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Combined aerobic exercise and task practice improve health-related quality of life after stroke: a preliminary analysis

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Abstract

Objective: The aim of this project was to determine the effects of lower extremity aerobic exercise coupled with upper extremity repetitive task practice (RTP) on health related quality of life (HRQOL) and depressive symptomology in individuals with chronic stroke.

Design: Secondary analysis of data from two randomized controlled trials.

Setting: Research laboratory.

Participants: Individuals (N=40) with chronic stroke.

Interventions: Participants received one of the following interventions: forced exercise + RTP (FE+RTP, n=16), voluntary exercise + RTP (VE+RTP, n=16), or stroke education + RTP (EDU +RTP, n=8). All groups completed 24 sessions, each session lasting 90 minutes.

Main Outcome Measure: The Center for Epidemiological Studies-Depression Scale (CES-D) and Stroke Impact Scale (SIS) were used to assess depressive symptomology and HRQOL.

Results: There were no significant group-by-time interactions for any of the SIS domains or composite scores. Examining the individual groups following the intervention, those in the FE +RTP and VE+RTP groups demonstrated significant improvements in the following SIS domains: strength, mobility, hand function, activities of daily living, and the physical composite. Additionally, the FE+RTP group demonstrated significant improvements in memory, cognitive

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Conflicts of Interest: JLA has authored intellectual property associated with the algorithm used in the control of the FE bicycle. The remaining authors declare no conflicts of interest.

Suppliers:

composite, and percent recovery from stroke. The HRQOL did not change in the EDU+RTP group. While CES-D scores improved predominately for those in the FE+RTP group, these improvements were not statistically significant. Overall, results were maintained at the four week follow-up.

Conclusion: Aerobic exercise, regardless of mode, preceding motor task practice improved HRQOL in patients with stroke. The potential of aerobic exercise to improve cardiorespiratory endurance, motor outcomes, and HRQOL following stroke justifies its use to augment traditional task practice.

Keywords

stroke; depression; health related quality of life; aerobic exercise; forced exercise; repetitive task practice

Every year, approximately 795,000 people in the United States incur a stroke[1] with approximately 25–50% of survivors experiencing long-term disability.[2,3] Rehabilitation interventions following stroke aim to improve physical limitations, restore health-related quality of life (HRQOL), and reduce depressive symptomology. Investigating outcomes that extend beyond motor function is imperative, as an increasing body of literature has shown that survivors of stroke experience feelings of social isolation, difficulty re-integrating into the community,[4] and post-stroke depression (PSD).[5] Post-stroke depression is associated with increased disability, lower HRQOL, and higher mortality,[6–8] and approximately 1 in 3 survivors of stroke exhibit symptoms of PSD.[6,9,10] A challenge to reducing depression and improving HRQOL after stroke is the persistent upper extremity (UE) paresis experienced by >60% of survivors of stroke,[11] which leads to greater dependency in mobility and activities of daily living (ADLs). Dependence in mobility and ADLs is associated with an increased risk of developing PSD.[6,12,13] Interestingly, the degree of PSD or HRQOL experienced by survivors of stroke has not been shown to be affected by whether the stroke led to impairment in the dominant versus non-dominant UE.[1415]

It is plausible that HRQOL and depressive symptomology may improve if a survivor of stroke can improve UE function. It has been theorized that aerobic exercise may be administered immediately preceding motor task practice to enhance motor recovery.[17] To examine this theory, a preliminary trial was conducted examining the impact of pairing a high intensity aerobic exercise intervention, termed forced exercise (FE), with UE repetitive task practice (RTP).[18,19] Results indicated that FE followed by UE RTP resulted in significant improvements in UE motor function compared to those who performed voluntary exercise (VE) followed by RTP and those who performed RTP alone.[19] Improvements in motor recovery following a FE intervention provided initial support for the concept that high intensity aerobic exercise may facilitate motor recovery via an endogenous increase in central neurotrophic factor levels.[18,19]

It is unclear if a high intensity aerobic exercise combined with RTP leads to improvements in HRQOL and depressive symptomology following stroke. The aim of this project was to determine whether two different modes of aerobic exercise coupled with UE RTP affected HRQOL and depressive symptomology following stroke. Previous data indicated that FE

was a more effective mode of exercise in terms of enhancing motor recovery;[19] therefore, it was hypothesized that individuals who completed FE coupled with UE RTP would exhibit greater improvements in depressive symptomology and HRQOL compared to those who completed VE or those completing RTP in the absence of an aerobic intervention.

METHODS

This report is a secondary analysis of data from two randomized controlled trials (clinicaltrials.gov registration numbers NCT02076776; National Institute of Health and NCT02494518; American Heart Association). Both studies recruited from the same demographic area and included individuals with chronic stroke and residual UE impairment (see inclusion/exclusion below). Figure 1 displays the participant flow for both studies. The most common reasons for exclusion were: level of impairment (too high or low functioning UE), lack of reliable transportation, and the individual declining to participate.

The FE and VE aerobic exercise protocols were identical in both studies. The studies differed in the intervention of the non-aerobic exercise control group. Six individuals in the NIH trial were randomized to a non-dose matched group (i.e. 90 minutes of RTP), thus were not included in this analysis. A dose-matched RTP group was included in the American Heart Association study; thus, those patients served as a control group in this analysis (i.e. stroke education + RTP; N=8). Both preliminary trials were approved by the *(blinded)* Institutional Review Board and participants completed the informed consent process prior to participation. All testing and interventions occurred at the main campus of the *(blinded)* located in *(blinded)*.

Subjects

Inclusion criteria were as follows: 1) single, unilateral stroke ≥ 6 months prior, 2) 19–55 on the Upper Extremity Motor section of the Fugl-Meyer Assessment, 3) between 18–85 years of age, 4) able to provide informed consent, and 5) approval from the primary care physician to undergo cardiopulmonary exercise test. Exclusion criteria were: 1) hospitalization for myocardial infarction, congestive heart failure, or heart surgery within 3 months of study enrollment, 2) serious cardiac arrhythmia, 3) hypertrophic cardiomyopathy, 4) severe aortic stenosis, 5) cardiac pacemaker, 6) pulmonary embolus, 7) other medical or musculoskeletal contraindication to exercise, 8) significant cognitive impairment (inability to follow 1–2 step commands) or major psychiatric disorder resulting in difficulty participating in the study, 9) anti-spasticity injection in the upper extremity within 3 months of study enrollment, 10) pregnancy, 11) resting systolic blood pressure >200mmHg or diastolic blood pressure >110 mmHg, and 12) symptomatic fall in systolic blood pressure >20 mmHg with exercise.[20,21] To ensure safe cardiac response to high-intensity exercise, participants meeting enrollment criteria underwent a cardiopulmonary exercise test.[a]

[a]Lode upright bicycle ergometer, Groningen, Netherlands;

Outcome Measures

The Stroke Impact Scale (SIS) version 3.0 and the Center for Epidemiological Studies-Depression Scale (CES-D) were administered by a blinded rater at three time points: baseline, end of treatment (EOT) and four weeks following EOT (EOT+4).

Stroke Impact Scale 3.0 (SIS)

The SIS version 3.0 is a validated, self-reported questionnaire that uses a 5-point Likert scale to measure HRQOL. The 59 item questionnaire assesses eight domains: strength (4 items), hand function (5 items), mobility (9 items), ADL (10 items), communication (7 items), emotions (9 items), memory (7 items), and meaningful activities (8 items) for individuals after stroke.[22,23] The domains can be combined to form two composite categories: physical (strength, hand function, mobility, ADL) and cognitive (communication, memory).[24] Scores are normalized to a 100 point scale with a higher score indicating better self-rating in that category. Individuals also rank their global assessment of percentage of recovery on a 0–100 scale, with 100 being full recovery from the stroke.

Center for Epidemiological Studies-Depression (CES-D)

The CES-D is a 20-item measure that assesses self-reported symptoms of depression. It is a recommended screening tool for PSD,[25] with established validity and reliability in a stroke population.[26] Participants rate how frequently they experience various symptoms, with 0 indicating “rarely” and 3 indicating “most or almost all the time.” The highest possible score is 60, and scores ≥16 are indicative of depressive symptomology.[26]

Intervention

Following baseline testing, participants were randomized via an envelope pull to one of three groups: 1) Forced exercise + UE RTP (FE+RTP), 2) Voluntary exercise + UE RTP (VE +RTP), or 3) Stroke education + RTP (EDU+RTP). All participants attended a total of 24 sessions, each lasting 90 minutes.

Forced Exercise + Repetitive Task Practice (FE+RTP)

Individuals randomized to the FE+RTP group exercised for 45 minutes on a recumbent stationary cycle ergometer equipped with an electric motor and control algorithm to mechanically augment pedaling rate by 30% greater than the participant’s voluntary pedaling rate achieved during the exercise stress test.[27–29] Each 45-minute FE session was monitored by an exercise physiologist or physical therapist and included a five-minute warm-up, 35-minute main exercise set, and a five-minute cool-down. While assistance was provided in the FE mode via the motor to augment pedaling rate, it is important to note that the participant was actively contributing to the pedaling action. Participants were instructed to maintain their heart rate between 60–80% of their heart rate reserve calculated using the Karvonen formula,[21] and heart rate was continuously monitored.[b] Blood pressure and rate of perceived exertion were obtained every 10 minutes, while cadence and power (Watts) was

[b] Garmin™Edge® 800, Olathe, KS

recorded every five minutes. Following a 10-minute rest period, participants completed a 45-minute session of UE RTP.

Repetitive task practice emphasizes highly-repetitious blocked practice tasks that are goal-oriented and relevant to the individual.[30] The RTP activities were administered by a neurologic physical therapist who tailored each task to ensure appropriate difficulty and relevance. During the 45 minute RTP session, the therapist typically selected 3–5 tasks and targeted 70–100 repetitions of each task.

Voluntary Exercise + Repetitive Task Practice

The VE+RTP sessions were conducted in an identical manner to the FE+RTP sessions, except participants in the VE+RTP group exercised for 45 minutes on a stationary recumbent cycle ergometer at a self-selected cadence without assistance from a motor. Target heart rate range was identical to the FE+RTP group, at 60–80% of heart rate reserve. Exercise monitoring and RTP sessions were also conducted in an identical manner to the FE +RTP group.

Stroke Education +Repetitive Task Practice Group

The control group underwent a time-matched intervention consisting of a 45-minute session of stroke-related education followed by a 45-minute session of UE RTP. Each education session covered a different stroke-related topic such as stroke pathology, nutrition, pharmacology, fatigue, etc. The RTP sessions were administered in an identical manner to the FE+RTP and VE+RTP groups.

Statistical Analysis

The analysis included participants who completed all study-related interventions and clinical testing. A total of 48 individuals were randomized into the two studies and eight participants withdrew from the study (Figure 1). At EOT, there were a total of 16, 16, and 8 individuals included in the FE+RTP, VE+RTP, and EDU+RTP groups, respectively. At EOT+4, one participant in the FE+RTP group experienced an unrelated injury and was excluded from analysis at that time point.

Demographic variables were summarized per group using summary statistics. The intervention effects were assessed using a linear mixed effects model including a random intercept, a main effect for time, and the group-by time interaction. Normality assumptions of the residuals were met, as normality was checked visually using a QQ-plot and fitted values were plotted against residuals. The model adjusted for baseline differences between groups by incorporating the baseline metric in the outcome vector and by excluding the group main effect term from the model.[31] The model estimated the changes from baseline to EOT and from baseline to EOT+4.

The group-by-time interaction was assessed from this model at the 0.05 significance level. Regardless of interaction statistical significance, post hoc contrasts were performed estimating the change from baseline to EOT and EOT+4 within each randomized group. The CES-D outcome was not normally distributed, and paired Wilcoxon tests were performed

within each group from baseline to EOT and baseline to EOT+4. Within each outcome, comparisons were Bonferroni corrected to maintain a 5% type I error rate per outcome. Analyses were conducted using R version 3.4.2 (R Foundation for Statistical Computing, Vienna, Austria) and the "nlme" package.[32]

RESULTS

A total of 40 participants successfully completed the intervention and were included in the analyses. Participant demographics and baseline characteristics are summarized in Table 1. There were no significant differences among demographic variables across groups ($p>0.05$).

Effect of exercise on the Stroke Impact Scale (SIS)

The mean ± standard deviation for the SIS outcome variables are summarized in Table 2. In contrast to our hypothesis, there were no significant group-by-time interactions for any of the SIS domains or the SIS composite scores ($p>0.05$). Post hoc contrasts to examine within group differences over time revealed those in the FE+RTP group demonstrated a significant improvement in the following domains of the SIS from baseline to EOT: strength ($p=0.002$), mobility ($p<0.001$), hand function ($p<0.001$), ADL ($p=0.005$), and memory ($p=0.04$). With the exception of memory, improvements in these domains persisted at the 4-week follow-up, and the communication domain became significant ($p=0.03$). Participants in the VE+RTP group exhibited significant improvements in the physical domains of strength ($p=0.03$), mobility ($p=0.001$), hand function ($p<0.001$), and ADL ($p<0.001$) following the intervention. All of these improvements were maintained at the 4-week follow-up assessment. The EDU+RTP group only exhibited an improvement in hand function from baseline to EOT+4 ($p<0.001$).

The FE+RTP group displayed significant improvements in the cognitive composite from baseline to EOT ($p=0.007$) and baseline to EOT+4 ($p=0.01$). When examining the physical composite score, the FE+RTP and VE+RTP groups improved from baseline to EOT ($p<0.001$ for both) and from baseline to EOT+4 ($p<0.001$ for both). The EDU+RTP group exhibited a significant improvement in the physical composite from baseline to EOT+4 only ($p<0.001$). The FE+RTP group displayed a significant improvement in percent recovery from stroke for baseline to EOT ($p<0.001$) and EOT+4 ($p=0.02$). The VE+RTP group displayed a significant improvement in percent recovery from baseline to EOT+4 ($p=0.02$), while the EDU+RTP group did not significantly change.

Effect of exercise on the Center for Epidemiological Studies-Depression (CES-D)

There was no statistically significant change in any of the groups from baseline to EOT and EOT+4 ($p>0.05$). Notably, the FE+RTP group demonstrated a mean improvement of 6 points in the CES-D from baseline to EOT, while the VE+RTP and EDU+RTP groups improved by a mean of 0 and 2 points, respectively.

An exploratory analysis revealed a difference in baseline CES-D scores between individuals with hemiparesis in the dominant ($n = 22$; 15.7 ± 9.3 points) versus non-dominant side ($n = 18$; 7.8 ± 6.8 points) (Figure 2). A multivariable linear regression model with baseline CES-D as a function of affected side, age, gender, race, baseline Fugl-Meyer Assessment score,

and time since stroke was used to determine association. Dominant affected side was significantly associated with increased CES-D at baseline, with an estimated increase in mean CES-D (95% CI) of 7.7 (2.8, 12.8) compared to non-dominant affected side after controlling for baseline demographic variables (p=0.004).

DISCUSSION

Stroke rehabilitation traditionally targets motor impairments, and the impact of physical activity on mood and HRQOL are often secondary or not measured. Our primary analysis did not support the hypothesis that FE+RTP would result in the greatest improvements in HRQOL and depressive symptomology. However, when each group was examined separately, our post hoc analysis indicated that aerobic exercise, both VE and FE, when combined with RTP resulted in improvements in multiple domains of the SIS after the intervention, while motor task practice coupled with education did not impact SIS. Overall, this pattern of results was maintained at the 4-week follow-up.

It is intuitive that a motor intervention leads to improvements in physical domains of the SIS; yet a significant improvement was found in the memory domain and cognitive composite in the FE+RTP group from baseline to EOT and in the communication domain from baseline to EOT+4. The SIS is a self-reported questionnaire; thus, we cannot conclude that an individual's perception of improved cognition, memory, or communication resulted in an actual improvement. Notably, the role of intensive aerobic exercise in improving cognitive function in individuals with mild cognitive impairment is well documented.[33,34] While our results are encouraging in demonstrating the potential benefits of intensive aerobic exercise in impacting memory and communication after stroke, our study was underpowered to detect change in these domains and further study is warranted using standardized neuropsychological measures of multiple components of executive function such as working memory, information processing, processing speed, attention, and learning.

Stroke often causes a dramatic shift in lifestyle, with almost 1/3 of survivors reporting social isolation, rarely leaving their home, or not engaging in social activities.[35] Active participation in interventions such as in this study where participants traveled to a rehabilitation laboratory and interacted with a therapist (and potentially other study participants) for a minimum of 4½ hours per week for an 8-week period, may reduce feelings of social isolation.[36,37] Therefore, ensuring comparable total contact time and dosage of UE rehabilitation across groups was a critical component of our experimental approach. All three groups experienced identical contact time during their respective interventions; thus, it is unlikely that therapist interaction alone was a defining factor in HRQOL improvements. Given previous reports of aerobic exercise contributing to improvements in mood,[38] cognition,[33,34] and motor improvements,[18,19] it is plausible that the aerobic exercise interventions played a role in the observed improvements.

Although there was no statistically significant effect of group assignment on change in depressive symptomology, several observations can be made from the data that warrant further investigation. Those in the FE+RTP group improved by a mean of 6 points on the CES-D while modest or no changes were evident in the remaining groups. Aerobic exercise

has been recommended as an efficacious, non-pharmacological adjunct to the treatment of depression.[38] The exact mechanism as to how aerobic exercise impacts depression is not known; however, it is theorized that exercise-induced neurotrophic growth factors promote neurogenesis in the hippocampus, an area of the brain which plays a prominent role in depression.[39] The precise type, intensity, and dosage needed for optimal effect in humans are not known, although in stroke it appears that high intensity exercise has a greater effect on depressive symptomology than low intensity.[40] The intensive aerobic exercise intervention prescribed for the FE+RTP group may have contributed to the positive, albeit not statistically significant, outcomes observed in our study.

An unexpected and potentially meaningful finding was observed when participants' levels of depression was evaluated as a function of dominant versus non-dominant side affected by the stroke. Individuals with hemiparesis in their dominant UE were more likely to exhibit depressive symptomology at baseline, presenting with a mean score of approximately 8 points greater on the CES-D than their counterparts. This finding may appear intuitive – those whose dominant side was affected likely experienced greater difficulty performing unimanual ADL's such as brushing teeth and hair, and ADL dependence is related to PSD.[12] However, our findings are in contrast with Nam and colleagues who found that dominance and side of hemiparesis had no bearing on HRQOL.[15] Further investigation is warranted to examine the relationship between hand dominance, PSD, and HRQOL, and how those factors may potentially be used to trigger additional neuropsychological or behavioral therapy.

Study Limitations

While including HRQOL and depressive symptomology outcomes is justified when examining the impact of aerobic exercise on survivors of stroke, these studies were underpowered to detect differences between groups in these outcomes. It is likely that the EDU+RTP group experienced a ceiling effect in several of the SIS cognitive domains (Memory, Communication, and Cognitive Composite), and thus limited the ability to detect improvement in that group. Future studies should consider including individuals with more severe depressive disorder, as that patient subgroup was excluded from this study and thus limits the generalizability. A larger randomized controlled trial powered to investigate the impact of aerobic exercise on HRQOL and depressive symptomology in individuals with chronic stroke would address these limitations and provide significant value to the stroke community.

CONCLUSION

The results from this study indicated that a combined intervention of aerobic exercise and RTP may improve HRQOL in individuals with chronic stroke. While we cannot claim superiority due to the lack of interaction effect, following the intervention both aerobic exercise groups demonstrated enhanced HRQOL in the motor domains of the SIS and FE combined with UE RTP improved in the non-motor domains of the SIS. Changes in depressive symptomology did not change statistically following the intervention; however, there was a numerical improvement in the FE+RTP group, indicating that the impact of high

intensity aerobic exercise on depression in stroke may be improve with a FE intervention. These results are promising and warrant further investigation with a larger clinical trial powered to detect differences in these outcomes. Our future work includes examining these outcomes in a larger randomized clinical trial and investigating the economic impact of these interventions form the perspectives of the individual, healthcare sector, and society. The additional benefits of aerobic exercise training in improving aerobic functional capacity and reducing cardiovascular risk factors cannot be overstated,[41–43] and thus it should be considered as an adjunct to traditional motor rehabilitation.

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Clinical Trail Registration: This trial is registered at clinicaltrials.gov, registration numbers NCT02076776; NIH and NCT02494518; AHA

Abbreviations:

ADLs	activity of daily living
CES-D	Center for Epidemiological Studies-Depression Scale
EDU	education
EOT	end of treatment
FE	forced exercise
FMA	Fugl-Meyer assessment
PSD	post-stroke depression
HRQOL	health-related quality of life
RTP	repetitive task practice
SIS	Stroke Impact Scale
UE	upper extremity
VE	voluntary exercise

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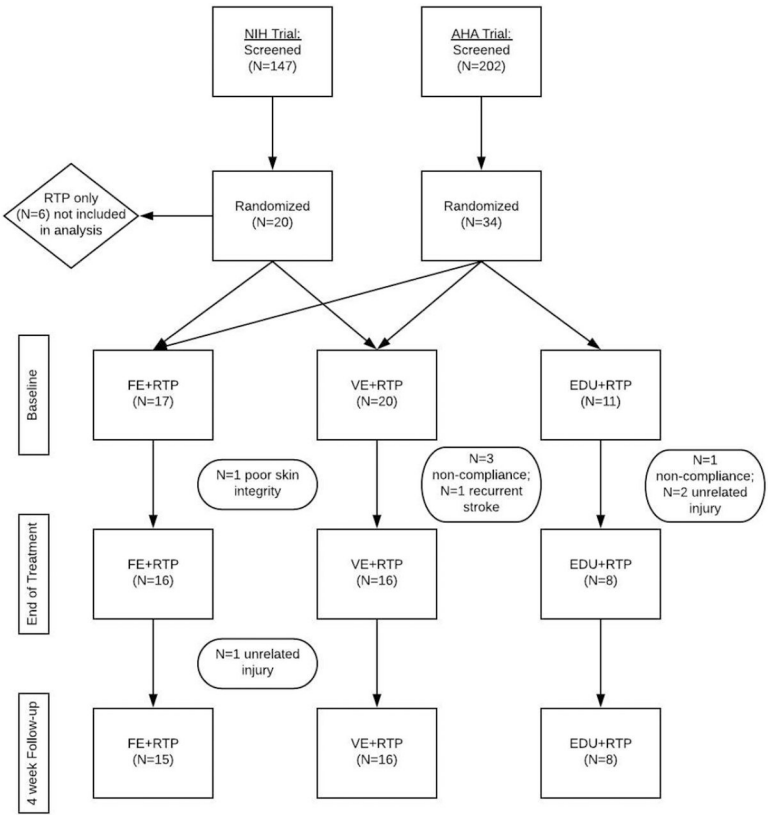

Figure 1:
Flow chart of the two randomized controlled clinical trials used for data analysis.

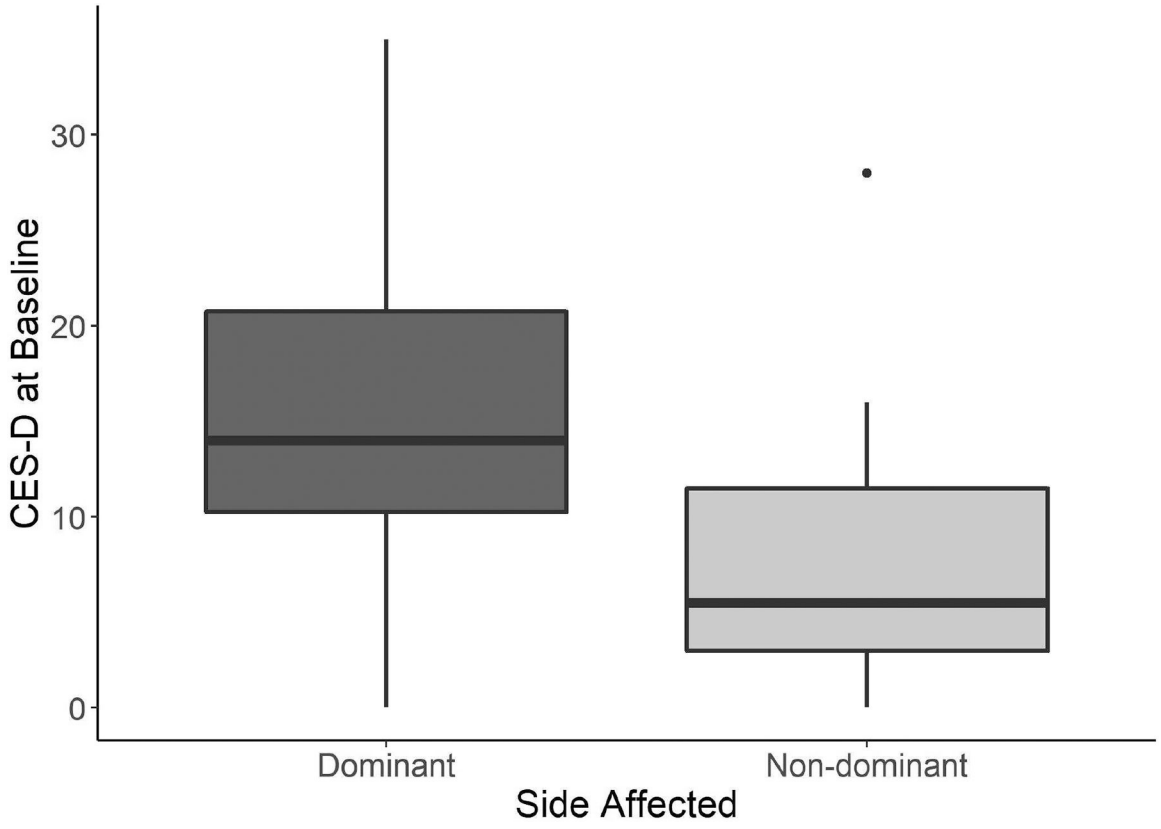

Figure 2:
Box plot of baseline CES-D scores separated by dominant (n=22) and non-dominant (n=18) side. Those whose dominate UE was affected by stroke experienced significantly higher CES-D scores, indicating increased depressive symptomology.

Table 1.

Subject demographics and baseline characteristics by group

Factor	FE+RTP (N = 16)	VE+RTP (N = 16)	EDU+RTP (N = 8)
Age (years)	51 ± 12	60 ± 14	58 ± 12
Male	12 (75%)	10 (62%)	7 (88%)
Race			
African American	8 (50%)	3 (19%)	4 (50%)
Asian	1 (6%)	1 (6%)	0 (0%)
Other	2 (12%)	0 (0%)	1 (12%)
White	5 (31%)	12 (75%)	3 (38%)
Hispanic Ethnicity	1 (6%)	0 (0%)	1 (12%)
Months since stroke	12 [7, 16]	16 [11, 32]	17 [12, 35]
Baseline Fugl Meyer Assessment score	37 ± 8	33 ± 11	33 ± 9

EDU, education; FE, forced exercise; RTP, repetitive task practice; VE, voluntary exercise Summary statistics presented as mean ± standard deviation (normally distributed characteristics), median [first quartile, third quartile] (characteristics with skewed data), or N (%) (categorical data). T-tests were used for normally distributed variables, while Wilcoxon rank sum tests were used for skewed data.

* There was no significant difference between groups ($p>0.05$)

Table 2.

Stroke Impact Scale (SIS) and Center for Epidemiological Studies-Depression Scale (CES-D) results by group

	FE + RTP (N = 16)			VE +RTP (N = 16)			EDU+RTP (N = 8)		
Outcome	**Baseline**	**EOT**	**EOT+4***	**Baseline**	**EOT**	**EOT+4**	**Baseline**	**EOT**	**EOT+4**
SIS domains									
Strength	55 ± 15	**69 ± 13**†	**66 ± 18**†	53 ± 18	**64 ± 17**†	**66 ± 18**†	51 ± 17	56 ± 12	62 ± 15
Mobility	75 ± 13	**87 ± 8**†	**85 ± 11**†	78 ± 19	**88 ± 10**†	**88 ± 10**†	77 ± 15	81 ± 10	86 ± 11
Hand Function	56 ± 23	**72 ± 14**†	**73 ± 17**†	43 ± 26	**58 ± 30**†	**61 ± 31**†	52 ± 23	61 ± 16	**73 ± 18**†
Activities of Daily Living	75 ± 10	**82 ± 10**†	**84 ± 10**†	72 ± 17	**81 ± 15**†	**80 ± 14**†	73 ± 10	78 ± 11	81 ± 7
Memory	77 ± 19	**85 ± 16**†	83 ± 18	82 ± 21	81 ± 22	85 ± 21	91 ± 6	88 ± 13	95 ± 8
Emotions	81 ± 14	89 ± 13	86 ± 13	87 ± 9	85 ± 14	89 ± 13	83 ± 15	85 ± 12	91 ± 8
Communication	84 ± 19	91 ± 12	**92 ± 13**†	83 ± 26	84 ± 24	87 ± 19	96 ± 5	93 ± 6	95 ± 5
Meaningful Activities	63 ± 20	71 ± 16	68 ± 19	64 ± 19	70 ± 22	71 ± 21	58 ± 20	58 ± 17	71 ± 19
SIS Physical Composite	58 ± 10	**69 ± 9**†	**67 ± 10**†	57 ± 14	**66 ± 15**†	**67 ± 14**†	56 ± 10	60 ± 8	**68 ± 7**†
SIS Cognitive Composite	80 ± 18	**88 ± 13**†	**87 ± 15**†	82 ± 22	82 ± 21	86 ± 19	94 ± 5	91 ± 7	95 ± 6
Stroke Recovery (%)	67 ± 10	**77 ± 10**†	**73 ± 14**†	58 ± 19	63 ± 15	**68 ± 14**†	62 ± 11	64 ± 18	68 ± 12
CES-D	15 ± 10	9 ± 8	10 ± 8	10 ± 8	10 ± 10	8 ± 7	10 ± 9	8 ± 7	7 ± 6

CES-D, Center for Epidemiological Studies-Depression Scale; EDU, education; FE, forced exercise; RTP, repetitive task practice; SIS, stroke impact scale; VE, voluntary exercise

Data are presented as mean ± SD. There was no interaction effect among any of the outcome variables ($p>0.05$)

† indicates a significant difference from baseline ($p<0.05$)

* One FE patient did not complete an EOT + 4 follow-up and was thus excluded from analyses.

The CES-D outcome was not normally distributed so paired Wilcoxon tests were performed within each group.