Psychological Profile of the Amyotrophic Lateral Sclerosis (ALS) Patients*: A Descriptive Pilot Study base on the Cognitive Systemic Approach

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Abstract

The aim of this study was to evaluate if the changes in the behavioral and emotional aspects of the patients with ALS are secondary to a cognitive deficit or correspond to an increased/adaptive activation of the mental functioning of the patients. The study was carried on 17 Italian patients with ALS in the initial phase of the disease being treated at the Nemo Clinical Center department in Rome. We evaluated the presence of FTD or Cognitive Impairment, the presence of psychopathology and finally the psychological profile, according to Cognitive Systemic Post-rationalist approach, in terms of “Personal Meaning Organization” or PMO. The absence of cognitive impairment in half of the patients leads us to reflect on the need to integrate psychological evaluation with tools that, in addition to behavior, allow us to grasp the personal meaning dimension of the patient and his relational reciprocity. We conclude by saying that the psychological characteristics observed in these patients do not seem to be caused by the onset of the disease but represent configurations of Personal Meaning Organization stable over time.

Keywords: Amyotrophic lateral sclerosis; Psychology profile; Cognitive systemic post-rationalist

Introduction

Amyotrophic Lateral Sclerosis (ALS) is a fatal neurodegenerative disorder involving upper and Lower Motor Neurons (LMN)” [1].

ALS is sometimes associated with frontotemporal lobes degeneration (ALS-FTD frontotemporal dementia). In cases where there is no indication for this diagnosis, the occurrence of cognitive impairment along with deficits in social cognition, linguistic deficits, memory and neuropsychiatric symptoms is frequently detected at the early onset of the disease [2,3]. Question arises, therefore, on the compromised ability of the patients to cope with this illness and their insight, especially regarding therapeutic choices.

The clinical approach to patients with Amyotrophic Lateral Sclerosis (ALS) has been largely modified by the identification of novel genes, the detection of gene mutations in apparently sporadic patients, and the discovery of the strict genetic and clinical relation between ALS and Frontotemporal Dementia (FTD). The frequency of ALS-related genes is unevenly distributed in different populations. For example, SOD1 mutations account for ~10% of ALS cases in Sweden and Finland, with the p.D90A homozygous mutation being far the most common missense mutation, while they are found in less than 1% of Dutch patients. Similarly, C9ORF72 is the commonest gene in Caucasian populations, but is less frequent in patients of Chinese or Japanese ancestry. C9ORF72 than any other gene, is more frequently associated with comorbid FTD and psychotic-like symptoms both in the index case and in the extended family [4-6].

The 10%-15% of cases patients develop the behavioral variant of frontotemporal dementia (bvFTD) characterized by low insight, apathy, emotional lability, oddities, which can also be accompanied by deficits in verbal fluency, executive functions and social cognition [7].

In another 30%/50% of cases, patients with ALS develop cognitive impairment [2,3,8-10] even if not appear as a frank dementia [11].

Cognitive impairment doesn’t always increase over time. Some studies concluded that those who do not show cognitive deficits at the onset tend to remain stable over time [12-14]. In addition to what has already been described, there is a significant number of ALS patients without cognitive impairment, whom manifest behavioral impairments of clinical relevance or clinical sub threshold. Others maintain a good psychosocial compensation and a good quality of life even if they have a higher sensitivity to emotional stimuli compared to healthy subjects [15,16]. The literature is consistent in placing these behavioral forms in the anxious/depressive sphere and there are more and more researches that talk about possible premorbid profiles and/or morbid profiles typical for patients with ALS. The first studies published in the seventies, while not finding typical psychological profiles, had already highlighted the tendency for patients with ALS to show higher scores in some relevant clinical syndromes (hypochondria, depression, hysteria, schizophrenia). They also found out that the locus of control changes from internal to external over time that these patients use negation and emotional control to remove from their consciousness the negative effects of the disease, essentially creating a constant depressive condition, albeit with adaptive connotations [17-19]. More recently, references to breakable self have been observed, along with the tendency to avoid new situations, a marked use of strategies aimed at maintaining autonomy, as well as denial and the tendency to use emotional control to avoid awareness of suffering above all [20].

These aspects would confirm the hypothesis of an anxious/depressive...
psychological profile characteristic for these kinds of patients. However, the data seem to support the indication of a greater risk of developing depressive symptoms for these patients and caregivers compared to the healthy population [10,21,22].

To conclude, the research on cognitive decline and behavioral manifestations in patients with ALS, describes a complex interrelation between neurological and cognitive behavioral aspects, corroborated by studies on genetics. Clinical phenotype is placed in the context of anxious/depressive manifestations, with predominance of depressive aspects ingravescent and adaptive, that can take the form of actual behavioral disorders or, in the most severe cases, the expression of a psychosis associated with FTD [23-25].

The psychodiagnostics assessment has the aim to evaluate if the emotional and behavioral changes in the patients with ALS are secondary to a cognitive deficit or correspond to an increased/adaptive activation of the mental functioning of the patients, without necessarily being the expression of a deficit [26-28].

The research would be a contribution to this ongoing debate. The results, which will be described and discussed based on the state of the art and the Cognitive Systemic Post-rationalist psychological model [29,30]. This would provide a mean to lay out the best therapeutic plan and the best possible care path for the patient and his family. Moreover we would contribute to outline a psycho diagnostic profile of the patient with ALS as well as possible guidelines on treatments, especially regarding the issue of therapeutic choices.

Method

The study uses an observational method and is mainly descriptive. The study is configured as a pilot study aimed preliminary data. The subjects of the sample were recruited during the first visits and routine checks at the multidisciplinary clinic of the Nemo Clinical Center (NEuroMuscular Omnicientre). The research protocol was administered at the same time as the neurological visit with duration of about two hours. The results were collected in a database and categorized by descriptive analysis at the end of the study.

Statistical sample

The study was carried on 17 patients with ALS (10 males and 7 females, aged between 31 and 76 years of age, 4 of which harboring the C9or72 expansion, being treated at the Nemo Clinical Center department in Rome (Table 1). Patients received a confirmed diagnosis of ALS according to the El Escorial criteria [8].

To determine the phase of the disease, the motor function was evaluated in its two aspects:

1) Quantification of segmental muscle strength through the Manual Assessment Test of muscular strength and respiratory capacity (MMT) derived from the Medical Research Council (MRC) [31];

2) Quantification of the degree of disability through the ALS Functional Rating Scale-revised (ALSFRS-R) which is the currently most used tool [32-35].

Inclusion criteria for the pilot study were:

- Confirmed diagnosis;
- age ≥ 18;
- score ≥ 2 in each ALSFRS-R item;
- respiratory function characterized by a value of Forced Vital Capacity (CVF) ≥ of 80% of the theoretical;
- ≤ 2 years duration of illness from the onset of symptoms.

Materials

The Assessment includes a battery of tests for cognitive screening, possible psychopathology in progress, Personal Meaning Organization -PMO- [29,30] and a clinical psychological interview.

Cognitive screening

To assess the presence of cognitive functions deterioration, it had been applied a validated screening tools for Italian [36] and the related diagnostic criteria indicated by the current Consensus Criteria [37] for patients with ALS. These tools, shared by the scientific community, allow to confirm the diagnosis of Frontotemporal Dementia (bvFTD) or Cognitive Impairment (ALSci) and/or Behavioral Impairment (ALSbi) in patients with ALS.

The cognitive screening tools are:

1. Descriptive criteria for identifying the behavioral variant of FTD (bvFTD), which is the most common in the patient with ALS (Table 2);
2. Edinburgh Test Cognitive and Behavioral ALS Screen-Italian version [36].

It evaluates the presence vs. absence of cognitive impairment. The tests are ALS specific (3 language tests - denomination, comprehension, spelling; - 2 tests of verbal fluency; 4 tests of executive functions - inverse digit span, alternation, completion sentences-social cognition) as well as ALS-nonspecific (2 memory test-immediate and deferred recall-and 3 tests of visuospatial abilities-counting points, cubes and position numbers). If at least 2 behaviors are reported in the interview, we can give an indication for ALSBI.


Psychopathology assessment

For the personalities descriptive clinical assessment and indications on the psychopathology we used the Million Clinical Multiaxial Inventory-II test [38]. The test refers to the clinical scales present in the DSM-IV (Diagnostic and Statistical Manual of Mental Disorders) estimates the prevalence in the clinical population of each measured

<table>
<thead>
<tr>
<th>N</th>
<th>Gender</th>
<th>Age</th>
<th>Years of Education</th>
<th>Region of Onset</th>
<th>Disease Duration</th>
<th>Genetic Screening</th>
</tr>
</thead>
<tbody>
<tr>
<td>17</td>
<td>F 7</td>
<td>M 10</td>
<td>31-76</td>
<td>5 1</td>
<td>8 4</td>
<td>13 8</td>
</tr>
</tbody>
</table>

Table 1: Demographic and clinical characteristics of ALS patients. Data are expressed in absolute number or average.
dimension, using this value to establish a level of clinical significance (cut off). A BR score ≥ 60 (50th percentile) indicates the clinical attention threshold for a given trait or syndrome in a non-clinical population; BR ≥ 75 (95th percentile) indicates the prevalence and pervasiveness of the trait or syndrome in a clinical population; BR ≥ 85 indicates severe disorder or syndrome.

**Psychological profile**

For the indication of the psychological profile, finally, the theoretical background is the Cognitive Systemic Post-rationalist approach and the concepts of "Personal Meaning Organization" or PMO [29,30]. Here it is not possible to describe in detail the concept of Personal Meaning Organization (PMS) but we will try to provide a map through which read the results of this work.

It is useful clarify that with the term meaning, we mean the way in which an individual understands, that is, assigns value, evaluation, explanation, meaning to his experiences, to the world, to his relationship with it and with others, as well as how he create a personal way of seeing the reality and therefore the complementary idea of himself forming throughout all his individual development. It is also intended that this meaning is constructed, (starting perhaps from the same fetal life) based on genetic epigenesis and the biological self-regulatory tendency of living systems, which continuously express the close biological and psychological integration of the progress of all development.

Clinical, neurotic or psychotic decompensations can therefore be “re-read” as critical, problematic reorganizations that personal meaning may have encountered in the various stages of the individual life cycle, thus providing the clinician with a point of view that allows them to relocate the symptom observed in a systemic perspective [30].

The Personal Meaning Organization is built around 3 dichotomous axes (Inward/Outward; Dependency field/Independence field; Diachrony/Synchrony), each corresponding to a specific personal style in cognitive, emotional, affective and relational terms. Basing on this we can obtain four different Personal Meaning Organization” or PMO (Table 3):

| 1. Outward, Independent field, Diachronic or Obsessive type (OSS) |
| 2. Inward, Dependent field, Diachronic or Phobic type (FOB) |
| 3. Outward Organization, Dependent Field, Synchronous or Eating Disorders type (ED): |
| 4. Inward, Independent, Synchronous or Depressive Organization type (DEP) |

In order to identify the Personal Meaning Organization, this study uses an ad hoc clinical interview and compares the obtained data from two questionnaires that differ in number of items, their content and the articulation of information to identify the PMO profile.

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**Table 2: Criteria for diagnosis of bvFTD.**

<table>
<thead>
<tr>
<th>Possible bvFTD</th>
<th>Clinical, neurotic or psychotic decompensations can therefore be “re-read” as critical, problematic reorganizations that personal meaning may have encountered in the various stages of the individual life cycle, thus providing the clinician with a point of view that allows them to relocate the symptom observed in a systemic perspective [30]. The Personal Meaning Organization is built around 3 dichotomous axes (Inward/Outward; Dependency field/Independence field; Diachrony/Synchrony), each corresponding to a specific personal style in cognitive, emotional, affective and relational terms. Basing on this we can obtain four different Personal Meaning Organization” or PMO (Table 3):</th>
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</tr>
<tr>
<td>1.</td>
<td>Outward, Independent field, Diachronic or Obsessive type (OSS)</td>
</tr>
<tr>
<td>2.</td>
<td>Inward, Dependent field, Diachronic or Phobic type (FOB)</td>
</tr>
<tr>
<td>3.</td>
<td>Outward Organization, Dependent Field, Synchronous or Eating Disorders type (ED):</td>
</tr>
<tr>
<td>4.</td>
<td>Inward, Independent, Synchronous or Depressive Organization type (DEP)</td>
</tr>
</tbody>
</table>
1. Clinical interview conducted with reference to the Cognitive Systemic Post-rationalist model [29,30].

2. Personal Meaning Questionnaire-PSQ [39].

3. ESQ III questionnaire on emotional style [40].

**Statistical analysis**

The statistical analysis focuses on the description of the sample through descriptive statistics. The categorical variables were synthesized by percentages.

**Results**

**Cognitive evaluation outcome**

<table>
<thead>
<tr>
<th>Axis</th>
<th>ED</th>
<th>FOB</th>
<th>OSS</th>
<th>DEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Outward</td>
<td>Inward</td>
<td>Outward</td>
<td>Inward</td>
</tr>
<tr>
<td>2</td>
<td>Field Dependent</td>
<td>Field Dependent</td>
<td>Field Independent</td>
<td>Field Independent</td>
</tr>
<tr>
<td>3</td>
<td>Synchronic</td>
<td>Diachronic</td>
<td>Diachronic</td>
<td>Synchronic</td>
</tr>
</tbody>
</table>

Table 3: ESQ classification for PMO.

<table>
<thead>
<tr>
<th>N17</th>
<th>bvFTD</th>
<th>ALSci</th>
<th>ALSbi</th>
<th>ALSci+ALSbi</th>
</tr>
</thead>
<tbody>
<tr>
<td>C9orf72</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>5.8</td>
<td>2</td>
<td>11.76</td>
</tr>
<tr>
<td>Others</td>
<td>1</td>
<td>5.8</td>
<td>3</td>
<td>17.64</td>
</tr>
<tr>
<td>TOT</td>
<td>2</td>
<td>11.76</td>
<td>4</td>
<td>29.41</td>
</tr>
</tbody>
</table>

Table 4: ECAS results (data expressed in absolute number and percentage).

<table>
<thead>
<tr>
<th>N 1-17</th>
<th>Cognitive Assessment</th>
<th>Behavioural Assessment</th>
<th>ECAS filed subtests</th>
</tr>
</thead>
<tbody>
<tr>
<td>1(C9orf72)</td>
<td>bvFTD</td>
<td>Apathy; Careless Actions; Anger; Suspiciousness (Anger, Control)</td>
<td>Visuoperceptual and Spatial Functions</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>Diminished response to other people's needs and feelings (Anger, Control)</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>bvFTD</td>
<td>Impulsive Actions; Hyperorality; Suspiciousness (Anger, Control); Apathy</td>
<td>Executive Functions; Memory; Verbal Fluency</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>Diminished response to other people's needs and feelings (Anger, Control)</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>Diminished response to other people's needs and feelings (Anger, Control)</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td></td>
<td>Diminished response to other people's needs and feelings (Anger, Control)</td>
<td>-</td>
</tr>
<tr>
<td>8</td>
<td></td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>9</td>
<td>ALSci</td>
<td>-</td>
<td>Executive Functions; Memory; Visuoperceptual and Spatial Functions</td>
</tr>
<tr>
<td>10</td>
<td></td>
<td>-</td>
<td>Language</td>
</tr>
<tr>
<td>11(C9orf72)</td>
<td>ALSci</td>
<td>-</td>
<td>Executive Functions; Language</td>
</tr>
<tr>
<td>12</td>
<td>ALSci</td>
<td>-</td>
<td>Executive Functions;</td>
</tr>
<tr>
<td>13(C9orf72)</td>
<td></td>
<td>-</td>
<td>Visuoperceptual and Spatial Functions</td>
</tr>
<tr>
<td>14</td>
<td></td>
<td>ALSbi</td>
<td>Apathy; Diminished response to other people's needs and feelings (Anger, Control)</td>
</tr>
<tr>
<td>15(C9orf72)</td>
<td>ALSci</td>
<td>-</td>
<td>Memory; Executive Functions; Visuoperceptual and Spatial Functions</td>
</tr>
<tr>
<td>16</td>
<td>ALSbi</td>
<td>-</td>
<td>Anger; Diminished response to other people's needs and feelings (Anger, Control)</td>
</tr>
<tr>
<td>17</td>
<td>ALSbi</td>
<td>-</td>
<td>Apathy; Diminished response to other people's needs and feelings (Anger, Control)</td>
</tr>
</tbody>
</table>

Table 5: Ci (Cognitive impairment), ECAS caregiver observed behaviours (ALSbi) and ECAS filed subtests.
from the scores of the three scales with the highest BR. In our study all subjects (100%) receive BR scores ≥ 60 in 2 up to 10 scales out of the 27 total predicted by the administration protocol; 16 subjects (94%) also obtained BR scores ≥ 75 in 3 up to 6 scales and BR scores ≥ 85 in 1 up to 3 scales.

The obsessive-compulsive scale gets the highest score ever (BR up to 115) in 70.58% of the subjects (12/17). The following are: desirability (BR between 84 and 94) in 17.64 of the subjects (3/17); somatization (BR between 85 and 105) in 11.76% of subjects (2/17); anxiety (BR 88-89) in 11.76% of subjects (2/17); histrionic (BR 85-86) in 11.76% of subjects (2/17); major depression (BR 87) in 5.8% of subjects (1/17); openness (BR 85) in 5.8% of subjects (1/17).

In the BR ≥ 75 range of scores the frequency of the scales percentages are: desirability (52.94%), dysthymia (35.29%), major depression (23.52%), narcissistic, histrionic, dependent, avoidant, somatization and negativism (11.76%), obsessive compulsive, anxiety, borderline and delusional disorder (5.8%).

Overall, these data indicate that the profile of patients in our sample is characterized by control behaviors, depressive symptoms (as a whole, indeed dysthymia and major depression reach 58.54%), attention to their social image, with the presence of anxiety symptoms.

Outcome of psychological evaluation

The percentages of occurrence of Personal Meaning Organizations are shown in Figure 2. As we can see the results obtained from the PSQ and ESQ questionnaires don’t overlap, probably because they capture different aspects of the same PMO as a result of their specific personality structure. In this research we describe the results, reserving a specific treatment of the topic in a next dedicated paper. However, we report that the clinical interview confirms data obtained from the ESQ questionnaire.

The PSQ questionnaire indicates the presence of the combination of Obsessive Organization (OSS) and Phobic (FOB) in 76.47% of cases. In 11.76% of cases the OSS type results in combination with the Eating Disorders type (ED); in 5.8% of cases the Eating Disorders type (ED) is in combination with the Fobic (FOB) and Depressive (DEP) of Personal Meaning Organization.

ESQ: the OSS/FOB combination is not present. There are ED/FOB combinations in 41.17% of cases; ED/OSS in 25.59% of cases; DEP/ED in 35.29% of cases.

Discussion

We await further ECAS validation data specific to the individual tests and for a stratification of the results in terms of severity.

The psychodiagnostic Assessment follows what emerges in the literature regarding the presence of control behaviors and depressive anxiety symptoms. As it is already known [41], in fact, anxiety and sadness have as a cognitive equivalent the expectation and loss. In line with this statement and with the literature considered in this paper, our sample presents essential anxiety-depressive characteristics in a degenerative pathology such as ALS. In fact, in confronting with this disease both for the patient and for the family, the concept of loss coincide with that of definitive loss (death). The clinical interview performed according to the post-rationalist systemic cognitive model allows to better determine these aspects because it orients and directs the clinician in understanding the organization of the patient’s thought. In fact, if the patient appears apathic, undecided, directive, controlling or excessively dependent on the outward context, that does not mean that it represents a pathological pattern but that it may express the personal functioning, the search and the maintenance of one’s own organization and personal narrative consistency [42].
This information is useful for guiding the careers towards a better understanding of the patient's emotions and therefore towards a better harmony between the career and the patient's state of mind. Furthermore, it opens the possibility for a better understanding of the decision-making processes that influence the therapeutic choices and possible conflictual family dynamics.

We conclude by saying that the psychological characteristics observed in these patients do not seem to be caused by the onset of the disease but represent configurations of personal meaning stable over time. In this regard, we point out that the protocols of the psychodiagnostic tests are arranged along a continuum in correspondence with specific configurations of Personal Meaning Organizations, which deserve to be studied in the future. Finally, the absence of cognitive impairment in half of the patients leads us to reflect on the need to integrate psychological evaluation with tools that, in addition to behavior, allow us to grasp the personal meaning dimension of the patient and his relational reciprocity.

Conclusion

We used a battery of ad hoc tests able to highlight the presence of cognitive deficits, psychopathology in progress and psychological profile in a sample of 17 patients affected by ALS, obtaining a picture of the current situation of each patient.

We care to stress the fact that this research is an observational pilot study. The data described are expressed in categories and percentages of occurrence and in this moment they cannot be used for predictive purposes. However, they can serve as pilot data to direct further lines of research.

The percentages of occurrence that we have found in our sample regarding the presence of the behavioral form both of Frontotemporal Dementia (bwFTD) and Cognitive Impairment (ALSci) follow what described in literature.

The behavioral assessment (ECAS caregiver) detects about 17% of patients with behavioural disorder (ALSbi) or problematic behavior (41%). According to the reports of the caregivers, these patients seem to have a strong propensity to autonomy, trying to conquer or exercise control strategies, whether outsourced or internalized (anger vs. apathy). They also show impulsivity as behavioural disinhibition. The caregivers also point out that these behaviors did not occur with the onset of the disease but were previously present as personality traits.

The psychodiagnostic evaluation performed with the Millon test shows a high percentage of subjects with a clinically relevant disorder (41%) and a high percentage of subjects showing pervasive traits with emotional and behavioral difficulties (55%) of clinical significance. The group with a clinically relevant disorders show less flexibility and the highest scores. Based on the psychological interviews we think that these patients attempt to maintain autonomy without losing relationships and care.

The group showing pervasive traits with emotional and behavioral difficulties of modest clinical significance, the control trait is present but is not predominant. These are the diagnostic frameworks in which, whereas presenting emotional difficulties deserving of clinical attention, there is a greater flexibility that benefits the personal and relational dynamics.

The PSQ-ESQ questionnaires we have administered show different configurations, probably due to the sensitivity of the items with respect to the variables to be observed and the way in which the profile is articulated. The clinical interview confirms the ESQ questionnaire results. In 41% of cases we found the Outward, Dependent Field, Diachronic (ED/FOB) type form in which the bodily sensorial experience is perceived intensely but the definition of internal emotional state is difficult. These patients in fact constantly need to refer to the context (caregivers and carers) in order to recognize and define themselves. They also feel high sensitivity to judgment and at the same time they need to find a personal distance from caregivers and carers to recover a sense of personal effectiveness. The difficulty in understanding their intense internal states and the attempt to feel adequate can reach such high levels that often these patients seem apathic or even give the impression of not understanding what is being said. This framework, furthermore, defines patients with a marked tendency to control. They employ both a search for autonomy and a need to constantly refer to the context (involvement of the caregiver and carers). Based on this way of functioning of the personality, these patients show a difficulty to express explicit and defined decisions.

In 35% of cases we found the Inward, Independent, Diachronic (DEP/ED) type in which the so-called depressive component pushes the subjects to seek solitude, perceived as the maximum form of autonomy; whereas the PMO ED component, while on the one hand allows them to maintain minimal social contact, on the other hand can determine a state of indefiniteness that accentuates the feeling of inadequacy and inability. Overall this configuration can lead the subject into a state that oscillates between apathy and anger.

In 25% of cases we find an Outward functioning, Independent Field, Synchronic (OSS/ED). The presence of specific ED/OSS themes determines a greater risk of insight failure since the examination of reality is done with reference to the context rather than with reference to internal states.

To conclude, the PMOs emphasize the general aspects of psychological functioning and the implications in relational reciprocity rather than individual problem behaviors or behavioral disturbances. As far as the control data is concerned, our assessment confirms what has been found in the literature, since some form of control is present in every operation described, but we are also able to add information about the content of the control. Finally, anxiety and depression do not seem to characterize our sample as much as the theme of personal autonomy is.

So, it seems plausible to assume that the difficulties presented by these patients may not be entirely attributed to the disease. We also think that cognitive impairment, where present, could make the management of problematic behaviors by the patient and the caregivers more complex. Therefore, appropriate pharmacological support therapies for these patients could be used as well as psychological support for the caregiver and the patient.

References
