Valkenborghs Sarah (Orcid ID: 0000-0003-2259-4682)

Title

Aerobic Exercise prior to Task-specific Training to improve post-stroke motor function: A Case Series

Abstract

Background

Aerobic exercise can improve upper limb motor function in both healthy and stroke populations. Research in animals after stroke has shown that aerobic exercise combined with forelimb motor training improved forelimb motor function more than aerobic exercise or motor training alone. There is a lack of knowledge about this combined intervention in humans after stroke.

Purpose

These two case reports describe the exploratory implementation of a combined aerobic exercise and task-specific training intervention to improve upper limb motor function in one person in subacute stroke recovery and one person in chronic stroke recovery.

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/pri.1707

Methods

Case Descriptions

Subacute participant: 45-year-old female, 3 months after ischemic stroke resulting in left-sided hemiparesis affecting her non-dominant upper limb, with a baseline Action Research Arm Test (ARAT) score of 10/57 and Wolf Motor Function Test (WMFT) score of 39/75.

Chronic participant: 69-year-old female, 14 years after ischemic stroke resulting in right-sided hemiparesis affecting her non-dominant upper limb, with a baseline ARAT score of 13/57 and WMFT score of 34/75.

Intervention

Participants performed 30 minutes of lower limb cycling immediately prior to 30 minutes of upper limb task-specific training. Sessions were undertaken three times a week for eight weeks in a university rehabilitation laboratory.

Results

The combined intervention was feasible and perceived as acceptable and beneficial. Participants improved their upper limb motor function on the ARAT (subacute participant =

4 points; chronic participant = 2 points) and WMFT (subacute participant = 5 points; chronic participant = 3 points). Participants improved their aerobic fitness (subacute participant = +4.66mL O_2/kg/min; chronic participant = +7.34mL O_2/kg/min) and six-minute walking distance (subacute participant = +50m; chronic participant = +37m).

Discussion

Combining aerobic exercise with task-specific training may be a worthwhile therapeutic approach to improve upper limb motor function suitable for persons in the subacute or chronic phase after stroke.

Key words: exercise; motor learning/control; neuroplasticity; rehabilitation; stroke;

Main Text

Introduction

Upper limb dysfunction is common after stroke (National Stroke Foundation, 2012) and affects well-being and quality of life (Nichols-Larsen, Clark, Zeringue, Greenspan, & Blanton, 2005). Persons after stroke, their carers, and therapists have ranked improving upper limb rehabilitation as a 'top ten' stroke research priority (Pollock, St George, Fenton, & Firkins, 2014).

Improvements in motor function coincide with structural and functional reorganization of the brain (Richards, Stewart, Woodbury, Senesac, & Cauraugh, 2008). The brain's ability to undergo these modifications, termed neuroplasticity, may occur when frequently repeated movements reinforce particular network connectional patterns (Classen, Liepert, Wise, Hallett, & Cohen, 1998). Extensive training to perform upper limb movements causes reorganization of the upper limb motor cortex area, particularly when repetitions are associated with skill learning (Mawase, Uehara, Bastian, & Celnik, 2017). Capitalization and enhancement of neuroplasticity in peri-infarct and non-primary motor regions may stimulate recovery via an increased response to motor training.

Aerobic exercise also increases neuroplasticity (Ploughman, Austin, Glynn, & Corbett, 2015) and even motor function in unrelated limbs. A single session of treadmill training can improve performance of upper extremity tasks in people with chronic stroke by almost half the minimum clinically important difference (MCID) on the ARAT (Ploughman, McCarthy, Bosse, Sullivan, & Corbett, 2008). An eight-week program of lower extremity cycling improved upper extremity fine motor control in people with chronic stroke (Quaney et al., 2009). By preceding upper limb task-specific training with aerobic exercise the brain may be primed to be more responsive to subsequent motor training (Mang, Campbell, Ross, & Boyd, 2013). Aerobic exercise facilitates greater relearning of forelimb reaching in post-stroke animals compared to running alone, reaching alone, or no rehabilitation (Ploughman, Attwood, White, Doré, & Corbett, 2007). The potential efficacy and feasibility of this combined intervention has not been established in human stroke.

The aim of this case study was to explore the feasibility of implementing a combined aerobic exercise and task-specific training intervention to improve upper limb motor function in two people: one in the subacute and one in the chronic stage of recovery from stroke. Specific feasibility objectives were acceptability, attendance (percentage of training sessions attended), and adherence (what intensity of exercise was tolerable without compromising subsequent TST, how many repetitions of TST were achievable after aerobic exercise training, etc.). We also wanted to explore whether the responses would: (a) achieve a minimum clinically important difference, and (b) whether the type or magnitude of responses would differ between two people who had similar levels of impairment but different levels of time since stroke.

Methods

Participants

The subacute participant was a 35-year-old female with right middle cerebral artery thrombosis three months prior to enrolment. Upon enrolment, her non-dominant left upper limb lacked active wrist or finger extension but did not have high tone in the finger flexors (Modified Ashworth scale = 1). Her left lower limb had foot drop resulting in reduced step length and walking speed. She was ambulatory over short distances in the community with a walking stick, but had fallen once on a treadmill since her stroke.

The chronic participant was a 69-year-old female who suffered an ischemic stroke 14 years prior to enrolment. Upon enrolment, her non-dominant right upper limb lacked active finger extension and had high tone in her finger flexors (Modified Ashworth scale = 3). Her gait was affected by clubfoot in her right lower limb since childhood, and she started wearing an orthotic since her stroke due to footdrop that reduced her step length and walking speed. She was ambulatory over short distances in the community without an aid and went to a gym three times per week with no history of falls.

< Insert Table 1 - Neuropyschometric Characteristics here >

Participants provided informed written consent. Neither participant had any medical contraindications to exercise testing (American College of Sports Medicine, 2013) and their general practitioner provided medical clearance. This study was approved by The Hunter New England Human Research Ethics Committee (14/12/10/4.07) and The University of Newcastle Human Research Ethics Committee (H-2015-0105).

Procedure

Participants commenced an 8-week program, which consisted of three sessions per week, totalling 24 sessions. Each session included 30 minutes of aerobic exercise followed immediately by 30 minutes of task-specific training supervised by a neurorehabilitation physical therapist in a university rehabilitation laboratory. Participant attendance, protocol deviations, and informal unsolicited feedback were recorded in training diaries. Structured interviews were conducted with participants immediately following post-intervention assessments regarding the perceived benefits and acceptability of the combined intervention.

Intervention

Aerobic Exercise

Aerobic exercise was performed on a low entry level upright cycle ergometer (928G3, Monark, Sweden) in 5 x 5 minute intervals interspersed by 1 minute of rest. A T31 Polar Australia chest strap transmitter was used to monitor heart rate (HR) during the last 15 seconds of each interval, along with ratings of perceived exertion (RPE) (Borg 6-20 scale (Scherr et al., 2013)), workload and duration of exercise achieved; data were recorded in training diaries. The initial training workload in Watts (W) was prescribed individually based on data from the baseline cycle ergometer test, which correlated with a target HR zone of 50-76% HR_{max} and an RPE of 10-13 (American College of Sports Medicine, 2013). Intensity was adjusted by means of workload if the participant's HR and RPE score were not within these ranges. Cycle ergometry training was chosen as it is a common type of aerobic exercise training after stroke and improves functional capacity and $VO2_{peak}$ (Marsden, Dunn, Callister, Levi, & Spratt, 2013). It has been the main modality used in studies using exercise to improve upper limb motor function in healthy and stroke populations (Mang, Snow, Campbell, Ross, & Boyd, 2014; Quaney et al., 2009; Roig, Skriver, Lundbye-Jensen, Kiens, & Nielsen, 2012; Skriver et al., 2014), as it minimizes movement of the upper limb as a possible confounder, and is the most accessible modality for those with lower limb motor impairment or balance issues allowing inclusion of more severe stroke patients. Both participants required extra support straps to maintain their foot position on the pedal.

Task-specific Training

Within 5 minutes of completion of aerobic exercise, participants commenced task-specific training. The task-specific training comprised of breaking down everyday skills into functional components that maintained a strong resemblance to the original skill. As goal-oriented training enhances patient compliance, motivation and self-efficacy (Levack et al., 2006), task prescription considered individual goals by allowing each participant to choose activities that they would like to accomplish within eight weeks. Appropriate exercises were selected from an upper limb rehabilitation manual containing 142 activities and movements (Cunningham, Turton, Van Wijck, & Van Vliet, 2015) and adapted based on individual needs and impairments. Examples of tasks practiced included eating with cutlery, combing hair, knocking, pouring liquid from one cup to another, putting a jacket on/off, and switching a light on/off. The difficulty of each component exercise was graded, reviewed and progressed according to the individual ability of each participant, with the aim of completing 100-150 repetitions per 30-minute session (Birkenmeier, Prager, & Lang, 2010). Participants initially trained on component movements of a skill (e.g., extend elbow and flex shoulder to reach to cup, open fingers and thumb to grasp cup) until each component was mastered, and then combined into its functional sequence to perform the whole skill, or as much of the whole skill as possible. Participants were encouraged to use objects that varied in terms of shape, size and texture (e.g. empty/full cup, narrow/wide cup). In order to maximally challenge participants, each task was adjusted according to the above characteristics until they could just manage to perform the task successfully without the use of compensatory strategies. Where necessary, activities were performed with manual assistance until active movement could be achieved without support, during which trajectory deviation was corrected by the therapist or via feedback mechanisms (e.g. boundary markings/obstacles/objects).

Assessments

Participants underwent a series of assessments at baseline and eight weeks later. The ARAT and WMFT were used as primary outcome measures for motor function based on activity limitation and impairment, respectively. Additional outcome measurements included the Motor Activity Log (MAL), the Stroke Impact Scale (SIS), six-minute walk test (6MWT) and an incremental cycle ergometer test.

The incremental cycle test was conducted on an upright cycle ergometer (928G3, Monark, Sweden) with a portable metabolic system (K4b^2, Cosmed, Italy) to measure oxygen consumption (VO_{2peak}, mL.kg^{-1}.min^{-1}). A portable electrocardiogram (Quark T12x, Cosmed, Italy) monitored cardiac rhythm and HR. Participants pedalled at a cadence of 60 revolutions per minute beginning at a workload of 25W. Workload increased by 25W every 30 seconds by adjusting resistance. HR and RPE were recorded every 30 seconds. The test was terminated when the participant reached 85% age-predicted HR_{max} or was unable to continue due to volitional exhaustion.

Results

Attendance was 96% for the sub-acute participant and 83% for the chronic participant and there were no adverse events. The subacute participant progressed from training with a workload of 25W to 65W with an average HR of 153 bt.min^{-1} (90% HR_{max}) and RPE of 13. The chronic participant progressed from 60W to 85W with an average HR of 132 bt.min^{-1} (87% HR_{max}) and RPE of 13. Session by session attendance and exercise training data are summarised in Table 2.

< Insert Table 2 – Attendance and Training loads at exercise sessions here>

The mean number of repetitions per 30-minute session for the subacute participant was 155, the lowest number of repetitions was 40 (in one session) and the highest number of repetitions was 255 (in two sessions). The mean number of repetitions per 30-minute session for the chronic participant was 255, the lowest number of repetitions was 110 (in one session) and the highest number of repetitions was 350 (in one session) (Birkenmeier et al., 2010).

Both participants improved in motor and non-motor outcomes as outlined in Table 3.

<Insert Table 3 – Quantitative Clinical and Self-reported Outcomes here>

Results of brief structured interviews

Intervention

Both participants reported that the aerobic exercise intensity could have been higher, as they did not feel it was sufficiently challenging. Both agreed the task-specific training was meaningful to them and relevant to their daily activities. They also stated that it provided a focus for using their affected arms, reflected by an increased perceived use of their affected upper limb in the SIS and MAL.

Program structure

Both participants reported that although the frequency (three times a week) was good, the training sessions should be longer. The subacute participant felt the changeover from aerobic exercise to task-specific training interrupted the flow of the session and reduced recovery potential. Both participants agreed eight weeks for the program was too short as it took 2-3 weeks to get used to the routine of the program. They also felt that based on the benefits seen after eight weeks, further gains could have been achieved if the program had been extended.

Perceived benefits

In addition to increased strength and function in the upper limb, participants reported increased participation in daily activities, which was supported by improved scores on the SIS for the participation and activities of daily living categories. Additional benefits included feeling fitter, education of compensatory movements, and social interaction. Completing the program provided hope and optimism that they could participate in meaningful activities they had not participated in since their stroke.

Discussion

Both participants exceeded the target of 100-150 task repetitions per 30-minute session and improved their upper limb motor function as measured by the ARAT (4 points for the subacute participant and 2 points for the chronic participant) and WMFT (5 points for the subacute participant and 3 for the chronic participant). These change scores represent a MCID on the WMFT (3 points) (Lin et al., 2009) but not on the ARAT (5.7 points) (Lang, Edwards, Birkenmeier, & Dromerick, 2008). This difference could be because the WMFT includes several gross movements not requiring grasp, giving both participants more scope for improvement than the ARAT. Also, a recent Cochrane review determined that more than 20 hours of task-specific training is required to achieve a moderate, statistically significant effect size (Pollock, Farmer Sybil, et al., 2014), whereas our participants performed only 12 hours of task-specific training. Notably, both participants suggested that a longer program would be beneficial based on the improvements gained in eight weeks. Importantly, despite very different levels of time since stroke and assumed differences in recovery potential, both participants responded well and to a similar extent, which suggests that level of impairment is a more important influence on benefit than stroke chronicity.

Adherence to protocol was good and attendance was consistent with average attendance at outpatient stroke rehabilitation (Ogwumike, Badaru, & Adeniyi, 2015). The high mean training HR values elicited in participants reflect a protocol variation. The original aerobic exercise prescription was based on the most recent guidelines for physical activity and exercise after stroke, which recommend low-moderate intensity exercise for functional capacity, ambulation and cardiovascular benefits (Billinger et al., 2014), however the focus of our research was to enhance upper limb motor function for which there are no guidelines. Although the only studies investigating aerobic exercise and upper limb motor function after stroke in humans found that moderate-intensity exercise (70% age-predicted HR_{max}) increased motor learning (Ploughman et al., 2008; Quaney et al., 2009), the strong correlations between peripheral lactate concentration and motor skill acquisition and retention in healthy subjects (Skriver et al., 2014) suggest that larger effects may be obtained with higher intensity exercise. Moderate-high intensity exercise also appears to be more effective for increasing motor learning and memory in healthy humans (Mang et al., 2014; Roig et al., 2012), as well as increasing levels of proposed underlying mechanisms, such as neurotrophic factors and synaptogenesis in animals after stroke (Ploughman et al., 2015). Both participants tolerated their initial workloads well and independently asked if they could increase the intensity to high, which had been shown to be feasible after stroke (Askim et al., 2014), but had not been combined with task-specific training in humans after stroke until this study.

Both participants reported that the combined intervention was acceptable and that the task-specific training was meaningful and relevant to their daily activities, which is vital to rehabilitation efficacy (Bayona, Bitensky, Salter, & Teasell, 2005). They also stated that the task practice provided a focus for using their affected limb outside of therapy sessions, which increased participation in daily activities and quality of life; improved scores in the MAL and SIS "Use of Hand" and "ADL" categories support these self-reports. Whether improvements were due to a reversal of learned disuse or recovery was considered. The chronic participant reported less improvement in the amount and quality of use of her upper limb, as well as the percentage of tasks that scored ≥3 on the MAL. If improvements were due to a reversal of disuse we would have expected this participant to have made greater improvements.

Implications for Physiotherapy Practice

Combining aerobic exercise with task-specific training may be a feasible approach to improve upper limb motor function in both subacute and chronic persons after stroke. This combined intervention could expand therapeutic possibilities for patients and merits further investigation.

References

American College of Sports Medicine. (2013). *ACSM's guidelines for exercise testing and prescription*: Lippincott Williams & Wilkins.

Askim, T., Dahl, A. E., Aamot, I. L., Hokstad, A., Helbostad, J., & Indredavik, B. (2014). High-Intensity Aerobic Interval Training for Patients 3–9 Months After Stroke. A Fe *Physiotherapy Research International, 19*(3), 129-139. doi: 10.1002/pri.1573

Bayona, N. A., Bitensky, J., Salter, K., & Teasell, R. (2005). The role of task-specific training in rehabilitation therapies. *Topics in Stroke Rehabilitation, 12*(3), 58-65. doi: 10.1310/bqm5-6ygb-mvj5-wvcr

Billinger, S. A., Arena, R., Bernhardt, J., Eng, J. J., Franklin, B. A., Johnson, C. M., . . . Roth, E. J. (2014). Physical activity and exercise recommendations for stroke survivors. *Stroke, 45*(8), 2532-2553.

Birkenmeier, R., Prager, E., & Lang, C. (2010). Translating animal doses of task-specific training to people with chronic stroke in one hour therapy sessions: a proof-of-concept study. *Neurorehabilitation and Neural Repair, 24*(7), 620 - 635.

Classen, J., Liepert, J., Wise, S. P., Hallett, M., & Cohen, L. G. (1998). Rapid plasticity of human cortical movement representation induced by practice. *Journal of Neurophysiology, 79*(2), 1117-1123.

Cunningham, P., Turton, A., Van Wijck, F., & Van Vliet, P. (2015). Task-specific reach-to-grasp training after stroke: Development and description of a home-based intervention. *Clinical Rehabilitation*, 0269215515603438.

Lang, C. E., Edwards, D. F., Birkenmeier, R. L., & Dromerick, A. W. (2008). Estimating minimal clinically important differences of upper-extremity measures early after stroke. *Archives of physical medicine and rehabilitation, 89*(9), 1693-1700. doi: 10.1016/j.apmr.2008.02.022

Levack, W. M., Taylor, K., Siegert, R. J., Dean, S. G., McPherson, K. M., & Weatherall, M. (2006). Is goal planning in rehabilitation effective? A systematic review. *Clinical Rehabilitation, 20*(9), 739-755.

Lin, K. C., Hsieh, Y. W., Wu, C. Y., Chen, C. L., Jang, Y., & Liu, J. S. (2009). Minimal detectable change and clinically important difference of the Wolf Motor Function Test in stroke patients. *Neurorehabilitation and Neural Repair, 23*(5), 429-434. doi: http://dx.doi.org/10.1177/1545968308331144

Mang, C. S., Campbell, K. L., Ross, C. J., & Boyd, L. A. (2013). Promoting neuroplasticity for motor rehabilitation after stroke: considering the effects of aerobic exercise and genetic variation on brain-derived neurotrophic factor. *Physical Therapy, 93*(12), 1707-1716.

Mang, C. S., Snow, N. J., Campbell, K. L., Ross, C. J., & Boyd, L. A. (2014). A single bout of high-intensity aerobic exercise facilitates response to paired associative stimulation and promotes sequence-specific implicit motor learning. *Journal of Applied Physiology, 117*(11), 1325-1336.

Marsden, D. L., Dunn, A., Callister, R., Levi, C. R., & Spratt, N. J. (2013). Characteristics of Exercise Training Interventions to Improve Cardiorespiratory Fitness After Stroke A Systematic Review With Meta-analysis. *Neurorehabilitation and Neural Repair, 27*(9), 775-788.

Mawase, F., Uehara, S., Bastian, A., & Celnik, P. (2017). Motor learning enhances use-dependent plasticity. *Journal of Neuroscience*, 3303-3316.

National Stroke Foundation. (2012). National Stroke Audit: Rehabilitation Services Report.

Nichols-Larsen, D. S., Clark, P., Zeringue, A., Greenspan, A., & Blanton, S. (2005). Factors influencing stroke survivors' quality of life during subacute recovery. *Stroke, 36*(7), 1480-1484.

Ogwumike, O. O., Badaru, U. M., & Adeniyi, A. F. (2015). Barriers to treatment adherence among stroke survivors attending outpatient phy-siotherapy clinics in North-western Nigeria.

Ploughman, M., Attwood, Z., White, N., Doré, J. J., & Corbett, D. (2007). Endurance exercise facilitates relearning of forelimb motor skill after focal ischemia. *European Journal of Neuroscience, 25*(11), 3453-3460.

Ploughman, M., Austin, M. W., Glynn, L., & Corbett, D. (2015). The effects of poststroke aerobic exercise on neuroplasticity: a systematic review of animal and clinical studies. *Translational stroke research, 6*(1), 13-28.

Ploughman, M., McCarthy, J., Bosse, M., Sullivan, H., & Corbett, D. (2008). Does treadmill exercise improve performance of cognitive or upper-extremity tasks in people with chronic stroke? A randomized cross-over trial. *Archives of physical medicine and rehabilitation, 89*(11), 2041-2047.

Pollock, A., Farmer Sybil, E., Brady Marian, C., Langhorne, P., Mead Gillian, E., Mehrholz, J., & van Wijck, F. (2014). Interventions for improving upper limb function after stroke. *Cochrane*

Database of Systematic Reviews, (11). Retrieved from: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010820.pub2/abstract

http://onlinelibrary.wiley.com/store/10.1002/14651858.CD010820.pub2/asset/CD010820.pdf?v=1&t=i7zpqtvc&s=2b72b548c3ccb299dd94e25a6cf2e56e82527fa3 doi:10.1002/14651858.CD010820.pub2

Pollock, A., St George, B., Fenton, M., & Firkins, L. (2014). Top 10 research priorities relating to life after stroke--consensus from stroke survivors, caregivers, and health professionals. *International Journal of Stroke, 9*(3), 313-320. doi: 10.1111/j.1747-4949.2012.00942.x

Quaney, B. M., Boyd, L. A., McDowd, J. M., Zahner, L. H., He, J., Mayo, M. S., & Macko, R. F. (2009). Aerobic exercise improves cognition and motor function poststroke. *Neurorehabilitation and Neural Repair*.

Richards, L. G., Stewart, K. C., Woodbury, M. L., Senesac, C., & Cauraugh, J. H. (2008). Movement-dependent stroke recovery: a systematic review and meta-analysis of TMS and fMRI evidence. *Neuropsychologia, 46*(1), 3-11.

Roig, M., Skriver, K., Lundbye-Jensen, J., Kiens, B., & Nielsen, J. B. (2012). A single bout of exercise improves motor memory. *PloS one, 7*(9), e44594.

Scherr, J., Wolfarth, B., Christle, J. W., Pressler, A., Wagenpfeil, S., & Halle, M. (2013). Associations between Borg's rating of perceived exertion and physiological measures of exercise intensity. *European journal of applied physiology, 113*(1), 147-155.

Skriver, K., Roig, M., Lundbye-Jensen, J., Pingel, J., Helge, J. W., Kiens, B., & Nielsen, J. B. (2014). Acute exercise improves motor memory: exploring potential biomarkers. *Neurobiology of learning and memory, 116*, 46-58.