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The role of pain, perseverative cognition and goal adjustment in Vasculitis associated fatigue.

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Abstract

Fatigue is a common symptom associated with Vasculitis and contributes significantly to impaired quality of life. Motivational Control Theory (Hockey, 2013) suggests a role for perseverative cognition and goal adjustment in fatigue. Therefore, this study investigated these potential predictors of fatigue in individuals with Vasculitis. 249 participants completed online questionnaires assessing fatigue, perseverative cognition, goal disengagement and goal reengagement, in addition to demographic and disease related variables. Hierarchical regression analysis found only pain, sleep disturbance, disease activity and perseverative cognition to significantly predict fatigue. This highlights the importance of psychological factors in determining fatigue in those with Vasculitis.

Keywords

Fatigue, Goal Adjustment, Motivational Control Theory, Perseverative Cognition, Vasculitis

Introduction

Vasculitis is a group of rare chronic autoimmune conditions characterised by inflammation of the blood vessels. Vasculitis subtypes are classified according to the size of blood vessel affected. For example, Giant Cell Arteritis and Takayasu's Arteritis affect large blood vessels such as the aorta, Polyarteritis Nodosa affect small to large arteries and Granulomatosis with Polyangiitis (GPA), Churg-Strauss Syndrome (CSS) and Microscopic Polyangiitis (MPA) affect arterioles, capillaries, veins and venules (Jennette et al., 2013). Many forms of Vasculitis have historically been acute fatal conditions, however developments in treatments has led to improved outcomes (Holle et al., 2011). Consequently, individuals with Vasculitis are now living with the challenges associated with a chronic remitting and relapsing condition (Koutanji et al., 2003).

Fatigue has consistently been identified as one of the most significant burdens of Vasculitis. Individuals are twice as likely to have severe fatigue compared to the general population (Basu et al., 2010) impairing quality of life in over 75% of people with the condition (Abularrage et al., 2008; Bernabé et al., 2010; Hajj-Ali et al., 2011). Indeed, Herlyn et al. (2010) found fatigue to be the greatest disease burden (higher than pain and musculoskeletal symptoms) reported by

patients with vasculitis. Despite this, few studies have specifically examined the contributors to fatigue in Vasculitis. The limited evidence available supports multifactorial determinants, with biopsychosocial variables appearing to play an important role. For example, pain has emerged as one of the most consistent predictors of fatigue across several Vasculitis studies (Basu et al., 2010; Basu et al., 2013; Kountantji et al., 2003). Depression, sleep disturbance, negative illness perceptions and dysfunctional coping strategies such as denial and behaviour disengagement have also all been found to contribute to fatigue (Basu et al., 2013; Grayson et al., 2013) beyond disease related (e.g. time since diagnosis) and demographic variables.

While the previous research is useful for gaining a broad understanding of the contribution of clinical and biopsychosocial factors, the selection of potential determinants is not informed by pre-existing theories of fatigue. Consequently, insight into the underlying mechanisms of fatigue is limited. One conceptual approach that may provide a useful framework for exploring fatigue in Vasculitis is Motivational Control Theory (MCT; Hockey, 2011). MCT conceptualises fatigue as an adaptive emotion serving to interrupt tasks, allowing a cost/benefit analysis of task continuation and preventing fixation on low value activities. In addition to this adaptive model of fatigue, Hockey (2013) also proposes an

explanatory mechanism for the occurrence of persistent or maladaptive fatigue. An effort-fatigue disengagement spiral is suggested to become activated when unresolved stressors prevent recovery from effortful engagement with the environment. Emotional states associated with stress then distract from tasks, meaning that more effort is required to maintain them. An increase in effort also increases feelings of fatigue, consequently leading to a downward spiral whereby more and more effort is required to persist with goals. This cannot be sustained and disengagement occurs when the perceived costs of maintaining the current activity outweigh the benefits. A low effort mode is then utilised, leading to an increased sense of effort when engaging in any further activity.

Perseverative Cognition and Fatigue

Perseverative Cognition (PC) is thought to be a key driver within the stress-fatigue process, occurring as a result of unresolved stress and maintaining engagement with stressors through repetitive negative thinking (Hockey, 2013). PC can be defined as “the repeated or chronic activation of the cognitive representation of one or more psychological stressors” (Brosschot, Gerin & Thayer, 2006, p.114). Worry and rumination are both types of perseverative cognition, with worry regarded as repetitive negative thinking (RNT) about future stressors and rumination as RNT about past stressors (Brosschot, 2010).

Hockey (2013) argues that due to the pervasive and persistent nature of PC, high effort is required to suppress such thinking, further increasing effort demands within the effort-fatigue disengagement spiral and limiting attentional resources for other activities. In support, rumination has previously been reported to limit mental concentration within academic environments and also to impair executive function in individuals with depression (Lyubomirsky, Kasri, & Zehm, 2003; Watkins & Brown, 2002). However, the ability to generalise the findings of these two studies is limited due to small sample sizes and specific populations (undergraduates and individuals with clinical depression).

There is limited direct evidence for the impact of PC on fatigue due to a paucity of research within this area. However, organisational psychology research has contributed to the evidence base, with one study finding RNT to significantly predict work-related fatigue in a sample of 719 workers from a diverse range of occupations (Querstret & Cropley, 2012). Further research also identified PC to mediate the relationship between perfectionism and post-vacation fatigue in academic employees. PC whilst on leave was found to negatively affect fatigue when individuals with high self-set standards returned to work (Flaxman et al., 2012). Although focussed on work populations, these findings suggest that PC is important in the process of fatigue and recovery from stress.

Goal Adjustment and Fatigue

In addition to perseverative thinking, goal adjustment may be a secondary factor influencing individual vulnerability to the effort-fatigue disengagement spiral. It is thought that individuals with high goal commitment may be predisposed to persisting with high effort strategies despite increasing fatigue (Hockey, 2013). In support, Wrosch et al. (2003) suggest that disengaging from unattainable goals avoids a build-up of failure experiences and allows personal resources to be directed elsewhere. Goal reengagement, which is the ability to identify and pursue new goals is also thought to be important to adaptive self-regulation, lessening the psychological distress associated with giving up goals or equally, continuing to pursue unachievable goals (Wrosch et al., 2003).

There is limited and contradictory evidence for the relationship between goal adjustment and fatigue. Research conducted into Chronic Fatigue Syndrome (CFS) found individuals with CFS do have a greater tendency to persist with goals despite fatigue compared to the general population (Van Campen et al., 2009; Van Houdenhove et al., 1995). However, research from other chronic conditions fails to replicate this finding. For example, no association was found between the goal adjustment variables and fatigue in a sample of 305

individuals with Polyarthrititis (autoimmune arthritis causing multiple sites of inflammation) (Arends et al., 2013). In addition, research investigating fatigue in cancer patients reported that changes in goal disengagement and reengagement after beginning psychosocial care did not explain decreases in fatigue symptoms (Zhu et al., 2015). The proposed role for goal persistence within the effort-fatigue disengagement spiral consequently requires further investigation to assess the relevance of this factor to Vasculitis associated fatigue.

In light of the hypothesised importance of perseverative cognition and goal persistence in motivational control theory (Hockey, 2011) the aim of this study, therefore, was to determine whether perseverative cognition and/or goal adjustment are predictors of fatigue after controlling for demographic and disease related variables within a sample of individuals with Vasculitis.

Method

Design

A cross-sectional correlational study was conducted to investigate the predictors of fatigue. Participants were invited to complete an online questionnaire via a link posted in online Vasculitis support forums.

Participants

Participants diagnosed with one or more types of Vasculitis completed the questionnaire. Participants <18 years old were excluded from the study. The sample comprised 249 participants, 78.7% female, age range 18-77yrs (M=50.3, SD=14.03). Table 1 below presents the demographic and clinical characteristics of the sample. The majority of the participants were in drug maintained remission and lived within the UK. The most common types of Vasculitis within the sample were GPA, MPA, CSS and Behçet's Disease.

INSERT TABLE 1 HERE.

Measures

Demographic and Disease-Related Information. Demographic information on age, gender, and country of residence were collected. Self-reported disease-related information regarding disease activity (active vs remission), time since diagnosis (yrs.), current prednisolone dosage (mg) and pain (number of days in the last month) was also collected.

Sleep Disturbance. The Estimation of Sleep Problems Questionnaire (ESQ; Jenkins et al., 1988) is a four item measure assessing sleep quality in relation to falling asleep, staying asleep and waking. A six point scale indicates the number of days in the last month participants experienced sleep problems (not at all, 1-3 days, 4-7days, 8-14 days, 15-21 days or 22-31 days). A sample item is “How often in the last month did you have trouble falling asleep?” A total score from the four items is calculated (range 0-20), with a higher score indicating a greater level of sleep disturbance. Jenkins et al. (1988) report good internal consistency with an alpha reliability of 0.79. This questionnaire was included as sleep disturbance has previously been shown to be significantly related to fatigue in patients with Vasculitis (e.g. Basu et al., 2013).

Fatigue. The Multidimensional Fatigue Inventory (MFI-20; Smets et al., 1995) has been widely used to assess fatigue and is validated in both clinical and non-clinical populations (Lin et al., 2009; Smets et al., 1995). The MFI-20 consists of five fatigue subscales (General fatigue, physical fatigue, mental fatigue, reduced activity and reduced motivation). Four statement items measure each subscale and a five point Likert scale is used to indicate level of agreement. There is good internal consistency for all subscales ($\alpha > 0.8$) and good convergent validity with Visual Analogue Scales of fatigue (Smets et al., 1995). Within this study the general fatigue subscale was used due to the recommendation of this being the best measure of overall fatigue (Smets et al., 1995). A General Fatigue scale sample item is "I tire easily". A higher score indicates greater fatigue severity (range 4-20). A score ≥ 13 has previously been used as a threshold to indicate significant fatigue (Grayson et al., 2013).

Perseverative Cognition. The Perseverative Thinking Questionnaire (PTQ; Ehring et al., 2011) was utilised to assess PC due to the scale measuring the characteristic processes of PC while being independent of content relating to specific disorders such as depression and anxiety. The PTQ has been validated in both clinical and non-clinical populations. It has high internal consistency for the overall scale ($\alpha > 0.90$) and good convergent validity with other measures of

repetitive negative thinking (RNT see Ehring et al., 2011). The PTQ consists of fifteen statement items and contains three subscales (Core Characteristics of PC, Perceived Unproductiveness and Capturing Mental Capacity). A sample item is “I keep thinking about the same issue all the time”. Frequency of occurrence of the statement items are indicated on a five point scale (Never, Rarely, Sometimes, Often, Almost Always). The total PTQ score was used within this study with a higher score indicating a higher level of PC (range 0-60).

Goal Adjustment. The Goal Adjustment Scale (GAS; Wrosch et al., 2003) is a ten item scale with two subscales of goal disengagement (four items) and goal reengagement (6 items). Both subscales have good internal consistency ($\alpha > 0.80$). Goal disengagement represents the ease with which individuals can reduce their effort towards unattainable goals. A sample item is “I stay committed to the goal for a long time, I can’t let it go”. Goal reengagement represents the ease with which individuals can identify and pursue new goals. A sample item is “I seek other meaningful goals”. Agreement with items is ranked on a 5 point scale. A total score can be obtained by summing the items, however, the individuals subscale scores were used within this study (Disengagement range 4-20, Reengagement range 6-30). The GAS has been

used both within the general population (Wrosch et al., 2003) and illness populations (Arends et al., 2013; Zhu et al., 2015).

Statistical Analysis

Hierarchical multiple regression was used to investigate whether PC and goal adjustment are predictors of fatigue. General fatigue score (MFI-20) formed the dependent variable. Demographic variables of age and gender were entered into the regression at step 1. Disease related and clinical variables of time since diagnosis, disease activity, prednisolone dosage, pain and sleep disturbance were entered in at step 2. Perseverative cognition was entered at step 3 and the goal adjustment variables of goal disengagement and goal reengagement were entered at step 4. The order of entry was determined by the theoretical and empirical importance of the variables. Categorical variables (gender and disease activity) were dummy coded.

Results

Descriptive statistics for fatigue and the predictor variables are detailed in Table 1. This shows that 91.2% of the sample scored above the threshold for significant fatigue (≥ 13). The sample comprised individuals who have been

diagnosed with Vasculitis for a number of years ($M=5.99$, $SD=6.78$). Pain was reported as experienced on more than half the days in the month by 62.7% of participants and sleep disturbance on half or more of the days in the month was reported by 46.6%. Perseverative Cognition was found to be similar to the mean score of participants ($M=28.14$) reported within the validation study for individuals without anxiety or depression (Ehring et al., 2011). The mean scores for goal disengagement and reengagement were similar to those reported previously in a sample of arthritis patients by Arends et al. (2013).

All assumptions for the regression analysis were met, although there were nine participants who had inflated Cook's distance scores (> 0.02) and these were removed from the analysis. The results from regression analysis are shown in Table 2. After entering the predictor variables in four steps, a significant overall regression model was found ($F(10, 228) = 10.60$, $p<.001$), accounting for 29% of the variance in fatigue.

The demographic variables entered in Step 1 did not produce a significant regression model ($F(2, 236) = 1.76$, $p=.18$). When the disease related variables were entered in Step 2 this produced a significant model ($F(7,231) = 11.96$, $p<.001$). Of the disease related variables pain, sleep disturbance and disease

activity were significantly associated with fatigue, accounting for 25% of the variance in fatigue. Entering perseverative cognition at Step 3, accounted for a further 3.4% of the variance and this represented a statistically significant increase in R^2 . There was, however, no significant increase in R^2 when the goal disengagement and goal reengagement variables were entered in Step 4 ($F(2, 228) = 2.85, p = .06$).

INSERT TABLE 2 HERE

Discussion

Motivational Control Theory (MCT: Hockey, 2013) provided a conceptual framework for this study, informing the investigation of potential determinants of Vasculitis associated fatigue. The results indicate that pain, sleep disturbance and disease activity play a significant role in Vasculitis fatigue. This is consistent with previous research reporting pain and sleep disturbance as the strongest predictors of fatigue (Basu et al., 2013). With regard to disease activity, the findings corroborate those of Grayson et al. (2013) and are also compatible with the evidence that C-Reactive Protein blood levels, a marker of inflammation, predict fatigue (Basu et al., 2013). Other research also supports the role of inflammation in fatigue, suggesting that increased release of cytokines, such as

interleukins 1 β and 6 contribute to symptoms of fatigue (See Norheim et al., 2011 for review). Currently, there is little evidence regarding the impact of immunosuppressant agents on fatigue symptoms in Vasculitis. However, recent clinical trial standards for Vasculitis treatments include patient reported outcomes such as fatigue (Merkel et al., 2011). Therefore, it is likely that greater evidence on the efficacy of pharmacological treatments for fatigue will be gained in future.

In relation to the variables suggested by MCT (Hockey, 2011) to play an important role in persistent fatigue, perseverative cognition was found to independently predict fatigue, accounting for an additional 3% of the variance. This is consistent with organisational psychology research reporting a relationship between PC and fatigue (Querstret & Cropley, 2012). Conversely, the goal adjustment variables were not significantly associated with fatigue. The relationship between PC and fatigue can be understood within the framework of MCT (Hockey, 2013). Persistent PC prolongs engagement with stressors leading to the effort-fatigue disengagement spiral, whereby increased effort is required in order to maintain goals. Individuals with Vasculitis are constantly coping with the stress associated with managing a chronic remitting and relapsing health condition. Therefore, the relationship between PC and

Vasculitis associated fatigue may be explained by PC increasing cognitive demand, meaning greater effort is required to continue with other tasks leading to increased fatigue and eventual behavioural disengagement.

The lack of association between the goal adjustment variables and fatigue is consistent with previous Polyarthritis and Cancer study findings (Arends et al., 2013; Zhu et al., 2015). However, it contradicts the reported relationship between goal persistence and fatigue in CFS (Van Campen et al., 2009; Van Houdenhove et al., 1995). This is compatible with there being greater similarities between Vasculitis and Polyarthritis (autoimmune inflammatory disorders) than between Vasculitis and CFS. Consequently, the proposal within MCT (Hockey, 2013) that high goal persistence may leave individuals more prone to the disengagement spiral is unsupported by the present study. However, it is plausible that the study outcome was affected by measurement issues. Due to goal type being unspecified, a variety of goals may have been considered when completing the goal adjustment measure, e.g. daily vs long term, career related vs leisure/social. Goal content and goal importance is suggested to be important in motivational control, with differing goal types influencing behaviour in diverse ways (Deci & Ryan, 2000; Sheldon & Elliot, 1998; Sheldon et al., 2004). It should also be acknowledge that Hockey's theory

relates more specifically to cognitive rather than chronic fatigue. Thus it could be that goal persistence leads to task specific fatigue rather than the general fatigue as measured in this study. We should note, however, that separate analysis of the cognitive fatigue sub-scale of the MFI replicated the findings with general fatigue. Notwithstanding, further research should seek to control the type of goals considered and also to investigate potential differences in goal adjustment for a range of goal types as well as examining more closely the potential dynamical nature of the relationship of goal persistence and fatigue.

Limitations

A significant limitation of this study is the distinct overrepresentation of female participants. Epidemiological studies of Primary Systemic Vasculitis (GPA, CSS and MPA) report an equal male: female ratio or a slightly greater prevalence of Vasculitis in males (Lane et al., 2005; Fujimoto et al., 2011), consequently further research is required to investigate the generalisability of the study findings to males. A greater proportion of females compared to males have been reported to seek support and advice from peers from groups and online forums (Krizek et al., 1999; Seale, 2006). Therefore the female bias can likely be attributed to the online forum recruitment method used within this study. Another point of concern is the percentage of individuals scoring above the

threshold for significant fatigue was higher (91.2%) within this study compared to previous studies (76%, Grayson et al., 2013). This is a potential problem as it indicates a fairly restrictive range of fatigue scores in the sample, with high scores dominating. Again, this may be reflective of the recruitment method, with highly fatigued individuals self-selecting to participate. A further potential limitation relates to the inherent problem of causality associated with correlational designs. It may be that fatigue leads to PC, rather than the opposite causal association. It would be impractical to carry out a prospective analysis of PC in individuals with Vasculitis, however intervention studies aimed at reducing PC through therapy or training would allow further exploration of the direction of causation between PC and fatigue. Such studies could also re-evaluate the impact of goal persistence and goal type given the hypothesised dynamical nature of this relationship with fatigue in Hockey (2011).

Future research might usefully re-examine the variables identified to predict fatigue within previous Vasculitis research. For example, PC and RNT are recognised as core thinking styles associated with depression (McEvoy et al., 2013), therefore further exploring depression in combination with PC will allow the individual contribution of each to be established. Additionally, Grayson et al. (2013) reported illness perceptions to account for 18% of the variance in fatigue

beyond clinical and demographic variables. Therefore, research should seek to investigate the relationship between PC and illness perceptions within the context of MCT. There is evidence to suggest that depression predicts illness perceptions in individuals with other health conditions such as those requiring dialysis and with heart diseases (Chilcot et al., 2013; Dickens et al., 2008). Consequently, further research into a possible mediating role for PC and depression in the relationship between illness perceptions and fatigue should also be carried out.

Clinical Applications

The results of this study are preliminary and require confirmation by further research. However, if the relationship between PC and fatigue is supported, this finding can be used to inform therapeutic interventions for fatigue in Vasculitis. Existing treatments targeting PC include Rumination-Focussed Cognitive Behavioural Therapy (RFCBT; Watkins et al. 2007), Metacognitive Therapy (Wells, 1999) and mindfulness based interventions (Kabat-Zinn, 1982). A systematic review of nineteen interventions targeting PC identified both CBT and mindfulness based interventions to be effective in reducing PC (Querstret & Copley, 2013). Mindfulness based interventions have also been reported to improve fatigue outcomes in conditions such as Rheumatoid Arthritis, Multiple

Sclerosis and Cancer (Carlson & Garland, 2005; Grossman et al., 2010; Zangi et al., 2012). Furthermore, both CBT and mindfulness based interventions have been used to successfully reduce sleep disturbance and pain (Hewlett et al., 2011; Reiner et al., 2013; Williams et al., 2012) and therefore would enable several of the contributors to fatigue to be targeted within one intervention.

Conclusion

The use of MCT (Hockey, 2013) as a framework to investigate Vasculitis associated fatigue was partially supported by this study, demonstrating the utility of cross-discipline thinking and the application of research from other psychological perspectives. The use of pre-existing models of fatigue to inform the selection of potential determinants allows greater consideration of the underlying mechanisms, whilst also testing the validity of fatigue models in Vasculitis. The findings from this study add to the emerging evidence base which suggests that psychological variables contribute to Vasculitis associated fatigue beyond disease related variables. This highlights the importance of moving beyond pharmacological treatment approaches and the requirement to explore the efficacy of psychological therapeutic interventions for Vasculitis associated fatigue.

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Table 1. Sample Characteristics and Descriptive Statistics for predictor and outcome variables (N=249)

Sample Characteristics	N	%
<i>Gender</i>		
Male	N= 53,	21.3%
Female	N= 196,	78.6%
<i>Country of Residence</i>		
United Kingdom	N=151	60.9%
United States	N= 62	25.0%
Rest of World	N=35	14.1%
<i>Vasculitis Type</i>		
Churg Strauss Syndrome	N= 20	8.0%
Microscopic Polyangiitis	N= 25	10.0%
Granulomatosis Polyangiitis	N= 100	40.0%
Central Nervous System Vasculitis	N= 9	3.6%
Behcet's Disease	N= 21	8.4%
Giant Cell Arteritis	N= 7	2.8%
Henoch-Schönlein Purpura	N= 9	3.6%
Hypersensitivity Vasculitis	N= 2	0.8%
Polyarteritis Nodosa	N= 8	3.2%
Polymyalgia Rheumatica	N= 6	2.4%
Rheumatoid Vasculitis	N= 5	2.0%
Takayasu's Arteritis	N= 10	4.0%
Urticarial Vasculitis	N= 9	3.6%
<i>Disease Activity</i>		
Complete Remission	N= 10	4.0%
Drug Maintained Remission	N= 110	44.2%
Mildly Active	N= 65	26.1%
Moderately Active	N= 51	20.5%
Severely Active	N= 13	5.2%

Table 1. Continued

Descriptive Statistics	Mean (S.D.)
Age (Years)	50.28 (13.98)
Time Since Diagnosis (Years)	5.99 (6.78)
Prednisolone Dosage (mg)	7.58 (9.36)
Sleep Problems	14.16 (2.85)
Pain (Days)	18.62 (11.79)
Perseverative Cognition	27.42 (12.84)
Goal Disengagement	11.09 (2.96)
Goal Reengagement	20.24 (4.15)
General Fatigue	16.27 (2.73)

Table 2. R², Adjusted R², R² change, B, standard error of B and β for each predictor of fatigue in each step of the hierarchical regression analysis.

	B	SEB	β	R²	Adjusted R²	R² Change
Step One:				0.02	0.01	0.02
Age	0.00	0.01	0.04			
Gender	0.73	0.39	0.05			
Step Two:				0.27	0.24	0.25***
Time Since Diagnosis	0.03	0.02	0.09			
Prednisolone Dosage	-0.01	0.02	-0.04			
Sleep Problems	0.20	0.05	0.21***			
Pain	0.05	0.01	0.24***			
Disease Activity	1.11	0.30	0.19***			
Step Three:				0.30	0.28	.034**
Perseverative Cognition	.04	.01	.017**			
Step Four:				0.32	0.29	0.02
Goal Disengagement	-0.08	0.05	-0.10			
Goal Reengagement	-0.06	0.03	-0.10			

*p<.05, **p<.01, ***p<.001