Commentary: Enuresis and ADHD in Older Children and an Adolescent Treated with Stimulant Medication: A Case Series

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This interesting case series points again to the association between ADHD (especially inattentive symptoms) and PNE. Their concurrent improvement with stimulant treatment reported here, however, should not conceal that:

- 1. follow-up studies showed that ADHD persists well after children become dry (Baeyens, D., Roeyers, H., Van, E. S., Hoebeke, P., & Vande, W. J, 2007);
- 2. there are no double-blind randomized placebo-controlled trials (RCTs) on the effects of stimulants on PNE in children with ADHD; and
- there is, however, one RCT (Sumner, C. R., Schuh, K. J., Sutton, V. K., Lipetz, R., & Kelsey, D. K. 2006), as well as case series (Shatkin, J. P. 2004) and open-label trials (Gepertz, S., & Neveus, T. 2004; Lundmark, E., & Neveus, T. 2009), on the efficacy of norepinephrine reuptake inhibitors.

This series also reminds us that functional immaturity of the brainstem plays a role in children with PNE, as well as in some children with ADHD-inattentive subtype, through a failure to inhibit involuntary responses (prepulse inhibition, PPI) (Ornitz, E. M., Russell, A. T., Hanna, G. L., Gabikian, P., Gehricke, J. G., Song, D., & Guthrie, D., 1999). This central deficit can be restored by desmopressin (Schulz-Juergensen, S., Rieger, M., Schaefer, J., Neusuess, A., & Eggert, P. 2007), one of the PNE mainstay treatments. Methylphenidate was also found to improve this deficit, but only to voluntarily attended prepulses (Ashare, R. L., Hawk, L. W., Shiels, K., Rhodes, J. D., Pelham, W. E., & Waxmonsky, J. G., 2010). It is not clear thus how methylphenidate might enhance micturition inhibition in response to a distended bladder during sleep. Decreasing sleep arousal threshold and allowing the enuretic child to awaken to void is an alternative hypothesis. It is, however, inconsistent with the reports that auditory arousal threshold was increased, not decreased, by stimulant medication in hyperkinetic children (Busby, K., & Pivik, R. T. 1985), and that, more generally, children with ADHD do not have more night awakenings (Cortese, S., Faraone, S. V., Konofal, E., & Lecendreux, M. 2009).

References

- Ashare, R. L., Hawk, L. W., Shiels, K., Rhodes, J. D., Pelham, W. E., & Waxmonsky, J. G. (2010). Methylphenidate enhances prepulse inhibition during processing of task-relevant stimuli in attention-deficit/hyperactivity disorder. *Psychophysiology*, 47, 838-845.
- Baeyens, D., Roeyers, H., Van, E. S., Hoebeke, P., & Vande, W. J. (2007). The prevalence of attention deficit-hyperactivity disorder in children with nonmonosymptomatic nocturnal enuresis: A 4-year followup study. *Journal of Urology*, 178, 2616-2620.
- Busby, K., & Pivik, R. T. (1985). Auditory arousal thresholds during sleep in hyperkinetic children. *Sleep*, *8*, 332-341.
- Cortese, S., Faraone, S. V., Konofal, E., & Lecendreux, M. (2009). Sleep in children with attention-deficit/hyperactivity disorder: Mmeta-analysis of subjective and objective studies. *Journal of the American Academy of Child and Adolescent Psychiatry*, 48, 894-908.
- Gepertz, S., & Neveus, T. (2004). Imipramine for therapy resistant enuresis: a retrospective evaluation. *Journal of Urology*, 171, 2607-2610.
- Lundmark, E., & Neveus, T. (2009). Reboxetine in therapy-resistant enuresis: a retrospective evaluation. *Scandinavian Journal of Urology* and Nephrology, 43, 365-368.
- Ornitz, E. M., Russell, A. T., Hanna, G. L., Gabikian, P., Gehricke, J. G., Song, D., & Guthrie, D. (1999). Prepulse inhibition of startle and the neurobiology of primary nocturnal enuresis. *Biological Psychiatry*, 45, 1455-1466.
- Schulz-Juergensen, S., Rieger, M., Schaefer, J., Neusuess, A., & Eggert, P. (2007). Effect of 1-desamino-8-D-arginine vasopressin on prepulse inhibition of startle supports a central etiology of primary monosymptomatic enuresis. *Journal of Pediatrics*, 151, 571-574.
- Shatkin, J. P. (2004). Atomoxetine for the treatment of pediatric nocturnal enuresis. *Journal of Child and Adolescent Psychopharmacology*, *14*, 443-447.
- Sumner, C. R., Schuh, K. J., Sutton, V. K., Lipetz, R., & Kelsey, D. K. (2006). Placebo-controlled study of the effects of atomoxetine on bladder control in children with nocturnal enuresis. *Journal of Child and Adolescent Psychopharmacology*, *16*, 699-711.

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