Depressive and Cognitive Symptoms and Psychiatric Comorbidity of Taiwanese Patients with Machado-Joseph Disease

Chih-Wan Huang, M.D.¹, Chia-Yih Liu, M.D.¹²³, Chin-Song Lu, M.D.²⁵⁶⁷, Yeong-Yuh Juang, M.D.¹²⁴*

Objectives: The objectives of this study were to investigate the psychiatric and cognitive symptoms as well as psychiatric comorbidity in Taiwanese patients with Machado–Joseph disease (MJD). Methods: Fourteen patients with genetically confirmed Machado-Joseph disease and eight sex- and age-matched healthy volunteers were recruited. A board-certified psychiatrist conducted structured diagnostic interview. The Wechsler Adult Intelligence Scale was assessed by clinical psychologists. Both groups received assessment with Symptoms Checklist (SCL-90-R) and Zung’s Depression Scale and GHQ/QL-12. Results: Nine of 14 MJD patients (64.3%), had depressive or anxiety disorders. MJD patients showed significant severity of psychiatric symptoms including somatization (p < 0.05), obsession (p < 0.001), depression (p < 0.05), phobia (p < 0.05), hostility (p < 0.01), paranoia (p < 0.01) and psychotism (p < 0.01). They showed significantly lower scores in verbal (p < 0.05), performance (p < 0.001), and full IQ test (p < 0.01). The life quality was also significantly poorer in patients with MJD compared to normal control (p < 0.001). Conclusion: The Taiwanese patients with MJD have more psychiatric and cognitive disturbance than controls. The disturbances influence their life quality. This condition needs more attention and treatment.

Key words: spinocerebellar ataxia type 3, cerebellar cognitive affective syndrome, Symptoms Checklist-90-R, Zung’s Depression Scale

Introduction

Machado-Joseph disease (MJD), also known as spinocerebellar ataxia type 3 (SCA3), is a rare autosomal dominant degenerative disorder of the central nervous system [1]. This disease is one of many polyglutamine neurodegenerative diseases in North America, Europe and many areas of Asia [2]. MJD is caused by an expansion of CAG trinucleotide repeats in a gene located at chromosome 14q32.1 and characterized by progressive ataxia due to cerebellar and brainstem dysfunction, typically beginning between the ages of 20 and 50 years [3]. It is a highly disabling disease with progressive gait imbalance accompanied by ophthalamoplegia, dysarthria, dysphagia, dystonia, rigidity, sensitive loss, and distal muscle atrophies. In advanced stages of this disease, patients are wheel chair-bound and later bed-ridden with great impact on life quality [1, 4].

Cerebellar lesions in MJD do not always manifest with ataxic motor syndromes only. But cognitive and mood disturbances have been proved to be related to cerebellar lesions in previous studies by anatomical, physiological, clinical, and functional neuro-imaging data [3,5]. Some published articles have showed that MJD may develop cognitive and mood disorders. The prevalence and severity of cerebellar cognitive affective syndrome (CCAS) vary considerably in SCA populations which include impairment of executive function and linguistic abilities [3], visual-spatial [4], and sleep disorders [6], mood disturbance ranging from emotional blunting, depression, to disinhibition and psychotic features [7-9].

In those studies, rating scales and neuropsychological testing were used to assess the patients and found some possible psychiatric problems [10]. But no studies exist using structure interview to investigate specific psychiatric morbidities of MJD. There is a paucity of literature on the psychiatric disease related with MJD. The objectives of this study were intended to investigate the cognitive and mood symptoms in Taiwanese patients with MJD, and to determine the psychiatric comorbidity using structured interview schedule.

Methods

Study subjects

Fourteen patients with MJD were enrolled from neurology clinic in this study. Diagnosis of MJD was confirmed by screening the expanded trinucleotide repeats using standard methods and by neurologists. We also recruited eight sex- and age-matched healthy volunteers without any history of movement disorder or psychiatric diseases were recruited as a control group.

The institutional review board of Chang Gung Memorial Hospital approves this study protocol with the requirement of obtaining the signatures of all study subjects.

Assessments

Psychiatric diagnosis

A structured interview with MINI (Mini Neuropsychiatric Interview). MINI was conducted by board-certificated psychiatrists. The diagnosed were made according to the DSM-IV criteria.

Psychiatric symptomatology

A self-rating scale, the Symptoms Checklist (SCL-90-R) [14] was applied to detect clinical symptoms including somatization, anxiety, depression, and psychosis. The Zung’s Depression Scale [11] was also applied to detect the patients’ subjective severity of depression.
General intellectual abilities

The subjects’ intellectual condition was evaluated by the Wechsler Adult Intelligence Scale [12], which was conducted by clinical psychologists.

Life quality

Life quality of the subjects and controls were evaluated using GHQ/QL-12 for life quality [13]

Statistical analysis

The diagnoses and psychiatric symptoms of MJD patients were presented using descriptive statistics. We compared scores of each scale between MJD group and the normal control group with the Mann-Whitney U test.

We used Statistical Package for Social Science software version 17.0 for Windows (SPSS, Inc., Chicago, Illinois, USA) to compute all Inc., study data. The differences between group were considered significant if p-values were smaller than 0.05.

Results

There were 14 subjects with MJD were recruited. The ages of the disease onset were from 23 to 53 years, with an average of 34.08 ± 7.6 years. The duration of illness before their visiting this special clinic was from 3 to 14 years with a mean of 7.6 ± 3.6 years. Nine of these 14 patients (64.3%) have psychiatric diagnosis: Two of them have major depression, another 2 patients have major depression comorbid with dysthymic disorder, 3 patients have generalized anxiety disorder and 1 patient has generalized anxiety disorder with obsessive-compulsive disorders. Besides, one patient was found to have schizophrenia (not related to MJD) in this study.

Table 1 compares SCL-90-R subscale scores between Machado-Joseph disease patients and normal control group.

<table>
<thead>
<tr>
<th>Subscales</th>
<th>MJD patients (n = 14)</th>
<th>Normal control (n = 8)</th>
</tr>
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<tbody>
<tr>
<td>Somatization</td>
<td>18.9 ± 10.4</td>
<td>5.1 ± 4.8*</td>
</tr>
<tr>
<td>Obsession</td>
<td>14.5 ± 5.4</td>
<td>6.1 ± 2.7***</td>
</tr>
<tr>
<td>Interpersonal</td>
<td>13.7 ± 7.8</td>
<td>5.5 ± 3.9</td>
</tr>
<tr>
<td>Depression</td>
<td>20.7 ± 9.9</td>
<td>5.6 ± 4.9*</td>
</tr>
<tr>
<td>Anxiety</td>
<td>11.2 ± 8.9</td>
<td>2.5 ± 2.6</td>
</tr>
<tr>
<td>Phobia</td>
<td>7.7 ± 6.3</td>
<td>1.8 ± 1.8*</td>
</tr>
<tr>
<td>Hostile</td>
<td>4.5 ± 3.7</td>
<td>0.9 ± 0.8**</td>
</tr>
<tr>
<td>Paranoia</td>
<td>7.1 ± 6.0</td>
<td>2.0 ± 2.3**</td>
</tr>
<tr>
<td>Psychoticism</td>
<td>8.1 ± 5.1</td>
<td>2.4 ± 1.5***</td>
</tr>
</tbody>
</table>

* p < 0.05; ** p < 0.01; *** p < 0.001 (N = 22)
Compared using Mann-Whitney U test
SCL-90-R (Symptom Checklist 90-R)
Table 2. Compares Zung’s Depression Scale and Life Quality Scale between two groups

<table>
<thead>
<tr>
<th>Scales</th>
<th>MJD patients (n = 14)</th>
<th>Normal control (n = 8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ZDS</td>
<td>45.9 ± 7.7</td>
<td>33.9 ± 5.6**</td>
</tr>
<tr>
<td>Life Quality</td>
<td>16.8 ± 6.1</td>
<td>26.4 ± 6.0***</td>
</tr>
</tbody>
</table>

**p < 0.01; ***p < 0.001 (N = 22)
Compared using Mann-Whitney U test
MJD, Machado-Joseph disease

Discussion

In this study, we described psychiatric burden including depression and intelligence in MJD patients with different scales. Previous studies have shown deficits on gait disturbance, muscle dysfunction, cognitive impairment and emotional problems [4, 8, 9, 15]. But there is a lack of information about the psychiatric comorbidity of MJD patients. To our best knowledge, this report is the first paper focusing on the psychiatric diagnosis using structured interview.

In the present study, MJD group got higher score in SCL-90-R and showed significant higher scores in most dimensions of SCL-90-R (Table 1) suggesting that MJD patients have more serious psychological problems than those in general population. In Zung’s scale, which is self-administered questionnaire (Table 2), we found that people with MJD were significantly more depressed than control group (p < 0.01). Though the case number is small, we demonstrated that Taiwanese patients with MJD also developed more severe psychopathology. In concordance with symptomatology, the present study revealed that high percentage of MJD patients fulfilled the criteria of psychiatric diagnoses. Most of them had depressive disorders or anxiety disorders. In association with cognitive impairment, the manifestation is probably due to the cerebellar lesions in MJD [5, 8].

In the second parts of this study, we provided evidence to prove that psychiatric disorders may affect MJD patients significantly (p < 0.001) in their life quality (Table 2). In the Life Quality Scale, MJD group also reported less satisfaction compared with that of the control group. Through this study, we need to take care of not only physical discomforts but we also have to deal with psychological problems. In the Wechsler Adult Intelligence Scale (Table 3), MJD patients showed significantly lower scores in verbal (p < 0.05), performance (p < 0.001) and full IQ (p < 0.01).

Table 3. lists comparison of global intellectual abilities in both groups

<table>
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<tr>
<th>Scales</th>
<th>MJD patients (n = 14)</th>
<th>Normal control (n = 8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verbal IQ</td>
<td>83.2 ± 26.8</td>
<td>97.1 ± 8.3*</td>
</tr>
<tr>
<td>Performance IQ</td>
<td>74.9 ± 23.7</td>
<td>97.0 ± 12.3***</td>
</tr>
<tr>
<td>Full IQ</td>
<td>78.7 ± 24.7</td>
<td>96.1 ± 8.8**</td>
</tr>
</tbody>
</table>

*p < 0.05; **p < 0.01; ***p < 0.001 (N = 22)
Compared using Mann-Whitney U test
IQ, intelligent quotient; MJD, Machado-Joseph disease
Cognitive impairment might be due to the original genetic disorder, cerebellar disorder, or poor learning ability due to multiple causes including poor life quality and depression.

Limitations of the study

Our study should be interpreted in the context of five limitations.

- MJD patients were compared with general population in all scales directly. As we have known, somatic discomfort and neurological dysfunction also affect mood and cognitive function so the life quality impairment may be affected as well.
- MJD is a rare disease so we have relative small sample size that may miss some other differences. This study only enrolled 8 subjects as controls so it may not been seen exactly as general population. In addition, our psychiatrist conducted interview with MJD group but not in control group so we do not know the psychiatric problems in control group.
- There was no following information and we cannot know how their disease process would be going. This will be the next target of such studies.
- The information we collected only suggest cross-sectional but not longitudinal condition.
- For some CAG-repeat disorders, the repeat number is correlated with clinical symptoms. But in this study, we did not have specific data about GAG-repeat numbers of our study patients and did not compare them with symptoms although the diagnosis of these MJD patients were confirmed genetically.

In summary, the findings from this study provide clinical data using structured interviews and diverse scales. Based on the results, we should pay more attention and effort to manage both physical and psychiatric disturbances in clinical practice when dealing with MJD patients.

Acknowledgements

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