Mental health of spinocerebellar ataxia patients during COVID-19 pandemic: a cross-sectional study

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Research Article

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Abstract

COVID-19 is a global concern nowadays, and the psychological impact of the pandemic cannot be overlooked. People are under insurmountable pressure, which may lead to psychological problems such as anxiety and depression. The purpose of this study was to evaluate the mental health of spinocerebellar ataxia (SCA) patients during COVID-19 pandemic and to analyze its influencing factors. We conducted an online questionnaire survey among 307 SCA patients from China. The contents of the questionnaire included general information, the self-rating anxiety scale (SAS), the self-rating depression scale (SDS). The relevant influencing factors included COVID-19 risk factors, age, gender, BMI (body mass index), educational background, disease course, and score of the scale for the assessment and rating of ataxia (SARA). Results indicate the 307 SCA patients had an anxiety rate of 34.9%, along with a depression rate of 56.7%. Their SAS and SDS scores were significantly higher than those of the Chinese norm group (SAS: 45.8 ± 10.1 vs. 37.2 ± 12.6 , $P < 0.01$; SDS: 55.1 ± 12.2 vs. 41.9 ± 10.6 , $P < 0.01$). Risks of exposure to COVID-19, educational level, and disease course may be factors affecting mental health status. The existence of a positive correlation among the scores of SARA, SAS and SDS scale was demonstrated, the higher the SARA score, the higher the risk of anxiety and depression. Anxiety and depression were more prevalent in SCA patients compared with the normal population, and depression was more common than anxiety during this pandemic. More psychological attention should be paid to SCA patients during COVID-19 pandemic.

1. Introduction

The coronavirus disease 2019 (COVID-19) pandemic has spread across China since the end of December 2019, and the disease rapidly spread throughout many countries around the world, becoming a global health emergency [1]. At present, the pandemic has been effectively controlled in China, but the psychological impact of the pandemic cannot be overlooked. Addressing the psychological crisis of COVID-19 has become an essential part of pandemic prevention and control. The National Health Commission has issued guidelines for emergency psychological crisis intervention. Medical institutions and universities across China have opened online platforms to provide psychological counseling services for doctors, patients, and others affected by the pandemic [2, 3].

Spinocerebellar Ataxia (SCA) is an autosomal dominantly inherited and progressive neurodegenerative disorder, the clinical hallmark of which is the loss of balance and coordination accompanied by slurred speech [4]. Its prevalence varies with subtypes, geography, and ethnicity, and SCA3 is the primary subtype of patients in China [5]. Affected by factors like (CAG)_n length, SCA mainly occurs in adults aged 30–40 years old, but can also occur in children and the elderly [6–9]. As ataxia progresses, the coordination of the extremities deteriorates, resulting in difficulties with writing and the loss of fine motor skills. Besides, SCA patients have many non-ataxia symptoms, such as spasticity, dystonia, parkinsonism, oculomotor abnormalities, sleep disorders [10–13]. Therefore, with the considerably complex clinical manifestations, SCA patients' ability to move and communicate is significantly limited, which seriously impedes the quality of life and even makes them vulnerable for anxiety and depression.

Previous studies have shown that depression affects 17–26% of SCA patients, which not only affects their life and social functions, but also may reduce their compliance with the treatment of SCA, increase their disease burden, and lead to a poor prognosis [14, 15]. Because of the higher susceptibility to stress compared with the general population, SCA patients could be more substantially influenced by the emotional responses brought on by the COVID–19 pandemic, which values to manage SCA patients during the outbreak, with particular attention to their mental health [16]. Nevertheless, rare studies are focusing on the mental health of SCAs patients during the pandemic. The purpose of the current study is to evaluate the psychological status of SCA patients in China during COVID–19 pandemic and facilitate better mental support for SCA patients.

2. Materials And Methods

2.1 Patients

We recruited 307 patients in the Chinese spinocerebellar ataxia online group to participate in this survey from February 20, 2020, to April 8, 2020. Criteria were as follows: (1) a definite genetic diagnosis of SCA; (2) participants could understand the content and meaning of the questionnaire; (3) participants signed the informed consent; (4) No recent traumatic experiences or other stressful events. For a pre-investigation, we randomly sampled 100 SCA patients, of whom 60% had anxiety or depression. The calculation of sample size was based on the formula " $n = 400 \times p / (1 - p)$ ", where "n" was the minimum sample size, "p" was the prevalence rate of mental illness of 60% in the preliminary survey [17]. The sample size of this study was calculated to be 266. We sent a total of 360 questionnaires and finally collected 307 valid questionnaires, with a valid response rate of 85.3%.

2.2 Questionnaire

The questionnaire consisted of three parts: basic demographic characteristics, risks of exposure to COVID–19, and mental health assessment.

2.2.1 Demographic characteristics

Basic demographic data consisted of gender (male or female), age (years), height and weight (to calculate BMI), educational level (primary school education level, middle school education level, university education level), course of the disease (years).

2.2.2 *Risks of exposure to COVID–19*

We determined risks of exposure to COVID–19 through the following questions asked to SCA patients: Have you ever had any suspected symptoms such as fever, fatigue, dry cough? Have you or your family

been diagnosed with COVID–19? Have your neighbors been diagnosed? Have you ever been to Hubei Province or contact people came from there? The answer to each question was yes or no.

2.2.3 Mental health assessment

We used two scales to assess the mental health status of SCA patients. The SAS scale is a self-rating scale to evaluate the severity of anxiety with excellent reliability and validity [18]. The standard scores are categorized as follows: minimal/no anxiety (<50), mild anxiety (50–59), moderate anxiety (60–69), or severe anxiety (>69). The SAS scale score of the Chinese norm group is (37.2 ± 12.6), which is the result of 1158 ordinary Chinese people [19]. The SDS scale is a self-report scale applied to assess the severity of depression, with the standard scores categorized as follows: minimal/no depression (<53), mild depression (53–62), moderate depression (63–72), or severe depression (>72) [20]. The SDS scale score of the Chinese norm group is (41.9 ± 10.6), which is the consequence of 1340 normal Chinese people.

2.3 Clinical Assessment

The severity of ataxia was assessed clinically with the scale for the assessment and rating of ataxia (SARA), scoring from 0 (no ataxia) to 40 (most severe ataxia) [21]. Owing to the COVID–19 outbreak, we were unable to conduct a home visit. Therefore, we consulted the data of 55 SCA3 patients who participated in the questionnaire and recently visited the department of neurology in Xiangya Hospital Central South University (from January 2019 to January 2020), and recorded their SARA score results of the last visit.

2.4 Statistical analysis

We conducted a descriptive analysis of the general data and risks of exposure to COVID–19. For counting data, we used frequencies and percentages. The single sample t-test was utilized to compare the scale scores of patients and Chinese norms. SAS scale scores and SDS scale scores of SCA patients in different groups were compared with independent-samples t-test and one-way analysis of variance (ANOVA). We used Bonferroni post hoc for pairwise comparison. With all of the demographic variables as independent variables and psychological scale scores as the outcome variable, multivariable linear regression analysis was conducted to determine the factors related to mental health status. Pearson correlation analysis was examined for the correlation of scores of SAS scale, SDS scale and SARA scale. SPSS (version 22.0) statistical software was used for data analysis. Statistical significance was set at $P < 0.05$, two-sided.

3. Results

3.1 Mental health status of SCA patients under COVID–19 pandemic

A total of 307 participants completed the survey questionnaire. The SCA subtype distribution was shown in Fig. 1b, and SCA3 was the primary subtype in our study. Among this final sample, the average age was 40.0 years (standard deviation [SD]: 8.8, range: 25–66), 138 (45.0%) patients held university education level, 126 patients (41.0%) had 5–10 years course of the disease. Further demographic characteristics are shown in Table 1.

In this study, participants came from different provinces in China but were mainly distributed in Hunan, Hubei, Guangdong, and Jiangxi provinces (Fig. 1a). None of the 307 subjects had been diagnosed with COVID–19. There was a total of 38 patients with risks of exposure to COVID–19: 18 of them had recently developed symptoms such as fever, fatigue, dry cough and dyspnea; 17 of them had been to Hubei region or had contacted with people from there; six patients replied that there were confirmed patients in their community.

Our results showed that of all participants, the total rate of anxiety was 34.9%, including 82 patients with mild anxiety (26.7%), 18 patients with moderate anxiety (5.9%), and seven patients with severe anxiety (2.3%) (Fig. 2a). Depressive symptoms were more common than anxiety symptoms in the study subjects, the total rate of depression was 56.7%, including 92 patients with mildly depressed (30.0%), 54 patients with moderately depressed (17.6%), and 28 patients with severely depressed (9.1%) (Fig. 2b). Besides, the mean standard score of SAS scale of SCA patients was higher than that of the Chinese norm group ($p < 0.01$) (Fig. 2c). Similarly, the average standard score of the SDS scale of SCA patients was also higher than that of the Chinese norm group ($p < 0.01$) (Fig. 2d).

3.2 Risk factors for anxiety and depression in SCA patients

SAS scores and SDS scores significantly differed across different education levels, and risks of exposure to COVID–19, course of the disease ($P < 0.05$) (Table 1). Scores of those patients whose course of the disease were more than ten years were significantly higher than those less than five years ($P < 0.05$). Scores of patients with college education were significantly higher than those with middle and primary school education ($P < 0.05$).

The multiple linear regression analysis showed that after excluding the influence of other variables, risks of exposure to COVID–19 ($\beta: 0.152$, $P < 0.01$), education levels ($\beta: -0.192$, $P < 0.01$), course of the disease ($\beta: 0.126$, $P < 0.05$) were significantly associated with SDS scores. Meanwhile, educational levels ($\beta: -0.239$, $P < 0.001$) and risks of exposure to COVID–19 ($\beta: 0.190$, $P < 0.01$) were correlated with scores of SAS scales (Table 2).

3.3 Correlation analysis of SARA scale score with SAS scale and SDS scale score

Pearson correlation analysis results showed that there was a positive correlation between the SARA score and the SAS scale score ($r = 0.47$, $P < 0.01$) (Fig. 3a). There was also a positive correlation between the SARA score and the SDS score ($r = 0.40$, $P < 0.01$) (Fig. 3b).

4. Discussion

In our study, 307 SCA patients were assessed for psychological assessment and health status during the COVID-19 outbreak. Wherein most of them live in Hunan, Hubei, Guangdong, and Jiangxi provinces, which provinces were on the brink of Wuhan city, Hubei province, the area that COVID-19 was mainly concentrated in China. Nevertheless, the results of this questionnaire showed that none of the 307 subjects infected with COVID-19. This may be related to the decreased motor ability of SCA patients, resulting in a reduced range of activities and fewer opportunities for them to go out to work and migrate. However, the COVID-19 virus is mainly transmitted through close contact with the respiratory tract. With less exposure to the outside world, SCA patients are less likely to be infected despite their feeble physical condition.

SCA patients who comorbidity with depression often have symptoms such as dejected mood and loss of interest, accompanying somatic symptoms such as weight change, sleep disorder, as well as psychological symptoms such as self-blame and suicidal thoughts [22]. A cohort study of 526 SCA patients recapitulated three independent predictors of health status in SCA patients, including ataxia severity, non-cerebellar symptom severity, and depressive symptoms [15]. Another two-year cohort study used the Patient Health Questionnaire (PHQ) to investigate the depression status of 300 patients with different subtypes of SCA. The results showed that 26% of SCA patients had depression, and suicidal ideation was even as high as 65% in SCA3 patients [14].

However, we observed that among the 307 SCA patients, the anxiety rate was 34.9% along with the depression rate was 56.7% during this pandemic. The standard scores of SAS scale and SDS scale were significantly higher than those of the Chinese norm group, indicating that most of the SCA patients had different degrees of anxiety and depression. Our results showed that depressive symptoms were more prevalent than anxiety symptoms among the 307 SCA patients, more than half of the SCA patients had depression, and even 28 patients had severe depression.

Univariate analysis and multivariate linear regression analyses showed that risks of exposure to COVID-19 were independently associated with SAS and SDS scale scores in SCA patients. According to the latest guidelines, fever, fatigue, dry cough, and dyspnea are the main symptoms of COVID-19; therefore, patients with SCA who develop these symptoms during the pandemic may feel uneasy about suspecting that they are infected with the virus. SCA patients who have been to the Hubei region are also at increased risk of infection. If someone nearby infected with the virus, the whole community would be closed, affecting the patient's psychological state inevitably. At the same time, SCA patients are susceptible to infectious diseases due to the lower immunity, so their mental state is more susceptible to the COVID-19 pandemic. Furthermore, many hospitals did not open the regular neurology outpatient

department during this pandemic, so SCA patients could not go to the clinic on time to get the medicine, which may cause more adverse emotions. Consequently, it is quite necessary to take corresponding protective measures and appropriate psychological counseling for SCA patients during the pandemic.

Additionally, the average scores of SAS and SDS scales decreased with increasing educational levels among SCA patients. Previous studies have reported a momentous association between lower education and severe depression [23]. In contrast, patients with college education can better regulate themselves, communicate better with doctors, actively collect the latest research advances of SCA, and learn more about the current situation about COVID-19 from the media, which can reduce anxiety and depression to some extent. This may suggest that we can relieve the psychological pressure of SCA patients by preaching disease-related knowledge for them.

It also concluded that course of the disease could affect SDS scores. The longer the course of the disease, the more severely the cerebellar function is impaired, which may lead to unhealthy psychological outcomes. Intriguingly, no significant difference was observed in the influence of different disease courses on SAS scores, which may be related to the fact that the prevalence of anxiety in SCA patients is lower than the rate of depression. Moreover, we need to expand the sample size for further study.

Our results showed that there was a positive correlation between the SARA score and SAS score, as well as between the SARA score and SDS score. Comparatively, the more severe the dyskinesia, the higher the SARA score, the higher the risk of anxiety and depression. Previous studies presented that the degree of ataxia symptoms and the state of depression jointly determined the subjective health rating of SCA patients [24], a direct correlation between depression scale scores and motor disability was found [25]. Nevertheless, in the natural history study of SCA, the ataxia symptoms of different SCA subtypes progressed at different rates (SCA1>SCA3>SCA2>SCA6). The prevalence of depression (SCA3>SCA1>SCA2>SCA6) does not follow the same developmental order, suggesting that depression may not be entirely attributable to motor impairments, other factors such as non-motor symptoms must be considered as well [26]. Given the insufficient sample size and the small number of patients with other subtypes except for SCA3, we did not explore the differences in psychological states among different SCA subtypes, and we need to explore further whether there is a cause and effect relationship between mental health state and ataxia progression.

There may also be other reasons for anxiety and depression in SCA patients: Their ability to exercise and communication is considerably limited, affecting the quality of life seriously; till date, there is no specific drug to cure SCA, which cannot stop the progress of the disease; with the prevalence ranged from 0 to 5.6 cases per 100,000 individuals, SCA is a rare disease that may not get enough social attention; severe patients cannot take care of themselves and may be under pressure from family and society. Pathological studies show that depression may be associated with some brain regions' pathological changes. Several brain stem regions and limbic systems related to depression have neuronal polyglutamine inclusion bodies, such as the raphe nucleus and locus coeruleus [27]. In summary, mental health has a severe impact on SCA patients. We should give them a professional psychological

assessment, as well as some psychological intervention and medication. At present, many experimental studies have shown that selective serotonin reuptake inhibitors (SSRIs) can reduce the neurotoxicity of SCA3 animal models [28, 29], but whether the drug is effective in clinical trials and whether antidepressants can be used as a routine treatment for SCA still requires further exploration.

Compared with previous studies, our psychological assessment is an online cross-sectional survey, which is convenient to involve more influencing factors on psychological states, such as risks of exposure to COVID-19 and demographic characteristics. It can instantly reflect the psychological characteristics of SCA patients in the current pandemic, which is conducive to targeted treatment after the pandemic. Too little work has been devoted to investigating the anxiety rate in SCA patients, while SAS scale was used to investigate the anxiety symptoms of SCA patients in our study. It showed that more than one-third of the subjects had anxiety, and the scores of SAS scale were correlated with the scores of SDS scale. In addition, the results revealed that the depression rate of the 307 SCA patients was significantly higher than that of previous studies, which may be due to the different depression scales used in the study and the impact of the COVID-19 pandemic. Compared with the PHQ scale, SDS scale has a reverse scoring standard, which is more scientific from the perspective of the scale design. Overall, the Zung scales are superior in terms of sensitivity in comparison [30].

However, there are also several limitations in our questionnaire. First, SCA patients need long-term care, and financial sources from family members have a significant influence on the psychological state of SCA patients. Nevertheless, family income was not included in our study due to the negligence of the questionnaire design. Secondly, affected by COVID-19, we can only issue questionnaires online, which may limit the collection of samples and cause selection bias, leading to the inability of elderly patients who cannot use the Internet to fill in the questionnaire, as well as the reluctance of patients with severe negative psychology. Thirdly, the SARA score for dyskinesia is not the patient's current score, which may lead to biased results. Finally, this study was conducted using a cross-sectional design, so the causal relationship between factors and psychological states cannot be determined, and more well-designed prospective cohort studies are needed to investigate these associations further.

5. Conclusion

This study shows that anxiety and depression were more prevalent in SCA patients compared with the normal population, which needs the attention of doctors and caregivers. We call on doctors to pay attention to the mental health of SCA patients, and to prioritize psychiatric interventions for SCA patients with high-risk mental health problems, contributing patients to better understanding the disease and sustaining optimism. In addition, we also appeal to the families of SCA patients for giving patients more psychological support and care during COVID-19 pandemic.

Declarations

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Authors' Contributions

All authors contributed to the study conception and design. Yiqing Gong wrote the manuscript. Yiqing Gong, Zhao Chen and Hong Jiang designed the project. Mingjie Liu and Linlin Wan organized and executed the experiment. Chunrong Wang, Huirong Peng, Yuting Shi, Yun Peng and Rong Qiu analyzed and interpreted the data. Kun Xia, Beisha Tang and Hong Jiang revised the manuscript. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Compliance with Ethical Standards

Conflict of Interest: The authors declare that they have no conflict of interest.

Ethical Approval: The studies involving human participants were reviewed and approved by Ethics Committee of Xiangya Hospital of Central South University in China.

Consent to Participate: Informed consent was obtained from all individual participants included in the study.

References

1. Lipsitch M, Swerdlow DL, Finelli L. Defining the Epidemiology of Covid-19 - Studies Needed. *N Engl J Med*. 2020;382(13):1194-6.
2. Duan L, Zhu G. Psychological interventions for people affected by the COVID-19 epidemic. *Lancet Psychiatry*. 2020;7(4):300-2.

3. Bao Y, Sun Y, Meng S, Shi J, Lu L. 2019-nCoV epidemic: address mental health care to empower society. *Lancet*. 2020;395(10224):e37-e8.
4. Klockgether T, Mariotti C, Paulson HL. Spinocerebellar ataxia. *Nat Rev Dis Primers*. 2019;5(1):24.
5. Chen Z, Wang P, Wang C, Peng Y, Hou X, Zhou X, et al. Updated frequency analysis of spinocerebellar ataxia in China. *Brain*. 2018;141(4):e22.
6. Chen Z, Sequeiros J, Tang B, Jiang H. Genetic modifiers of age-at-onset in polyglutamine diseases. *Ageing Res Rev*. 2018;48:99-108.
7. Wang P, Chen Z, Peng Y, Cao L, Li X, Wang C, et al. (CAG)_n loci as genetic modifiers of age at onset in patients with spinocerebellar ataxia type 1 from mainland China. *Eur J Neurol*. 2019;26(8):1130-6.
8. Li T, Martins S, Peng Y, Wang P, Hou X, Chen Z, et al. Is the High Frequency of Machado-Joseph Disease in China Due to New Mutational Origins? *Front Genet*. 2018;9:740.
9. Chen Z, Zheng C, Long Z, Cao L, Li X, Shang H, et al. (CAG)_n loci as genetic modifiers of age-at-onset in patients with Machado-Joseph disease from mainland China. *Brain*. 2016;139(Pt 8):e41.
10. Schmitz-Hubsch T, Coudert M, Bauer P, Giunti P, Globas C, Baliko L, et al. Spinocerebellar ataxia types 1, 2, 3, and 6: disease severity and nonataxia symptoms. *Neurology*. 2008;71(13):982-9.
11. Stephen CD, Schmahmann JD. Eye Movement Abnormalities Are Ubiquitous in the Spinocerebellar Ataxias. *Cerebellum*. 2019;18(6):1130-6.
12. Pedroso JL, Braga-Neto P, Felicio AC, Dutra LA, Santos WA, do Prado GF, et al. Sleep disorders in machado-joseph disease: frequency, discriminative thresholds, predictive values, and correlation with ataxia-related motor and non-motor features. *Cerebellum*. 2011;10(2):291-5.
13. Kuo PH, Gan SR, Wang J, Lo RY, Figueroa KP, Tomishon D, et al. Dystonia and ataxia progression in spinocerebellar ataxias. *Parkinsonism Relat Disord*. 2017;45:75-80.
14. Lo RY, Figueroa KP, Pulst SM, Perlman S, Wilmot G, Gomez C, et al. Depression and clinical progression in spinocerebellar ataxias. *Parkinsonism Relat Disord*. 2016;22:87-92.
15. Schmitz-Hubsch T, Coudert M, Tezenas du Montcel S, Giunti P, Labrum R, Durr A, et al. Depression comorbidity in spinocerebellar ataxia. *Mov Disord*. 2011;26(5):870-6.
16. Manto M, Dupre N, Hadjivassiliou M, Louis ED, Mitoma H, Molinari M, et al. Management of Patients with Cerebellar Ataxia During the COVID-19 Pandemic: Current Concerns and Future Implications. *Cerebellum*. 2020:1-7.
17. Wang W. *Clinical Epidemiology-basic principles and practical applications*. Beijing: Higher Education Press; 2012.
18. Zung WW. A rating instrument for anxiety disorders. *Psychosomatics*. 1971;12(6):371-9.
19. Tanaka-Matsumi J, Kameoka VA. Reliabilities and concurrent validities of popular self-report measures of depression, anxiety, and social desirability. *J Consult Clin Psychol*. 1986;54(3):328-33.
20. Zung WW. A SELF-RATING DEPRESSION SCALE. *Arch Gen Psychiatry*. 1965;12:63-70.
21. Schmitz-Hubsch T, du Montcel ST, Baliko L, Berciano J, Boesch S, Depondt C, et al. Scale for the assessment and rating of ataxia: development of a new clinical scale. *Neurology*. 2006;66(11):1717-

- 20.
22. Malhi GS, Mann JJ. Depression. *The Lancet*. 2018;392(10161):2299-312.
23. Schlax J, Junger C, Beutel ME, Munzel T, Pfeiffer N, Wild P, et al. Income and education predict elevated depressive symptoms in the general population: results from the Gutenberg health study. *BMC Public Health*. 2019;19(1):430.
24. Schmitz-Hubsch T, Coudert M, Giunti P, Globas C, Baliko L, Fancellu R, et al. Self-rated health status in spinocerebellar ataxia—results from a European multicenter study. *Mov Disord*. 2010;25(5):587-95.
25. Cecchin CR, Pires AP, Rieder CR, Monte TL, Silveira I, Carvalho T, et al. Depressive symptoms in Machado-Joseph disease (SCA3) patients and their relatives. *Community Genet*. 2007;10(1):19-26.
26. Diallo A, Jacobi H, Cook A, Labrum R, Durr A, Brice A, et al. Survival in patients with spinocerebellar ataxia types 1, 2, 3, and 6 (EUROSCA): a longitudinal cohort study. *Lancet Neurol*. 2018;17(4):327-34.
27. Seidel K, Siswanto S, Brunt ER, den Dunnen W, Korf HW, Rub U. Brain pathology of spinocerebellar ataxias. *Acta Neuropathol*. 2012;124(1):1-21.
28. Teixeira-Castro A, Jalles A, Esteves S, Kang S, da Silva Santos L, Silva-Fernandes A, et al. Serotonergic signalling suppresses ataxin 3 aggregation and neurotoxicity in animal models of Machado-Joseph disease. *Brain*. 2015;138(Pt 11):3221-37.
29. Ashraf NS, Duarte-Silva S, Shaw ED, Maciel P, Paulson HL, Teixeira-Castro A, et al. Citalopram Reduces Aggregation of ATXN3 in a YAC Transgenic Mouse Model of Machado-Joseph Disease. *Mol Neurobiol*. 2019;56(5):3690-701.
30. Dunstan DA, Scott N, Todd AK. Screening for anxiety and depression: reassessing the utility of the Zung scales. *BMC Psychiatry*. 2017;17(1):329.

Tables

Table 1. Demographic characteristics of participants and psychometric scores by demographic variables
n=307

Characteristics		Number of participants (%)	Anxiety		Depression	
			SAS	P	SDS	P
Risks of exposure to COVID-19						
	yes	38 (12.4%)	50.6±7.9	0.001	60.1±14.2	0.022
	no	269 (87.6%)	45.1±10.1		54.3±11.8	
Gender						
	male	146 (47.6%)	46.1±10.6	0.703	54.5±12.9	0.534
	female	161 (52.4%)	45.5±9.4		55.4±11.5	
Age						
	<30	41 (13.4%)	43.2±9.9	0.056	53.3±10.8	0.121
	30~40	124 (40.4%)	45.1±8.7		53.8±11.5	
	40~50	99 (32.2%)	47.8±11.1		57.2±11.4	
	>50	43 (14.0%)	45.3±10.2		54.9±16.2	
Education						
	university	138 (45.0%)	43.5±8.9	<0.001	52.4±12.4	0.004
	middle school	139 (45.3%)	46.8±11.1		56.9±12.2	
	primary school	30 (9.7%)	51.1±5.9		58.1±9.2	
BMI						
	BMI<18.5	64 (20.8%)	46.1±9.8	0.950	57.2±12.2	0.196
	BMI 18.5~24	189 (61.6%)	45.7±10.4		54.1±12.2	
	BMI >24	54 (17.6%)	45.9±9.1		55.7±12.2	
Course of disease						
	0~5 years	107 (34.9%)	43.9±9.7	0.031	52.8±12.5	0.021
	5~10 years	126 (41.0%)	46.3±10.5		55.2±12.2	
	>10 years	74 (24.1%)	47.8±9.2		57.9±11.4	

Abbreviations: SCA, spinocerebellar ataxia; SDS, self-rating depression scale; SAS, self-rating anxiety scale; BMI, body mass index.

Table 2. Results of multiple linear regression on factors associated with scores of SAS scale and SDS scale [n=307]

Variables	SAS		SDS	
	Coefficient	P	Coefficient	P
Risks of exposure to COVID-19	0.190	0.001	0.152	0.007
Gender	-0.038	0.504	0.380	0.704
Age	0.052	0.373	0.597	0.551
Education	-0.239	<0.001	-0.192	0.001
BMI	-0.050	0.381	-0.066	0.256
Course of disease	0.103	0.069	0.126	0.029

Abbreviations: SCA, spinocerebellar ataxia; SDS, self-rating depression scale; SAS, self-rating anxiety scale; BMI, body mass index.

Figures

Figure 1

The approximate geographic locations map and subtype distribution for SCA patients (a) Map of the approximate geographic locations for SCA patients in this study. Participants came from different provinces in China but were mainly distributed in Hunan, Hubei, Guangdong, and Jiangxi provinces, which provinces were on the brink of Wuhan city, Hubei province, the area that COVID-19 was mainly concentrated in China. (b) SCA subtype distribution in the 307 SCA patients and SCA3 was the primary subtype in our study. Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.

Figure 2

Mental health state of the 307 SCA patients (a) Prevalence of anxiety in all participants. 307 SCA patients had an anxiety rate of 34.9%. (b) Prevalence of depression in all participants. 307 SCA patients had a depression rate of 56.7%. (c) Comparison of SAS scores between SCA patients and Chinese norms. The mean standard score of SAS scale of SCA patients was higher than that of the Chinese norm group (45.8 ± 10.1 vs. 37.2 ± 12.6 , $P < 0.01$). (d) Comparison of SDS scores between SCA patients and Chinese norms. The mean standard score of SDS scale of SCA patients was higher than that of the Chinese norm group (55.1 ± 12.2 vs. 41.9 ± 10.6 , $P < 0.01$).

a

b

Figure 3

Fig. 3 Correlation of SARA scale score with SAS scale and SDS scale score (a) Graph depicting significant positive correlation between SARA score (the higher the score the more severe the ataxia) vs SAS score (the higher the score the more anxiety) in 55 patients with SCA3. The correlation was significant with correlation coefficient $r=0.47$, $p=0.0002$. (b) Graph depicting significant positive correlation between

SARA score vs SDS score (the higher the score the more depression) in 55 patients with SCA3. The correlation was significant with correlation coefficient $r=0.40$, $p= 0.0023$.