**The clinical utility of metacognitive beliefs and processes in emotional distress in people with multiple sclerosis**

Running Title: Metacognitions and Multiple Sclerosis

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**Abstract**

**Aim:** Multiple sclerosis (MS) is a chronic demyelinating disease that poses significant life challenges. Depression and anxiety often occur in people with MS (PwMS). An information processing model of psychopathology, the Self-Regulatory Executive Function (S-REF) model specifies that maladaptive metacognitive beliefs play a fundamental role in the development and maintenance of distress. The model also asserts that a style of thinking known as the cognitive attentional syndrome (CAS), which consists of worry and rumination, focusing on sources of threat, and unhelpful coping responses, is common across all psychological conditions. This study investigated for the first time whether metacognitive beliefs explained additional variance in distress in PwMS, after accounting for demographic, clinical, and illness appraisal variables. **Method**: One hundred and thirty-two participants with MS completed self-report questionnaires measuring distress, fatigue, pain, metacognitive beliefs, illness appraisals, and the CAS. Hierarchical regression modelling was used to test whether metacognitive beliefs accounted for distress. Mediational modelling examined if the CAS mediated the association between metacognitive beliefs and distress. **Results:** Metacognitive beliefs made a unique contribution to distress, over and above demographic and clinical variables, and illness appraisals. The CAS fully mediated the relationship between positive metacognitive beliefs and distress, and partially mediated the relationship between negative metacognitive beliefs and distress. **Conclusions:** Metacognitive beliefs are associated with emotional distress in PwMS, and the CAS mediates this relationship. Future studies should examine if modification of metacognitive beliefs and processes in PwMS will lead to effective alleviation of emotional distress.

**Keywords:** Multiple sclerosis; depression; anxiety; metacognition; fatigue; pain

1. **Introduction**

Multiple sclerosis (MS) is a chronic and progressive inflammatory disease of the central nervous system, which affects around 2.5 million people worldwide [1, 2]. MS manifests in a variety of disabling symptoms, including motor and sensory disabilities, cognitive impairment, sexual dysfunction, pain, fatigue, and bladder and bowel disturbances [1, 3-7]. The often variable and unpredictable nature of the clinical symptoms can be frightening for people with MS (PwMS) [2]. Along with physical, sensory and cognitive symptoms, there are profound psychosocial challenges [7]. The onset for many PWMS occurs around early-to-mid adulthood [1], and there is frequent disruption to employment, family life, social roles, and leisure activities [7]. Emotional distress adds further disruption to the lives of PwMS [8]. Approximately a third of PwMS meet the diagnostic threshold for anxiety, and around half for depression [9], although some studies suggest the prevalence of anxiety is higher than depression [8, 10-12].

Acknowledging the significant psychosocial impact of MS, clinical guidance recommends cognitive-behavioural therapy (CBT) to treat distress in chronic physical health conditions [13]. While CBT has been shown to reduce distress in PwMS [14], effect sizes have been modest [15]. The limited efficacy of CBT could be due to the difficulties modifying negative cognitions. Research suggests PwMS often make realistic and accurate appraisals of their illness (e.g., “MS has major consequences on my life” and “MS is a serious condition”) [16], which is unsurprising given the challenging nature of the condition. A potentially more effective approach would be to address modifiable factors that maintain heightened distress. For example, persistent worry has been shown to be higher in PwMS compared to the healthy controls and is associated with higher levels of depression, fatigue and sleep disturbance [17].

The transdiagnostic Self-Regulatory Executive Function (S-REF) model [18, 19] is an information processing model of emotional disorder that may be applicable to PwMS experiencing emotional distress. According to the S-REF model, it is not the content of negative thoughts or negative appraisals related to MS that prolong distress *per se*, but metacognitive beliefs that drive a deleterious style of thinking and responding to those thoughts, known as the cognitive-attentional syndrome (CAS) [20]. The CAS consists of engaging in worry/rumination (i.e., perseverative thinking), focusing attention on sources of threat (e.g., focusing attention on bodily sensations), and coping responses that backfire (e.g., avoidance, drinking too much alcohol). According to the S-REF model, all aspects of the CAS are activated and maintained by metacognitive beliefs [18]. Positive metacognitive beliefs (PMCBS) encourage the selection of worry/rumination as a coping response (“Worrying about the future keeps me prepared”) with a heightened focus on threat monitoring (e.g., paying close attention to physical sensations). Negative metacognitive beliefs (NMCBS) further fuel distress because worry/rumination is appraised as uncontrollable and dangerous (“I have no control over my worry; I am losing my mind”), whilst also giving rise to unhelpful patterns of cognitive self-regulation (e.g., thought suppression, avoidance).

Although the utility of the S-REF model has been tested in several chronic health populations [21-24], so far, the model is untested in PwMS. Given that metacognitive therapy (MCT) [25] is an effective intervention for a range of anxiety and affective disorders [26], with techniques that target and modify metacognitive beliefs and interrupt the CAS [25], it raises the possibility that similar approaches may be applicable in chronic health populations such as PwMS. However, before MCT can be developed for PwMS, the predictions of the S-REF model must be empirically investigated whilst also considering how the predictions fit within current psychological understandings of the condition.

Consistent with the common-sense model [27, 28], the S-REF model also predicts that negative illness appraisals will be associated with distress, theoretically in the form of negative intrusions related to the illness, or as the specific of content of worry/rumination (e.g., “Nothing I do will affect my MS”). However, the S-REF model makes a further prediction that metacognitive beliefs will explain additional variance in distress after controlling for illness appraisals. This is because according to the model, it is not necessarily the content of thoughts or illness-specific appraisals that are fundamental to emotional distress, but the psychological factors involved in the control and regulation of cognition. Positive and negative metacognitive beliefs are hypothesised to influence distress via different pathways. Research examining the pathways between metacognitive beliefs and depression, via rumination support these predictions, with levels of rumination fully mediating the relationship between PMCBS and depression, and partially mediating the association between NMCBS and depression [29].

Metacognitive beliefs and processes are associated with emotional distress in other neurological populations [23, 24], therefore this study tested the predictions of the S-REF model in PwMS, whilst controlling for demographic and clinical variables, and illness appraisals [18, 19, 27, 28]. Specifically, this study makes the following predictions; 1) metacognitive beliefs will be positively associated with distress, 2) metacognitive beliefs will explain significant variance in distress after controlling for established covariates (i.e., demographic and clinical variables, and illness appraisals), and consistent with previous research [29], 3) the CAS will fully mediate the relationship between PMCBS and distress, and partially mediate the relationship between NCMBS and distress, whilst controlling for potential clinical and socio-demographic confounders (i.e., education, pain, fatigue and treatment control illness appraisals). These predicted pathways are based on the premise that PMCBS lead to distress indirectly by promoting the selection of unhelpful coping responses (e.g., worry/rumination), and NMCBS directly result in distress because these beliefs are both intrinsically distressing when worrying/ruminating, and in parallel they fuel distress promoting maladaptive coping responses (i.e., thought suppression, avoidance).

1. **Method**
	1. **Design**

This study reports data collected from an online cross-sectional survey. The study was approved by the University of Liverpool Ethics Committee (Reference: IPHS-1516-30).

* 1. **Participants and Procedure**

One hundred and thirty-two participants were recruited consecutively via an advert placed on the MS Society, MS Trust and National MS Society websites. PwMS were invited to complete an anonymous survey asking them about their beliefs about worry, perceptions of their illness and experiences of fatigue, pain, and depression and anxiety. They were informed before taking part that if they completed the survey they could enter a prize draw for a chance to win one of three £50 retail vouchers. Inclusion criteria were; 1) current diagnosis of MS, 2) aged 18 and over, and 3) the ability to understand written English. Data was obtained by self-report questionnaires using an online survey platform (Qualtrics).

* 1. **Measures**

2.3.1 Dependent variable

The Hospital Anxiety and Depression Scale (HADS) – Total Score [30] was used to measure distress. The HADS has been used widely in physical health populations [31] and has also been validated for use in PwMS [32]. In the present study, a cut-off score of eight or more for both the anxiety and depression subscales was used to define caseness of depression and anxiety [32, 33]. The HADS consists of 14 items, which are statements about symptoms of depression or anxiety, scored on a 4-point scale (e.g., 0 = *not at all* to 3 = *most of the time*; 0 = *definitely as much* to 3 = *hardly at all*). The HADS- Total showed adequate levels of internal consistency in this sample (α = 0.85).

* + 1. Independent variables

Demographic and clinical data was collected which included; gender, age, years in full-time education, ethnicity, employment status, duration of MS, clinical course, and history of treatment for depression and anxiety (i.e., current and past treatment for depression or anxiety).

The Fatigue Severity Scale (FSS) [34]was used to assess severity of fatigue. The FSS contains nine items, which are questions about how fatigue interferes with a range of activities, each scored on a 7-point scale (1 = *strongly disagree* to 7 = *strongly agree*). In this study, a mean score was used as an index for fatigue (i.e., total score/number of items). However, to designate severe levels of fatigue, a cut-off total score of 36 and over was used [34]. The FSS was designed and validated for use in MS and shows good psychometric properties [34]. The scale showed high internal consistency in this sample (α = 0.94).

Pain was measured with a visual analogue scale, a unidimensional measure used extensively in adult physical health populations [35]. Participants were asked to select a level of pain intensity on a visual continuum ranging from 0-100. A higher score indicated greater pain.

The Illness Perception Questionnaire-Revised (IPQ-R) [36]was used to measure cognitive appraisals of MS. The IPQ-R is valid and reliable measure in MS samples [36, 37]. This study used the core section of questionnaire, which consists of 38 items assessing beliefs and emotional responses to MS (e.g., “Nothing I do will affect my MS; There is very little that can be done to improve my MS”). Participants responded to each item using a 5-point scale (1 = *strongly disagree* to 5 = *strongly agree*). The IPQ-R has seven subscales; timeline (acute vs. chronic), consequences (effects and outcome), personal control, treatment control, coherence, timeline cyclical, and emotional representations. In the present study, as the scale was used to assess cognitive appraisals of MS, the emotional representation subscale was not used. The six subscales utilised showed acceptable-to-good levels of reliability in this sample (α = 0.73 to α = 0.86).

The Metacognitions Questionnaire-30 (MCQ) [38] was used to assess metacognitions. The MCQ-30 consists of five subscales; positive beliefs about worry (PMCBS), negative beliefs about the uncontrollability and dangerous nature of worry (NMCBS), cognitive confidence (CC), need to control thoughts (NC), and cognitive self-consciousness (CSC). The MCQ-30 has been used in other neurological populations, for example Parkinson’s disease and epilepsy [23, 24]. The scale consists of 30 items (e.g., “My worrying is dangerous for me; Worrying helps me avoid problems in the future”), scored on a 4-point scale (1 = *do not agree* to 5 = *agree very much*). Total subscales scores range from 6-24. Higher scores on the subscales indicate greater prominence of metacognitive beliefs. Subscales in this sample showed good levels of internal consistency (i.e., ranged from α = 0.8 to α = 0.93).

* + 1. Mediator variable

Cognitive Attentional Syndrome-10 (CAS-10) [25]. The CAS-10 is a 10 item self-report questionnaire that assesses metacognitive beliefs and processes. Items 7-10 duplicates the assessment of metacognitive beliefs and were thus disregarded. Items 1- 6 assess the extent to which individuals have been using the main aspects of the CAS; perseverative thinking in the form of worry/rumination (e.g., “How much time in the last week have you been dwelling on your problems?”), threat monitoring (e.g., “How much time in the past week have you been focusing your attention on things you find threatening?”), and unhelpful coping responses (e.g., “How much time in the past week have you tried to not think certain thoughts?”) [25]. Participants responded to each item with the degree to which they had engaged in the particular style of thinking or coping, on a continuous scale. For this study, an index score was calculated by dividing the total score by the number of items summed for the index. The CAS index score showed good levels of internal consistency in this sample (CAS α = 0.82).

* 1. **Statistical Analysis**

Intercorrelations between the primary predictor variables (i.e., distress, pain, fatigue, illness appraisals, metacognitive beliefs, and the CAS) were tested with parametric and non-parametric methods. Due to the large number of correlations calculated, a significance criterion of 0.01 was adopted to reduce Type 1 error. In the main analysis, hierarchical regression was used to test whether metacognitions explained additional variance in distress in PwMS, after controlling for demographic, clinical variables (i.e., pain, fatigue, and the CAS), and illness appraisals. Multicollinearity was inspected by examining the variable inflation factor (VIP) and tolerance for all variables entered in the regression (cut offs; VIP < 10, tolerance > 0.2) [39]. The order of the variables and method of entry into the regression equation was based on methodological and logical precedence. Each block of variables was entered using forced entry. Step 1 controlled for demographic variables (age, gender, education, and employment status); Step 2 controlled for clinical variables (pain, fatigue, and the CAS); Step 3 controlled for cognitive appraisals of illness (IPQ-R subscales); and Step 4 tested the prediction that metacognitive beliefs (MCQ-30 subscales), would contribute to distress after controlling for the aforementioned variables.

To test the hypothesised relationships between metacognitive beliefs, the CAS and distress, two mediational analyses were performed; Model 1, *x* = PMCBS, *m* = CAS, *y* = distress, and Model 2, *x* = NMCBS, *m* = CAS, *y* = distress. Both mediation models controlled variables that made significant independent contributions in the hierarchical regression (education, pain, fatigue, and treatment control). Three criteria for carrying out mediation analyses were satisfied in this study [40]; 1) all variables entered into the mediational model were significantly correlated, 2) the design of the model used was based on previous prospective research suggesting metacognitive beliefs play a causal role in distress [22, 41], and 3) the relationship between metacognitive beliefs and distress was reduced or eliminated when accounting for variance in the CAS. All analyses were carried out using SPSS version 20.0.0 Hayes [42]. The PROCESS macro for SPSS was used to run the mediational analyses. Bootstrapping with 5,000 samples was used in line with recommendations [43].

**3. Results**

**3.1 Sample Characteristics**

Table 1 provides a summary of the sample characteristics. Of the 132 participants that completed the survey, 100 (75.8%) reported having relapse-remitting MS (RRMS). A large proportion of the sample had received or were in receipt of treatment for anxiety or depression (84.8%). Seventy-two participants met the threshold for caseness of comorbid depression and anxiety (54.5%) [32, 33] with anxiety being more prevalent than depression (80% and 60%, respectively). One hundred and thirteen (85.6%) participants reported severe levels of fatigue [34]. One hundred and twenty-five (94.7%) identified themselves as White, which is a moderately higher composition of Caucasian people compared to African or Asian as found in epidemiological studies of PwMS [44].

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| **Table 1**Sample characteristics (N= 132) |
| **Variable** | **N (%) or Mean (SD)** |
| Demographic Variables: |  |
| Gender |  |
| Female | 111 (84.1%) |
| Male | 21 (15.9%) |
| Age in years | M = 43.3 (SD = 11.94) |
| Years full-time education | M = 14.43 (SD = 3.2) |
| Ethnicity |  |
| White | 125 (94.7%) |
| African | 1 (0.8%) |
| Caribbean | 2 (1.5%) |
| Asian | 1 (0.8%) |
| Mixed ethnicity | 1 (0.8%) |
| Other | 2 (1.5%) |
| Number employed | 65 (49.2%) |
| Clinical Variables: |  |
| Duration of MS in years | M = 7.31 (SD = 7.5) |
| Disease course |  |
| RRMS | 100 (75.8%) |
| SPMS | 15 (11.4%) |
| PPMS | 8 (6.1%) |
| PRMS | 2 (1.5%) |
| Unknown | 7 (5.3%) |
| Received treatment for depression / anxiety | 81 (61.4%) |
| Past treatment for depression / anxiety | 100 (75.8%) |
| HADS caseness for depression | 82 (62.1%) |
| HADS caseness for anxiety | 105 (79.5%) |
| HADS comorbid depression & anxiety | 72 (54.5%) |
| Fatigue | M = 5.71 (SD = 1.4) |
| Pain | M = 3.98 (SD = 3.1) |
| *Note*. RRMS = relapse remitting MS; SPMS = secondary progressive MS; PPMS = primary progressive MS; PRMS = progressive lapsing MS. Caseness for depression and anxiety was defined by a score of 8 or more on both HADS subscales [30]. A mean score from the FSS was used in the present study (i.e., total score/number of items). Pain was scored on a VAS ranging from 0 *no pain* – 10 *unbearable pain.*  |

* 1. **Correlations and Descriptive Statistics**

Intercorrelations and descriptive statistics for the independent and dependent variables (i.e., IPQ-R, MCQ-30 subscales and the CAS) are presented in Table 2. Three illness appraisal subscales were significantly associated with distress (i.e., positive correlation for consequences, and negative correlations for personal and treatment control, *r=* 0.30 to 0.35, *p <* 0.01). Of the metacognition subscales, four were positively associated with distress (PMCBS, NMCBS, CC, and NC, *r=* 0.37 to 0.49, *p <* 0.01), confirming the first prediction of this study. Positive and negative metacognitive beliefs did not correlate with any of the illness appraisal subscales, but did correlate with the CAS.

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| **Table 2**Descriptive statistics and intercorrelations between the study independent variables, mediator variable and distress (HADS Total Score) |
|  | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | **11** | **12** | **13** | **M** | **SD** |
| 1     HADS | .18 | .30\* | -.24\* | -.35\* | -.15 | .22 | .22\* | .49\* | .45\* | .37\* | 0.1 | .67\* | 19.46 | 6.92 |
| 2     T |  | .26\* | -.25\* | -.46\* | .06 | .04 | -.05 | .02 | .24\* | .01 | -.09 | .05 | 26.74 | 3.9 |
| 3     C |  |  | -.08 | -.37\* | -.08 | .18 | -.05 | .10 | .31\* | .10 | .20 | .28\* | 24.64 | 4.18 |
| 4     PC |  |  |  | .49\* | .12 | .03 | .06 | .03 | -.10 |  .01 | .23\* | -.20\* | 19.35 | 5.17 |
| 5     TC |  |  |  |  | .01 | .04 | .07 | -.11 | -.33\* | -.09 | .08 | -.26\* | 13.79 | 4 |
| 6     IC |  |  |  |  |  | -.29\* | -.09 | -.05 | -.18 | -.16 | .04 | -.23\* | 16.46 | 5.42 |
| 7     TLC |  |  |  |  |  |  | .06 | .11 | .29\* |  .19 | .07 | .23\* | 14.16 | 3.66 |
| 8     PMCBS |  |  |  |  |  |  |  | .45\* |  .09 | .59\* | .31\* | .26\* | 10.84 | 4.38 |
| 9     NMCBS |  |  |  |  |  |  |  |  | .28\* | .61\* | .42\* | .59\* | 14.61 | 4.49 |
| 10   CC |  |  |  |  |  |  |  |  |  | .28\* | .10 | .35\* | 15.08 | 5.52 |
| 11   NC |  |  |  |  |  |  |  |  |  |  | .43\* | .41\* | 11.89 | 4.33 |
| 12   CSC |  |  |  |  |  |  |  |  |  |  |  | .27\* | 16.24 | 4.46 |
| 13   CAS |  |  |  |  |  |  |  |  |  |  |  |  | 4.15 | 2.01 |
| *Note.* M = Mean; SD = Standard deviation; HADS = Total Distress; *IPQ-R Subscales*: T = Timeline; C = Consequences; PC = Personal Control; TC = Treatment Control; IC = Illness Coherence; TLC = Timeline Cyclical. *MCQ-30 Subscales*: PMCBS = Positive Metacognitive Beliefs; NMCBS = Negative Metacognitive Beliefs; CC = Cognitive Confidence; NC = Need to Control; CSC = Cognitive Self-consciousness; CAS = Cognitive Attentional Syndrome Index; \* *p* < 0.01 |

* 1. **The Unique Contribution of Metacognitive Beliefs to Distress**

Table 3 shows the results from the hierarchical regression predicting distress, whilst controlling for demographic and clinical variables (age, gender, employment, pain, fatigue, and the CAS), and illness appraisals. Demographic variables entered at Step 1 were non-significant (*F* = 1.89, *df =* 4,127, *p =* 0.11). Levels of pain, fatigue, and the CAS entered as a block at Step 2 were significant (*Fchange* = 46.24, *df* = 3,124, *p* < 0.001), accounting for an additional 49.8% of the variance in distress. The illness appraisal variables entered at Step 3 did not make a significant contribution (*Fchange* = 0.89, *df* = 6,118, *p* = 0.506). In the final step of the model, Step 4, the metacognitive variables made a significant contribution to the variance in distress accounting for an additional 4.5% of the variance (*Fchange* = 2.695, *df* = 5,113, *p* < 0.05), and thus confirmed the second prediction of the study. Overall the final model explained 55.9% of the variance in distress. There were four independent predictors in the final model, fewer years in full time education (*β* = -0.20, *p* < 0.05), severity of the CAS (*β* = 0.57, *p* < 0.001), severity of fatigue (*β* = 0.24, *p* < 0.001), and conviction in NMCBS (*β* = 0.19, *p* < 0.05).

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| **Table 3** Summary of the hierarchical regression predicting distress (HADS Total Score) |
| **Step** | **Variable** | **Δ*R*2** | **Sig.** | ***Standardised*** ***βeta*** | ***T*** | **Sig.** |
| 1 |  | 0.056 | 0.115 |  |  |  |
|  | Age |  |  | -0.076 |  -0.820 | 0.414 |
|  | Gender |  |  |  0.011 |  0.121 | 0.904 |
|  | Education |  |  | **-0.202** |  **-2.260** | **0.026** |
|  | Employment |  |  | -0.125 |  -1.342 | 0.182 |
| 2 |  | **0.498** | **0.000** |  |  |  |
|  | Pain |  |  | 0.083 |  1.131 | 0.260 |
|  | Fatigue |  |  | **0.244** |  **3.382** | **0.001** |
|  | CAS |  |  | **0.568** | **8.572** | **0.000** |
| 3 |  | 0.019 | 0.506 |  |  |  |
|  | Timeline |  |  | 0.055 | 0.786 | 0.434 |
|  | Consequences |  |  | -0.020 | -0.259 | 0.796 |
|  | Personal Control |  |  | 0.140 | 0.187 | 0.852 |
|  | Treatment Control |  |  | -0.113 | -1.356 | 0.178 |
|  | Illness Coherence |  |  | 0.049 | 0.741 | 0.460 |
|  | Timeline Cyclical |  |  | 0.015 | 0.220 | 0.826 |
| 4 |  | **0.045** | **0.024** |  |  |  |
|  | PMCBS |  |  | 0.031 | 0.399 | 0.691 |
|  | **NMCBS** |  |  | **0.194** | **2.139** | **0.035** |
|  | Cognitive Confidence |  |  | 0.098 | 1.275 | 0.205 |
|  | Need to Control |  |  | 0.082 | 0.897 | 0.371 |
|  | CSC |  |  | -0.104 | -1.423 | 0.157 |
| *Note.* CAS = Cognitive Attentional Syndrome; PMCBS = Positive Metacognitive Beliefs; NMCBS = Negative Metacognitive Beliefs; CSC = Cognitive Self-consciousness. Significant results highlighted in bold.  |

* 1. **Mediation of the Association between Metacognitive Beliefs and Distress by the CAS**

Results of the mediational analyses are presented in Figures 1 and 2. In both mediational models education, pain, fatigue and treatment control appraisals were controlled for as covariates. In the mediation model assessing the role of the CAS in mediating the relationship between PMCBS and distress, there was a significant indirect effect of the CAS (*ab* = 0.22, BCa 95% CIs = 0.08 to 0.39. The results indicated full mediation, as the direct effect between PMCBS and distress was non-significant when accounting for the CAS. Similarly, the mediation model assessing the CAS as a mediator of the relationship between NMCBS and distress was significant (*ab* = 0.35, BCa 95% CIs = 0.22 to 0.52). However, the direct effect remained significant when including the CAS in the model, indicating partial mediation (*b =* 0.38*, p* < 0.01).



*Notes*. PMCBS = positive metacognitive beliefs about worry; CAS = cognitive attentional syndrome; n.s = non-significant; \* *p* < 0.01; Model covariates; education, pain, fatigue and treatment control. Bootstrapping with 5,000 samples was used.



*Notes*. NMCBSs = negative metacognitive beliefs about worry; CAS = cognitive attentional syndrome; n.s = non-significant; \* *p* < 0.01; Model covariates; education, pain, fatigue and treatment control. Bootstrapping with 5,000 samples was used.

1. **Discussion**

This study investigated the role of metacognitive beliefs in distress in PwMS, specifically testing the predictions of the S-REF model for the first time in this population. In this sample, four types of metacognitive beliefs were positively associated with distress (i.e., PMCBS, NMCBS, Cognitive Confidence, and Need to Control), confirming the first prediction of the study. In addition, the second study prediction was supported which asserted that metacognitive beliefs would make an incremental contribution to distress after controlling for demographic variables, levels of pain and fatigue, the CAS (i.e., worry/rumination, focusing attention on sources of threat, and coping responses that backfire), and illness appraisals. Of the metacognitive variables measured, NMCBS emerged as a significant and unique predictor of distress. In the mediational analysis, the relationship between PMCBS and distress was fully mediated by the CAS, while the CAS partially mediated the association between NMCBS and distress, in line with the final prediction of the study and previous research [29].

* 1. **Metacognitive Beliefs and Distress**

Findings were consistent with the results from previous studies testing the role of metacognitive beliefs in emotional distress in other chronic health populations [22, 23]. However, while positive and significant correlations were evident for both PMCBS and NMCBS with distress in the correlational analysis, only NMCBS made an independent and significant contribution in the regression model. These results suggest that NMCBS about the uncontrollability and dangerous nature of worry (e.g., “Once I start worrying, I cannot stop; I am damaging my mind with worry”), and the extent to which participants engaged in the main aspects of the CAS and experienced fatigue, are particularly important factors involved in elevated distress in PwMS. The negative finding for PMCBS was noteworthy, given these metacognitive beliefs (e.g., “Worrying helps me avoid problems in the future”) have been implicated in other physical health populations such as people with cancer [22]. However, here we used the HADS total distress score, where previous research has modelled depression and anxiety separately [22]. This difference in the significance of PMCBS and NMCBS may have been due to the MCQ-30 lacking sensitivity to PMCBS about rumination, which is often a more prominent feature in depression [45] and less evident in anxiety, which tends to present with future-orientated perseverative thinking (i.e., worry). In this sample there were a high proportion of cases that presented with clinically significant depression and lower anxiety. As such, according to the S-REF model, these cases would be predicted to present with positive beliefs about the usefulness of rumination, as opposed to worry which the MCQ-30 measures.

* 1. **Illness Appraisals and Distress**

The results suggested that illness appraisals about the consequences (e.g., “My MS has major consequences on my life”), and personal and treatment control over the illness (e.g., “My actions will have no effect on the outcome of my illness; There is very little that can be done to affect the outcome of my MS”) were associated with distress in this sample, consistent with previous studies testing the assertions of the common-sense model in this population [16, 46]. However, after controlling for demographic and clinical variables, illness appraisals did not account for additional variance in distress. Given that previous studies have not controlled for levels of pain and fatigue [16, 46], it is possible that these variables play an important role in influencing the nature of an individual’s perceptions of illness. Thus by controlling for the variance in distress attributable to these strongly correlated covariates, little additional variance remains to be explained by the illness appraisal variables in which the research question is focused. Indeed, previous research has identified links between fatigue and illness appraisals [37, 47].

A further explanation for the negative findings for the range of illness appraisals measured, is that different illness appraisal domains may be differentially associated with depression and anxiety, which has been found when depression and anxiety have been modelled separately [16]. For example, higher levels of anxiety may be predicted by illness appraisals in relation a cyclical timeline (e.g., “I go through cycles in which my MS gets better and worse”) due to higher levels of anxiety in anticipation of relapse, whereas depression may predicted by illness appraisals about personal control of the illness (e.g., “Nothing I do will affect my MS”) which could potentially encourage rumination about failed attempts to influence the course of the illness.

* 1. **Metacognitive Beliefs and the CAS**

According to the S-REF model, PMCBS do not cause distress *per se*, but do so by promoting the selection of worry/rumination as a coping response (e.g., “Worrying helps me cope”) and increasing focus on sources of threat, whilst NMCBS lead to negative appraisals of worry/rumination (e.g., “My worrying could make me go mad” and “When I start worrying, I cannot stop”) and unhelpful self-regulation strategies (e.g., avoidance and thought suppression). The results of the mediational analysis supported these hypothesises, with a full mediation effect of the CAS between PMCBS and distress in which the significance of the relationship between PMCBS and distress was eliminated when accounting for the CAS, and a partial mediation effect of the CAS between NMCBS and distress whereby the relationship between NMCBS and distress remained significant when the CAS entered the mediational model. These findings cross-validate previous studies employing comparable mediational models in other chronic health populations [29, 48].

* 1. **Study Limitations**

While this study provides the first evidence implicating the deleterious role of metacognitive beliefs in PwMS, several limitations were evident. Firstly, relationships between the outcome and predictors could be reversed, in which distress causes the predictor variables rather than the assumed direction of causality. Nevertheless, the predictions were based on previous longitudinal research [22, 41). Secondly, while the study controlled for established clinical variables (i.e., pain and fatigue), there are other potentially important variables that warrant measurement, such as disease severity [49-53). Thirdly, the representativeness of the sample may have been limited, given most of the sample were female, and predominantly White, exceeding estimates from epidemiological research [44].

* 1. **Implications and Conclusions**

The findings largely support the relevance of the S-REF model in the maintenance of distress in PwMS, specifically the deleterious role of negative beliefs about the uncontrollability and harmful nature of worry. Psychological interventions with PwMS may be most effective when they target and modify metacognitive beliefs and the CAS (e.g., tackling worry/rumination, attentional focus, and unhelpful coping responses such as avoidance). Such an approach diverges from traditional cognitive-behavioural therapy, which would focus more on modifying cognitive content, both in relation to the distressing aspects of the illness (e.g., “I could have another relapse any day now”), and negative illness appraisals (e.g., “My illness has major consequences on my life”) that are often appropriate and realistic in PwMS [16].

To take forward the findings of this study, longitudinal research is necessary to investigate whether metacognitive beliefs measured at baseline predict distress over time, whilst controlling for baseline levels of distress, demographic variables, clinical variables including elements of the CAS, and illness appraisals. To support the translation of these empirical findings to clinical practice, psychological interventions that target and modify NMCBS in PwMS should be investigated in trials testing their efficacy against traditional cognitive-behavioural approaches.

**Acknowledgments**

We would like to thank the Multiple Sclerosis Trust, the Multiple Sclerosis Society, and the National Multiple Sclerosis Society for supporting this study; we would also like to thank Peter Salmon for his review and comments on an earlier draft of the paper.

**References**

1. Haussleiter IS, Brüne M, Juckel G. Psychopathology in multiple sclerosis: Diagnosis, prevalence and treatment. Therapeutic Advances in Neurological Disorders. 2009;2(1):13-29.

2. Compston A, Coles A. Multiple sclerosis (vol 359, pg 1221, 2002). Lancet. 2002;360(9333):648.

3. Bol Y, Duits AA, Lousberg R, Hupperts RMM, Lacroix MHP, Verhey FRJ, et al. Fatigue and physical disability in patients with multiple sclerosis: A structural equation modeling approach. Journal of Behavioral Medicine. 2010;33(5):355-63.

4. Harrison AM, McCracken LM, Bogosian A, Moss-Morris R. Towards a better understanding of MS pain: A systematic review of potentially modifiable psychosocial factors. Journal of Psychosomatic Research. 2015;78(1):12-24.

5. Kessler TM, Fowler CJ, Panicker JN. Sexual dysfunction in multiple sclerosis. Expert Review of Neurotherapeutics. 2009;9(3):341-50.

6. Brissart H, Morele E, Baumann C, Debouverie M. Verbal episodic memory in 426 multiple sclerosis patients: Impairment in encoding, retrieval or both? Neurological Sciences. 2012;33(5):1117-23.

7. Dennison L, Moss-Morris R. Cognitive-behavioral therapy: What benefits can it offer people with multiple sclerosis? Expert Review of Neurotherapeutics. 2010;10(9):1383-90.

8. Janssens AC, van Doorn PA, de Boer JB, van der Meché FG, Passchier J, Hintzen RQ. Impact of recently diagnosed multiple sclerosis on quality of life, anxiety, depression and distress of patients and partners. Acta Neurologica Scandinavica. 2003;108(6):389-95.

9. Jones KH, Ford DV, Jones PA, John A, Middleton RM, Lockhart-Jones H, et al. A large-scale study of anxiety and depression in people with Multiple Sclerosis: A survey via the web portal of the UK MS Register. PloS one. 2012;7(7):e41910.

10. Feinstein A, O'Connor P, Gray T, Feinstein K. The effects of anxiety on psychiatric morbidity in patients with multiple sclerosis. Multiple Sclerosis. 1999;5(5):323-6.

11. Korostil M, Feinstein A. Anxiety disorders and their clinical correlates in multiple sclerosis patients. Multiple Sclerosis. 2007;13(1):67-72.

12. Garfield AC, Lincoln NB. Factors affecting anxiety in multiple sclerosis. Disability & Rehabilitation. 2012;34(24):2047-52.

13. National Institute of Health and Care Excellence. Depression in adults with a chronic physical health problem: Recognition and management. London, UK: NICE; 2009.

14. Mohr DC, Boudewyn AC, Goodkin DE, Bostrom A, Epstein L. Comparative outcomes for individual cognitive-behavior therapy, supportive-expressive group psychotherapy, and sertraline for the treatment of depression in multiple sclerosis. Journal of Consulting & Clinical Psychology. 2001;69(6):942-9.

15. Hind D, Cotter J, Thake A, Bradburn M, Cooper C, Isaac C, et al. Cognitive behavioural therapy for the treatment of depression in people with multiple sclerosis: A systematic review and meta-analysis. BMC Psychiatry. 2014;14:5.

16. Vaughan R, Morrison L, Miller E. The illness representations of multiple sclerosis and their relations to outcome. British Journal of Health Psychology. 2003;8(Pt 3):287-301.

17. Bruce JM, Arnett P. Clinical correlates of generalized worry in multiple sclerosis. Journal of Clinical & Experimental Neuropsychology. 2009;31(6):698-705.

18. Wells A, Matthews G. Attention and emotion: A Clinical perspective. Hove, UK: Erlbaum; 1994.

19. Wells A, Matthews G. Modelling cognition in emotional disorder. Behaviour Research & Therapy. 1996;32:867-70.

20. Fisher P, Wells A. Metacognitive therapy: Distinctive features. London: Taylor & Francis; 2009.

21. Maher-Edwards L, Fernie BA, Murphy G, Wells A, Spada MM. Metacognitions and negative emotions as predictors of symptom severity in chronic fatigue syndrome. Journal Of Psychosomatic Research. 2011;70(4):311-7.

22. Cook SA, Salmon P, Dunn G, Holcombe C, Cornford P, Fisher P. A prospective study of the association of metacognitive beliefs and processes with persistent emotional distress after diagnosis of cancer. Cognitive Therapy & Research. 2015;39(1):51-60.

23. Allott R, Wells A, Morrison AP, Walker R. Distress in Parkinson's disease: Contributions of disease factors and metacognitive style. British Journal of Psychiatry. 2005;187:182-3.

24. Fisher PL, Cook SA, Noble A. Clinical utility of the Metacognitions Questionnaire 30 in people with epilepsy. Epilepsy & Behavior. 2016;57, Part A:185-91.

25. Wells A. Metacognitive therapy for anxiety and depression. New York: Guilford Publications; 2008.

26. Normann N, van Emmerik AAP, Morina N. The efficacy of Metacognitive Therapy for anxiety and depression: A meta-analytic review. Depression & Anxiety. 2014;31(5):402-11.

27. Leventhal H, Nerenz DR, Steel DJ. Illness representations and coping with health threats. In: Baum A, Singer J, editors. A Handbook of Psychology and Health. Hillsdale (NJ): Erlbaum; 1984. p. 411-6.

28. Leventhal H, Benyamini Y, Brownlee S, Diefenbach M, Leventhal E, Patrick-Miller L, et al. Illness representations: Theoretical foundations. In: Petrie KJ, Wieinman J, editors. Perceptions of health and illness: Current research and applications. Amsterdam: Harwood; 1997. p. 19-45.

29. Huntley CD, Fisher PL. Examining the role of positive and negative metacognitive beliefs in depression. Scandinavian Journal of Psychology. 2016;57(5):446-52.

30. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatrica Scandinavia. 1983;67(6):361-70.

31. Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. Journal of Psychosomatic Research. 2002;52(2):69-77.

32. Honarmand K, Feinstein A. Validation of the Hospital Anxiety and Depression Scale for use with multiple sclerosis patients. Multiple Sclerosis. 2009;15(12):1518-24.

33. Watson TM, Ford E, Worthington E, Lincoln NB. Validation of mood measures for people with multiple sclerosis. International Journal of MS Care. 2014;16(2):105-9.

34. Krupp LB, LaRocca NG, Muir-Nash J, Steinberg AD. The Fatigue Severity Scale: Application to patients with multiple sclerosis and systemic lupus erythematosus. Archives of Neurology. 1989;46(10):1121-3.

35. Hawker GA, Mian S, Kendzerska T, French M. Measures of adult pain: Visual Analog Scale for Pain (VAS Pain), Numeric Rating Scale for Pain (NRS Pain), McGill Pain Questionnaire (MPQ), Short-Form McGill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), Short Form-36 Bodily Pain Scale (SF-36 BPS), and Measure of Intermittent and Constant Osteoarthritis Pain (ICOAP). Arthritis Care & Research. 2011;63(S11):S240-S52.

36. Moss-Morris R, Weinman J, Petrie KJ, Horne R, Cameron LD, Buick D. The Revised Illness Perception Questionnaire (IPQ-R). Psychology & Health. 2002;17:1-16.

37. Jopson NM, Moss-Morris R. The role of illness severity and illness representations in adjusting to multiple sclerosis. Journal of Psychosomatic Research. 2003;54(6):503-11.

38. Wells A, Cartwright-Hatton S. A short form of the metacognitions questionnaire: Properties of the MCQ-30. Behaviour Research & Therapy. 2004;42(4):385-96.

39. Belsley DA, Kuh E, Welsch RE. Detecting and assessing collinearity. Regression Diagnostics. New Jersey, US: John Wiley & Sons; 2005. p. 85-191.

40. Kraemer HC, Wilson GT, Fairburn CG, Agras WS. Mediators and moderators of treatment effects in randomized clinical trials. Archives of General Psychiatry. 2002;59(10):877-83.

41. Yilmaz AE, Gencoz T, Wells A. The temporal precedence of metacognition in the development of anxiety and depression symptoms in the context of life-stress: A prospective study. Journal of Anxiety Disorders. 2011;25(3):389-96.

42. Hayes AF. An introduction to mediation, moderation, and conditional process analysis: A regression-based approach. New York: Guildford Press; 2013.

43. Preacher K, J., Hayes AF. SPSS and SAS procedures for estimating indirect effects in simple mediation models. Behavior Research Methods, Instruments, & Computers. 2004;36(4):717-31.

44. Flachenecker P. Epidemiology of neuroimmunological diseases. Journal of Neurology. 2006;253(*Suppl*.5):V2-V8.

45. Papageorgiou C, Wells A. Depressive rumination: Nature, theory and treatment. Chichester: Wiley; 2004.

46. Dennison L, Moss-Morris R, Silber E, Galea I, Chalder T. Cognitive and behavioural correlates of different domains of psychological adjustment in early-stage multiple sclerosis. Journal of Psychosomatic Research. 2010;69(4):353-61.

47. Schwartz CE, Coulthard-Morris L, Zeng Q. Psychosocial correlates of fatigue in multiple sclerosis. Archives of Physical Medicine & Rehabilitation. 1996;77(2):165-70.

48. Cook SA, Salmon P, Dunn G, Holcombe C, Cornford P, Fisher P. The association of metacognitive beliefs with emotional distress after diagnosis of cancer. Health Psychology. 2015;34(3):207-15.

49. Téllez N, Río J, Tintoré M, Nos C, Galán I, Montalban X. Fatigue in multiple sclerosis persists over time: A longitudinal study. Journal Of Neurology. 2006;253(11):1466-70.

50. Šabanagić-Hajrić S, Suljić E, Sulejmanpašić-Arslanagić G. Depression during multiple sclerosis relapse: Relation to disability and relapse severity. Medicinski Glasnik: Official Publication Of The Medical Association Of Zenica-Doboj Canton, Bosnia And Herzegovina. 2016;13(1):44-9.

51. Jones KH, Jones PA, Middleton RM, Ford DV, Tuite-Dalton K, Lockhart-Jones H, et al. Physical disability, anxiety and depression in people with MS: An internet-based survey via the UK MS Register. PloS one. 2014;9(8):e104604-e.

52. Arnett PA, Randolph JJ. Longitudinal course of depression symptoms in multiple sclerosis. Journal of Neurology, Neurosurgery & Psychiatry. 2006;77(5):606-10.

53. Huber SJ, Rammohan KW, Bornstein RA, Christy JA. Depressive symptoms are not influenced by severity of multiple sclerosis. Neuropsychiatry, Neuropsychology, & Behavioral Neurology. 1993;6(3):177-80.