Exertion Fatigue and Chronic Fatigue Are Two Distinct Constructs in People Post-Stroke

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Abstract

Background and Purpose—Post-stroke fatigue is a common and neglected issue despite the fact that it impacts daily functions, quality of life, and has been linked with a higher mortality rate because of its association with a sedentary lifestyle. The purpose of this study was to identify the contributing factors of exertion fatigue and chronic fatigue in people post-stroke.

Methods—Twenty-one post-stroke people (12 males, 9 females; 59.5±10.3 years of age; time after stroke 4.1±3.5 years) participated in the study. The response variables included exertion fatigue and chronic fatigue. Participants underwent a standardized fatigue-inducing exercise on a recumbent stepper. Exertion fatigue level was assessed at rest and immediately after exercise using the Visual Analog Fatigue Scale. Chronic fatigue was measured by the Fatigue Severity Scale. The explanatory variables included aerobic fitness, motor control, and depressive symptoms measured by peak oxygen uptake, Fugl-Meyer motor score, and the Geriatric Depression Scale, respectively.

Results—Using forward stepwise regression, we found that peak oxygen uptake was an independent predictor of exertion fatigue (*P*=0.006), whereas depression was an independent predictor of chronic fatigue (*P*=0.002).

Conclusion—Exertion fatigue and chronic fatigue are 2 distinct fatigue constructs, as identified by 2 different contributing factors.

Keywords

fatigue; stroke; rehabilitation; exercise; behavioral changes

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After a stroke, the frequency of post-stroke fatigue has been reported to be as high as 76%[1] and persists >2 years after the stroke.[2] Post-stroke fatigue affects performance of daily activities[3] and is associated with other negative ramifications such as poor quality of life[4] and higher fatality rate.[2]

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Fatigue is difficult to characterize and measure.[5,6] A general classification of the fatigue dimensions includes perception, physiological, biochemical, and behavioral.[7] Fatigue can be associated with exertion such as exercise, household activities, or social activities.[8] Researchers have distinguished this type of fatigue as exertion fatigue. Exertion fatigue is acute in nature, with rapid onset, short duration, and short recovery period, and is commonly experienced after exertion of physical power or use of mental effort.[8-10] On the other hand, chronic fatigue is defined as a state of weariness unrelated to previous levels of exertion and is associated with pathological factors.[9,10] To date, no definition of fatigue clearly defines its associated dimensions.

In people post-stroke, researchers have proposed several potential contributing factors specific to post-stroke fatigue,[11] such as deconditioning, physical impairment, disuse, sleep disorders, medication side effects, and depression. However, it is unclear which factors contribute to fatigue and, more important, what type of fatigue. In this study, we examined 3 potential contributors to post-stroke fatigue based on the existing literature: aerobic fitness,[3,11,12] motor control,[2,11-13] and depression.[2,11,13-15] The present study aimed to identify the contributing factors of exertion fatigue and chronic fatigue in people post-stroke using forward stepwise regression, in which the response variables were exertion fatigue (measured by the Visual Analog Fatigue Scale[16]) and chronic fatigue (measured by Fatigue Severity Scale[17]). The explanatory variables were aerobic fitness (measured by peak oxygen uptake [VO_{2peak}]), motor control (measured by Fugl-Meyer [FM] Test[18]), and depressive symptoms (measured by the Geriatric Depression Scale [GDS][19,20]). We hypothesized that aerobic fitness, motor control capability, and depressive symptoms would simultaneously predict the presence and severity of exertion fatigue and chronic fatigue.

Materials and Methods

Design

This study used a descriptive, cross-sectional design with a sample of convenience.

Participants

Twenty-one people participated and completed this study. Initially, 59 people were identified via local stroke support groups and the ASTRA (Advancing Stroke Treatment through Research Alliances) participant database at the University of Kansas Medical Center. After a phone interview, 36 people either declined to participate or did not give a response, and 2 were excluded from the study based on our exclusion criteria.

To be included in this study, we required that all participants: (1) have a diagnosis of stroke ≥ 6 months and ≤ 5 years, (2) have the ability to perform the exercise movement on a total body recumbent stepper, (3) receive medical clearance from their primary care physician to confirm that they are medically stable and able to participate in exercise, and (4) score <2 on a dementia screening tool (the AD8).[21,22] Participants were excluded from the study if they presented with cardiovascular or pulmonary pathology that would be considered absolute contraindication to exercise,[23] were current smokers, had alcoholism issues or alcohol dependency, or were recreational drug users. The human subjects committee at the University of Kansas Medical Center approved the study. Institutionally approved informed consent was obtained in writing before participation in the study.

Procedure

Data collection was completed in 2 visits. The first visit involved assessment of chronic fatigue, depressive symptoms, motor control, and exertion fatigue after a fatigue-inducing exercise. A second visit (24 to 48 hours later) involved an assessment of VO_{2peak} during a

graded maximal exercise test, which was scheduled on a different day to allow recovery from the fatigue-inducing exercise on the first visit.

Response Variables

Assessment of Exertion Fatigue—The Visual Analog Fatigue Scale (VAFS)[16] was used to assess the level of exertion fatigue. The VAFS consists of score ranges from 0 to 100 measured in millimeters on a 10-cm vertical line using a pen. The score was obtained by measuring the line from "no fatigue" to the point indicated by participants to represent their fatigue level. Participants were presented the VAFS for the first time to measure fatigue at rest ($VAFS_{at-rest}$) after sitting for 5 minutes in a quiet room. Immediately afterward, a 15-minute standardized fatigue-inducing exercise was administered ($VAFS_{post-exercise}$). Participants were allowed 15 minutes for recovery, after which they were presented the VAFS for the third time ($VAFS_{post-recovery}$). Exertion fatigue was calculated by subtracting the $VAFS_{at-rest}$ score from the $VAFS_{post-exercise}$ score, and recovery rate was calculated using the formula: $(VAFS_{post-exercise} - VAFS_{post-recovery})/(VAFS_{post-exercise} - VAFS_{at-rest}) \times 100$). The VAFS, the assessment of exertion fatigue using the change score on the VAFS, and the calculation of recovery rate using the ratio of VAFS change score have been established previously and reported to have good validity in people post-stroke.[16]

Standardized Fatigue-Inducing Exercise—To induce exertion fatigue, participants were asked to perform a 15-minute standardized exercise protocol using a total body recumbent stepper (NuStep, Inc). To standardize the workload, all participants were asked to step at 75 steps per minute with an external power of 75 to 80 watts for 15 minutes. The device and workload of the fatigue-inducing protocol was chosen to allow participants to become fatigued at a moderate workload.

Assessment of Chronic Fatigue—Chronic fatigue was measured by the Fatigue Severity Scale.[17] The Fatigue Severity Scale is a 9-item scale that has been shown to be reliable and valid to assess fatigue level over the previous week in people post-stroke.[3,11,12]

Explanatory Variables

Aerobic Fitness (VO_{2peak})—To assess aerobic fitness, a maximal effort graded exercise test was conducted using a calibrated metabolic cart, total body recumbent stepper, and the modified total body recumbent stepper–exercise test protocol described previously.[24] Before the exercise test, participants were asked to refrain from consuming caffeine and food. Each participant's heart rate and rhythm was monitored using a 12-lead ECG during the exercise test. The exercise test was terminated using the following criteria: (1) the participant reached volitional fatigue and requested to end the test, (2) plateau of oxygen uptake despite the continuation of exercise, (3) the participant was unable to maintain the cadence, or (4) an adverse cardiovascular response to the exercise test was observed. When participants were unable to achieve their maximal effort, the aerobic fitness level at the peak values was collected (measured in VO_{2peak}).

Fugl-Meyer—The FM test was used to determine the level of motor function in the hemiparetic limbs after stroke. The FM test is a reliable and valid tool that was specifically designed as a clinical measure of sensorimotor impairment for stroke.[18] The total possible score is 124, which has components of sensation (FMSEN, 24 points), upper extremity (FMUE, 66 points), and lower extremity (FMLE, 34 points). Because the sensory component was less relevant, the combined total motor (FMTM) scores of the FMUE and FMLE were determined (FMTM=FMUE+FMLE),[25] with a total possible score of 100.

Geriatric Depression Scale—The GDS is a questionnaire that includes 30 items that refer to affective, cognitive, and behavioral symptoms of depression to assess mood. It has been tested extensively in older adults[19,20] and previously used in people post-stroke. The possible score ranges from 0 to 30.

Data Analysis

SPSS 16.0 (SPSS, Inc.) statistical software was used to perform all statistical analysis. Descriptive statistics were calculated; histograms for each variable were evaluated for normal distributions, and scatter plots were analyzed for outlying scores. To explore the relationship between variables, the Pearson correlation coefficient was performed. Subsequently, forward stepwise regression model with 3 predictors (VO_{2peak}, FMTM, and GDS scores) was calculated for exertion fatigue and for chronic fatigue. The validity of each model was assessed through analysis of colinearity statistics (variance inflation factor) and Q-Q plots of unstandardized residuals. A 0.05 level of significance was used for all statistical tests.

Results

Data were collected from 21 people with chronic stroke (12 men and 9 women; 59.5±10.3 years of age; 4.1±3.5 years after stroke). No adverse event was reported during the fatigue-inducing exercise or the graded maximal exercise test. Participant characteristics and descriptive statistics are shown in Table 1. The VAFS scores (at rest, post-exercise, and post-recovery) are illustrated in the Figure.

Correlations between all variables are shown in Table 2. Using the Pearson correlation coefficient, our data suggest that higher VO_{2peak} was associated with less exertion fatigue ($r=-0.582$; $P<0.01$) and better recovery ($r=.891$; $P<0.001$) after exercise, whereas higher GDS score and $VAFS_{at-rest}$ were associated with higher chronic fatigue ($r=0.639$, $P<0.01$; $r=0.752$, $P<0.01$, respectively). In addition, chronic fatigue did not show any correlation with either exertion fatigue or VO_{2peak}.

Using forward stepwise regression, we found that the regression models for exertion fatigue and chronic fatigue with 3 explanatory variables (VO_{2peak}, FMTM, and GDS scores) were both statistically significant, as shown in Table 3. VO_{2peak} was found to be a significant individual factor that explained 30.5% of variance in exertion fatigue, whereas GDS score was found to be a significant individual factor that explained 37.8% of variance in chronic fatigue. In addition, $VAFS_{at-rest}$ was found to contribute independently to chronic fatigue (adjusted $R^2=0.555$; $P<0.001$).

Discussion

We found that aerobic fitness and depression are strong independent predictors for exertion fatigue and chronic fatigue in people post-stroke, respectively. This finding supports our hypotheses and suggests that exertion fatigue and chronic fatigue are 2 unique constructs as identified by 2 distinct predictors.

Our data showed that all participants experienced some level of exertion fatigue immediately after exercise. The various severities experienced among participants and the large SD of exertion fatigue may be explained by the difference in VO_{2peak} between participants. Because VO_{2peak} was found to be a strong negative predictor for exertion fatigue, our data suggest that a person with higher aerobic fitness is likely to experience less exertion fatigue after exercise. In addition, we found a significant positive correlation

between recovery rate and VO_{2peak}, which concurs with our result and suggests that the higher the aerobic fitness, the quicker the recovery after exercise.

Contrary to our finding, one previous study examining the severity of fatigue using the Fatigue Severity Scale[17] and the Visual Analog Scale[26] reported no significant relationship between aerobic fitness and fatigue in people post-stroke.[12] Although aerobic fitness was assessed at the peak level using a graded exercise protocol on a treadmill in the previous investigation, the measurement of fatigue was not specific to exercise. Fatigue was measured as a single time-point assessment that represented overall fatigue on the testing day, which is likely separate from the type of fatigue that is activity induced with an acute onset nature such as exertion fatigue. In contrast, our use of the VAFS before and after the fatigue-inducing protocol ensured that the fatigue being measured attributed to the exertion during exercise. To faithfully report fatigue that is induced by exercise, exertion fatigue must be calculated by determining the difference between fatigue level at baseline and immediately after exercise. Existing fatigue assessments and questionnaires measure only fatigue level over an extended period of time (eg, 2 weeks); and most investigators used the visual analog assessment at a single time point to represent fatigue. The measure used in the present study was designed to quantify changes of fatigue level during real time.

In the present study, chronic fatigue assessment (mean score=4.2 of 7, as measured by the Fatigue Severity Scale) showed similar results compared with data from a previous study (mean score=3.9 of 7) using the same scale.[12] We found that depression is highly related to chronic fatigue, which supports previous findings;[13,14] and we also found that it may contribute to chronic fatigue in people post-stroke. Post-stroke depression is the most frequent psychiatric complication of stroke.[27] Among our 21 participants, we found that 10 were mildly depressive, 2 were severely depressive, and 9 were either subclinical or asymptomatic based on the GDS.[20] Many symptoms that are commonly experienced after stroke, such as cognitive impairment, aphasia, functional impairment, and social isolation, are considered post-stroke depression risk factors,[28] which may explain the close association between stroke and depression. In addition, it is important to recognize that fatigue can be one of the symptoms of depression and is difficult to separate because of the paradoxical relationship between fatigue and depression. Although the pathophysiology of post-stroke depression is still debated, the relationship between depression and stroke cannot be neglected because even with relatively low or moderate levels of depression, it was a strong contributor to chronic fatigue as shown in our study.

Post-stroke fatigue is a multifactorial phenomenon that involves both physiological and psychosocial properties[12] and can exist independently of depression.[14,15] According to the Portenoy integrated fatigue model,[29] exertion fatigue can be more closely associated with factors that are physiological (eg, inactivity and physical deconditioning) than those that are psychosocial (eg, depression and anxiety). On the other hand, chronic pain, medical treatment side effects, sleep disorders, and depression may better describe chronic fatigue. Our finding is congruent with the Portenoy model and suggests that exertion fatigue and chronic fatigue are 2 distinct fatigue constructs as identified by 2 different contributing factors.

Although previous investigations considered physical impairment a contributing factor to post-stroke fatigue,[11,30] we did not find that motor control ability in the hemiparetic limbs was an independent predictor of exertion fatigue or chronic fatigue in this study. One of the explanations may be that although our fatigue-inducing protocol involved all 4 limbs, the exercise may not have fully challenged participants' maximal motor control capability because it was performed on a total body recumbent stepper. Future studies should consider administering fatigue-inducing protocol that engages ambulatory movement such as

treadmill walk. This approach will challenge participants at a higher level and may better capture the poor biomechanical efficiency and increased energy expenditure attributable to limited range of motion, muscle tone, and malalignment often experienced in people post-stroke. In addition, subsequent studies may consider incorporating muscular endurance and strength measures (eg, isokinetic device) in the regression model to describe fatigue instead of motor control measured by the FM test. Although FM test is well accepted as an indication of motor impairment,[25,31,32] strength is a direct measure of muscular properties and could perhaps describe fatigue more appropriately than motor control.

Although statistical significance was achieved, the small sample size recruited from a single center did not allow us to perform subgroup analyses to determine whether fatigue level would be different among sex, stroke subtypes, and lesion locations, which may limit the generalizability of our findings. Interestingly, our data showed that the baseline fatigue detected (as represented by $VAFS_{at\text{-}rest}$) using the VAFS developed in our laboratory[16] was an independent predictor for chronic fatigue and accounted for 55.5% of the variance. Future studies may consider measuring fatigue at different times of the day to investigate the role of circadian fatigue in people post-stroke. Another limitation of this study is that pain and sleep were not assessed, and lesion location was not standardized. Future studies should consider lesion location differences and explore additional factors (eg, pain) that may potentially contribute to fatigue in people post-stroke.

Although our inferences are based on a relatively small sample size, the significant contribution of this work is that it provides a beginning framework to understand 2 distinct fatigue constructs in people post-stroke. Follow-up studies should use a larger sample size to further solidify the validity of these models.

Conclusions

We found that aerobic fitness is a strong independent predictor of exertion fatigue, whereas depression is an independent predictor of chronic fatigue in people post-stroke. We also found that exertion fatigue and chronic fatigue are 2 distinct constructs, as shown by each having its own unique contributing factor and a lack of relationship between constructs. Fatigue is prevalent and can have severe negative impacts in people post-stroke. Before individualized therapeutic treatment can be implemented, clinicians must distinguish the nature of fatigue by indentifying its contributing factors and provide appropriate countermeasures accordingly.

Acknowledgments

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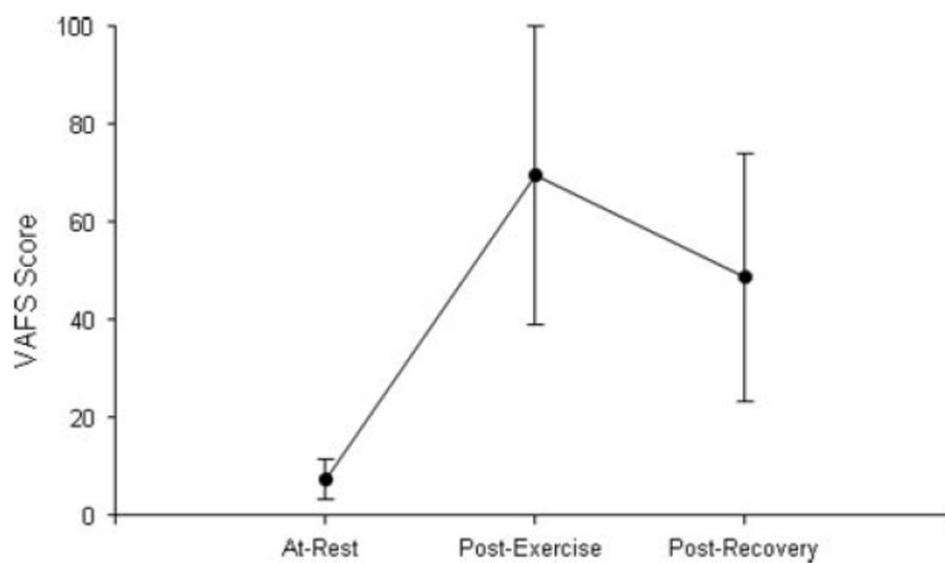
Figure.
Mean VAFS score at different time points. Values are means±SD.

Table 1

Participant Characteristics (n=21)

Characteristics	Values
Men/women	12 (57%)/9 (43%)
Stroke lesion side: right/left/brain stem	15 (71%)/4 (19%)/2 (10%)
Stroke subtype: ischemic/hemorrhagic	18 (86%)/3 (14%)
Age (y)	59.5±0.3
Time after stroke (y)	4.1±3.5
RR (%)	37.0±17.3
Variables	Values
Response variables	
Exertion fatigue	62.4±29.3
Chronic fatigue	4.2±1.7
Explanatory variables	
VO_{2peak} (mL/kg/min)	16.2±6.5
FMTM	70.8±28.8
GDS	10.2±7.3

Values are means±SD.

RR indicates recovery rate after fatigue-inducing exercise.

Exertion fatigue is calculated by ($VAFS_{post-exercise}$−$VAFS_{at-rest}$); chronic fatigue 4 indicates the presence of chronic fatigue. VO_{2peak} (mL/kg/min), normal sedentary males in the same age group (>31; females >22); FMTM, upper extremity+lower extremity motor scores; 99≈85=mild/moderate motor deficits; 84≈50=marked; <50=severe. GDS scores: <9, normal; >9, mildly depressive; >19, severe.

Table 2

Relationship Between Variables

	CF	VO$_{2peak}$	FMTM	GDS	RR	VAFS$_{at-rest}$
EF	0.332	−0.582 **	−0.270	0.221	−0.649	0.242
CF		−0.125	0.142	0.639 **	−0.161	0.752 **
VO$_{2peak}$			0.404	−0.057	0.891 **	−0.076
FMTM				0.159	0.495	0.156
GDS					−0.123	0.289
RR						−0.150

EF indicates exertion fatigue; CF, chronic fatigue; RR, recovery rate.

FMTM is composed of upper extremity+lower extremity motor scores.

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P value<0.01.

Table 3

Predictors for Exertion and Chronic Fatigue

Regression Model for Exertion Fatigue		
Adjusted R^2		0.305
F		9.76
P		0.006
Explanatory Variables	B-Weights	*P*
VO_{2peak}	−2.633	0.006 [**]
FMTM (excluded)	−0.410	0.845
GDS (excluded)	0.190	0.326
Regression Model for Chronic Fatigue		
Adjusted R^2		0.378
F		13.130
P		0.002
Explanatory Variables	B-Weights	*P*
VO_{2peak} (excluded)	−0.089	0.628
FMTM (excluded)	0.041	0.824
GDS	0.149	0.002 [**]

[**] *P* value<0.01.

F indicates F-statistics in regression models.