Abstract

Introduction: One of the strongest predictors of successful coping in multiple sclerosis (MS) is the extent to which one can accept the diagnosis and limitations associated with the disease. Acceptance is also one of three core processes of *psychological flexibility* – a malleable treatment target of some psychological therapies. This is the ability to notice and accept the presence of thoughts and feelings without being swept along by them, engaging in the present moment, and making decisions in line with personal values.

Poor psychological flexibility is associated with elevated levels of distress in the general population. However, we do not know the level of psychological flexibility in people with MS, or its relationship to distress or quality of life when the disease becomes more physically disabling. The aims of this study were to determine the level of psychological flexibility, and its relationship with distress and quality of life in secondary progressive multiple sclerosis (SPMS), a subtype of MS with increased severity of disability and distress.

Method: This cross-sectional analytic study used data collected by the UK MS Register. Pre-existing data on distress, quality of life, disability, and demographics collected by the UK MS Register were combined with a psychological flexibility measure and its component parts, collected for the purpose of this study.

Patient demographics and questionnaire data were recorded for distress, quality of life, and psychological flexibility. Pearson's correlations were used to examine bivariate relationships between distress, quality of life, disability and psychological flexibility. Whether psychological flexibility moderated the relationship between disability (predictor), distress and quality of life (outcomes) was also investigated.

Results: Between February and March 2020, 628 participants with SPMS completed the CompACT and had a recent (<12 months) HADS questionnaire (M^{age} = 60.66, 70.90% women). On the HADS questionnaire subscales, 44% of the sample scored above the MS clinical cut-off (≥8) for anxiety (*M* = 7.09, *SD* = 4.57), and 30% above the clinical cut off (≥11) for depression (*M* = 8.35, *SD* = 4.21). Psychological flexibility (*M* = 81.94, *SD* = 22.60) and its components were each moderately negatively correlated with total distress (*r* = -0.65), anxiety (*r* = −0.58), and depression (*r* = -0.56). A second subsample (*n* = 434) completed the EQ-5D-5L health-related quality of life measure, which was moderately positively correlated with psychological flexibility (*r* = 0.47). A third subsample (*n* = 210) found a weak negative relationship between psychological flexibility and disability (*r* = -0.16), a weak positive relationship between distress and disability (*r* = 0.26), and a moderate negative relationship between quality of life and disability (*r* = -0.56). Psychological flexibility was not found to moderate the rate of change in anxiety, depression, or quality of life as disability increases in SPMS.

Discussion: Greater psychological flexibility was associated with lower self-reported distress and higher quality of life in this SPMS sample. It was not shown to moderate the extent to which physical disability predicts distress or quality of life in SPMS.

These findings demonstrate that greater psychological flexibility is related to better coping outcomes (lower distress, higher quality of life) in SPMS. If psychological flexibility can be increased in people with SPMS, this could lead to a reduction in distress and improvement in quality of life, although directionality could not be attributed with these methods. Further longitudinal evidence and trials of psychological flexibility-focussed interventions are needed.

Keywords: multiple sclerosis, psychological flexibility, cross-sectional, distress, quality of life

Psychological Flexibility, Distress, and Quality of Life in Secondary Progressive Multiple Sclerosis: A Cross-sectional Study

Multiple Sclerosis (MS) is a chronic inflammatory demyelinating disease of the central nervous system. It has a prevalence of approximately 2.2 million people worldwide, with 106,000 in the United Kingdom (UK) (Wallin et al., 2019). It is the most common cause of non-traumatic disability in young adults and typically begins between the ages of 20 and 40. Secondary Progressive Multiple Sclerosis (SPMS) is a subtype of MS, which is defined by a gradual decline in function and a progressive accumulation of disability after an initial relapsing remitting course. Gradual worsening of symptoms, lack of clear recovery and an increased severity, and presence of new symptoms are markers for this stage of the disease (Lublin et al., 2014). SPMS has a high personal cost: those with MS already experience a higher prevalence of clinical depression and anxiety than the general population (Boeschoten et al., 2017), with progressive forms most severely affected (Jones et al., 2012).

Those who manage the difficulties associated with MS most successfully often have better access to social support, but also use an acceptance-focussed coping style demonstrated in relapsing remitting MS (RRMS) (Topcu et al., 2020) and SPMS (Meek et al., 2020). Topcu et al. (2020) found that the ability to balance internal and external stressors in MS with acceptance-based coping and support can assist with adjustment. This mirrors adapting to broader chronic illness where successful adjustment involves accepting illness challenges and making adaptations to maintain 'equilibrium' in the face of new stressors (Moss-Morris, 2013).

Acceptance is also one of three core processes of *psychological flexibility* – the ability to notice and accept the presence of thoughts and feelings without being swept along by them, engaging in the present moment, and making decisions in line with personal values (Cherry et al., 2021). It is a treatment target of some psychological therapies, and a set of interpersonal and intrapersonal processes which can be trained (McCracken & Gutiérrez-Martínez, 2011). Psychological flexibility is a fundamental determinant of health (Kashdan & Rottenberg, 2010), because it encompasses an individual's ability to recognise and adapt to situational demands, shift their mindset or behaviour when existing strategies compromise personal or social functioning, and maintain a sense of balance among important life domains to ensure behaviour which is congruent with deeply held values. This differs from traditional understandings of psychological health, where positive internal experiences (i.e., emotions and thoughts) are to be embraced, whilst negative internal experiences are to be challenged or avoided (Kashdan & Rottenberg, 2010).

Psychological flexibility has been measured in general and clinical populations through self-report measurements such as the Acceptance and Action Questionnaire (AAQ) (Bond et al., 2011). In a representative adult sample, psychological flexibility was found to consistently moderate the relationship between stress and other life outcomes (wellbeing, mental health, physical health), with higher psychological flexibility conferring greater protection, following a dose-response (Gloster et al., 2017). It has also been shown to be particularly important in long-term chronic or degenerative conditions that share features with SPMS. In a chronic pain study (n = 239), McCracken and Velleman (2010) found that psychological flexibility accounted for 24.1% of variance in health status, having a greater impact than other variables such as pain intensity (9.2% of variance). In cancer, several common negative outcomes reported in cancer patients (such as pain and quality of life) were shown to improve with interventions focussed on increasing psychological flexibility (Hulbert-Williams et al., 2015). Finally, in muscular dystrophy, which like in SPMS causes decline in physical

functioning and mobility, psychological flexibility was found to account for small but significant levels of variance in life satisfaction, depression and anxiety (Graham, Gouick, Ferreira, et al., 2016).

As a determinant of health across similar degenerative conditions, psychological flexibility could also be a determinant of wellbeing within SPMS. Sadly, those with MS currently have far higher levels of anxiety and depression scores than a non-clinical general population (Crawford et al., 2001), which worsen as disability increases and patients move towards the progressive stage of the disease (Jones et al., 2012). Those with SPMS have greater levels of psychological distress and less input than other stages of the disease (Croft et al., 2016).

The relationship between psychological flexibility and wellbeing in MS is not well studied. A cross-sectional study (*n* = 128) on a 73% RRMS sample did find that increased *cognitive defusion* (a synonym for acceptance), a component of psychological flexibility, positively correlated with reduced distress and increased quality of life in MS (Valvano et al., 2016). We have not identified any studies conducted mainly in patients with progressive forms of the disease (e.g., primary progressive, or SPMS) which pose greater risks to wellbeing than non-progressive forms. In addition, Valvano et al. (2016) only included one component of psychological flexibility (i.e., acceptance), but did not measure components such as behavioural awareness or valued action. Gathering an understanding of this relationship is important because it could inform whether those with SPMS could benefit from a psychological flexibility-targeted psychological support, which may have important clinical implications.

The link between psychological flexibility and distress can inform psychological treatment approaches to SPMS. If psychological flexibility is associated with anxiety, depression, and quality of life, then this provides additional justification for using therapies in SPMS that target psychological flexibility, because they could lead to improved clinical outcomes relevant to patients. Alternatively, if they are not found to be linked – or that higher psychological flexibility is associated with poorer outcomes, then it would suggest more caution in applying psychological flexibility-targeted therapy in SPMS. A systematic review did find some evidence for efficacy of using such a psychological flexibility-targeted approach in chronic and long-term conditions, but studies were of a low quality and not conducted in SPMS (Graham, Gouick, Krahé, et al., 2016). A one-arm evaluation of a group psychological therapy suggested psychological flexibility was malleable to change in MS in an 81% RRMS sample (Giovannetti et al., 2021). However, more research is needed to better understand the association between psychological flexibility and distress, and more high-quality studies are needed in this area, and specifically for people with SPMS.

Aims

Our aim was to determine the level of psychological flexibility in people with SPMS and to assess its relationship with anxiety, depression, and quality of life (outcomes). Specifically, we wanted to:

- Describe levels of anxiety, depression, quality of life, and psychological flexibility in this UK SPMS population.
- Measure the strength and direction of any correlation between outcomes and psychological flexibility.
- Separate the component parts of psychological flexibility and measure the strength and direction of correlation to outcomes.
- Assess whether psychological flexibility moderates the relationship between disability and outcomes.

Method

Design

We used a cross-sectional design. Pre-existing distress, quality of life, disability, and demographic data collected by the UK MS Register were combined with a psychological flexibility measure and its component parts, collected for the purpose of this study.

Participants

Participants were recruited through the MS Register, a large database of those with MS in the UK. The MS Register has >19,000 people with MS (>3500 SPMS) recruited from 48 UK National Health Service (NHS) sites (Ford et al., 2021). The web portal of the MS Register functions as a questionnaire platform for those with an MS diagnosis. Baseline demographic data such as age, gender, and date and type of diagnosis are collected as part of the registration process. Individuals can then provide information on their MS experiences using several validated scales, which individuals are asked to complete biannually. The MS Register has been found to be a valid method of self-report diagnosis, highly analogous to clinical cohorts (Middleton et al., 2018) and has been found feasible for use in characterising a cohort of people with MS (Ford et al., 2012). Ethical approval for UKMSR studies was obtained from South West-Central Bristol Research Ethics Committee (16/SW/0194).

The MS Register has an existing demographic and clinical dataset, which it allows for use by researchers. Ethical approval was given for the authors to obtain and use the requested demographic (Age, Gender) and clinical data: Type of MS, Expanded Disability Status Scale (EDSS), Hospital Anxiety and Depression Scale (HADS), and EuroQol Quality of Life (EQ-5D-5L) in March 2020. For our study, the MS Register placed a version of the Comprehensive Assessment of Acceptance and Commitment Therapy Processes (CompACT) questionnaire (Francis et al., 2016) online for one month, available for those with SPMS to complete.

Measures

Psychological Flexibility

The CompACT (Francis et al., 2016) was used to detect changes in psychological flexibility and its constituent components (*openness to experience*, *behavioural awareness* and *valued action*). Other psychological flexibility measures, such as the AAQ-II (Bond et al., 2011), have been criticised for conflating process and outcomes measurements, lack of consistency between items, and being a measure of distress rather than psychological flexibility (Ong et al., 2019; Wolgast, 2014). The CompACT provides a more nuanced and clinically meaningful understanding of psychological flexibility and was selected for this study on this basis (Rogge et al., 2019). It also has a greater discriminant validity than alternative psychological flexibility measures (Ong et al., 2020), with good internal consistency (α = .92), and test-retest reliability (r = .88) (Bayliss, 2018). It has 23 items, rated on a Likert scale with 7 response options. It has a maximum score of 138 and minimum score of 0; higher scores indicating greater psychological flexibility.

Distress

Distress (anxiety, depression) was measured through the Hospital Anxiety and Depression Scale (HADS) questionnaire (Zigmond & Snaith, 1983). It is the most frequently used measure of distress in MS populations, and has been routinely collected by the MS Register since its inception (Jones et al., 2012). The HADS has been validated for use in MS (Honarmand & Feinstein, 2009; Watson et al., 2014). It has 14 items, with a 4 response-option Likert scale. It has a maximum score of 42 (21 anxiety, 21 depression) and minimum score of 0; higher scores indicate greater distress.

Quality of Life

Health-related quality of life was measured through the EuroQol Quality of Life (EQ-5D-5L), which is a widely used and reliable measure for use in MS with excellent psychometric properties (Feng et al., 2021; Feng et al., 2015; Kuspinar & Mayo, 2014). The EQ-5D-5L produces two scores: firstly, an EQindex which is calculated between 0.00 (a state equivalent to dead) and 1.00 (full health) and normed to a UK population (Devlin et al., 2018) using descriptive five-point Likert scales (assessing self-care, mobility, usual activities, pain/discomfort, anxiety/depression). Secondly, a Health State score (0-100) from a single visual analogue scale (VAS), with higher scores indicating greater health related quality of life.

Disability

The Expanded Disability Status Scale (EDSS) (Kurtzke, 1983) was used to measure disability, and is the most widely used suitable measure of disability in MS (Meyer-Moock et al., 2014). It ranges from 0-10 in 0.5-unit increments, with higher scores representing increased levels of disability.

Statistical Analysis

Descriptive statistics included the age (*M*, range, *SD*, *SE*) and gender (percentages) of participants. Those who completed the CompACT but were excluded from the analysis were reported (*n*) along with the reasons for their exclusion.

Clinical characteristics were reported for the HADS (anxiety, depression, and total distress [*M*, *SD*, *SE*]), EQ-5D-5L (EQindex, Health State visual analogue scale [*M, SD, SE*]), EDSS (*M, SD, SE*), and CompACT (openness to experience, behavioural awareness, valued action, and total psychological flexibility [*M*, *SD*, *SE*]). All clinical scores were compared to a UK general population reference group (Bayliss, 2018; Crawford et al., 2001; Feng et al., 2021; Hernandez et al., 2018) and norms created for the CompACT using its *SD*.

Internal consistency of measures (apart from EQ-5D-5L) were determined through use of the alpha coefficient ($\alpha > 0.9$ = excellent, $\alpha > 0.8$ good, $\alpha > 0.7$ acceptable) to determine the reliability of the measure result (Henson, 2001; Tavakol & Dennick, 2011). Internal consistency is not a relevant psychometric property for the EQ-5D-5L as the EQindex items measure different aspects of health (Feng et al., 2021).

Pearson's correlations were used to examine bivariate relationships between psychological flexibility and outcomes (anxiety, depression, total distress, quality of life). The correlations between the subscales of psychological flexibility (openness to experience, behavioural awareness, and valued action) and outcomes were also measured. We used the Dancey and Reidy (2004) categorisation to report the strength of the correlation relationship (0.1-0.3 = weak, 0.4-0.6 = moderate, 0.7-0.9 = strong).

We also used a multiple regression model (Model 1; Hayes, 2012) with psychological flexibility as moderator, disability as predictor, and distress (anxiety, depression, total distress) and quality of life (index value, visual analogue scale) as outcomes. A separate linear model was conducted for each predictor x outcome combination.

Results

Participants

Not all participants answered all questionnaires, so they were separated into three subgroups to maximise use of the available data. All participants in Subgroup 2 were also in Subgroup 1, and all participants in Subgroup 3 were in Subgroup 1 and 2. We needed to exclude some participants accumulatively from subgroup 1 (total *n* = 148 [not SPMS *n* = 50, no HADS *n* = 98]), subgroup 2 (*n* =

194, no EQ-5D-5L) and subgroup 3 (*n* = 224, no disability data). See Table 1 for the measures, constructs, and descriptive statistics for each.

Table 1.

Measures and descriptive statistics of participants across subgroups

Subgroup Characteristic	Subgroup		
	1	2	3
n	628	434	210
Mean age (*SD*, range)	60.66 (8.02, 33-86)	60.91 (7.65, 38-84)	61.30 (6.97, 41-84)
Gender (% f)	70.9	72.1	74.3
Measure (Construct)			
HADS (Distress)	X	X	X
C-ACT (Psyc. Flexibility)	X	X	X
EQ-5D-5L (Quality of Life)		X	X
EDSS (Disability)			X

Note. *SD* = Standard Deviation, *n* = Number in sample, HADS = Hospital Anxiety and Depression Scale, C-ACT = Comprehensive Assessment of Acceptance and Commitment Therapy Processes, EQ-5D-5L: EuroQol Quality of Life Scale, EDSS = Expanded Disability Status Scale, X = Present

Subgroup 1: Psychological Flexibility and Distress

Clinical Descriptive Statistics & Correlations

All correlations demonstrated a statistically significant moderate negative relationship, with Valued Action and Anxiety the only exception with a weak-to-moderate relationship (See Table 2). As psychological flexibility scores increased, anxiety and depression scores decreased. The CompACT demonstrated that the average psychological flexibility is approximately 82 in this population, and to assist with clinical application, cut-off scores for the CompACT have been suggested in this population, using +/- 1SD in Table 3. These measures demonstrated good to excellent internal consistency in the current sample.

The Valued Action subscale of psychological flexibility has a stronger negative relationship with depression (*r* = -0.53) than anxiety (*r* = -0.38). The reverse is seen in the Openness to Experience subscale where a stronger negative relationship is seen with anxiety (*r* = -0.55) than depression (*r* = -0.42). The Behavioural Awareness subscale is similar in both anxiety and depression.

Table 2.

Subgroup 1: Descriptive statistics and Pearson product-moment correlations (n = 628)

Clinical Descriptive Statistics				
Measure	Mean	*SD*	Range	α
$HADS^{T}$	15.53	7.88	0-42	-
$HADS^{Anx}$	7.21[a]	4.57	0-21	0.89
$HADS^{Dep}$	8.32[a]	4.18	0-21	0.84
$C\text{-}ACT^{T}$	81.94[b]	22.60	0-138	0.90
$C\text{-}ACT^{OTE}$	31.33[b]	11.67	0-60	0.84
$C\text{-}ACT^{BA}$	16.53[b]	7.49	0-30	0.85
$C\text{-}ACT^{VA}$	34.08[b]	8.40	0-48	0.83

Correlations (*r*)		
CompACT Subscale	HADS Subscale	

	$HADS^{T}$	$HADS^{Anx}$	$HADS^{Dep}$
$C\text{-}ACT^{T}$	-0.65**	–0.59**	-0.58**
$C\text{-}ACT^{OTE}$	-0.54**	-0.55**	-0.42**
$C\text{-}ACT^{BA}$	-0.55**	-0.50**	-0.48**
$C\text{-}ACT^{VA}$	-0.50**	-0.38**	-0.53**

Note. SD = Standard Deviation, *SE* = Standard Error, α = Cronbach's alpha, *r* = Pearson's r, HADS = Hospital Anxiety and Depression Scale, $HADS^{T}$ = Total Distress, $HADS^{Anx}$ = Anxiety, $HADS^{Dep}$ = Depression, CompACT = Comprehensive Assessment of Acceptance and Commitment Therapy Processes, $C\text{-}ACT^{T}$ = Total Psychological Flexibility, $C\text{-}ACT^{OTE}$ = Openness to Experience, $C\text{-}ACT^{BA}$ = Behavioural Awareness, $C\text{-}ACT^{VA}$ = Valued Action, - = not reported, ** = <0.01, [a] : UK population reference group (*n* = 1792) $HADS^{Anx}$ = 6.14 (*SD* = 3.8) $HADS^{Dep}$ = 3.68 (*SD* = 3.1), [b] : UK population reference group (*n* = 313) $C\text{-}ACT^{T}$ = 85.07 (*SD* = 20.62) $C\text{-}ACT^{OTE}$ = 31.85 (*SD* = 11.79) $C\text{-}ACT^{BA}$ = 16.05 (*SD* = 6.73) $C\text{-}ACT^{VA}$ = 37.17 (*SD* = 6.59)

Table 3.

Cut-off score interpretation for CompACT in SPMS

Interpretation	Cut-off	*SD*
Above Average	> 106	+1
Average	60-105	
Below Average	< 59	-1

Note. CompACT = Comprehensive Assessment of Acceptance and Commitment Therapy Processes

A regression analysis using a line of best fit was conducted to determine at which point the CompACT flexibility score predicts the "cut-score" for the HADS. Below this point in psychological flexibility predicts a clinical level of distress. The anxiety "cut-score" (≥8) is reached at a score of 75, and depression "cut-score" (≥11) is reached at a score of 57.

Subgroup 2: Psychological Flexibility and Quality of Life

Clinical Descriptive Statistics & Correlations

Pearson's coefficient was used to assess relationships between quality of life and psychological flexibility. A moderate positive relationship was found between psychological flexibility and quality of life scores on the EQindex and weak-to-moderate relationship on the Health State VAS. A range of non-significant to moderate positive relationships were observed between the components of the EQ Index and the CompACT (See Table 4). As psychological flexibility scores increased, quality of life scores increased. Valued Action, the subscale of psychological flexibility, had the strongest positive relationship with both the EQ Index and Health State VAS, although differences between subscales were small.

Table 4.

Subgroup 2: Descriptive statistics and Pearson product-moment correlations (n = 434)

Clinical Descriptive Statistics			
Measure	*M*	*SD*	*SE*
EQ Index	0.76[a]	0.08	0.00
HS-VAS	52.63[b]	21.16	1.02
$C\text{-}ACT^{T}$	83.64	22.38	1.07
$C\text{-}ACT^{OTE}$	32.20	11.45	0.55
$C\text{-}ACT^{BA}$	16.96	7.35	0.35

C-ACT^{VA}	34.49	8.38	0.40

	Correlations (*r*)						
CompACT	EQ-5D-5L						
	Subscales					Totals	
	MB	SC	UA	PD	AD	EQ Index	HS-VAS
C-ACT^{T}	0.10*	0.19**	0.13**	0.28**	0.53**	0.47**	0.37**
C-ACT^{OTE}	0.07	0.10*	0.04	0.23**	0.49**	0.39**	0.27**
C-ACT^{BA}	0.04	0.15**	0.09	0.21*	0.41**	0.36**	0.29**
C-ACT^{VA}	0.13**	0.24**	0.20**	0.25**	0.38**	0.40**	0.36**

Note. M = Mean, *SD* = Standard Deviation, *SE* = Standard Error, *r* = Pearson's r, EQIndex = Quality of Life Index Value, HS-VAS = Quality of Life Health State Visual Analogue Scale, CompACT = Comprehensive Assessment of Acceptance and Commitment Therapy Processes, C-ACT^{T} = Total Psychological Flexibility, C-ACT^{OTE} = Openness to Experience, C-ACT^{BA} = Behavioural Awareness, C-ACT^{VA} = Valued Action, ** = <0.01, * = <0.05, [a]: General population reference group (0.91, *n* = 52380), [b]: General population reference group (84.31, *n* = 20587), MB = Mobility, SC = Self Care, UA = Usual Activities, PD = Pain and Discomfort, AD = Anxiety and Depression

Subgroup 3: Psychological Flexibility, Distress, Quality of Life, and Disability

Clinical Descriptive Statistics & Moderation

Pearson correlations, clinical descriptive statistics, and α coefficients can be seen in Table 5.

A moderate negative relationship was found between psychological flexibility, anxiety, and depression, with a strong negative relationship found between psychological flexibility and total distress. Mirroring subgroup 1, as psychological flexibility increased, anxiety, depression and total distress decreased.

A moderate positive relationship was found between psychological flexibility and quality of life scores on the EQindex, and weak-to-moderate relationship on the Health State VAS. Mirroring subgroup 2, as psychological flexibility increased, quality of life also increased. A moderate negative relationship was found between distress and quality of life. As distress increased, quality of life decreased.

A weak negative relationship was found between psychological flexibility and disability. As psychological flexibility increased, disability decreased. Of the components of psychological flexibility, Valued Action had the strongest relationship (*r* = -0.21) and Openness to Experience the weakest (*r* = -0.07). A weak positive relationship was found between anxiety, depression, distress and disability. As anxiety, depression and distress increased, disability increased. A moderate negative relationship was found between quality of life and disability. As quality of life increased, disability decreased.

Five moderation analyses were conducted. None of these analyses found a significant moderation effect of psychological flexibility on relationships between the predictor (i.e., disability level) and outcomes (i.e., distress, quality of life) (*B* range: -0.02-0.01).

Table 5.

Subgroup 3: Pearson product-moment correlations, descriptive statistics, and α coefficients (n = 210)

Focal Variables	1	2	3	4	5	6	7	8	9	10	Scale	Range	Mean	*SD*	α
Psychological Flexibility (1)		.89**	.80**	.78**	-.66**	-.59**	-.70**	.48**	.35**	-.16*	C-ACT^{T}	0-138	82.29	23.26	.90
Openness to Experience (2)			.60**	.52**	-.60**	-.44**	-.58**	.43**	.23**	-.07	C-ACT^{OTE}	0-60	31.61	11.62	.82
Behavioural Awareness (3)				.46**	-.58**	-.55**	-.63**	.35**	.28**	-.14*	C-ACT^{BA}	0-30	16.41	7.59	.85
Valued Action (4)					-.46**	-.52**	-.54**	.41**	.37**	-.21**	C-ACT^{VA}	0-48	34.26	8.77	.83
Anxiety (5)						.62**	.90**	-.55**	-.34**	.16*	HADS^{Anx}	0-21	6.94	4.51	.89
Depression (6)							.89**	-.52**	-.54**	.30**	HADS^{Dep}	0-21	8.12	4.31	.85
Distress^{T} (7)								-.60**	-.49**	.26**	HADS^{T}	0-42	15.06	7.92	.91
Quality of Life (8)									.47**	-56**	EQIndex	0-1	0.76	0.08	
Health State (9)										-.31**	HS-VAS	0-100	54.08	21.12	
Disability (10)											EDSS	0-10	6.49	1.17	
Demographic Variables															
Age	.22**	.20**	.20**	.14*	-.18*	-.12	-.16*	.18**	.10	-.09					
Male	.09	.09	.01	.09	-.11	.03	-.05	.07	.01	-.03					

Note. n = number included in sample*, SD* = Standard Deviation, EDSS = Expanded Disability Status Scale, HADS^{T} = Total Distress, HADS^{Anx} = Anxiety, HADS^{Dep} = Depression, EQIndex = Quality of Life Index Value, HS-VAS = Quality of Life Health State Visual Analogue Scale, C-ACT^{T} = Total Psychological Flexibility, C-ACT^{OTE} = Openness to Experience, C-ACT^{BA} = Behavioural Awareness, C-ACT^{VA} = Valued Action, ** = <0.01, * = <0.05

Discussion

Descriptive statistics in all subgroups of our sample are approximately representative of the SPMS population in terms of gender and age (Koch et al., 2010) and clinical descriptive statistics across all subgroups align with the SPMS literature for distress (Jones et al., 2012), quality of life (Jones et al., 2013), and disability (Iaffaldano et al., 2020). We were therefore able to achieve a representative sample of the SPMS population.

This study achieved some important significant novel findings. Firstly, it demonstrated that greater psychological flexibility was negatively correlated with anxiety and depression (i.e., those that were more flexible were typically less distressed) and positively correlated with quality of life (those that were more flexible had a better quality of life) in those with SPMS. This has also, been reported in the adult general population (Dawson & Golijani-Moghaddam, 2020), and it aligns with prior qualitative research into the importance of acceptance in adjustment in MS (Meek et al., 2020; Topcu et al., 2020).

Secondly, this study presents the level of psychological flexibility in the SPMS population, which had not previously been explored. We found that people with SPMS had … compared to…? Mention the cut-off here. This allows future researchers or clinicians working with those with SPMS to put psychological flexibility scores into context (See Table 3).

All psychological flexibility subscales demonstrated that they were important aspects of psychological health, however Valued Action/Depression and Openness to Experience/Anxiety appeared to have the strongest negative relationships. This may be because a symptom of depression is a reduction in activity (i.e., so the individual may not be motivated to pursue their values), and anxiety is known to be maintained through avoidance (i.e., so the individual may not be open to internal and external experiences).

We did not find a moderating effect of psychological flexibility. There was a weak positive predictive relationship between disability and distress, and a moderate positive predictive relationship between disability and quality of life, neither of which were moderated by psychological flexibility. This suggests that, whilst psychological flexibility was directly predictive of distress and quality of life, it did not buffer the (weak) relationship between disability and distress or the (moderate) relationship between disability and quality of life. This contrasts with general population literature, which suggests psychological flexibility acts as a “buffer” against negative outcomes, such as stress (Gloster et al., 2017) and depression (Fonseca et al., 2020). It may be that… (insert explanation).

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By increasing the malleable attribute of psychological flexibility in this population, we could expect this to lead to improved quality of life and anxiety and depression outcomes for patients which are closely related, even if no “buffer” to increased disability was found. This is consistent with pilot study evidence for the application of psychological flexibility-specific interventions reducing distress and quality of life in a broader MS sample (Pakenham et al., 2018), and distress in other chronic health conditions (e.g., Hughes et al., 2017).

Future research should look towards implementing psychological flexibility-targeted interventions to SPMS populations to improve psychological outcomes as at each stage of disability, higher levels of psychological flexibility are associated with better quality of life and distress outcomes. As access to

mental health specialists in Neurology services are limited (Chiu et al., 2018; Mynors et al., 2016), an easy-to-implement standardised intervention may be most feasible.

Limitations and Strengths

Our findings should be considered in the contexts of the strengths and limitations of this study. The large (largely representative) sample of SPMS patients, which allowed the measurement of separate subcomponents of psychological flexibility against the components of distress to identify and compare the strength of the relationships is a strength. The study also allowed us to create cut-offs for future clinicians and researchers to use in practice.

As a cross-sectional investigation, causation cannot be determined, and further longitudinal research is needed to determine any directionality between psychological flexibility and outcomes. Secondly, the psychological flexibility, quality of life, and disability clinical characteristics were all measured at the same timepoint, however the HADS collected were at two timepoints (one several months before, one at the same time as the rest of the data). This may mean that for some who completed their HADS earlier, their distress scores may have changed over time, although test-retest reliability is high in HADS in MS (Marrie et al., 2018).

Conclusions

Greater psychological flexibility is related to better coping outcomes (lower distress, higher quality of life) in SPMS. If psychological flexibility can be increased in people with SPMS, this could lead to a reduction in distress and improvement in quality of life, although directionality could not be attributed within our study design. Further longitudinal evidence and trials of psychological flexibility-focussed interventions are needed.

Conflict of Interest

NE has received lecture fees from Biogen and participated in paid advisory board for Biogen, Roche and Merck. RdN has received funding to prepare and deliver lectures (speakers bureau) from Novartis, Merck, and Biogen.

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