Review Article

Autonomic Dysfunction in Patients with Vertigo

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Abstract

Autonomic function and vertebral blood flow were measured in patients with vertigo. Based on our findings obtained in a series of studies, we propose the following hypothesis of sympatho-vascular mechanisms of vertigo. Hyporesponse of the sympathetic nervous system to stress observed in patients with vertigo induces asymmetrical blood flow of the vertebral artery. Asymmetrical activity of the sympathetic nervous system observed in patients with vertigo also induces asymmetrical blood flow of the vertebral artery. The asymmetrical vertebral blood flow induces asymmetrical activities of the inner ear and/or the vestibular nuclei, resulting in the development of vertigo.

Key words Vertigo, Sympathetic nervous system, Parasympathetic nervous system, Vertebral artery, Stress

Introduction

Autonomic dysfunction has been proposed to be an underlying mechanism of the development of vertigo, although there is little evidence.[1,2] In the present review, a series of our studies on autonomic nervous activity and the vertebral blood flow in patients with vertigo is summarized and how the autonomic dysfunction triggers the onset of vertigo is discussed.

Systemic Autonomic Dysfunction in Patients with Vertigo

Systemic autonomic nervous function was examined in patients with vertigo including Meniere's patients by means of power spectral analysis of heart rate variability.[3] The power spectral density (PSD) of beat-to-beat heart rate intervals was analyzed using a continuous non-invasive finger blood pressure recording system. A fast-Fourier transform algorithm was used to compute the PSD. In frequencies up to 5 Hz, the PSD of heart rate variability contains three major components: a low frequency (P1), a middle frequency (P2) and a high frequency (P3). Each component was normalized by dividing the absolute values of total power (T). P2 and P3 were used as an index of sympathetic and parasympathetic nervous functions, respectively. In patients with vertigo at rest, the normalized power of P2 slightly increased and the normalized power of P3 significantly decreased, in comparison with healthy subjects at rest (Fig. 1). These findings indicated that the parasympathetic nervous activity at rest was suppressed in patients with vertigo. Yamada et al. used power spectral analysis of heart rate variability and reported that parasympathetic hypofunction in patients with Meniere's disease.[4]

Then, the effects of passive tilt up on the autonomic nervous activity were examined in patients with vertigo. In healthy subjects, the normalized power of P2 increased and the normalized power of P3 decreased with passive tilt up. These findings indicated that the sympathetic nervous activity was stimulated and the parasympathetic nervous activity was suppressed in response to passive tilt up. On the contrary, in spite of a decrease of the normalized power of P3, passive tilt up did not increase the normalized power of P2 in patients with vertigo (Fig. 2). These find-

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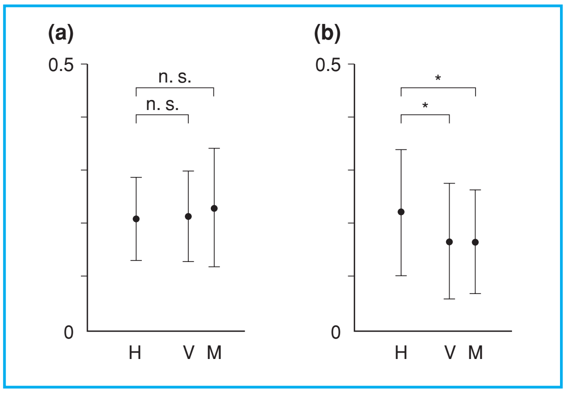

Fig. 1 Normalized power of P2 as an index of sympathetic activity (a) and normalized power of P3 as an index of parasympathetic activity (b) in health subjects (H), patients with vertigo (V) and patients with Meniere's disease (M) at rest

Points are means ± SD. *$P<0.05$.

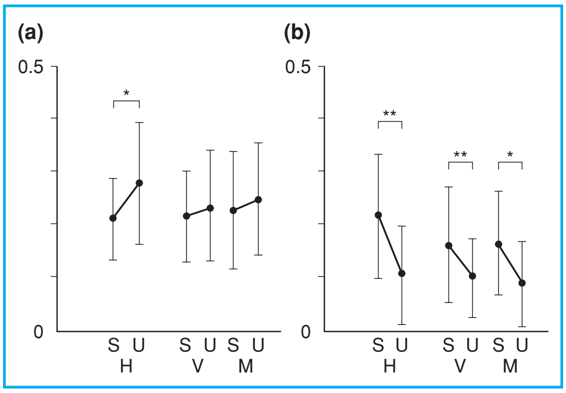

Fig. 2 Normalized power of P2 as an index of sympathetic activity (a) and normalized power of P3 as an index of parasympathetic activity (b) in health subjects (H), patients with vertigo (V) and patients with Meniere's disease (M) in response to passive tilt up

Points are means ± SD. S: supine, U; upright. *$P<0.01$, **$P<0.05$.

ings indicated that response of the sympathetic nervous system to passive tilt up was impaired. Yamada et al. also reported that sympathetic response to postural changes was suppressed in patients with Meniere's disease.[4]

It has been speculated that both mental and physical stress played an important role in the onset of vertigo.[5] On the other hand, because of neurotic personality in patients with vertigo, vertigo itself can be a stress.[6] Therefore, it is suggested that a reciprocal causal relationship between vertigo and stress induced the suppression of the parasympathetic nervous activity and the repeated stimulation of the sympathetic nervous activity. The present finding of the impaired response of the sympathetic nervous system to passive tilt up might be explained by the desensitization of the sympathetic nervous system after repeated activations in patients with vertigo. Accordingly, it is suggested that the response of the sympathetic nervous system to stress is also desensitized in dizzy patients.

Asymmetrical Sympathetic Activity in Patients with Vertigo

The right-left differences of sympathetic nervous activity were examined in patients with vertigo including Meniere's patients by means of recovery curve of palm skin temperature after cold exposure.[7] A contact skin thermometer was attached to the palm of both hands. Both hands were immersed in iced water for 30 sec. Subsequently, palm skin temperature of both hands was recorded at 1 min intervals. Figs. 3 and 4 represent the thermal recordings of both hands in a healthy subject and a Meniere's patient, respectively. There is no difference in the recovery of palm skin temperature between right and left hands of the healthy subject (Fig. 3). However, asymmetrical recovery of palm skin temperature was observed in patients with Meniere's disease during an active spell. After immersion in iced water, the patient showed an abnormal slow recovery time in the side affected by Meniere's disease. Then, the asymmetrical recovery of palm skin temperature disappeared in the interval between active spells in the same patient (Fig. 4). During active spells, a significantly high proportion of Meniere's patients had an anisothermal recovery of palm skin temperature after immersion in iced water, in comparison with that of healthy subjects. However, during intervals between active spells, the frequency of anisothermal recovery of palm skin temperature in Meniere's patients did not differ from that of healthy subjects (Table 1). Since the palm skin temperature is regulated by anastomotic skin blood flow, and its blood flow through arteriovenous anastomoses is controlled by efferent sympathetic nerve fibers,[8] these findings indi-

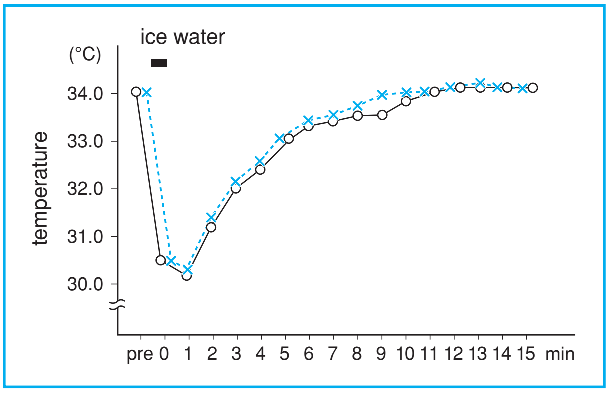

Fig. 3 Changes in palm skin temperature in a healthy subject after hand being immersed in iced water

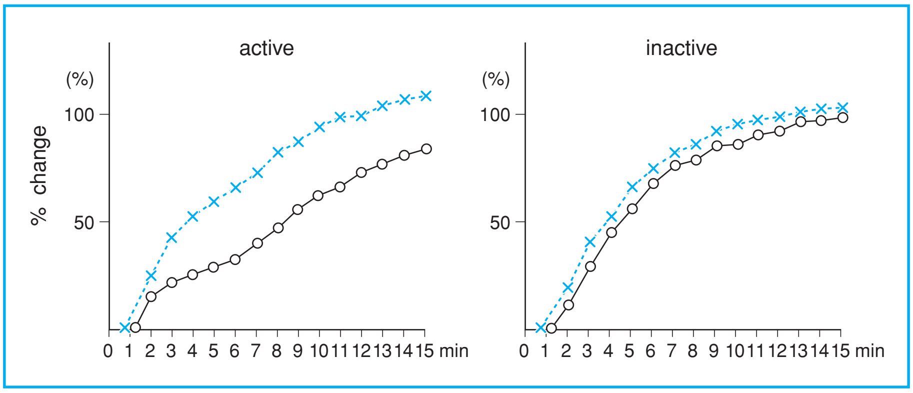

Fig. 4 Changes in palm skin temperature in a patient with Meniere's disease after hand being immersed in iced water

Active: during active spells, inactive: during intervals between active spells. Points are percentages of the palm skin temperature before immersion in iced water

Table 1 Appearance of anisothermal recovery of palm skin temperature after hand immersed in iced water

Healthy	Meniere's disease	
	active	inactive
18.2% (6/33)	60.0%* (12/20)	19.2% (5/26)

*$P<0.05$

cated the asymmetrical activity of the sympathetic nervous activity in patients with vertigo. Because of the correlation between the sympathetic asymmetry and active spells, it is suggested that the asymmetrical activity of the sympathetic nervous activity contributed to vertigo attacks. Uemura et al. reported autonomic dysfunction revealed by mecholyl test on the affected side of Meniere's patients.[9] Yamada et al. also reported sympathetic hypofunction in Meniere's patients at the attack stage, but not at the interval stage.[4]

Asymmetrical Vertebral Blood Flow in Patients with Vertigo

The blood supply of both inner ear and vestibular nuclei in the brain stem originates from the vertebral artery, of which blood flow is mainly controlled by the sympathetic nervous system. A question arises whether the asymmetrical activity of the sympathetic nervous activity in patients

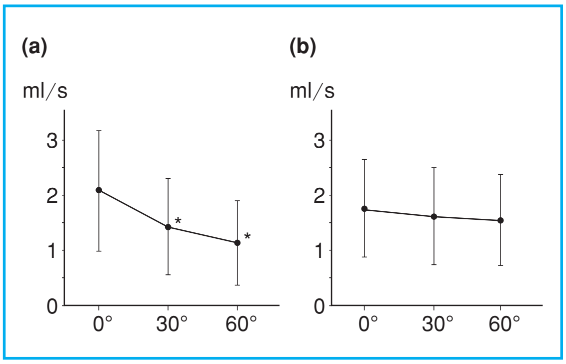

Fig. 5 Blood flow of the vertebral artery in patients with vertigo (a) and in healthy subjects (b)

Points are means ± SD. **P*<0.01 vs. 0 degree.

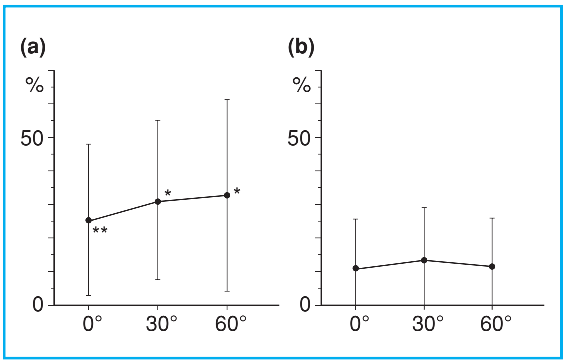

Fig. 6 Right-left differences of the vertebral blood flow in patients with vertigo (a) and in healthy subjects (b)

Points and bars means ± SD of asymmetrical percentage calculated as follows:

$$\%\text{Asymmetry} = \frac{|\text{Right blood flow} - \text{Left blood flow}|}{\text{Right blood flow} + \text{Left blood flow}} \times 100$$

**P*<0.05 vs. 0 degree,
***P*<0.01 vs. healthy subjects at 0 degree

with vertigo may affect the blood flow of the vertebral artery. To clarify the question, the effects of passive tilt up on the vertebral blood flow were examined in patients with vertigo.[10] The blood flow of the vertebral artery was measured at the level of C2-C3 by means of Doppler spectral analysis. There were no differences of vertebral blood flow at rest between patients with vertigo and healthy subjects at rest. In healthy subjects, the vertebral blood flow did not change with passive tilt up. By contrast, the vertebral blood flow significantly decreased in response to passive tilt up in patients with vertigo (Fig. 5).

Then, the right-left differences of the vertebral blood flow were analyzed. The right-left differences of the vertebral blood flow in patients with vertigo at rest were significantly more than those in healthy subjects at rest. In response to passive tilt up, the right-left differences of the vertebral blood flow were significantly higher in dizzy patients. However, the asymmetry of vertebral blood flow did not increase with passive tilt up in healthy subjects (Fig. 6). Since the vertebral blood flow is mainly regulated by the sympathetic nervous system, it is suggested that in patients with vertigo, both poor response of the sympathetic nervous system to stress and asymmetrical activity of the sympathetic nervous activity induce asymmetrical vertebral blood flow.

Furthermore, changes in the right-left differences of the vertebral blood flow were examined in patients with Meniere's disease. The right-left differences of the vertebral blood flow were significantly higher during active spells, in comparison with those during intervals between active spells (Table 2). These findings suggested that the asymmetrical vertebral blood flow contributed to the onset of vertigo in patients. Asymmetrical vertebral blood flow might induce asymmetrical activities of the inner ear and/or the vestibular nuclei, resulting in the development of vertigo.

Table 2 %Asymmetry of vertebral blood flow in healthy subjects and patients with Meniere's disease

Healthy	Meniere's disease	
	active	inactive
2.9 ± 3.8%	36.8 ± 6.7%*	18.1 ± 4.3%

Values are means ± SD, **P*<0.05

Hypothesis of Sympatho-Vascular Mechanisms of Vertigo

In conclusion, in patients with vertigo, parasympathetic nervous activity at rest was suppressed and the response of the sympathetic nervous system to passive tilt up was impaired. These findings suggested that a reciprocal causal relationship between vertigo and stress induced the suppression of parasympathetic nervous activity and desensitized sympathetic nervous activity in response to stress. Patients with vertigo also have asymmetrical sympathetic nervous activity. Because of the correlation between the sympathetic asymmetry and active spells, it is suggested that asymmetrical sympathetic nervous activity contributed to vertigo attacks. In addition to the above mentioned autonomic dysfunction in patients with vertigo, their vertebral blood flow was significantly lower in response to passive tilt up. In response to passive tilt up, the right-left differences of the vertebral blood flow significantly increased in these dizzy patients. Since vertebral blood flow is mainly regulated by the sympathetic nervous system, it is suggested that in patients with vertigo, both poor response of the sympathetic nervous system to stress and asymmetrical activity of the sympathetic nervous system induce asymmetrical vertebral blood flow. Because of the correlation between asymmetry of the vertebral blood flow and active spells, it is suggested that asymmetrical vertebral blood flow induces asymmetrical activities of the inner ear and/or the vestibular nuclei, resulting in the development of vertigo. In an animal study, it was reported that unilateral electrical stimulation of the cervical sympathetic ganglion induced directional preponderance of per-rotatory nystagmus in rabbits, suggesting that asymmetrical sympathetic activity causes asymmetric vestibular activities.[11]

Based on our findings, we proposed the following hypothesis of sympatho-vascular mechanisms of vertigo: Hyporesponse of the sympathetic nervous system to stress observed in patients with vertigo induces asymmetrical blood flow of the vertebral artery. Asymmetrical activity of the sympathetic nervous system observed in patients with vertigo also induces asymmetrical blood flow of the vertebral artery. The asymmetrical vertebral blood flow induces asymmetrical activities of the inner ear and/or the vestibular nuclei, resulting in the development of vertigo.

Acknowledgements

I would like to dedicate this review to the memory of Dr. Toru Matsunaga, Professor Emeritus of Osaka University.

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