and compared between groups
- There appears to be very little practice effect for the tests, as assessed by the lack of improvement from T1 to T2 and T3 for the placebo group; there is no information about whether there is a practice effect in a group of healthy individuals
- The single dose of MP with a cognitive task two hours later provides insufficient information about the drug effect in daily practice

Assessment: Inadequate for evidence of the treatment effect of methylphenidate (too small a sample size, single dose only with test improvement only when the drug level is expected to be at its peak, effect of MP appears to be transient)