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Case Report

Neuropsychology of Spinocerebellar Ataxia Type 2, a Case Study in Stage I Disease

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Abstract

Currently, the evaluation of cognitive disorders in Spinocerebellar Ataxia Type 2 is of great interest, given that the identification of its neuropsychological characteristics allows for a deeper understanding of the disease. However, its approach from the field of study of neuropsychology, based on the integration of the cognitive, affective and behavioral state, is insufficient. The objective of study is characterized from a neuropsychological point of view, a series of cases with Spinocerebellar Ataxia Type 2 in stage I. A multiple case study was carried out with four patients with diagnosis of Spinocerebellar Ataxia Type 2 in stage I genetically confirmed and intentionally chosen. Psychological and neurocognitive tests were applied to evaluate the cognitive, affective and behavioral spheres. Patients with SCA2 stage I presented cognitive impairment in the neuropsychological examination, only one of the subjects showed normal global cognitive functioning, although in the evaluation by specific domains he evidenced various cognitive deficits. Anxiety and depression at pathological levels were not identified in the patients. They showed satisfaction and self-actualization with their lifestyles. The neuropsychological characterization of the cases studied with SCA2 in stage I contributed to a greater understanding of the disease. The identified deficits speak in favor of carrying out a neuropsychological evaluation from the initial stages, to project more effective neuropsychological rehabilitation strategies, which is of interest to the scientific community in the field of Neurosciences.

Keywords

Spinocerebellar Ataxia Type 2, Neuropsychology, Cognitive Impairment, Lifestyle

1. Introduction

Spinocerebellar Ataxia Type 2 (SCA2) is characterized by a cerebellar syndrome associated with slow saccades, early hyporeflexia, severe postural tremor, peripheral neuropathy, cognitive impairments, and other multisystem features [7]. In

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this sense, the scientific literature consulted supports the presence of cognitive alterations in SCA2 [2, 4, 15, 20, 27]. However, despite being one of the most frequent forms of hereditary ataxias, its approach from the field of study of Neuropsychology is insufficient.

Studies carried out report the presence of cognitive impairment in early stages of the disease [21], identifying between 5-39% of patients with SCA2 [3, 6, 22, 27]. More specifically, cognitive deficits are reported involving domains such as attention, executive function, verbal, visuospatial and visuoperceptual memory, speed of information processing, semantic and phonological verbal fluency [6, 15, 16, 22, 27]. However, the decline of the cognitive procceses varies among studies [10]. This does not allow a homogeneous neuropsychological characterization in SCA2.

In researchs developed by Karamazovova [11] it was stablished that the cerebellum has a modulating role not only in cognition, but also in emotion. He reported that in addition to depression, there is a high level of anxiety in Spinocerebellar Ataxia (SCA); although other symptoms such as: apathy, agitation, lack of impulse control and psychosis are among the least addressed, several studies suggested their presence in this type of patient. Besides, there is evidence that environmental factors, including lifestyle, influence on the onset and progression of neurodegenerative disorders [5, 28].

The absence of studies in SCA2 that cover the three axes of neuropsychology: cognition, affection and behavior, requires the integration of these dimensions in the neuropsychological evaluation, not only to achieve a better description of the disease, but also to develop more effective rehabilitation forms.

In Cuba, the latest epidemiological study carried out identified 848 subjects with SCA2, which is equivalent to 87.42% of patients with autosomal dominant cerebellar ataxias, belonging to 124 families [33]. The high prevalence of patients constitutes a health problem for the country, especially for the municipality of Baguanos, Holguín province, which concentrates the largest sick and at-risk population reported worldwide so far. Therefore, the neuropsychological characterization of SCA2 in the Cuban context is a pending issue and of special relevance for the Holguín province in particular.

In this way, the objective of this study is: To characterize, from a neuropsychological point of view, a series of cases with Spinocerebellar Ataxia Type 2 in stage I in the province of Holguín.

2. Methods

2.1. Type of Study and Participants

To fulfill the objective, a multiple case study was carried out using qualitative methodology. The participants were chosen based on genetic confirmation at the Center for Research and Rehabilitation of Hereditary Ataxias (CIRAH), reside in the municipality of Báguanos in the province of Holguín, aged between 18-60 years, without confusional mental state, psychopathological disorders, cognitive impairment or neurodegenerative condition, in addition to ataxia, which would prevent the understanding of the tasks to be accomplished.

A review of the registry of patients with SCA2 was carried out at the "Rolando Ricardo Estrada" Polyclinic, Baguanos. Subsequently, the medical records of all registered patients were reviewed to select the subjects according to the established criteria. Then a semi-structured interview was applied to the patients who met the selection criteria, based on obtaining their consent to participate in the research and corroborate the data obtained.

2.2. Neuropsychological Evaluation

The instruments to evaluate cognitive functioning were: Montreal Cognitive Assessment (MoCA): it was used to measure general cognitive status [12]. Forward and backward digit repetition scale: it was used to evaluate sustained attention [18]. Toulouse test: it was applied to explore the functioning of selective attention [8]. Learning 10 words proposed by AR Luria: it was used in the exploration of verbal memory in the process of fixation and evocation, in addition to fatigue and attention activity [1]. From the Holguín Neuropsychological Evaluation Battery, the Visual Memory subtest was used to evaluate the process of fixation, free evocation and visual recognition; the Expression subtest to measure expressive language, the Nomination subtest for the evaluation of the language naming process and the Ideational Praxis subtest [19, 25] were used as well. The animal category was explored in case of Verbal Fluency Test, in the semantic modality. In the phonological modality the letters F,A,S were evaluated [23]. From the Neuropsi Battery, the Comprehension subtest was used to explore comprehensive language; the Calculus subtest for the evaluation of the concept of number, the ability to calculate and to solve problems related to executive functioning; the Reading subtest for the evaluation of oral reading fluency, reading comprehension and parallelies [24]. Zoo map was included in the Behavioral Assessment of Dysexecutive Syndrome (BADS) to measure executive functions in planning ability [26]. Stroop test was used to explore inhibitory control in executive functioning [9]. Analogies Test I and II was used to evaluate the capacity for abstraction in executive functioning [1].

The instruments to evaluate the affective-behavioral state were: The Beck Depression Inventory, for the evaluation of depressive symptoms. The Beck Anxiety Inventory, to assess the severity of anxiety symptoms [8]. Lifestyle Characterization Questionnaire (EV-3) was used to evaluate the behavioral expression of the personality of the subjects participating in the study [17].

The results of the applied instruments were interpreted

according to the criteria of the referenced authors.

2.3. Procedure and Data Processing

The neuropsychological evaluation was carried out in two work sessions. In the first session, global cognitive, affective and behavioral functioning was explored. In the second session, the evaluation was developed by specific cognitive domains. In data processing, each technique was interpreted separately, then triangulation of the information was carried out to achieve greater validity and reliability of the results.

2.4. Ethical Aspects

The subjects signed an informed consent to participate in the study, in accordance with the ethical aspects of the Health Institution. The information contained on the applied instruments is kept preserved and confidential. The case study is related with the Declaration of Helsinki.

3. Cases Presentation

3.1. Case 1

Female patient, 44 years old, white, university studies, retired due to illness, two children, married, with a history of mental health. She presents as a Personal Pathological History: Arterial Hypertension and SCA2 in stage I, with a history of SCA2 in her paternal family. She was diagnosed with the disease 5 years ago, showing symptoms since that time. She currently presents dysarthria, imbalance and difficulties in walking, she walks alone without the help of another person or implement.

Neuropsychological evaluation revealed global cognitive impairment (MoCA = 21). In the deeper exploration by cognitive domains, alterations were identified in the selective and sustained attention of direct and reverse digits, visual recognition memory, expression, comprehension, semantic and phonological verbal fluency of language, reading, planning and inhibitory control of the executive functioning. Orientation, verbal and visual memory of fixation and evocation, nomination, ideational praxis, calculation and abstraction of executive functioning were evidently preserved.

From the affective-behavioral point of view, she did not show anxiety or depression at pathological levels. The lifestyle was oriented toward the present, playing the main roles of daughter and mother. She showed satisfaction with her lifestyle, although she wanted to be as healthy as before and for her illness to have a cure. She expressed self-realization from her work, family and personal point of view. She considers that there is a relationship between SCA2 and her lifestyle; she believes that the symptoms of the disease influence the modification of behaviors to assume a healthy lifestyle.

3.2. Case 2

Male patient, 48 years old, white, 11th grade of education, retired due to illness, one child, divorced, smoker, with a history of mental health. As Personal Pathological History he presents SCA2 in stage I, with a history of SCA2 in the maternal family. Diagnosed with the disease whenhe was 8 yearsold, showing symptoms since that time. Currently he has dysarthria and mild imbalance in open spaces, he walks alone without the help of another person or implement.

Neuropsychological evaluation revealed global cognitive impairment (MoCA = 21). In the more specific exploration by cognitive domains, alterations were identified in selective attention, visual evocation memory, expression, comprehension, semantic and phonological verbal fluency of language, planning and inhibitory control of executive functioning. Orientation, sustained attention of direct and reverse digits, verbal memory of fixation and evocation, visual memory of fixation and visual recognition, nomination, reading, ideational praxis, calculation and abstraction of executive functioning were evident as preserved.

From the affective-behavioral point of view, he did not show anxiety or depression at pathological levels. Her lifestyle was oriented towards the present, playing the main roles of son and father. He showed satisfaction with his lifestyle. He manifested self-realization in the work and personal spheres. However, he claims to feel partially self-realized in his relationship, due to his divorce after the diagnosis of the disease. He said that there is a relationship between SCA2 and his lifestyle, because he had to retire due to the disease and thus develop other alternative activities to obtain financial remuneration.

3.3. Case 3

Female patient, 49 years old, white, university studies, teacher, three children, married, with a history of mental health. As Personal Pathological History she presents Arterial Hypertension and SCA2 in stage I, with a history of SCA2 in her paternal family. She has been diagnosed with the disease for 22 years. In the last 6 years she has shown slight imbalance and memory problems, she walks alone without the help of another person or implement.

Neuropsychological evaluation revealed global cognitive impairment (MoCA = 24). In the deeper exploration by cognitive domains, alterations were identified in sustained attention of reverse digits, verbal fixation memory, semantic verbal comprehension and fluency of language, planning in executive functioning. Orientation, selective and sustained attention of direct digits, verbal evocation memory, visual fixation and evocation memory, visual recognition, nomination, expression and phonological verbal fluency of language, ideational praxis, reading, inhibitory control, were evident as preserved, calculation and abstraction of executive functioning.

From the affective-behavioral point of view, she did not show anxiety or depression at pathological levels. Her life-

style was future-oriented, playing the main roles of mother and worker. She showed satisfaction with her lifestyle and with self-realization in the work and personal spheres as well. She reported feeling partially self-realization in her relationship due to communication problems between them. She did not express a relationship between SCA2 and her lifestyle, since she considers that she is a strong person.

3.4. Case 4

Male patient, 59 years old, white, 12th grade of education, retired due to illness, married, with a history of mental health. As Personal Pathological History he presents Arterial Hypertension and SCA2 in stage I, with a history of SCA2 in his paternal family. Diagnosed with the disease for 21 years. In the last 11 years he has manifested dysarthria and imbalance in open spaces, walking alone without the help of another person or implement.

Neuropsychological evaluation revealed normal global cognitive functioning (MoCA = 26). In the more specific exploration by cognitive domains, alterations were identified in sustained attention of direct digits, verbal memory of fixation and evocation, phonological verbal fluency of language and planning in executive functioning. Orientation, selective and sustained attention of reverse digits, visual memory of fixation and evocation, visual recognition, nomination, expression, comprehension, semantic verbal fluency of language, reading, ideational praxis and inhibitory control, calculation and abstraction were evident as preserved of executive functioning.

From the affective-behavioral point of view, he did not show anxiety or depression at pathological levels. His lifestyle was oriented towards the present, playing the main roles of father and husband. He showed satisfaction with his lifestyle, although he would like to increase activities of a pleasurable nature. He expressed self-realization from his work and family relationship, but not in his personal life, in which he reported partial self-realization, due to the influence of his illness on the achievement of goals. He proposed a relationship between SCA2 and his lifestyle, because he cannot carry out daily activities as quickly as before and now he needs more time to perform them.

4. Discussion

From a neuropsychological view, a series of cases with SCA2 in stage I of the disease, genetically confirmed, were described. All cases presented ataxic manifestations, among which dysarthria, imbalance in open spaces and walking difficulties stand out. These symptoms are consistent with cerebellar syndrome, in which the cerebellum was long believed to be responsible for motor functions. However, in lastyear's the role of the cerebellum in cognitive functions has become visible [15].

Previous studies report the presence of cognitive impairment in early stages of the disease [3, 21, 22, 27]. Of the four patients analyzed, three presented global cognitive impairment in the initial stage of the disease. This finding means that cognitive deterioration can set in from the onset of SCA2, a fact that is rarely addressed in the international literature, precisely because, in the authors' opinion, the neuropsychological evaluation is performed late, when the disease has progressed as far as possible enough to impair cognition. This result is probably related to the hypothesis that there is a very early contribution of the cerebellum to cognition [13].

In the four patients studied, the cognitive deficits are mild, which may be related to the stage I of the disease in which they are found, whose clinical severity is mild. This result is associated with the study developed by Le Pira [13] in which they proposed that cognitive status was partially related to clinical severity rather than to the duration of the disease or the age of onset of symptoms. Furthermore, the subjects' educational level is high, which means greater cognitive reserve. This is in line with various scientific findings that affirm that, in people with high intellectual enrichment, estimated by educational achievements, there is a better capacity to resist cognitive deterioration in neurological diseases [29, 30].

Although executive dysfunction is frequently reported in ataxic patients [14, 34], in the deeper exploration of the subjects evaluated, deficits in inhibitory control and planning were identified, which corresponds to the results from the study on executive functions in SCA2 developed by Sánchez [31] and Vaca-Palomares [32].

Recent studies suggest that cognitive deficits involve other domains such as: alterations in attentional matrices, verbal, visuospatial and visuoperceptivememory, speed of information processing, semantic and phonological verbal fluency [15, 16, 22, 27]. The neurocognitive characteristics identified in the patients evaluated coincide with these studies. In the cases addressed, alterations were evident in sustained and selective attention, semantic and phonological verbal fluency. To a lesser extent, deficits were seen in verbal memory, with damage being more evident in the fixation process than in evocation. Visual memory showed higher performance, with lower efficiency reported in free recall and recognition. The results obtained in memory support the hypothesis of a difficulty in retrieval rather than a storage problem [3, 14, 21].

The deficits in language expression and comprehension are significant; as well as text comprehension in reading, little explored processes and for which no previous references to these results were found.

The analysis of the four patients revealed that not all cognitive domains are impaired. So they preserve orientation, visual memory in the process of fixation, naming, the capacity for abstraction and calculation.

Regarding the analysis of the affective component, the four patients had a history of mental health, so they were not receiving treatment with psychotropic drugs. The tests used to identify states of anxiety and depression were negative. These

results can be related to the presence of a preserved functional capacity in the subjects, which favors their active performance in society and in daily life. Furthermore, denying the emotional symptoms of the disease could be interpreted as a way of coping with it.

The findings identified differ from the actual systematic review conducted by Karamazovova [11] in which high levels of depression and anxiety were reported in SCA. However, in the cases analyzed, the possibility that, given the isolated presence of some symptoms such as palpitations, fear, irritability and difficulties for falling asleep, is indicative of an evolution towards anxious and depressive states, is notruled out. Therefore, it must be monitored to prevent affective alterations that aggravate the clinical condition of these patients.

In the evaluation of lifestyle as a behavioral expression, the four cases were satisfied and self-fulfilled with their lifestyle. They manifested a temporal orientation focused more on the present, aimed at the search for pleasurable activities from a family, work and social point of view. These behaviors can be related to a way of coping with the disease, which means taking advantage of the current moment to achieve configurations of behaviors in the present that serve as compensation for the future, when the wear and tear imposed by SCA2 is greater.

There was a predominance of patients who perceived a relationship between their disease and lifestyle, associated with the modification of habits that could negatively influence the evolution of SCA2; as well as the adoption of behaviors that compensate for the physical limitations of the disease.

Only one participant did not report links between the disease and lifestyle, arguing the presence of personological qualities that allow him to cope with the disease. This self-perception of the patient could be interpreted as a mechanism of denial of the disease and become a risk factor for her health because it can lead to non-compliance with treatment.

5. Limitations and Future Directions

The present set of studies has a number of clear limitations. First off all, certain information relating to the participants' genetic characteristics were not collected, which does not allow an analysis of possible associations between genetic variables and cognitive impairment. Future studies could be conducted to examine how genetic variables explain individual differences associated with neropsychological changes in SCA2. Secondly, although the study allows an in-depth description of the cases beyond their cognitive state; it is recommended to extend the study to a larger number of cases. However, despite the limitations noted above, the results of the present research are sufficiently robust to attest to the reliability of the data collected from the qualitative analysis of the cases.

6. Conclusions

From a cognitive point, global cognitive deterioration predominated in the subjects studied in the initial stage of SCA2. Alterations in sustained and selective attention were identified; in the comprehension, expression and verbal fluency of language, in planning and inhibitory control of executive functioning; as well as in verbal memory of fixation and evocation, visual memory of evocation and recognition and in reading. Orientation, visual fixation memory, nomination, ideational praxis, calculation and abstraction were found preserved.

The patients analyzed did not show a depressed or anxious mood, which is related to the adoption of a healthy, present-oriented lifestyle; so that it constitutes a compensatory behavioral strategy for coping with the disease in more advanced stages.

The neuropsychological characterization of the case series with SCA2 stage I contributed to a greater understanding of the disease. The identified deficits speak in favor of carrying out a neuropsychological evaluation from the initial stages, to project more effective neuropsychological rehabilitation strategies, which is of interest to the scientific community in the field of Neurosciences.

Abbreviations

SCA2: Spinocerebellar Ataxia Type 2

SCA: Spinocerebellar Ataxia

CIRAH: Center for Research and Rehabilitation of Hereditary Ataxias

MoCA: Montreal Cognitive Assessment

BADS: Behavioral Assessment of Dysexecutive Syndrome

EV-3: Lifestyle Characterization Questionnaire

Ethical Approval

The research protocol was approved by the local ethics committee of the corresponding author's academic institution, and all participants provided written informed consent to participate in the research.

Author Contributions

Diana Rosa Hidalgo Martinola: Conceptualization, Methodology, Writing-Original Draft Preparation

Ana Karina Gutiérrez Alvarez: Writing-Review & Editing, Project Administration

Yarily Martínez Fernández: Supervision

Mairelys Guillén Reyes: Supervision

María Victoria González Jover: Validation

Data Availability Statement

The raw data supporting the conclusions of this research will be made available by the authors, without any undue reservation.

Conflicts of Interest

The authors declare no conflicts of interest.

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