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This is the **accepted version** of the journal article:

Morris, Timothy P.; Costa Miserachs, David; Rodriguez-Rajo, Pablo; [et al.].  
«Feasibility of aerobic exercise in the subacute phase of recovery from traumatic  
brain injury : A case series». Journal of Neurologic Physical Therapy, Vol. 42  
Núm. 4 (october 2018), p. 268-275. DOI 10.1097/NPT.0000000000000239

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# **Feasibility of Aerobic Exercise in the Subacute Phase of Recovery from Traumatic Brain Injury: A Case Series**

Timothy P. Morris MSc<sup>1,3,4</sup>, David Costa-Miserachs PhD<sup>3</sup>, Pablo Rodriguez-Rajo MSc<sup>1,2</sup>  
Jordi Finestres MSc<sup>1,2</sup>, Montserrat Bernabeu MD<sup>1,2</sup>, Joyce Gomes-Osman PhD<sup>3,5</sup>, Alvaro Pascual-Leone MD PhD<sup>1,3</sup> and Jose Maria Tormos-Muñoz MD PhD<sup>1,2</sup>

<sup>1</sup>Institut Guttmann, Institut Universitari de Neurorehabilitació adscrit a la UAB, Badalona, Barcelona, Spain

<sup>2</sup>Fundació Institut d'Investigació en Ciències de la Salut Germans Trias i Pujol, Badalona, Barcelona, Spain

<sup>3</sup>Berenson-Allen Center for Noninvasive Brain Stimulation, Division of Cognitive Neurology, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, Massachusetts, United States

<sup>4</sup>Departament de Psicobiologia i Ciències de la Salut, Institut de Neurociències, Universitat Autònoma de Barcelona, Bellaterra, (Cerdanyola del Vallès) Spain

<sup>5</sup>Department of Physical Therapy, University of Miami, Miller School of Medicine, Miami, United States

**Abstract word count:** 191

**Manuscript word count:** 3,541

**Conflicts of interest and sources of funding:** This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. No authors declare any significant conflicts of interest. In part supported by the Barcelona Brain Health Initiative.

**Acknowledgments:** We extend our thanks and gratitude to Dr. Josep Medina Casanova (Institut Guttmann), Dr Alberto Garcia Molina (Institut Guttmann) and Dr. Antonia Enseñat Cantallops (Institut Guttmann) for their help during the running of this study. We extend our thanks to Dr Alexandra M. Stillman (BIDMC) for her guidance in the preparation of this manuscript.

28

29 **Abstract**

30

31 **Background and purpose:** Injuries associated with traumatic brain injury (TBI) are  
32 common and can complicate rehabilitation. The objective of this study is to examine the  
33 feasibility of introducing aerobic physical exercise programs into the subacute phase of  
34 multidisciplinary rehabilitation from moderate-to-severe TBI, which includes computerized  
35 cognitive training.

36 **Case description:** Five individuals undergoing inpatient rehabilitation with moderate or  
37 severe TBIs who also have concomitant physical injuries. All of these individuals are in the  
38 subacute phase of recovery from their TBIs.

39 **Intervention:** An 8-week progressive aerobic physical exercise program. Participants were  
40 monitored to ensure that they could both adhere to and tolerate the exercise program. In  
41 addition to the physical exercise, individuals were undergoing their standard rehabilitation  
42 procedures which included cognitive training. Neuropsychological testing was performed to  
43 gain an understanding of each individuals' cognitive function.

44 **Outcomes:** Two minor adverse events were reported. Participants adhered to both aerobic  
45 exercise and cognitive training. Poor correlations were noted between heart rate reserve  
46 and ratings of perceived effort.

47 **Discussion:** Despite concomitant injuries and cognitive impairments, progressive aerobic  
48 exercise programs seem feasible and well tolerated in subacute rehabilitation from  
49 moderate-to-severe TBI. Some findings highlight the difficulty in measuring exercise  
50 intensity in this population.

51 **Abstract word count:** 196

52 **Manuscript word count:** 3,544

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54 **1. Introduction**

55 Traumatic brain injury (TBI) leads to many behavioural, sensorimotor and cognitive deficits,  
56 which result in significant social, personal and economic burdens. Cognitive impairment is  
57 an important statistical predictor of return to work <sup>1</sup> and with a mere 40% of individuals with  
58 severe TBI returning to work within 1-year of injury <sup>2</sup>, long-term treatments aimed at  
59 combating these deficits are critical for quality of life. Aerobic exercise, an inexpensive,  
60 easily administered and potentially long-term therapeutic intervention has been shown to  
61 have many physiological, structural and cognitive effects on the brain <sup>3-7</sup>. In non-injured  
62 adults, aerobic exercise appears capable of improving a variety of cognitive functions  
63 including attentional processes <sup>8</sup> and executive functions such as working memory and task  
64 switching <sup>9,10</sup>. In clinical studies improved attention, delayed memory and executive  
65 functions <sup>11,12</sup> have been observed in individuals with traumatic brain injury who participated  
66 in aerobic exercise. Additionally, a cardiorespiratory benefit of aerobic exercise in  
67 individuals with TBI has been shown <sup>13,14</sup>. However, these studies are few, with small  
68 sample sizes. A recent systematic review on aerobic exercise and cognitive recovery after  
69 TBI <sup>15</sup> highlighted some shortcomings inherent in these studies, including grouping together  
70 of individuals in different phases of recovery (subacute and chronic) and inadequate  
71 information on multidisciplinary rehabilitation procedures. Moreover, cognitive impairment  
72 and concomitant physical injuries may limit the participation in, and adherence to, an  
73 aerobic exercise program.

74

75 Common concomitant injuries associated with TBI include musculoskeletal injuries <sup>16</sup> and  
76 gait and balance impairments <sup>17</sup>. Apraxia and/or hypokinesia <sup>18</sup>, pain <sup>19</sup> and spasticity <sup>20</sup> are  
77 also seen. These injuries may constitute barriers to aerobic exercise, especially in the

subacute phase of injury. It is possible that the duration, intensity and frequency needed to induce an adaptive plastic response to enhance functional and cognitive recovery may not be achieved in individuals who present with serious concomitant injuries. It has been suggested that individuals with TBI have poor awareness of subjective fatigue however <sup>21</sup>. Assessing the feasibility of how to measure and control for these exercise parameters (frequency, duration and intensity), is therefore important

Inpatient, as well as early outpatient rehabilitation for TBI includes intensive sessions of physical therapy, occupational therapy, behavioural speech therapy and cognitive rehabilitation. This multidisciplinary approach means outcomes are unlikely to be influenced greatly by any single therapeutic input <sup>22</sup>. Meta-analyses on cognitive rehabilitation outcomes suggest computerized cognitive training is beneficial for improving cognitive functions such as executive function and attention <sup>23,24</sup> and is a common therapeutic tool in neurorehabilitation clinics <sup>25</sup>. Research has postulated that the combination of aerobic exercise with cognitive training may be more effective than either one alone <sup>26</sup>. Since fatigue <sup>27</sup> and apathy <sup>28</sup> are common symptoms in subacute TBI, the addition of aerobic exercise to traditional rehabilitation may pose challenges regarding the adherence to both programs. Should both interventions prove efficacious, it is important that individuals can participate in both.

Therefore, the development of successful aerobic exercise programs early after TBI requires the assessment of their feasibility. The aim of this case series study is to assess the feasibility of the inclusion of an 8-week progressive aerobic exercise program in addition to standard multidisciplinary rehabilitation, which includes computerized cognitive training, for moderate-to-severe TBI in the subacute phase of recovery.

103

104 **2. Case description**

105

106 The demographics of five individuals with moderate or severe TBIs who were undertaking  
107 inpatient rehabilitation at the time of recruitment are seen in Table 1.

108

109 A.A – The participant was a 19-year-old male who collided at high velocity with a wooden  
110 shed whilst skiing. He was wearing a helmet at the time but the impact caused the helmet  
111 to split into two. He lost consciousness immediately and upon being admitted to the hospital  
112 was awake but minimally conscious. His injury resulted in gait impairments including ataxia  
113 and apraxia. He had been an active adult prior to the injury, participating in regular sport  
114 and activity. He had undertaken the first year of undergraduate studies in computer  
115 engineering and spoke four languages.

116

117 B.B – The participant was a 56-year-old male who sustained a head injury in a motorcycle  
118 accident. He lost control of the motorcycle and was subsequently hit by a moving car. He  
119 presented with concomitant injuries of a cervical fracture at C4. He had been an active adult  
120 prior to injury participating in cycling multiple days per week. He had vocational education in  
121 mechanics.

122

123 C.C – The participant was a 34-year old male who sustained a head injury in a motor traffic  
124 accident. He fell from a motor cycle and hit the pavement with the front part of his head,  
125 breaking his helmet in two. He sustained a brachial plexus injury to the right arm, which  
126 caused severe pain as well as cervical compression myelopathy and a fractured right

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## 147

148 The education and ethics committee of the participating institution approved this study. All  
149 patients signed an informed consent prior to participating in the study. The informed  
150 consent documents were left with the participant and family members overnight and family  
151 members were active in all consent processes. This manuscript has been prepared under

the CARE guidelines: consensus-based clinical case reporting guideline development <sup>29</sup>. Participants were recruited from an acquired brain injury inpatient ward and were assessed by both a trained neuropsychologist and physiotherapist to assure they met the inclusion criteria for the study. Participants were considered eligible to participate in this study if they: i) had a diagnosis of moderate or severe TBI (3-8 or 9-13 on the Glasgow Coma Scale, respectively <sup>30</sup>) ii) had sufficient cognitive ability to understand written and verbal instructions (>6 on the Rancho Los Amigos Scale <sup>31</sup>); and iii) if they no longer displayed post-traumatic amnesia (measured by an average score of >75 on the Galveston Orientation Amnesia Scale over 3 consecutive days). Participants were excluded from the study if they had a history of a previous moderate or severe TBI, if they presented with any neurological or cardiorespiratory complications that were a contraindication to perform physical exercise, as described by the American College of Sports Medicine <sup>32</sup> or if they presented with aphasia, which would limit their ability to perform the cognitive assessments and study procedures. All participants began the study as inpatients and were discharged from the hospital during the 8-week intervention period. A.A, B.B and C.C returned as outpatients to continue their rehabilitation and the study whereas D.D and E.E did not live in the local area and did not come back for treatment in the outpatient clinic.

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### 170 3.1.2 Description of rehabilitation procedures

171

All participants were undergoing standard and individualised multidisciplinary rehabilitation programs throughout the entire study period, which involved intensive 5 hours a day, 5-7 days a week of occupational therapy, physical therapy, and behavioural speech therapy. Cognitive training using a computerized cognitive training platform (Guttman NeuroPersonal Trainer®, Barcelona, Spain) was performed by each participant at a similar



177 frequency to the physical exercise (three times per week for one hour during the 8-week  
178 study period). The cognitive training consists of a set of computerised cognitive tasks that  
179 cover different cognitive functions (attention, memory and executive functions) and sub-  
180 functions. For a full list of sub-functions see Solana et al., (2015) <sup>25</sup>. A baseline  
181 neuropsychological assessment determines the cognitive training program (which tasks, at  
182 what frequency and at what difficulty level to begin) and an automated algorithm, 'Intelligent  
183 therapy assist' <sup>33</sup> continuously monitors and updates an individual's progress.

184

#### 185 *Measures of neuropsychological function*

186

187 Participants were administered a clinical battery of neuropsychological tests by a trained  
188 neuropsychologist prior to (<1-week) the 8-week intervention period. The trail making test A  
189 <sup>34</sup>, where the participant is instructed to connect 25 numbered dots consecutively, as quickly  
190 and accurately as possible was used as a measure of processing speed and attention. The  
191 digit span forward, digit span backward and letter/numbers tests of the Wechsler adult  
192 intelligence scale part III (WAIS <sup>35</sup>), a series of tests during which the participant is read a  
193 series of numbers (or numbers and letters for letters/numbers) and asked to repeat them in  
194 the same order, or backwards were undertaken and which have been asserted to measure  
195 working memory. The Rey auditory verbal learning tests (RAVLT <sup>36</sup>) which measures  
196 episodic memory using a word-list learning task where 15 unrelated words are verbally  
197 presented and the participant is asked to recall as many as possible was performed. Five  
198 trials are presented which give measures of immediate word span (trial 1), total acquisition  
199 (all trials) and retention (after 20 to 45-minute delay). The block design task from the WAIS  
200 was also administered which measures visual abstract processing, spatial perception and  
201 problem solving. The participant is presented with red and white blocks (with two red sides

and two white) and is asked to construct replicas of designs previously presented by the examiner. Lastly, the verbal fluency task (FAS<sup>37</sup>) which consists of three word-naming trials where the participant has to say as many words beginning with a given letter of the alphabet (typically F A or S although in this study P M and R were used as part of the Spanish language version<sup>38</sup>) was administered.

### *3.2 Progressive aerobic exercise program*

The aerobic exercise intervention took place 3 times per week for 8-weeks. An introductory session took place to introduce participants to the equipment and aerobic exercise program. Each participant's physical abilities dictated which exercise equipment was used. Two machines was available- an active/passive exercise trainer that delivered resistance for active exercising of the arm, leg or arms and legs (Motomed Muvi, RECK, Betzenweiler, Germany), and an upright cycle ergometer (Keiser M3 indoor, Fresno, CA). As an example, if the participant was non-ambulatory they initially began with the active/passive trainer, performing arm cycling only. Weekly assessments by the participant's physiotherapist assessed whether a move from active/passive arm cycling to both arm and leg cycling or to the cycle ergometer was appropriate. Decisions were based on functional capacity of the participant (e.g has the participant regained sufficient leg strength to perform active leg cycling? Or, has the participant regained ambulation and sufficient balance to ride the cycle ergometer?). The target exercise intensity zone was defined as 50-70% of heart rate reserve (HRR). The corresponding heart rate (HR) in beats per minute (BPM) was calculated using the Karvonen equation ( $[(220 - \text{age}) - \text{resting heart rate}] \times \text{intended goal \% of HRR} + \text{heart rate rest}$ ) and monitored continuously by a Polar A380 wrist-based photoplethysmographic heart rate monitor (Polar Electro, Kemple, Finland). Nursing staff

227 recorded resting heart rate periodically during the early mornings, according to standard  
228 hospital protocol, and the average of the three lowest values in the three days prior to  
229 enrolment in study was recorded as pre-intervention resting heart rate. Ratings of perceived  
230 exertion using the 6-20 Borg scale <sup>39</sup> were taken every 15-minutes. Borg's scale of  
231 perceived exertion is a widely used rating scale with both verbal anchors and corresponding  
232 numbers whereby 6 represents "no exertion at all" and 20 represents "maximal effort". The  
233 scale is based on the physical sensations a person experiences during exercise, including  
234 increases in HR. A high correlation between the numerical anchors (times by 10) and actual  
235 heart rate during exercise has been shown <sup>40</sup>. The target HR zones of 50-70% of HRR are  
236 said to correspond to 12-14 ("somewhat hard") on this scale <sup>32</sup>. Each aerobic exercise  
237 session was designed to last between 45 minutes and one hour with a 10-minute warm-up  
238 and cool-down worked into each session. Warm-up sessions consisted of light resistance  
239 exercise. The exercise protocol aimed to allow each participant to become familiar with  
240 aerobic exercise, thus initially, participants were asked to undertake exercise at their own  
241 pace and were allowed to stop at any time. Upon having completed week one, the physical  
242 therapy staff asked participants to attempt to progressively increase their intensity (HR) and  
243 the duration of each session until they reached a consistent performance in each session  
244 that comprised 25 to 35 minutes of aerobic exercise within the target HRR zone. As patient  
245 engagement in health care may lead to greater outcomes <sup>41</sup> physical therapy staff  
246 attempted to engage participants to play a role in increasing the resistance of the exercise  
247 by using positive language as verbal motivation and feedback. The physical therapy staff  
248 monitored the participants HR and RPE to ensure intensity was increased in a progressive  
249 manner (i.e. not abruptly). Figure 1 shows a decision diagram of the aerobic exercise  
250 program.

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Table 2 shows the neuropsychological profile of each participant at the beginning of the intervention. Two adverse events were reported during the study. A.A complained of

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## 5 Discussion

Inpatient as well as early outpatient rehabilitation from severe TBI involves intensive multidisciplinary treatments. However, damage to frontal lobes and networks integral to drive and motivation can be problematic to the rehabilitation process <sup>42</sup>. Low motivation in individuals with TBI is often observed and commitment to, and perseverance in, rehabilitation can be negatively affected <sup>43</sup>. Fatigue <sup>27</sup> and apathy <sup>28</sup> are also common in this phase of recovery and so, aerobic exercise may be challenging to initiate and sustain. More recently, adherence to minimally supervised aerobic exercise programs within community-dwelling individuals with TBI was deemed feasible <sup>44</sup>. Importantly, such aerobic exercise programs may improve mood in chronic TBI <sup>45,46</sup>. Less is known about adherence to aerobic exercise in sub-acute rehabilitation however, and so the results from the present study suggest the addition of three, one-hour sessions of aerobic exercise per week for 8-weeks to the multidisciplinary rehabilitation schedule can be feasible.

Up to 78% of individuals with TBI may present with concomitant extracranial injuries, which have been significantly associated with long-term disability<sup>47</sup>. These physical barriers to aerobic exercise can also contribute to a sedentary lifestyle and result in long-term sedentary behaviour upon discharge from the hospital<sup>48</sup>. Therefore, the re-introduction of aerobic exercise soon after injury may be important. Indeed, aerobic exercise has been shown to improve clinical disability scores in other clinical populations<sup>49</sup> and so successful adherence to an early 8-week aerobic exercise program in individuals with concomitant injuries to TBI, such as loss of ambulation (A.A), cervical and clavicle and rib fractures (B.B and C.C and E.E) has the potential to improve long term disability. Nevertheless, despite adhering to both the exercise program and traditional rehabilitation, only two participants exercised for more than 50% of the time within the target intensity zones. A previous study showed that just 28% of individuals with severe TBI exercised above 50% of their heart rate reserve (HRR) during circuit class therapy<sup>13</sup>. The authors did not report on physical limitations of participants in that study. It is possible that the concomitant injuries sustained by the participants in this case series limited their ability to exercise at higher HR intensities. However, contributions beyond physical limitations (which dictated exercise type) may also account for this. Participants A.A and B.B performed different exercises (arm/leg cycling and static upright cycling, respectively) and neither participant exercised within the target HR training zones. The Karvonen equation, used to calculate HR training zones, uses 220-age to predict HR maximum and may be a contributing factor. The peak aerobic capacity of individuals with TBI has been reported at 65-74% of non-injured adults<sup>50-52</sup> and so this widely used equation may underestimate intensity zones in this population.

The possible inability of the Karvonen equation to capture true HRR in individuals who have lower peak aerobic capacity could also explain the poor correlation between HRR and RPE

351 seen. However, participant D.D reported the same RPE value at most time points  
352 regardless of HR and so it is more likely that this individual had difficulty in accurately  
353 communicating their true perception of effort. Indeed poor awareness of subjective fatigue  
354 in individuals with TBI compared to healthy controls has previously been reported <sup>21</sup>.  
355 Importantly, the Borg scale is not validated in individuals with TBI and discrepancies in the  
356 meaning of the verbal anchors may exist in this population <sup>53</sup>. Nevertheless, RPE is the  
357 preferred method to assess intensity in individuals who take medications that affect HR or  
358 pulse <sup>54</sup>. This is of particular importance as if the peak aerobic capacity of individuals with  
359 TBI is reduced <sup>50-52</sup> and/or medications that affect resting heart rate are taken, then heart  
360 rate measures to control for the intensity of exercise may be invalid. Yet the use of RPE  
361 may also prove inaccurate <sup>53,55</sup>. Larger studies to assess this phenomenon in individuals in  
362 this phase of recovery and a search for optimal methods to control for exercise intensity are  
363 required.

364

365 The results from this case series should be interpreted in light of their limitations. The  
366 recording of RPE at 15-minute intervals in a small sample is a limitation. Yet  
367 implementation of RPE recordings at greater frequencies within the clinic might be  
368 impractical. The use of wrist-based photoplethysmography (PPG) technology to monitor  
369 HR is also a limitation with its susceptibility to motion artifact <sup>56</sup>. However, this may  
370 represent a best-case scenario as the use of the gold standard chest straps may be  
371 impractical in individuals with severe TBI who present with behavioral and cognitive  
372 impairments. Additionally, by not re-measuring resting heart rate prior to each exercise  
373 session changes in resting heart rate (which dictates heart rate training zones) over the 8-  
374 week intervention period an unaccounted for.

375



#### 4. Summary

The inclusion of three, one-hour sessions of aerobic exercise for 8-weeks into intensive multidisciplinary rehabilitation for moderate-to-severe TBI was feasible. Individuals tolerated the aerobic exercise well and concomitant physical injuries did not hinder their participation. Despite this feasibility, future studies are required to better understand how the intensity of exercise can be controlled in this population.

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## Tables

Table 1. Demographics

Participant	A.A	B.B	C.C	D.D	E.E
Age	19	56	34	43	32
Gender	M	M	M	M	M
Severity of Injury (GCS)	Severe (4)	Moderate (10)	Severe (3)	Moderate (11)	Severe (5)
Pre-intervention resting HR	58	79	67	58	58
Time since injury (days)	91	24	30	51	48
PTA time (days)	78	24	18	36	38
Cause of injury	Skiing accident	Traffic accident	Traffic accident	Traffic accident	Traffic accident
Concomitant injuries / barriers to exercise	Complete loss of independent ambulation, Apraxia / ataxia	C4 vertebral fracture	Brachial plexus injury / fractured clavicle / chronic pain	n/a	Rib fractures 10/11
Pre-injury activity level	Active	Active	Active	Active	Active

GCS, Glasgow coma score; PTA, post traumatic amnesia

Table 2. Neuropsychological test scores

Participant	A.A		B.B		C.C		D.D		E.E	
Test										
RAVLT Short term ( <i>verbal</i> )	28	VS	33	M	34	VS	42	S	20	VS

memory)

RAVLT long term ( <i>verbal memory</i> )	n/a*	VS	5	M	1	M	8	S	2	VS
RAVLT retention ( <i>verbal memory</i> )	n/a*	VS	12	N	9	M	12	S	5	VS
WAIS digit span forward ( <i>short term memory</i> )	6	N	4	S	6	N	6	N	5	S
WAIS digit span backwards ( <i>working memory</i> )	7	N	4	N	4	N	5	N	3	S
WAIS letters/numbers ( <i>working memory</i> )	5	S	10	N	11	N	8	S	n/a*	VS
WAIS block design ( <i>visual construction</i> )	n/a^		26	N	46	N	27	M	15	S
TMT-A ( <i>attention</i> )	77	VS	84	S	56	N	31	N	57	M
FAS ( <i>executive function</i> )	20	VS	n/a*	VS	20	VS	19	VS	16	VS

Left column = test score, right column = level of deficit, based on age and level of education: VS = very severe, S = severe, M = moderate, N = normal. RAVLT, Rey auditory verbal learning test; WAIS, Wechsler adult intelligence scale; TMT-A, trail making test part A; FAS, phonemic verbal fluency test. n/a\*, participant unable to complete test due to severe deficit; n/a^, participant unable to complete test due to motor impairment.

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Table 3. Feasibility data from the aerobic exercise and cognitive training programs

Participant	A.A	B.B	C.C	D.D	E.E
<i>Aerobic exercise</i>					
Total number of sessions	24	23	23	12	13
% adherence	100%	95%	95%	80%	87%
Mean session duration (mins)	45	47	41	45	49
Mean % HRR	33%	40%	40%	55%	56%
Mean time spent in HRR training zone (%)	0	4%	0%	55%	62%

Mean BPM	102	109	108	116	128
Mean RPE	12	13	11	12	

### *Cognitive training*

Total number of sessions	24	24	24	11	12
% adherence	100%	100%	100%	73%	80%
# tasks performed	363	222	252	157	234

% adherence based on 24 sessions for A.A, B.B AND C.C and on 15 sessions for D.D and E.E. HRR, heart rate reserve; BPM, beats per minute; RPE, ratings of perceived exertion.

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## 576 **Figure Legends**

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578 Figure 1. Flow diagram of the progressive aerobic exercise intervention

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580 Figure 2. **A.** Individual mean %HRR at 15-minute intervals (1 minute average of HRR before and after each 15-minute  
 581 mark) with standard error bars.**B-E.** Scatter plots for individual mean %HRR and mean RPE at 15-minutes intervals with  
 582 Pearson's correlation coefficient values.

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