

## LETTERS TO THE EDITOR

## Inflammation, Sleep and ADHD

Response to Araz Altay. Sleep disorders and attention deficit: a consequence of proinflammatory state? *J Clin Sleep Med*. 2018;14(6):1081.

Dora Wynchank, MD<sup>1</sup>; Denise Bijlenga, PhD<sup>1</sup>; J.J. Sandra Kooij, MD, PhD<sup>1,2</sup>

<sup>1</sup>PsyQ Expertise Center Adult ADHD, The Hague, The Netherlands; <sup>2</sup>Department of Psychiatry, Amsterdam Public Health Research Institute, VU University Medical Center, Amsterdam, The Netherlands

We thank Dr. Araz Altay for raising the important issue of inflammation, sleep and ADHD<sup>1</sup> and the editors of the *Journal of Clinical Sleep Medicine* for giving us the opportunity to respond.

Our group previously investigated adult ADHD symptoms, Metabolic Syndrome (MetSyn) and obesity-related variables in a large population study with different stages of comorbid affective disorders (Netherlands Study of Depression and Anxiety, NESDA).<sup>2</sup> Interestingly, we showed few clear associations: ADHD was not associated with MetSyn. It is possible that these associations are difficult to detect and therefore we failed to find them. Also, both the concept and definition of MetSyn have been questioned<sup>3</sup> as it is possible that not *all* MetSyn risk factors contribute significantly to cardiovascular diseases/diabetes in the general population.<sup>4</sup>

Concerning *obesity*, a meta-analysis showed that it was significantly associated with ADHD.<sup>5</sup> Both obesity and MetSyn are considered proinflammatory conditions.<sup>6</sup>

Another possible link includes *sleep disturbance*, which was associated with systemic inflammation markers in the NESDA cohort.<sup>7</sup> ADHD is comorbid with insomnia, RLS and circadian dysregulation.<sup>8</sup> Preliminary evidence links ADHD to inflammatory processes.<sup>9</sup> The circadian system and clock genes control both the sleep-wake cycle and metabolism.<sup>10</sup> Fasting glucose, lipid levels, blood pressure and the sleep-wake cycle are rhythmically coordinated by the biological clock. Disruption of either the circadian or metabolic system can lead to derangement of the other, predisposing to MetSyn, obesity or diabetes.<sup>10</sup> Once again, inflammatory processes may be the link between ADHD, circadian rhythm and metabolic disturbance. We therefore support further investigation of these overlapping processes, as causality is unknown.

## CITATION

Wynchank D, Bijlenga D, Kooij JJ. Inflammation, sleep and ADHD. *J Clin Sleep Med*. 2018;14(6):1083.

## REFERENCES

1. Araz Altay M. Sleep disorders and attention deficit: a consequence of proinflammatory state? *J Clin Sleep Med*. 2018;14(6):1081.
2. Wynchank D, Bijlenga D, Lamers F, et al. The association between metabolic syndrome, obesity-related outcomes, and ADHD in adults with comorbid affective disorders. *J Atten Disord*. 2016;200:74–81.
3. Kahn R, Buse J, Ferrannini E, Stern M; American Diabetes Association; European Association for the Study of Diabetes. The metabolic syndrome: time for a critical appraisal: joint statement from the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetes Care*. 2005;28(9):2289–2304.
4. Reaven GM. The metabolic syndrome: time to get off the merry-go-round? *J Intern Med*. 2011;269(2):127–136.
5. Cortese S, Moreira-Maia CR, St Fleur D, Morcillo-Penalver C, Rohde LA, Faraone SV. Association between ADHD and obesity: a systematic review and meta-analysis. *Am J Psychiatry*. 2016;173(1):34–43.
6. Stafeev IS, Menshikov MY, Tsokolaeva ZI, Shestakova MV, Parfyonova YV. Molecular mechanisms of latent inflammation in metabolic syndrome. Possible role of sirtuins and peroxisome proliferator-activated receptor type gamma. *Biochemistry (Mosc)*. 2015;80(10):1217–1226.
7. Prather AA, Vogelzangs N, Penninx BW. Sleep duration, insomnia, and markers of systemic inflammation: results from the Netherlands Study of Depression and Anxiety (NESDA). *J Psychiatr Res*. 2015;60:95–102.
8. Instanes JT, Klungsoyr K, Halmoy A, Fasmer OB, Haavik J. Adult ADHD and comorbid somatic disease: a systematic literature review. *J Atten Disord*. 2018;22(3):203–228.
9. Verlaet AA, Noriega DB, Hermans N, Savelkoul HF. Nutrition, immunological mechanisms and dietary immunomodulation in ADHD. *Eur Child Adolesc Psychiatry*. 2014;23(7):519–529.
10. Huang W, Ramsey KM, MarcheVA B, Bass J. Circadian rhythms, sleep, and metabolism. *J Clin Invest*. 2011;121(6):2133–2141.

## SUBMISSION &amp; CORRESPONDENCE INFORMATION

Submitted for publication March 20, 2018

Submitted in final revised form March 20, 2018

Accepted for publication March 29, 2018

Address correspondence to: Dora Wynchank, PsyQ Expertise Center Adult ADHD, Carel Reinierszkade 197, 2593 HR The Hague, The Netherlands; Tel: +31 (0)88 35 73604; Fax: +31 (0)88 35 73020; Email: wynchank@gmail.com

## DISCLOSURE STATEMENT

Dr. Wynchank has served on the advisory boards of Janssen BV, Novartis and Eli Lilly for activities outside the scope of this letter (2009–2014). The authors report no conflicts of interest.