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Abstract

Occupational therapy (OT) is a profession concerned with promoting health and well-being through occupation, by enabling handicapped people to participate in the activities of everyday life. OT is part of the clinical rehabilitation of progressive genetic neurodegenerative diseases such as spinocerebellar ataxias; however, its effects have never been determined in these diseases. Our aim was to investigate the effect of OT on both physical disabilities and depressive symptoms of spinocerebellar ataxia type 3 (SCA3) patients. Genomically diagnosed SCA3 patients older than 18 years were invited to participate in the study. Disability, as evaluated by functional independence measurement and Barthel incapacitation score, Hamilton Rating Scale for Depression, and World Health Organization Quality of Life questionnaire (WHOQOL-BREF), was determined at baseline and after 3 and 6 months of treatment. Twenty-six patients agreed to participate in the study. All were treated because OT prevents blinding of a control group. Fifteen sessions of rehabilitative OT were applied over a period of 6 months. Difficult access to food, clothing, personal hygiene, and leisure were some of the main disabilities focused by these patients. After this treatment, disability scores and quality of life were stable, and the Hamilton scores for depression improved. Since no medication was started up to 6 months before or during OT, this improvement was related to our intervention. No association was found between these endpoints and a CAG tract of the MJD1 gene (CAGn), age, age of onset, or neurological scores at baseline (Spearman test). Although the possibly temporary stabilization of the downhill disabilities as an effect of OT remains to be established, its clear effect on depressive symptoms confirms the recommendation of OT to any patient with SCA3 or spinocerebellar ataxia.

Key words: Spinocerebellar ataxia 3; Occupational therapy; Rehabilitation; Depression; Machado-Joseph disease; Polyglutamine diseases

Introduction

Spinocerebellar ataxia type 3 (SCA3), also known as Machado-Joseph disease, is a rare neurodegenerative disease caused by expansions of a CAG tract of the MJD1 gene (1-3). The expanded allele is dominant, and there is an important correlation of the repeat amplification with both symptom severity and age at onset in affected individuals. There is no treatment.

SCA3 affects at least 3:100,000 individuals in the Brazilian population (4). SCA3 is a highly disabling disease, which imposes a severe burden on the patients and their families. Clinical manifestations usually start during adulthood, with a mean (± SD) age at onset of 32 ± 12 years (5). Patients end up confined to a wheelchair and later become bedridden (6). Age at onset distribution is very wide and ranges between 5 and 73 years (6). Median survival time after onset is 21 years (7).

The disease is related to neuronal loss and neuronal intranuclear inclusions, detected mainly in the dentate nucleus of the cerebellum, the nucleus dorsalis of Clarke in the spinal cord, cranial motor nerve nuclei, pontine nuclei, substantia nigra, and the lenticular fasciculus of the globus pallidus (8-11). Clinical manifestations usually start with cerebellar ataxia affecting gait, limb movements, speech articulation, and deglutition. Patients also present a variety of other dysfunctions, including pyramidal involvement; a supranuclear, progressive external ophthalmoplegia with...
limitation of upward gaze and convergence; extrapyramidal
signs, including dystonia, rigidity, bradykinesia, and even a
full parkinsonian syndrome; lower motor neuron disease,
with fasciculation and atrophy; sensitive loss; eyelid
retraction, contraction fasciculation, weight loss, and sleep
disorder (6). All of these findings lead to a progressive bur-
den and incapacitation. In addition, depressive symptoms
are rather frequent and may be related to the inexistence
of an effective treatment (12). In SCA3, depressive scores
have been associated with the level of incapacitation,
conditions that probably reinforce each other.

To our knowledge, very few studies of rehabilitation inter-
enventions in SCAs in general and in SCA3 in particular have
appeared in the literature. Among rehabilitation techniques,
occupational therapy (OT) aims to adapt a particular patient
to the activities of his/her daily living in order to obtain the
maximum possible independence. OT is a common clinical
practice, although its effects have never been measured
in patients with SCA. In order to identify the role of OT in
SCA3, the present study describes the disabilities associ-
ated with the disease, the effect of occupational therapy on
these disabilities, on depressive symptoms and on quality
of life, and the possible associations of these endpoints
with risk factors, such as a CAG tract of the MJD1 gene
(CAGn) and age of onset.

**Material and Methods**

Genomically diagnosed SCA3 patients older than 18
years were invited to participate. The inclusion criterion
was independent gait on neurological examination. Patients
who had started any therapy less than 6 months before or
who had previously been on OT were excluded. The pres-
ent study was approved by the Grupo de Pesquisa e de
Pós-Graduação do Hospital de Clínicas de Porto Alegre
(GPPG, process #05-254), and all patients gave written
informed consent before participating.

After the patients agreed to participate in the study, a
structured interview, which included four instruments to
measure endpoints, was performed. The disability scores
included the functional independence measurement (FIM)
in its Portuguese version (13,14), and Barthel Incapacitation
scores (15). FIM scores were classified as follows: under
18, total dependence; 18 to 60, 50% dependence; 61 to
103, 25% dependence, and over 104, preserved indepen-
dence. Barthel scores were classified as follows: 0 to 45,
severe motor disability; 46 to 75, moderate disability; 76
to 99, mild disability, and 100, no disability. Depressive
symptoms were measured by the Hamilton Rating Scale
for Depression (16). Scores over 25, between 18 and
24, and between 17 and 7 were associated with severe,
moderate and mild depression, respectively. Quality of
life was investigated with the Portuguese version of the
World Health Organization Quality of Life questionnaire
(WHOQOL-BREF) (17,18). At baseline, the Neurological
having a longer CAGn when compared to the general sample (78 vs 74) and consequently earlier ages at onset (28.6 ± 13.3 vs 37.1 ± 10 years). The quality of life of cases lost to follow-up also tended to be worse than that of the general group (45.8 ± 14.4 vs 58.1 ± 9.6; P = 0.06).

Follow-up of depressive symptoms

Hamilton scores (mean ± SD) for depression obtained for the 23 patients who completed the study were 8.65 ± 6.6 and 6.04 ± 6.2 before and after 6 months of OT treatment, respectively. This improvement was not only significant (P < 0.0001, paired t-test), but the mean (after trial) also reached normal values. Individual scores are presented in Figure 1.

The difference between the 6th month score and baseline score, hereafter referred to as ∆ Hamilton, was not related to the independent variables under study (age, age at onset, schooling, CAGn, SARA, and NESSCA scores) or to the other endpoints measured (Barthel, WHOQOL, and FIM) at baseline or at the patients own progression slopes.

Individuals with higher depressive scores at baseline showed apparently better responses to treatment (OT) after 6 months (Figure 2A; r = -0.619, P < 0.002, Spearman).

Follow-up of FIM and Barthel scores for disability

The incapacities most referred to by patients were...
difficulty in dynamic balance resulting in walking deficits, difficulty in word articulation, and difficulty in handling tableware and pens.

Mean ± SD scores for disability did not change after 6 months of OT: FIM scores were 120.17 ± 4.8 and 120.26 ± 6.5, and Barthel scores were 96.9 ± 5.9 and 96.9 ± 6.3 at baseline and after 6 months. When the group was stratified according to CAGn (two groups of patients, with cut-off at 73 CAGs) and to disease duration (cut-off at 5 years of disease duration), no differences were found in FIM progression.

Some individuals actually got worse after 6 months of follow-up. Regarding Barthel scores, an inverse relation was observed between response (Δ Barthel) and baseline; the better the baseline, the worse the response after 6 months. This phenomenon is illustrated in Figure 2B.

Follow-up of quality of life

Mean ± SD scores of global WHOQOL did not change after 6 months of OT; they were 58.1 ± 9.6 and 58.1 ± 14.4 at baseline and after 6 months (paired t-test). Since patients lost to follow-up tended to have worse WHOQOL and in order to test if their exclusion could have biased these results, we also compared the WHOQOL of the overall sample at baseline (26 cases) to that of the remaining sample at 6 months (23 cases). No differences were found.

Actually, 4 patients improved according to WHOQOL, 15 remained the same, and 4 worsened at the end of observation. When these three subgroups were analyzed, no differences were found in their independent variables or in the other endpoints studied.

Discussion

OT is currently part of common clinical practice, although its effects have rarely been measured. Since interventions are individually tailored in any rehabilitation therapy but especially in OT, the variability of interventions or their qualitative nature can partially explain the lack of studies on their effects. OT is particularly important in progressively incapacitating diseases, especially those without any known treatment. The objective of OT is to improve abilities and capacities of daily living in handicapped individuals. And due to the progressive nature of neurodegenerative diseases, OT should not only be a permanent management but also change as disease progresses.

Studies on the impact of OT on SCAs in general are lacking. Two open-label trials on SCA2 studied the impact of physical training and of group psychotherapy (23,24). Both studies reported favorable follow-ups, but intervention, disease under study and endpoints were diverse, and therefore their results are hardly comparable to ours. Expert opinions are also rare: in a review article, neuroanatomical characteristics were analyzed regarding rehabilitative choices in SCA2 and SCA3 (25).

Since we routinely indicate OT to our patients, we tried to improve our knowledge about the role of this rehabilitation technique. Our challenge started when we tried to figure out what the specific effect of OT would be, for instance, on capacities and abilities, social adaptation, or personal adaptation to the disease. The existing instruments used to measure these endpoints are multiple, and there is no unique severity score with all these domains. Because of this, we decided to test disabilities, quality of life, and depressive manifestations. Our second challenge was the study design, and we decided for an open trial. This design was chosen for two main reasons. First, OT is an acclaimed management, which is no longer prone to randomized studies. Second, blinding OT would be rather impossible.

Our results indicate that OT improved the Hamilton scores for depression of SCA3 patients. This response to OT was not related to the independent variables under study, i.e., gender, age, age at onset, schooling, CAGn, NESSCA, and SARA scores. Moreover, improvement of depression did not correlate with the other endpoints.

Incapacitation scores - Barthel score and FIM - and quality of life were stable throughout this study. However, since the natural history of these parameters in SCA3 is unknown, interpretation of these data was not possible. This is a drawback of this study design, where no control group was monitored. When the natural history of a progressive disorder like SCA3 is unknown, open trials do not allow stabilizations to be interpreted as positive results. Stable states may theoretically be related to the natural course of a disease. Only improvements can be seen as definite results of open trials, in relentless diseases like SCA3.

Although the paired t-test did not detect any statistically significant differences in Barthel or FIM after 6 months of observation, a careful exam of the data revealed a sad reality. Baseline Barthel had an inverse correlation with responses, or Δ. In other words, patients with the best functional independence parameters at the beginning of the study tended to get worse after 6 months. This was clearly the result of the natural course of the disease.

The observation started with 26 cases; 3 dropped out, but there was apparently no bias due to these losses. In any case, it is possible that patients with more social networks and consequently better quality of life were inadvertently selected. Keeping in mind that this sample was limited to independent ambulatory patients, we still believe that this group was representative of SCA3 patients with an A-C-A ancestry, since general parameters such as age, age at onset, gender, CAGn ranges, and NESSCA scores were similar to those found in previous studies on these populations (5,19).

OT improved the depressive symptoms of SCA3 patients, which are an important clinical problem already shown to be common among these patients (12). Organic or reactive depressive symptoms can affect 33.5% of SCA3 individuals. The relation between depressive scores and
incapacitation levels observed in previous studies was not found in the present sample (12). We speculate that our lack of association was due to the recruitment of patients with relatively shorter disease duration and lower impact on their capabilities. Of course, incapacitation and depression may reinforce each other. Depressive symptoms should be looked for in SCA3 and probably in other SCAs in order to offer appropriate support to these individuals. We have already reported positive results of fluoxetine treatment on depression in these patients (26), and now a similar effect concerning OT was found. Comparisons of costs and effects of both treatments (OT and pharmacological) are prevented, due to the lack of data about them.

Although the possibly temporary stabilization of the downhill disabilities as an effect of OT remains to be established, the clear effect on depressive symptoms is enough to confirm the recommendation of OT to any given patient with SCA3 or a spinocerebellar ataxia.

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