Cardiovascular autonomic dysfunction and sleep abnormalities in children with Prader-Willi syndrome

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Abstract

Purpose: Prader-Willi syndrome (PWS) is a rare genetic neurodevelopmental condition characterized by cognitive disabilities, behavioral problems, hypothalamic dysfunction with obesity, and sleep disorders. A few studies have reported autonomic nervous system dysfunction. Our aim was to investigate dysautonomia by combining sleep studies and standard autonomic testing in regularly followed children with PWS.

Methods: In this retrospective study, heart rate variability was analyzed during each sleep stage (polysomnography) using time and frequency domains in PWS children (N = 37) compared with age-matched controls (N = 20). Cardiovascular autonomic testing (Ewing tests) and sweating assessment (electrochemical skin conductance) were also performed in patients over 6 years (N = 23).

Results: Autonomic testing: Heart rate changes with active standing and with deep breathing were impaired in 47% and 22% of the children, respectively. Asymptomatic orthostatic hypotension (OH) was found in 26%. Baroreflex sensitivity in supine position was in normal range (14.1 ± 6.7 ms/mmHg). Electrochemical skin conductance was normal. Sleep study: 46% of the children with PWS had obstructive sleep apnea and 24% had central sleep apnea. None of these events were observed in the control group. Mean R-R and time domain heart rate variability parameters were significantly lower compared with controls in N2 and Rapid Eye Movement (REM) sleep stages. Narcoleptic-like phenotype was found in 47% associated with lower low-frequency (LF) power (sympathetic index) in REM sleep.

Conclusion: Our study confirms a decreased vagal modulation during both wakefulness and sleep in children with PWS. OH in some patients suggests a sympathetic dysfunction. These changes may contribute to the increased cardiovascular risk in PWS.

Keywords: Autonomic nervous system; Cardiovascular regulation; Heart rate variability; Polysomnography; Prader–Willi syndrome.

Conflict of interest statement

Declarations. Conflict of interest: The authors have no competing interests to declare that are relevant to the content of this article. Ethical approval: A retrospective analysis of the data of patients with PWS and control patients was performed over the years 2014–2017 in the Toulouse University Hospital Center. Sixty-two evaluations and/or data items were gathered. In line with the French law on ethics, patients

were informed that their codified data would be used for the study. According to French ethics and regulatory law (public health code), retrospective studies based on the exploitation of usual care data do not have to be submitted to an ethics committee but they do have to be declared or covered by the reference methodology of the French National Commission for Informatics and Liberties (CNIL). The collection and computer processing of personal and medical data were carried out to analyze the results of the research. The Toulouse University Hospital Center signed a commitment of compliance to the reference methodology MR-004 of the CNIL. After evaluation and validation by the data protection officer and according to the General Data Protection Regulation*, this study met all criteria and was then registered in the study data registry of the Toulouse University Hospital Center (number's register: RnIPH 2018-34) and covered by the MR-004 (CNIL number: 2206723 v 0).This study was approved by Toulouse University Hospital Center, which confirms that the ethical requirements were fully respected in the above report. *Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016.

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