

RESEARCH PAPER

# The effects of hybrid cycle training in inactive people with long-term spinal cord injury: design of a multicenter randomized controlled trial

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**Purpose:** Physical activity in people with long-term spinal cord injury (SCI) is important to stay fit and healthy. The purpose of this study is to evaluate the effects of hybrid cycle training (hand cycling in combination with functional electrical stimulation-induced leg cycling) on fitness, physical activity and health among a group of inactive people with long-term SCI. **Method:** This study will be a 16-week multicenter randomized controlled trial (RCT) with a 26-week follow-up. Forty inactive people, aged 28–65 years, with paraplegia or tetraplegia for at least 10 years, will be randomly assigned to either an experimental group (hybrid cycle group) or control group (hand cycle group). During 16 weeks, both groups will train twice a week 30 minutes at an intensity of 65–75% of their heart rate reserve. The primary outcome measure is fitness. Secondary outcome measures are physical activity and health-related parameters. The primary and secondary outcome measures will be assessed just before the training program (T1), after 8 weeks of training (T2), directly after (T3), and 26 weeks after the training program (T4). **Conclusion:** The results of this RCT may provide future implications for exercise prescription that preserve long-term functioning in people with SCI.

**Keywords:** fitness, functional electrical stimulation, hand cycling, health, paraplegia, physical activity, tetraplegia

## Introduction

With today's specialized medical care, life expectancy of people with a spinal cord injury (SCI) has considerably improved. However, many people with long-term SCI show a seriously inactive lifestyle, associated with deconditioning and secondary health complications (e.g. pressure sores,

## Implications for Rehabilitation

### Spinal cord injury (SCI)

- Many people with SCI show a serious inactive lifestyle, associated with deconditioning and secondary health problems, resulting in a reduced participation and quality of life.
- Physical activity in people with SCI is important to avoid this downward spiral that threatens people with SCI.
- Physical activity in people with SCI has traditionally involved upper-body exercise (e.g. hand cycling) due to the lower-limb paralysis.
- Hybrid exercise training (electrical stimulation-induced leg exercise combined with voluntary arm exercise) is expected to be more effective in preventing deconditioning and several secondary health problems (e.g. osteoporosis and cardiovascular disease) compared to arm exercise alone.

osteoporosis and cardiovascular disease), resulting in a reduced participation and quality of life [1,2]. It is important to avoid this downward spiral that threatens persons with long-term SCI. Therefore, the research program “Active Lifestyle Rehabilitation Interventions in long-term Spinal Cord injury” (ALLRISC) was developed to address inactive lifestyle, deconditioning, and secondary complications in people who have a SCI for at least 10 years [3]. The current study is part of ALLRISC and focuses on the lower-body disuse paradigm.

Exercise for individuals with SCI has traditionally involved upper-body activities (e.g. hand cycling) due to their lower-limb

paralysis. Unfortunately, this approach can limit successful health outcome since the dynamics of conventional arm exercise are not conducive to the development and maintenance of the superior levels of fitness that can be achieved with leg exercise. In addition, arm exercise alone may not markedly contribute to the prevention of some common secondary complications such as lower-limb muscle atrophy, osteoporosis, pressure sores and a host of cardiovascular disorders [4,5]. Several physiological factors related to SCI and arm exercise may account for some of these problems including: the relatively small muscle mass available, deficient cardiovascular reflex responses and inactivity of the skeletal muscle pump of the legs. Due to the specificity of exercise principle, arm exercise alone would be expected to do little to prevent lower-body deterioration.

Use of the paralyzed lower-limb musculature, accomplished through functional electrical stimulation (FES), could alleviate some of these problems. A major advantage of FES-induced exercise of the paralyzed legs over voluntary arm exercise is that it can utilize a large muscle mass that otherwise would be dormant. This can potentially provide benefits to improve the integrity of the paralyzed lower limbs, augment the circulation by activating the skeletal muscle pump, as well as elicit relatively large exercise responses for better aerobic training capability. One of the developed exercise techniques uses a computer-controlled leg cycle ergometer which is pedalled via FES-induced contractions of the paralyzed lower-limb muscle groups. Several studies suggest benefits not only on physical capacity and endurance [6–10], but also on vascular [11], muscle [12,13] and bone systems [14] in the lower extremities. Altogether, these studies have shown evidence strongly suggesting that this type of exercise can offer multiple therapeutic benefits, encompassing improved physical fitness, as well as reduced risk of acquiring secondary health complications.

To further activate more muscle mass and subsequently provide greater exercise responses to enhance aerobic fitness training capability, a hybrid mode of exercise consisting of FES-induced leg exercise combined with voluntary arm exercise can be used (e.g. rowing or cycling) [15–17]. Several training studies performed on hybrid exercise suggest benefits on aerobic capacity [18–22] and vascular characteristics [23,24]. However, these studies had relatively small sample groups (6 to 11 participants) and investigated only one aspect of hybrid training (e.g. aerobic capacity or vascular function). Moreover, these studies had no control group (except for Mutton et al. [22], where participants acted as their own control). There are no randomized controlled trials (RCTs) to date that investigated multiple aspects of hybrid cycle training in people with long-term SCI.

Therefore, the aim of this RCT is to examine the effectiveness of a 16-week hybrid cycle training program among a group of 40 inactive people with long-term SCI on fitness, health and physical activity.

## Methods

### Participants

The participant group will consist of 40 inactive individuals, aged 28–65 years, with paraplegia or tetraplegia for at least 10 years (age at onset SCI  $\geq$  18 years). People will be qualified

as “inactive” if their score on the Physical Activities Scale for Individuals with Physical Disabilities (PASIPD) [25] is lower than the 75th percentile of a Dutch cohort study population [26]. Individuals will be eligible to be included if they are dependent on a handrim-propelled wheelchair, and if they have a spastic paralysis as well as no or limited sense in the lower extremity. Individuals will be excluded if they have contra-indications for physical training and testing (such as pressure sores, serious cardiovascular problems, or severe musculoskeletal complaints), or psychiatric problems that could interfere with the study. Individuals will also be excluded if they have plans to start another lifestyle (e.g. changes in physical activity and diet) in the months that the experiment is going on or if they have insufficient knowledge of the Dutch language to understand the purpose and protocol of the study. These eligibility criteria will be checked by the research assistant in a telephone interview with the participant and by the rehabilitation physician during a thorough screening.

Potential participants will be selected from the databases of the two participating SCI-specialized Dutch rehabilitation centers: Reade Amsterdam and St. Maartenskliniek Nijmegen. An information letter will be sent to these people to inform them about the study. All participants have to provide written informed consent indicating voluntary participation in the study. Participants can withdraw from the study at any time for any reason if they wish to do so, without any consequences. Reasons for withdrawal will be registered. The study has been approved by the Medical Ethics Committee of the VU University Medical Centre Amsterdam.

### Design

This study will be a 16-week RCT with a 26-week follow-up, performed in two rehabilitation centres between November 2011 and November 2013. Within each rehabilitation center, participants will be randomly assigned to either the experimental group (hybrid cycle group) or control group (hand cycle group). A blinded independent researcher will provide the allocation in sealed envelopes. The experimental group will receive a 16-week hybrid cycle training program, while the control group will receive a 16-week hand cycle training program (Figure 1). The primary outcome measure is fitness. Secondary outcome measures are physical activity and health-related parameters. The primary and secondary outcome measures will be assessed just before the training program (T1), after 8 weeks of training (T2), directly after (T3), and 26 weeks after the training program (T4).

### Training device

#### *The hybrid cycle*

The hybrid cycle (BerkelBike Pro, BerkelBike B.V., St. Michielsgestel, the Netherlands; Figure 2) combines synchronous hand cycling with asynchronous FES-induced leg cycling. The backrest and seat position can be adjusted to the participant's anthropometry. The feet can be fastened in the foot pedals. A 6-channel stimulator (Impuls, BerkelBike B.V., St. Michielsgestel, the Netherlands; Figure 2A) provides electrical stimulation via self-adhesive 50 x 90 mm surface electrodes (Stimex, Pierenkemper GmbH, Germany) placed

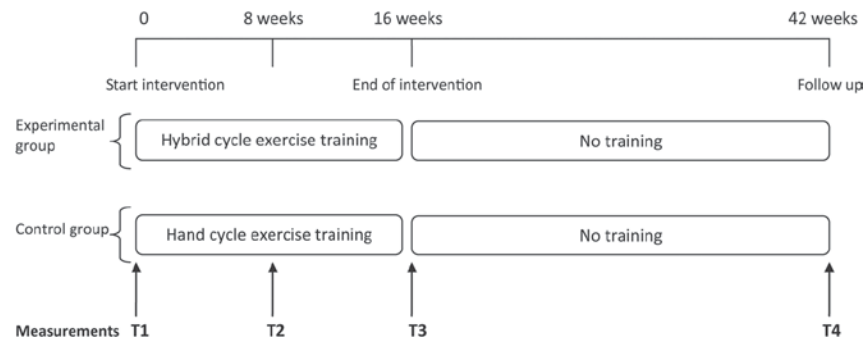


Figure 1. Experimental design of the study (intervention and measurements).

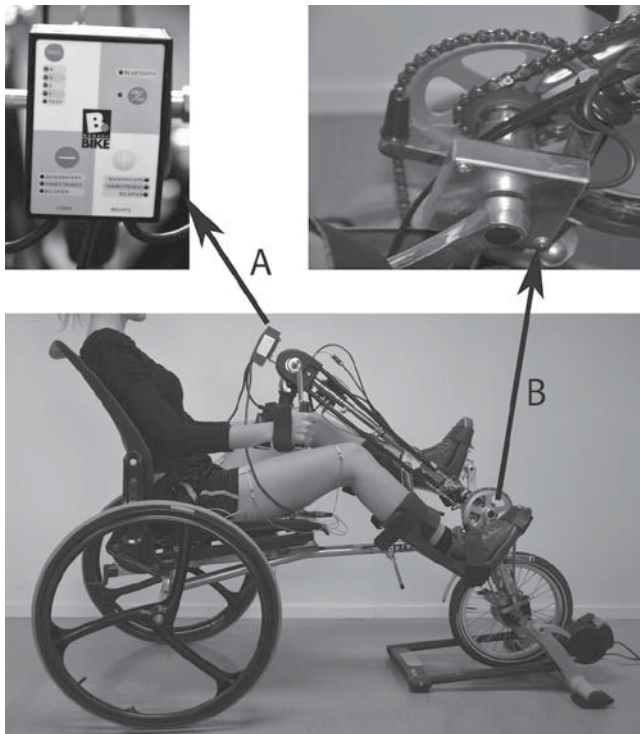


Figure 2. The hybrid cycle with stimulator (A) and crank angle encoder (B).

bilaterally over the quadriceps, hamstrings and gluteus muscles. The stimulator receives information from the crank angle encoder (Figure 2B) about pedal position and velocity to control the cyclic stimulation pattern. The stimulator has five preset stimulation programs (program test, 1, 2, 3 and 4), each with different FES firing angles and stimulation frequency (program test: 35 Hz; program 1–4: 20 Hz). In all programs, pulse duration is 400  $\mu$ s and maximum current amplitude is 150 mA. During cycling, the legs move together with the arms and the current amplitude of the electrical stimulation can be changed manually with steps of 15 mA. When the leg musculature fatigues, arm activity can take over the entire propulsion. The hybrid cycle is equipped with 8 gears that can be changed manually. If necessary, it is possible to equip the hybrid cycle with quad grips.

### The hand cycle

The hand cycle (Speedy-Bike, Reha-Technik GmbH, Delbrück, Germany; Figure 3) is equipped with a wide

synchronous bull-horn crank, and with 8 gears that can be changed manually. The hand cycle can be equipped with quad grips, if necessary.

### Training protocol

Participants will perform 32 training sessions within a continuous period of 16 weeks. Each training session will consist of a short warm-up and cool-down period. After the warm up, the interval training protocol for that training session will start (Table I). During the training period, total cycle time will increase from 18 to 32 min. To provide sufficient recovery time, at least one day of rest will be scheduled in between training days. A week before the first training session, participants will perform a graded exercise test in their own handrim-propelled wheelchair to measure their maximal exercise responses (see section on “primary outcome measure”). Based on this test, the training load will be chosen such that the participant achieves an average heart rate response of 65–75% heart rate reserve (HRR) during training.

The first training will be a practice session, during which participants can become familiarized with cycling in either the hybrid cycle or hand cycle. The familiarization session is particularly important for the hybrid cycle group, since what is tested here is the participant’s response to the different stimulation programs.

Training sessions will be performed on an ergotrainer (Taxc Flow, Technische Industrie Taxc B.V., Wassenaar, the Netherlands) adapted to the wheel size of the hybrid cycle and hand cycle. During training, heart rate will be monitored using radiotelemetry (Polar, Polar Electro Inc., Woodbury, NY) to ensure the proper training intensity is maintained as the training progresses. Since the use of heart rate as an indicator for training intensity can be unreliable in a part of the tetraplegic population [27], rating of perceived exertion (RPE) will serve as a subjective measure of training intensity. RPE will be measured after each training block and should 4–7 on the Borg’s 10-point scale [28].

Training intensity can be controlled by the participant making adjustments in cycle velocity, or by the trainer adjusting the gear of the cycle or the resistance of the ergotrainer. In addition, during hybrid cycling the current amplitude of the stimulation can be adjusted manually by the trainer to control the degree of muscle activation. The trainer will try to induce strong muscle contractions during training. However, if the





Figure 3. The hand cycle.

Table I. Interval training protocol.

Session	Exercise bout		Reps	Total cycle time (min)
	(min)	Rest (min)		
1-3	3	2	6	18
4-5	3	2	7	21
6-7	3	1.5	7	21
8-11	3	1.5	8	24
12-13	3	1	8	24
14-15	4	2	7	28
16-18	4	1.5	7	28
19-20	4	1	7	28
21-24	4	1.5	8	32
25-32	4	1	8	32

Reps: Repetitions

legs are moving too fiercely due to the stimulation or if the participant indicates that the stimulation is too intense, the trainer will decrease the current amplitude. Before and immediately after each training session, participants will be asked to report local pain and/or complaints. If serious musculoskeletal complaints occur, the researcher can decide to withdraw a participant from the study.

### Primary outcome measure

The primary outcome measure in this study is fitness, which we define as the peak power output.

*Peak power output* ( $PO_{peak}$ ) will be assessed during a graded exercise test in the participant's own handrim-propelled wheelchair on a motor-driven treadmill using the protocol of Dallmeijer et al. [29]. First, participants will perform a 3-min familiarization and warm-up session, followed by a 5-min rest interval. Then, two 3-min submaximal exercise blocks on two different constant workloads, with a 2-min rest period between blocks, will be performed to determine submaximal exercise responses. After the two submaximal blocks and a 2-min rest interval, the workload will be increased every minute by increasing the incline of the treadmill belt. The velocity of the treadmill belt will be held constant during testing, and depends on the participant's physical capability. The test will end when the participant can no longer maintain the velocity due to fatigue, or when the participant indicates

that he/she wants to stop. Before the test, a separate drag test will be performed to determine the drag force ( $F_{drag}$ ) of the wheelchair-user system on different inclines using the protocol of Van der Woude et al. [30]. Power output (PO) will be calculated from  $F_{drag}$  and the velocity of the belt ( $v$ ), according to:  $PO (W) = F_{drag} (N) * v (m/s)$ .  $PO_{peak}$  will be defined as the highest PO maintained for at least 30 s. During testing, respiratory gas exchange will be measured using open circuit spirometry (K4b<sup>2</sup>, COSMED, Rome, Italy). Heart rate will be measured using radiotelemetry (Polar, Polar Electro Inc., Woodbury, NY).

### Secondary outcome measures

The secondary outcome measures are physical activity and health-related parameters (metabolic syndrome, vascular structure and function, and bone mineral density of the distal femur and proximal tibia).

*Physical activity* will be measured objectively with an odometer as well as subjectively with the Dutch Physical Activities Scale for Individuals with Physical Disabilities (PASIPD). The odometer will be mounted on the wheel of the participant's wheelchair to record every forward and backward revolution of the large wheels [31]. Participants will be asked to keep a diary in which they register the number of wheel revolutions on a daily basis during 7 consecutive days. The distance covered will be calculated by multiplying the number of wheel revolutions by the wheel circumference. The Dutch PASIPD will be used to subjectively assess physical activity [25]. This 12-item questionnaire requests the number of days a week and hours a day of participation in leisure (six items), household (five items) and occupational (one item) activities over the past 7 days. Participants will be asked to fill out this questionnaire at home.

*Metabolic syndrome* is defined as having  $\geq 3$  of the following symptoms: abdominal obesity (waist circumference  $> 102$  cm for males,  $> 88$  cm for females), high blood pressure ( $> 130/85$  mm Hg or use of medication for hypertension), high triglycerides ( $\geq 1.7$  mmol/L), low high-density lipoprotein cholesterol ( $< 1.03$  mmol/L for males,  $< 1.29$  mmol/L for females), high fasting plasma glucose ( $\geq 5.6$  mmol/L or use of medication for hyperglycemia) [32]. Waist circumference will be measured using a tape measure with the participant in the supine position. Blood pressure will be taken on the right arm in a sitting position. Fasting blood samples will be taken to determine levels of triglycerides, high-density lipoprotein cholesterol and plasma glucose.

*Vascular structure and function* will be measured under standardized conditions using high resolution ultrasound (T3000, Terason, Burlington, MA). Wall thickness and diameter will be examined across arteries in the neck, arm and leg [33]. Forearm blood flow and vascular resistance will be measured using venous occlusion plethysmography [34]. Physiological (flow-mediated dilation (FMD)) and pharmacological (nitroglycerine (NTG)) vasodilation will be examined after occlusion.

*Bone mineral density (BMD) of the distal femur and proximal tibia* will be measured using dual energy X-ray absorptiometry

(DXA; Hologic Discovery, Hologic Inc., Waltham, Mass). Distal femur and proximal tibia are common fracture sites in people with SCI [35]. However, distal femur and proximal tibia are not standard measurement sites and will therefore be analyzed using a adapted forearm protocol [36]. In addition, biochemical markers of bone turnover (CTX and P1NP) will be determined from fasting blood samples [37,38].

### Other outcome measures

Besides the primary and secondary outcomes, several other outcome measures will be assessed, among others things, for comparison with the other three ALLRISC studies. These other outcome measures will not be fully described, but will only be mentioned here: wheelchair skill performance [39,40], pulmonary function [41], immune function (immunoglobulin A) [42], inflammatory state (C-reactive protein, interleukins 6 and 10) [43], health-related quality of life (World Health Organization Quality of Life- 5) [44], participation (Utrecht Scale for Evaluation of Rehabilitation- Participation) [45], mood (Hospital Anxiety and Depression Scale) [46], sleep quality (Pittsburgh Sleep Quality Index) [47], fatigue (Fatigue Severity Scale) [48], upper extremity pain (Wheelchair User's Shoulder Pain Index) [49,50], bowel function (Neurogenic Bowel Dysfunction Score) [51], functional independence (Spinal Cord Independence Measure III) [52], self-efficacy (Spinal Cord Injury- Exercise Self-Efficacy Scale [53]; Self-Efficacy in Wheeled Mobility Scale) [54].

### Statistical analysis

The sample size was calculated with the formulas given by Twisk [55] on the main outcome measure peak power output. This calculation, based on data of a preliminary study [41,56], revealed that a group size of 18 was required to detect a difference of 9W between the experimental and control group on the main outcome measure. The power was 0.8 and the alpha was set at 0.05. With an expected drop-out of 10–15%, we aim to recruit at least 20 participants per group. Descriptive statistics will be used for the outcome measures and for the relevant participant characteristics. Student t-tests will be performed to evaluate group differences at baseline. Multifactor analysis of variance with repeated measures will be used to determine differences in change over time (treatment effect) between the experimental and the control group. To assess the potential relationship between outcome measures, a multivariate multi-level regression analysis will be performed. The level of significance will be set at 0.05. The data will be analyzed with the Statistical Package for the Social Science, version 18.0 (SPSS Inc, Chicago, Illinois, USA).

### Discussion

This paper outlines the design of a multicenter RCT that examines the integrated effects of a hybrid cycle training intervention in physically inactive people with long-term SCI on fitness, health and physical activity. During hybrid cycling, voluntary upper-body exercise is combined with FES-induced exercise of the paralyzed lower body. We expect this training modality to be more effective in preventing

deconditioning and several secondary health problems compared to arm exercise alone (e.g. hand cycling). The results of this study may provide future implications for exercise prescription that preserve long-term functioning in people with SCI.

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