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Ischemic Lesion Formation in Solitary Tract Nuclei During Central Sleep Apnea With Heart Failure – Reply –

We thank Dr Jaster for his interest in the recent 2 papers published in the *Circulation Journal*, including ours.[1,2] Dr Jaster and his colleagues previously reported that excessive afferent signals can damage the solitary tract nuclei with resultant cerebral ischemia and infarction, which could disrupt medullary brain autonomic regulation and cause severe cardiac arrhythmias.[3,4] Regarding the interaction between the brain and the heart, it is an interesting opinion that fatal arrhythmias in chronic heart failure (CHF) patients with sleep-disordered breathing (SDB) are caused by impairment of the solitary tract nuclei with various negative prognostic impacts. Indeed, several reports showed that various cerebral brain regions, including those in the hippocampus and the solitary tract nuclei, are impaired in CHF patients with SDB.[3,5] Repeated apneic and hypopneic events during sleep with intermittent hypoxemia increase sympathetic vasoconstriction and decrease vascular protective mechanisms, resulting in structural and functional changes of the brain.[6] On the other hand, Canessa et al reported that cognitive and structural deficits in patients with obstructive sleep apnea could be improved by nocturnal respiratory treatment.[7] Thus, improvement of SDB may ameliorate the impairment of various cerebral brain regions, including those in the hippocampus and the solitary tract nuclei in CHF patients with SDB. It has been previously reported that fatal arrhythmic events are associated with the severity of SDB.[1,8] Those reports support the notion that SDB is an independent risk factor for the occurrence of malignant ventricular arrhythmias.[1,8] Javaheri et al also reported that the improvement of SDB by CPAP was associated with a significant reduction in ventricular arrhythmias.[9] Thus, we consider that effective treatment of SDB could reduce fatal arrhythmias in CHF patients.

As Dr Jaster pointed out, the effects of nocturnal respiratory therapy for CHF with SDB remain controversial because conflicting results have recently been reported.[8–10] In the Canadian Continuous Positive Airway Pressure for Patients with Central Sleep Apnea and Heart Failure Trial (CANPAP), the post hoc analysis showed that CPAP may be beneficial for both cardiac function and prognosis of CHF patients with central sleep apnea (CSA) when the apnea-hypopnea index is <15 per hour.[10] Yoshihisa et al also reported that nocturnal adaptive servo-ventilation (ASV) reduces sympathetic nervous activity and myocardial damage in CHF patients with SDB.[11] In contrast, the Treatment of Sleep-Disordered Breathing with Predominant Central Sleep Apnea by Adaptive Servo Ventilation in Patients with Heart Failure (SERVE-HF) Trial in CHF patients with CSA found a statistically significant 2.5% increase in annual risk of cardiovascular mortality in those with LVEF ≤45% compared with the control group.[12] One possible explanation for this adverse effect is the high pressure induced by ASV, which could worsen the hemodynamics of CHF patients. Indeed, the effective therapeutic strategy for respiratory interventions remains to be developed for the management of CHF patients with SDB.[13]

We consider that effective treatment of SDB ameliorates the vicious circle, including hypoxia, increased sympathetic nerve activity and excessive afferent signals, and improves the prognosis of CHF patients with SDB.

Conflict of Interest

The authors declare no conflicts of interest that relate to this work.

References

1. Satake H, Sugimura K, Fukumoto Y, Fukuda K, Nakano M, Kondo M, et al. Effect of respiratory therapy on the prognosis of chronic heart failure patients complicated with sleep-disordered breathing: A pilot efficacy trial. *Circ J* 2016; **80:** 130–138.
2. Momomura S, Seino Y, Kihara Y, Adachi H, Yasumura Y, Yokoyama H, et al; for the SAVIOR-C investigators. Adaptive servo-ventilation therapy for patients with chronic heart failure in a confirmatory, multicenter, randomized, controlled study. *Circ J* 2015; **79:** 981–990.
3. De Caro R, Parenti A, Montisci M, Guidolin D, Macchi V. Solitary tract nuclei in acute heart failure. *Stroke* 2000; **31:** 1187–1193.
4. Jaster JH, Ottaviani G, Matturri L, Lavezzi AM, Zamecnik J, Smith TW. Sudden unexpected death related to medullary brain lesions. *Am J Forensic Med Pathol* 2008; **29:** 371–374.
5. Suzuki H, Sumiyoshi A, Matsumoto Y, Duffy BA, Yoshikawa T, Lythgoe MF, et al. Structural abnormality of the hippocampus associated with depressive symptoms in heart failure rats. *Neuroimage* 2015; **105:** 84–92.
6. Gozal E, Row BW, Schurr A, Gozal D. Developmental differences in cortical and hippocampal vulnerability to intermittent hypoxia in the rat. *Neurosci Lett* 2001; **305:** 197–201.
7. Canessa N, Castronovo V, Cappa SF, Aloia MS, Marelli S, Falini A, et al. Obstructive sleep apnea: Brain structural changes and neurocognitive function before and after treatment. *Am J Respir Crit Care Med* 2011; **183:** 1419–1426.
8. Yamada S, Suzuki H, Kamioka M, Suzuki S, Kamiyama Y, Yoshihisa A, et al. Sleep-disordered breathing increases risk for fatal ventricular arrhythmias in patients with chronic heart failure. *Circ J* 2013; **77:** 1466–1473.
9. Javaheri S. Effects of continuous positive airway pressure on sleep apnea and ventricular irritability in patients with heart failure. *Circulation* 2000; **101:** 392–397.
10. Arzt M, Floras JS, Logan AG, Kimoff RJ, Series F, Morrison D, et al. Suppression of central sleep apnea by continuous positive airway pressure and transplant-free survival in heart failure: A post hoc analysis of the Canadian Continuous Positive Airway Pressure for Patients with Central Sleep Apnea and Heart Failure Trial (CANPAP). *Circulation* 2007; **115:** 3173–3180.
11. Yoshihisa A, Suzuki S, Miyata M, Yamaki T, Sugimoto K, Kunii H, et al. 'A single night' beneficial effects of adaptive servo-ventilation on cardiac overload, sympathetic nervous activity, and myocardial damage in patients with chronic heart failure and sleep-disordered breathing. *Circ J* 2012; **76:** 2153–2158.
12. Cowie MR, Woehrle H, Wegscheider K, Angermann C, d'Ortho MP, Erdmann E, et al. Adaptive servo-ventilation for central sleep apnea in systolic heart failure. *N Engl J Med* 2015; **373:** 1095–1105.
13. Koyama T, Watanabe H, Ito H. Respiratory intervention in patients with chronic heart failure. *Circ J* 2016; **80:** 60–61.

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