



Clinical trial

The mediating effect of health-related hardiness on the degree of physical disability and perceived stress in Chinese female patients with neuromyelitis optica spectrum disorder

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ABSTRACT

Background: Neuromyelitis optica spectrum disorder (NMOSD) is a rare and chronic disease of the central nervous system. The characteristics and main symptoms of recurrent NMOSD lead to an increase in psychological stress and accelerate a decline in the patients' quality of life. The incidence of NMOSD in the Chinese population is much higher than that for other countries and the majority of NMOSD patients are female. In general, there are sex differences in the perception and management of stress, with females experiencing higher levels of perceived stress than males. Thus, we should be concerned about the psychological issues experienced by Chinese female NMOSD patients. Health-related hardiness is a psychological adjustment factor that could affect perceptions of illness that impact on NMOSD patients. The objective of this study was to evaluate the mediating role of health-related hardiness on physical disability and perceived stress in Chinese NMOSD female patients.

Methods: Participants were 68 females patients with NMOSD treated at the Department of Neurology, Huashan Hospital, Fudan University, China, between March and September 2018. Patients were evaluated for their degree of physical disability, perceived stress, and health-related hardiness. Measures included the Expanded Disability Status Scale (EDSS), Perceived Stress Scale (PSS), and Health-related Hardiness Scale (HRHS). Pearson's correlation analyses and stepwise multiple linear regression analysis were used.

Results: Findings indicated a positive correlation between the PSS and EDSS ($r = 0.735, P < 0.001$) and a negative correlation between the PSS and HRHS total score ($r = -0.441, P < 0.001$). After adjusting for the confounding factors, the EDSS was found to have a positive predictive effect on the PSS ($\beta = 2.743, P = 0.000$), and the HRHS was found to have a negative predictive effect on the PSS ($\beta = -0.152, P = 0.04$). Mediation analysis showed a direct effect of the EDSS on the PSS, and as a mediating variable for health-related hardiness ($\alpha = -1.928, b = -0.152, c = 2.743, c' = 2.481$), which was statistically significant ($P < 0.05$). The mediating effect of health-related hardiness accounted for 10.68% of the total effect.

Conclusions: As a mediating variable, health-related hardiness indirectly affected perceived stress caused by physical disability and improved health-related hardiness. This was beneficial in reducing psychological stress and promoting mental health in NMOSD female patients.

Abbreviations: EDSS, Expanded Disability Status Scale; HRHS, Health-related Hardiness Scale; NMOSD, neuromyelitis optica spectrum disorder; PSS, Perceived Stress Scale

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1. Introduction

Neuromyelitis optica spectrum disorder (NMOSD) is an immune-mediated inflammatory demyelinating disease of the central nervous system involving the optic nerves and spinal cord (Jarius et al., 2014). From an epidemiological perspective, the incidence of neuromyelitis optica in the global population is 0.57/100,000 (Marrie and Gryba, 2013) and in the Asian population is 1.57/100,000 (Houzen et al., 2017). However, the incidence of NMOSD in the Chinese population is as high as 3.31/100,000 (Hor et al., 2018). On this basis, more attention should be focused on this population in China.

The main clinical manifestations of neuromyelitis optica are sudden or successive unilateral or bilateral optic neuritis and/or severe acute transverse myelitis, accelerating the development of blindness and paraplegia (Patterson and Goglin, 2017) as well as pain (Asseyer et al., 2018). Among NMOSD patients, 80–90% have recurrent NMOSD, with an average annual rate of recurrence of 0.93 (Tackley et al., 2016). As a result of recurrence, neurological dysfunction from the previous episode tends not to be fully recovered and the long course of the disease and rate of recurrence cause neurological deficit symptoms, such as blindness in both eyes, dysuria, paralysis, and pain (Jarius et al., 2014; Patterson and Goglin, 2017; Shosha et al., 2017; Tackley et al., 2016). In addition, the characteristics and main symptoms of recurrent neuromyelitis optica lead to an increase in psychological stress, accelerate the decline in patients' quality of life (Barzegar et al., 2018; Chanson et al., 2011; Kanamori et al., 2011; Seok et al., 2017; Shi et al., 2016; Zhao et al., 2014), and also cause the emergence of high-risk behaviors, such as suicide, self-injury, and reduced treatment compliance (Fernandez et al., 2018). The majority of NMOSD patients are female. A Chinese study has shown that the female to male ratio of NMOSD patients in China is 8.7:1 (ZhangBao et al., 2017).

It is also known that there are sex differences in the perception and management of stress, with females experiencing higher levels of psychological stress than males (Yang and Wang, 2003). Sawada et al. (2016) surveyed female breast cancer patients and found that their levels of psychological stress were much higher than for healthy females. Female patients with NMOSD face similar problems to those experienced by breast cancer patients in that they also use immunosuppressive medication and have disabilities that affect appearance and physical function. Therefore, it is necessary to investigate the perceived stress of female patients with NMOSD to provide evidence to support the development and application of future interventions. Solutions to help to reduce perceived stress are urgently needed for female NMOSD patients.

Humans are biopsychosocial beings, constantly interacting with the environment and exchanging information, matter, and energy. Human life is a process of continued adaptation to various stimuli in our internal and external environments. In the process of interacting with internal and external environments, people will adopt appropriate ways to maintain the integrity of their body structures. At this time, the scope and intensity of the stimuli that an individual can withstand, or cope with, constitute the coping mechanisms and adaptation levels of each individual. Therefore, the strength of the coping mechanisms of an individual affects his/her adaptation to the stimuli (Roy, 1976).

Health-related hardiness (HRH) originated from the concept of toughness or resilient personality, which includes a strong sense of commitment, control, and challenge. It helps individuals to adapt to illness (Pollock, 1989). In 1984, a nursing scholar, Pollock, proposed the Health-related Hardiness Scale (HRHS) to assess the psychological features of self-adjustment in individuals encountering health problems (Pollock and Duffy, 1990). Patients suffering from chronic illness also experience tremendous stress, increased number of hospitalizations and thus, also increase the workload of health care providers (Brooks, 2008). However, previous research has shown that individuals with higher HRH have better psychosocial adjustment in terms of decreasing their perception of illness impact (Pollock, 1986).

No recent research has considered the role of HRH in the experiences of NMOSD patients. Given the significant challenges experienced by female NMOSD patients over the various stages of the disease, this study aimed to investigate the mediation effect of HRH on physical disability and perceived stress in Chinese female NMOSD patients.

2. Materials and methods

2.1. Participants

This was a cross-sectional study. It used a continuous sampling method of 68 Chinese female NMOSD patients who were treated in the outpatient clinic for demyelinating disease in the Huashan Hospital affiliated to Fudan University, China, between March and September 2018. The inclusion criteria for patients were as follows: (I) a diagnosis of NMOSD from neurologists in our hospital, (II) female and aged 18–70 years old, (III) been diagnosed for at least one year, (IV) basic reading and comprehension skills, and (V) willingness to participate after being informed about the study. The exclusion criteria were patients: (I) with blindness or paralysis caused by other diseases or congenital factors, and (II) with a diagnosis accompanied by diabetes, cancer, or other chronic diseases or diseases that seriously affect the quality of life. The severity of the disability of the patients was measured by two neurologists using the expanded disability status scale (EDSS) (Kahraman et al., 2016).

2.2. Demographic data

General demographic data for each NMOSD patient, including gender, age, marital status, education level, family financial status, and the number of family members, were collected.

2.3. Instruments and measures

2.3.1. Perceived Stress Scale (PSS)

The PSS was included as a measure of psychological stress. This self-report scale was developed by Cohen et al., (1983) to assess the stress level experienced by an individual. We used the Chinese version of the PSS developed by Yang who translated and revised the measure in 2003 (Yang and Wang, 2003). This version contains 14 items divided into two dimensions: crisis perception and perception of coping ability. Each item was rated on a 5-point Likert scale, with a higher score representing higher levels of perceived stress. In this study, the Cronbach's α coefficient was 0.78.

2.3.2. Health-related Hardiness Scale (HRHS)

The HRHS was established by Pollock et al. in 1990 based on Kobasa's concept of health-related hardiness (Kobasa et al., 1983) to measure the impact of health-related hardiness on health problems in individuals. It is the most commonly used measurement of health-related hardiness to date. In 2008, Li and Wang translated and revised the HRHS to measure the impact of having a resilient personality on individual health problems (Li, 2008). The HRHS Chinese version consists of three subscales: (1) control subscale with a total of 11 items; (2) commitment subscale with a total of six items; and (3) challenge subscale with a total of 13 items. In this study, the Cronbach's α coefficient of the total scale was 0.89.

2.4. Quality control

Two questionnaire administrators were trained by a member of our research team holding a national certified psychological counselor qualification to ensure that the surveyors fully understood the survey methods, precautions, knowledge and contents of the scale, and evaluation methods, and could also accurately explain the questionnaire contents to the respondents. In addition, members of our research team

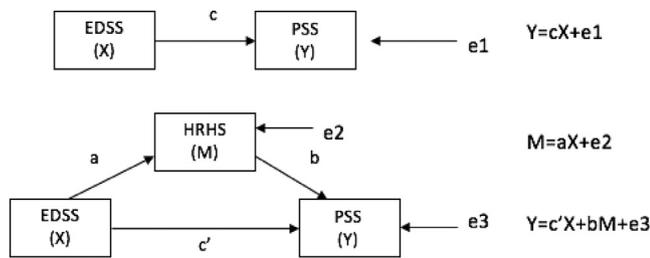


Fig. 1. Diagram of the meditating effect of HRHS on EDSS and PSS. Abbreviations: EDSS = Expanded Disability Status Scale; HRHS = Health Related Hardiness Scale; PSS = Perceived Stress Scale.

explained the research objective and significance to the patients and their families and informed them that there were no potential health hazards as a result of participation. The questionnaire content and completion requirements were carefully explained to each patient after receiving his/her informed consent. Each patient completed the paper-based questionnaire independently. An anonymous survey method was adopted in the questionnaire, which required that the respondent did not miss any questions. All on-site questionnaires were collected immediately after completion and checked by the administrators; if there were any missing answers, the administrators would ask the patients to complete the missing questions to ensure the completeness of the questionnaires. Visually impaired patients were allowed to select their answers after listening to the questions presented verbally by the surveyors. In this study, a total of 68 questionnaires were distributed and collected, all of which were correctly completed.

2.5. Statistical analysis

We hypothesized that correlations would be found between disability, perceived stress, and HRH. We have presented the proposed mediating effect as a diagram (Fig. 1), assuming that the EDSS is a risk factor (independent variable X) of the PSS (dependent variable Y), and that HRHS is a mediating variable (M) of X and Y. This proposes that the degree of physical disability would directly affect psychological stress and play a role through the HRH of patients (i.e., the total effect of EDSS on PSS is c; the effect of EDSS on HRHS is a; and the effect of HRHS on PSS is b. After adding the mediating variable, HRHS, the direct effect of EDSS on PSS is c'). The diagram of the mediating effect was used to compare the difference between the total effects of the degrees of physical disability on the perceived stress and the effect of the additional HRH, in order to verify the role of HRH in the relationship between physical disability and perceived stress.

SPSS 19.0 software (IBM SPSS, Chicago, IL) was used for statistical analysis. The total score for HRH, the scores for the different dimensions, the total score of the EDSS and the total score of perceived psychological stress were analyzed using Pearson's correlations. AMOS 17.0 software was used to verify the mediating effect. Three equations were established to successively test the mediating effect and HRH using stepwise regression analysis. Since the mediating effect was an indirect effect, a structural equation model could be used to replace the path analysis of the mediating effect, regardless of the variables involving latent variables or not (Bollen, 1989). The calibration level was $\alpha = 0.05$.

2.6. Ethical considerations

The study was reviewed by the Ethics Review Committee of Huashan Hospital affiliated to Fudan University and met the ethical standards of the Helsinki Declaration. Each patient signed a written informed consent form before participation.

Table 1
Demographic characteristics of the NMOSD patients.

Duration of disease (x ± s)	46.88 ± 46.02
Age (x ± s)	38.72 ± 12.54
Number of recurrences [P ₅₀ (P ₂₅ , P ₇₅)]	2.00 (0.00, 3.00)
PSS score (x ± s)	25.68 ± 7.40
EDSS score (x ± s)	3.54 ± 1.76
HRHS score (x ± s)	105.99 ± 12.16

*: Continuous variables are presented as means ± standard deviations; categorical variables are presented as medians.

Abbreviations: EDSS = Expanded Disability Status Scale; HRHS = Health Related Hardiness Scale; NMOSD = neuromyelitis optica spectrum disorder; PSS = Perceived Stress Scale.

3. Results

3.1. Demographic data

The average age of the recruited NMOSD patients was 38.72 ± 12.54 years. The average disease duration was 46.88 ± 46.02 months and the average number of NMOSD recurrences was 2.34 ± 3.05. Table 1 summarizes the PSS, EDSS, and HRHS scores of the NMOSD patients.

3.2. Correlation and regression analysis of HRHS, the EDSS, and PSS of NMOSD patients

Correlation analysis showed that the PSS score was positively correlated with the EDSS score ($r = 0.735, P < 0.001$) and negatively correlated with the HRHS score ($r = -0.441, P < 0.001$). The EDSS score was negatively correlated with HRHS score ($r = -0.312, P = 0.013$) (Table 2).

3.3. Evaluating the effect of HRHS on EDSS and PSS by multiple regression analysis

With the PSS as the dependent variable, the EDSS as the independent variable, the HRHS total score as the mediating variable, and influencing factors, such as age, number of recurrences, education level, family financial status, and number of family members living together, as the adjustment variables entered into the stepwise, multivariate, hierarchical linear regression model, the EDSS had a positive predictive effect on the PSS ($\beta = 2.743, P = 0.000$). After including the mediating variable of HRHS in the model, we found that it had a negative predictive effect on the PSS ($\beta = -0.152, P = 0.04$), and the degree of interpretation of the PSS also increased by 3.7%. The mediating effect of the EDSS on PSS dropped from the original value of 2.743 to 2.481 (Table 3).

3.4. Validation and analysis of the theoretical model proposing a mediating effect of HRH on disability and psychological stress

As shown in Table 4, analysis of the mediating effect in the model showed that the effect of the EDSS on HRH was $\alpha = -1.928$. The effect

Table 2
Correlations between the PSS, EDSS, and HRHS.

	PSS	HRHS	EDSS
PSS	-	-0.441**	0.735**
HRHS	-	-	-0.312*

* $P < 0.05$.

** $P < 0.001$.

Abbreviations: EDSS = Expanded Disability Status Scale; HRHS = Health Related Hardiness Scale; PSS = Perceived Stress Scale.

Table 3
Multiple regression analysis among the PSS, EDSS, and HRHS.

	First step			Second step			Third step		
	β	<i>t</i>	<i>P</i>	β	<i>t</i>	<i>P</i>	β	<i>t</i>	<i>P</i>
Age	0.035	0.444	0.658	-0.036	-0.602	0.549	-0.046	-0.794	0.431
Relapse times	0.237	0.779	0.439	0.241	1.054	0.296	0.335	1.477	0.145
Education	-0.809	-0.963	0.339	-0.822	-1.301	0.198	-0.488	-0.770	0.445
Family financial situation	-0.095	-0.159	0.874	-0.016	-0.036	0.972	0.122	0.277	0.783
Family member	-0.863	-0.957	0.342	-1.068	-1.574	0.121	-1.368	-2.027	0.047
EDSS				2.743	6.853	0.000	2.481	6.074	0.000
HRHS							-0.152	-2.105	0.040
<i>F</i> value		0.838			9.061			8.851	
<i>R</i> ² value		0.065			0.480			0.516	
<i>R</i> ² variation		0.065			0.414			0.037	

Abbreviations: EDSS = Expanded Disability Status Scale; HRHS = Health Related Hardiness Scale; PSS = Perceived Stress Scale.

of HRH on psychological stress was $b = -0.152$, and the total effect of the EDSS on the PSS was $c = 2.743$. After adding the mediating variable, the direct effect of the EDSS on the PSS was $c' = 2.481$. The step-by-step effect coefficient was statistically significant ($P < 0.01$). We used the formula to account for the mediating effect of the HRHS (Wen et al., 2004) being 10.68% $[(-1.928) \times (-0.152) / 2.743 \times 100\%]$ of the total effect. The mediating effect of the HRHS was also verified in the structural equation model. The HRHS was a mediating variable between EDSS and PSS ($P = 0.009$), i.e., HRH partially relieved the increase in psychological stress caused by the degree of physical disability (Fig. 2).

4. Discussion

4.1. Relationship between HRH, physical disability, perceived stress

In this study, physical disability, perceived stress, and HRH were all significantly correlated with each other. NMOSD is a neurological disease with high disability and recurrence (Jarius et al., 2014). Previous studies on different populations with chronic disease have shown that low levels of HRH are associated with negative emotions, adaptive ability, loneliness, and insomnia (Akkasilpa et al., 2000; Bahrami et al., 2018; Brooks, 2003; Kowalski and Schermer, 2018; Ng and Lee, 2019). Chinese scholar Shi et al., (2016) investigated the health-related quality of life (HRQOL) of 73 Chinese NMOSD patients (67 females and six males). They found that negative emotions such as anxiety and depression, were independent predictors of HRQOL. Therefore, we inferred that low levels of HRH can lead to the decline of quality of life by affecting the emotions of patients. In this study, we found that the degree of physical disability, perceived stress, and health resilience were also significantly correlated. Higher levels of physical disability induced higher perceived stress. The perception of the disability caused by chronic disease is an important factor in the process of adjustment (Pollock, 1993). Neuman systems model was first proposed by Betty Neuman, a nursing scholar, in 1972. It is based on the relationship between individuals and stressor. This nursing theory explains how individuals cope with stress. The Neuman systems model believes that people are an open system that continuously interacts with the environment. As the central core of the whole system, the human body is

Table 4
The mediation effect sequential test of the HRHS to the PSS and EDSS.

Step	Dependent	Independent	Regression equation	Coefficient test <i>t</i>	<i>P</i>
1	PSS (Y)	EDSS (X)	$Y = 2.743X + e_1$	6.853	< 0.001
2	HRHS (M)	EDSS (X)	$M = -1.928X + e_2$	-2.674	0.009
3	PSS (Y)	HRHS (M) EDSS (X)	$Y = -0.152M + 2.481X + e_3$	-2.105 6.074	0.040 < 0.001

Abbreviations: EDSS = Expanded Disability Status Scale; HRHS = Health Related Hardiness Scale; PSS = Perceived Stress Scale.

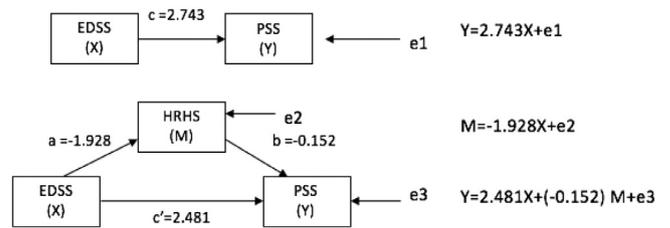


Fig. 2. Relationships among the HRHS, EDSS, and PSS. Abbreviations: EDSS = Expanded Disability Status Scale; HRHS = Health Related Hardiness Scale; PSS = Perceived Stress Scale.

surrounded by three defense lines. When the body encounters a stressor, the three defense lines play the roles in helping the body resist the stress. The efficiencies of the three defensive lines is affected by six variables: physiology, psychology, spirit, society, culture, and development (Neuman, 1982). HRH is one of the psychological factors for defensive lines (Pollock, 1989). Due to the degree of HRH for handling health problems differing between individuals, NMOSD patients at the same degree of disability in this study showed different adaptation scores and different degrees of psychological stress. This may be the mechanism underlying the mediating effect between HRH, disease-related disability, and perceived stress.

4.2. The mediating effect of HRH in Chinese patients with NMOSD

Our study showed that HRH, as a mediating variable, indirectly affected the relationship between physical disability and psychological stress. We inferred that NMOSD, as a source of stress, caused physical disability in patients. These patients were subjected to different levels of psychological stress, through which psychological coping processes were initiated. This may be the mechanism underlying the mediating effect among HRH, disease-related disability, and perceived stress. Nakazawa et al. (2018) have reported the effect of resilience as a personal characteristic on anxiety and depression in 77 patients with MS and NMOSD. They found that resilience can reduce the anxiety and depression and improve quality of life. This conclusion is similar to that obtained from our study. However, perceived stress can predict anxiety

and depression in patients, and paying attention to perceived stress and providing timely intervention can improve mental health (Ghorbani et al., 2008). Furthermore, this study identified the statistical extent of impact of HRH on perceived stress caused by disability.

4.3. Clinical implications

Findings from this study suggest that HRH may promote an individual's positive response to disease and reduce their psychological stress. Some studies have shown that perceived stress is related to quality of life and mental health (Leung et al., 2010; Teh et al., 2015). As a protective and stress-adaptive factor, HRH plays an important role in perceived stress caused by physical disability. Exploring the importance of HRH and the methods for improving the levels of HRH in NMOSD patients remains of great significance in promoting their physical and mental health. Previous studies have only focused on how to reduce psychological stress (Umanodan et al., 2014; van Oorsouw et al., 2014; Yamagishi et al., 2007). Our results suggest that in addition to stress management training, measures should be taken to increase HRH in chronic illness patients. Although HRH is a psychological trait, a study by Judkins et al. (2006) in which hardiness training was completed by 13 nurse managers, showed that hardiness could be increased and sustained among this group. Thus, HRH is not a fixed trait but can be amenable to change. Thus, future research should focus on the design of hardiness training for patients with NMOSD to improve their mental health.

5. Limitations

Our study also has some limitations. First, we did not set a fixed time for each patient to complete the questionnaire. Second, the small sample size may have biased the results. Third, we did not take into account the treatments the patients received. Thus, further research should recruit more participants and undertake a longitudinal study design.

6. Conclusion

Although disability caused by optic neuromyelitis is inevitable, a high level of HRH is beneficial in reducing psychological stress and negative emotions caused by physical disability in NMOSD patients. HRH in this study was related to each individual's control of psychological stress, their response to health-related activities, and personal vitality when facing stress. Therefore, investigations focusing on the development of psychological interventions for stress in NMOSD patients aiming to reduce negative emotions, as well as the evaluation of these in improving the HRH of NMOSD patients, remain important avenues for future research.

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Conflict of interest

None.

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