
Impact of Passive Leg Cycling in Persons With Spinal Cord Injury: A Systematic Review

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Background: Passive leg cycling is an important clinical tool available for rehabilitation after spinal cord injury (SCI). Passive cycling can be used to derive exercise-related benefits in patients with poor motor control. There have been a number of studies examining the effects of passive cycling on a variety of outcomes. There is need for a systematic assessment of the cycling parameters and the associated clinical changes in cardiovascular, neuromuscular, and musculoskeletal outcomes after passive cycling. **Objectives:** To assess the effectiveness of passive leg cycling interventions on cardiovascular, neuromuscular, and musculoskeletal outcomes post SCI, and to describe intensity, duration, and type of passive leg cycling post SCI. **Methods:** PRISMA guided systematic review of literature based on searches in the following databases: PubMed/MEDLINE, PEDro, EMBASE, Cochrane Library, and Google Scholar. Peer-reviewed publications that were written in English were included if they described the effects of a single session or multiple sessions of passive leg cycling in persons post SCI. **Results:** Eleven papers were included: two were randomized controlled trials (RCTs), one was a crossover trial, and the rest were pre-post single-group designs. Three studies (including two RCTs) reported statistically significant benefits of multiple sessions of passive cycling on leg blood flow velocity, spasticity, reflex excitability and joint range of motion, and markers of muscle hypertrophy. About half of the single session studies showed statistically significant improvement in acute responses. **Conclusion:** Multiple sessions of passive leg cycling showed benefits in three categories – cardiovascular, musculoskeletal, and neurological – with medium to large effect sizes. **Key words:** blood flow velocity, ergometry, H-reflex, muscle spasticity, muscle strength, oxygen, spinal cord injury

Spinal cord injury (SCI) can result in sensory-motor deficits such as spasticity, impaired motor control, impaired sensation, impaired walking, and other functions.¹ In persons with chronic SCI, circulatory impairments such as decreased venous capacity and blood flow and increased venous flow resistance have been observed.^{2,3} Rehabilitation after an SCI is complex because it requires addressing deficits across multiple body systems. Active or self-driven cycling can address deficits in multiple body systems⁴ and can be incorporated into clinical rehabilitation as well as a personal exercise regimen. Recent guidelines recommend moderate aerobic exercise for persons with SCI,³ and cycling interventions offer a good option to promote aerobic exercise in patients with poor lower limb motor control and walking difficulty. However, active cycling

interventions can also be difficult to administer post SCI⁵ because of impaired motor control and completeness of the injury. In addition to neurological issues, active cycling may be limited in SCI by cardiovascular limitations (decreased aerobic capacity) as well as musculoskeletal issues (reduced joint range of motion and stiffness and muscle weakness).⁶

Passive (motorized) cycling can be used to elicit rhythmic limb movements and allow patients with poor motor control to perform exercise. Passive cycling is particularly helpful in patients with a complete SCI who have no motor control or their motor output is not sufficient to engage in active cycling. The effects of passive cycling have been reported to be similar to active cycling in terms of improvement in cortical excitability,⁶ spasticity, bone mineral density, and myofibrillar protein

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content.⁴ The neurological impairments such as spasticity and musculoskeletal impairments such as range of motion limitation can limit cycling ability and can also be addressed using passive cycling as an intervention. Cardiovascular effects such as increased blood flow have also been reported after passive cycling. Thus, passive cycling has the potential to target multiple bodily systems in a rehabilitation program and may be seen as a favorable method compared with active cycling in persons with poor motor control post SCI.

There have been a number of studies that have examined the effects of passive cycling and a recent review summarized these effects⁴; however, that review was not systematic in nature and focused predominantly on the neurological impact of passive cycling in animal studies and included adults as well as children with SCI. Additionally, the review did not clearly describe two important intervention characteristics – the training parameters and whether the included studies were single or multiple sessions. Active cycling parameters can be influenced by heart rate, muscle strength, endurance, and motor control; however, these may not play a significant role during passive cycling. Passive cycling training parameters are important to understand in relation to the observed effects as a starting point for determining effectiveness. Both single and multiple session studies are helpful in understanding the mechanism of change, but it is not clear in the literature what the effects of single or multiple passive cycling sessions are. Considering that passive cycling does not involve active muscle pumping actions like those seen in active cycling, it can be hypothesized that a single session of passive cycling may not accrue any significant changes; however, this needs to be ascertained systematically. Other clinical benefits such as maintenance of flexibility and range of motion and circulatory benefits such as improvement in blood flow were also not examined in this review. Thus, it is important to examine the effectiveness of passive cycling on different body systems within the context of the variety of training parameters employed.

Therefore, to understand the value of passive cycling, there is a need to systematically review the effectiveness of passive cycling on various

rehabilitation outcomes assessing cardiovascular, neurological, and musculoskeletal systems in the SCI population. The objectives of this systematic review were to describe exercise training parameters such as intensity, duration, type of passive leg cycling interventions, and types of outcomes used in persons post SCI and to assess the effectiveness of single and multiple sessions of passive leg cycling interventions on cardiovascular, neuromuscular, and musculoskeletal outcomes post SCI.

Methods

Search strategy

We conducted a systematic review of the literature using PubMed, PEDro, Cochrane Library, Google Scholar, and EMBASE databases including all studies from the inception of the database until May 28, 2018. In the PubMed database, the following search strategy was used: “spinal cord injuries” [MeSH] AND “motion therapy, continuous passive” [MeSH] OR “passive cycling” [All Fields] OR “passive movement” [All Fields] OR “cycle ergometer” [All Fields]. A filter to only include studies with subjects over 18 years of age was applied: “Adult” [terms]. The search strategy was adapted to the other databases following the same principles to identify all relevant articles. We did not register the protocol for this systematic review. Corresponding authors were contacted to provide full texts when not accessible via electronic databases.

Study selection

In the first phase, two reviewers (L.V. and C.P.) independently looked for the titles and abstracts of the articles retrieved. Articles that assessed passive leg cycling prospectively in adult participants (age ≥ 18 years) with SCI were included in this review. Studies with a retrospective design, single case studies, studies with healthy subjects or athletes, or studies using arm cycling were excluded. Next, both reviewers screened all remaining abstracts independently. Results of screening were compared, and any discrepancies between reviewers were discussed and a consensus-based

decision was arrived at in consultation with a third reviewer (S.M.). Finally, full text screening was performed in a similar way (see **Figure 1**).

Data extraction

The study information was first independently extracted by two reviewers (L.V. and C.P.) using

a standardized data extraction form. Then, individual cycling protocols among the included studies were summarized. The following data were extracted: study information year, author, study design, publication type, sample size, patient demographics (age, sex, and body mass index), completeness of injury, times since injury, functional status, parameters of intervention, and details of

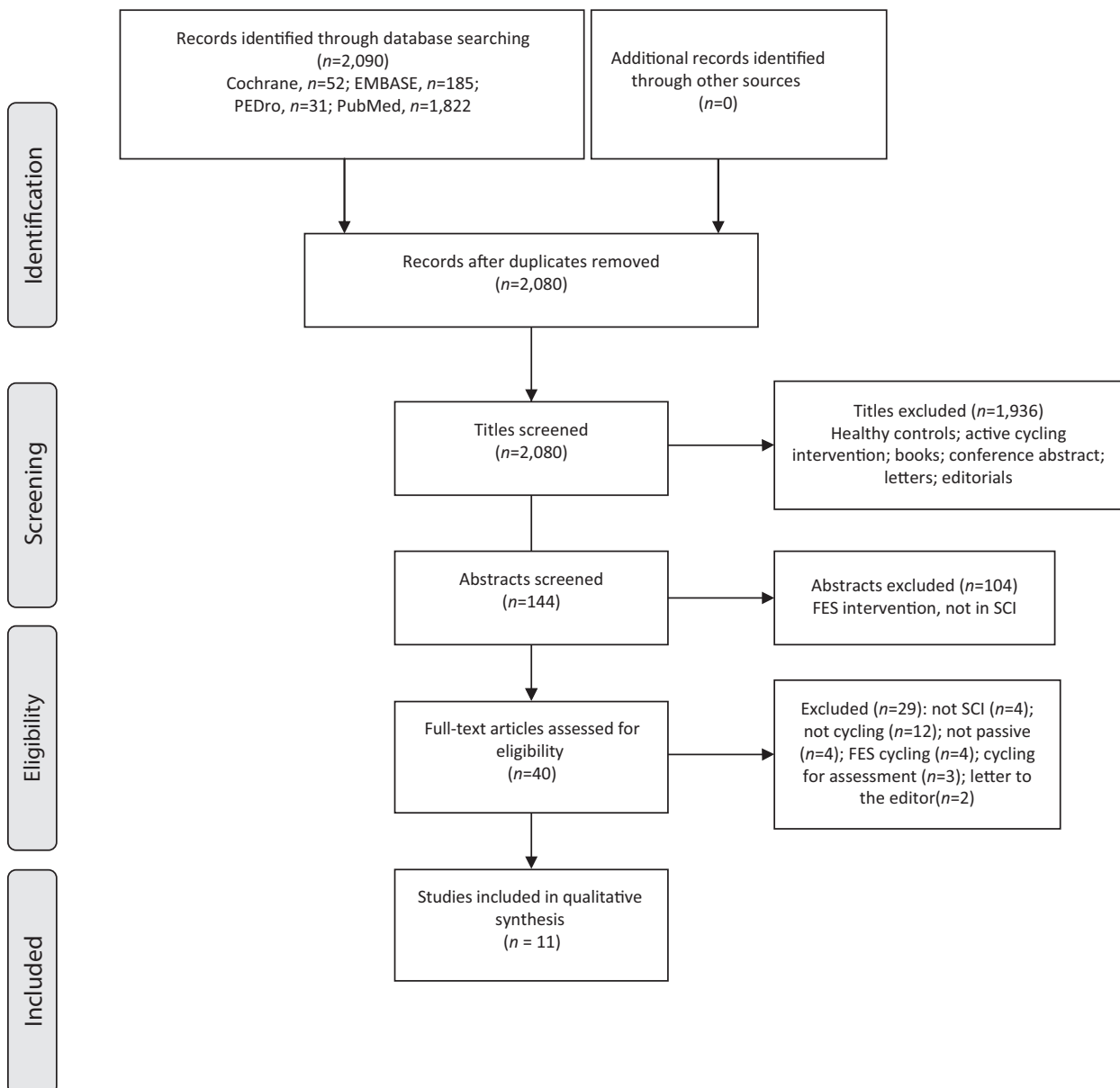


Figure 1. PRISMA flow diagram showing the results of the searches. Adapted from Moher D, Liberati A, Tetzlaff J, Altman DG; The PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *PLoS Med.* 2009;6(6):e1000097. doi:10.1371/journal.pmed1000097 Copyright © 2009 Moher et al.

outcomes. The study outcomes were categorized into groups based on the body systems they targeted (cardiovascular, neurological, and musculoskeletal). When available, change scores and percent changes from baseline were calculated from the included studies so that they could be statistically analyzed. If pre/post outcome scores were only available, percent change from baseline was calculated using the formula: [(post - pre) / pre] x 100]. The extracted data are presented in **Tables 1-3**.

Statistical analysis

Effect size was calculated in all studies for the primary outcome measure pre and post passive cycling with Microsoft Excel using the following formulae⁷:

$$\text{Cohen's } d = \frac{\text{Mean pre} + \text{Mean (post)}}{\text{pooled Standard Deviation (SD)}}$$

$$\text{Effect size } r = \frac{d}{\sqrt{d^2 + 4}}$$

An effect size of 0.2 was considered small, 0.5 medium, and 0.8 and above large.⁸

Quality of studies and risk of bias

The Oxford levels of evidence (LOE) was used to indicate the methodological quality of the included studies.⁹ We assessed the risk of bias using the Study Quality Assessment Tools developed by the National Heart, Lung and Blood Institute¹⁰ to examine biases in the included studies. Sequence generation, allocation concealment, blinding, incomplete and selective outcome data, and other biases¹⁰ were assessed for each study by two reviewers (C.P. and S.M.) and discrepancies were resolved by consensus.

Results

Overview of the studies

A summary of the studies is presented on **Table 1**. Two of the 11 studies were randomized controlled trials,^{11,12} one was a crossover trial,¹³ and eight studies were pre-post type including

case series designs (see level of evidence categories in **Table 1**). The time since injury in persons with SCI tested in the included studies was at least 1 year post SCI and chronicity ranged from 1 to 25 years. Total number of subjects in the included studies was 179 (81 in the two RCTs and 98 in the non-RCT studies; see **Table 1**). The majority of patients (69%, $n = 123/169$) in the studies had a motor complete SCI (ASIA Impairment Scale levels A or B).

Cycling training parameters

Summary of the cycling training parameters is presented in **Table 2**. Of the studies that examined effects of a single intervention, four studies tested the effects of <10 minutes of cycling duration: 5 minutes¹⁴ and 7 minutes⁶; and two studies tested the effect at 10 minutes^{15,16} of passive cycling. Four studies tested the effects of 20 to 100 minutes of a single cycling intervention (see **Table 2**). Multiple session studies ranged from 18 to 36 sessions of cycling intervention over a 6- to 12-week period. The pedaling frequency appeared to be lower for multiple session studies (range, 25-40 rpm) compared to single session studies (range, 35-60 rpm).

Outcome measures used to assess the effects of cycling

Six studies^{2,12,14-17} examined outcomes in the cardiovascular category, two studies^{11,18} used musculoskeletal outcome measures, and four studies^{6,11,13,19} used neurological outcome measures (see **Table 2**). Rayegani et al¹¹ used outcomes in two categories – neurological and musculoskeletal. Cardiovascular outcomes measured during cycling were (1) blood volume pulse signals, (2) blood flow velocity, (3) oxygen uptake (VO₂), (4) stroke volume, (5) cardiac output, (6) pulmonary ventilation, (7) heart rate, (8) mechanical efficiency, and (9) peripheral vascular resistance. Musculoskeletal outcome measures were (1) thigh girth, (2) joint range of motion, and (3) messenger ribonucleic acid (mRNA) to examine myosin heavy chain expression of the vastus lateralis muscle. Neurological outcome measures were (1) modified Ashworth Scale, (2) stretch reflex peak torque, (3) pendulum test,

Table 1. Key characteristics

Year	Author	Study design	LOE	n	AIS	Severity of SCI	Chronicity, years	Age	Sex % male	Device used
2008	Ballaz ¹²	RCT (passive cycling vs no cycling)	2	17 (9 cycling, 8 control)	A-C	—	cycling 20±8; control 17±11	cycling 48±8; control 48±7	NA	Ergo-dom; DCO Engineering, Zoopôle développement, 22 440 Ploufragan, France
2007	Ballaz ¹⁶	Pre-post (single group; single session)	4	15	A-C	2 I, 13 C	19±8	47±8	80%	Ergo-dom; DCO Engineering Pack, Technologie du Zoopôle Développement, 22 440 Ploufragan, France
1990	Figoni ¹⁴	Pre-post (single group; single session)	4	30 (13 PP, 17 QP)	Frankel A-C	I	PP 5.5±3.9; QP 6.0±4.7	PP 27.8±7.4; QP 31.6±7.9	PP 85%; QP 88%	FNS leg cycle ergometer, Model ERGYS 1 Therapeutic Alliances Inc. Tampa, FL
2005	Kakebeeke ¹⁹	Pre-post	4	10	A-B	C	2	42	90%	Motorized cycle THERA-vital, Medica Medizin GmbH Hochdorf, Germany
2008	Krause ¹³	Crossover	4	5	A	C	6.2±1.9	46.6±10.3	60%	Ergometer not described
2007	Muraki ¹⁵	Pre-post (single group; single session)	4	4	A	C	≥3	PP 35±11; control 30±10	100%	ERGYS 1 leg cycle ergometer Therapeutic Alliances, Inc. Dayton, OH
2016	Nardone ⁶	Pre-post (single group; single session)	4	10	A-D	5 I, 5 C	2-17	46.6	60%	Sevo-dynamically controlled recumbent ergometer Cybex International, Inc. Medway, MA
2011	Rayegani ¹¹	RCT (passive cycling vs PT)	2	64	A-B	C	~25	43	95%	Motorized cycle THERA-vital, Medica Medizin GmbH Hochdorf, Germany
2006	Ter Woerds ²	Pre-post	4	8	A-B	C	8.3±6.1	SCI 35±8.4; control 26±4.5	100%	Cycle ergometer Reck Motomed Viva 1
2011	Tran ¹⁷	Matched repeated measures cohort design	4	8	A-B	C	9±7.8	41±13.4	88%	Isokinetic Motomed cycle Multi-Tems Pty Ltd
2000	Willoughby ¹⁸	Pre-post	4	8	A-C	2 I, 6 C	3.87±3.24	27.87±10.93	63%	Psychic ergometer; passive leg exercise (no assistance from motor-driven apparatus)

Note: AIS = American Spinal Injury Association Impairment Scale; C = complete; I = incomplete; LOE = Oxford levels of evidence; NA = not available; PP = paraplegia; PT = physical therapy; QP = quadriplegia; RCT = randomized controlled trial.

Table 2. Summary of cycling parameters

Year	Author	Pedaling frequency, rpm	Total no. of sessions	Minutes/day	Days/week	Total duration of intervention, weeks	Comparison intervention
2008	Ballaz ¹²	40	36	30 ^a	6	6	No cycling intervention
2007	Ballaz ¹⁶	40	1	10	—	—	—
1990	Figoni ¹⁴	50	1	5	—	—	FES cycling
2005	Kakebeeke ¹⁹	40	1	30	—	—	Resting
2008	Krause ¹³	—	1	60-100	—	—	FES cycling
2007	Muraki ¹⁵	50	1	10	—	—	Active+FES cycling
2016	Nardone ⁶	60	1	7	—	—	Active cycling
2011	Rayegani ¹¹	NA	2 months	60 ^b	3x/day	~8	No cycling intervention
2006	Ter Woerds ²	35	1	20	—	—	Passive movements
2011	Tran ¹⁷	40	1	30	—	—	FES cycling
2000	Willoughby ¹⁸	25	24	20-90	2	12	—

Note: Shaded rows indicate multiple session intervention effects. FES = functional electrical stimulation.

^aThe duration of the session and the pedaling rate were increased regularly during the first week to reach 30 minutes at 40 rpm at the beginning of the second week of the training period.

^b20 min/set = 60 min/day.

(4) spasticity perception, (5) H-reflex amplitude, and (6) short-interval intracortical inhibition. None of the included studies measured activity or participation as described in the ICF domains.

Effectiveness of passive leg cycling

The impact of cycling on various outcome measures is summarized in **Table 3**. Although not all studies reported a statistical significance, seven out of nine studies reported large effect sizes and the other two reported moderate effect sizes (**Tables 3A and B**).

Cardiovascular responses to passive cycling

Single session studies: In general, studies showed a trend toward improvement in acute responses to passive cycling. Ballaz et al¹⁶ showed a medium effect size (Cohen's $d = -0.75$) increase in blood flow velocity and decrease in peripheral vascular resistance after cycling. Muraki et al¹⁵ ($n = 4$, Cohen's $d = -1.5$), Figoni et al¹⁴ ($n = 30$, Cohen's $d = -1$), and Ter Woerds et al² ($n = 8$; Cohen's $d =$ not available) also showed large effect sizes with the

small increase in blood flow, stroke volume, cardiac output, and pulmonary ventilation. The fourth study by Tran et al¹⁷ did not show any significant difference in the markers of vascular resistance between healthy controls and persons with SCI.

Multiple session studies: Only one study by Ballaz et al¹² showed a large effect size (Cohen's $d = 1.01$) in blood flow velocity and decrease in peripheral vascular resistance after cycling.¹²

Neurological responses to passive cycling

Single session studies: Overall, most studies found some form of improvement in the acute responses to passive cycling. Two studies found a large effect size with an improvement in outcomes such as short-interval intracortical inhibition (Cohen's $d = -1.84$) and spasticity (Cohen's $d = 1.53$) measured using the relaxation index and the modified Ashworth Scale.^{6,13} Kakebeeke et al¹⁹ found no change in spasticity measured by the peak knee torque evoked as a result of knee stretching; however, in this study, 6 of 10 participants reported subjective improvements in spasticity. None of the studies except one⁶ tested whether these acute

Table 3A. Summary of effects of passive cycling

Year	Author	Outcome category	Primary outcomes	Improvement	Statistical significance ^a
2008	Ballaz ¹²	Cardiovascular	Femoral artery blood flow velocity by Doppler US (mean blood flow velocity), used as an indicator of peripheral resistance	Yes	Yes
2007	Ballaz ¹⁶	Cardiovascular	Femoral artery blood flow velocity by Doppler US (mean blood flow velocity), used as an indicator of peripheral resistance	Yes	Yes
1990	Figoni ¹⁴	Cardiovascular	Oxygen uptake, stroke volume, total peripheral resistance, and cardiac output	Yes	No
2007	Muraki ¹⁵	Cardiovascular	Cardiorespiratory, mechanical efficiency, and quadriceps muscle oxygenation (NIRS)	Yes	No
2006	Ter Woerds ²	Cardiovascular	Leg blood flow doppler US	Yes	No
2011	Tran ¹⁷	Cardiovascular	Blood volume pulse signals (marker of cardiac activity and peripheral cardiovascular resistance)	No	NR
2016	Nardone ⁶	Neurological	Short-interval intracortical inhibition	Yes	Yes
2005	Kakebeke ¹⁹	Neurological	Spasticity perception	Yes	NA
2005	Kakebeke ¹⁹	Neurological	Stretch reflex – peak torque (isokinetic dynamometer)	No	No
2008	Krause ¹³	Neurological	Spasticity (modified Ashworth Scale and pendulum test of spasticity)	Yes	Yes
2011	Rayegani ¹¹	Neurological	Modified Ashworth scale and electrodiagnostic parameters	Yes	Yes
2011	Rayegani ¹¹	Musculoskeletal	Hip, knee, and ankle range of motion	Yes	Yes
2000	Willoughby ¹⁸	Musculoskeletal	Anthropometric measures (weight, thigh girth, and body mass index) and mRNA and myosin heavy chain expression (muscle biopsy)	Yes	Yes

Table 3B. Summary of effects of passive cycling

Year	Author	Outcome category	% change	Effect size (<i>d</i>) ^b	Effect size (<i>r</i>)
2008	Ballaz ¹²	Cardiovascular	45% increase in blood flow velocity ($p < .05$), and 14% decrease ($p < .05$) in peripheral vascular resistance (velocity index)	1.01	0.45
2007	Ballaz ¹⁶	Cardiovascular	Maximum and mean blood flow velocity increased by 20% and 31%, respectively ($p < .01$). Heart rate did not change. Peripheral resistance (velocity index) decreased by 11% ($p < .05$) after passive cycling.	-0.75	-0.35
1990	Figoni ¹⁴	Cardiovascular	31% increase in pulmonary ventilation, 17% increase in stroke volume, and 15% increase in cardiac output (peripheral resistance decreased by 7%)	-1	-0.45
2007	Muraki ¹⁵	Cardiovascular	Expired ventilation increased by 29% and VO ₂ max increased by 20%, heart rate decreased by 8%.	-1.5	0.6

(Continued)

Table 3B. Summary of effects of passive cycling (CONT.)

Year	Author	Outcome category	% change	Effect size (<i>d</i>) ^b	Effect size (<i>r</i>)
2006	Ter Woerds ²	Cardiovascular	~25% increase in blood flow after passive cycling. No changes in peripheral vascular resistance, or blood pressure were observed during or after the interventions.	—	—
2011	Tran ¹⁷	Cardiovascular	No difference between healthy controls and SCI subjects after cycling	—	—
2016	Nardone ⁶	Neurological	Short-interval intracortical inhibition decreased by 62% ($p < .001$)	-1.84	-0.68
2005	Kakebeeke ¹⁹	Neurological	In 6/10 subjects immediately post cycling and in 3/10 subjects after 30 minutes rest post cycling, self-report indicated that spasticity decreased.	—	—
2005	Kakebeeke ¹⁹	Neurological	No change in stretch reflex activation related knee peak torque assessed at 10 and 120 degrees/second speeds	—	—
2008	Krause ¹³	Neurological	Relaxation index increased after passive cycling by about 12% ($p < .05$), MAS decreased by 33% ($p < .05$) and peak velocity showed small increase after the passive cycling (1%; $p < .05$).	1.53	0.61
2011	Rayegani ¹¹	Neurological	MAS decreased significantly after passive cycling ($p < .05$). Hmax/Mmax decreased by 51% (right, $p < .05$) and 50% (left, $p < .05$).	1.22	0.52
2011	Rayegani ¹¹	Musculoskeletal	Hip (22%), knee (68%), and ankle (280%) range of motion significantly increased after passive cycling (all joints, $p < .05$).	-1.71	-0.65
2000	Willoughby ¹⁸	Musculoskeletal	No significant changes from pretraining to posttraining for the 3 anthropometric measures (thigh girth increased by 2.8%). For mRNA expression, there were significant increases in expression of MHC types IIa (49%) and IIx (61%) and significant decreases in expression for UBI (45%), E2 (68%), and 20S (96%), all analyses $p < .05$.	-0.79	-0.37

Note: Shaded rows indicate multiple session intervention effects. Hmax = maximum H-reflex amplitude; MAS = modified Ashworth Scale; MHC = myosin heavy chain; Mmax = maximum M-wave amplitude; UBI = ubiquitin; US = ultrasound.

^aAt least one measure showed statistically significant improvement.

^bEffect size measured using only the primary outcome variable.

responses to passive cycling persisted. Nardone et al⁶ showed that short-interval intracortical inhibition seen immediately after passive cycling had disappeared at 30 minutes post cycling.

Multiple session studies: One study found an improvement in spasticity measured using the pendulum test and the modified Ashworth Scale as well as H-reflex amplitude (Cohen's *d* for H-reflex = 1.22).¹¹ None of the studies that tested cardiovascular, musculoskeletal, or neurological outcomes after multisession cycling training tested whether the benefits persisted for any duration after the end of training.

Musculoskeletal responses to passive cycling

Single session studies: None of the studies that examined musculoskeletal outcomes were single session designs.

Multiple session studies: In general, there was a trend for improvement after passive cycling among the studies reviewed. Willoughby et al¹⁸ reported a medium effect size with an increase (Cohen's *d* = -0.79) in genetic expression of myosin heavy chain filament proteins (MHC types IIa and IIx), which are associated with fast-twitch muscle fiber type, after 24 sessions of passive cycling intervention. In addition, there was also a concomitant decrease

in genetic expression of markers of protein degradation (ubiquitin). Thigh girth was reported to have not changed statistically after training, however a small positive change was noted.¹⁸ Rayegani et al¹¹ reported an improvement in joint range of motion with passive cycling intervention with a large effect size (Cohen's $d = -1.71$) that occurred over a 2-month period of regular training.

Quality of studies and risk of bias

The LOE in the studies included in this review ranged from levels 2 to 4. Two papers were randomized controlled trials (LOE 2),^{11,12} and the remaining studies were case series or case control type trials (LOE 4). Ratings of the risk of bias for individual studies are reported in **Tables 4** and **5**. Quality and the risk of bias of the studies ranged

from poor to good, but were in general in the fair risk of bias category. Missing information that typically led to fair or poor ratings was small sample size, lack of prespecified inclusion criteria, lack of assessor blinding, lack of statistical analysis or p value reporting, lack of clarity in the eligibility criteria in the pre-post trials, lack of treatment allocation (so that assignments could not be predicted), lack of double-blinding, inadequate sample size, and lack of baseline between-group comparisons in the randomized controlled trials.

Discussion

Rehabilitation after SCI requires addressing deficits across multiple body systems. In this systematic review, we examined the acute responses (single session) and effects (multiple session) of

Table 4A. Risk of bias in pre-post studies

Author, year	Objective clarity	Eligibility prespecified	Participants representative of SCI population	Eligible participants enrolled	Large sample size	Tests or intervention clarity	Outcomes prespecified, valid and reliable
Ter Woerds, 2006 ²	Yes	NR	Yes	NR	No	Yes	Yes
Ballaz, 2007 ¹⁶	Yes	Yes	Yes	NR	Yes	Yes	Yes
Figoni, 1990 ¹⁴	Yes	NR	Yes	NR	Yes	Yes	Yes
Kakebeeke, 2005 ¹⁹	Yes	Yes	Yes	Yes	No	Yes	Yes
Krause, 2008 ¹³	Yes	Yes	No	NR	No	Yes	Yes
Muraki, 2007 ¹⁵	Yes	No	No	NR	No	Yes	Yes
Nordone, 2016 ⁶	Yes	Yes	Yes	NR	No	Yes	Yes
Tran, 2011 ¹⁷	Yes	No	No	NR	No	Yes	NR
Willoughby, 2000 ¹⁸	Yes	Yes	Yes	NR	No	Yes	Yes

Table 4B. Risk of bias in pre-post studies

Author, year	Assessor blinding	Loss to follow-up $\leq 20\%$	Statistical analysis, p values	Outcome measures multiple times pre/post	Risk of bias
Ter Woerds, 2006 ²	NR	Yes	Yes	No	Fair
Ballaz, 2007 ¹⁶	No	Yes	Yes	No	Good
Figoni, 1990 ¹⁴	No	Yes	Yes	No	Good
Kakebeeke, 2005 ¹⁹	No	Yes	No	No	Fair
Krause, 2008 ¹³	No	Yes	Yes	No	Fair
Muraki, 2007 ¹⁵	No	Yes	Yes	No	Fair
Nordone, 2016 ⁶	NR	Yes	Yes	No	Good
Tran, 2011 ¹⁷	NR	Yes	No	No	Poor
Willoughby, 2000 ¹⁸	NR	Yes	Yes	No	Good

Note: NR = not reported.

Table 5A. Risk of bias in randomized controlled trials

Author, year	RCT description	Randomization adequate	Treatment allocation concealed	Double blinding	Baseline group comparison	Dropout rate $\leq 20\%$	Differential dropout rate $\leq 15\%$
Ballaz, 2008 ¹²	Yes	NR	NR	NR	NR	No	Yes
Rayegani, 2011 ¹¹	Yes	Yes	No	NR	NR	Yes	Yes

Table 5B. Risk of bias in randomized controlled trials

Author, year	High intervention adherence	Other interventions similar or avoided	Outcomes valid and reliable	Power analysis ($\geq 80\%$)	Outcomes/subgroup analyses prespecified	Intention to treat analysis	Risk of bias
Ballaz, 2008 ¹²	Yes	Yes	Yes	No	Yes	No	Fair
Rayegani, 2011 ¹¹	Yes	Yes	Yes	NR	Yes	No	Fair

Note: NR = not reported; RCT = randomized controlled trial.

passive cycling intervention on cardiovascular, musculoskeletal, and neurological outcomes and summarized passive cycling training parameters such as intensity, duration, and type of passive leg cycling interventions. Our study builds on the previous systematic review that focused on neurological outcomes and animal studies⁴ by additionally reviewing cardiovascular and musculoskeletal effects of passive cycling in human studies. Two RCTs reported significant benefits of multiple sessions of passive cycling on cardiovascular (improved leg blood flow velocity), musculoskeletal (improved joint range of motion and markers of muscle hypertrophy), and neurological outcomes (improved spasticity and reflex excitability). No clear picture emerged with single session studies, with about half the studies showing a statistically significant improvement in acute responses in cardiovascular (blood flow velocity) and neurological outcomes (short interval intracortical inhibition and spasticity),^{6,13,16} while the rest reported no change. The studies reviewed here showed a diversity of cycling protocols and outcomes across multiple body systems.

Training parameters

Number of factors such as comfort level, tolerance, joint range of motion, stiffness, and ergometer motor capacity will determine the pedaling frequency. In the multiple session

studies, frequency of the exercise sessions ranged from one to three times per day, 20 to 90 minutes per session, 2 to 6 days per week, and 6 to 12 weeks total duration. This large variation in training parameters makes it difficult to determine the optimal patterns for maximizing improvement. The mix of acute responses to a single session of passive cycling may be a result of the variation in the single session duration in these studies, which ranged from 5 to 100 minutes per session; however, we did not observe any patterns that would indicate that there was a relationship between length of the cycling session and statistically significant results. Thus, it is difficult to make conclusive statements about the nature of acute responses to a single session of passive cycling. It is important that future studies include a follow-up period after end of training to assess how long these effects can last. The duration of these effects will help in determining optimal training protocols to maximize the beneficial changes post training.

Types of outcome measures

We identified three broad categories of outcome measures in this study—cardiovascular, neurological, and musculoskeletal—to assess the impact of passive cycling exercise. Although only a few outcomes were statistically significant, the moderate to large effect sizes warrant future larger studies.

Cardiovascular effects

Two parameters indicative of adaptive changes after SCI are the decreased blood flow to the lower limb muscles and increased peripheral vascular resistance.^{2,3} Thus, an improvement in these two parameters reported by Ballaz et al^{12,16} and Figoni et al¹⁴ after passive cycling is a desirable impact on the vascular system. Most studies that found decrease in peripheral vascular resistance used a more direct assessment of peripheral resistance by calculating the velocity index (difference in maximum and minimum blood velocity divided by the maximum velocity). Tran et al¹⁷ showed a nonsignificant 4% increase in peripheral vascular resistance (after 30 minutes of cycling); however, they used a different method of assessing peripheral resistance than the rest of the studies, which may explain the contradictory results. Tran et al¹⁷ used assessment of the dicrotic notch of the blood volume pulse (BVP) waveform, which is known to be influenced by physical stress even in healthy controls. It is possible that their findings are related to the duration of exercise (an indicator of physical stress), which was six times longer (30 minutes) than other studies and may reflect physical stress more than the peripheral vascular resistance. In the studies that showed no statistical change, the results may have been affected either by a small sample size^{2,15} or a shorter duration of cycling.¹⁴ Overall, it appears that passive cycling can improve blood flow to the lower limbs and can potentially help prevent and address conditions related to impaired blood flow such as skin breakdown lesions.²⁰ Decreased circulation can also result in vascular disorders such as thrombosis and muscle atrophy,²¹ and thus passive cycling has the potential to induce preventive effects.

Neurological effects

In addition to cardiovascular changes, three studies reviewed here found significant neurological benefits of passive cycling, namely decrease in spasticity and H-reflex amplitude and an increase in intracortical inhibition. A fourth study also examined a measure of spasticity (stretch-induced muscle torque) but did not find any significant changes.¹⁹ The lack of change in torque reported by

Takebeke et al¹⁹ can be attributed to the slow stretch speed chosen (120 degrees per second) to assess spasticity. Knee velocity during walking can be up to 169 degrees per second in healthy controls and up to 153 degrees per second in persons with cervical SCI.²² Animal SCI model spasticity assessments indicate that spasticity can only be assessed at stretch speeds in a range of 350 to 612 degrees per second.²³ Thus, it is possible that 120 degrees per second, certainly not a functional speed,²² may not have been fast enough to elicit a reflex response.²³ Although, Rayegani et al¹¹ reported a significant change in spasticity (with a large effect size), they did not report actual change scores. They also reported greater inhibition of H-reflexes, which are known to be hyperexcitable in the SCI population.²⁴ Previous reports have indicated that H-reflex amplitude is correlated with functional independence and spasticity in the SCI population.²⁴ Thus, these changes amount to positive changes with potentially meaningful functional impact on persons with SCI.

These results suggest that neurological outcomes may be more readily influenced after a single session and multiple sessions of passive cycling. The improvement in these outcome measures indicates that passive cycling can induce beneficial changes in the central nervous system. One of the underlying mechanisms of spasticity is thought to be increased sensitivity of the muscle spindles²⁵ as well as an increase in spinal excitability (higher H-reflex amplitude).²⁶ Improvement in outcome measures such as modified Ashworth Scale and H-reflex amplitude are indicative of the positive effects of passive cycling. Cortical excitability is known to be higher after SCI and is associated with a decrease in intracortical inhibition.²⁷ Thus, an increase in intracortical inhibition is an indicator of improved neuromodulation within the cortical neurons as a result of passive cycling. It is important to note that all these improvements in outcome measures such as spasticity,²⁸ H-reflex,²⁶ and cortical inhibition⁶ are all indicators of neuroplasticity associated with functional improvement after SCI.

Musculoskeletal effects

Musculoskeletal improvements in range of motion after multiple sessions of passive cycling

movements suggest that passive movements may not only maintain but also improve joint mobility post SCI.²⁹ In addition to overt musculoskeletal changes, one study examined the impact of multiple sessions of passive cycling on genetic expression of markers of muscle building and degradation.¹⁸ The results of the study by Willoughby et al¹⁸ are encouraging because they show an increase in the expression of fast-twitch myosin heavy chain and a concomitant decrease in genetic expression of markers of protein degradation (ubiquitin). These results suggest that passive cycling has the potential to attenuate muscle atrophy¹⁸; however, further studies are needed to determine whether a passive cycling intervention can protect muscle size. As anticipated, none of the single session studies assessed musculoskeletal outcomes because these changes most likely require a longer period of training.³⁰

Mechanisms of change

The common mechanism likely involved in the circulatory effects seen after passive cycling is the mechanical effect of rhythmic cycles of stretch and shortening. Large muscles like plantar flexors and quadriceps can exert mechanical pumping action as well as stretch reflex activation to trigger muscle pump and improve venous return.^{31,32} Peripheral vasculature resistance is prone to decrease with a decrease in movement typically seen after SCI. It appears that even a single session of cycling can elicit an acute response of enhanced blood flow and improved circulation through an increase in arterial diameter possibly because of preserved endothelial function in arteries below the lesion. Range of motion probably improved as a result of decrease in hyperreflexia⁵ as well as decrease in muscle and tendon stiffness.³³ Increased genetic expression of myosin heavy chain filament proteins and decreased expression of ubiquitin suggests that passive cycling may have upregulated pathways for muscle hypertrophy, which could help in the prevention of muscle atrophy and stimulate hypertrophy in people with SCI.³⁴

Limitations

Majority of the studies reviewed here were nonrandomized studies with a fair risk of bias,

and the results must be cautiously interpreted. This limitation should be weighed against the large effect sizes seen in the studies reviewed here. In addition, it is difficult to ascertain the clinical meaningfulness of the benefits of passive cycling reported here. The protocols used for cycling were diverse and so were the outcome measures precluding meta-analyses. In addition, all outcome measures were limited to the body structure and function category of the International Classification of Functioning, Disability and Health³⁵ with no outcomes in the activity or participation domains. The cutoff values for a clinically meaningful difference in the outcome measures after passive cycling in the studies reviewed here have not been established. Most outcome measures reported in this study were research tools but not routine clinical measurements; future studies need to examine the impact of passive cycling on assessments routinely used in the clinical environment. Finally, none of the studies barring one⁶ examined the duration of the effects of passive cycling lasted.

Conclusion

Evidence from this systematic review indicates that multiple sessions of passive leg cycling showed some form of beneficial changes across cardiovascular, musculoskeletal, and neurological systems in persons with SCI, based on two RCTs. More evidence is required to understand the best parameters for single and multiple sessions of passive cycling. More randomized controlled trials are needed to systematically understand the effects of passive cycling in persons with SCI. We recommend that future studies not only assess outcomes for body function and structure, but also include outcomes for activity and participation and include both objective as well as patient-reported outcomes.

Conflicts of Interest

Drs. Phadke, Ismail, and Boulias have received research grants from Merz Pharma. Drs. Ismail and Boulias have received speaker fees from Merz and Allergan. The other authors report no conflicts of interest.

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