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### Mechanisms of fatigue: Determinants of observational effort judgement of exercising individuals

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PRIFYSGOL  
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UNIVERSITY

**Thesis for the degree of Masters by Research (MSc Res)**

**Mechanisms of fatigue: Determinants of observational effort  
judgement of exercising individuals**

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July 2023

## DECLARATION

'I hereby declare that this thesis is the results of my own investigations, except where otherwise stated. All other sources are acknowledged by bibliographic references. This work has not previously been accepted in substance for any degree and is not being concurrently submitted in candidature for any degree unless, as agreed by the University, for approved dual awards.'

I confirm that I am submitting the work with the agreement of my Supervisor(s)'

'Yr wyf drwy hyn yn datgan mai canlyniad fy ymchwil fy hun yw'r thesis hwn, ac eithrio lle nodir yn wahanol. Caiff ffynonellau eraill eu cydnabod gan droednodiadau yn rhoi cyfeiriadau eglur. Nid yw sylwedd y gwaith hwn wedi cael ei dderbyn o'r blaen ar gyfer unrhyw radd, ac nid yw'n cael ei gyflwyno ar yr un pryd mewn ymgeisiaeth am unrhyw radd oni bai ei fod, fel y cytunwyd gan y Brifysgol, am gymwysterau deuol cymeradwy.'

Rwy'n cadarnhau fy mod yn cyflwyno'r gwaith gyda chytundeb fy Ngrichwylwr (Goruchwylwr)'

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## ABSTRACT

**Background:** Fatigue is a hugely common problem and symptom amongst patients in numerous chronic disease states. It negatively impacts patients' quality of life and subsequently has a major social and economic burden. A crucial concept of better understanding fatigue is the perception of effort. Perception of effort can be measured using the Rating of Perceived Exertion (RPE) scale. Fatigue sufferers have a generally higher perception of effort. We can say that their world is a "higher effort world" whereby general tasks and activities require more effort. Reasons for this elevation of effort are not clear, however learning processes are suggested. If learning is part of the causes of elevated fatigue, then it is also likely that prediction of higher effort for actions extends to observation of actions i.e. 'spill over'. **Aims:** Our first aim was to see if individuals can predict effort using RPE through observation alone. If this was possible, our second aim was to investigate how fatigue levels in patients influence this observational predictive capability and whether they have a prediction bias. **Hypotheses:** We propose that observer RPE (scores given by participants) and observed RPE (scores given by exercising subjects) will be strongly correlated in the patient and healthy participant groups. We also hypothesise that patients will have a significantly higher bias for observational RPE than healthy participants. **Methods:** Two online studies were designed whereby a patient group with fatigue symptoms (n=49) and a healthy group (n=74) were shown a series of videos of individuals with variable fitness levels exercising on a treadmill at different speeds (4km/h; 8km/h; 10km/h; 12km/h; 14km/h) and asked to rate the effort they felt the individuals were exerting using the Rating of Perceived Exertion (RPE) scale. The two groups were also shown an image of a flight of stairs and asked to rate the effort they feel they would need to exert using the RPE scale. Bias was calculated by subtracting observed RPE from the observer RPE. **Results:** Observer and observed RPE had a strong positive correlation amongst both healthy ( $\rho(1848) = .74, p < .001$ ), and patient ( $\rho(1223) = .68, p < .001$ ) participants. The patient group had a significantly higher prediction bias for higher RPE, which we found to be influenced by their own characteristics and fatigue levels. **Conclusions:** Findings indicate that observational judgment of RPE is a measurable outcome. Higher prediction bias for higher effort observed in patients was mainly influenced by their own characteristics rather than cues from the observed characteristics in the videos suggesting learning processes

secondary to own experiences. This potentially helps improve our understanding of the possible mechanisms behind the persistent nature of fatigue

## CONTENTS PAGE

Declaration.....	1
Acknowledgments.....	2
Thesis Abstract.....	3
1.0 Introduction.....	7
1.1 Biological mechanisms of fatigue.....	8
1.1.1 Central versus peripheral fatigue.....	9
1.1.2 Exercise induced versus pathological fatigue .....	10
1.2 Psychological mechanisms of fatigue.....	13
1.3 Effort perception.....	15
1.4 Linking effort perception and fatigue: context to thesis.....	17
2.0 Aim and hypotheses.....	19
2.1 Aim of study.....	19
2.2 Proposed hypotheses.....	19
3.0 Methods.....	20
3.1 Participants.....	20
3.2 Survey design.....	20
3.3 Procedures and preparation of video recordings.....	21
3.4 Measurements .....	23
4.0 Analysis.....	27
5.0 Results.....	28
5.1 Demographic data and body characteristics.....	28
5.2 Medical conditions and characteristics of the patient group.....	29
5.3 Outcome measures from questionnaires and imagined stair task .....	31
5.4 Correlation analysis .....	32
5.5 Multiple regression analysis .....	37
6.0 Discussion.....	45
6.1 Key findings .....	45
6.2 Interpretations.....	45
6.3 Limitations.....	47
6.4 Future Research .....	47
7.0 Conclusions .....	48
References.. ..	49
Appendix.....	56

## LIST OF FIGURES

<b>Figure 1</b>	Borg 15-point Rating of Perceived Exertion (RPE) scale	Page 16
<b>Figure 2</b>	Schematic of online survey design (healthy and patient group)	Page 21
<b>Figure 3</b>	Example display of video recordings in the survey (face and body side view of the volunteers during treadmill sessions)	Page 26
<b>Figure 4</b>	Slider function for RPE selection used in the online survey	Page 26
<b>Figure 5</b>	Image of flight of stairs used in the imagined stair task	Page 27
<b>Figure 6</b>	Graph showing the correlation between observed RPE and observer RPE in both healthy and patient participant groups	Page 33
<b>Figure 7</b>	Graph showing the correlation between RPE bias and observed RPE in both healthy and patient participant groups	Page 34
<b>Figure 8</b>	Graph showing the correlation between speed (km/h) and RPE bias of both healthy and patient groups	Page 35
<b>Figure 9</b>	Q-Q plot of RPE bias for healthy group	Page 37
<b>Figure 10</b>	Q-Q plot of RPE bias for patient group	Page 38



## LIST OF TABLES

<b>Table 1</b>	Physical characteristics (age, sex, ethnicity) of volunteers in video recordings, RPE scoring and RHR at each speed (4km/h, 8km/h, 10km/h, 12km/h, 14km/h), average HR per speed	Page 22
<b>Table 2</b>	Physical data and body characteristics of the healthy and patient group	Page 29
<b>Table 3</b>	Distribution of medical conditions in the patient group, including years since diagnosis, years of fatigue and the average FAS and LADLs; normally distributed data, averages displayed as mean and standard deviation	Page 30
<b>Table 4</b>	Distribution of medical conditions in the patient group, including years since diagnosis, years of fatigue and the average LADLs; non-normally distributed data, averages displayed as median and percentiles	Page 30
<b>Table 5</b>	Outcome measures from questionnaires and imagined stair task	Page 32
<b>Table 6</b>	Average observed RPE score (displayed as median) and RPE bias scores of the healthy and patient groups	Page 36
<b>Table 7</b>	Linear multiple regression analysis between dependent variables and RPE bias in the healthy group	Page 40
<b>Table 8</b>	Linear multiple regression analysis between dependent variables and RPE bias in the patient group	Page 41
<b>Table 9</b>	Linear multiple regression analysis between dependent variables and Observer RPE in the healthy group	Page 43
<b>Table 10</b>	Linear multiple regression analysis between dependent variables and Observer RPE in the patient group	Page 44

## 1.0 Introduction

Fatigue is a persistent and debilitating sense of exhaustion that negatively impacts daily functions, activities, and tasks (Matura et al., 2018). It is a common symptom experienced in many chronic illnesses, such as chronic obstructive pulmonary disease (COPD), cancer, chronic kidney disease (CKD), heart failure (HF), multiple sclerosis (MS), and numerous rheumatological disorders. Chronic fatigue syndrome (CFS) or Myalgic Encephalomyelitis (ME) is defined as fatigue exceeding 6 months without a demonstrable organic pathology (M. P. Davis et al., 2010). The consequences of fatigue can be severe enough to lead to social withdrawal, work disability, family conflicts, and a general decrease in quality of life (McElhone et al., 2016). Fatigue is also persistent in some patient groups extending beyond disease activity (Walter et al., 2018). Considering the heavy personal impact and economic burden of fatigue, a better understanding of its mechanisms is crucial to prioritise finding effective treatments and thus improving patients' quality of life. One avenue for exploring mechanisms of fatigue is improving the understanding of effort perception. Fatigue sufferers have a generally higher perception of effort, whereby general tasks and activities require more effort (Iodice et al., 2017). The reasons for this elevation of effort are not clear however, learning processes are suggested. If learning is part of the causes of elevated fatigue, then it is also likely that the prediction of higher effort for actions extends to observation of actions.

### *1.1. Biological mechanisms of fatigue*

Fatigue is a complex phenomenon that can be understood broadly as having both peripheral and central mechanisms, which are at interplay with each other (Lambert et al., 2005). In the literature, peripheral fatigue refers to the processes at or distal to the neuromuscular junction (Tornero-Aguilera et al., 2022). Central fatigue is attributed to the physiological processes within the central nervous system (CNS). Simultaneously, it is also important to differentiate between exercise-induced (i.e. exertional or transient) fatigue and pathological (i.e. disease-induced, prolonged or chronic) fatigue as a separation currently exists between the two in their respective research fields (Greenhouse-Tucknott et al., 2022). This section will focus on summarising the key proposed biological mechanisms

of fatigue through the lens of these sub-definitions: central versus peripheral fatigue, and exercise-induced versus pathological fatigue.

### 1.1.1. *Central versus peripheral fatigue*

#### Central fatigue

Central fatigue can be described as “the failure to initiate and/or sustain attentional tasks and physical activities requiring self-motivation” (Chaudhuri & Behan, 2000). Central fatigue mechanisms are divided into spinal and supraspinal. Proposed central causes of fatiguability include; recruitment of high threshold motor units, a reduction in central drive as a result of increased inhibitory interneuron input to the motor cortex, central conduction block from motor neuron dropout, and afferent inhibition from types III and IV sensory neurons (M. P. Davis et al., 2010; Sharpe & Wilks, 2002).

Key to the central fatigue hypothesis is the influence of central monoamines – in particular, serotonin (5-HT), dopamine (DA), and catecholamines (NA) (Meeusen et al., 2007). Researchers in 1987, first proposed that higher brain serotonergic activity during exercise leads to loss of neural drive and subsequently less motor unit recruitment (Meeusen et al., 2007). This original central fatigue hypothesis was revised in 1997 to recognise the synchronous role of dopamine; researchers suggested that a higher ratio of 5-HT to DA is associated with a quicker onset of fatigue symptoms, whereas a lower ratio was associated with better physical performance (J. M. Davis & Bailey, 1997; Meeusen et al., 2012). A group of researchers further included the role of noradrenaline in supraspinal fatigue when noticing a decrease in cycling performance in a group of well-trained men after ingesting a noradrenaline reuptake inhibitor (Klass et al., 2012). Central fatigue is now thought to be an interplay of all these neurotransmitters, with dopamine and noradrenaline being the main players (Connell et al., 2017).

#### Peripheral fatigue

Peripheral or muscle fatigue can be described as progressive loss of maximal voluntary contraction (MVC) during a task (M. P. Davis et al., 2010). Allen et al proposed that this force reduction is split into two phases (Allen et al., 2008). The earlier, shorter phase is caused by increased concentrations of inorganic phosphate ( $P_i$ ) (Allen et al., 2008). Higher  $P_i$

concentrations and poor muscle function have been linked in multiple studies, for example, one study highlighted a significant inverse relationship between resting Pi levels and force generation in a group of patients following cast immobilisation (Pathare et al., 2005). The second, more predominant phase is attributed to impaired calcium activity, including impaired calcium release from the sarcoplasmic reticulum, impaired reuptake of calcium, and reduced calcium sensitivity of the contractile units (Allen et al., 2008; Kent-Braun, 1999). Other recognised mechanisms in the literature include: loss of electrical conduction from the muscle membrane to tubule systems and an impairment of the interaction between actin and myosin during cross-bridge cycling (M. P. Davis et al., 2010).

### *1.1.2. Exercise-induced versus pathological fatigue*

#### Exercise-induced fatigue

Non-pathological or acute fatigue is a well-recognised phenomenon in sports competition. It is defined as an acute impairment in performance or in the ability to generate force secondary to exercise (Wan et al., 2017). Both central and peripheral mechanisms influence it (Ma et al., 2018). An eventual reduction in motor neuron firing rates is observed during exercise secondary to the following reasons: lower excitatory drive from the motor cortex, reduced excitability of motor neurons due to repeated activation, and decreased firing of motor neurons due to increased firing of group III/IV muscle afferents (Luc Darques et al., 1998; Taylor et al., 2016). Studies suggest that these processes hasten during prolonged exercise secondary to higher noradrenergic neurotransmitter system, which also corresponds with a larger increase in the rating of perceived exertion (Connell et al., 2017).

#### Pathological fatigue

Stephan et al. use the metacognitive theory of dyshomeostasis to define pathological fatigue (Stephan et al., 2016). They state that disease-induced fatigue arises as a result of a mismatch between prior cognitive predictions and the ascending sensory evidence, which undermines the individuals' control mastery and self-efficacy over precision beliefs, resulting in the phenomenological experience of fatigue. Recently, Greenhouse-Tucknott et al proposed that this loss of confidence in control predictions in response to repeated

prediction errors is a common foundation for fatigue in health and disease (Greenhouse-Tucknott et al., 2022). Research on biological mechanisms of fatigue tend to investigate separate disease pictures, with the greatest focus in the literature being cancer-related fatigue (Matura et al., 2018). The key biological changes in various chronic disease states that appear to be associated with fatigue are: (i) inflammation; (ii) hypothalamic-pituitary-adrenal (HPA) axis dysregulation and (iii) activation of the autonomic nervous system (Bower, 2014a). These mechanisms can also activate each other, for example, sympathetic nervous activation leads to a pro-inflammatory response (Pongratz & Straub, 2014). Other biological features to be discussed include, (iv) sleep and (v) cardiorespiratory fitness (Bower, 2014b).

- i) *Inflammation.* The link between inflammation and fatigue levels is widely reported. Inflammation is a key part of immune function, which is exaggerated in many disease states (Louati & Berenbaum, 2015). Patients with ovarian carcinoma were found to have raised levels of interleukin-6 (IL-6), which were associated with fatigue (Lutgendorf et al., 2008). Investigators also found fatigue levels to be associated with IL-6 levels in breast cancer patients undergoing chemotherapy (Bower, 2014b). One study investigating the link between inflammatory markers and fatigue in COPD only found a link with raised levels of TNF-alpha (not CRP or IL-6) (Al-Shair et al., 2011). However, this link between inflammation and fatigue is not always consistent in the literature. For example, Giovannani et al concluded that there was no association between self-reported fatigue levels and markers of systemic inflammation in multiple sclerosis (Giovannoni, 2006) . Furthermore, RA-related fatigue has an inconsistent relationship with inflammatory activity (measured by erythrocyte sedimentation rates (ESR), c-reactive protein (CRP), number of swollen/tender joints and disease activity score (Matura et al., 2018). Fatigue can also be persistent in disease states when inflammation levels are low, for instance, in one study, fatigue was persistent in a group of RA patients after a year of strict treatment protocol and the main predictors of fatigue levels were baseline fatigue and depression levels (Walter et al., 2018).
- ii) *Hypothalamic-pituitary-adrenal axis.* Various studies investigating fatigue have also reported dysregulation of the HPA axis (Bower, 2014b). In MS patients, one

study observed that lower waking cortisol and higher post-awakening cortisol were linked to higher levels of self-reported fatigue (Powell et al., 2015). Several studies have suggested that the HPA axis is underactive in patients with chronic fatigue syndrome and fibromyalgia syndrome (Tanriverdi et al., 2007). For example, Ottenweller et al compared ACTH levels between 20 CFS patients and 15 sedentary controls, finding similar baseline levels but lower ACTH response in CFS patients after exercise (Ottenweller et al., 2001). Cleare et al. suggested that low cortisol levels found in CFS patients could result from reduced adrenal gland activity (Cleare et al., 2004). However other studies show contradictory results, for instance, Jerjes et al found that urinary-free cortisol and cortisone concentrations had a normal diurnal pattern in CFS patients with no difference compared to controls (Jerjes et al., 2006). Furthermore, the conclusion of three randomized placebo-controlled trials using low-dose hydrocortisone treatment and combination therapy with fludrocortisone, is that steroids are not the treatment of choice for CFS (Tanriverdi et al., 2007).

- iii) *Autonomic nervous system.* Fagundes et al, investigated fatigue in breast cancer patients and found that higher fatigue levels correlated with elevated noradrenaline levels, reflecting higher sympathetic activity (Fagundes et al., 2011). One study investigating MS found higher vagal (parasympathetic) activity in patients who reported fatigue compared to those who did not (Keselbrener et al., 2000). Another study posited a positive association between impaired autonomic activity and fatigue in patients with end-stage renal disease compared to healthy individuals (Fujii et al., 2013). No studies have investigated the link between fatigue and the autonomic nervous system in HF, RA and COPD (Matura et al., 2018). Autonomic dysfunction in ME/CFS is described as “sympathetic nervous system predominance” (Martínez-Martínez et al., 2014). Meeus et al used heart rate variability (HRV) as a marker of the relative sympathetic and parasympathetic activity and found that CFS patients had reduced HRV and increased sympathetic activity at night (Meeus et al., 2013).
- iv) *Sleep.* There is a recognised link between biologically disturbed sleep and fatigue, whether experimentally induced, self-imposed, or as a result of a primary sleep disorder (Mariman et al., 2013). However, the link is not fully understood.

Unrefreshing sleep is a prominent feature in CFS however, in the Wichita CFS surveillance study, researchers could not demonstrate a significant difference in sleep architecture, using polysomnography, when comparing a group of CFS patients with self-reported sleep problems and healthy subjects (Reeves et al., 2006).

- v) *Cardiorespiratory fitness, physical activity, and BMI.* One of the hallmark features of fatigue is a reduction in overall physical activity. Wouters et al evaluated how physical activity levels in 300 patients with primary Sjögren's syndrome were associated with their fatigue levels, compared to 100 demographically matched controls (Wouters et al., 2012). They observed that the patient group had higher fatigue scores ( $p < 0.001$ ) and lower physical activity scores ( $p < 0.001$ ) when compared to the control subjects. A meta-analysis of five randomised control trials looking at the effect of an aerobic exercise training program on fatigue levels in rheumatoid arthritis patients concluded that an exercise program was effective in improving fatigue levels, but only in the short term (Rongen-Van Dartel et al., 2015). Obesity has been recognised as a predictor of fatigue in some inflammatory conditions, such as RA and SLE (Feldthusen et al., 2016; Oeser et al., 2005). Some potential explanations include mitochondrial dysfunction in skeletal muscles, an altered state of energy distribution and a higher inflammatory burden due to oxidative stress (Davies et al., 2021; Osborn & Olefsky, 2012). However, it is important to remember that the relationship between high BMI and fatigue remains multifactorial as obesity is strongly linked to many determinants of health such as an individual's behaviours and socio-economic and physical environment (Davies et al., 2021).

## 1.2 Psychological mechanisms

### Mood disturbances

Fatigue and mood disturbances such as anxiety, stress and depression commonly co-occur in many diseases states (Vassend et al., 2018). It is important to note that fatigue is included in the DSM-5 diagnostic criteria for depression (Uher et al., 2014). As fatigue is a reported symptom in 90% of patients with major depressive disorder, fatigue and

depression may share a mechanistic pathway (Ghanean et al., 2018). One possible shared pathophysiological pathway is inflammation. Similar to findings in fatigued patients, an increased level of pro-inflammatory cytokines and microglial activation in the brain has been observed in depressed patients (Bårdsen et al., 2016). Kallaur et al concluded that in MS, the manifestation of depression is driven by circulating peripheral pro-inflammatory markers (Kallaur et al., 2016). However, further studies examining if this inflammation is also concurrently linked to fatigue have produced inconsistent results (Ormstad et al., 2020). It is pertinent to remember that the co-occurrent nature of fatigue and mood disturbances can also be explained by social factors and consequent health behaviours (Gold et al., 2020).

### Sickness behaviour model

Sickness behaviour is an evolutionary conceptual model that describes changes in behaviour, such as depressive mood, social withdrawal, and fatigue during infection and inflammation (Omdal et al., 2021). Many animal studies have highlighted the key role of IL-1beta signalling in the pathway of sickness behaviour (Dantzer et al., 2008). In disease states of chronic inflammation, these temporary pathways become continuously active due to persistent signalling, driving chronic fatigue. Human studies in RA patients looking at IL-1beta blockade, using the anti-inflammatory drug Anakinra, demonstrated a substantial decrease in fatigue symptoms (Omdal & Gunnarsson, 2005).

### The conscious perception of fatigue

Gibson et al. describe fatigue as a conscious sensation and emotional construct rather than a physiological sensation (St et al., 2003). They argue that the consciousness-producing areas of the brain sense fatigue due to the difference between the subconscious representation of the baseline physiological state and the physiological activity induced by physical activity. The subconscious element is dictated by previous experiences and memory of fatigue, which allows one to estimate their reserve levels, therefore, allowing decision-making on whether to continue the physical activity. The interaction between working memory and long-term memory occurs in the pre-frontal cortex, therefore the origin of the conscious perception of fatigue is postulated to arise from these prefrontal cortical systems (Miller, 2000; St et al., 2003).



Damasio and Parvizi put forward a theoretical framework of the subconscious ‘proto-self’ to describe how conscious perception develops, which can be used to understand how the sensation of fatigue arises (Parvizi & Damasio, 2001). The theory suggests that the proto-self arises from a series of neural patterns that map out the physiological changes associated with emotions manifesting as “feelings” through our conscious response to these changes. When changes occur in the external or the internal physiological environment, they are compared to this original “homeostatic” proto-self to create a subconscious mental image. This secondary subconscious image can only indicate to the consciousness that a change has occurred by inducing a “feeling” or emotion; if the feeling is negative, for example, fatigue, it will likely lead to avoidant behaviour.

### *1.3 Perception of exertion and effort*

Perceived “effort” and “exertion” are important regulators of human physical activity and although related constructs, can be defined separately (Hutchinson & Tenenbaum, 2019). Perception of exertion was recognised as early as 1894 by the French philosopher, Guillauma Ferrero and later defined in 1962 by Gunnar Borg as “the feeling of how heavy, strenuous and laborious exercise is” (Pageaux, 2016). The Borg Rating of Perceived Exertion (RPE) scale is validated as a numerical scale for perceived effort as shown in Figure 1 (G. Borg, 1990). In contrast, perception of effort, or sense of effort, is defined as the “amount of mental or physical energy being given to a task” (Preston et al., 2009). The distinction is that perceived exertion integrates peripheral feedback from the body whilst exercising whereas perceived effort relies primarily on central feedback (Hutchinson & Tenenbaum, 2019).

Figure 1. Borg 15-point Rating of Perceived Exertion (RPE) scale (G. Borg, 1990)

<b>Rating</b>	<b>Perceived exertion</b>
6	No exertion
7	Extremely light
8	
9	Very Light
10	
11	Light
12	
13	Somewhat hard
14	
15	Hard
16	
17	Very hard
18	
19	Extremely hard
20	Maximal exertion

The neurophysiology of effort perception is not extensively researched leaving much to debate. There are three different models; (i) the afferent feedback model; (ii) the corollary discharge model; (iii) the combined model (Pageaux, 2016).

- i. The afferent feedback model postulates that the neuronal process of effort perception is driven by afferent feedback from working muscles (Pageaux, 2016). This argument is based on an increase in the perception of effort as lactate and metabolite concentrations in the blood increase (Noble, 1982). In particular, it has been hypothesized that group III-IV muscle afferent signals, which have projections to the sensory cortex, are involved in generating of perception of effort (Craig, 2002). However, these observations are not replicated in a further study where an injection of physiological concentrations of metabolites is used (Pollak et al., 2014) . Borg conceptualised this in his early work as a gestalt phenomenon combining peripheral feedback from muscles as well as feedback from other sites such as the cardiovascular and respiratory systems (G. Borg, 1990).
- ii. The corollary discharge model suggests that effort perception arises from central motor commands (Marcora, 2009). Zenon et al demonstrated that continuous

theta-burst stimulation disrupting the supplementary motor led to a higher perception of effort (Zénon et al., 2015). An increase in effort was observed by Kjaer et al., during a cycling exercise, by using epidural anaesthesia to reduce afferent feedback (Kjær et al., 1999).

- iii. The combined model postulates that perceived effort is an assimilation of both afferent feedback and corollary discharge, however this model has not been tested in studies (Amann et al., 2010).

#### *1.4 Linking effort perception and fatigue: context to Thesis*

There is a link between perceiving a task to be effortful and the experience of fatigue (Iodice et al., 2017). Kahneman's "resource capacity theory" suggests that the effort required to perform a task is dictated by both task complexity and the individual's general capacity to perform the task (i.e. resource capacity) (Sarà et al., 2019). If the demand for resources is high and as a result, the individual recognises that performance suffers, then the task is perceived as effortful. Repetitively perceiving tasks to be more effortful manifests as the sensation of fatigue, which theoretically can become a learned phenomenon.

A similar concept is the affordance theory. Gibson et al define the perception of affordance as one's ability to perceive what is offered by the environment, concerning a task, relative to their own abilities (Seifert et al., 2018). A critical study led by Warren et. al in 1984 investigated the visual perception of stair climbing using a 'body-scaled' metric (Warren, 1984a). Two groups (a tall group and a short group) were presented with stairs of varying heights to determine their perceptual critical point i.e. the transition point in behaviour of an affordance behaviour, in this case, the boundary between "climbable" and "unclimbable" stair risers. These critical points, or boundaries, were found to be at a riser height in proportion to their leg length across the two groups. Konczak et al further added that this critical point differed in older adults due to reduced strength and joint flexibility (Konczak et al., 1992). These findings indicate that affordance is intrinsically regulated between the observer and their environment.

This integration between the visual environment and perception is also explored by the Rubber Hand Illusion (RHI) (Costantini & Haggard, 2007). This was first experimentally reported in 1998 by Botvinick and Cohen (Botvinick & Cohen, 1998). They observed that

when they stroked a rubber hand placed in front of a subject and stroked their real hand which was hidden out of their sight, the subjects started to feel the rubber hand as their own. This demonstrates how visual and tactile feedback influences subjective experiences, which speaks to our area of interest; the visual perception of effort (Pazzaglia et al., 2019). There are observations that the perception of effort is elevated in disease states. In a study looking at post-stroke fatigue, investigators found a significant relationship between fatigue levels and perceived effort (De Doncker et al., 2020). In another study, Solomon et al concluded that patients with fatigue in Parkinson's disease had a higher sense of effort during handgrip and tongue elevation tasks compared to a neurologically matched normal control group (Solomon & Robin, 2005).

Perception of effort is also increasingly used in the prescription of individualised rehabilitation for patients (Pageaux, 2016). Any decrease in effort perception should improve physical performance, which is a potentially highly relevant concept in clinical practice; manipulating effort perception could have long-term benefits for patients.

There is also mounting literature to suggest that there is a learned component to fatigue. Fatigue and its precursors shape a threatening and negative mental representation and thus becomes learned as an undesirable experience, leading to fear-related avoidant behaviour (Lenaert et al., 2018). For example, a series of studies measured stair-climbing performance in patients with chronic fatigue after asking them to rate their anticipated fatigue; higher levels of anticipated fatigue predicted poorer stair-climbing performance (Heins et al., 2013; Nijs et al., 2012). Other studies propose evidence for perceptual-cognitive biases in fatigue. For example, Hou et al demonstrated through a visual probe experiment, that patients with CFS had an attentional bias towards 'health-threat stimuli' compared to non-threatening stimuli, and this bias was not replicated in the healthy control group (Hou et al., 2008). There is also mounting literature to suggest that fatigue sensations can become a conditioned response to stimuli or precursors that were previously associated with the experience of fatigue (Lenaert et al., 2018). Ishii et al. were able to observe this through acoustic stimuli, where subjects were exposed to the sound of a metronome whilst performing a mentally fatigue-inducing task and showed increased fatigue levels when this was repeated on the next day compared to the control group who were not exposed to the acoustic stimulus (Ishii et al., 2013).

From the above studies, we can appreciate that patients who suffer from fatigue have a higher perception of effort. We can even say that their world is a “higher effort world”, where general tasks and activities require more effort through their eyes. Having this bias towards fatigue due to their own experiences and sensations can potentially spill over to any observations of the world around them. Therefore in this study, we aim to investigate observational effort perception and judgement of others and imagined tasks, rather than self-judgment of effort whilst exercising. If we were to ask fatigued patients to rate their effort during exercise, this would only tell us that they have higher effort, which is known (Lea et al., 2022). This would not enable us to evaluate if there is a change of perception. If the brain is predicting individual tasks to be more effortful, this will accumulate and spill over, changing one’s world to a “higher effort world”.

## **2.0 Aim and Hypotheses**

### *2.1 Aim*

The primary aim of this study is to investigate psycho-physiological influences on the ability of people to judge someone’s exercise effort level. Firstly, we aim to see if individuals can predict RPE through observation. If so, we then aim to examine how fatigue levels in patients influence this observational predictive capability and whether they have a prediction bias (by subtracting observed RPE from the observer RPE) .

### *2.2 Proposed Hypotheses*

- i) We predict that observer RPE and observed RPE will be strongly correlated in both patients and healthy participant groups.
- ii) We hypothesise that patients with fatigue will have a significantly higher bias for observational RPE than healthy participants. Any prediction bias in patients will also correlate with higher stair RPE.

### **3.0 Methods**

#### *Ethical Approval*

This study was ethically approved by the Ethics Committee of School of Human and Behavioural Sciences at Bangor University (ethics number for first study: 2021-17055, second study: 2022-17197).

#### *3.1 Participants*

A total of 123 participants were recruited. 74 healthy participants were recruited (individuals who do not suffer from pathological fatigue or any chronic illnesses) and 49 patient participants (individuals who suffer from pathological fatigue secondary to a chronic illness). The healthy group participants were recruited from the student population of Bangor University through online and paper advertisements and from the general public using social media advertisements. The patient group participants were recruited via social media advertisements through self-help groups on Facebook; these included patient support groups for sleep apnoea, chronic fatigue syndrome/myalgic encephomyelitis, rheumatoid arthritis, and long COVID.

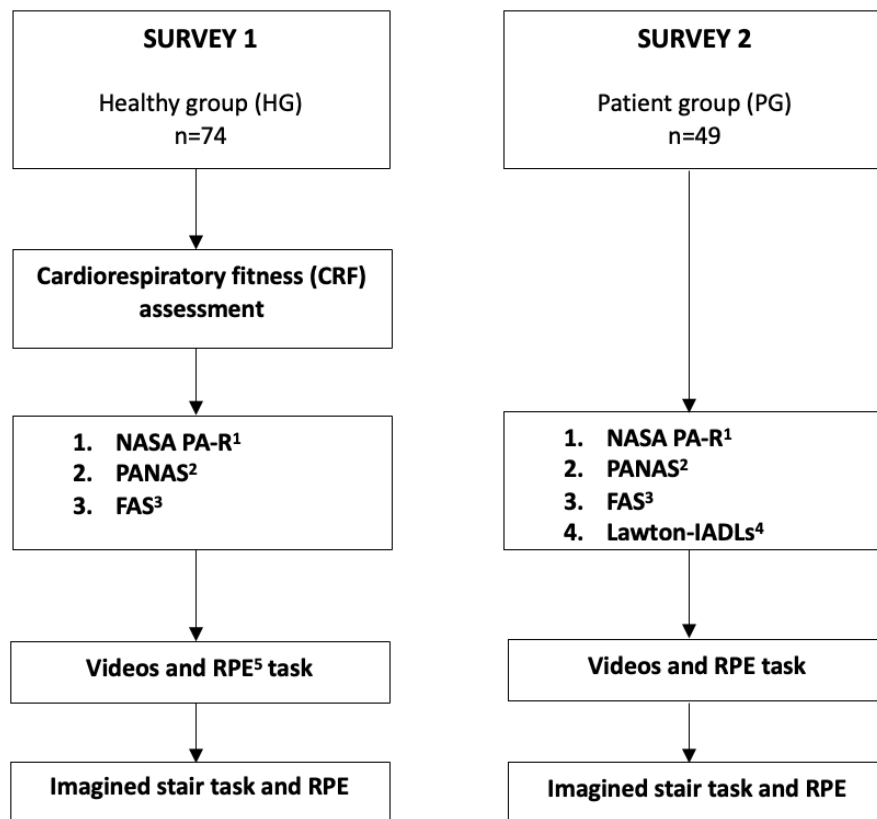
An external link to detailed study information was included in the advertisements using Qualtrics. The final page summarised essential participant study information (Appendix. 1). Those who agreed to participate clicked “I consent” as part of the informed consent process and were directly linked to their respective survey.

Participants in each group were offered entry into a prize draw to win an iPad.

#### *3.2 Survey design*

Two online surveys were designed using Qualtrics software; one for the healthy group and one for the patient group (Figure 2).

Figure 2. Schematic of online survey design (healthy and patient group)



- 
1. NASA PA-R (National Aeronautics and Space Administration physical activity rating)
  2. PANAS (Positive and Negative Affect Schedule)
  3. FAS (Fatigue Assessment Scale)
  4. Lawton-IADLs (Lawton-Brody Instrumental Activities of Daily Living Scale)
  5. RPE (Rating of Perceived Exertion)

### 3.3 Procedures and preparation of video recordings

Video recordings of exercising individuals were prepared. Five healthy volunteers were recruited from the university and filmed exercising on a treadmill at different speeds. These videos were then used in both surveys for the study participants to watch. The order of the videos of the five volunteers at different speeds was randomized to remove any order effect in the output data. The volunteers were filmed individually on separate days. The volunteers were asked to run on a treadmill at five different speeds for 3 minutes at each speed (4km/h; 8km/h; 10km/h; 12km/h; 14km/h). Their heart rate was monitored throughout and at each speed they were asked to rate their exertion using the Borg Rating of Perceived Exertion (RPE) scale (G. Borg, 1990) (Figure 1). Individual

characteristics (age, sex, ethnicity) of these volunteers including their RPE scoring and RHR at each speed are summarised in Table 1. We also calculated ‘HR per speed’ (increase in heart rate for every km/h) to get a measure of the volunteers’ cardiovascular fitness levels. Heart rates of the volunteers were recorded at each speed and these data points were used to plot a linear regression line for each volunteer via enter method on SPSS, which represented HR per speed.

Table 1. Physical characteristics (age, sex, ethnicity) of volunteers in video recordings, RPE scoring, and RHR at each speed (4km/h, 8km/h, 10km/h, 12km/h, 14km/h), average HR per speed

	<b>Volunteer 1</b>	<b>Volunteer 2</b>	<b>Volunteer 3</b>	<b>Volunteer 4</b>	<b>Volunteer 5</b>
<b>Age (years)</b>	25	42	59	25	23
<b>Sex</b>	Male	Male	Male	Female	Female
<b>Ethnicity</b>	White	White	White	Other (Arab)	White
<b>RPE (6-20)</b>					
<b>4km/h</b>	6	7	6	6	6
<b>8km/h</b>	8	9	8	10	7
<b>10km/h</b>	12	10	10	12	11
<b>12km/h</b>	14	12	12	16	14
<b>14km/h</b>	18	15	14	20	19
<b>RHR (bpm)</b>					
<b>4km/h</b>	87	80	64	100	95
<b>8km/h</b>	150	128	111	162	143
<b>10km/h</b>	175	157	125	174	162
<b>12km/h</b>	193	169	138	189	178
<b>14km/h</b>	201	180	150	195	189
<b>HR per speed (bpm)</b>	49.24	44.27	35.67	72.87	62.13



The study was entirely remote for the participants completing the survey, no travel was required.

Three 3-minute breaks were offered during the patient group survey to minimise any effects of potential cognitive fatigue from the already 'fatigued' participants in the patient group.

### *3.4 Measurements*

#### *Demographic and Body Characteristics*

Participants in both groups were asked to enter their age, sex, ethnicity, height, and weight (to calculate their body mass index – BMI). The patient group participants were further asked about which chronic disease(s) they suffered from, for how long they have had their diagnosis, and how long they have had problems with fatigue.

#### *Questionnaires*

1. The Positive and Negative Affect Schedule (PANAS) scale (Appendix .2). This is used to evaluate mood using two 10-item self-reported mood scales (Watson et al., 1988). The scoring is calculated using the sum of a scale (from very slightly or not at all – extremely) of 10 positive affect (excited, alert, interested, strong, enthusiastic, proud, inspired, determined, attentive, and active) scores and 10 negative affect (irritable, afraid, jittery, nervous, ashamed, hostile, scared, guilty, upset and distressed) scores. Higher total positive scores indicate a greater positive affect (PA), whilst lower total negative scores indicate a lower negative affect (NA). This scale is a strong valid measure in detecting general distress, depression, and anxiety and is viewed as being adequately reliable and internally consistent, with measurements by Cronbach's alpha for PA being 0.89 and for NA, 0.85 (Crawford & Henry, 2004).
2. The Fatigue Assessment Scale (FAS), (Appendix .3). This is a one-dimensional 10-item self-reported questionnaire, which evaluates symptoms of chronic fatigue levels (Michielsen et al., 2003a). Ten statements are provided that describe five physical and five mental difficulties surrounding fatigue, such as "I get tired very quickly", "mentally I feel exhausted" and "physically, I feel exhausted". Subjects choose from

a five-point response; “1=never”, “2=sometimes”, “3=regularly”, “4=often” or “5=always” leading to a total sum score between 10 and 50, reflecting the severity of their fatigue levels (< 22 indicates ‘normal’ fatigue levels; 22-34 indicates mild-moderate fatigue; >= 35 indicates severe fatigue)(De Vries et al., 2004). The total score can be subdivided into total ‘physical fatigue’ (physical impact of fatigue) score and total ‘mental fatigue’ (cognitive impact of fatigue) score. FAS has good internal consistency (Cronbach’s alpha 0.9) and is consistently considered the most reliable self-reported questionnaire in evaluating fatigue in patients with chronic diseases (Lookzadeh et al., 2018; Michielsen et al., 2003b)

3. National Aeronautics and Space Administration Physical Activity Rating (NASA PA-R) Scale (Appendix .4). NASA PA-R is used to rate physical activity status on a scale of 1-5 depending on how often the subjects engage in aerobic exercises; 1 is scored for little activity other than usual daily activities, 3 for aerobic exercise for 20-60 minutes per week and 5 for aerobic exercise for over 3 hours a week (Jurca, Jackson, LaMonte, Morrow, Blair, Wareham, Haskell, Van Mechelen, et al., 2005).
4. Lawton-Brody Instrumental Activities of Daily Living (IADL) scale, (Appendix .5). This is an eight-item questionnaire, which evaluates functional status and independent living skills (Graf, 2008). It is a scoring system that is used to score the independence levels of each of the following functional domains; ability to use a telephone, shopping, food preparation, housekeeping, laundry, mode of transportation, responsibility for own medications, and handling finances(Lawton & Brody, 1969). Competence of each domain is scored using descriptors of the subjects’ independent ability to perform each activity (for example, for shopping the following four competence levels are described: takes care of shopping needs independently; shops independently but only for small purchases; needs accompaniment and assistance on all shopping trips; cannot shop independently at all) (Fish, 2011). The total summary score ranges from 0 (dependent, low functional status) to 8 (independent, high functional status). It is the most commonly used scale for assessing the independence of activities of daily living in older adults (Isik et al., 2020). This questionnaire was only included in the patient group survey.

### *Cardiorespiratory fitness*

We assessed Cardiorespiratory fitness (CRF) in the healthy group without performing exercise testing using the methods described by Jurca, Jackson et al (Jurca, Jackson, LaMonte, Morrow, Blair, Wareham, Haskell, van Mechelen, et al., 2005). The variables we used were as follows; gender, age, BMI ( $\text{kg}/\text{m}^2$ , using self-reported height and weight), resting heart rate (RHR), and the National Aeronautics and Space Administration self-reported physical activity levels (NASA SR-PA). Resting heart rate was obtained using the 'Instant Heart Rate' application (<https://apps.apple.com/us/app/instant-heart-rate-hr-monitor/id409625068>), which participants were instructed to download on their mobile phones and guided on how to use during the survey. Before measuring their RHR, participants were asked to ensure they had not engaged in strenuous activity within an hour, nor consumed any caffeine within 2 hours, and to ensure a minimum 3-hour gap before their last meal.

### *Videos and RPE*

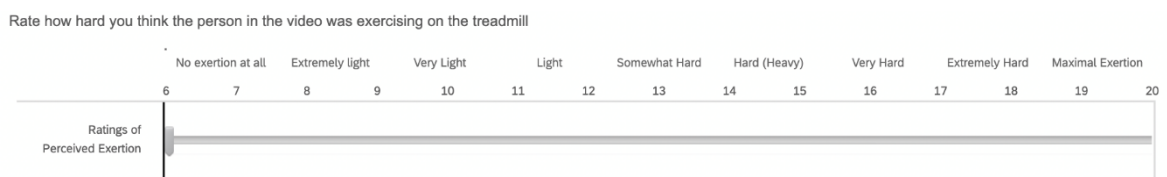
The last 30 seconds of the 3-minute videos of volunteers exercising at each of the 5 different speeds was used in the survey. The ideal length of the videos was tested in a pilot with healthy volunteers, where 15 seconds was required for judgment by healthy volunteers. An additional 15 seconds was therefore added to cater to patients with fatigue. The videos were grouped according to speed within the survey and the order of volunteers shown at each speed was randomly generated using the Qualtrics random selection feature. Each video recording of the volunteers included a front view of the face and a side view of their whole body (see Figure 3). Front view of the face was essential to observe facial expression as frowning muscle activity has been shown to reflect effort during physical tasks (de Morree & Marcora, 2010). The participants completing the survey watched each of these videos and were then asked to provide an RPE score to rate the effort they felt the individuals were exerting. The RPE score was rated using a slider function on their screen (see Figure 4). Throughout the thesis, 'observed RPE' and 'observer RPE' will be referred to; 'observed RPE' is the RPE given by the volunteers in the videos whereas 'observer RPE' is the RPE given by the healthy and patient group subjects watching the videos. Bias was calculated by subtracting the observed RPE from the observer RPE, in the following equation:

$$\text{Bias} = \text{Observer RPE} - \text{Observed RPE}$$

Figure 3. Example display of video recordings in the survey (face and body side view of the volunteers during treadmill sessions)



Figure 4. Slider function for RPE selection used in the online survey



### *Imagined stair task and RPE*

An imagined stair task was used to test affordance, similar in principle to the study led by Warren et. al (see section 1.4) (Warren, 1984a). Imagined exercise was also used by E.Borg to study the multi-dimensional character of perceived exertion in an important study resulting in adjustments to the Borg scale (E. Borg, 2007). In our study, an image of one flight of stairs consisting of 12 steps was shown at the end of the survey (Figure 5). We

asked the participants to imagine themselves walking up these steps and rate the exertion they would expect using the RPE slider scale.

Figure 5. Image of flight of stairs used in the imagined stair task



#### 4.0 Analysis

Statistical Package for the Social Science (IBM SPSS) version 27 was used for data analysis. The following outcome variables were tested using parametric testing e.g. independent t-test; BMI, FAS physical scores and RPE bias at 4km/h. Transformation of non-normally distributed data was not successful and so the remaining variables were analysed using non-parametric analysis e.g. Pearson's chi-squared test, Mann & Whitney U-test, and Kruskal-Wallis test. These included age, sex, ethnicity, NASA scores, PANAS scores, total FAS and mental FAS scores, and RPE bias at remaining speeds (8km/h, 10km/h, 12km/h, 14km/h). Effect size is reported as Eta squared. Multiple regression

analysis was performed using the enter method of selected parameters; observed characteristics were entered in the first block and observer characteristics were entered in the second block, as indicated in the results section. Based on the work published by Williams et al., use of multiple regression analysis was possible for our dataset as they met the following assumptions: (1) Zero conditional mean of errors; (2) Independence of errors; (3) Homoscedasticity of errors; (4) Normal distribution of errors (Williams et al., 2019). Correlation analysis was performed using Spearman's correlation analysis. Data is displayed as mean and standard deviation or as a median with 25 and 75 percentiles. Significance levels were reported as less than 0.05, 0.01 and 0.001.

## 5.0 Results

### 5.1 Demographic data and body characteristics

123 participants were recruited in total (healthy group, n=74; patient group, n=49). Physical data and body characteristics are presented in Table 2. The mean age for the healthy group was 33.40 years (SD = 13.31). The patient group on average was significantly older with a mean age of 52.27 years (SD = 14.83),  $U = 573.50$ ,  $p < 0.05$ . From the healthy group: 69% (n=51) were white British, 61% (n=67) were female and 39% (n=7) were male. From the patient group: 84% (n=41) were white British, 80% (n=39) were female and 20% (n=10) were male. Independent t-test revealed a significant effect for BMI between the two groups,  $t(109) = -3.235$ ,  $p < 0.05$ , with the patient group having higher BMIs (mean = 29.84 kg/m<sup>2</sup>, SD = 6.70) than the healthy group (mean = 25.73 kg/m<sup>2</sup>, SD = 6.43). The patient group also had lower NASA physical activity scores on average (mean = 1.49, SD = 0.82) than the healthy group participants (mean = 3.24, SD = 1.49); Pearson chi-square test showed a significant difference of NASA scores between the two groups,  $\chi^2(4) = 37.55$ ,  $p < 0.05$ .

Table 2. Physical data and body characteristics of the healthy and patient group

	Healthy ( <i>M</i> ± <i>SD</i> )	Patients ( <i>M</i> ± <i>SD</i> )
	<i>N</i> = 74	<i>N</i> = 49
<b>Age (years)</b>	33.40 ± 13.31	52.27 ± 14.83 <sup>†</sup>
<b>NASA</b>	3.24 ± 1.49	1.49 ± 0.82*
<b>Ethnicity</b>	(White British; n=51; 69%)	(White British; n=41; 84%) **
<b>Sex</b>	(Females n=67; 61%)	(Females n=39; 80%) ***
<b>Body Mass Index (kg/m<sup>2</sup>)</b>	25.73± 6.43	29.84± 6.70 <sup>††</sup>

NASA: Level of physical activity; range 1-5; 1-> little or no activity; 5-> Max level of activity

\*Pearson chi-square shows a significant difference between groups  $X^2(4) = 37.55 p < 0.05$

\*\*Pearson chi-square shows no significant difference between groups  $X^2(4) = 8.14 p = 0.08$

\*\*\* Pearson chi-square shows a significant difference between groups  $X^2(1) = 4.55 p < 0.05$

<sup>†</sup> Mann-Whitney *U* statistic (573.50) shows a significant difference between groups  $p < 0.05$

<sup>††</sup> An independent t-test shows a significant difference between groups  $t(109) = -3.235 p < 0.05$

### 5.2 Medical conditions and characteristics of the patient group

The most common medical diagnosis reported was ME/CFS (17 patients), followed by long COVID (13 patients). This was followed by OSA (5 patients) and RA (4 patients). The least commonly reported diagnoses were CKD (3 patients) and HF (1 patient). Long COVID patients had the highest FAS scores ( $M = 37.76$ ,  $SD = 7.03$ ), followed by ME/CFS patients ( $M = 37.41$ ,  $SD = 3.51$ ). Mean FAS scores for the remaining medical conditions are displayed in Table 3, alongside all other normally distributed results. Non-normally distributed results are shown in Table 4. The highest average LADL score was observed in OSA patients with a median score of 8 (maximum possible score). There was a large variation of years since diagnosis between the medical conditions; CKD patients had the highest average of years since diagnosis (median = 20 years) and Long Covid patients had the lowest average (median = 1 year). However, very similar averages of years of fatigue were reported in all medical conditions (RA ( $M = 2.75$ ,  $SD = 1.75$ ); OSA ( $M = 2.60$ ,  $SD = 0.89$ ); CKD ( $M = 2.33$ ,  $SD = 1.52$ ); HF (2.00), LCOVID (median = 2), ME/CFS (median = 3).

Table 3. Distribution of medical conditions in the patient group, including years since diagnosis, years of fatigue and the average FAS and LADLs; normally distributed data, averages displayed as mean and standard deviation

Condition	No of People	Years Post Diagnosis	Fatigue (Yrs.)	FAS	LADLS
		<i>M±SD</i>	<i>M±SD</i>	<i>M±SD</i>	<i>M±SD</i>
RA	4	9.75 ± 2.62	2.75 ± 1.75*	26.50 ± 4.12*	7.25 ± 0.95*
OSA	5	6.33 ± 4.16	2.60 ± 0.89*	25.80 ± 7.19*	-
CKD	3	-	2.33 ± 1.52*	33.00 ± 2.64*	-
HF	1	10.00	2.00	22.00	6.00
LCOVID	13	-	-	37.76 ± 7.03*	-
M.E/CFS	17	-	-	37.41 ± 3.51*	-

RA = Rheumatoid arthritis

OSA = Obstructive Sleep Apnoea

HF = Heart Failure

LCOVID = Long Covid

M.E/CFS = Myalgic Encephalomyelitis /Chronic Fatigue Syndrome

FAS = Fatigue Assessment Scale (> 22 (no fatigue); ≤ 22 (fatigue); ≤ 35 (severe fatigue))

LADLS = Lawton Activities of Daily Living (range from 0 (low function, dependent) to 8 (high function, independent))

\*Normal Distribution

- Non-parametric Distribution (median and percentile values are displayed in Table below)

Table 4. Distribution of medical conditions in the patient group, including years since diagnosis, years of fatigue and the average LADLs; non-normally distributed data, averages displayed as median and percentiles.

Years Post Diagnosis	Condition	No of People	Median	70 <sup>th</sup> Percentile
	CKD	3	20	20
	LCOVID	13	1	2.1
	M.E/CFS	17	4	6.2
Fatigue (Yrs.)	Condition	No of People		
	LCOVID	13	2	2.40
	M.E/CFS	17	3	3.20
LADLS	Condition	No of People		
	OSA	5	8	8
	CKD	3	7	7.40
	LCOVID	13	6	7
	M.E/CFS	17	7	7



### 5.3 Outcome measures from questionnaires and imagined stair task

A summary of these measures is presented in Table 5. Participants in the patient group had lower mood levels than the healthy group, reflected by their lower PANAS positive affect scores (patient group mean = 22.89, SD = 7.97; healthy group mean = 27.8, SD 7.84) and higher negative affect scores (patient group mean = 24.12, SD = 7.37; healthy group mean = 21.13, SD = 7.97). Mann-Whitney U-statistical testing showed a significant difference ( $U=1175.5$ ;  $p<0.05$ ) in the positive and negative affect scores between the two groups. The patient group had more severe fatigue levels with total FAS scores being higher (mean 34.08, SD = 8.95) than the healthy group (mean = 25.89, SD = 9.59); independent t-test showed a significant effect for the patient group having higher scores,  $t(121) = -4.764$ ,  $p < 0.05$ . There is a statistically significant difference between the FAS scores in the physical domain ( $t(119) = -5.646$ ,  $p < 0.05$ ), with the patient group ( $M=18.80$ , SD = 4.89) having higher mean scores than the healthy group (13.29, SD = 4.43). A Mann-Whitney U test also showed that the patient group ( $M= 15.23$ , SD = 4.65) scored higher than the healthy group ( $M= 12.59$ , SD = 4.72) in the mental domain of the FAS ( $U=1148.00$ ,  $p < 0.05$ ).

In the imagined stair task, Mann-Whitney U statistical test revealed a significant difference between the RPE ratings of both groups; participants in the patient group gave a higher RPE rating (mean = 13.53, SD = 3.11) than the participants in the healthy group (mean = 10.31, SD = 7.89), ( $U = 754.50$ ;  $p < 0.05$ ).

Table 5. Outcome measures from questionnaires and imagined stair task

	Healthy ( $M \pm SD$ )	Patients ( $M \pm SD$ )
<b>LADLS</b>	-	6.20 $\pm$ 1.65
<b>PANAS (Positive)</b>	27.81 $\pm$ 7.84	22.89 $\pm$ 7.97*
<b>PANAS (Negative)</b>	21.13 $\pm$ 7.97	24.14 $\pm$ 7.37**
<b>FAS (Total)</b>	25.89 $\pm$ 9.59	34.08 $\pm$ 8.95***
<b>FAS (Physical)</b>	13.29 $\pm$ 5.43	18.80 $\pm$ 4.89 <sup>†</sup>
<b>FAS (Mental)</b>	12.59 $\pm$ 4.72	15.23 $\pm$ 4.65 <sup>††</sup>
<b>Stair RPE</b>	10.31 $\pm$ 7.89	13.53 $\pm$ 3.11 <sup>†††</sup>

LADLS: Lawton Activities of Daily Living; Range: 0 (low function, dependent) to 8 (high function, independent)

PANAS (Positive): Positive and Negative Affect Schedule (Positive); Range:10-50; higher scores representing higher levels of positive affect.

PANAS (Negative): Positive and Negative Affect Schedule (Negative); Range:10-50; higher scores representing higher levels of negative affect.

FAS: Fatigue Assessment Scale; Range: > 22 (no fatigue);  $\leq$  22 (fatigue);  $\leq$  35 (severe fatigue)

FAS (Physical): Physical impact of fatigue

FAS(Mental): Cognitive impact of fatigue

Stair RPE: Image based Ratings of Perceived Exertion; Range:6-20; 6(no exertion), 20(maximal exertion)

\*Mann-Whitney  $U$  statistic (1175.50) shows a significant difference between groups  $p < 0.05$

\*\* Mann-Whitney  $U$  statistic (1314.00) shows a significant difference between groups  $p < 0.05$

\*\*\* An independent t-test shows a significant difference between groups  $t(121) = -4.764$   $p < 0.05$

<sup>†</sup> An independent t-test shows a significant difference between groups  $t(119) = -5.646$   $p < 0.05$

<sup>††</sup> Mann-Whitney  $U$  statistic (1148.00) shows a significant difference between groups  $p < 0.05$

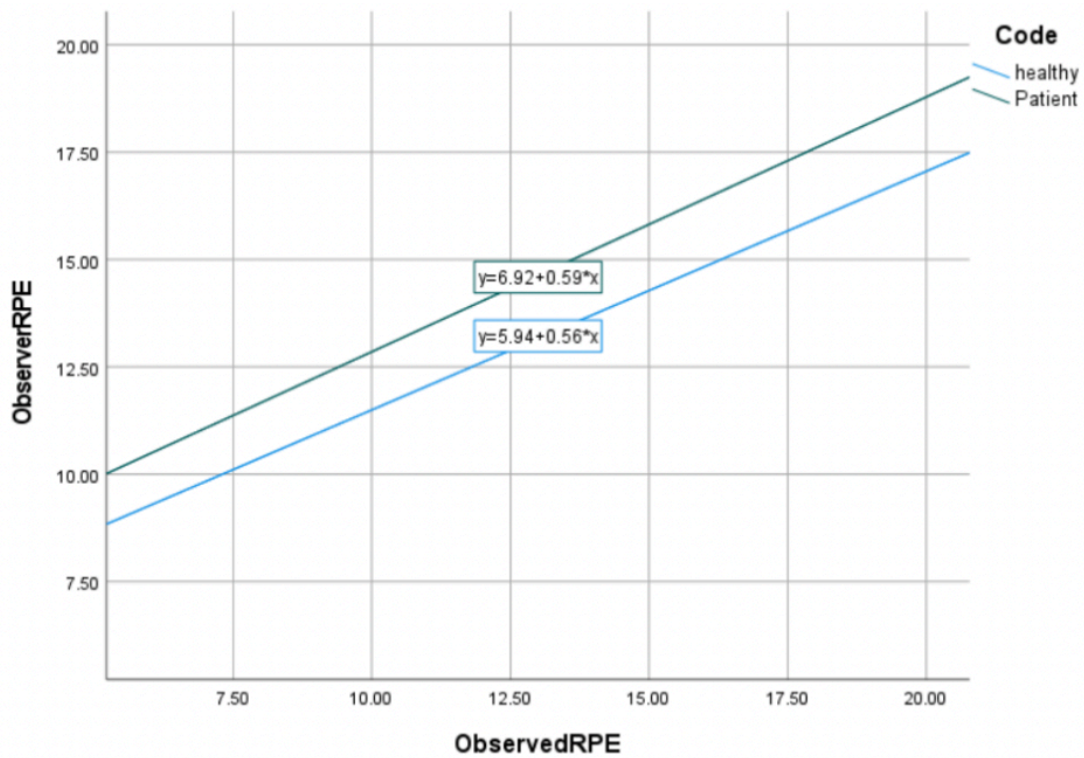
<sup>†††</sup> Mann-Whitney  $U$  statistic (754.50) shows a significant difference between groups  $p < 0.05$

#### 5.4 Correlation analyses

##### Observed RPE and observer RPE

Our first hypothesis was that judgment of RPE was possible through observation. Results of the Spearman correlation indicated that there was a significant and strong positive association between observer RPE and observed RPE in the healthy group, ( $\rho(1848) = .74$ ,  $p < .001$ ). Spearman correlation also revealed a significantly strong association between observer RPE and observed RPE in the patient group, ( $\rho(1223) = .68$ ,  $p < .001$ ), showing that patients were also able to judge RPE. These correlations are displayed in Figure 6.

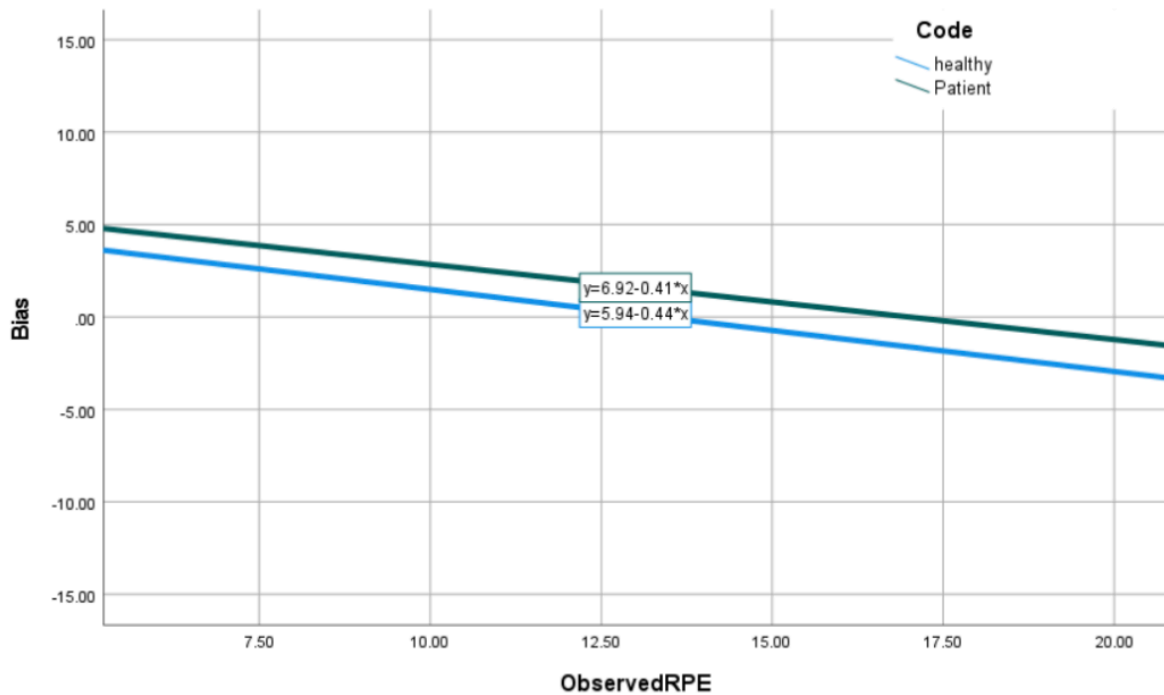
Figure 6. Graph showing the correlation between observed RPE and observer RPE in both healthy and patient participant groups



### RPE bias and observed RPE

In the healthy group, the higher the observed RPE, the lower the bias i.e. there was a negative correlation. RPE bias went from positive to negative as the mean observed RPE of the five volunteers in the videos increased at each of the five speeds (Figure 8). In other words, healthy individuals showed an overestimation in bias at lower observed RPE and an underestimation in bias of higher observed RPE. In the patient group, the same overestimation in bias at lower observed RPE and underestimation at higher observed RPE was noted (Figure 9).

Figure 7. Graph showing the correlation between RPE bias and observed RPE in both healthy and patient participant groups

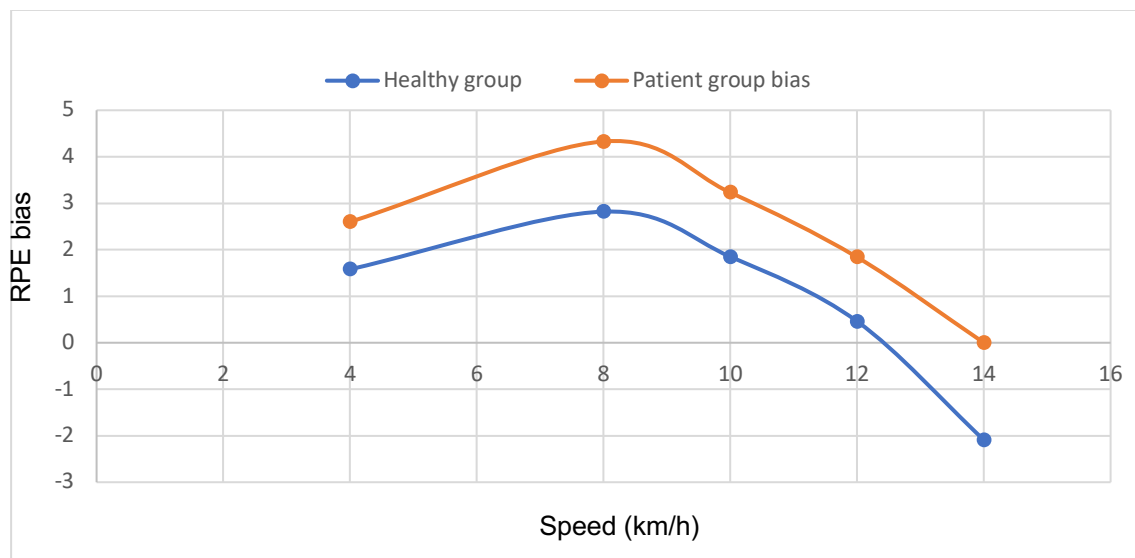


Bias = Observer RPE - Observed RPE  
 Observed RPE = Rating of Perceived Exertion given by subject in the video  
 Observer RPE = Rating of Perceived Exertion given by subject watching the video

RPE bias and speed

There was also a reciprocal relationship between RPE bias and speed; as treadmill speed increased, mean bias score went from positive to more negative in both groups, as shown in Figure 10. This shows that the both healthy and patient group participants watching the videos overestimated RPE at lower speeds but underestimated RPE at higher speeds.

Figure 8. Graph showing the correlation between speed (km/h) and RPE bias of both healthy and patient groups



A comparison of RPE bias between healthy and patient groups at each treadmill speed is summarised in Table 6. As the results of four out of the five speeds had a non-normal distribution, the Kruskal-Wallis H test was used to test the significance of any differences between the two groups. The mean RPE bias score was higher at all five speeds in the patient group compared to the healthy group, which was consistently a statistically significant difference (see Figure 5.4). At 4km/h, the mean bias score was 2.60 (SD = 1.92) for the patient group and 1.58 (SD = 1.35) for the healthy group (statistically significant difference; Kruskal-Wallis H test,  $\chi^2(1) = 9.937, p = 0.000$ ). At 8km/h, the mean bias score was higher at 3.70 (SD = 2.41) for the patient group compared to 2.14 (SD = 1.76) for the healthy group (statistically significant difference; Kruskal-Wallis H test,  $\chi^2(1) = 15.644, p = 0.000$ ). At 10km/h, the mean bias score was again higher for the patient group at 3.27 (SD = 2.56) in comparison to the healthy group, 1.85 (SD = 1.54), (statistically significant difference; Kruskal-Wallis H test,  $\chi^2(1) = 12.365, p = 0.000$ ). A greater mean bias score was also observed in the patient group at the highest treadmill speeds used, 12km/h and 14km/h, compared to the healthy group (respectively, 1.84 (SD = 2.47) (patient group), 0.46 (SD = 1.46) (healthy group); -0.37 (SD = 2.10) (patient group), -2.09 (SD = 1.91) (healthy group)). There was a statistically significant difference in the bias RPE score between the

two groups at these higher speeds (Kruskal-Wallis H test, 12km/h =  $\chi^2(1) = 15.898, p = 0.000$ ; 14km/h  $\chi^2(1) = 19.534, p = 0.000$ ).

Table 6. Average observed RPE score (displayed as the median) and RPE bias scores of the healthy and patient group

Speed	Observed RPE (Median; percentile25; percentile75) [Min; Max]	Bias (RPE 6-20)	
		Healthy ( $M \pm SD$ )	Patient ( $M \pm SD$ )
4km/h †	(6;6;6) [6;7]	1.58 ± 1.35	2.61 ± 1.93*
8km/h ††	(8;8;9) [7;10]	2.82 ± 1.87	4.33 ± 2.54**
10km/h ††	(11;10;12) [10;12]	1.85 ± 1.55	3.23 ± 2.56***
12km/h ††	(14;12;14) [12;16]	0.46 ± 1.46	1.84 ± 2.47****
14km/h ††	(18;15;19) [14;20]	-2.09 ± 1.91	-0.36 ± 2.10*****

Bias = Observer RPE – Observed RPE  
† Normal Distribution  
†† Non-Normal Distribution  
\*Kruskal-Wallis H test showed that there was a statistically significant difference between two groups  $\chi^2(1) = 9.397, p = 0.002, \eta^2 = 0.05$  with a mean rank bias score of 54.00 for Group 0, and 74.08 for Group 1.  
\*\* Kruskal-Wallis H test showed that there was a statistically significant difference between two groups  $\chi^2(1) = 13.796, p = 0.000, \eta^2 = 0.09$  with a mean rank bias score of 52.29 for Group 0, and 76.66 for Group 1.  
\*\*\* Kruskal-Wallis H test showed that there was a statistically significant difference between two groups  $\chi^2(1) = 11.595, p = 0.001, \eta^2 = 0.07$  with a mean rank bias score of 53.10 for Group 0, and 75.44 for Group 1.  
\*\*\*\* Kruskal-Wallis H test showed that there was a statistically significant difference between two groups  $\chi^2(1) = 15.898, p = 0.000, \eta^2 = 0.11$  with a mean rank bias score of 51.58 for Group 0, and 77.73 for Group 1.  
\*\*\*\*\*Kruskal-Wallis H test showed that there was a statistically significant difference between two groups  $\chi^2(1) = 19.809, p = 0.000, \eta^2 = 0.14$  with a mean rank bias score of 50.36 for Group 0, and 79.57 for Group 1.

### Stair RPE and fatigue scores

Results of the Spearman correlation indicated that there was a significant positive association between RPE scores for the imagined stair task and FAS scores in the healthy group, ( $\rho(1848) = .41, p < .01$ ). A similar correlation was also observed between FAS and stair RPE scores in the patient group ( $\rho(1223) = .42, p < .01$ ).

## 5.5 Multiple regression analysis

### RPE bias

To show that the assumptions, mentioned in Section 4.0, for the use of multiple regression analysis are met, a Q-Q plot for both healthy (figure 9) and patient group (figure 10) datasets are shown, respectively (Williams et al., 2019).

Figure 9. Q-Q plot of RPE bias for healthy group

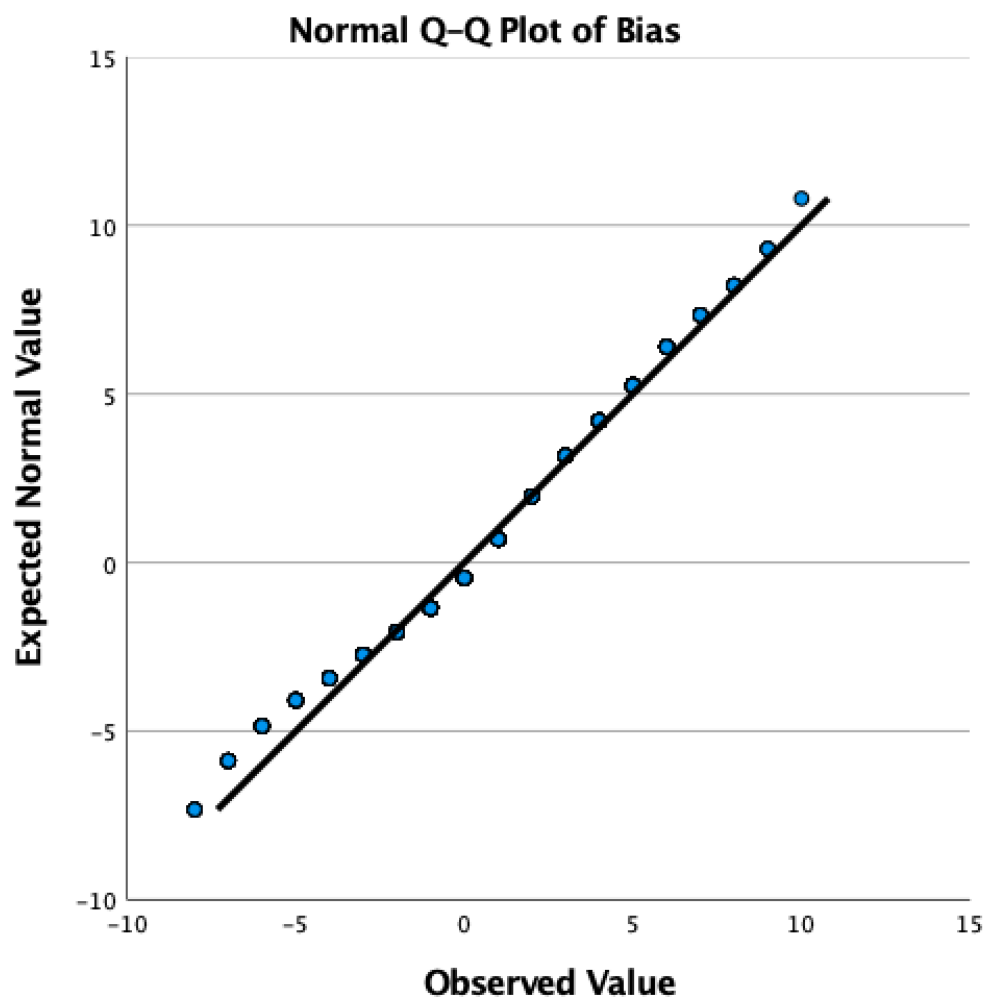
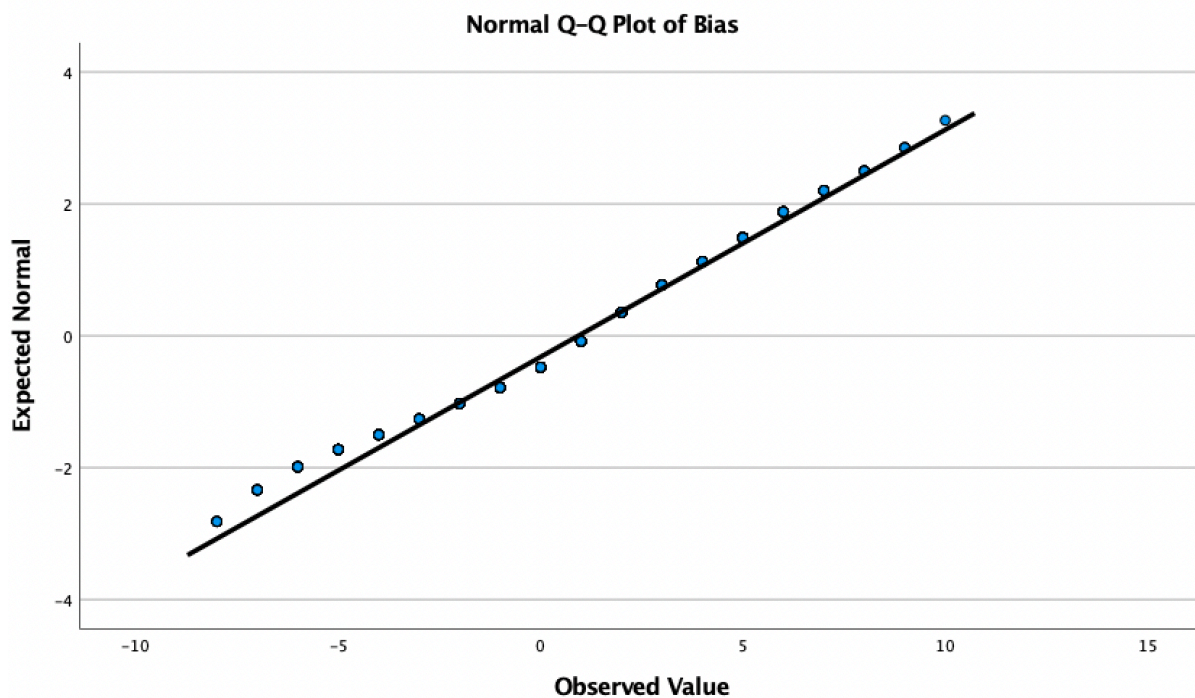


Figure 10. Q-Q plot of RPE bias for patient group



Multiple regression analysis of observed and observer characteristics was performed on the RPE bias of both the healthy group,  $n=1850$ , (Table 7) and the patient group,  $n=1225$  (Table 8). In the first step, observed characteristics were added and observer characteristics were added in the second step. In the healthy group, the greatest proportion of variance in RPE bias came from the characteristics of the observed individuals. The addition of observer characteristics from the healthy group only added 2% ( $R^2 = .26$  for Step 1,  $\Delta R^2 = .28$  for Step 2 ( $p < .001$ )) to the model. Observer characteristics including fatigue had little overall influence on RPE bias. However, the characteristics of the observed individuals in the videos had the greatest influence on bias in the healthy group. The most significant characteristics were speed, age and ethnicity. The speed at which the volunteers were running resulted in a significantly negative beta value ( $-.40$  ( $p < .05$ )), showing that the higher the speed, the higher the negative bias. On the other hand, the lower the speed the bigger the positive bias. Observed age significantly affected RPE bias ( $\beta = .41$  ( $p < .05$ )), so the older the person was in the videos, the higher the RPE bias from the healthy individuals watching the videos. Observed ethnicity also significantly contributed to RPE bias; the negative value ( $\beta = -.36$  ( $p < .05$ )), represents a stronger negative bias towards non-white ethnic groups, i.e. their RPE was significantly more underestimated.



In contrast, the biggest contribution of RPE bias variance in the patient group came from their own, or observer, characteristics. Addition of the observer characteristics added 13% ( $R^2 = .17$  for Step 1,  $\Delta R^2 = .30$  for Step 2 ( $p < .001$ )) to the model. This is almost a six-fold increase compared to the healthy group upon adding observer characteristics. The observer characteristics of the patient group that were found to have the highest influence on RPE bias was fatigue and disability scores, in particular, mental fatigue had the biggest contribution to RPE bias (which was even bigger than the contribution of speed). Higher mental fatigue FAS scores resulted in a higher bias (beta value =  $.36$ ,  $< .001$ ). Interestingly, the opposite was true for physical FAS scores; high physical fatigue levels resulted in significantly less bias (beta value =  $-.23$ ,  $< .001$ ). Patients with higher LADL scores i.e. less independent in their daily activities and so higher disability showed a significantly higher bias and overestimated RPE (beta value =  $.29$ ,  $< .001$ ). Patients with lower NASA scores and so lower activity levels, also overestimated RPE as there was a significant negative bias with higher NASA scores (beta value =  $-.14$ ,  $< .001$ ). Higher stair RPE scores also resulted in a significantly positive bias (beta value =  $.28$ ,  $< .001$ ) for the patient group, however higher stair RPE had almost no effect on bias in the healthy group (beta value =  $-.03$ ).

Table 7. Linear multiple regression analysis between dependent variables and RPE bias in the healthy group

<b>Healthy</b>			
	B (Constant)	Std. Error	$\beta$
<b>STEP 1</b>			
<b>Speed</b>	-.34	.02	-.40*
<b>HRperSpeed</b>	.09	.10	.41
<b>Observed Age</b>	.09	.04	.41*
<b>Observed Sex</b>	-.60	1.22	-.10
<b>Observed Ethnicity</b>	-.66	.31	-.36*
<b>STEP 2</b>			
<b>Speed</b>	-.34	.02	-.40*
<b>HRperSpeed</b>	.09	.10	.41
<b>Observed Age</b>	.09	.04	.41*
<b>Observed Sex</b>	-.60	1.20	-.10
<b>Observed Ethnicity</b>	-.66	.30	-.36*
<b>NASA</b>	-.14	.05	-.07*
<b>Physical Activity</b>			
<b>Observer Ethnicity</b>	-.05	.06	-.02
<b>Observer Age</b>	.03	.01	.13*
<b>Observer Sex</b>	-.66	.15	.11*
<b>Observer Stair RPE</b>	-.04	.03	-.03
<b>Physical Fatigue</b>	-.03	.02	-.05
<b>Mental Fatigue</b>	.07	.03	.10*
<b><math>R^2 = .26</math> for Step 1, <math>\Delta R^2 = .28</math> for Step 2 (<math>p &lt; .001</math>)</b>			
<b>*<math>p &lt; .05</math></b>			

Table 8. Linear multiple regression analysis between dependent variables and RPE bias in the patient group

<b>Patients</b>			
	<b>B (Constant)</b>	<b>Std. Error</b>	<b>β</b>
<b>STEP 1</b>			
<b>Speed</b>	-.29	.03	-.30*
<b>Observed Age</b>	.05	.05	.21
<b>Observed Ethnicity</b>	-.51	.39	-.24
<b>Observed Sex</b>	-.01	1.5	-.002
<b>HRperSpeed</b>	.03	.13	.10
<b>STEP 2</b>			
<b>Speed</b>	-.29	.02	-.30*
<b>Observed Age</b>	.05	.05	.22
<b>Observed Ethnicity</b>	-.51	.36	-.25
<b>Observed Sex</b>	-.03	1.4	-.01
<b>HRperSpeed</b>	.03	.12	
<b>NASA Physical Activity</b>	-.54	.12	-.13*
<b>Observer Age</b>	.01	.01	.06*
<b>Observer Sex</b>	.63	.24	.08*
<b>Observer Ethnicity</b>	.82	.16	.18*
<b>LADLS</b>	.60	.08	.29*
<b>Observer Stair RPE</b>	.31	.03	.28*
<b>Physical Fatigue</b>	-.16	.04	-.23*
<b>Mental Fatigue</b>	.26	.04	.36*
<b>R<sup>2</sup> = .17 for Step 1, ΔR<sup>2</sup> = .30 for Step 2 (p&lt;.001)</b>			
<b>*p&lt;.05</b>			

## Observer RPE

We also ran a multiple regression analysis of observed and observer characteristics on the raw observer RPE value as the outcome, in addition to RPE bias. RPE bias as an outcome showed us what factors made people deviate from the observed RPE of exercising individuals as it went up with higher speeds. However, here we want to see which independent factors directly contributed to the raw observer RPE value given by the healthy (Table 9) and patient groups (Table 10).

In the healthy group, the greatest proportion of variance, which was significant, in observer RPE came from observed RPE (beta value  $-.20$  ( $p < .001$ )) from the individuals in the videos and their treadmill speed (beta value  $.97$  ( $p < .001$ )). As observed RPE was an independent factor next to speed, the participants did not just rely on speed to make a judgment but also used observed RPE to reach a judgement for their observer RPE score. The addition of their own, observer, characteristics added only 3% ( $R^2 = .62$  for Step 1,  $\Delta R^2 = .65$  for Step 2 ( $p < .001$ )) to the model. Although the contribution is very small, some of the observer characteristics (age, sex, NASA scores and mental fatigue scores) still significantly affected observer RPE.

In the patient group, speed again gave the largest contribution out of the observed characteristics in step 1 of the regression analysis. Observed RPE was the second largest contributor to observer RPE i.e. the higher the observer RPE, the lower the RPE from the observed (beta value  $-.20$ ,  $p < .001$ ). The addition of the patients' own, observer, characteristics in step 2 added 10% ( $R^2 = .53$  for Step 1,  $\Delta R^2 = .63$  for Step 2 ( $p < .001$ )) to the model. Therefore, similar to the previous regression model, the biggest contribution of observer RPE variance in the patient group came from their own, or observer, characteristics. The largest contributors from these observer characteristics were LADL and mental fatigue scores. Patients with lower functional levels reflected by their higher LADL scores, showed a significant bias for higher RPE scores and overestimated RPE (beta value  $-.26$ ,  $p < .001$ ). Overestimation of RPE was also seen in patients with higher mental fatigue scores (beta value  $-.31$ ,  $p < .001$ ).

Table 9 . Linear multiple regression analysis between dependent variables and Observer RPE in the healthy group

<b>Healthy</b>			
	<b>B (Constant)</b>	<b>Std. Error</b>	<b>β</b>
<b>STEP 1</b>			
<b>Speed</b>	.92	.05	<b>-.97*</b>
<b>Observed RPE</b>	-.16	.04	<b>-.20*</b>
<b>HRperSpeed</b>	-.04	.08	<b>-.15</b>
<b>Observed Age</b>	-.02	.03	<b>-.08</b>
<b>Observed Sex</b>	.60	.96	<b>.09</b>
<b>Observed Ethnicity</b>	.14	.24	<b>.07</b>
<b>STEP 2</b>			
<b>Speed</b>	.92	.05	<b>.97*</b>
<b>HRperSpeed</b>	-.04	.08	<b>-.15</b>
<b>Observed Age</b>	-.02	.03	<b>-.08</b>
<b>Observed Sex</b>	.60	.93	<b>.09</b>
<b>Observed Ethnicity</b>	.14	.24	<b>.07</b>
<b>NASA</b>	.14	.04	<b>-.06*</b>
<b>Physical Activity</b>			
<b>Observer Ethnicity</b>	-.05	.05	<b>-.02</b>
<b>Observer Age</b>	.03	.01	<b>.12*</b>
<b>Observer Sex</b>	.66	.12	<b>.10*</b>
<b>Observer Stair RPE</b>	-.04	.02	<b>-.03</b>
<b>Physical Fatigue</b>	-.03	.02	<b>-.05</b>
<b>Mental Fatigue</b>	.07	.02	<b>.09*</b>
<b>R<sup>2</sup> = .62 for Step 1, ΔR<sup>2</sup> = .65 for Step 2 (p&lt;.001)</b>			
<b>*p&lt;.05</b>			

Table 10. Linear multiple regression analysis between dependent variables and Observer RPE in the patient group

<b>Patients</b>			
	B (Constant)	Std. Error	$\beta$
<b>STEP 1</b>			
<b>Speed</b>	.98	.06	.89*
<b>Observed RPE</b>	-.17	.06	.18*
<b>Observed Age</b>	-.05	.05	-.20
<b>Observed Ethnicity</b>	.28	.39	-.24
<b>Observed Sex</b>	1.1	1.3	.15
<b>HRperSpeed</b>	-.10	.12	-.34
<b>STEP 2</b>			
<b>Speed</b>	.98	.06	.88*
<b>Observed RPE</b>	-.17	.05	-.18*
<b>Observed Age</b>	-.05	.04	-.20
<b>Observed Ethnicity</b>	.28	.30	.12
<b>Observed Sex</b>	1.1	1.2	.15
<b>HRperSpeed</b>	-.10	.10	-.34
<b>NASA Physical Activity</b>	-.54	.10	-.12*
<b>Observer Age</b>	.01	.01	.05*
<b>Observer Sex</b>	.63	.20	.07*
<b>Observer Ethnicity</b>	.83	.13	.16*
<b>LADLS</b>	.60	.06	.26*
<b>Observer Stair RPE</b>	.31	.03	.25*
<b>Physical Fatigue</b>	-.16	.03	-.20*
<b>Mental Fatigue</b>	.26	.03	.31*
<b><math>R^2 = .53</math> for Step 1, <math>\Delta R^2 = .63</math> for Step 2 (<math>p &lt; .001</math>)</b>			
<b>*<math>p &lt; .05</math></b>			

## 6.0 Discussion

### 6.1 Key findings

- i) Our first key finding is that judgement of RPE is possible through observation. Although the healthy group judged RPE more accurately and gave scores closer to the observed RPE, the patient group could still judge RPE.
- ii) The patient group had a prediction bias for higher effort judgement, which was influenced by their own characteristics and fatigue levels. Multiple regression analysis of various dependent variables on RPE bias and observer RPE in section 5.4 demonstrated that the patient's own/observer characteristics influenced their bias in effort judgement. Whereas the healthy group was not influenced by their characteristics but instead by observed characteristics of the exercising individuals. This supports the notion that patients suffering with fatigue have an increased prediction bias towards higher effort leading them live in a world of "higher effort", which consequently causes spill over to the observations of effort around them.

### 6.2 Interpretations

We propose a novel paradigm and approach to understanding effort and fatigue from our key findings. Kahneman's "resource capacity theory" and Gibson's "affordance theory" are based on one's perceptual ability to physically perform a task as a result of one's awareness of their inherent capacity (Sarà et al., 2019; Warren, 1984b). Our paradigm takes the affordance theory further and answers whether people can also judge other people's level of effort through observation. In our first regression model, the healthy group demonstrated that much of their bias was coming from observed characteristics, i.e. they are looking at the people in the videos and directly taking cues (age, ethnicity, speed) from them rather than being influenced by their own characteristics. When we added observer characteristics in the second part of the regression model, there was hardly any change in the model. Therefore, the theory of perceived affordance seems to work through observation for healthy patients. This group was able to take visual cues from their

environment and so could judge accurately another person's level of effort at different speeds.

Our study is unique because the participants who were watching the videos were exerting no physical effort; the study focused on judging someone else's perception of effort using only observation. This is critical as it allows interpreting our results in context to Gibson's theory of fatigue being a subconscious sensation dictated by own memories and experiences, rather than a physical sensation. Our findings in the first regression model support this notion since much of the RPE bias from participants in the patient group came from their level of effort (stair RPE), having higher fatigue and disability scores and lower physical activity levels. In other words, the patients were so subconsciously influenced by their own experiences, that they cannot take visual cues from their environment leading to a misjudgement of other people's level of effort. This finding also adds to Konczak's extension of Warren's leg length model, where the perceptual judgement of stair climbing ability was limited by own leg strength and joint flexibility (Konczak et al., 1992). Our study also highlights the influence of one's own characteristics on affordance ability, in particular how own fatigue levels influenced RPE judgement.

In our second regression model, when looking at the influence of variables on observer RPE, we found that even in the healthy group, RPE judgement remains influenced by their own fatigue levels and capability. Although this was on a much smaller scale than the patient group, it was still significant and so highlights how the severity of fatigue and own negative experiences dictate the degree of impairment in effort judgement, i.e. it is a universal phenomenon, not just amongst patients.

Our findings could explain why fatigue can persist even after optimal medical treatment. One study showed how fatigue persisted in a group of RA patients even after a year of strict treatment protocol; the main predictor of post-treatment fatigue was baseline fatigue levels and not disease activity levels (Walter et al., 2018). Our study could potentially explain this observation; baseline fatigue levels led to becoming stuck in a "higher effort world" so even after optimally treating the patients, they continued to be dictated by their own altered perception (initially afflicted by the disease) instead of picking up on new cues around them (less disease activity) to reduce their bias. This supports Damasio and Parvisi's theory of the subconscious "proto-self" in understanding the development of fatigue, where changes in one's own internal or external environment, for example, the experience of



fatigue, produce new neural patterns to create a new subconscious “proto-self” (Parvizi & Damasio, 2001). Therefore, a potential approach for the future management of fatigue should consider how we get patients to disconnect safely beyond their own experiences with effort judgment and instead practice being able to pick up on environmental visual cues around them to manipulate this “proto-self”.

### *6.3 Limitations*

This study is not free from limitations. Our patient group was recruited from self-help support groups via social media, which may not be reflective of the general population. Also, the representation of different medical conditions in the patient group was limited; the largest representation was for ME/CFS patients, so our results may be more applicable to these patients. All participants completed the surveys virtually and under no observation from ourselves, which makes it a less controlled environment. However, we attempted to minimise large variations in how people completed the survey by including a detailed brief on ensuring they were on an empty stomach for at least 3 hours and advising no consumption of caffeine before completion of the survey. We also advised participants to use a desktop computer or laptop to minimise any issues with the video section and slider function for rating RPE. Also, using self-reported questionnaires is a subjective approach to quantify fatigue, physical activity and independence levels; participants may have different personal thresholds for quantifying these characteristics. Another potential subjective influence is varying levels of empathy, or alexithymia. However, there is currently no literature reporting whether patients with chronic fatigue have higher or lower levels of empathy. BMI was calculated using self-reported height and weight measurements instead of direct measurements which could have implicated BMI accuracy as people tend to underestimate their weight and overestimate their height (Engstrom et al., 2003). Finally, the volunteers in the videos only included one non-white individual so interpretations of any racial bias for RPE ratings is limited.

### *6.4 Future research*

We have demonstrated that people can judge effort by observation, a novel paradigm which, can be used in future research. As our study did not require participants to exercise

or physically move, the paradigm we have introduced has the potential to be further tested by scanning participants using functional MRI to see if the spill over of observed prediction bias correlates with changes in the brain.

## **7.0 Conclusion**

In summary, this work has established that effort judgement through observation is a possible phenomenon and opens a potential path for further research on effort and fatigue. Patients suffering from fatigue have a higher prediction bias as a direct result of being influenced by their own characteristics and fatigue levels. In contrast, healthy individuals are influenced by observed characteristics and visual cues taken from the environment rather than their own. This is a crucial observation as it highlights a dissociation between visual environmental cues and observational judgment of effort in those who suffer from fatigue. Instead, fatigue sufferers appear to be trapped in their own experiences, which translated into a prediction bias in their observations of other individuals and their environment i.e. they are experiencing the world around them through a higher effort lens. This altered experience and perception of the world has the potential to explain the persistent nature of fatigue as a symptom in various medical conditions, especially as fatigue can be persistent beyond disease duration and can be out of proportion to disease activity.

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# APPENDICES

## Appendix 1: Participant Study Information and Consent Page on survey

### PARTICIPANT STUDY INFORMATION AND CONSENT

To take part in this study, it is essential for you to have read the following information before you give your consent.

- It will take approximately 40 minutes of your time to complete this survey.
- To be eligible to take part you must be an individual age 18 or above.
- If you wish to withdraw from this survey at any point, you may do so without having to give a reason.
- Any information collected about you will remain confidential and only to the knowledge of the researchers involved in this study.
- If you are uncomfortable with any question/s and do not wish to answer them, then you may skip and go to the next question
- All video footage in the survey is the proprietary property of the University. Taking screenshots or recording with a mobile or hand-held camera is strictly prohibited.

**Important:** Do not try to do this survey on your mobile phone. Open the link only on either your laptop or desktop computer. If you are reading this on your mobile, kindly close it and open the link again on your desktop or laptop.

This survey contains four sections:

1. **Details about you** (which includes questions about your current diagnosis, demographics (height, weight, age) and your physical activity)
2. **THREE Questionnaires;** A questionnaire which is asking questions about your current mood mood status; PANAS, Magyar-Moe, 2009 A questionnaire which is asking about the severity of your fatigue and how it affects you in daily life; FAS, Michielsen et al, 2003 A questionnaire which assesses your ability to perform daily tasks; IADL scale, Graf, 2007
3. **Video Section:** this section will introduce you to a scale of effort perception followed by watching videos of individuals exercising on treadmill. You will be asked to rate the effort the exercising people might perceive in the videos.
4. **Imagined Task Section:** in this section, you will be asked to imagine yourself walking up a distinct staircase (photo provided) and to rate the effort you would feel.

You will be asked at the end of the survey to enter your email address, should you wish to be entered in the prize draw for a chance to win an iPad.

### Any Questions?

Please ask us if you have any questions (see email addresses below). You should not consenting to take part in the study if you still have unanswered questions or any doubts.

Dr Hans-Peter Kubis and Prof Paul Mullins the supervisor and co-supervisor of this study, Vinod Ramakrishnan PhD student and Principal Investigator and Dr Yakeen Hafouda, junior doctor and MRes student, will be glad to answer your questions about this study at any time.

Vinod Ramakrishnan (vlr20bpg@bangor.ac.uk). (07587872351) (Principal Investigator)

Dr. Yakeen Hafouda (ykh21xbv@bangor.ac.uk) (MRes Student)

Dr Hans Peter Kubis (h.kubis@bangor.ac.uk) (Supervisor)

Prof Paul Mullins (p.mullins@bangor.ac.uk) (Co-Supervisor)

Dr Joe Butler (joe.butler@sunderland.ac.uk) (Co-supervisor)

**By clicking "I consent" I am confirming that I am at least 18 years old and have problems with fatigue. I have read and understood the study information sheet. I understand what is required of me for my participation in this study. I have had the opportunity to consider the information, ask questions, and have had them answered satisfactorily, if I had any.**

I CONSENT

I DO NOT CONSENT

## Appendix 2: The Positive and Negative Affect Schedule (PANAS) scale

Q22

### PANAS Mood Questionnaire

This questionnaire assesses your **feelings and emotions** over the past week.

Read each statement and select the appropriate answer from the choices immediately below the statement. You can choose one out of five answer categories

Q21

Indicate how **interested** you have felt over the past week

- Very slightly or not at all
- A little
- Moderately
- Quite a bit
- Extremely

Q36

Indicate how **guilty** you have felt over the past week

- Very slightly or not at all
- A little
- Moderately
- Quite a bit
- Extremely

Q30

Indicate how **distressed** you have felt over the past week

- Very slightly or not at all
- A little
- Moderately
- Quite a bit
- Extremely

Q35

Indicate how **scared** you have felt over the past week

- Very slightly or not at all
- A little
- Moderately
- Quite a bit
- Extremely

Q31

Indicate how **excited** you have felt over the past week

- Very slightly or not at all
- A little
- Moderately
- Quite a bit
- Extremely

Q34

Indicate how **hostile** you have felt over the past week

- Very slightly or not at all
- A little
- Moderately
- Quite a bit
- Extremely

Q32

Indicate how **upset** you have felt over the past week

- Very slightly or not at all
- A little
- Moderately
- Quite a bit
- Extremely

Q33

Indicate how **enthusiastic** you have felt over the past week

- Very slightly or not at all
- A little
- Moderately
- Quite a bit
- Extremely

Q151

Indicate how **strong** you have felt over the past week

- Very slightly or not at all
- A little
- Moderately
- Quite a bit
- Extremely

Q40

Indicate how **proud** you have felt over the past week

- Very slightly or not at all
- A little
- Moderately
- Quite a bit
- Extremely

Q39

Indicate how **irritable** you have felt over the past week

- Very slightly or not at all
- A little
- Moderately
- Quite a bit
- Extremely

Q44

Indicate how **determined** you have felt over the past week

- Very slightly or not at all
- A little
- Moderately
- Quite a bit
- Extremely

Q37

Indicate how **alert** you have felt over the past week

- Very slightly or not at all
- A little
- Moderately
- Quite a bit
- Extremely

Q43

Indicate how **attentive** you have felt over the past week

- Very slightly or not at all
- A little
- Moderately
- Quite a bit
- Extremely

Q38

Indicate how **ashamed** you have felt over the past week

- Very slightly or not at all
- A little
- Moderately
- Quite a bit
- Extremely

Q47

Indicate how **jittery** you have felt over the past week

- Very slightly or not at all
- A little
- Moderately
- Quite a bit
- Extremely

Q41

Indicate how **inspired** you have felt over the past week

- Very slightly or not at all
- A little
- Moderately
- Quite a bit
- Extremely

Q46

Indicate how **active** you have felt over the past week

- Very slightly or not at all
- A little
- Moderately
- Quite a bit
- Extremely

Q42

Indicate how **nervous** you have felt over the past week

- Very slightly or not at all
- A little
- Moderately
- Quite a bit
- Extremely

Q45

Indicate how **afraid** you have felt over the past week

- Very slightly or not at all
- A little
- Moderately
- Quite a bit
- Extremely

## Appendix 3: The Fatigue Assessment Scale (FAS)

Q51

### Fatigue Assessment Scale (FAS)

The following 10 statements refer to **how you feel**.

Select how often you have **each** feeling from the choices immediately below.

Q50

### I am bothered by fatigue

- Never
- Sometimes
- Regularly
- Often
- Always

Q53

### I have problems starting things

- Never
- Sometimes
- Regularly
- Often
- Always

Q57

### I get tired very quickly

- Never
- Sometimes
- Regularly
- Often
- Always

Q52

### I feel no desire to do anything

- Never
- Sometimes
- Regularly
- Often
- Always

Q56

### I don't do much during the day

- Never
- Sometimes
- Regularly
- Often
- Always

Q58

### I have problems thinking clearly

- Never
- Sometimes
- Regularly
- Often
- Always

Q55

### I have enough energy for everyday life

- Never
- Sometimes
- Regularly
- Often
- Always

Q60

### Mentally, I feel exhausted

- Never
- Sometimes
- Regularly
- Often
- Always

Q54

### Physically, I feel exhausted

- Never
- Sometimes
- Regularly
- Often
- Always

Q62

### When I am doing things, I can concentrate quite well

- Never
- Sometimes
- Regularly
- Often
- Always

Appendix 4: National Aeronautics and Space Administration Physical Activity Rating (NASA PA-R) Scale

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Q64

**NASA Physical Activity Rating Scale**

Each box below describes a pattern of daily physical activities.

Select the statement that best describes your activity.

You can only pick **one** option

- Inactive or little activity other than usual daily activities
  - Regularly (more than 5 days a week) participate in physical activities requiring low levels of exertion that result in slight increases of breathing and heart rate for at least 10 minutes at a time
  - Participate in aerobic exercises such as brisk walking, jogging or running, cycling and swimming or vigorous sports at a comfortable pace or other activities requiring similar levels of exertion for 20 to 60 minutes per week
  - Participate in aerobic exercises such as brisk walking, jogging or running, cycling and swimming or vigorous sports at a comfortable pace or other activities requiring similar levels of exertion for 1 to 3 hours per week
  - Participate in aerobic exercises such as brisk walking, jogging or running, cycling and swimming or vigorous sports at a comfortable pace or other activities requiring similar levels of exertion for over 3 hours per week
-

## Appendix 5: Lawton-Brody Instrumental Activities of Daily Living (LADL) scale

Q135

### Lawton-Brody Instrumental Activities of Daily Living Scale (IADLs)

This part assesses your ability to perform daily tasks. For each task select the option that most applies to you.

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Q130

Ability to use your PHONE

- I use my phone on my own initiative; look up and dial numbers
  - I dial a few well-known numbers
  - I only answer my phone and don't dial
  - I don't use a phone at all
- 
- 

Q131

SHOPPING

- I take care of all my shopping needs independently
  - I only shop independently for small purchases
  - I need to be accompanied on any shopping trip
  - I am completely unable to shop
- 
- 

Q132

FOOD PREPARATION

- I plan, prepare and serve meals independently
  - I prepare meals if supplied with ingredients
  - I heat and serve prepared meals
  - I need to have my meals prepared and served to me
- 
- 

Q133

HOUSEKEEPING

- I maintain my house alone with occasional assistance for heavy work
  - I perform light daily tasks such as dishwashing and bed making
  - I perform light daily tasks, but can not maintain an acceptable level of cleanliness
  - I need help with all home maintenance tasks
  - I do not participate in any housekeeping tasks
- 
-

**Q134**

**LAUNDRY**

- I do all my personal laundry
- I only launder small items, rinse socks etc
- All my laundry is done by others

**Q137**

**TRANSPORT**

- I drive my own car or travel independently on public transport
- I arrange my own travel via taxi, but do not otherwise use public transport
- I travel on public transport when accompanied by another
- My travel is limited to taxi or car with assistance of another
- I do not travel at all

**Q138**

**RESPONSIBILITY FOR OWN MEDICATIONS**

- I take my own medications in correct doses at the correct time
- I take my own medication if prepared in advance in separate dosage
- I am not capable of dispensing my own medications

**Q139**

**FINANCES**

- I manage my financial matters independently (budgets, write cheques, pay rent, bills, go to bank), collect and keep track of my income
- I manage day to day purchases, but need help with banking, major purchases, etc
- I am incapable of handling money