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Independent, Community-Based Aerobic Exercise Training for People with Moderate-to-Severe Traumatic Brain Injury

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Running head: COMMUNITY BASED EXERCISE IN MODERATE-TO-SEVERE TBI

**INDEPENDENT, COMMUNITY-BASED
AEROBIC EXERCISE TRAINING FOR PEOPLE WITH
MODERATE-TO-SEVERE TRAUMATIC BRAIN INJURY**

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DISCLOSURES

Dr. Devine has nothing to disclose.

Dr. Wong has nothing to disclose.

Dr. Gervino has nothing to disclose.

Dr. Pascual-Leone serves on the scientific advisory boards for Nexstim, Neuronix, Starlab Neuroscience, Neuroelectrics, and Neosync; and is listed as an inventor on several issued and pending patents on the real-time integration of transcranial magnetic stimulation (TMS) with electroencephalography (EEG) and magnetic resonance imaging (MRI).

Dr. Alexander has nothing to disclose.

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ACCEPTED MANUSCRIPT

1 **INDEPENDENT, COMMUNITY-BASED AEROBIC EXERCISE**
2 **TRAINING FOR PEOPLE WITH MODERATE-TO-SEVERE**
3 **TRAUMATIC BRAIN INJURY**

4
5
6 **ABSTRACT**

7 Objective: To determine if people with moderate-to-severe TBI can adhere to a minimally
8 supervised, community-based vigorous aerobic exercise program.

9 Design: Prospective trial.

10 Setting: Eastern Massachusetts YMCA facilities.

11 Participants: Ten community-dwelling volunteers (8 men, 2 women; ages 22-49) 6-15 months post
12 moderate-to-severe TBI.

13 Intervention: Participants received memberships to local YMCAs and brief orientations to exercise,
14 then were asked to independently complete ≥ 12 weeks of ≥ 3 training sessions/week, performed at
15 65-85% of maximum heart rate for ≥ 30 minutes per session. Participants could self-select exercise
16 modality, provided they met intensity/duration targets. Programmable heart rate monitors captured
17 session intensity/duration.

18 Main Outcome Measures: Independence with equipment/facility use, compliance with training
19 goals (session frequency, duration, intensity and total weeks of training).

20 Results: All participants achieved independence with equipment/facility use. All met at least 2 of 4
21 training goals; half met all 4 goals. Participants averaged 3.3 sessions/week (SD +/- 0.7) for 13
22 weeks (range 6 – 24). Average session duration was 62 minutes (SD +/- 23), of which 51 minutes
23 (SD +/- 22) occurred at or above individual HR training targets.

24 Conclusions: People in recovery from moderate-to-severe TBI can, with minimal guidance,
25 perform vigorous, community-based exercise. This suggests decentralized exercise may be
26 logistically and economically sustainable after TBI, expanding its potential therapeutic utility and
27 rendering longer duration exercise studies more feasible.

28 Key Words: aerobic exercise; traumatic brain injury; community-based.

29 Habitual aerobic exercise improves cardiovascular endurance and positively affects mood and
30 functional capacity. Increasing evidence suggests it also influences cognition in many populations,
31 including stroke^{1,2}, brain injury^{3,4}, Alzheimer's disease^{5,6} and people at increased risk of dementia^{7,8}
32 . As impairments in cognition, endurance, functional capacity and mood are all sources of morbidity
33 after TBI, aerobic exercise may represent a valuable non-pharmacologic adjunct. Improvements in
34 cardiovascular endurance are demonstrable after 12-week aerobic exercise programs in most
35 populations⁹, while mood and cognition changes can take > 6 months to manifest^{5,6}. TBI survivors
36 can safely perform vigorous exercise¹⁰ and comply with short, supervised group training^{3,4,10}.
37 However, they frequently have limited transportation access, which restricts participation in longer
38 exercise programs requiring multiple weekly visits to distant training sites. Decentralized,
39 independent exercise may offer an alternative, if reliable participation can be assured. The goal of
40 this study was to determine if community-dwelling people with moderate-to-severe TBI could
41 demonstrate the physical, cognitive and behavioral skills necessary to adhere to an independent,
42 community-based cardiovascular exercise program, and whether they could maintain an intensity,
43 duration and frequency known to improve cardiovascular endurance.

44

45

46 **METHODS**

47 Screening: After obtaining approval by the Committee for Clinical Investigation at Beth Israel
48 Deaconess Medical Center and Braintree Rehabilitation Hospital, a query of Braintree Hospital's
49 admission database identified patients aged 18-50 with moderate-to-severe TBI during an 18-month
50 period. Chart review identified those who met study criteria. Inclusion criteria were: 1) English
51 speaking; 2) visual acuity adequate for safe participation; 3) resident of a community served by the
52 participating Eastern MA YMCA; 4) competent to give informed consent. Exclusion criteria were:

53 1) Pre-morbid or injury-related musculoskeletal or neurological impairment that would render
54 cardiovascular exercise dangerous; 2) Pre-morbid or injury-related medical disorders for which
55 rigorous cardiovascular exercise is contraindicated (deep venous thrombosis, active coronary artery
56 disease, valvular heart disease, peripheral vascular disease, obstructive lung disease, uncontrolled
57 hypertension, uncontrolled diabetes). Figure 1 summarizes screening and enrollment.

58
59 Enrollment: Ten patients replied to telephone contact and completed in-person evaluations on a
60 rolling, first-come basis, including history and physical examination with study physician. Where
61 possible barriers to participation arose, participants furnished current medical records to confirm
62 they could safely participate. Brain injury clinical diagnoses and injury severity were extracted
63 directly from hospital notes. Neuropsychological screening showed residual memory and executive
64 function impairments, but confirmed cognitive recovery sufficient to safely comply with pre-
65 intervention exercise testing instructions.

66
67 Pre-Intervention Cardiovascular Testing: Participants underwent maximal effort cardiovascular
68 testing (modified Bruce Protocol with continuous 12-lead ECG and blood pressure monitoring
69 using treadmill or bicycle) to confirm cardiovascular safety for exercise. Observed maximum heart
70 rates were used to calculate individual aerobic training zones (65-85% of maximum). Two
71 participants withdrew from the study prior to intervention: participant #2 withdrew due to interval
72 DVT diagnosis, and participant #10 withdrew when her nearest YMCA left the study.

73
74 Intervention: Participants received complimentary individual memberships at local YMCA's for the
75 duration of the study, where they had access to exercise equipment during normal hours. Each was
76 asked to complete ≥ 12 weeks of exercise, maintaining ≥ 3 exercise sessions/week of ≥ 30

77 minutes/session, and to keep heart rates between 65-85% of their observed maximum. Participants
78 received individually programmed, recordable heart rate monitors (HRM; Polar Electronics model
79 RS-400) that continuously displayed heart rate, personal training zone and session duration, and
80 wore monitors for all exercise. Initial sessions were supervised by study staff until participants
81 showed they could: 1) exercise for ≥ 30 minutes at target intensity, 2) navigate the gym milieu
82 [negotiate external facilities and entry, find and use locker room/restroom, find cardiovascular
83 exercise area within facility, comply with facility rules], 3) safely operate at least two pieces of
84 stationary exercise equipment, and 3) independently operate HRM. After demonstrating these skills,
85 participants were permitted to exercise independently. Participants were given no additional support
86 beyond what general YMCA members receive. YMCA staff was informed that participants were
87 involved in an exercise study, given P.I.'s contact information and told to share any concerns
88 if/when they arose. Participants were encouraged to exercise outdoors when safe opportunities
89 existed, but received no additional financial support for this. In the event of technical/operational
90 error with HRM's, participants also kept training logs. Study staff met participants every 3 weeks at
91 their YMCA to download HRM data and review training logs. HRM training intensity parameters
92 were increased incrementally to insure continued cardiovascular challenge. Participants unable to
93 perform exercise for medical reasons (illness, injury, surgery) during a given study week were
94 permitted to make up sessions at the end of the 12-week period. Downloaded HRM data was
95 analyzed individually for each participant to obtain individual total minutes of exercise and volume
96 of time spent within individual target training zone.

97

98

99 **RESULTS**

100 Table 1 summarizes participant demographics and exercise performances.

101

102 Compliance: All participants achieved independence with use of YMCA facilities, demonstrated
103 proficiency with programmable HRM's and could safely and independently use 2 pieces of
104 stationary exercise equipment within 4 training sessions or less. One participant was unable to write
105 in a training log, but used a HRM for all training sessions.

106

107 Training performance: All 8 participants met goals for session duration and intensity. Half of
108 participants (3, 7, 8, 9) met all of the training goals (session duration, intensity, session frequency
109 and overall program duration. Two participants met 3 of 4 goals (#5 averaged 2.7 sessions /week;
110 #6 completed 10 weeks of training). Participants 1 and 4 documented < 12 weeks of training and
111 averaged < 3 sessions/week during weeks they exercised. Participant 4's HRM was lost before final
112 data extraction. Mean performance data was calculated for each participant; individual means were
113 then used to create the group mean. This assured that each participant's efforts were represented
114 equally in summary statistics, regardless of how many sessions s/he completed. Participants
115 completed a mean of 3.3 exercise sessions/week (SD +/- 0.7) for a mean of 13 weeks (range 6 – 24
116 weeks). Mean session duration was 62 minutes (SD +/- 24 minutes), of which 51 minutes (SD +/-
117 22 minutes) was spent at or above target intensity. This represented 81.9% of total training time
118 spent at or above target intensity (SD +/- 0.1).

119

120 Adverse events: No serious events were reported during this study. Two participants developed
121 overtraining injuries (ankle soreness, delayed onset muscle soreness) sufficient to briefly suspend
122 exercise (≤ 7 days' rest). Two participants (#4, #7) underwent planned outpatient surgery during the
123 12-week training period for pre-existing orthopedic injuries not impacted by exercise. Participant 7
124 resumed training once medically cleared and made up missed sessions at the end of the study. We

125 received no reports of inappropriate behavior in the training milieu, or of participants requiring
126 support beyond what was available to all YMCA members. The most commonly cited reason for
127 missed training sessions was lack of transportation (no ride, insufficient funds for public transit).

128

129

130 **DISCUSSION**

131 The purpose of this study was to see whether TBI survivors could independently exercise at the
132 same intensity, frequency and duration known to cause a training effect, utilizing local facilities and
133 common training tools. Our findings show that community-dwelling people with moderate-to-
134 severe TBI can do this. With neither a structured exercise program nor therapist supervision, our
135 participants safely and effectively performed aerobic exercise and met most frequency, duration and
136 intensity goals. All were capable of independently navigating exercise facilities, using exercise
137 equipment and operating programmable HRM's. These findings suggest aerobic exercise may be
138 promoted for TBI survivors independent of insurance or therapist supervision, and that exercise can
139 be safely and effectively done in facilities convenient to participants, alongside the general
140 population. Our findings further suggest that longer duration community-based exercise may be a
141 viable alternative to centralized research interventions.

142

143 Without reliable, uniform exercise interventions, attribution of effect, or confirmation of non-effect
144 is impossible. By using individually programmed HRM's, we gave participants real time exercise
145 guidelines, and confirmed intensity/duration were comparable both between sessions and among all
146 participants. HRM's supplied data unobtainable from training session attendance records alone, and
147 eliminated recall bias as an error source – critical for populations with cognitive impairments.

148 Tailoring exercise intensities to individual baseline cardiovascular fitness and increasing intensity

149 throughout the study to maintain constant challenge insured our participants trained at an intensity
150 that existing literature suggests is sufficient to provoke a cardiovascular training response⁹.

151

152

153 **STUDY LIMITATIONS**

154 With eight participants generalizability is limited. Older individuals comprise a growing subgroup
155 of TBI survivors; it is unclear whether independent exercise is equally safe for them. Our
156 participants used standard gym equipment; mobility-impaired TBI survivors may require
157 specialized equipment not widely available in the community. Only patients with interest in
158 exercise replied to screening, biasing selection in favor of compliance. While this bias exists in all
159 exercise trials, it is more problematical in those where degree of participation or some derivative
160 thereof is an outcome.

161

162

163 **CONCLUSIONS**

164 People in recovery from moderate-to-severe TBI can, with minimal guidance, perform vigorous,
165 community-based exercise. This suggests decentralized exercise may be logistically and
166 economically sustainable after TBI, expanding its potential therapeutic utility and rendering longer
167 duration exercise studies more feasible.

168

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- 197

198 **SUPPLIERS**

199 Programmable Heart Rate Monitors (Polar RS-400) supplied by Polar Electro Inc., 1111 Marcus
200 Avenue, Suite M15, Lake Success, NY 11042-1034, telephone 1-800-227-1314.

PARTICIPANTS

DEMOGRAPHICS

	1	2 ¹	3	4	5	6	7	8	9	10 ²	Mean	Standard deviation
Age	31	48	26	29	22	42	49	40	42	24	36	10
Gender	female	male	male	male	male	male	male	male	male	female	--	--
Brain Injury Clinical Diagnosis	severe	moderate	severe	moderate	moderate	severe	severe	moderate-to-severe	severe	severe	--	--
Mechanism of injury	fall	motorcycle accident	pedestrian vs. MVA	MVA	MVA	MVA	fall	bicycle vs. MVA	pedestrian vs. MVA	MVA	--	--
Inpatient hospitalization (days)	74	11	185	36	10	91	≥ 47	40	67	121	68	54
Months post-injury at enrollment	10	6	15	9	12	6	7	6	7	12	9	3
Concomitant neuro / MSK injuries	radial, mandibular fractures	mandibular fracture, pre-morbid chronic neck pain	clavicular, rib, acetabular and femoral head fractures	brachial plexus injury, femoral & tibial fracture with foot drop	transient right hemiparesis	rib fractures	clavicular, distal radius, wrist and digit fractures	tibia and fibular fracture, ankle fracture	left hemiparesis	vertebral, iliac wing, rib and hand fractures	--	--
Pre-injury exercise experience	regular aerobic & resistance exercise	regular aerobic & resistance exercise	physically demanding job	physically demanding job	regular aerobic & resistance exercise	no prior exercise	physically demanding job	no prior exercise	no prior exercise	former high school athlete	--	--
Distance from residence to YMCA (miles)	0.6	10.4	4.6	4.2	4.4	8.4	5.4	1.4	7	4.3	5.1	3

EXERCISE PERFORMANCE

GOAL ACHIEVEMENT

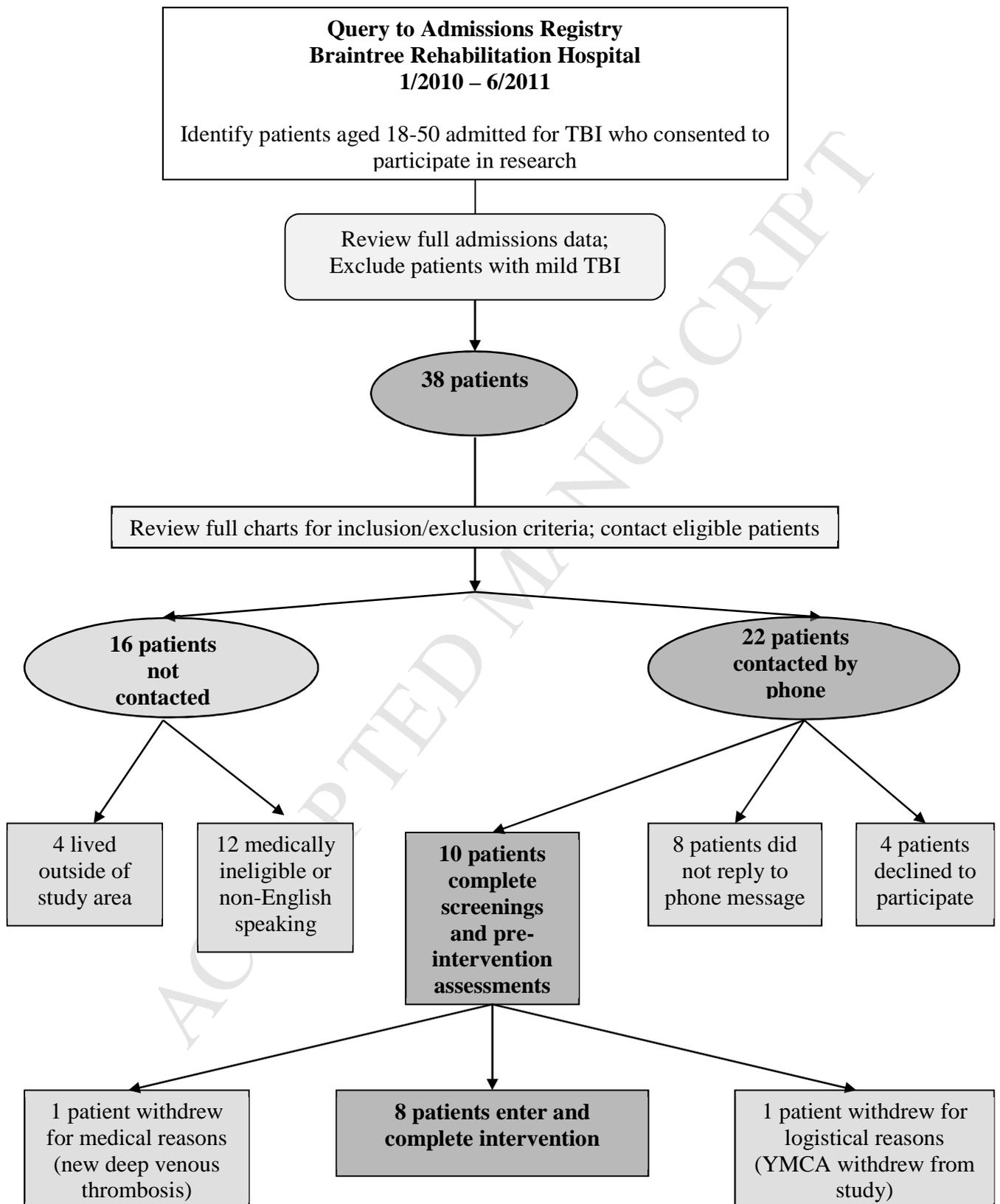
	1	2 ¹	3	4	5	6	7	8	9	10 ²
Independent in facility, safely used equipment and HRM	yes	--	yes	--						
Averaged ≥ 30 minutes per session	yes	--	yes	--						
Able to sustain 65-85% max HR for 30 minutes	yes	--	yes	--						
Averaged ≥ 3 sessions per week	no	--	yes	no	no	yes	yes	yes	yes	--
Completed 12 weeks of training	no	--	yes	no	yes	no	yes	yes	yes	--

TRAINING DATA

	1	2 ¹	3	4	5	6	7	8	9	10 ²	Mean	Standard deviation
Total Sessions	13	--	79	17	30	43	47	52	41	--	40	21
Total Weeks of Exercise	6	--	24	9	15	10	13	14	13	--	13	5
% weeks with > 1 session	50	--	87	58	93	83	92	100	100	--	83	19
Mean sessions/week exercise	2.3	--	4.2	2.4	2.7	3.9	3.8	3.7	3.2	--	3.3	0.7
Mean session duration (minutes)	55	--	85	48	44	38	50	108	65	--	62	24
Mean training time at 65-85% max HR (minutes)	39	--	80	38	36	33	35	86	63	--	51	22

¹ Participant withdrew from study for medical reasons prior to exercise intervention.

² Participant withdrew from study for logistical reasons prior to exercise intervention.

FIGURE 1: Screening and Enrollment Pathway

HIGHLIGHTS

Per Dr. Basford's reply to us on April 11, 2016 (included in the uploaded "Response to Reviewers" document), is our understanding that Highlights and Graphical Abstract are optional. If this is not the case for this revision, we are happy to create and add these to our submission materials.

Thank you.