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Physiological Adaptations Following Endurance Exercises after Stroke: Focus on the Plausible Role of High-Intensity Interval Training

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Abstract

The endurance training is considered as an integral part of stroke rehabilitation. However, medical institutions did not systematically include aerobic exercises because of the lack of scientific evidence. It is mainly the case for high-intensity interval training (HIT) for which very few experiments were focused on after stroke. This review was designed to examine and compare the neurophysiological and physiological adaptations associated with two effective modalities of endurance training after stroke: the continuous low-intensity endurance training and the HIT. Based on the beneficial adaptations induced by HIT in healthy people and in patients with cardiovascular disorders, we postulate that this training modality might be involved in endurance program as complement or alternate of the traditional low intensity training in stroke patient. Therefore, including HIT in stroke rehabilitation may improve functional recovery by inducing rapid and significant beneficial physiological adaptations. Moreover, no clear recommendations were found on the appropriate timing for using HIT and other endurance training after stroke despite that the intervention timing is one of the major determinant of an effective recovery. The optimal time to initiate endurance program rehabilitation is thus discussed. Further studies are required to investigate the physiological adaptations to HIT compared to traditional endurance training as well as the combination of these two training modalities.

Keywords: Rehabilitation; Cerebral ischemia; Aerobic program; Cardiovascular fitness; Functional recovery

Introduction

When functional rehabilitation is stopped, stroke survivors frequently preserve chronic sensorimotor dysfunctions as well as metabolic and cardiovascular complications [1]. Moreover, they are still subjected to recurrent stroke within 5 years despite optimal medical management [2]. Therefore, it is crucial that scientists and therapists continue to investigate the effectiveness of different stroke rehabilitation components in order to improve functional recovery and reduce both dependence and the economic burden associated with the lack of effective treatments.

Endurance training has been developed as part of stroke rehabilitation (and post-rehabilitation period) to prevent complications relating to prolonged inactivity, to decrease the risk of recurrent stroke and to improve cardiorespiratory fitness, muscular endurance and motor function [3,4]. However, the lack of practical and physiological evidence-based exercise recommendations put a damper on medical institutions to include such physical training in stroke rehabilitation [5,6]. To date, no optimal endurance program has currently established itself as a dominant strategy but two endurance training modalities begin to be confronted in the stroke literature: the traditional continuous low-intensity aerobic exercise and the high-intensity interval training (HIT). The latter is defined as a brief and intermittent intense exercise that is interrupted by periods of active or passive rest [7,8]. This training modality could induce greater improvements in endurance performance and associated physiological adaptations than the traditional aerobic training in both health and disease. Over the last decade, HIT-induced physiological adaptations have been more investigated for cardiovascular diseases as heart failure or hypertension than for stroke patients. But, all the findings, discussed in this review, could give us insight on the plausible role of HIT as complement or alternate to the traditional endurance modality for stroke patient [9,10].

The purpose of the present review is to examine and compare the physiological adaptations associated with continuous low-intensity endurance training and HIT in order to clarify the benefits of these training modalities for stroke patients. Given that HIT have received little attention after cerebral ischemia, it is also necessary to use evidence from healthy adults and patients with heart disease. We will also discuss the optimal time to initiate such endurance training modalities because an effective functional recovery needs to take into account the timing of intervention.

Continuous Low Intensity Aerobic Training Generates Beneficial Neurophysiological and Physiological Adaptations After Stroke

Aerobic training recommendations

Since the last decade, it has been considered that aerobic exercise should be characterized by a progressive increase of intensity from 40 to 80% of the maximum heart rate reserve (HRR) with a frequency comprised between 3 and 5 sessions/week. The duration of continuous aerobic exercise should also be up to 20-60 min/session and is mainly performed on treadmill and/or cycle ergometer [4,11,12].

Safety of continuous aerobic exercises

It was frequently postulated that such physical exercise could be undertaken with a high level of safety by most people including stroke survivors [11,13,14]. Nevertheless, given that physical exercise is never performed without injury risks, the potential adverse effects of exercise is minimized by appropriate screening, monitoring and patient education [11]. To date, no major adverse events were reported after the above aerobic training program [4,12]. For example, Marzolini et al. demonstrated that no serious cardiovascular events occurred during 349 cycle ergometer or treadmill continuous aerobic exercises on a 6 months period [15]. In addition, as stroke patients exhibited more or less poorer standing balance, cycle ergometer appeared to be more safe approach than treadmill exercise [12,16,17].

Beneficial effects and physiological adaptations

Aerobic training improves the cardiorespiratory fitness, exercise tolerance to fatigue, quality of life and reduces the risk of cardiovascular disease and recurrent stroke [4]. Indeed, endurance-training programs using treadmill or cycle ergometer are now well known to induce higher peak work rate, higher walking velocity (10-m and 6-min walking tests) and improve peak oxygen consumption ($VO_{2\text{peak}}$) [3,18-20]. Such aerobic training also elicits significant reduction in submaximal energy expenditure. Indeed, the steady-state VO2 is reduced by 21 % during a standardized walking treadmill task (representative of typical slow hemiparetic gait) after 12 weeks of aerobic training [21]. These findings suggest that endurance training might enable activities of daily living to be performed at a lower percentage of the aerobic capacity.

Moreover, after 10 weeks of aerobic training, stroke patients showed lower systolic blood pressure at submaximal workloads during the graded exercise test [20]. Such events may be explained by vascular adaptations following physical training. Indeed, Billinger et al. proved that aerobic training focused on single paretic limb induced an increase of the femoral artery diameter, peak blood flow velocity and thus improved muscle blood flow (+42%) [22]. Moreover, it was recently confirmed that treadmill training during 6 months increased blood flow at both paretic and non-paretic limb contrary to the effects of traditional stroke rehabilitation [23] The same authors also indicated later that the vasomotor function could be improved at the cerebral level by measuring the middle cerebral artery blood flow velocity before and after 6-month of aerobic training [24]. However, the benefits of improved cardiovascular fitness did not systematically appear to extend to measurable change in disability and dependence functions or psychological state [25]

On a metabolic point of view, treadmill aerobic training is also known to improve glucose tolerance and insulin sensitivity that limit insulin resistance often observed in stroke patients [26].

Very few information were found on the brain activity following aerobic training. Only one study indicated that effective gait training on treadmill with body weight support, improving walking speed and endurance, was characterized by an increase of brain activity in the bilateral primary sensorimotor cortices, the cingulate motor areas, the caudate nuclei bilaterally and in the thalamus of the affected hemisphere during movement of the paretic foot [27]. In addition, improvement in sensorimotor function, assessed with the Fugl-Meyer Index, was significantly related to the improvement in aerobic capacity [20].

Several studies using rat models of cerebral ischemia enabled to better understand the aerobic training outcomes on the infarct volume and underlying neuromuscular adaptations. Indeed, several authors indicated that endurance training reduced infarct volume during the first weeks after cerebral ischemia [28-31]. Moreover, an early and daily treadmill exercise during 1 month increased the cellular expression levels of some neurotrophic factors, promoted cell growth and neural plasticity, but also reduced the expression of apoptosis markers [28,31,32]. Others studies indicated that early endurance exercise improved blood flow in the ischemic region and promoted angiogenesis [33]. Such finding was reinforced by the fact that daily treadmill training induced an increase of GFAP expression (proteins playing a role in vascular cerebral plasticity) [32]. Furthermore, it is noteworthy to add that only 3 days of aerobic exercise reduced microvascular endothelial cells apoptosis in brain related by shear stress increase following modest improvement of cerebral blood flow [34]. In addition, the hind-limb muscle atrophy was attenuated just after 6 sessions of daily low-intensity endurance exercise in both the type I and II fiber cross-sectional area (both in affected and non-affected limbs) [35]. Moreover, it was shown that aerobic treadmill training (20min/day, during 21 days) improved cholinergic system regulation/homeostasis and it was suggested that such adaptation allowing better limb motor function [36]. The muscle electromyographic activity returned to normal activity only after 10 days of treadmill training, optimizing balance and motor coordination during locomotion [37]. Unfortunately, the underlying neuromuscular adaptations at the spinal and supraspinal levels remain poorly understood in animal as well as in human models and deserves more attention. Indeed, it is important to notice that these parameters could give important information on the quality of treatments.

The recovery plateau may be counteracted by varying endurance-training program

A recovery plateau was mainly observed after 6 to 12 months post-stroke traditional functional rehabilitation meaning that no additional motor improvements were expected after this time period [38-40]. Given that current therapy termination decisions are predicted on the existence of such plateau, patients were discharged without recovered all their motor functions.

The exercise physiology gives us information on the way to avoid the performance stagnation and demotivation. Page et al. were the first authors to speak about periodization in stroke inspired from the athlete training [38]. If an athlete repeats the same training, a performance plateau occurs. Indeed, physical training needs to be varied in terms of training variables such as intensity, volume and type of exercise in order to induce long-term performance improvement. In accordance to Page et al., the absence of functional improvement observed in stroke patients may be avoided by changing the rehabilitation exercise characteristics. It was already shown that stroke patients who exhibited the presence of recovery plateau can show substantial motor improvement after participation in novel program requiring task-specific, repeated motor practice [41].

It seems reasonable to suppose that varying the way of performing aerobic exercises may be beneficial for stroke patients. Several authors reported that greater improvements were observed with higher exercise intensity after stroke [4,19]. For example, it was demonstrated that chronic mild to moderate stroke patients were able to tolerate 30 to 50 minutes of training at 60% to 80% of the HRR (3x/week), which could be considered as a high-intensity aerobic treadmill exercise [18]. Such program led to an increase in VO_{2peak}, HRR, maximum walking speed on 10 m and balance. Interestingly, gains in VO_{2peak} were still higher 1 year after the end of training compared to baseline value [18]. Given that high-intensity exercises could be supported by most stroke patients, we will now argue that the HIT should be considered as a plausible effective alternate or complement to traditional low-intensity endurance training in order to avoid recovery plateau and optimize cardiorespiratory fitness and motor function after stroke.

Including Interval-Training Exercises in Rehabilitation Program Seems to be an Effective Strategy after Stroke

Principles of HIT exercise

The use of HIT is based on the hypothesis that higher exercise intensity optimally stimulates the oxygen transport and utilization systems and thus induces greater improvements in VO_{2peak}. For that, this endurance training modality consists to work in the high-intensity training zone in order to elicit VO_{2peak}, or at least approach it at a very high percentage (85-95% of VO_{2peak}) [42,43]. The way to enhance VO_{2peak} by using HIT is thus very different than continuous low-intensity exercise in which the intensity is frequently fixed around the ventilatory threshold [43]. Moreover, HIT offers the opportunity to combine numerous factors including intensity and duration of exercise, number of intervals (active or passive), duration of recovery and the type of exercise (running, cycling, rowing…). It thus may allow varying the physiological response to endurance exercise during stroke rehabilitation. Therefore, the use of HIT in complement with continuous submaximal exercise may enable to avoid plateau recovery often observed after stroke. In addition, HIT could be perceived to be more enjoyable than moderate-intensity continuous exercise [44]. With such endurance exercise, stroke patients may perform high endurance intensities without high psychological constraints.

Rapid physiological adaptations following HIT program

HIT stimulates physiological remodeling comparable with moderate-intensity continuous training in healthy people despite a substantially lower time commitment (67% lower after HIT than continuous training) and reduced total exercise volume (90% lower after HIT than continuous training) [**8,45-49**]. For example, the HIT programs increased VO_{2peak}, compliance in peripheral arteries and improved endothelial function in the trained legs to the same extent as continuous endurance training despite a markedly reduced time commitment per session and total training volume [45,49,50]. Consequently, HIT may improve effectively the cardiorespiratory fitness of stroke patients in a shorter period of time.

Beneficial effects of HIT for people with cardiovascular disorders

Several authors demonstrated that HIT is more effective than continuous moderate-intensity exercise training for improving quality of life and cardiovascular fitness of hypertensive patients and heart failure patients [9,51-54]. Indeed, it was found that HIT was effective on hypertensive patients, and normotensive at high familial risk for hypertension, as shown by 1) a higher increase in VO_{2peak} (36% vs. 16% after continuous moderate-intensity exercise), 2) an improvement of endothelial function as indicated by an increase of nitric oxide (NO) release associated with higher NOx and lower endothelin-1 plasma levels, 3) a reduction in norepinephrine levels in both resting conditions, during and just after exercise, and 4) a reduction in arterial stiffness [9].

Likewise, HIT elicited the largest increases in VO_{2peak} for heart failure patients although all physical training modalities have proven to be beneficial [10,55]. Moreover, endothelial function and left ventricular morphology were improved to a greater extent following HIT compared with continuous moderate-intensity training as indicated by a decrease of systolic and diastolic blood pressure [52,54]. Authors also indicated that mitochondrial biogenesis and maximal rate of Ca^{2+} reuptake into sarcoplasmatic reticulum were higher after HIT [54]. Warburton et al. revealed that HIT also improved anaerobic tolerance to a greater importance than traditional continuous exercise modality [56]. Consequently, we can observe that HIT could act on many parameters known to determine the endurance performance and physical health of a subject.

As for healthy subjects, these beneficial adaptations were realized even though the training time commitment was much lower than traditional aerobic exercises without increasing the risk to patients [53,57,58]. If HIT is effective for patients with cardiovascular disorders, there are no reasons to believe that HIT could not be applied to stroke patients.

Beneficial effects of HIT in stroke patients

Despite the above evidence, very few studies were focused on HIT-induced neurophysiological or physiological adaptations after stroke. HIT can induce similar or even higher changes than traditional low-intensity continuous exercise in aerobic fitness and related-physiological adaptations in stroke patients. Katz-Leurer et al. demonstrated the beneficial effect of progressive interval training on cycle ergometer during 2 weeks, following by continuous exercises during 6 weeks, on the HR at rest, workload, work time and stair climbing [5]. However, the intensity was limited to 60 % of HRR during the protocol that is considered as moderate exercise intensity. Likewise, Duncan et al. also used interval training to improve endurance abilities for stroke patients but each bout of cycling effort involved different intensities (measured as rpm, higher then lower intensities in the same cycling bout) [57]. No reasons were advanced for this strategy choice. Nevertheless, authors found higher endurance capacities associated with gains in VO_{2peak}, an increase in duration of bike exercise and distance on the 6-min walk and the 10 m gait velocity compared with traditional aerobic training [57]. As it was mentioned above, low to moderate stroke patients were able to maintain high-intensity exercise [18]. Consequently, authors have recently used higher intensities in their HIT programs. In one study, stroke patients performed HIT on treadmill (4 x 4 minutes work periods separated by 3 min of active rest; intensity: 85-95% of HRpeak) during 4 weeks (5 days per week) [59]. Such HIT program induced an increase in VO_{2peak} (+11.6%) and in peak pulmonary ventilation compared to baseline values. Interestingly, the increase of VO_{2peak} was similar to that observed in other experiments after 6 months of low-moderate intensity treadmill training [3]. The increase in VO_{2peak} after HIT was assumed to be considerable from this short training intervention [59]. Given that the oxygen consumption, HR and pulmonary ventilation were lower during treadmill walking at the same submaximal intensity after HIT program, the authors also found that the walking economy was improved by such training [59]. The reduced effort of walking post-training exhibited strong implications for everyday life energy expenditure. However, these results were not in accordance with Askim et al. who did not found a significant increase of VO_{2peak} whereas they used the same HIT characteristics during a 6 weeks training [60]. They attributed this difference by a too small sample and/or too few training sessions.

It seems important to add that VO_{2peak} measurement is crucial but not sufficient to assess the cardiorespiratory fitness of a subject. Indeed, VO_{2peak} was frequently measured for stroke patients because their baseline VO_{2peak} level was frequently below the 18 ml/kg/min that was suggested as a minimum required for independent living [4]. Other exercise parameters as the cardiac remodeling, the ventilatory threshold adaptation, the muscle mass, the anaerobic contribution to energy support, but also neuromuscular adaptations are lacking despite such information may bring us important evidence on the HIT effectiveness and the outcomes on quality of life of stroke patient.

Timing of Endurance Training Initiation?

Although the timing of functional rehabilitation appears to be one of the critical factor determining a successful recovery, the optimal time of aerobic training initiation remains controversial [61-64]. It was found that late intervention was associated with lower discharge, lower functional outcomes and longer period of rehabilitation [62,63]. Some authors suggested that a very early rehabilitation (during the first week post-stroke) shortened the hospitalization period, improved functional outcomes, limited the deconditioning period inducing by patient immobilization and presented a low relative risk for adverse effects [61-63,65]. Animal studies reinforced this hypothesis by showing that early rehabilitation induced more important decrease in infarct volume than late intervention [66]. Moreover, some authors strongly recommended a more intense rehabilitation during the first 3 months [63]. They assumed that early and aggressive interventions should be implemented, even for severely affected stroke patients showing the most functional benefits from early rehabilitation. It is noteworthy to add that the use of cycle ergometer for performing HIT seems us to be more appropriate for stroke patients because it allows bypassing the early balance impairments that could delay the physical intervention [17]. However, the physiological-based evidence of endurance exercises effectiveness in the very early period after stroke are still lacking [17].

New advances in the understanding of the neural adaptations following stroke injury could help us to found the critical period to obtain the best recovery [67]. Functional abilities strongly decreased in the 1st to the 4th weeks after stroke suggesting important neurophysiological adaptations [61]. Indeed, there are numerous early changes at the molecular and cellular levels that increase the potential for activity driven changes in spared cerebral regions [67]. Initiating rehabilitation may be more effective during this period of only few weeks/months post-stroke where cerebral motor areas were hyperexcitable.

Given that stroke patients need to improve their functional recovery into a short window of time after stroke, we postulate that HIT with progressive increase of intensity seems appropriate during the acute phase in order to promote rapid and effective physiological adaptations observed in just few sessions.

Conclusion

All these findings suggest that HIT appears to be promising for stroke patients. It could be assumed that this training strategy may assist or replace the traditional moderate intensity exercise in order to promote more effective and rapid physiological adaptations. However, large-scale studies in human and animal models are clearly needed to ensure that HIT is a realistic and time-efficient exercise, but also, to determine the specific and beneficial neurophysiological and physiological adaptations following HIT intervention. The comparison and the combination of these two-endurance exercise modalities need to be deepened in further studies. It is also necessary to precisely define when stroke rehabilitation incorporating HIT should commence after stroke. If achieved, HIT will probably be considered as an integral component of stroke rehabilitation.

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