

1 Concurrent impact of bilateral multiple joint functional electrical stimulation and treadmill walking
2 on gait and spasticity in post-stroke survivors: A Pilot Study

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23 on gait and spasticity in post-stroke survivors: A Pilot Study
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25 **ABSTRACT**

26 **Background:** Stroke causes multi-joint gait deficits, so a major objective of post-stroke rehabilitation
27 is to regain normal gait function. **Design and Setting:** A case series completed at a neuroscience
28 institute. **Aim:** The aim of the study was to determine the concurrent impact of functional electrical
29 stimulation (FES) during treadmill walking on gait speed, knee extensors spasticity and ankle plantar
30 flexors spasticity in post-stroke survivors. **Participants:** Six post-stroke survivors with altered gait
31 patterns and ankle plantar flexors spasticity (4=male; age 56.8 ± 4.8 years; Body Mass Index (BMI)
32 26.2 ± 4.3 ; since onset of stroke: 30.8 ± 10.4 months; side of hemiplegia [L/R]: 3:3) were recruited.
33 **Intervention:** Nine treatment sessions using FES bilaterally while walking on a treadmill. **Main**
34 **Outcome Measures:** Primary outcome measures included the Modified Modified Ashworth Scale
35 (MMAS), Timed Up and Go test (TUG), 10-m walking test, gait speed, and Functional ambulation
36 category (FAC). Secondary outcome measures included the Step Length Test (SLT), and active range
37 of motion (ROM) of the affected ankle and the knee. Measurements were taken at baseline (T0), at
38 the end of last treatment (T1), and one month after the final treatment session (T2). **Results:** The TUG,
39 10-m walking test, gait speed, FAC, active ROM, and SLT all significantly improved following
40 treatment ($P < 0.05$), while ankle plantar flexors spasticity ($P = 0.135$), and knee extensors spasticity
41 ($P = 0.368$) did not show any significant decrease. **Conclusions:** A short duration of bilateral FES in
42 conjugation with treadmill walking contributed to significant improvement in gait speed, functional
43 mobility, functional ambulation, range of motion and step length in post-stroke survivors. In contrast,
44 no significant decrease were identified in the spasticity of the ankle plantar flexors and knee extensors
45 muscles.

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47 **Keywords:** functional electrical stimulation; gait; neurorehabilitation; stroke

48 **INTRODUCTION**

49 Stroke is one of the main contributors of death and disability (Feigin et al, 2015). In developing
50 countries, the incidence of stroke and its associated disabilities, continues to increase annually (Feigin
51 et al, 2015). In Iran, stroke is the second highest cause of death and disability (Forouzanfar et al,
52 2014), and physical complications include spasticity, that negatively affect walking ability and gait
53 patterns (Watkins et al, 2002).

54 One of the major objectives of post-stroke rehabilitation is to regain normal gait function (Noma et al,
55 2012). Stroke causes multi-joint gait deficits (Kesar et al, 2009), consequently, treadmill training has
56 received special attention in post-stroke rehabilitation (Kesar et al, 2009). As speed and gradient are
57 fully controllable, the treadmill may allow patients to train gait function without some of the challenges
58 faced with walking on a regular surface (Barbeau and Visintin, 2003).

59 Functional electrical stimulation (FES) may be an effective treatment for reducing muscle spasticity
60 and improving movement in post-stroke survivors (Howlett, Lannin, Ada, and McKinstry, 2015).
61 Previous rehabilitation studies have shown that FES is effective for increasing muscle activation (Kafri
62 and Laufer, 2014; Shariat et al, 2018). In addition, FES appears to engage the sensorimotor cortex of
63 the brain by stimulating Type 1 afferent nerve endings in post-stroke survivors. The process of these
64 repetitive sensory inputs may provide sensory and visual feedback to the brain, aiding the
65 rehabilitation process (Howlett, Lannin, Ada, and McKinstry, 2015). The effectiveness of a single
66 channel of FES for increasing gait velocity and reducing energy expenditure has been previously
67 reported (Kafri and Laufer, 2014). A single channel of FES has also been shown to help improve the
68 swing phase of the gait cycle in 20% of post-stroke survivors (Kafri and Laufer, 2014; Kesar et al,
69 2009). However, in patients where multiple joints are affected by paralysis this method may not be

70 effective (Kesar et al, 2009). Therefore, FES should be used to target multiple muscle groups, for
71 example, dorsiflexors and plantar flexors during gait training as part of the rehabilitation process.
72 Previous studies have shown that FES may help patients improve ankle and knee impairment during
73 the swing and stance phases of the gait cycle (Kesar et al, 2009), and a dose response relationship
74 appears to be evident between the number of muscle groups stimulated and the improvement observed
75 in the gait cycle (Daly et al, 1996).

76 Bilateral stimulation of the affected and unaffected limb (either the upper or lower extremities) has
77 not often been studied in the rehabilitation setting. Chan, Tong, and Chung (2009) have suggested that
78 bilateral upper limb training with FES could be an effective method for upper limb rehabilitation of
79 stroke patients. A study conducted by Cauraugh and Kim (2002) using 2 coupled motor recovery
80 protocols with electromyography (EMG)-triggered neuromuscular stimulation and bilateral
81 movements, showed that the motor improvement of the bilateral group for upper extremity function
82 was better than the improved motor function of the unilateral group. However, they noted that the
83 unilateral group did improve significantly compared to the control group. One study examined
84 bilateral (versus unilateral) TENS combined with task-oriented training (e.g. stepping up and down,
85 squatting, standing up from a chair and walking short distances) on lower extremity function (Kwong,
86 Ng, Chung, and Ng, 2018). Kwong, Ng, Chung, and Ng (2018) found that bilateral electrical
87 stimulation was better for improving ankle dorsiflexion strength and the timed up and go test, but
88 balance and motor coordination were not improved. No studies were found to indicate if lower
89 extremity bilateral stimulation (compared to unilateral stimulation of the involved limb) would
90 improve gait function in individuals with stroke. No studies combining bilateral lower extremity FES
91 and treadmill training were found.

92 There is emerging evidence that FES may be more beneficial than skeletal muscle training alone
93 following stroke (Howlett, Lannin, Ada, and McKinstry, 2015). A decrease in plantar flexors spasticity
94 and increased ankle active dorsiflexion following FES training has been previously reported (Wang et
95 al, 2016). Further, in patients with spinal-cord-injury, FES may reduce quadriceps tone, increase
96 voluntary muscle strength, and increase stride length (Granat, Ferguson, Andrews, and Delargy, 1993).
97 The aim of the study was to determine the concurrent impact of bilateral multiple joint functional
98 electrical stimulation (FES) during treadmill walking on gait parameters and ankle plantar flexors and
99 knee extensors muscle spasticity in post-stroke survivors. It was hypothesized that the involvement
100 of multi-channel bilateral FES during treadmill walking would decrease muscle spasticity and increase
101 gait speed in post-stroke survivors.

102 **METHODOLOGY**

103 Design

104 A pilot study was performed based on a single group (pre-test, post-test design; STROBE guidelines).
105 The study protocol was approved by the ethical committee of (REMOVED FOR REVIEW) and all
106 participants signed an informed consent form prior to the study.

107 Participants

108 Thirty-six patients were screened as potential subjects to participate in this study. Twenty-one were
109 excluded based on the exclusion criteria of the study; and among the fifteen patients who met all
110 inclusion criteria, nine agreed to participate in this study (Figure 1). The inclusion criteria were: 1) no
111 past history of electrical stimulation; 2) only one episode of stroke; 3) patients with 30-65 years of age 4)
112 ability to sit supported for 40 minutes; 5) sufficient communication skills to indicate yes/no verbally
113 or via gestures; 6) ability to walk without any support for at least 10 meters; 7) Ambulation ability \geq

114 3 based on functional ambulation classification; 8) stroke onset > 6 months, and < 5 years prior to
115 study recruitment; and 9) unilateral hemiplegia.

116 **FIGURE 1 ABOUT HERE**

117 The exclusion criteria were: 1) pregnancy; 2) patients with aphasia with inability to follow instructions;
118 3) contractures of the lower extremities; 4) arrhythmias during resting EKG, and/or implanted cardiac
119 pacemaker; 5) major circulatory disturbances; 6) severe osteoporosis or arthritis; 7) metallic implants
120 in the upper legs; 8) open wounds in the lower extremities; 9) allergic to electrode gel; 10) history of
121 deep coma (coma recovery scale <12); 11) peripheral neuropathy; and 12) cognitive impairment.

122 A physiotherapist, who was blinded to group assignments performed, all measurements. Research was
123 performed at the Sports Medicine Research Center, Neuroscience Institute, under the supervision of a
124 neurorehabilitation specialist, and a specialist in sports medicine.

125 Outcome Measurements

126 Outcome measurements included plantar flexors and knee extensors spasticity assessment using
127 Modified Modified Ashworth Scale (MMAS), functional mobility assessed by Timed Up and go test
128 (TUG), gait speed assessed by the 10-m walking test and Functional ambulation category (FAC). Step
129 length and active range of motion in the ankle and knee joints was also assessed. Each measurement
130 was performed at baseline, immediately after the final treatment session, and one month following the
131 final treatment session.

132 **Spasticity Assessment**

133 The Modified Modified Ashworth Scale (MMAS) was used to assess the spasticity of the ankle plantar
134 flexors and knee extensors (Ansari, Naghdi, Younesian, and Shayeghan, 2008; Ghotbi, Ansari,
135 Naghdi, and Hasson, 2011). The MMAS assesses the level of spasticity on an ordinal scale from 0 to
136 4 based on the level of resistance in response to a passive movement. According to the MMAS scale,

137 0 represents no increase in muscle tone, and 4 represents rigidity of the affected part in flexion or
138 extension (Ansari, Naghdi, Moammeri, and Jalaie, 2006). The MMAS has been shown to be a reliable
139 tool in post-stroke survivors: inter-rater reliability for plantar flexors was good ($Kappa = 0.74$); knee
140 extensors was very good ($Kappa = 0.81$) (Ghotbi et al, 2009); and kappa values were very good for
141 intra-rater in ankle plantar flexors ($Kappa = 0.85$ and knee extensors ($Kappa = 0.82$) (Ghotbi, Ansari,
142 Naghdi, and Hasson, 2011). All the tests were performed in the same position, lying in a supine
143 position with knees in flexed (soleus) and extended (gastrocnemius) position for ankle plantar flexors
144 movement, and lying on the side for knee extensors movement by same rater.

145 **10-m Walk Test and Gait Speed**

146 To test changes in ambulation ability we used the 10-meter walk to measure walk time and calculated
147 gait speed (Alon and Ring, 2003). Patients were asked to walk as fast as possible over a straight, level
148 10m surface. Patients performed one trial, and the time (seconds) was recorded. Time was measured
149 for the intermediate 6 meters and gait speed was determined. Start and stop the timing
150 of procedure was synchronized by passing the 2 meter and 8 meter mark on the
151 toes of the leading foot (Scivoletto et al, 2011). Scivoletto et al showed inter- and intra-rater
152 reliabilities were between 0.97 and 0.99 intra-class correlation coefficient (ICC) for 10-m Walk Test
153 and Gait Speed.

154 **Timed Up and Go Test (TUG)**

155 TUG was used to evaluate functional mobility. The patient sat in a chair (seat height 46 cm, arm height
156 67 cm), and following a command from the assessor, would stand up (the patient was allowed to use
157 the chair arms), walk 3 meters in a straight line, turn around, walk back to the chair, and re-seat
158 themselves. This test was performed in one practice trial, followed by a timed trial, and the time

159 (seconds) was recorded. The test showed to be a reliable tool ($ICC > 0.95$) for quantifying functional
160 mobility after a stroke (Ng and Hui-Chan, 2005).

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163 **Functional Ambulation Category (FAC)**

164 The FAC is a common clinical assessment scale which has high test-retest reliability (Cohen
165 $Kappa=0.950$) and inter-rater reliability ($Kappa=0.905$) in patients with stroke (Mehrholz et al, 2007).

166 FAC includes 6 functional levels: “0” (nonfunctional ambulator) indicates a patient who is not able to
167 walk at all or needs the help of 2 therapists. Level of “1” (ambulator, dependent on physical assistance
168 [level II]) indicates a patient who requires continuous manual contact to support body weight as well
169 as to maintain balance or to assist coordination. “2” (ambulator, dependent on physical assistance
170 [level I]) indicates a patient who requires intermittent or continuous light touch to assist balance or
171 coordination. “3” (ambulator, dependent on supervision) indicates a patient who can ambulate on level
172 surface without manual contact of another person but requires stand by guarding of one person either
173 for safety or for verbal cueing. “4” (ambulator, independent, level surface only) indicates a patient
174 who can ambulate independently on level surface but requires supervision to negotiate (e.g. stairs,
175 inclines, nonlevel surfaces). “5” (ambulator, independent) indicates a patient who can walk
176 everywhere independently, including stairs (Holden et al, 1984).

177 **Step Length**

178 A spatial characteristic of the gait cycle was measured using an ink footprint record. Patients were
179 asked to walk 10 meters at a self-selected and comfortable speed while wearing non-permanent ink
180 patches on their footwear. A perpendicular distance (meters) from foot contact to the contact of the
181 opposite foot was recorded for each step taken during the 10-meter walk. The first and final two meters

182 of the walk were not calculated due to changes in walking gait/velocity. The test was performed on
183 two trials, and mean step length was recorded; both sound and affected side were assessed for each
184 participants. The validity of the test has been previously demonstrated in patients with hemiparesis
185 (Graham et al, 2008), Inter-rater and test-retest reliability has been showed in patients with
186 hemiparesis (Holden et al, 1984).

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188 **Range of Motion- Ankle and Knee**

189 Active range of motion was measured by standard manual goniometer (Youdas, Bogard, and Suman,
190 1993). Active range of motion of the ankle plantar flexion was measured with patients in a supine
191 position, with knees extended to 20 degrees of flexion. Patients were asked to perform active
192 dorsiflexion of the ankles. Knee range of motion was evaluated in the supine position with the hip in
193 neutral as starting position , patients were encouraged to bend their knees without losing heel contact
194 from the table. Each measurement was repeated on three times and the highest score was reported.

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196 Intervention

197 The treatment intervention involved 10 sessions of concurrent FES during treadmill walking.
198 However, the first session acted as a familiarization, and the following nine sessions were provided
199 over a 3-week period. We used a current-controlled 8-channel stimulator (FES, Hasomed, Germany),
200 with surface electrodes (rectangular auto-adhesive gel electrodes, Flextrode, Krauth + Timmermann
201 Ltd. Hamburg, Germany, size 4.5 x 9.5 cm) in a bipolar configuration situated on the quadriceps,
202 hamstrings, peroneals, and plantar flexors muscle groups. The pulse width was 350 μ s, stimulation
203 frequency was 35 Hz, and amplitude was set to achieve motor responses as determined by contractions
204 produced under the electrode. Intensity in the first session was variable from 20mA to 34mA between

205 subjects, the amplitude was increased for each participant based on the acceptable personal tolerance
206 during next sessions and reached ultimately to 40-45 mA (Figure 2). In the first week, the intervention
207 consisted of ten minutes of treadmill walking and FES was utilized in two, 5-minute bouts. In the
208 second and third weeks, treadmill walking increased to 15-20 minutes, with FES introduced in three
209 and four, 5-minute bouts, respectively. Between any therapeutic treatments, a rest period of one to two
210 minutes was incorporated. Before each treatment session, patients performed a two-minute warm up
211 on the treadmill. Likewise, a two-minute cool-down session was incorporated at the end of each
212 treatment session when no FES was performed. During each session, treadmill speed was set to a
213 minimum speed in the warm-up phase, and gradually increased based on individual gait limitations.
214 The inclination of the treadmill was set to zero in all sessions.

215

216

FIGURE 2 ABOUT HERE

217

Statistical Analysis

218 Statistical analysis was performed using SPSS version 21 for Windows. Values are presented as mean
219 \pm SD or 95% confidence intervals unless otherwise specified. Data normality was checked for all
220 variables with the Shapiro-Wilk test. One-way repeated measure analysis of variance (ANOVA) was
221 applied to test the effects of the treatment on primary and secondary outcome measures over time (pre,
222 post, and follow up). A Bonferroni post-hoc adjustment was used for multiple comparisons. The
223 Friedman test was performed for non-normally distributed, as well as ordinal variables (i.e. FAC),
224 followed by the Wilcoxon Signed Ranks Test (WSRT) for pairwise comparisons of dependent
225 variables measured on three occasions. Partial η^2 (η_p^2), effect sizes were also calculated, with 0.25,
226 0.40, and > 0.40 representing small, medium, and large effect sizes, respectively (Richardson, 2011).

227 For ordinal variables Kendall's W (Coefficient of concordance) was calculated to determine effect
228 size (Schmidt, 1997). An alpha level of $P < 0.05$ was used as a threshold for statistical significance.

229 **RESULTS**

230 Initially 15 participants were eligible for the study, however only nine consented to participate. Of the
231 nine individuals three participants dropped out for the reasons unrelated to the study (transportation
232 issues) (Figure 1). After exclusions six patients (4=male; age 56.8 ± 4.8 years; body mass index (BMI)
233 26.2 ± 4.3 ; since onset of stroke: 30.8 ± 10.4 months; side of hemiplegia [L/R]: 3:3) completed the
234 intervention.

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236 Ankle Plantar Flexors MMAS

237 There was no statistically significant difference in ankle plantar flexors spasticity after the FES
238 intervention, $\chi^2(2) = 4.000$, $P = 0.135$. Post hoc analysis showed no significant changes at T0 compared
239 to T1 ($Z = -1.41$, $P = 0.157$), and T1 compared to T2 ($Z = 0.00$, $P = 1.000$) (Table 2).

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241 Knee Extensors MMAS

242 There was no statistically significant difference in knee extensors spasticity, $\chi^2(2) = 2.000$, $P = 0.368$
243 following the intervention. Post hoc analysis showed no significant changes at T0 compared to T1
244 ($Z = 1.00$, $P = 0.317$), and T1 compared to T2 ($Z = 1.00$, $P = 0.317$) (Table 2).

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246 Timed Up and Go

247 A statistically significant improvement in TUG was evident ($F(1,076, 5.382) = 14.347$, $P = 0.011$, $\eta_p^2 = 0.742$).
248 Post hoc testing revealed that FES training during treadmill walking elicited a mean improvement of
249 2.89 seconds (between T0 and T1), but was not maintained one month later (T1 to T2).

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10-Meter Walk Test

A significant improvement in 10-meter walk test performance was evident following the intervention [$F(1.045, 5.227) = 8.598, P = 0.031, \eta_p^2 = 0.632$]. Post hoc testing with Bonferroni correction revealed that mean time improved by 2.98 seconds between T0 and T1 ($p = 0.032$). The improvement remained consistent between T1 and T2 ($P = 0.307$).

Gait Speed

A significant change in gait speed was reported after intervention ($F(2, 10) = 13.456, P < 0.001, \eta_p^2 = 0.729$). Post hoc testing with Bonferroni correction revealed that walking improved by .345 meter/ seconds between T0 and T1 ($P < 0.001$). The improvement remained consistent between T1 and T2 ($P = 0.460$).

Functional Ambulation Category (FAC)

There was statistically significant difference in FAC, $\chi^2(2) = 2.000, P = 0.039$ following the intervention. Post hoc analysis showed significant changes at T0 compared to T1 ($Z = 2.00, P = 0.046$), while T1 compared to T2 showed no evident change ($Z = 1.00, P = 0.317$) (Table 3). Kendall's W (Coefficient of concordance) for FAC was 0.542.

Active Range of Motion: Ankle

272 Improvements in active range of motion of the ankle were evident following the intervention between
273 time points ($F(2, 10) = 10.588, P = 0.003, \eta_p^2 = 0.679$). Post hoc testing with Bonferroni correction
274 revealed that ankle range of motion increased by 4 degrees between T0 and T1 ($P = 0.049$). The
275 improvement remained consistent between T1 and T2 ($P = 0.123$).

276 Active Range of Motion: Knee

277 Active range of motion of the knee significantly improved between time points following the
278 intervention ($F(1.067, 5.241) = 12.045, P = 0.015, \eta_p^2 = 0.707$). A mean improvement of 27.2° was evident
279 between T0 and T1 ($P = 0.044$). Improvements remained between T1 and T2 with ($P = 0.064$).

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281 Step Length – Sound Side

282 Step length (sound side) improved significantly between time points following the intervention (F
283 $(1.010, 5.051) = 13.294, P = 0.014, \eta_p^2 = 0.727$). A mean improvement of 17.6 cm was evident between T0
284 and T1 ($P = 0.042$). The improvement remained from T1 to T2 ($P = 0.807$).

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286 Step Length - Affected Side

287 Step length on the affected side improved significantly following the intervention ($F(1.086, 5.429) =$
288 $20.845, P = 0.005, \eta_p^2 = 0.807$). A mean improvement of 11.6 cm was evident between T0 and T1 (P
289 $= 0.018$), this improvement did remain consistent at T2 assessment ($P = 0.152$).

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291 **TABLES 1, 2 and 3 ABOUT HERE**

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293

294 **DISCUSSION**

295 The study examined the effect of FES with treadmill walking on gait parameters and spasticity in post-
296 stroke survivors. To our knowledge, this is the first study which has investigated the impact of a
297 bilateral FES application in conjunction with gait training. Each patient reported no adverse events
298 while undertaking the intervention. One ultimate goal of therapy for lower-limb motor impairment is
299 to improve the function of walking (Hattem et al, 2016), and our novel intervention showed that a short
300 duration of bilateral FES combined with treadmill walking training contributed to significant
301 improvements in gait speed, functional ambulation, and step length.

302 Increased gait speed is the most common effect reported after FES application (Kafri and Laufer,
303 2014). FES has been demonstrated to improve gait through repetitive practice during retraining by
304 restoring the motor program of a more normal gait performance in stroke (Kim, Chung, Kim, and
305 Hwang, 2012). In this study we reported a significant gait speed improvement of 0.345 m/s difference
306 after intervention and this progression maintained by 0.223 m/s from T0 to T2 assessment with a large
307 effect ($\eta_p^2=0.729$) exceeding the meaningful change of walking speed which has been reported as 0.10
308 m/s in stroke (Howelt et al, 2015) suggesting that the improvement made by the participants in gait
309 speed is considered clinically important. A gait speed improvement of 0.18 m/s has been reported
310 based on a meta-analysis of three control trials (Robbins, Houghton, Woodbury, and Brown, 2006),
311 while another systematic review reported 0.08 m/s difference after FES during walking (Howlett,
312 Lannin, Ada, and McKinstry, 2015). Differences reported in gait speed improvement can be influenced
313 by patients characteristics (i.e. severity, age and initial gait speed) (Peurala, Tarkka, Pitkänen, and
314 Sivenius, 2005). Another reason for significant improvement in gait speed in our study could relate to
315 bilateral and multiple muscle stimulation; the more muscles stimulated the better gait improvement
316 expected (Daly et al, 1996). We reported evident improvement in FAC score with Kendall's $W=0.542$
317 (indicating moderate effect size). However, no minimal clinically important difference (MCID) and

318 minimal detectable change (MDC) data are available for the FAC (Louie and Eng, 2016); it seems
319 that FAC which classifies walking ability both indoors and outdoors (Holden, Gil, and Magliozzi,
320 1986) are associated with improvements in gait performance (Holden et al, 1984; Holden, Gil, and
321 Magliozzi, 1986). It has been suggested that FAC scores correlate significantly with walking speed
322 and step length (Mehrholtz et al, 2007). In this study, only 5.6% of subjects had level 5 based on FAC
323 scores at baseline while after 3 weeks of intervention this value reached 16.7% among participants
324 and maintained by 11.1% after one month. It seems that bilateral FES with treadmill training not only
325 improved gait speed in stroke survivor, it might also change their functional category.

326 We found significant improvement after 3 weeks of intervention in TUG score; however, the
327 improvement did not last after 1 month. Therapeutic effect of FES on TUG has not demonstrated any
328 clear effects (Kafri and Laufer, 2014). Yan, Hui-Chan, and Li (2005) did not demonstrate any
329 significant changes after FES application on 4 muscle groups, 5 days per week, after 3 weeks of
330 intervention. Since TUG does include walking, it is expected to have a strong relationship with gait
331 speed. However it should be noted that TUG test is not a simple walking task, it includes a series of
332 motor tasks requiring rising from a chair, walking and turning; thus balance control in addition to
333 muscle strength, coordination and walking endurance could impact the score (Ng and Hui-Chan,
334 2005).

335 Correlation between slower gait speed and decreased propulsive force generation has been shown after
336 stroke (Bowden, Balasubramanian, Neptune, and Kautz, 2006). It has been reported that FES to the
337 ankle plantar flexors and dorsiflexors muscles during gait while on a treadmill can correct mechanics
338 resulting in an increase in knee flexion swing phase, greater plantar flexion at toe-off and better
339 forward propulsion (Kesar et al, 2009). Another investigation by Patterson, Rodgers, Macko, and
340 Forrester (2008) also demonstrated an increase in step length after combined treadmill walking and

341 FES. The authors concluded that improvement in non-paretic step length resulted from increased
342 propulsion. Conversely, increased paretic step length may be due to an increased range of motion in
343 the paretic leg joints allowing the limb to swing farther forward. Previous studies have shown a
344 positive impact of FES on muscle strength and active range of motion (Daly et al, 2011; Peurala,
345 Tarkka, Pitkänen, and Sivenius, 2005). In our study, significant improvement in active range of motion
346 of the ankle and the knee demonstrating large effects for the affected limb, respectively ($\eta_p^2= 0.679$
347 and 0.707); and significant improvement in step length for both the sound and affected limb (again
348 with large effects, respectively $\eta_p^2= 0.727$ and 0.807) occurred. Minimal detectable changes were 6.0
349 degrees for ankle dorsiflexion (Krause et al, 2011) and 6.3 degrees for knee flexion (Mehta et al,
350 2017). Our results demonstrated 27.2° increase in knee active ROM after 3 weeks of intervention and
351 these changes maintained by 22° after one month; therefore these improvements not only exceeded
352 the minimal detectable changes but also showed over 15% change which is considered clinically
353 important (Albright et al, 2001). For the ankle we did not meet the above value with 4° improvement
354 after treatment (though large effect size). In regards to step length, it has been suggested a clinical
355 meaningful improvement would be > 15% change (Albright et al, 2001) . Step length in the affected
356 limb improved by approximately 20% and the sound limb by approximately 40% and these percent
357 improvements maintained in follow-up (again with large effect size).

358 We did not find any significant decrease in muscle spasticity which was similar to the Peurala, Tarkka,
359 Pitkänen, and Sivenius (2005) findings. They did not find any decrease in ankle, knee, and hip
360 spasticity after three weeks of over-ground walking with FES. In addition, another study suggested
361 that unchanged spasticity after FES applications on two antagonist muscles like plantar flexors and
362 dorsi flexors may represent positive messages to clinicians (Embrey et al, 2010) disallowing clinical
363 concerns about stimulating antagonist muscle groups for fear of increasing spasticity.

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367 **Study Limitation**

368 The study included a relatively small number of participants. Future studies with larger sample sizes,
369 over a longer period, are needed to support or refute our findings. We did not test lower extremity
370 muscle strength which might have been improved from the intervention and may be an important
371 factor for improvement of step length and gait speed. The knee and ankle spasticity of our participants
372 was not severe, therefore, generalization of our results to patients with progressed stages is
373 unwarranted. Also, we did not separate out the impact of multiple joint stimulation and bilateral
374 stimulation in this study as we used these concurrently.

375

376 **CONCLUSION**

377 In conclusion, a short duration (ten sessions) of bilateral FES combined with treadmill walking training
378 contributed to significant improvements in gait speed, functional mobility, functional ambulation,
379 range of motion and step length in post-stroke survivors while no significant decrease were identified
380 in the spasticity of the ankle plantar flexors and knee extensors muscles.

381

382 **Declaration of Interest**

383 The authors declare no conflict of interest.

384

385 **REFERENCES**

- 386 Albright J, Allman R, Bonfiglio RP, Conill A, Dobkin B, Guccione A, Hasson S, Russo R, Shekelle
387 P, Susman JL; Ottawa Methods Group 2001 Philadelphia Panel evidence-based clinical practice
388 guidelines on selected rehabilitation interventions: Overview and methodology. *Physical*
389 *Therapy* 81: 1629-1640.
- 390 Alon G, Ring H 2003 Gait and hand function enhancement following training with a multi-segment
391 hybrid-orthosis stimulation system in stroke patients. *Journal of Stroke and Cerebrovascular*
392 *Diseases* 12: 209-216.
- 393 Ansari NN, Naghdi S, Moammeri H, Jalaie S 2006 Ashworth Scales are unreliable for the
394 assessment of muscle spasticity. *Physiotherapy Theory and Practice* 22: 119-125.
- 395 Ansari NN, Naghdi S, Younesian P, Shayeghan M 2008 Inter-and intrarater reliability of the
396 Modified Modified Ashworth Scale in patients with knee extensor poststroke spasticity.
397 *Physiotherapy Theory and Practice* 24: 205-213.
- 398 Barbeau H, Visintin M 2003 Optimal outcomes obtained with body-weight support combined with
399 treadmill training in stroke subjects. *Archives of Physical Medicine and Rehabilitation* 84:
400 1458-1465.
- 401 Bowden MG, Balasubramanian CK, Neptune RR, Kautz SA 2006 Anterior-posterior ground reaction
402 forces as a measure of paretic leg contribution in hemiparetic walking. *Stroke* 37: 872-876.
- 403 Cauraugh JH, Kim S 2002 Two coupled motor recovery protocols are better than one:
404 electromyogram-triggered neuromuscular stimulation and bilateral movements. *Stroke* 33:
405 1589-1594.
- 406 Chan MK, Tong RK, Chung, KY 2009 Bilateral upper limb training with functional electric
407 stimulation in patients with chronic stroke. *Neurorehabilitation and Neural Repair* 23: 357-365.
- 408 Christensen MS, Grey MJ 2013 Modulation of proprioceptive feedback during functional electrical
409 stimulation: An fMRI study. *European Journal of Neuroscience* 37: 1766-1778.
- 410 Daly JJ, Marsolais EB, Mendell LM, Rymer WZ, Stefanovska A 1996 Therapeutic neural effects of
411 electrical stimulation. *IEEE Transactions on Rehabilitation Engineering* 4: 218-230.
- 412 Daly JJ, Zimbelman J, Roenigk KL, McCabe JP, Rogers JM, Butler K, Burdsall R, Holcomb JP,
413 Marsolais EB, Ruff RL 2011 Recovery of coordinated gait: Randomized controlled stroke trial
414 of functional electrical stimulation (FES) versus no FES, with weight-supported treadmill and
415 over-ground training. *Neurorehabilitation and Neural Repair* 25: 588-596.
- 416 Embrey DG, Holtz SL, Alon G, Brandsma BA, McCoy SW 2010 Functional electrical stimulation
417 to dorsiflexors and plantar flexors during gait to improve walking in adults with chronic
418 hemiplegia. *Archives of Physical Medicine and Rehabilitation* 91: 687-696.
- 419 Feigin VL, Krishnamurthi RV, Parmar P, Norrving B, Mensah GA, Bennett DA, Barker-Collo S,
420 Moran AE, Sacco RL, Truelsen T et al 2015 Update on the global burden of ischemic and
421 hemorrhagic stroke in 1990-2013: The GBD 2013 study. *Neuroepidemiology* 45: 161-176.
- 422 Forouzanfar MH, Sepanlou SG, Shahrzad S, Dicker D, Naghavi P, Pourmalek F, Mokdad A, Lozano
423 R, Vos T, Asadi-Lari M, et al 2014 Evaluating causes of death and morbidity in Iran, global
424 burden of diseases, injuries, and risk factors study 2010. *Archives of Iranian Medicine* 17: 304-
425 320.
- 426 Francis S, Lin X, Aboushoushah S, White TP, Phillips M, Bowtell R, Constantinescu CS 2009 fMRI
427 analysis of active, passive and electrically stimulated ankle dorsiflexion. *Neuroimage* 44: 469-
428 479.
- 429 Ghotbi N, Ansari NN, Naghdi S, Hasson S 2011 Measurement of lower-limb muscle spasticity:
430 Intrarater reliability of Modified Modified Ashworth Scale. *Journal of Rehabilitation Research*

431 Development 48: 83-88.

432 Ghotbi N, Ansari NN, Naghdi S, Hasson S, Jamshidpour B, Amiri S 2009 Inter-rater reliability of
433 the Modified Modified Ashworth Scale in assessing lower limb muscle spasticity. *Brain Injury*
434 23: 815-819.

435 Graham JE, Ostir GV, Kuo YF, Fisher SR, Ottenbacher KJ 2008 Relationship between test
436 methodology and mean velocity in timed walk tests: A review. *Archives of Physical Medicine*
437 *and Rehabilitation* 89: 865-872.

438 Granat MH, Ferguson AC, Andrews BJ, Delargy M 1993 The role of functional electrical
439 stimulation in the rehabilitation of patients with incomplete spinal cord injury - Observed
440 benefits during gait studies. *Paraplegia* 31: 207-215.

441 Hatem SM, Saussez G, Della Faille M, Prist V, Zhang X, Dispa D, Bleyenheuft Y 2016
442 Rehabilitation of motor function after stroke: A multiple systematic review focused on
443 techniques to stimulate upper extremity recovery. *Frontiers in Human Neuroscience* 10: 442.

444 Holden MK, Gil KM, Magliozzi MR 1986 Gait assessment for neurologically impaired patients:
445 standards for outcome assessment. *Physical Therapy* 66: 1530-1539.

446 Holden MK, Gill KM, Magliozzi MR, Nathan J, Piehl-Baker L 1984 Clinical gait assessment in the
447 neurologically impaired: reliability and meaningfulness. *Physical Therapy* 64: 35-40.

448 Howlett OA, Lannin NA, Ada L, McKinstry C 2015 Functional electrical stimulation improves
449 activity after stroke: A systematic review with meta-analysis. *Archives of Physical Medicine*
450 *and Rehabilitation* 96: 934-943.

451 Iftime-Nielsen SD, Christensen MS, Vingborg RJ, Sinkjær T, Roepstorff A, Grey MJ 2012
452 Interaction of electrical stimulation and voluntary hand movement in SII and the cerebellum
453 during simulated therapeutic functional electrical stimulation in healthy adults. *Human Brain*
454 *Mapping* 33: 40-49.

455 Joa KL, Han YH, Mun, CW, Son BK, Lee CH, Shin YB, Ko HY, Shin YI 2012 Evaluation of the
456 brain activation induced by functional electrical stimulation and voluntary contraction using
457 functional magnetic resonance imaging. *Journal of Neuroengineering and Rehabilitation* 9: 48.

458 Johannsen L, Wing AM, Pelton T, Kitaka K, Zietz D, Brittle N, van Vliet P, Riddoch J, Sackley C,
459 McManus R 2010 Seated bilateral leg exercise effects on hemiparetic lower extremity function
460 in chronic stroke. *Neurorehabilitation and Neural Repair* 24: 243-253.

461 Kafri M, Laufer Y 2014 Therapeutic effects of functional electrical stimulation on gait in
462 individuals post-stroke. *Annals of Biomedical Engineering* 43: 451-466.

463 Kesar TM, Perumal R, Reisman D S, Jancosko A, Rudolph KS, Higginson JS, Binder-Macleod SA
464 2009 Functional electrical stimulation of ankle plantarflexor and dorsiflexor muscles: effects
465 on poststroke gait. *Stroke* 40: 3821-3827.

466 Kim JH, Chung Y, Kim Y, Hwang S 2012 Functional electrical stimulation applied to gluteus
467 medius and tibialis anterior corresponding gait cycle for stroke. *Gait and Posture* 36: 65-67.

468 Krause DA, Cloud BA, Forster LA, Schrank JA, Hollman JH 2011 Measurement of ankle
469 dorsiflexion: a comparison of active and passive techniques in multiple positions. *Journal of*
470 *Sport Rehabilitation* 20: 333-344.

471 Kwong PW, Ng GY, Chung RC, Ng SS 2018 Bilateral transcutaneous electrical nerve stimulation
472 improves lower-limb motor function in subjects with chronic stroke: A randomized controlled
473 trial. *Journal of the American Heart Association* 7: e007341.

474 Louie DR, Eng JJ 2016 Powered robotic exoskeletons in post-stroke rehabilitation of gait: A
475 scoping review. *Journal of Neuroengineering and Rehabilitation* 13: 53

476 Luft AR, McCombe-Waller S, Whittall J, Forrester LW, Macko R, Sorkin JD, Schulz JB, Goldberg

477 AP, Hanley DF 2004 Repetitive bilateral arm training and motor cortex activation in chronic
478 stroke: A randomized controlled trial. *JAMA* 292: 1853-1861.

479 Mehrholz J, Wagner K, Rutte K, Meissner D, Pohl MI 2007 Predictive validity and responsiveness
480 of the functional ambulation category in hemiparetic patients after stroke. *Archives of Physical
481 Medicine and Rehabilitation* 88: 1314-1319.

482 Mehta SP, Barker K, Bowman B, Galloway H, Oliashirazi N, Oliashirazi A 2017 Reliability,
483 concurrent validity, and minimal detectable change for iphone goniometer app in assessing
484 knee range of motion. *Journal of Knee Surgery* 30: 577-584.

485 Ng SS, Hui-Chan CW 2005 The timed up & go test: Its reliability and association with lower-limb
486 impairments and locomotor capacities in people with chronic stroke. *Archives of Physical
487 Medicine and Rehabilitation* 86: 1641-1647.

488 Noma T, Matsumoto S, Shimodozono M, Etoh S, Kawahira K 2012 Anti-spastic effects of the direct
489 application of vibratory stimuli to the spastic muscles of hemiplegic limbs in post- stroke
490 patients: A proof-of-principle study, *Journal of Rehabilitation Medicine* 44: 325-330.

491 Patterson SL, Rodgers MM, Macko RF, Forrester LW 2008 Effect of treadmill exercise training on
492 spatial and temporal gait parameters in subjects with chronic stroke: A preliminary report.
493 *Journal of Rehabilitation Research and Development* 45: 221-229.

494 Peurala SH, Tarkka IM, Pitkänen K, Sivenius J 2005 The effectiveness of body weight-supported
495 gait training and floor walking in patients with chronic stroke. *Archives of Physical Medicine
496 and Rehabilitation* 86: 1557-1564.

497 Richardson JT 2011 Eta squared and partial eta squared as measures of effect size in educational
498 research. *Educational Research Review* 6: 135-147.

499 Robbins SM, Houghton PE, Woodbury MG, Brown JL 2006 The therapeutic effect of functional and
500 transcutaneous electric stimulation on improving gait speed in stroke patients: A meta-analysis.
501 *Archives of Physical Medicine and Rehabilitation* 87: 853-859.

502 Sabut SK, Sikdar C, Mondal R, Kumar R, Mahadevappa M 2010 Restoration of gait and motor
503 recovery by functional electrical stimulation therapy in persons with stroke. *Disability and
504 Rehabilitation* 32: 1594-1603.

505 Schmidt R C 1997 Managing Delphi surveys using nonparametric statistical techniques. *Decision
506 Sciences* 28: 763-774.

507 Scivoletto G, Tamburella F, Laurenza L, Foti C, Ditunno JF, Molinari M 2011 Validity and
508 reliability of the 10-m walk test and the 6-min walk test in spinal cord injury patients. *Spinal
509 Cord* 49: 736-740.

510 Shariat A, Ansari NN, Shaw BS, Kordi R, Kargarfard M, Shaw I 2018 Cycling training and
511 functional electrical stimulation for post-stroke patients. *Revista Brasileira de Medicina Do
512 Esporte* 24: 300-302.

513 Wang Y, Meng F, Zhang Y, Xu M, Yue S 2016 Full-movement neuromuscular electrical
514 stimulation improves plantar flexor spasticity and ankle active dorsiflexion in stroke patients: A
515 randomized controlled study. *Clinical Rehabilitation* 30: 577-586.

516 Watkins CL, Leathley MJ, Gregson JM, Moore AP, Smith TL, Sharma AK 2002 Prevalence of
517 spasticity post stroke. *Clinical Rehabilitation* 16: 515-522.

518 Youdas JW, Bogard CL, Suman VJ 1993 Reliability of goniometric measurements and visual
519 estimates of ankle joint active range of motion obtained in a clinical setting. *Archives of
520 Physical Medicine and Rehabilitation* 74: 1113-1118.

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522