Cardiocirculatory responses to human passive walking-like leg movement in the standing posture

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Abstract Passive walking-like leg movement in the standing posture (PWM) has been used to activate neural mechanisms responsible for generating gait movement and to prevent disuse syndrome including muscle atrophy, bone mass loss and joint contracture as a rehabilitation tool for individuals with gait disturbance. However, circulatory responses to PWM have not been fully determined, despite the potential risk of orthostatic intolerance from standing posture. Quiet standing (QS) causes a decrease in blood volume in the ventricles due to the pooling of blood in the lower extremities and subsequent decrease in stroke volume. On the other hand, cardiac contractility and heart rate increase to maintain cardiac output due to enhancement of sympathetic nerve activity. The enhancement of cardiac activity is linked to vasovagal responses characterized by bradycardia and the drop in arterial blood pressure and symptoms such as pallor, lightheadedness, hyperventilation and blurred vision, especially in young individuals. In addition, QS can cause orthostatic hypotension due to loss of sympathetic control of the heart and vasculature in individuals with cervical spinal cord injury. Vasovagal response and orthostatic hypotension may lead to syncope. However, PWM has been shown to induce a decrease in cardiac activity compared to that during QS in young individuals and a large increase in arterial blood pressure in individuals with cervical spinal cord injury, suggesting that PWM reduces the risks of vasovagal responses and orthostatic hypotension and, consequently, syncope. The efficacy and safety of PWM suggests that PWM is a useful tool for rehabilitation in individuals with gait disturbance.

Keywords: gait, orthostatic intolerance, rehabilitation, standing

Introduction Passive walking-like leg movement in the standing posture (PWM) has been shown to induce locomotor-like muscle activities in passively moved lower extremities in humans, because neural mechanisms responsible for generating gait movement can be activated. In addition, PWM has the potential to prevent disuse syndrome including muscle atrophy, bone mass loss, joint contracture and pressure sores - that arises in paralyzed lower limbs in individuals with disabilities. Thus, PWM is considered to be an effective tool for rehabilitation in individuals with gait disturbance. On the other hand, circulatory responses to PWM have not been fully determined, despite the potential risk of orthostatic intolerance from standing posture. Quiet standing (QS) causes a decrease in blood volume in the ventricles due to the pooling of blood in the lower extremities and subsequent decrease in stroke volume. Cardiac contractility and heart rate increase to maintain cardiac output due to the enhancement of sympathetic nerve activity. The enhancement of cardiac activity is linked to vasovagal response, which is characterized by bradycardia and a drop in arterial blood pressure, and symptoms such as pallor, lightheadedness, hyperventilation and blurred vision. This response occurs with a high incidence in young individuals (aged 10-20 years). In addition, QS can cause orthostatic hypotension. Individuals with spinal cord injury (SCI) at cervical levels are prone to orthostatic hypotension because they have lost sympathetic control of the heart and vasculature. Since the vasovagal response and orthostatic hypotension may lead to syncope, it is important to know how the vasovagal response and orthostatic hypotension are affected by PWM in order to establish safe PWM.

In this review, the effects of PWM on vasovagal responses in young individuals and orthostatic hypotension in individuals with SCI are mainly discussed on the basis of the results of the authors’ own work.

How to conduct PWM and QS

In a series of the author’s studies, a commercially avail-
Cardiac activity responses to PWM in young individuals

Ogata et al.\(^3\) compared cardiac activity responses during PWM to those during QS in healthy young individuals aged 19 ± 1 years. The subjects (n = 13) underwent PWM and QS trials. In the PWM trial, subjects spent 5 minutes in a sitting position, followed by a 5-minute QS period to determine baseline levels in sitting and standing states with a 1-minute transition period for postural change from sitting to standing. The subjects then underwent 25 minutes of rhythmic PWM at 1 Hz. This movement frequency corresponds to 120 steps per minute during normal walking. The protocol of the QS trial was the same except that the subjects underwent 25 minutes of QS instead of 25 minutes of PWM. In the PWM trial, HR, which had been increased by postural change from sitting to standing, decreased to the sitting level during PWM. In the QS trial, on the other hand, HR increased gradually with time. The decrease in HR during PWM was shown to be caused by predominance of parasympathetic nerve activity according to HR variability analysis. It is thought that increased venous return due to the muscle pump effect by PWM increases afferent input from cardiopulmonary baroreceptors, which would inhibit efferent sympathetic nerve activity, resulting in a shift of the sympathovagal balance towards parasympathetic activation. Ogata et al.\(^3\) also determined changes in double product (DP; HR × systolic arterial blood pressure) as an index of cardiac oxygen consumption. DP, which had been increased by postural change from sitting to standing, increased gradually with time in the QS trial, whereas it remained unchanged during PWM. These results suggest that cardiac activity responses to orthostatic stress are suppressed during PWM.

Ogata et al.\(^3\) reported that two of thirteen subjects showed vasovagal responses during a 25-min QS period in the QS trial, but that they completed the PWM trial without any vasovagal response. The most commonly used model for triggering a vasovagal response is the Bezold-Jarisch reflex. In a literature review by Fenton et al.\(^3\), the mechanism underlying the Bezold-Jarisch reflex was summarized as follows. Upright posture causes a pooling of blood in the lower extremities, decreasing blood volume in the ventricles and at the level of the aortic arch and carotid sinus. This results in decreased afferent neural activity from baroreceptors, producing increased sympathetic tone to the vasculature and heart, with subsequent vasoconstriction and increased inotropy (contractility) and HR. The Bezold-Jarisch reflex is initiated by a decrease in ventricular volume and an increase in ventricular inotropy. This activates sensory receptors that respond to wall tension in the inferoposterior portion of the left ventricle, paradoxically increasing neural traffic to the central nervous system through afferents in the vagus nerve. Sympathetic output to the vasculature and heart decreases and parasympathetic activity increases. Based on this putative mechanism, it is suggested that the avoidance of vasovagal response in the PWM trial is caused by suppression of cardiac activity responses to orthostatic stress.

The effect of movement frequency during PWM on cardiocirculatory responses in young individuals was examined by Ogata et al.\(^3\). The subjects (n = 8) in their study spent 4 minutes in a sitting position, and this was followed by a 4-minute QS period with a 1-minute transition period for postural change from sitting to standing. The subjects then underwent 10-minute rhythmic PWM. Three types of movement frequency were used: 0.33 Hz, 0.66 Hz and 1 Hz. These frequencies correspond to 40 steps per minute, 80 steps per minute and 120 steps per minute during normal walking, respectively. Patterns of changes in HR and DP from the QS period to the PWM period were similar in the three types of PWM. According to a study by Sekiya et al.\(^9\), the tempos of walking with instruction to walk at the slowest speed are 67.4 steps per minute in males aged 26.3 years and 60.4 steps per minute in females aged 21.6 years. These findings suggest that PWM with a tempo during normal walking of less than the slowest speed is sufficient to avoid vasovagal responses.

Blood pressure responses to PWM in individuals with SCI

Ogata et al.\(^3\) determined blood pressure responses to PWM in individuals with SCI. In their study, individuals with SCI were divided into two groups: individuals with lesion level between thoracic (T) 6 and cervical (C) 6 (higher SCI; HSCI) and individuals with lesion level between T10 and T12 (lower SCI; LSCI). The reason for this is as follows: it is known that spinal sympathetic reflex activity can be induced in the paralyzed region in response to a stimulus originating below the level of the
SCI. Although spinal reflexes can be seen in upper and lower thoracic injured individuals, systemic pressure response is confined to upper level injured individuals who have lost supraspinal control of most of the greater splanchnic nerve (GSN) outflow. The uppermost ganglion contributing to the GSN resides in T5–7 and the lowermost ganglion contributing to the GSN resides in T9–11 in most cases. Therefore, a pressor response should be greater in HSCI than in LSCI if spinal sympathetic reflexes are induced during PWM. The subjects in the study by Ogata et al. spent 6 minutes in a sitting position, and this was followed by a 6-minute QS period. Thereafter, they performed 12-minute rhythmic PWM at 1 Hz. Blood pressure responses to PWM in HSCI (n=7) and LSCI (n=5) as well as able-bodied individuals (n=12) were compared. In HSCI, two individuals with cervical SCI in HSCI showed decreases in systolic blood pressure and diastolic blood pressure to levels in the definition of orthostatic hypotension by postural change from sitting to standing (20 mmHg and 10 mmHg, respectively). Several studies have shown that individuals with cervical SCI are prone to orthostatic hypotension by postural change from the supine position to upright position, but this is not the case in individuals with thoracic SCI or able-bodied individuals. On the other hand, there were greater pressor responses to PWM in HSCI than in the other two groups. The levels of blood pressure during PWM exceeded the levels of blood pressure during sitting. These greater pressor responses in HSCI are thought to be caused in part by spinal sympathetic reflex.

Ogata et al. observed a linear relationship between a decrease in mean arterial blood pressure and an increase in minute ventilation (VE) during QS in individuals with SCI. It is thought that a sensation of breathlessness is closely related to excessive ventilation for the level of activity (generally measured as O2 uptake). A sensation of breathlessness is a possible symptom that occurs with orthostatic hypotension. Thus, Ogata et al. determined whether pressor responses during PWM suppress an increase in VE and, consequently, decrease the ventilatory equivalent (VE/V̇O2) and breathlessness. Subjects (n = 8) had lesion levels between C6 and T7. They spent 5 minutes in a sitting position, and this was followed by a QS period with a 1-min transition between sitting and QS periods. Subjects remained in a QS position for as long as they could tolerate, but the maximal duration was limited to 15 minutes. If subjects showed mild presyncope symptoms, PWM at 1 Hz was immediately commenced and was sustained for 6 minutes. The intensity of the breathlessness sensation was assessed with the use of a modified Borg category scale. This scale has 11 scores ranging from 0 to 10 with adjectival descriptions (0, not at all; 1, very slight; 2, slight; 3, moderate; 4, somewhat severe; 5, severe; 7, very severe; 9, very very severe; 10, maximal). VE/V̇O2 during QS was significantly higher than that during sitting. The increase was attributed to a significant increase in VE without a significant change in V̇O2. On the other hand, VE/V̇O2 during PWM was significantly lower than that during QS. The breathlessness score during sitting was 0 or 1. Two subjects reported severe breathlessness (scores of 5 and 6) in the last 3 minutes of QS, but these subjects reported only slight or moderate breathlessness (scores of 1 and 3) during PWM. Consequently, the breathlessness scores during PWM became less or equal to 3.

Ogata et al. reported an individual with cervical SCI. The subject spent 6 minutes in a sitting position followed by a 6-minute QS period. Thereafter, the subject performed 12-minute rhythmic PWM at 1 Hz. The subject showed a unique blood pressure response during PWM, i.e., a decrease in blood pressure during PWM below the sitting level. This subject showed a severe muscle spasm during QS and an abrupt decrease in spasm during PWM. It is thought that some vasodilator effects associated with muscle spasm that arise during QS might have overcome the pressor effect of PWM and caused the fall in blood pressure below the sitting level during PWM. The findings of that study suggest that PWM does not always prevent hypotension.

In summary, PWM induces pressor response and a subsequent decrease in ventilatory equivalent and associated breathlessness in HSCI. However, responses of blood pressure and ventilation may be different if there is a severe muscle spasm during QS before the onset of PWM.

**Conclusions**

Besides the efficacy of PWM in individuals with gait disturbance, a series of the author’s studies have demonstrated the safety of PWM in terms of orthostatic intolerance. The efficacy and safety of PWM suggests that PWM is a useful tool for rehabilitation in individuals with gait disturbance. However, the possibility of PWM not preventing orthostatic intolerance should be taken into consideration. Furthermore, there might be other unknown risks during PWM, especially for individuals who have not taken a standing posture for a long period. To resolve these problems, further study is needed to determine whether the efficacy of PWM can be achieved even during passive leg movement in the sitting or supine position.

**Conflict of Interests**

The author declares that there is no conflict of interests regarding the publication of this article.

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