Stress modulates key psychological processes and characteristic symptoms in females with fibromyalgia

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ABSTRACT

Objective. *To examine how stress interacts with psychological processes and key phenotypic symptom characteristics in females with fibromyalgia.*

Methods. *Ninety-eight women with fibromyalgia, diagnosed according to ACR 1990 criteria, and 35 female healthy controls without pain were studied. Applied questionnaires included the following: Perceived Stress scale [PSS], Fibromyalgia Impact Questionnaire [FIQ], Perceived Control of Internal States (PCOIS), Mastery scale and the Profile of Mood States scale (POMS).*

Results. *Perceived stress correlated significantly with the characteristic features of fibromyalgia including pain ($p<0.05$) and sleep change, fatigue and cognitive dysfunction (all $p<0.001$). Perceived stress correlated inversely with measures of control and positively with mood and neuroticism (all $p<0.001$). When controlling for stress, most of these variables were no longer significant, suggesting that stress impacts on the majority of variables associated with FM.*

Conclusion. *Stress in females with fibromyalgia associates with both key symptoms and a range of relevant psychological variables. Stress appears to have a major role in modulating several key "up-stream" processes in fibromyalgia.*

Introduction

Stress has been associated with a number of major chronic health conditions (1, 2), including fibromyalgia (3). Stress has been suggested to trigger, exacerbate or perpetrate the clinical features of fibromyalgia (4, 5). The triggering role of stress at the onset of fibromyalgia is thought to originate from negative life events, lack of social support or a specific psychological-associated trauma (6, 7). The evidence for such a triggering role of stress in fibromyalgia is not clear (8). This may relate to an individual's response to different types of stress. One study examining work-related stress reported a 2–4 times greater risk of developing fibromyalgia when confronted with high levels of work stress (4), whereas another conducted on the 9/11 tragedy was unable to correlate stress with any new onset of fibromyalgia symptoms (9, 10).

Stress and changes in mood can also directly impact on the functioning of an individual who already has fibromyalgia with significant effects on their quality of life (11). For instance, through its influence on ability to cope stress subsequently modulates fibromyalgia symptoms, often causing a so-called "flare-up" of the condition (12). Also unclear is the evidence associated with stress as a perpetrator of ongoing symptoms in fibromyalgia. This is because a stress response can result from the symptoms of fibromyalgia in themselves and hence it is difficult to identify which components of a person's stress might be in the background acting as potential perpetrators of fibromyalgia and which components are those that result from the condition itself (13). This classic chicken and egg situation typifies many considerations of stress, as does the complexity in differing operational definitions of stress (14). Thus some argue that the central sensitisation that characterises fibromyalgia activates the stress response and contributes to the complex picture of fibromyalgia (15), while others suggest that psychological stress is by itself the fundamental initiator of the neurophysiological mechanisms that lead to the clinical phenotype of fibromyalgia (16, 17). It has been shown that the level of stress may also influence the severity of fibromyalgia symptoms (18).

The ultimate aim of the stress response is to restore equilibrium or homeostasis. The stress response induces changes in autonomic nervous system function, the hypothalamic pituitary

adrenal axis (HPA) and brain-related control systems related to spinal cord sensory processing. Changes or perturbations in all of these systems are present in fibromyalgia (19) suggesting links between stress and important "down-stream" mechanisms in fibromyalgia (19-24).

These changes may be further confounded by the effects of certain comorbidities, such as depression. Why stress links with pain in the contemporary individual is unclear but may relate to a survival advantage to humans in the distant past.

Taken together, stress is deemed to be a key feature of fibromyalgia but it remains unclear how psychological aspects of stress interact with brain-related pain processes involved in fibromyalgia. It has been shown that personality, control styles and mood associate with the predictable phenotypic symptom characteristics of fibromyalgia, such as pain, fatigue, sleep and confusion (18, 25-27). Stress seems important in these relationships.

We hypothesised that as the level of stress increases other variables, including the phenotypic symptoms and psychological variables, would also increase. We were also interested in the effects of age on stress-related outcomes, given increased neuroticism personality trait in younger females with fibromyalgia (26). It is hypothesised that the impact of stress within this younger population would show significant change in this age group. We first investigated the association of stress with the fibromyalgia phenotype comprising pain, sleep disturbance, fatigue and cognitive disturbance. We then examined whether stress would modulate certain psychological styles, such as the type of control used in patients with fibromyalgia. Finally, we examined the impact of stress on the relationship between psychological variables and phenotypic features of fibromyalgia. The schema for our study is shown in Figure 1.

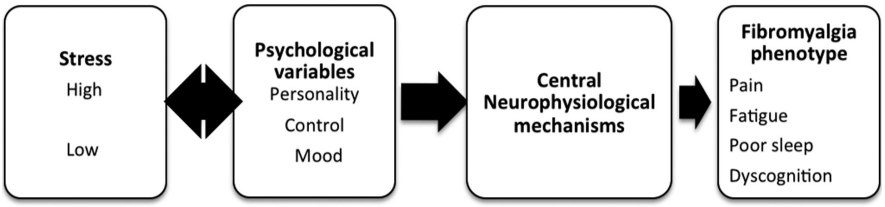

Fig. 1. The proposed linear model used in this study comprised a "top-down" view of fibromyalgia with stress and psychological factors modulating brain-related pain control mechanisms linking to the fibromyalgia phenotype. We examined associations between symptom-related variables in these categories but not neurophysiological mechanisms.

Methods

Ethics approval was obtained through relevant committees of Monash University and Monash Medical Centre, Melbourne, Australia. The participants were volunteer women sourced from a variety of areas including: a FM self-management program, notices in local newspapers, a FM treatment clinic and local rheumatologists. Ninety-eight female FM patients fulfilling ACR 1990 classification criteria (28, 29) and 35 female healthy controls (HC), all healthy individuals with no pain condition and recruited by word of mouth, were identified. All participants were sent written information regarding the study along with a consent form which, when signed, was followed by a series of questionnaires. These included: The Big 5 personality Inventory, The Fibromyalgia Impact Questionnaire (FIQ), (28) the Profile of Mood States (POMS), Perceived Stress scale (PSS), Perceived Control of Internal States scale (PCOISS), and the Mastery scale.

Table I. Demographic variables of fibromyalgia (FM) and healthy control (HC) participants in the study.

		Overall group		Subset	
		FM %	HC %	FM %	HC %
Number		98	35	25	27
Age	18 – 29	8.7	42.9	32	56
	30 – 39	18.5	34.3	68	44
	40 – 49	22.8	11.4		
	50 – 59	31.5	11.4		
	60 – 69	18.5	0.00		
Marital Status	Single	6.5	32.8	16	33
	Married / Defacto / Significant relationship	78.5	59.3	51	37
	Separated/Divorced	13.0	7.9	33	30
Education	Secondary	43.5	22.9	32	0
	Tertiary	41.4	28.5	48	81
	Higher degree	14.1	48.6	20	19
Work Status	Full time	17.6	68.5		
	Part time	34.8	28.6		
	Casual	7.6	2.9		
Occupation	Semi professional	25.0	11.4	32	4
	Professional	20.7	54.3	32	59
	Self employed	3.3	5.7		
	Retired	14.1	0.00		
	Unemployed	3.3	0.00	36	37
	Home/Caring	19.6	2.9		
	Student	4.3	2.9		
				Average income	
Income: (AUS)	<$20,000	38.6	17.1	<$20, 000	$41 – 60,000
	$ 20 – 40,000	33.7	25.7		
	$ 41 – 60,000	14.5	34.3		
	$ 61 – 80,000	3.6	11.4		
	+ $100,000	6.0	0.00		

FM: fibromyalgia; HC: healthy controls.

Instruments

The following instruments were applied to all fibromyalgia and HC subjects.

1. The Big 5 Personality Inventory (BFI): A validated 44-item personality scale, scored as 1 (disagree strongly) through to 5 (agree strongly) to indicate the extent of agreement with the items. The 44 items comprise 5 subscales of extraversion, agreeableness, conscientiousness, neuroticism and openness (31).

2. Fibromyalgia Impact Questionnaire (FIQ): A validated 20 item functional ability questionnaire, which measures how an individual's symptom characteristics impact their daily functioning for the preceding week. Individual subscales include sleep, depression, anxiety and pain and use a 0 to 10 cm visual analogue scale (VAS), measuring extreme left of line for "no impact of subscale" through to the far right, "worst possible impact" (30).

3. Perceived Stress Scale (PSS):

A validated scale that assesses the degree that an individual experiences feelings of being overwhelmed by stressful life events over the previous month. The scale is a 10 item, 5-point likert scale ranging from 0 (never) to 4 (very often) with scores ranging from 0 to 40 (32).

4. Profile of Mood States (POMS)-confusion subscale: A validated scale that measures individual aspects of mood as well as a total overall mood score. The POMS identifies adjective words that describe feelings that are indicative of mood states. The questionnaire asks individuals to rate on a scale from zero (not at all) to four (extremely) which best describes how they have felt over the past week. The scale includes a total of 65 definitions that represent the 6 subscales that include: Tension-Anxiety, Depression-Dejection, Anger-Hostility, Vigour, Fatigue and Confusion. A total mood score is obtained by summing all subscale scores with vigour inversed. The subscale of confusion was used to represent the cognitive dysfunction seen in fibromyalgia, here termed dyscognition (33). The single word items that reflect confusion include, bewildered, confused, unable to concentrate, forgetful, uncertain and efficient (score reversed) (34).

Table II. Symptom and psychological characteristics for the total FM and HC groups.

	FM (n=98) Mean ± SD	HC (n=35) Mean + SD	*t*-tests t	df	*p*
Pain	6.35 ± 2.41	0.19 ± 0.47	14.31	127	0.001
Sleep	7.74 ± 2.13	3.46 ± 2.73	9.34	130	0.001
Fatigue	7.97 ± 2.04	2.72 ± 2.28	12.33	128	0.001
Dyscognition	9.88 ± 5.08	6.03 ± 5.46	3.75	126	0.001
Depression	3.74 ± 2.79	1.51 ± 2.56	4.14	130	0.001
Anxiety	4.40 ± 2.86	1.86 ± 2.25	4.76	130	0.001
Neuroticism	25.95 ± 5.22	23.91 ± .6.04	1.89	129	NS
Control	57.41 ± 9.99	63.83 ± 10.83	-3.13	120	0.01
Mastery	16.72 ± 3.27	18.54 ± 3.23	-2.82	127	0.01
Stress	28.61 ± 5.99	24.49 ± 7.04	3.32	128	0.001

FM: fibromyalgia, HC: healthy controls.

Table III. Symptom and psychological characteristics for the younger age-matched FM and HC groups.

	FM (n=25) Mean ± SD	HC (n=25) Mean ± SD	*t*-tests t	df	*p*
Pain	6.36 ± 2.25	0.17 ± 0.48	13.18	47	0.001
Sleep	8.24 ± 1.67	3.33 ± 2.75	7.71	50	0.001
Fatigue	8.52 ± 1.33	2.88 ± 2.44	10.16	48	0.001
Dyscognition	11.00 ± 4.45	6.19 ± 5.87	3.32	50	0.01
Depression	4.72 ± 2.49	1.41 ± 2.56	4.72	50	0.001
Anxiety	4.76 ± 301	1.74 ± 2.16	4.13	50	0.001
Neuroticism	27.08 ± 4.79	23.52 ± 5.98	2.36	50	0.05
Control	56.79 ± 9.57	63.44 ± 12.01	-2.17	49	0.05
Mastery	16.24 ± 2.89	18.67 ± 3.40	-2.81	50	0.01
Stress	30.16 ± 5.89	24.15 ± 7.30	3.52	50	0.01

FM: fibromyalgia; HC: healthy controls; PCIOSS: perceived control of internal states scale.

5. Perceived control of internal states scale (PCOISS): A validated scale that assesses the degree of control based on the individuals thoughts, feelings and behaviours. The PCOISS measures the degree to which individuals feel they have control of their thoughts, emotions, and physical reactions, which, in turn, moderates the impact of events on their wellbeing. A 5-point Likert scale, rated from 1 = strongly agree to 5 = strongly disagree, is used to assess 14 items. High scores indicate a high level of perceived control (35).

Statistical analysis

Initial descriptive analysis was conducted, along with normality checks, using SPSS (PASW version 18). T tests, means and standard deviations were used to explore the differences between groups in symptom characteristics and stability of personality traits. ANOVAs were performed to compare the differences between the groups that explored levels of stress (high, medium and low) for symptom characteristics of fibromyalgia within the fibromyalgia group. Bivariate (Pearson) correlation was used to compare the relationships between the variables of FM and levels of stress. Initial descriptive analysis was conducted, along with normality checks.

Results

Table I summarises the demographics of the total group and a subset matched specifically for age. The total study group consisted of 133 individuals, 98 of whom met the 1990 ACR criteria for fibromyalgia. The age-matched subset group (p=0.1) were all under 39 years and consisted of 25 women with fibromyalgia and 27 female HCs.

The means, standard deviations and *t*-tests for all the examined symptoms

and selected psychological domains of fibromyalgia of the total group are shown in Table II. The major symptoms contributing to the fibromyalgia phenotype showed significantly higher means for pain, sleep, fatigue and dyscognition in the fibromyalgia group. The levels of anxiety and depression reported by the fibromyalgia patients were only moderate in severity, whereas sleep and fatigue rated at high levels. Fatigue rated higher than pain. Depression, anxiety, and level of stress were all significantly higher in those with fibromyalgia than the HCs. Both elements of control (*i.e.* internal control, as measured by the PCIOSS and mastery, as measured by the Mastery scale) were higher in the HC group. The personality trait neuroticism did not differ significantly between the groups. Perceived stress was significantly higher in the fibromyalgia group. We matched a subset of the total group for age to explore whether there were age effects on these associations. The results shown in Table III indicate all variables, including neuroticism were significantly higher in the fibromyalgia group.

The relationships between the stress score and the various components that make up the fibromyalgia phenotype, namely pain, fatigue, sleep disturbance and dyscognition (measured as confusion in the POMS instrument) are shown in Figure 2. There is a signifi-

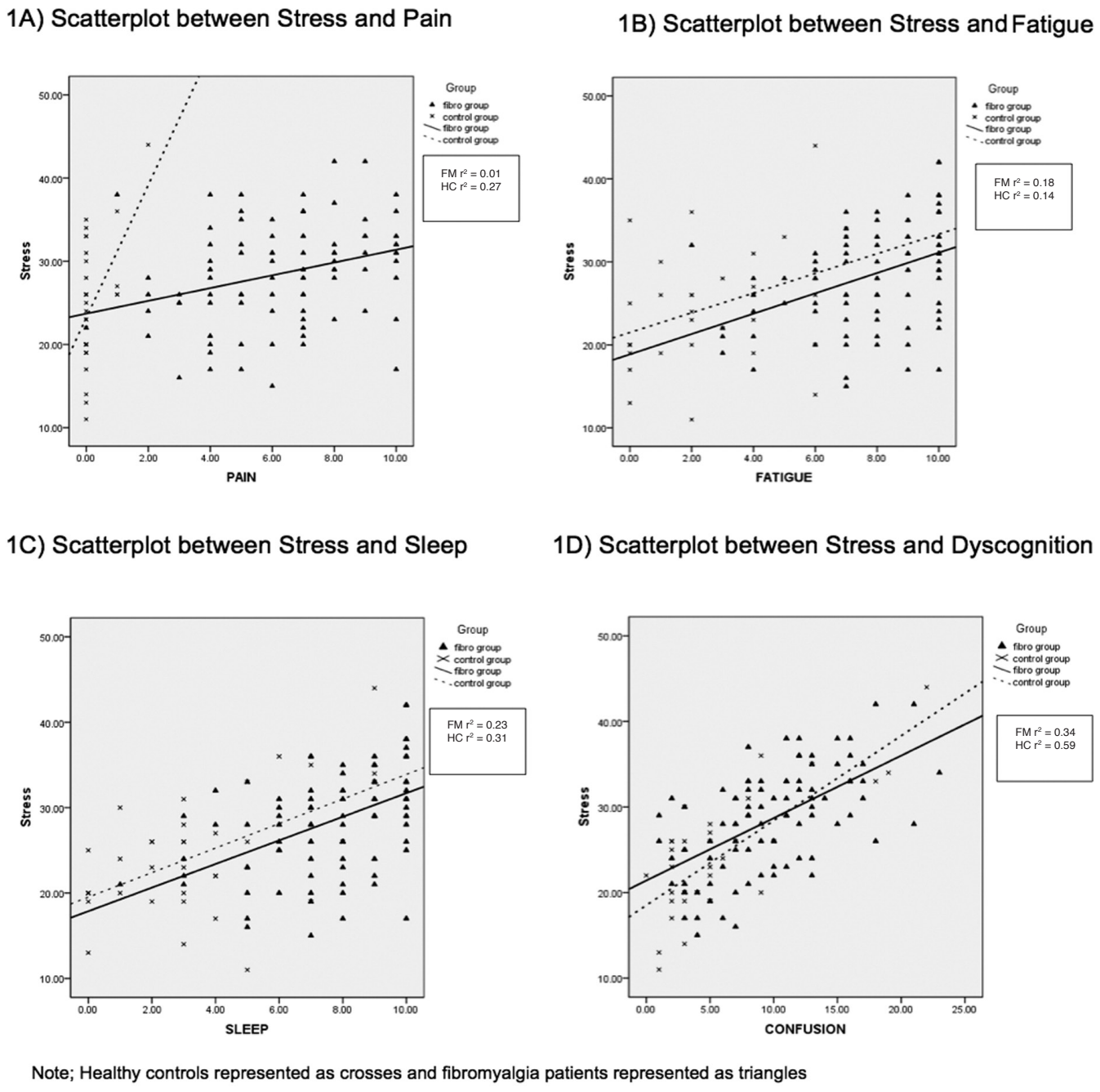

Fig. 2. Associations between stress score and the phenotypic components of fibromyalgia.

cant association between stress and all of these variables with the exception of pain, which is likely due to a ceiling effect. Both HC and fibromyalgia patients appear to belong to the different ends of the sample population with the fibromyalgia patients representing a shift to the right of the healthy normal control population.

Stress was explored in relation to its association with the phenotypic symptoms of fibromyalgia and selected psychological factors that are prevalent within this syndrome. There were moderate to strong correlations found between stress and the variables within both the total fibromyalgia and total HC groups, as shown in Table IV. We also examined the same age-matched subset of the total group described in Tables I and III. The results are also presented in Table IV.

In the total group, there was a moderate positive relationship between stress and pain, sleep, fatigue and dyscognition within both the fibromyalgia group and in the HC group. Thus as stress increases this relationship also increases in both groups. However within the age-matched younger sub group, the phenotypic variables did not correlate with stress in the fibromyalgia group but did in the HC group, suggesting that other variables might be influencing this relationship.

In both the total group and the subset, for both fibromyalgia and HCs, stress associated strongly with the personality characterised as neurotic. Stress also, in all groups, associated significantly with both mastery and internal control (as measured by PCIOSS), indicating that these important psychological processes interact actively with stress in both the fibromyalgia and the HC groups.

Stress positively correlated with mood disturbance in both the fibromyalgia and HC populations and within the age-matched subset group. Thus a similar relationship between stress and the selected psychological variables was found in all groups. Examining further the relationship between the fibromyalgia phenotype and the psychological variables and the influence that stress has on this relationship is presented in Table V. Presented within this table is the matched for age group. While the total group showed a moderate correlation within the relationships for both groups, fewer significant results were found in the matched for age group FM group compared to the HC group.

To further explore the influence of stress on the relationship between the phenotypic and psychological variables partial correlations, controlling for stress, were performed and are presented in Table VI. Again both the total group and the age-matched subset were examined.

Limited correlations were seen between the variables when controlling for stress. Depression and anxiety were both found to have moderate relationships to some of the fibromyalgia phenotypic symptoms including sleep, fatigue and dyscognition in the total groups. Similar but less powerful outcomes were seen in the subset groups. However the majority of variables no longer correlated when stress was not playing a role. Tertiles were calculated for stress and ANOVAs for the highest and lowest groups are reported. The results are presented in Table VII.

Within the fibromyalgia group all variables including the phenotypic symptoms and the psychological variables differed between the two levels

Table IV. Correlations between stress and fibromyalgia phenotype characteristics and psychological variables for the overall group and the subset group.

		Total group				Age-matched subset			
		FM		HC		FM		HC	
		r	*p*	r	*p*	r	*p*	r	*p*
FM phenotype									
	Pain	0.31	0.01	0.52	0.01	-0.14	NS	0.62	0.01
	Sleep	0.48	0.001	0.56	0.001	0.27	NS	0.56	0.01
	Fatigue	0.42	0.001	0.38	0.05	0.23	NS	0.45	0.05
	Dyscognition	0.59	0.001	0.77	0.001	0.60	0.001	0.80	0.001
Psychological									
	Control	-0.64	0.001	-0.77	0.001	-0.74	0.001	-0.81	0.001
	Mastery	-0.70	0.001	-0.74	0.001	-0.73	0.001	-0.76	0.001
	Depression	0.64	0.001	0.77	0.001	0.75	0.001	0.80	0.001
	Anxiety	0.65	0.001	0.60	0.001	0.68	0.001	0.61	0.001
	Neuroticism	0.72	0.001	0.64	0.001	0.75	0.001	0.70	0.001

FM: fibromyalgia; HC: healthy controls.

Table V. Correlations of fibromyalgia phenotype characteristics and psychological variables for the overall group and the subset group.

Total group:		Control	Mastery	Depression	Anxiety	Neuroticism
Pain	(FM)	-0.16	-0.23*	0.21*	0.17	0.23*
	(HC)	-0.64***	-0.45**	0.50**	-0.25	0.41*
Sleep	(FM)	0.42***	-0.39***	0.47***	0.34**	0.42***
	(HC)	-0.40*	-0.27	0.69***	0.66***	0.38*
Fatigue	(FM)	-0.34**	-0.32**	0.41***	0.42***	0.31**
	(HC)	-0.52**	-0.28	0.43*	0.32	0.25
Confusion	(FM)	-0.47***	-0.46***	0.57***	0.48***	0.44***
	(HC)	-0.58***	-0.60***	0.81***	0.67***	0.41*
Subset:		**Control**	**Mastery**	**Depression**	**Anxiety**	**Neuroticism**
Pain	(FM)	-0.05	0.01	-0.28	-0.23	0.01
	(HC)	-0.69***	-0.55**	0.61***	0.31	0.47*
Sleep	(FM)	-0.31	-0.27	0.34*	-0.02	0.40*
	(HC)	-0.47*	-0.27	0.71***	0.65***	-0.20
Fatigue	(FM)	-0.38	-0.30	0.03	0.10	0.46*
	(HC)	-0.46*	-0.35	0.58**	0.45*	0.35
Confusion	(FM)	-0.34	-0.49*	-0.35	-0.47*	0.30
	(HC)	-0.60**	-0.69***	0.84**	0.69**	0.41*

FM: fibromyalgia; HC: healthy pain-free controls. ***p<0.000, **p<0.01, *p<0.05.

Table VI. Partial correlations of fibromyalgia phenotype characteristics and psychological variables for the overall group and the subset group when controlling for stress.

Controlling for stress:						
Total group:		Control	Mastery	Depression	Anxiety	Neuroticism
Pain	(FM)	0.07	-0.12	-0.05	-0.01	-0.07
	(HC)	-0.44*	-0.11	0.19	-0.08	0.23
Sleep	(FM)	-0.14	-0.13	0.23*	0.10	0.14
	(HC)	-0.06	0.10	0.51**	0.51**	0.42*
Fatigue	(FM)	-0.14	-0.08	0.23*	0.29**	0.02
	(HC)	-0.17	0.01	0.24	0.12	0.54**
Confusion	(FM)	-0.10	-0.23	0.34**	0.16	0.04
	(HC)	-0.09	-0.02	0.55**	0.40*	-0.16
Subset:		Control	Mastery	Depression	Anxiety	Neuroticism
Pain	(FM)	-0.19	-0.12	-0.32	-0.23	0.16
	(HC)	-0.39*	-0.13	0.24	-0.09	0.03
Sleep	(FM)	-0.16	-0.11	0.30	-0.23	0.30
	(HC)	-0.06	0.35	0.55**	0.50*	-0.20
Fatigue	(FM)	-0.17	-0.06	0.03	0.29**	-0.13
	(HC)	-0.04	0.01	0.40*	0.24	-0.07
Confusion	(FM)	-0.24	-0.21	-0.15	-0.01	-0.24
	(HC)	0.04	-0.14	0.63**	0.48*	-0.25

FM: fibromyalgia; HC: healthy pain-free controls. ***$p<0.000$, **$p<0.01$, *$p<0.05$.

of stress. Overall the results show that higher stress associates with higher symptoms. The HC group followed a similar pattern, with the exception of pain and fatigue, which showed no significant difference between the two levels of stress. A multiple regression analysis was conducted within the total fibromyalgia population in order to explore which psychological variable would be best predicting stress. The results are seen in Table VIII.

Discussion

Stress is an important feature of fibromyalgia. It appears relevant in the initiation, exacerbation and maintenance of FM. However, while stress is an acknowledged feature of fibromyalgia it is often difficult to know whether this is a cause or effect relationship. There are few prospective studies that look at stress in the pre-fibromyalgia situation in order to assess stress as a risk factor for fibromyalgia. Most studies are cross sectional and make associations between features of stress and other characteristics of the disorder.

In this study we examined 98 female patients with fibromyalgia and compared various clinical outcomes and psychological factors with 35 healthy female controls without pain. All the fibromyalgia patients fulfilled ACR 1990 classification criteria. The patients with fibromyalgia had typical clinical features compared to other studied groups. Our healthy controls did not completely match our patients in terms of age, and they also had higher rates of employment and yearly income than the fibromyalgia group that would likely attribute to the disability that associates with fibromyalgia. We examined an age-matched subset of the total population to assess the generalisability of our findings to all age groups. Our fibromyalgia population showed typical levels of clinical features as found in other studies with higher levels of fatigue and sleep disturbance rather than levels of pain (25). These characteristics shape the fibromyalgia phenotype (36). In addition, our analysis involved splitting both groups into tertiles to seek modulating effects of stress and explore its influence on psychological variables and features of fibromyalgia.

It was noted in the total group that the components of the fibromyalgia phenotype, namely sleep, fatigue and dyscognition rated much higher than the fourth, and essential, component of pain. All of these components of the fibromyalgia phenotype were significantly higher than the control group although it is noteworthy that dyscognition (representative of cognitive dysfunction and measured by the item of confusion in the POMS instrument) rated at 6 out of 10 in the healthy control group. An explanation of this discrepancy may be partly attributed to the use of the self-rated POMS questionnaire. Adjectives are rated on 1-4 likert scale in items of "feeling confused" and "unable to concentrate" through to "uncertain about things". Factors such as interpretation or comprehension of the items may influence these results.

Both depression and anxiety were rated in the mild to moderate category in the fibromyalgia group and were much lower in the healthy control group. Self-perceived stress was significantly higher in fibromyalgia than healthy controls and there were significant associations between stress and pain, fatigue, sleep change and confusion in both fibromyalgia and healthy controls. It appeared that both the healthy control and fibromyalgia groups responded similarly in that when stress increased the particular component of fibromyalgia also increased accordingly. This would imply that the healthy control group and the fibromyalgia group are responding in the same fashion with the healthy control group being lower on the scale compared to the fibromyalgia group, as shown in Figure 1. Higher stress also associated with higher levels of fibromyalgia symptoms in both groups. This fits with the concept of fibromyalgianess, where the different components of the condition may be present at different levels in different persons and only when they reach a certain threshold do they reach criteria for FM fibromyalgia, as seen in the ACR 2010 clinical diagnostic criteria for the disorder (37).

This association between different levels of stress and clinical features is further illustrated when mean tertile levels are compared between the two groups. There are significant differences between the lowest and highest tertile in pain, sleep, fatigue and confusion in fibromyalgia and also significant differences between the lowest and high-

Table VII. ANOVA, means and standard deviations of high and low levels of stress on symptoms associated with FM.

		Stress level	Group	
			FM Mean ± SD	HC Mean ± SD
Symptom				
Pain		Low	5.32 ± 2.44	0.00 ± 0.00
		High	7.19 ± 2.29	0.43 ± 0.63
	ANOVA		4.96	3.30
	p-value		0.01	NS
Sleep		Low	6.46 ± 2.24	2.15 ± 2.27
		High	8.87 ± 1.54	4.94 ± 2.74
	ANOVA		12.15	5.51
	p-value		0.001	0.01
Fatigue		Low	6.96 ± 2.30	1.75 ± 2.34
		High	8.84 ± 1.67	3.63 ± 2.19
	ANOVA		6.87	2.74
	p-value		0.002	NS
Dyscognition		Low	6.29 ± 3.39	3.38 ± 2.14
		High	12.97 ± 4.85	9.19 ± 6.52
	ANOVA		19.86	6.53
	p-value		0.001	0.005
Depression:		Low	1.57 ± 1.20	0.77 ± 1.09
		High	5.90 ± 2.59	3.13 ± 3.07
	ANOVA		27.77	8.54
	p-value		0.000	0.001
Anxiety:		Lowest	2.14 ± 1.24	0.62 ± 1.44
		High	6.71 ± 2.30	2.94 ± 2.54
	ANOVA		31.63	4.67
	p-value		0.000	0.05
Neuroticism		Low	21.19 ± 4.29	19.23 ± 3.85
		High	29.71 ± 3.57	28.44 ± 4.18
	ANOVA		32.28	16.75
	p-value		0.000	0.000
Control		Low	65.28 ± 7.16	71.85 ± 5.34
		High	52.07 ± 9.09	54.94 ± 9.19
	ANOVA		16.50	22.70
	p-value		0.000	0.000
Mastery		Low	19.19 ± 2.51	20.69 ± 2.59
		High	14.37 ± 2.30	16.37 ± 2.55
	ANOVA		22.55	10.79
	p-value		0.000	0.000

FM: fibromyalgia; HC: healthy controls; ANOVA: analysis of variance.

Table VIII. Summary of significant multiple regression analyses in predicting variance in stress in the total fibromyalgia group.

Dependent	Adj. R^2	R^2	Independent	Standardised B
Perceived stress				
$F(9, 81) = 40.09$ $p<0.001$	0.72	0.75	Neuroticism	45***
			Mastery	- 26**
			Anxiety	21*
			Control	NS
			Depression	NS

***$p<0.000$, **$p<0.01$, *$p<0.05$.

est tertile means of the healthy control groups in sleep and dyscognition. The lack of change in the healthy control pain sub-group may be ascribed to the fact that the controls were chosen specifically as having no pain. The healthy control fatigue sub-groups were not significantly different but a trend was present. Higher numbers in the control group may have clarified this relationship.

There was a stronger association between the mean levels of the lowest and highest tertiles in both fibromyalgia and healthy controls in all of the psychological variables including neuroticism, aspects of control, depression and anxiety. Patients with high levels on the neuroticism scale of the Big 5 scale are characterised by abnormal reactivity to stress (13, 27). Hence this personality characteristic may be seen as one that promotes stress rather than is a reaction or response to it. Similarly the patients with poor mechanisms of control over internal psychological stressful factors or who have low control in relation to external factors are likely to generate stress. Hence, again it is likely that in these situations the stress follows changes in these psychological mechanisms rather than causes them. In contrast, it is less clear that depression promotes stress in this setting, and it is felt to be more likely to be a reaction to the predicament of the situation rather than a cause of it. Anxiety however may either drive stress or be a reaction to it.

In our study we found that mastery, anxiety and internal control all significantly contributed to the predicted ratings of stress in our fibromyalgia group. This was in addition to the prediction of stress by the majority of other psychological variables examined. In the healthy control group the lower numbers precluded appropriate analysis. This, together with the buffering effects of tertile levels of stress on clinical features and psychological factors, would imply that stress is a major contributor to the overall fibromyalgia phenotype.

There are some limitations to this study. There are some differences in the control group and differences in the group sizes. The control group were more educated, had higher incomes and were younger and usually employed. The fibromyalgia group had had various interactions with health care programmes. However, the study has strong internal consistencies in the fibromyalgia group that is large and is analysed in tertiles to identify important associations be-

tween variables.When controlling for stress, the fibromyalgia phenotype of pain, sleep and fatigue still show a significant positive relationship, including depression and to a lesser extent, anxiety. There is no significant relationship with internal control and a low inverse relationship with mastery and confusion. This again suggests that stress is a major factor contributor to the overall FM fibromyalgia phenotype.

We have shown that psychological stress strongly associates with most of the variables that have been identified as being important in fibromyalgia, not only the defining symptoms of fibromyalgia but also key background psychological processes. Stress appears to have a central role in modulating key "up-stream" processes in fibromyalgia.

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