Long lasting complex nocturnal hallucinations during Osmotic Release Oral System (OROS) methylphenidate treatment in a 7-year old girl

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Abstract

We report a case of a girl with Attention deficit hyperactivity disorder (ADHD) and Oppositional defiant disorder (ODD) who experienced a 3-hour episode of nocturnal complex bizarre visual hallucinations when treated with 18 mg Osmotic Release Oral System (OROS) methylphenidate (MPH). Nocturnal polysomnography performed two weeks later revealed REM sleep reduction (17%) and fragmentation. Two episodes of confusional arousals were recorded. This finding is typical of parasomnia associated with NREM sleep – disorder of arousal. We hypothesize that this preexisting sleep impairment represents a factor of vulnerability to MPH sleep side effects. In our search of literature, we found no report of nocturnal hallucination alone during treatment with stimulants.

Abbreviations:

ADHD	- Attention deficit hyperactivity disorder
ODD	- Oppositional defiant disorder
OROS	- Osmotic Release Oral System
MPH	- Methylphenidate
IR	- Immediate Release
REM	- Rapid eye movement
NREM	- Non Rapid eye movement

INTRODUCTION

The use of stimulants increased by several hundred percent during last two decades (Bohkari *et al.* 2005). They are prescribed to a wider age spectrum of patients (increased use in preschoolers and adults) (Vitiello *et al.* 2007, Biederman *et al.* 2010). This may confront clinicians with rare but serious adverse effects more often, and emphasize safety issues (Mosholder *et al.* 2009, Ptacek *et al.* 2009). We report the case of a girl with Attention deficit hyperactivity disorder (ADHD) and Oppositional defiant disorder (ODD) who experienced a 3-hour episode of nocturnal complex visual hallucinations in response to treatment with18 mg

CASE REPORT

Osmotic Release Oral System (OROS) methylphenidate (MPH). Visual and somatic hallucinations have been described in association with MPH given in terapeutical doses (Gross-Tsur *et al.* 2004; Rashid & Mitelman 2007; Halevy and Shuper 2009) or in combination (Coskun & Zoroglu 2008). Our literature search revealed no report of nocturnal only hallucination during treatment with stimulants.

CASE

The patient is a 7-year old girl with DSM-IV ADHD Combined subtype and ODD diagnosed when she was 6. Her family consulted a child psychiatrist because of the girl's maladaptation at school. At diagnosis, the Child Symptom Inventory score (CSI-4) ADHD subscore was 33 as rated by her mother, and 14 relative to ODD).

She had a positive perinatal history (mild perinatal asphyxia), normal psychomotor development, and daily enuresis till the age of 5. Neuropsychological assessment before entering school at 6 years of age found impaired fine motor coordination, high distractibility, hyperactivity and oppositional behavior. There was no evidence of autism or mental retardation. She had no history of psychotic symptoms. Neurological examination was normal, EEG revealed no abnormalities even after hyperventilation and photostimulation. Chronic sleep problems were reported – fear of darkness, restless sleep, repeated nighttime awakenings, inconsolable crying during the night. No excessive daytime sleepiness was recorded. Treatment with Immediate-Release (IR) MPH was initiated with the dosage gradually titrated up to 10 mg in two doses. Immediate-release MPH was switched to 18 mg Osmotic Release Oral System (OROS) MPH after three weeks. The girl´s mother reported significant improvement in her daughter's behavior, in particular fewer conflicts and longer involvement in one activity, with mild abdominal pain and decreased appetite as the side effects.

After 2.5 months of treatment with 18 mg OROS-MPH, the girl experienced a 3-hour episode of complex nocturnal visual hallucinations. She came to her parent's bedroom at 3 a.m. crying because she was scared by crocodiles which she claimed she saw in the house. The girl appeared to be fully awake, standing in the corner of the room, anxious and shaking. The mother tried to calm her down verbally, but the girl was afraid that the crocodiles could harm her mother so she told her not to approach. This went on for about three hours and then slowly disappeared. The girl remembered well what had happened during the night and was found unusually silent and inhibited the day after. The family consulted a psychiatrist, and OROS MPH was discontinued. The girl was found in good physical health with normal neurological findings. No recurrence of

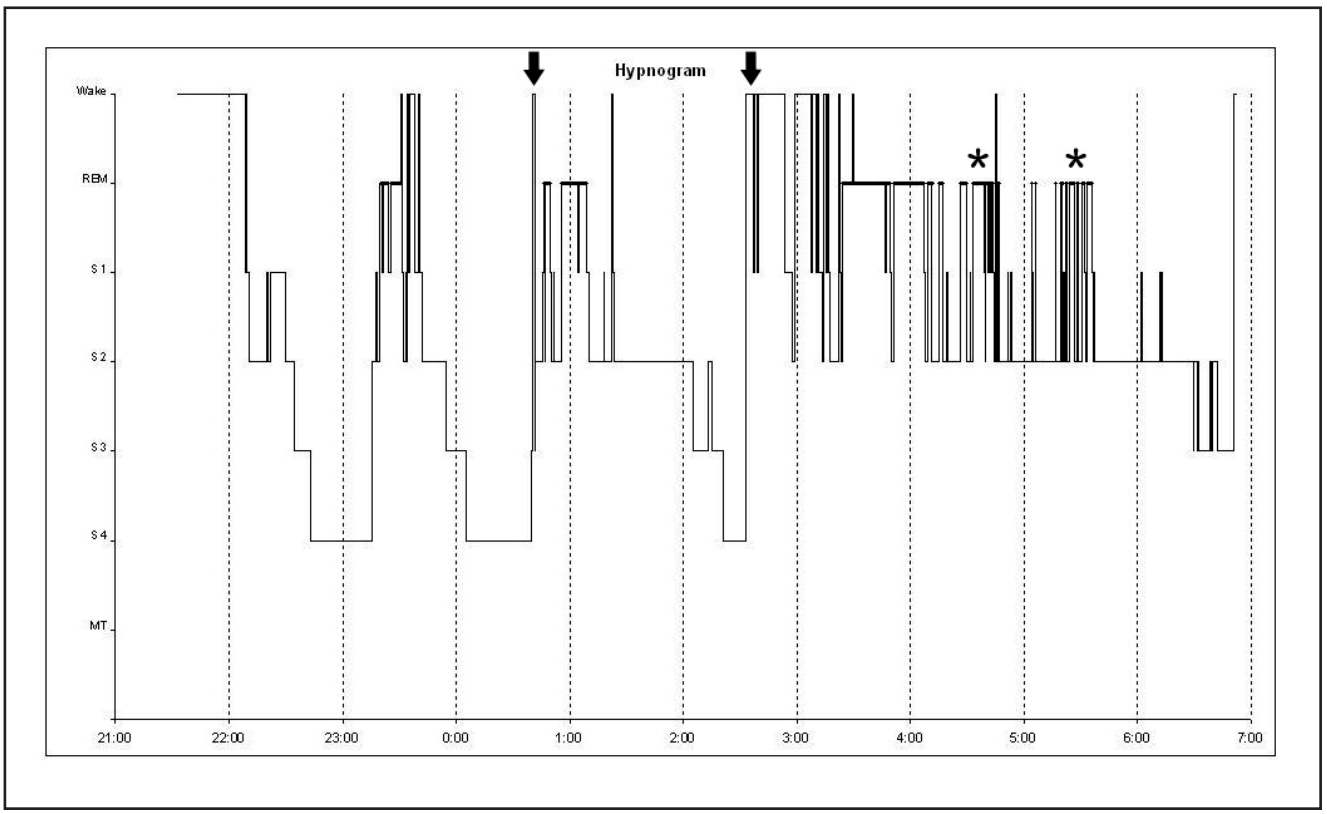

Fig. 1. Sleep examination – hypnogram. Confusional arousals from NREM sleep are marked with arrows. REM sleep fragmentation is apparent especially in the early morning hours (marked with stars).

hallucinations occurred after methylphenidate was withdrawn . Nocturnal polysomnography performed two weeks later revealed reduction (17%) and fragmentation of REM sleep, especially in the early morning hours. Two episodes of partial arousal from delta sleep were recorded connected with sitting on the bed, confusion and somniloquence (Figure 1). The second episode appeared at 2:30. The duration of the episodes was from 1 to 3 minutes. This finding was typical of parasomnia associated with NREM sleep – disorder of arousal. According to the type of behavior, the episodes were classified as confusional arousals.

After a 3-month drug-free period, treatment with atomoxetine was initiated, with no episode of psychotic symptoms or sleep impairment.

DISCUSSION

There are several reports of daytime psychotic perception disturbances in association with methylphenidate. Vivid visual hallucinations of creatures, mosquitoes, horseflies (Young 1981), snakes, roaches, mosquitos (Gross-Tzur *et al.* 2004), bugs (Rashid & Mitelman 2007) and most recently – rats – as reported by Halevy and Shuper (2009) in the case of a 15-year-old boy. The interval between the start pf MPH treatment and the onset of hallucination varies from days to years. Gross-Tzur *et al.* (2004) suggest stimulation of the sensory areas in the central nervous system as an underlying mechanism.

Sleep-related hallucinations represent a special type of parasomnia involving hypnagogic and hypnopompic hallucinations but also complex nocturnal hallucination as a distinct form (American Academy of Sleep Medicine 2005).

Complex nocturnal hallucinations typically occur following a sudden awakening, without a recall of the preceding dream. They usually take the form of complex, vivid, relatively motionless, images of people or animals, sometimes distorted in shape or size (Silber *et al.* 2005). Though wide awake, the patients often initially perceive the hallucinations as real and frightening. The hallucinations may persist for minutes and usually disappear if ambient illumination is increased. The pathophysiology is not clear and diverse etiology is discussed (Silber *et al.* 2005). Predisposing and precitipating factors are neurologic and visual disorders (narcolepsy, visual loss, midbrain and diencephalic pathology), use of beta adrenergic receptor blocking medication, anxiety and mood disorder, sleep-onset insomnia and previous insufficient sleep (American Academy of Sleep Medicine 2005). Complex nocturnal hallucinations are rare and, unlike other types of sleep hallucinations, reported to arise from NREM sleep. Association with disorder of arousal and complex nocturnal hallucinations has already been described in two patients (Kavey 1993).

The study Comparison of Methylphenidates in the Analog Classroom Setting (COMACS) found appetite and sleep problems, most commonly exacerbated by long acting MPH (Sonuga-Barke *et al.* 2009). On the other hand, Kim *et al.* (2010) did not find OROS-MPH as sleep affecting, but they had excluded children with ADHD and sleep disorders. This hardly represents a regular clinical sample. Children with ADHD are significantly more impaired than the controls in the subjective and objective sleep measures (Cortese *et al.* 2009). Although the clinical effects of OROS-MPH usually disappear within12 hours, residual levels of MPH may remain in the evening and at bedtime (Sonuga-Barke *et al.* 2009). Methylphenidate has relatively slow clearance from the brain, and the duration of the side effects parallels the temporal course of MPH in the brain (Volkow *et al.* 2003). Besides, the individual variability in response to MPH appears to be due to the differences in the responsivity of the dopamine and/or norepinephrine systems (Volkow et al.1996; Paclt *et al.* 2010). In order to identify any preexisting sleep impairment as a potential risk factor we performed nocturnal polysomnography two weeks after the episode of hallucinations. In our patient parasomnia associated with NREM sleep – disorder of arousal was apparent (Figure 1). We hypothesize that this represents a factor of vulnerability to MPH sleep side effects.

While nocturnal hallucinations usually last only minutes (Silber *et al.* 2005), in our patient they persisted for 3 hours, and, despite the mother´s attempts, the girl was unable to grasp reality and remained scared for all the time of the episode. She was repordetly anxious and behaviorally inhibited for all of the next day. This suggests considerable impact on the child´s mental health with the risk of posttraumatic stress disorder. Patients with complex nocturnal hallucinations may jump out of the bed in terror, act upon the influence of images, and injure themselves. As this type of parasomnia is potentially dangerous for the patient and family members, careful sleep history should be taken before treatment and reevaluated in the course of therapy, especially when the dose is increased, or switched to long acting formulas.

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