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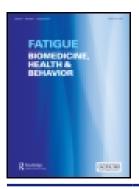
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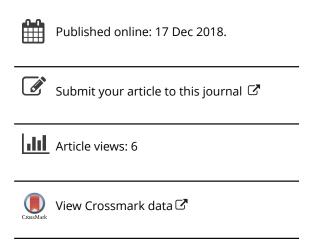
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## Predictors of feelings of energy differ from predictors of fatigue

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#### **ABSTRACT**

**Background:** Studies examining energy and fatigue as a bipolar mood have focused on a single variable, usually fatigue, when studying these moods.

**Objective:** The purpose of this study was to identify factors predicting feelings of energy and fatigue separately while simultaneously examining multiple domains related to these mood states in graduate health sciences students.

**Method:** Seventy-seven participants were recruited from a Physician Assistant, Physical Therapy and Occupational Therapy program at a small school in Northern New York. Participants completed a series of surveys to measure mood, diet, mental work load intensity on school days and non-school days, and physical activity. Participants also completed the Trail-making Test Part B task on an iPad and their Resting Metabolic Rate (RMR) and muscle oxygen consumption mVO2 was measured. A backwards linear regression was used to determine the relationship between energy, fatigue and multiple variables.

**Results:** The predictor variables accounted for 46.1% and 22.7% of the variance in fatigue and energy, respectively. More fatigue was associated with worse sleep quality, more time spent sitting and higher perceived intensity of mental workload on non-school days. More energy was associated with better sleep quality, higher muscle oxygen saturation, lower RMR, and faster psychomotor performance.

**Conclusion:** The results of this study indicate that energy and fatigue are separate, yet overlapping constructs that are predicted with different accuracy by different variables. Our results indicate that small lifestyle changes may be necessary to improve feelings of fatigue but comprehensive interventions may be necessary to improve feelings of energy and fatigue.

#### ARTICLE HISTORY

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#### **KEYWORDS**

Energy; fatigue; resting metabolic rate; mitochondrial function

#### Introduction

Both colloquially and in research, feelings of fatigue are usually defined as 'a feeling of weariness, tiredness or a lack of energy,' suggesting that energy and fatigue are a

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single bipolar mood [1,2]. However, recently Loy and colleagues have suggested defining feelings of energy as 'an individual's potential to perform mental and physical activity' with synonyms such as 'vigor', 'vitality', 'lively', and 'full of pep' [3]. Furthermore, these authors have defined feelings of fatigue as 'subjective perceptions of reduced mental or physical capacity' or 'persistent sense of physical, emotional, and/or cognitive tiredness or exhaustion that can interfere with function.' Synonyms included 'exhausted', 'sluggish', 'weary', 'tired' or 'feeling worn out' [3]. To date, theoretical approaches to these subjective states have been rare and those that have been developed, such as the motivational control theory of fatigue, have emphasized fatigue and ignored feelings of energy [4]. One unresolved issue is whether energy and fatigue are better conceptualized as two sides of the same construct or as separate constructs.

Our Google Scholar searches using the phrases 'fatigue was measured' and 'fatigue was assessed' yielded 342,000 results, compared to identical searches that used the words vitality and vigor in lieu of fatigue, which yielded 86,300 results. This suggest that fatigue symptoms are more commonly measured by researchers than energy symptoms, and when both fatigue and energy concepts are measured, the different assessment tools make comparisons difficult. Nevertheless, when similar, but separate assessments of energy and fatigue have been made, e.g. the Profile of Mood States questionnaire, substantial evidence suggests that the two are separate constructs [5,6].

There are over 250 instruments that measure fatigue [7], many assuming energy and fatigue as bipolar ends of the same continuum [8-14], while others treat them as two separate unipolar moods [9,15-18]. Studies that have measured changes in both energy and fatigue have shown that certain interventions impact energy only, while others impact fatigue only [19-30]. For example, engaging in low-to-moderate intensity physical activity almost invariably increases feelings of energy but has much less effect on reducing fatigue [19]. Moreover, a meta-analysis examining recovery from work-related mental effort found that psychological detachment from work was negatively related to fatigue while feelings of control and mastery after work were positively related to vigor [31]. Another limitation of the extant literature is that studies typically have focused on understanding one aspect of fatigue (e.g. the effect of either sleep or physical activity or cognitive workload or nutrition) rather than several relevant domains simultaneously (e.g. the effects of sleep, physical activity, workload and nutrition together).

Several lifestyle factors have well-established effects on feelings of energy and fatigue, including diet, physical activity, sedentary time, sleep and mental work. Food, especially carbohydrate consumption (including alcohol), generally has stronger effects on fatigue than energy [27,32,33]. Certain micronutrients, such as caffeine, cause similar sized changes in energy and fatigue [21,34-36]. Acute bouts of exercise and adoption of regular physical activity by sedentary groups result in larger increases in energy than decreases in fatigue [19,20,37]. In addition, when regular exercisers reduce their physical activity levels for five days, decreased energy is greater than increased feelings of fatigue [38]. Sleep duration is more strongly linked to fatigue compared to feelings of energy while sleep quality has associations with energy and fatigue that are similar in magnitude [26,29]. Studies have also noted decreases in subjective energy in association with acute mental work demands [21,39,40] as well as chronic mental work load demands [41]. It should also be noted that when office workers increased sedentary time by removing their standing workstation, decreased energy was reported but with insignificant

effects on fatigue [22]. However, fatigue has been associated with sedentary behavior in other studies [3,23,42].

In addition to the above variables, our study also examined several other factors such as mitochondrial function, body composition and resting metabolic rate that we hypothesize to be related to energy and fatigue. While the relationship between mitochondrial function and energy and fatigue has not been established in healthy adults, the chronic fatigue literature suggests a relationship between mitochondrial dysfunction and severity of fatigue [43–46]. A review of 25 studies suggested that the six most commonly proposed pathways to explain the association between subjective fatigue and mitochondrial dysfunction are: metabolism, energy production, protein transport, mitochondrial morphology, central nervous system dysfunction and post-viral infection [46].

Body composition although not directly linked to energy and fatigue has shown a correlational relationship with mood. A study conducted on obese women noted that as their body-mass index (BMI) improved, decreased fatigue and increased energy was reported regardless of the type of treatment received [47]. Additionally a study examining the relationship between body fat and fatigue noted that adolescents with low fatigue had significantly lower body fat than adolescents with high fatigue [48]. Another study noted a significant negative association between body weight and feelings of vitality in a sample of 8889 adults [49]. There is also evidence that thyroxine levels which influence resting metabolic rate (RMR) [50] also play a role in influencing subjective energy and fatigue [51-53]. Studies examining the influence of fatigue on RMR noted that after high volume training (>100% of their regular training loads) subjects reported increased fatigue and showed decreased RMR, including when RMR was normalized for fat free mass suggesting a possible relationship between fatigue and RMR [54,55].

The purpose of this study was to examine traditional (i.e. sleep, physical activity, diet, sitting behavior, mental workload) and novel (resting metabolic rate, mitochondrial function, body composition) variables known (or hypothesized) to be related to feelings of energy and fatigue and determine how well these variables predicted energy and separately fatigue. It was hypothesized that significant predictor variables would be different for energy as compared to fatigue.

#### Methods

#### Study design

A cross-sectional design was used. Data was collected from November 5–18, 2016 to minimize potential seasonal effects [26].

#### **Participants**

After obtaining Clarkson University Institutional Review Board (IRB) approval (approval #17-15), graduate health sciences students between the ages of 22-45 years were recruited from a population of 151 Physician Assistant (PA), Physical Therapy (PT) and Occupational Therapy (OT) students at a small private university in northern NY. The presence of cardiorespiratory disease was an exclusion criterion. Seventy-seven volunteered to participate (Females = 46, 1 person chose not to identify). The mean ± SD age, height and

weight of the sample was  $25.8 \pm 3.6$  yrs,  $169.1 \pm 10.0$  cm and  $71.2 \pm 15.5$  kg, respectively. The mean BMI was  $24.81 \pm 4.32$ . Most of the sample identified as Caucasian (80%).

This participant pool was considered to be potentially vulnerable to fatigue given that perceived stress is common among individuals pursuing graduate education in health professions, including occupational therapy, physical therapy, and physician assistant students [56–59]. The need to master an ever-increasing body of knowledge represents a challenge that students often struggle to meet. Students may use a variety of methods to attempt to cope with the substantial mental work load, including restricting sleep, reducing physical activity, and engaging in convenient but unhealthy eating patterns. These behavioral choices can contribute to feelings of low energy and fatigue [60–63]. Feelings of low energy and fatigue may cause significant cognitive and performance problems. Low energy and fatigue are also associated with reductions in sustained attention and learning as well as cognitive errors, especially lapses, during cognitive tests [4]. For health science practitioners, these effects plausibly could contribute to errors in treatment delivery and documentation [60]. Thus there is a need to better understand the potential causes of low energy and fatigue among allied health science students.

#### **Measures**

#### Dependent variables: energy and fatigue feelings

The 30-item Profile of Mood States (POMS) Short Form measures six mood states: energy (Vigor), fatigue, tension, depression, anger and confusion [64]. Participants indicated the intensity of these subjective states over the past 30 days on a five-point scale ranging from 'Not at all' (scored as 0) to 'Extremely' (scored as 4). Each of the mood states are scored from the sum of five questions (i.e. vigor = lively + energetic + active + full of pep + vigorous); thus, each mood variable has a 20-point range. Among healthy participants Cronbach's alpha, a measure of internal consistency, has been reported as 0.90 for the POMS-SF [17]. For the purposes of this study, only the energy and fatigue variables were used as dependent variables while tension, depression, anger and confusion were not used in the analysis because of the collinearity between these moods and energy and fatigue.

#### **Predictor variables**

#### Sleep

The Pittsburgh Sleep Quality Index (PSQI) was used to assess usual sleep quantity and quality during the prior month. This 19-question survey generates global sleep quality scores that distinguish between good and poor sleepers as defined by a gold standard objective measure [65]. Lower scores indicate better sleep quality [65].

#### Perceived mental workload

Perceived typical weekly mental workload was measured using mental work questions from the background information section of the Mental and Physical State and Trait Energy and Fatigue Scale, the reliability and validity of which has been supported

[20,34,40,66-79]. Data were obtained separately for school and non-school days using the same scoring rule. Perceived mental workload on school days was calculated from: (i) the number of days at school during a typical week multiplied by (ii) the typical number of hrs. of mental work performed on school days, and that product was multiplied by (iii) the average intensity of mental work performed on school days. Perceived mental intensity was rated using the following scale: 1 = very low intensity; 2 = low intensity; 3 = average; 4 = intense; 5 = very high intensity. Thus, individuals who perceived the intensity of mental work as average and completed work for eight hrs. per day on five days per week would have a total perceived mental workload score of 8 hrs. × 5 days × 3 intensity = 120 [16].

#### **Objective coanitive function**

The Trail-Making Test Part B, a measure of cognitive function, is a timed test involving attention, psychomotor speed and visual scanning and sequential abilities [16]. Participants were asked to connect numbers to letters in alphanumerical seguential order (i.e. 1 to A, A to 2, 2 to B) with their finger touching Apple iPad Pro (A1584) [80] Shorter completion times indicate better performance.

#### **Body composition**

The participants' height was measured using a stadiometer. Weight and body composition, including estimated body fat percentage and fat-free mass (fat free mass) were measured using the Total Body Composition Analyzer model TBF-410GS (Tanita Corporation, Tokyo, Japan). This device, uses bioelectrical impedance analysis (BIA), and has independent evidence to support its validity [81].

#### **Unhealthy eating behavior**

The Rapid Eating Assessment for Participants Short Form (REAP-S) was used to evaluate the nutritional status of the participants [82]. This survey contains 16 questions about eating behavior and has been validated against the Block Semi-Quantitative Food Frequency Questionnaire (Block FFQ) [19]. It is used by health care providers to flag patients who display unhealthy eating behaviors and are in need of nutritional counseling [83]. Each question has a response that is identified as a flag and the total number of flagged responses for each participant were calculated for this study. Participants were classified as at risk (> = 5 flags) or low risk (<5 flags) [82,83]

#### **Caffeine consumption**

A 20-item questionnaire was administered to assess caffeine consumption from beverages, food, over-the-counter and prescription medications. This questionnaire has been used by health care professionals to estimate the average number of milligrams (mg) of daily caffeine consumption [84].

#### **Physical activity**

Past week physical activity was measured using the International Physical Activity Questionnaire Short Form (IPAQ-SF). Participants completed the 16-question survey which asked about the duration (in min.) and frequency (in days) of physical activity in the domains of school, transportation, and leisure time; walking, moderate intensity and high intensity activities are also captured [85]. Metabolic equivalent (MET) min. of physical activity per week are used as the criterion scores.

#### Sitting time

Total time spent sitting was assessed by a single item on the IPAQ-SF asked which asks participants how much time is spent sitting (TSS) on week days, reported as the number of min. per week.

#### Resting metabolic rate

Resting metabolic rate (RMR) was measured using the Cosmed Fitmate Pro (CosMed, Rome, Italy) [86]. RMR was assessed after the participants had been in a seated position for 30 min. After 30 min. a facemask was affixed for 15 min. and the last 10 min. of data were used for the analysis. A normalized RMR was calculated by adjusting for fat free mass [87]. Fat free mass is a primary determinant of RMR but  $\sim$ 30% of the variation in RMR is accounted for by poorly understood other factors, such as genetics and prior weight loss, which may be related to feelings of energy or fatigue [88–90].

#### Muscle oxygen saturation

Resting right lateral gastrocnemius skeletal muscle oxygen saturation (mVO2) was measured using a portable near infrared spectroscopy (NIRS) monitor (BSXinsight, BSX Athletics, Texas, USA) which has been supported by independent reliability and validity data [91,92]. Reduced oxygen delivery to muscles has been investigated in patients with chronic fatigue syndrome [93]. The data here are exploratory as a potential objective index of feelings of energy or fatigue. Data were obtained after each participant had been seated for 30 min. The monitor was then placed on the right lateral gastrocnemius for 15 min. and the average of the last 10 min. was used for analysis.

#### **Procedure**

After screening and providing written informed consent, the participants were invited to complete the protocol in a quiet, climate-controlled lab (~72F). Participants were asked to not smoke or consume caffeine or alcohol for a minimum of 8 hrs. prior to testing. Height, weight and body composition were measured and participants then sat in a chair where they completed the surveys using surveymonkey.com on an Alienware laptop (17 R2 Model #P43F). The surveys took approximately 25 min. to complete. After the completion of the survey participants completed the Trails B using the Membrain platform (PsychTech-Solutions) on an Apple iPad Pro (A1584). Participants remained seated throughout the

duration of the surveys and cognitive tasks. Next, the participants were fitted with the mask to measure RMR and the BSXInsight monitor was worn using a sleeve with the sensor placed on the skin above the right lateral gastrocnemius. The entire data collection process took approximately 40 min.

#### Statistical analysis

Variables were evaluated for normality of distribution using a combination of histograms and the Shapiro-Wilks test for normality. Except for physical activity all other variables were normally distributed (p > .05). Physical activity (METS) was skewed to the left with more participants reporting being physically inactive. We removed the METS variable from the analysis and since there was no difference in final variables selected by the model we left the variable in our final analysis. The univariate method of outlier detection was used to eliminate outliers in the predictors. Multicollinearity of the predictor variables were tested. From the correlation matrix of the predictor variables, we eliminated the potential predictor variables of tension, depression, anger and confusion, total hrs. in bed and BMI. After making these adjustments the calculated variance inflation factors in our model were less than 1.5, which indicated no predictor had a strong linear relationship with the other predictors.

A backward multiple linear regression model was used to examine predictors of POMSfatigue, and POMS-Energy. All analyses were conducted using Minitab 18. The backward multiple linear regression model is a method of multiple regression which begins by placing all predictors in the model and then calculating the contribution of each one by looking at the significance value of the t-test for each predictor. This significance value is compared against a removal criterion. If a predictor meets the removal criterion it is removed from the model and the model is re-estimated for the remaining predictors. This process is repeated until no further predictors can be deleted without a statistically significant loss of fit. Since we have a relatively large set of candidate predictors, the backward multiple linear regression model enables us to obtain a reduced set, eliminating unnecessary predictors, simplifying data, and enhancing predictive accuracy.

A post-hoc power analysis was completed using F family tests and t-family tests using G\*Power (version 3.1.9.2) [94].

#### Results

In the current study, the Cronbach alphas ranged from 0.645 to 0.874 (Tension = 0.810, Depression = 0.811, Anger = 0.873, Confusion = 0.645, Vigor = 0.842, Fatigue = 0.874). There was a significant moderate correlation between energy and fatigue mood states (r = -.35, p = .002) (Table 1). Results of the correlations are presented in Table 1.

#### **POMS-Fatigue predictors**

The backward multiple linear regression accounted for 46.1% of the variance in POMSfatigue,  $R^2 = .490$ , F [4,71] = 17.031, p < .001. More intense feelings of fatigue were predicted by three variables: poor sleep quality ( $\beta = .520$ , t(71) = 5.228, p < .001), more time spent sitting ( $\beta = .409$ , t(71) = 4.615, p < .001) and higher mental work load on non-

**Table 1.** Intercorrelations\* and descriptive statistics for study variables.

Variable	Means (SD)	POMS- Energy	Global PSQI	Sleep (hrs.)	Total time spent sitting (mins/ week)	Physical activity (MET mins/week)	Perceived mental workload school days	Perceived mental workload non-school days	RMR Normalized	Muscle oxygen saturation	Body fat %	Trails B (s)	Caffeine (mg)	REAP-S (ratio at risk: low risk)
POMS-Fatigue	7.6	353	.515	237	.501	334	.261	.335	165	.131	.071	005	.020	.057
5	(4.1)	(.002)	(<.001)	(.038)	(<.001)	(.003)	(.022)	(.003)	(.151)	(.256)	(.540)	(.969)	(.860)	(.623)
POMS- Energy	7.5		340	.079	113	.224	001	162	088	.195	160	128	094	012
	(3.5)		(.002)	(.495)	(.329)	(.050)	(.991)	(.158)	(.446)	(.089)	(.165)	(.269)	(.417)	(.917)
Global Pittsburgh Sleep	6.1			526	156	232	.037	.147	-0.125	.009	.054	.096	.269	.005
Quality Inventory scores	(2.7)			(<.001)	(.175)	(.042)	(.748)	(.201)	(.280)	(.941)	(.638)	(.408)	(.018)	(.963)
Sleep (hrs.)	6.6				243	013	140	241	0.081	.118	.004	214	200	.011
	(1.0)				(.033)	(.912)	(.225)	(.035)	(.483)	(.307)	(.974)	(.062)	(.081)	(.927)
Total time spent sitting	628.6					239	.294	.231	240	199	097	072	054	054
(mins/week)	(275.4)					(.036)	(.009)	(.043)	(.036)	(.083)	(.403)	(.535)	(.642)	(.642)
Physical activity (MET mins /	1984.2						250	057	.209	.110	.081	.246	048	215
week)	(1858.4)						(.028)	(.624)	(.068)	(.341)	(.483)	(.031)	(.680)	(.061)
Perceived mental workload	190.1							.446	196	098	.016	041	044	.125
school days	(92.2)							(<.001)	(880.)	(.399)	(.894)	(.726)	(.701)	(.278)
Perceived mental workload	16.7								040	.191	051	.054	.114	.182
non-school days	(11.2)								(.728)	(.096)	(.660)	(.638)	(.322)	(.113)
Resting Metabolic Rate	34.4									.023	.247	212	.284	.232
Normalized	(5.6)									(.842)	(.030)	(.064)	(.012)	(.042)
Muscle oxygen saturation	26.7										167	033	.023	.010
	(4.3)										(.145)	(.778)	(.842)	(.931)
Body fat %	23.4											165	003	100
	(8.4)											(.152)	(.982)	(.388)
Trail-Making Test Part B (s)	64.1												074	009
	(20.8)												(.524)	(.937)
Caffeine (mg)	226.5													.131
	(198.4)													(.257)
Rapid Eating Assessment for Participants Short Form (ratio at risk: low risk)	19:58													

school days ( $\beta$  = .207, t(71) = 2.336, p = .022). Post-hoc power analysis revealed a calculated power of 0.998 (Table 2 and Figure 1 in supplemental material).

#### **POMS-Energy predictors**

The backward multiple linear regression accounted for 22.7% of the variance in POMS energy,  $R^2$  = .299, F(7,68) = 4.152, p = .001. More intense feelings of energy were predicted by four variables: higher sleep quality ( $\beta$  = -.399, t(68) = -3.232, p = .002), lower muscle oxygen saturation ( $\beta$  = -.240, t(68) = -2.192, p = .028), faster completion times on Trails B ( $\beta$  = -.216, t(68) = -2.018, p = .057) and lower normalized RMR ( $\beta$  = -.219, t(68) = -2.076, p = .047). Post-hoc power analysis revealed a calculated power of 1.000 (Table 2 and Figure 2 in supplemental material).

#### **Discussion**

The purpose of this study was to identify traditional and hypothesized variables known to be related to feelings of energy and fatigue and determine the degree to which these variables predicted feelings of energy and separately feelings of fatigue. One primary finding supported self-report energy and fatigue states as separate, yet overlapping constructs predicted by a number of variables. Sleep quality was the strongest predictor of both energy and fatigue albeit in opposite directions. Also fatigue and energy were negatively correlated. These findings suggest that these moods may be unique, yet overlapping. Our results are consistent with prior investigations that found sleep quality as a significant predictor of subjective energy and fatigue [42,95–97]. These findings suggest that when examining energy and fatigue, it is preferable to measure both mood states as certain interventions may impact only one, or both moods.

Sedentary behavior was also a significant predictor of fatigue. Health science students reported an average of over 10 hrs. of sedentary behavior per day which was significantly correlated with fatigue, but not energy. This observation is consistent with several prior investigations that noted associations between sedentary behavior and increased fatigue with smaller effects on feelings of energy [3,22,23].

Perceived mental workload was also a significant predictor of fatigue as has been observed previously [41]. Unique to the present study was that perceptions of typical

Table 2. POMS-Fatigue and POMS-Energy predictors.

	POMS Fatigue				POMS Energy				
Variable	β**	<i>t-</i> statistic	<i>p</i> - value	95% CI of b	β**	<i>t-</i> statistic	<i>p</i> - value	95% Cl of b	
Global Pittsburgh Sleep Quality Inventory Scores	.517	5.228	<.001	(.492, 1.088)	399	-3.232,	.002	(849,195)	
Perceived mental workload on non-school days	.208	2.336	.020	(.012, .139)					
Total time spent sitting	.417	4.615	<.001	(.004, .009)					
Muscle oxygen saturation					.240	-2.192	.028	(.021, .370)	
Resting Metabolic Rate Normalized					219	-2.076	.047	(270,002)	
Trail-making Test Part B					216	-2.018	.057	(073, .001)	

<sup>\*\*</sup> $\beta$  is the standardized coefficient.

school day workload were not significant in predicting fatigue but perceived mental work on non-school days was predictive of fatigue. Thus, the requirement to perform work on non-work days may be especially fatiguing or fatigue may contribute to reduced work efficiency if the completion of school work requires time on non-school days [98]. Regardless, these findings point to the importance of obtaining mental workload information on the days such work typically is done and on days when students are typically not formally required to be in school.

The objective measure of psychomotor performance, Trail-making Test Part B, was important in the prediction of self-report energy but not fatigue. This is consistent with research showing that the ability to sustain attention is a key component of mental energy [99]. Our findings are also generally consistent with a study of 766 right handed healthy young adults that found that self-report energy, rather than fatigue, was more strongly associated with reduced diffusivity in brain neuronal areas involved in motivation [100].

Other significant correlates of subjective energy observed in the present study relate to novel variables that rarely have been considered previously. Our study found a negative relationship between feelings of energy and resting metabolic rate (RMR) normalized for fat free mass. Resting metabolic rate is the energy required by the body in resting conditions [101]. The relationship between RMR and feelings of energy appear to be complex. There is evidence that hormones, such as thyroxine, can dramatically impact RMR and act on the brain and influence feelings of energy [51-53]. In contrast, studies show that caloric restriction reduces RMR but has no significant effect on feelings of energy [102]. Interestingly, Woods and colleagues [5455] noted declines in RMR, when normalized for fat free mass, as well as increased fatigue (without change in energy) during an overtraining protocol. It should be noted that feelings of energy were trending positively in both those studies [54,55]. Influence of leptin could underlie this observation as leptin is known to promote thermogenesis [103] and an increased secretion of this hormone is associated with psychological stress [104] . When fatigue and energy are measured on a bipolar scale, several studies examining patient populations have noted a positive relationship between serum leptin levels and fatigue severity [105-107]. Although our study did not measure thyroxine or leptin levels, our results warrant a closer examination of RMR on both energy and fatigue in healthy populations.

Another interesting finding in our study was the negative relationship between resting skeletal muscle oxygen saturation (mVO<sub>2</sub>) in the right lateral gastrocnemius and feelings of energy. To the best of the authors' knowledge there is no published research documenting the relationship between variations of mVO<sub>2</sub> at rest and feelings of fatigue and energy in healthy participants; however, multiple studies have found a relationship between cellular respiration dysfunction (i.e. mitochondrial disorders) and severity of symptoms in chronic fatigue syndrome [43-46]. Although our study examined healthy participants, it may be hypothesized that non-clinical deviations in mitochondrial function, i.e. the ability of the mitochondria to produce adenosine triphosphate (ATP), may be related to non-clinical variations in feelings of energy. This may be due to differences in ATP production by skeletal muscle mitochondria.

Lower resting mVO<sub>2</sub> may be the result of lower vascular tone or blood pressure which were not measured in the present study. It is plausible that the association between mVO2 and feelings of energy were mediated indirectly through processes that influence both the brain and skeletal muscle. For example, regular physical activity can reduce vascular tone and blood pressure as well as increase feelings of energy [108] . Since our study did not examine specific biomarkers and examined muscle O2 consumption, we may hypothesize that feelings of energy may be influenced by metabolism, energy production, protein transport, or mitochondrial morphology [46]. The studies reviewed by Filler and colleagues [46] examined patients with chronic fatigue syndrome and used fatigue measurements only. Our results warrant examining energy and fatigue as two separate constructs in healthy populations and perhaps even in patients with chronic fatigue syndrome.

#### Limitations

There were several limitations to this study including reliance on self-reported measures for physical activity and diet. Thus students can over-estimate their perceived physical activity compared to actual physical activity [109]. Prior studies, which used more precise measures of eating behavior, have found relationships between diet and these mood states [27,33,110]. Our analysis focused on overall sleep quality rather than the specific components of sleep quality. Information about the specific sleep components are presented in the supplementary section (see Tables A and B).

Based on the association indicating the influence of mitochondrial function on energy, the study could have benefited from a more nuanced measure of participation in physical activity to determine whether intensity [19], type of exercise [111] or duration [19] influences feelings of energy. Although we asked the participants to not consume alcohol, caffeine or nicotine 8 hrs prior to testing, we did not control their food intake prior to their lab visit, nor did we verify whether they followed our instructions such as by testing salivary caffeine level and/or blood alcohol content. These factors can influence measurement of RMR [112] and may have impacted the results of our study. Other limitations include a relatively small sample size and the cross-sectional design of the study.

Our findings imply that fatigue and energy are independent, yet overlapping moods where small lifestyle changes may promote improvements in fatigue, but improvements in feelings of energy may be more difficult. Changes in sleep habits, using a standing desk, and taking mental breaks on the weekends could promote improvements in feelings of fatigue. Improvements in energy will be more difficult because there is no evidencebased method to increase muscle oxygen saturation. An increase in RMR would require an increase in fat-free mass (the primary determinant of RMR) such as from a regular strength training program, and improvements in sleep. RMR and muscle oxygen saturation combined are less strongly related to energy (23% of the variance accounted for) than sleep, sitting and non-school day mental workload (46% of the variance) are to fatigue. Our findings potentially have the strongest implications for health science students and replication of the study would provide stronger evidence and provide information about the generalizability of the findings.

#### **Conclusion**

The purpose of this study was to identify factors predicting feelings of energy and fatigue while simultaneously examining multiple domains related to these mood states. The results of our study indicate that sleep quality, intensity of mental work on non-school



days and sedentary behavior are predictors of fatigue while energy was predicted by resting metabolic rate, resting skeletal muscle oxygen saturation, sustained attention and sleep quality. These variables predicted fatigue better than energy, and this study provided potential new insight into a multi-variable approach to predicting energy and fatique moods.

#### **Disclosure statement**

No potential conflict of interest was reported by the authors.

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