Acute effects of methylphenidate on neuropsychological parameters in adults with ADHD: possible relevance for therapy

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Summary. Recent research has demonstrated that attention-deficit/hyperactivity disorder (ADHD), one of the most common mental disorders in childhood, continues into adulthood. In adulthood, however, pharmacotherapy with psychostimulants still is an off-label treatment. Because of this we routinely administer a test dose of methylphenidate (MPH) prior to a continuous medication and measure MPH effects quantitatively and repeatedly employing a neuropsychological test battery. To probe if the acute effects of MPH are indeed helpful in predicting longer-term efficacy of MPH treatment we retrospectively analyzed the neuropsychological test results of 34 patients on continuous MPH medication. Two testing sessions had been performed without MPH (at baseline and 24 h after a single dose intake to control possible training effects), one after a single dose and one after 3–6 months of regular intake of MPH. A significant improvement of performance in tests assessing attentional, memory and executive functions after single medication was maintained on long term medication in those 23 patients available for follow-up. These results indicate that beneficial short term effects of MPH predict longer-term effects and may thus be helpful in the decision for an off-label treatment. Controlled prospective studies are now necessary.

Keywords: Adult ADHD; neuropsychology; methylphenidate effects

Introduction

Attention-deficit/hyperactivity disorder (ADHD) is one of the most common mental disorders in childhood with a prevalence of 5.3% (Polanczyk et al. 2007). It is characterized by symptoms of hyperactivity, impulsivity and inattention. ADHD continues into adulthood in about 60% of cases (Spencer 2002) with a prevalence among adults of between 1–6% (Wender et al. 2001; Faraone et al. 2005; Kessler et al. 2005; Fayyad et al. 2007). Symptom intensity decreases over time (Biederman et al. 2000) and hyperactivity becomes less apparent (Adler et al. 2002), but more sublime difficulties with impulsivity and attention are persistent (Faraone et al. 2000; Kordon et al. 2004).

An increasing number of studies therefore investigate the neuropsychology of adults with ADHD. Adults with ADHD have been reported to be impaired on measures of vigilance, perceptual motor speed, working memory, verbal learning, response inhibition and interference control (Seidman et al. 1997; Hervey et al. 2004; Spencer et al. 2005; King et al. 2007).

The therapy with the psychostimulant methylphenidate (MPH) is the medical treatment of choice. Studies analysing the effects of MPH on the neuropsychological performance of adults with ADHD report significant improvements in performance associated with marked therapeutic response (Wender et al. 1985; Turner et al. 2005; Tucha et al. 2006; Wilson et al. 2006).

As opposed to the USA in Germany and other countries the prescription of MPH is still off-label and it is licensed only for the treatment of children with ADHD and for the treatment of adults with narcolepsy (Fritze et al. 2003; Weih et al. 2007). It is therefore important to have stringent criteria for its prescription. Based on the extensive literature on its effects on neuropsychological functions we retrospectively analyzed if acute effects of a test dose of MPH on neuropsychological parameters predict long-term effects and thus may be helpful for the decision on a longer-term prescription.
Material and methods

Procedure
From October 2003 until October 2005 61 patients were consecutively clinically diagnosed with probable adult ADHD in a specialized out-patient service of the Department of Psychiatry at the University of Münster. The clinical diagnosis of probable ADHD, using DSM IV criteria, was made by two experienced psychiatrists. Psychometrical scales such as WURS-25 (Ward et al. 1993; Retz-Junginger et al. 2003) and GAF (Wittchen et al. 1997) were employed. Physical and technical examinations (EEG, MRT, blood tests) were conducted to exclude other diagnoses if necessary. A current, clinically relevant axis I disorder was an exclusion criterion for neuropsychological testing and was treated prior to it. All 61 patients thus clinically diagnosed with probable ADHD without currently clinically relevant axis I disorder were asked to do a neuropsychological test battery (T1, Fig. 1).

Of these 61 patients, 11 were either of less than average intelligence or did not demonstrate any relevant neuropsychological deficits. The remaining 50 patients with average or above average intelligence, less than average results and/or marked discrepancy between intelligence results and those in at least one neuropsychological test measuring attentional, memory and executive functions were elected to receive a test dose of MPH and to do a second and third test battery for evaluation of a potential therapeutic effect of MPH. The second test battery (T2, Fig. 1) was conducted 90 min after the intake of 10 mg MPH in order to obtain data on its efficacy. The third test battery (T3, Fig. 1) was done exactly 24 h after the second test battery. No medication was given at that point of time in order to control for possible learning effects.

Thirty four of these 50 patients, who showed improved test performance not explained by learning effects after intake of 10 mg MPH, were medicated with MPH or MPH extended-release. All patients started with a dose of 10 mg per day. The dose was increased with regards to the patients’ individual needs up to 40–60 mg per day (0.5–1.0 mg/kg weight). Patients were informed that in order to evaluate long term effects of medication a fourth test should be performed after three to six months (T4, Fig. 1). Of the 34 patients, 23 were finally available for the follow up test. 8 patients did not stay in contact, 1 patient did not take medication regularly and 2 patients had a personal feeling of not benefiting from MPH and discontinued the medication.

Patients
The mean age of the 34 patients on continuous MPH medication was 31.8 years (SD: 8.8; range: 19–51). More male than female patients were treated (21 males, 13 females). Twenty nine patients fulfilled DSM-IV criteria for the combined type, 3 for the predominantly inattentive subtype and 2 for the predominantly hyperactive-impulsive type. Symptom severity in childhood as measured by WURS-25 items was 54.97 ± 17.4 (mean and SD) and the level of social functioning in adulthood prior to treatment was 55.3 ± 11.1 (mean and SD) as measured by GAF. Twelve of the 34 patients had a lifetime comorbidity with affective disorders. At the time of our testing however none of these 12 patients had a current affective disorder. We regard this sample as representative for the general sample of patients we see at our department with regard to age, gender and clinical subtypes (Table 1).

Psychometric and neuropsychological evaluation
The WURS (Wender Utah Rating Scale) scale employed to obtain a parameter for symptom severity in childhood was the WURS-25 item version (Ward 1993; Retz-Junginger 2003) with a maximum degree of severity of 100. The GAF (Global Assessment of Functioning) measures the level of social functioning on a scale between 0 (worst) and 100 (best) (Wittchen 1997).

For neuropsychological evaluation we employed the MWT-B (Mehrfachwahl-Wortschatz-Intelligenztest/Multiple Choice Vocabulary Test, Lehrl 1999), the WT (Wortschatz-Test/Vocabulary Test, part of the Wechsler Adult Intelligence Scale revised (WAIS-R) German version: Hamburg-Wechsler Intelligenztest für Erwachsene, Tewes 1991), the LPS 3 (LeistungsprüfSystem Subtest 3, 1983) and 9 (LeistungsprüfSystem Subtest 9, 1983) as neuropsychological tests to measure intelligence. In order to assess neuropsychological functions believed to be specifically involved in ADHD such as attentional, memory and executive functions the following tests were selected: the ZVT (Zahlen-Verbindungs-Test/Trail-Making-Test, Oswald and Roth 1987), the ZST (Zahlen-Symbol-