
Progressive Agraphia, Acalculia, and Anomia:
A Single Case Report

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Abstract

Here we report the case of a 50 year-old, right-handed female, monolingual native Spanish-speaker with a university level education. Over about two years she presented with a progressive deterioration of writing abilities, associated with acalculia and anomia. An MRI disclosed a left parietal-temporal atrophy. Two years later, a further significant cognitive decline consistent with a dementia was observed. Amnesia, executive dysfunction, and ideomotor apraxia were found. Writing was severely impaired and some difficulties in reading were also observed. Copying abilities, however, were relatively well preserved and the patient could drive around and go to different city locations without significant spatial orientation difficulties. A second MRI taken at this moment showed that brain atrophy had significantly progressed. Spontaneous writing, and writing to dictation were impossible. Reading words was preserved, but reading pseudowords was impossible. Changes in calligraphy were also noted. This case clear illustrates the progression of focal cognitive defects over time and the spreading of abnormalities to other domains.

Key words: progressive agraphia, progressive acalculia, progressive anomia.
Progressive Agraphia, Acalculia, and Anomia

Progressive deterioration of a single domain of cognitive function is unusual in Alzheimer's disease (AD). Progressive aphasia, alexia, agraphia, amusia, visuospatial disturbances, anarthria, ideomotor apraxia, dressing apraxia, and visual agnosia with initial preservation of most other cognitive functions, has been described in histopathologically verified AD and is considered among the atypical clinical variants of Alzheimer dementia (e.g., Ardila et al., 1997; Benson et al., 1988; Berthier et al., 1991; Buxbaum et al., 2000; Caselli et al., 1999; Crystal et al., 1982; De Renzi et al., 1986; Fukui, 1996; Holf et al., 1993; Infante et al., 2000; Jagust et al., 1990; Kertesz et al., 1998; Kiyosawa et al., 1989; Otsuki et al., 1997; Polk & Kertesz, 1993; Rosen et al., 2002; Ross et al., 1996; Sanchez-Garcia et al., 1998; Yamaguchi et al., 1998; Wakai et al., 1994). Primary progressive aphasia is a condition of insidious onset and gradual progression, where there is typically a slow progressive and isolated impairment in language function for at least two years before additional cognitive impairments develop (e.g., Garcia-Sanchez et al., 1998; Graff-Radford et al., 1990; Hodges et al., 1992; Karbe et al., 1993; Kertesz et al., 1998; Kertesz & Munoz, 2002; Knott et al., 2000; Mesulam, 1982, 2001; Papagno & Capitani, 2001; Parkin et al., 1993; San Pedro et al., 2000; Snowden et al., 1992).

Alexia is often mentioned in many of cases of progressive aphasia and progressive posterior cortical dementia (e.g., Ardila et al., 1997; Chiacchio et al., 1993; Freeman et al., 1991). Several of these reports refer also to agraphia (e.g., Berthier et al., 1991; Benson et al., 1988; Grossman et al., 2001; Mendez et al., 1990; Kiyosawa et al., 1989). However, the severity of
these manifestations and the level of documentation and assessment are widely variable, and the type of alexia and agraphia are usually not specified or documented in sufficient detail. Furthermore, there is a wide range of individual variability in deficits encountered. Ardila et al. (1997) described a 65-year-old woman with progressive visuospatial dysfunctions associated with alexia and agraphia. MRI revealed cerebrocortical atrophy, which was especially more severe in both parieto-occipital regions. Alexia was significantly more severe than agraphia, fitting the pattern of a letter-by-letter reading alexia. Both lexical and spatial agraphia were also evident. The patient’s ability to write deteriorated as the orthographic ambiguity of the target word increased, and tendency to regularization in writing was observed (lexical agraphia). Misuse of spaces, iterations of strokes and letters, slanting of the lines, and underuse of the left side of the paper were also observed (spatial agraphia). Grossman et al. (2001) described a patient who presented with writing difficulty that deteriorated over time. While her graphemes were typically legible, her writing was extremely slow, and her letters were written in an inconsistent and heterogeneous manner. She also produced allographic and spelling errors (mainly omissions and perseverations) in her writing. Using a positron emission tomography scan superior parietal occipital and superior frontal defects more evident at the left were demonstrated. The authors proposed that the patient was presenting a deficit retrieving physical letter forms as manifested by her heterogeneous and slow production of letter forms.

Here we report a patient with a progressive loss of writing skills, associated with acalculia and anomia. MRI scans showed a focal left frontal-parietal temporal atrophy. Two different evaluations were performed, the first one in August 1999, and the second in July 2001. In the first evaluation the memory difficulties were mild, whereas in the second memory difficulties
were significant. Acalculia, agraphia, and anomia were also severe.

Case Presentation

**Background.** Fifty year-old, right-handed female (ARA), monolingual native Spanish-speaker with a university level education. Not any familiar history of neurological or psychiatric illness in two generations is found. ARA had 2 sisters and 3 brothers, all of them grew up until adults, they are all married, and they have a successful life without any evident cognitive deterioration. She is married and has two healthy boys of 25 and 17 years old. ARA worked as a successful psychologist in a government educational institute in Mexico. In her job she frequently had to write and lecture. About two years before the first evaluation, ARA noted difficulties in correctly writing the words and using Spanish orthography. She mentions that had to think hard how to write the words. ARA frequently had to write down the words several times, and correct them after seeing them. In her job also had to manage a budget, and noted errors in performing calculations. She had to ask somebody else to review the accounts and repeat the arithmetical operations. In addition, she began to present some word-finding difficulties that prevented her from lecturing. Due to these difficulties, ARA left her job one year before the first evaluation, and began to help in her brother’s business. According to her family, difficulties became significant from about one and half years before the first evaluation. Her family mentions difficulties in using numbers, handling money, word finding, and maintaining the topic while she was speaking. They reported that arithmetical errors were frequent but mild; i.e., that she usually got a result that was close to the correct answer. Her family also emphasized her writing disturbances, making it difficult for her to perform her daily working duties in her brother’s
business. At this time, ARA consulted a neurologist. The neurological exam was normal. MRI scans taken in June 1999 showed a left parietal-temporal atrophy (Figure 1). She was referred for neuropsychological testing.

**INSERT FIGURE 1 ABOUT HERE**

**First evaluation**

During the first evaluation performed in June 1999 the patient was fully oriented. Spontaneous language was nearly normal. Speech articulation, speed, and voice volume were normal. Fluency, phonology, grammar, and sentence length were normal during conversational speech. Mild word-find difficulties resulted in occasional semantic paraphasias and circumlocutions, however, were noted. Verbal IQ (Wechsler, 1981) was 86, Performance IQ was 103, and Full Scale IQ was 93 (Table 1). Total score in the Neuropsi –Brief Neuropsychological Test Battery for Spanish Speakers (Ostrosky et al., 1997, 1999) was 91 (mildly abnormal for her age and education). Decreased scores were observed in successively subtracting 3’s from 20, naming, phonological verbal fluency, semantic verbal fluency, writing, arithmetical problems solving, categories recall, language comprehension, sequences, changing right-hand position, and opposite reactions subtests. Verbal and nonverbal memory -recall condition, were borderline. Language repetition, reading, verbal memory –coding, copying a semi-complex figure, similarities, digits backwards, visual detection, words recognition, changing left-hand position and hands alternating movements tasks were within the normal range for her age and educational level. Scores on the Wechsler Memory Scale were within the normal range. Score on a Spanish naming test (Gardner, 1987) containing 80 items was 42 (abnormal). She recognized right and left in her body and the examiner’s body. Errors were noted in naming and pointing to fingers.
ARA recognized without any evident difficulty the faces of her relatives, friends, and the people around her.

**INSERT TABLE 1 ABOUT HERE**

A good calligraphy was observed in writing. Spatial distribution was appropriate and no spatial neglect was noted. Three different writing tasks were used: (1) Spontaneous writing: to report her history in writing (Figure 2), (2) Copying: to copy a 44 word story, and (3) Dictation: a short text (28 words), 8 words, and 10 pseudowords. For reporting her history, she used 130 words. The report contained 20 corrections. Orthographic errors were abundant (e.g., cercanas -> sercanas). Letter omissions and additions were noted (e.g., ortografia -> hortogafia). Non homophone errors were also observed (e.g., máquina -> magina). In writing words under dictation similar errors were found. In copying a text, one word from 44 was incorrectly written and the patient wrote an extra word. No reading errors were observed in reading the 109-word story included in the Neuropsi, however. Reading understanding was normal; she correctly answered all the Neuropsi reading understanding questions.

**INSERT FIGURE 2 ABOUT HERE**

Calculation abilities were abnormal. Defects were observed in basic arithmetical operations, both written and oral. Reading numbers was correct up to three-digit numbers. Writing single digits to dictation was correct, but writing two-digit numbers was abnormal (e.g., 45->25). She could not make four-digit comparisons (e.g., What four-digit number is bigger in an 8 numbers series; example, 2541-1859). In addition to the calculation subtest included in the Neuropsi, and the WAIS–Arithmetic subtest, the WRAT (Jaskat & Wilkinson, 1984) was administered. Her score of 7/ 40 is regarded as frankly abnormal. She was unable to add three
two-digit numbers. She could not use the multiplication tables. To the question “3 x 4” she answered 18. She confused arithmetical signs (e.g., 6/2=12, 33-17=50), she was unable to use fractions.

Over the following two years, the patient was attending a cognitive rehabilitation program. She continued helping in her brother’s business. She continued driving and no spatial or topographical difficulties were noted. In the rehabilitation program, special emphasis was placed on calculation abilities, writing, and language.

Second evaluation

In July/2001 a further neuropsychological evaluation was conducted (see Table 1). The patient was alert, oriented, and cooperative, with fluent speech. Attention level was normal. No articulation defects, apraxia of speech, or agrammatism were observed. However, a significant decrease in most test scores was found. Neuropsi scores in word recognition, language repetition, similarities, left-hand position and alternating movements with both hands subtests remained within the normal range. All the WAIS subtest scores were over one standard deviation below the expected score. Total score in the Neuropsi Neuropsychological Test Battery score was 79/130 (severely abnormal). Interesting to note, her spontaneous recall of the Semi-Complex Figure corresponds to the normal range but her score in the WMS Visual Reproduction subtest was 5/14. Some non verbal memory defects, in consequence, were observed. Using verbal information (words), her spontaneous recall was abnormal (1/6 words) but her recognition was normal (6/6). In consequence, no defects in encoding were observed but problems in retrieving verbal information can be assumed. Score on the WRAT was again 7/40. She could add and
subtract simple quantities, likely because this ability was intensively trained during the rehabilitation program, but any other arithmetical operation was impossible. Ideomotor apraxia was tested asking ARA, (1) to mimic different movements by oral command or by copying the examiner’s movements (7 items): to throw a ball, to ‘say goodbye’ with the hand, to ‘say come here’ with a hand, to brush her teeth, and comb her hair; (2) to imitate non sense movements presented by the examiner (4 items): to make “horns” with the fingers, to show the fist, to make a circle with the thumb and the index, and to make a “bunny” with the fingers, and (3) to perform buccofacial movements (4 tasks): to whistle, to inflate the cheeks, to blow, and to show the teeth. Performance in this test was frankly abnormal (see Table 1) indicating an evident ideomotor apraxia. ARA, however, continued to recognize without difficulty the faces of her relatives, friends, and people around her.

In spontaneous writing (describing her disease) she could report aloud what supposedly she was writing, but no word was recognizable (see Figure 2). Letters were well formed and could be easily recognized but calligraphy had changed in contrast with the first assessment. During the first evaluation, she used her normal cursive writing, whereas during this second evaluation she wrote using uppercase block letters. No clear relationship between the length of the spoken and written to dictation word was evident. Writing words and writing text to dictation had similar characteristics. The patient could report what she was going to write, letters were relatively well-formed but no word could be recognized. A few self-corrections were noted. Nonetheless, seemingly there was some tendency to alternate consonants and vowels, as most frequently observed in Spanish. Copying, however, was virtually perfect (Figure 3).

INSERT FIGURE 3 ABOUT HERE
Writing to dictation was tested using exactly the same procedure developed in the first evaluation. Initially a short text (28 words) was dictated (Figure 4). Even though the patient repeated what she was going to write, just a weak relationship between what she repeated and what she wrote was observed. For example, the first sentence was “La mañana era fría” (“the morning was cold”) and the patient wrote LA EINC EL FIEA (non-sense). Only the first word, the feminine article LA was correctly written. The patient’s writing contained 24 letter groups that may be supposed correspond to words.

Writing words and pseudowords to dictation was defective. She could write 2 out of 12 words and no pseudowords. The correctly written words contained only two or three letters (ir – to go, and sol - sun). On longer words, she failed. However, reading was easier and only one error in reading words and 10 errors in reading pseudowords was recorded. Lexicalization (reading pseudowords as real words; e.g., bosa – pseudoword as bolsa – bag) was observed in 7 items (Table 2). She presented, however, 17 errors when reading the short 109-word story history included in the Neuropsi neuropsychological test battery.

A new MRI demonstrated that the brain atrophy had significantly extended, and was not anymore limited to the left parietal-temporal area (Figure 5)

Discussion

Cognitive decline in our patient began with, (1) difficulties in using Spanish orthography, and (2)
errors in performing arithmetical operations. Interestingly, her family points out that her arithmetical errors were frequent but mild, and she usually got a result that was close to the correct answer. This type of approximative responses when solving arithmetical tasks is not unusual in cases of acalculia (Ardila & Rosselli, 2002). Some word finding difficulties were also recorded.

At the time of the first evaluation, arithmetical abilities were at a frankly abnormal level. Verbal fluency and lexical knowledge (according to the WAIS Vocabulary subtest and the Naming Test) were also decreased. Nonetheless, writing difficulties were almost limited to orthography in spontaneous writing. Calligraphy was appropriate and written copying and to dictation were nearly normal.

It is intriguing the strong association found between orthography and calculation ability. Our case would support the hypothesis that both share a common brain organization. It may be conjectured that both depend upon some spatial representation mediated through language. As a matter of fact, ARA was initially presenting an incomplete Gerstmann’s syndrome (acalculia, agraphia, and finger agnosia, but no right-left discrimination defects). Gerstmann’s syndrome has been some times interpreted as a defect in performing mental rotations and conceptualize the space through the language (Ardila et al. 2000; Gold et al., 1995). Some authors have proposed that Spanish orthography is -in a significant extent, a spatial ability (Ardila et al., 1996).

Two years later (i.e., about four years after the start of her symptomatology), the patient had a significant cognitive decline. Her mainly verbal but also non verbal abilities, had significantly decreased. Her memory scores corresponded to a pathological range. Her Full Scale IQ had decreased 26 points, with a similar decline in both the verbal and performance scales.
During the initial evaluation, her Full Scale IQ corresponded to a normal performance, whereas during the second evaluation it was found to be over two standard deviation below the mean. At this time, the patient clearly fulfilled the diagnostic criteria for dementia, according to the DSM-IV (APA 1994). However, she continued driving and going by herself to different places without any apparent difficulty. Her copying abilities were well preserved. She could copy figures and words without any significant difficulty. In consequence, even though she was technically demented, there was not a global cognitive deterioration yet, but multi-function impairments.

Her calculation abilities decreased between the first and the second evaluation, but as a matter of fact, in the first evaluation these abilities were already so seriously impaired that no significant further score decrease could be anticipated. Scaled score in the WAIS Arithmetic subtest was initially 4 (two standard deviations below the mean), and hence, no major decrease was possible. Digits was initially eight (first evaluation) and later four (second evaluation). Total digit forwards score was 6 in the first evaluation and 3 in the second evaluation. Total digit backwards scores were 5 (first evaluation) and 2 (second evaluation). She obtained a similarly abnormal score in both WRAT administrations. It should be taken into account that between the first and second evaluation, she was attending a cognitive rehabilitation program twice a week. Rehabilitation had a special emphasis on arithmetical abilities retraining. It can be conjectured that without this rehabilitation program, difficulties in arithmetical abilities may have been even more severe in the second evaluation.

Cognitive deterioration progressed significantly between the two evaluations. According to the Naming Test and the WAIS Vocabulary subtest, anomia was evident during the first evaluation and even more severe during the second one. Thus, since the initial evaluation an
anomic aphasia was evident. During the second evaluation concept-formation difficulties, ideomotor apraxia, right-left disorientation, and finger agnosia were also observed. Memory abilities during the second evaluation corresponded to an abnormal range.

Interestingly, her copying ability remained relatively well preserved, and no evident spatial or topographical orientation difficulties were found. The patient continued driving and going around the city without any significant difficulty. She correctly recognized places and people, and in consequence, no topographical agnosia or prosopagnosia were seen. A significant dissociation between some verbal and some non-verbal abilities was quite evident.

As a matter of fact, several important dissociations were observed in the second evaluation. They included, (1) dissociation between her reading and writing ability; (2) dissociation between her spontaneous writing and writing by copy. (3) Dissociation between her ability to read words and pseudowords. (4) Dissociation between her ability to repeat and to write. And most significant, (5) dissociation between verbal and spatial abilities. Some dissociation between her ability to write letters and her ability to write words was also found: word writing was notoriously more difficult than letter writing. During the second evaluation, she could write by dictation only two out of 12 words (the shortest ones, *ir* and *sol*), but she correctly wrote two (D and Z) out of six letters (D, J, L, V, and Z). When writing the alphabet, she wrote A, B, C, H, E, D, I, G, J, L, M, N, Ñ, O, P, S, Y, T, Z.

It is interesting to note that using Spanish orthography was the initial writing difficulty noted in ARA. The correct use of orthography (i.e., selecting between two or more homophone alternatives) represents for normal people the most difficult aspect in writing Spanish, and it is not surprising to find it was the most fragile writing ability. Further evolution (first evaluation)
demonstrated not only orthographic (homophone) errors, but also letter omissions and additions, and even non homophone errors. Noteworthy, regardless of her inability to write spontaneously or by dictation noted during the second evaluation, her writing by copy was virtually perfect. It can be conjectured that writing by copy does not really represent a linguistic ability but rather visuoperceptual and visuoconstructive ability.

Whereas in the second evaluation the patient clearly presented the major syndromes usually found associated with left hemisphere pathology (such as aphasia, alexia, agraphia, acalculia, and ideomotor apraxia), no major defects usually observed in cases of right hemisphere damage were evident (such as general spatial disturbances, prosopagnosia, and topographical agnosia). Nonetheless, some decline in visuoconstructive abilities was documented between the first and the second evaluation. Semi-Complex Figure copy score decreased in about 20% (12/12 and 9.5/12), Block Design score decreased in over one standard deviation (SS=9 and 4), and Picture Arrangement score decreased in one standard deviation (SS=9 and 6). This observation may support the hypothesis that in cases of progressive cognitive syndromes, brain dysfunction extends from a focus to surrounding areas, eventually involving the whole brain and resulting in a global cognitive deterioration. During the second testing, our patient presented with significantly severe defects in some cognitive domains, whereas other domains were relatively well preserved. It may be assumed that in a future, brain atrophy will become even more extended, and cognitive deterioration more severe, though some nonverbal abilities will be the last in becoming disturbed.

Reading and writing difficulties observed in ARA have some similarities with other cases of progressive deterioration of specific cognitive functions previously reported. Writing
difficulties in Ardila et al. (1997) English speaking patient partially corresponded to a lexical agraphia, even though alexia was significantly more severe than agraphia. The inability to correctly use orthographic rules in Spanish writing has been interpreted as a lexical agraphia (Ardila et al., 1996) and in consequence, the initial writing disturbance in ARA can be interpreted as a lexical agraphia. Further, a severe agraphia was found, even though the ability to write individual letters was better preserved. As a matter of fact, regardless of the severity of the agraphia found in the second evaluation, letters were in general clearly recognizable. In Grossman et al. (2001) case it is also pointed out that graphemes were typically legible, though letters were written in an inconsistent and heterogeneous manner. We did not note any inconsistency in writing the letters regardless of the task (spontaneous, coy, dictation), but in the second evaluation it was evident that the handwriting had dramatically changed. During the first evaluation while an evident writing defect (lexical agraphia) was documented, not changes in handwriting were noted. Changes in handwriting from cursive to block letters -as observed in ARA, have been reported in cases of right hemisphere pathology (Ardila & Rosselli, 1993). It can be conjectured that the dramatic change in handwriting observed during the second evaluation might be associated with some extension of the brain pathology to the right hemisphere. This hypothesis is congruent with the moderate deterioration of some non verbal abilities found in the second evaluation.

This case clearly illustrates the progression of focal cognitive defects over time and the spreading of abnormalities to other domains. Progressive focal neuropsychological syndromes can represent an excellent model for the study of brain organization of cognition.
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Table 1. Results obtained in the first and second neuropsychological testing

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<th>Test</th>
<th>First Evaluation</th>
<th>Second Evaluation</th>
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<td>June 1999</td>
<td>July 2001</td>
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<tr>
<td><strong>Neuropsi:</strong> Total score</td>
<td>91/130</td>
<td>80/130</td>
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<tr>
<td>Semi-Complex Figure: Copy</td>
<td>12/12</td>
<td>9.5/12</td>
</tr>
<tr>
<td>Semi-Complex Figure: Memory</td>
<td>9.5/12</td>
<td>7.5/12</td>
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<tr>
<td>Verbal Fluency: Phonologic (letter F)</td>
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<td>0</td>
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<tr>
<td>Verbal Fluency: Semantic (animals)</td>
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<td>9</td>
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<td>Repetition</td>
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<td>4/4</td>
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<td><strong>WAIS:</strong> Information</td>
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<td>5</td>
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<tr>
<td>Comprehension</td>
<td>12</td>
<td>4</td>
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<tr>
<td>Arithmetic</td>
<td>4</td>
<td>3</td>
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<tr>
<td>Digits</td>
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<td>Digits forward natural score</td>
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<tr>
<td>Digits backwards natural score</td>
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<td>Digit-Symbol</td>
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<tr>
<td>Picture Completion</td>
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<td>Block Design</td>
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<td>Associative Learning</td>
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<td>Visual Reproduction</td>
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<tr>
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<td>Naming test</td>
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<td>WRAT</td>
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<td>Ideomotor praxis Right hand</td>
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<tr>
<td>Left hand</td>
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Mouth 1/4
Right-left discrimination correct 2/10
Fingers naming abnormal 2/5
pointing abnormal 3/5

Note. Scores in the Neuropsi (excepting verbal fluency, referring to the total number of elements in that category) are “patient score/total score”. Scores in the WAIS (excepting “natural scores” in digits) are scaled scores. Scores in the Wechsler Memory Scale are “patient score/total score”. Scoring in the Wisconsin Card Sorting Test is according to the Manual. For the rest of the tests, scores are “patient score/total score”.

Table 2. Words and pseudowords reading and writing (second evaluation). The words and pseudowords that were used are presented in the first and fourth columns. In the following two columns toward the right it is presented what the patient wrote and read.

<table>
<thead>
<tr>
<th>WORDS</th>
<th>Writing to dictation</th>
<th>Reading</th>
<th>PSEUDOWORDS</th>
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<td>Correct</td>
<td>Pal</td>
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<td>NISO</td>
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<td>Turiposa</td>
<td>SIROM</td>
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<td>OSAONA</td>
<td>Estacionar</td>
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LEGENDS TO FIGURES

Figure 1. First MRI (June 1999)

Figure 2. Spontaneous writing, first (A) and second (B) evaluation. Written description of her condition.

Figure 3. Copying during the first (A) and second (B) evaluations.

Figure 4. Writing by dictation during the first (A) and second (B) evaluations.

Figure 5. Second MRI (July 2001)
Figure 1.
Figure 5.
Figure 2.

Hace más de 5 años empieza con las dificultades de equilibrar, como era de mal hacer, y cada vez que me equilibro, se me sigue pasando. A mi nieto, a mi sobrino, a mi sobrina, a mis abuelos. ¿Cómo me decía que tenía que entregar documentación de todo mi ser en forma legal y, ¿que generalmente soy responsable de mi trabajo, me hago de entregar documentación que es importante para la directora, pero a otros con estos dilatados, lo que me ocupa es el no poder equilibrar, como antes, la manera de equilibrar, todos esos dilatados, lo que me ocupa es el no poder hacerlo, como antes, para poder equilibrar algo, lo que me ocupa es el no poder equilibrar, como antes, la manera de equilibrar.
La Gallina de los huevos de oro.

Un hombre tenía una gallina que ponía huevos de oro. Deseando obtener más oro sin necesidad de estar esperándolo mató a la gallina, pero no encontró nada adentro de ella, ya que era como cualquier otra gallina.

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La mañana está fría, el algunos pasan en el patio, una leve bruma se levantaba del río y tapaba la vista de la carretera. Tejidos de los eucaliptos.

A

B

La fiebre, el frio, el crato, la IRA.
Ríon el rinatir roro, i tara la ista rto.
Rora el tós eicultos.