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CITALOPRAM, DEPRESSION AND PSEUDO DEMENTIA

A NEUROPSYCHOLOGICAL CASE STUDY

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SUMMARY - The author presents a case of (depressive) pseudo dementia, commenting on the clinical and neuropsychological findings before and after the use of citalopram, a serotoninergic anti depressive drug. The case portrays the current criticism about the old dichotomy between non-reversible ("functional") and reversible ("organic") dementia. The 73 year old woman initially diagnosed as pseudo demented showed some mild cognitive deterioration in neuropsychological evaluation after the improvement of her depressive symptoms. Some reasons for the divergent findings on pseudo dementia prognosis in the literature are proposed.

KEY-WORDS: depression, dementia, pseudo dementia, citalopram.

Citalopram, depressão e pseudodemência: um estudo neuropsicológico de caso.

RESUMO: O autor apresenta um caso de pseudodemência depressiva, tecendo comentários sobre os achados clínicos e neuropsicológicos antes e depois do uso de citalopram, um agente serotoninérgico. O caso apresentado ilustra as críticas atuais acerca da antiga dicotomia entre demências reversíveis ("funcionais") e não-reversíveis ("orgânicas"). A paciente de 73 anos inicialmente diagnosticada como pseudodemente demonstrou algum grau de deterioração cognitiva em testes neuropsicológicos após a melhora dos sintomas depressivos. São sugeridas algumas razões para os achados divergentes com relação ao prognóstico da pseudodemência encontrados na literatura.

PALAVRAS-CHAVE: depressão, demência, pseudodemência, citalopram.

Since the mid-nineteenth century, medicine has estabilished a dichotomy between the "reversible", "functional" or "non-organic" dementia on one side and the "irreversible", "structural" or "organic" on the other side. The term "pseudo dementia", has been widely used in the literature, comprising a broad class of disorders which historically includes not only depressive dementia but also schizophrenia, Ganser syndrome, delirium, normal-pressure hydrocephalus, deafness and much more[2]. The pseudo dementia clinical picture can be present in a number of psychiatric disorders, of which depression is by far the most common. Nowadays the term is commonly used to refer to patients with a depressive syndrome mimicking dementia but for whom this last diagnosis is abandoned because of the course of the illness. Some authors employ the terms depressive and non-depressive pseudo dementia[11].

This dichotomy has been based upon the presumption that the cognitive impairment seen in pseudo dementia, although having the appearance of organic deterioration, could remit with proper

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treatment, unlike the "true" degenerative dementia. In the case of depressive pseudo dementia, this clear-cut differentiation became increasingly criticized in the last decades. Many authors suggest that there is a continuum between depression and dementia, because many patients who initially respond favorably to antidepressant treatment do not demonstrate complete or permanent improvement on more lengthy follow-ups[4,6,12]. Many patients initially diagnosed as "pseudo demented" became truly demented few years later[2,8].

Although depression is usually associated with varying degrees of cognitive impairment, depressive patients with prominent cognitive impairment dominating the clinical picture, represent one of the very frequent diagnostic problems in clinical practice. As Emery and Oxman[2] state: *"The major issue is whether and how depressive illness itself causes the cognitive impairment or whether some form of degenerative brain disorder is present"*. This issue is a major problem for the physician, since depression commonly causes cognitive impairment, specially in those over 40 years old[1] and the prevalence rates of depression in primary degenerative dementia may range up to 50%, according to different series[3,10]. DSM-III R (American Psychiatric Association, 1987), in its criteria for dementia, had an exclusionary criterion of *"cannot be accounted for by any non organic mental disorder,e.g., major depression accounting for cognitive impairment"*, a statement that seems useless in face of current knowledge about dementia, depression and depressive pseudo dementia. On the other hand, DSM-IV (American Psychiatric Association, 1994) has an exclusionary criterion of *"the disturbance is not better accounted for by another axis I disorder (e.g., major depressive disorder...)"*. Although the authors of DSM-IV dropped the term "organic" from it, indicating there is no clear distinction between "functional" and "organic" disorders, they suggest (in the case of dementia) that the physician should distinguish between the cognitive impairment caused by depression from that caused by brain injury. If major depression is present, DSM-IV indicates that a second diagnosis is not given, and merely considers this case a "subtype" of dementia.

Reifler and Sherrill[9] introduced the expression "*excess disability*" (dementia symptoms worsened by depressive symptoms) in the literature providing a rationale for more aggressive treatment for the disability caused by the depressive syndrome and helping lower unrealistic expectations based on the old stereotypical concept of reversibility of pseudo dementia.

This case portrays the issues mentioned above and remarks two important considerations when treating patients with depressive pseudo dementia :

1. Cognitive function must always be evaluated through neuropsychological examination in patients suspected of dementia. It is noteworthy that although the NINCS-ADRS criteria clearly states that, many still rely on tomographic studies or bedside evaluations, like the Mini-Mental Status Examination which are often normal in the initial stages.

2. The drugs used for the treatment of depression should not impair cognitive function.

In the present case, we performed a neuropsychological examination (parts of which are shown below) before and after the treatment for depression.

CASE REPORT

MS is a 73 year-old white woman who was referred to the PIN (Projeto Integrado de Neuropsicologia da UFRJ) for neuropsychological assessment in November-1994. She came to consultation with her daughter, who provided some of the information. She had prominent memory complaints: she forgets appointments, loses personal objects (keys, purse, etc.) and is unable to recall a phone conversation shortly after she had hung up. She has became more repetitive (saying several times the same thing as if it were the first time) and has been referring more to the past than to the present. She is unable to recall a recent event, even a very important one (one of her daughter's birthday party a few days before, for example). She had already lost her way back home more than once. She also had a tendency to report events that have never happen, as if they were absolutely true (confabulation) and became angry when her relatives made any comments on it.

The symptoms had an insidious beginning about 3 years ago and had become more evident in the last 6 months. She was also obviously depressed: she cried very often, had severe insomnia with late awakening, felt

herself hopeless and helpless, reported vague suicide thoughts, was extremely pessimistic and reported diurnal variation (feeling worse in the morning). She obtained a score of 26 in the Hamilton Depressive Scale. She already had 3 previous depressive episodes (first at age 34) and always received medical attention for them. No manic symptoms were reported. No prophylactic treatment was ever suggested. None of the previous episodes presented prominent memory problems.

She was under treatment for hypothyroidism. No other diseases were reported in her past medical history. There were no history of depressive disorders or dementing disorders in the family.

Her physical examination was normal. There were no signs of thyroid dysfunction. The following laboratory exams were normal: blood count, T3, T4 and TSH, seric folate, seric iron, seric B12, creatinine, glucose, VDRL, sodium, calcium, potassium, hepatic enzymes and urine analysis. A CT scan revealed a very mild atrophy but it was considered normal for her age.

She was given citalopram 20 mg BID and this drug was elected for the following reasons :

- it has a better profile of side effects (compared to tricyclics) which may be specially prominent in the elderly, e.g., it does not promote orthostatic hypotension. This is particularly important in the old age because orthostatic hypotension may impair an already impaired mental functioning.
- it is devoid of anticholinergic effects which may impair to a significant degree cognitive functions, like speed of processing, attention and memory.
- it is easier to administer, compared to tricyclics or MAOI. This aspect is particularly important when treating dysmnesic or demented patients.
- although it is not available in Brazil yet, it has already been extensively and safely used in older patients in Europe.

FIRST NEUROPSYCHOLOGICAL EXAMINATION

Orientation: MS could not say the day and she answered September (instead of the correct answer, November) when asked about the month. She also could not say the day of the week, but she was able to say the place, the city and state.

Attention:

- Digit Span Forward (WAIS-R): normal
- Digit Span Backwards (WAIS-R): normal
- Word Span (Rey Auditory Verbal Learning Test): normal
- Alphabet, regressive counting and successive additions of 3 (Mental Control, WMS-R): normal
- Visual Memory Span (WMS-R): normal

Memory :

- Short-Term Verbal Memory: MS could not recall most of a long paragraph immediately after it was read aloud by the examiner (Logical Memory, WMS-R). She recalled only a few isolated facts about the story.
- Short-Term Visual Memory: MS could recall many parts of 4 different drawings that were displayed to her, one at a time, for 10 seconds, obtaining a normal score for her age (Visual Reproduction, WMS-R).
- Long-Term Verbal Memory (30 minutes): MS could not remember anything from her first recall of the paragraph.
- Long-Term Visual Memory (30 minutes): MS could not remember anything from the first presentation

The scores are presented below:

	Raw Score	Percentile
Logical Memory I	8	5%
Logical Memory II	0	2%
Visual Reproduction	20	24%
Visual Reproduction II	0	4%

It was not possible to calculate the MQ (memory quotient) because of the important impairment seen on several subtests.

• Verbal Learning

MS could not normally learn a list of six paired words (Verbal Paired Associates, WMS-R) after successive presentations by the examiner. She could remember the "easy" pairs (metal-iron) that had some logical link more often than the "hard" pairs (school-grocery). This result is typical of dysmnesia.

MS was able to learn most of a list of 12 words (List Acquisition, Memory Assessment Scale) along six successive presentations. She had low *span* of 4 words, but she was able to increase the numbers of words recalled along the six repetitions of the list by the examiner. The list contains words of four different categories (birds, colors, cities and countries) and MS gave evidence of using list clustering to help the remembering (normal performance for her age).

List	I	II	III	IV	V	VI
12	4	6	6	6	7	11
groups	2	1	0	2	1	3

List: initial presentation of 12 words. I to VI: numbers of words recalled, immediately after successive repetitions of the list read aloud by the examiner. Groups: number of logical groups (words grouped by category: colors, countries, birds and cities)

• Recognition: MS could recognize all the 12 words from the list after 30 minutes.

• Remote Memory: MS could say her birthday but was unable to say nor any of her daughters' birthdays neither the date of her marriage

Language Functions: All expressive and receptive functions were normal when examined through the Multilingual Aphasia Examination (MAE) Battery.

Abstraction: Normal performance on the Similarities test (WAIS-R)

Visual Gnosis, Visual-Spatial and Visual-Constructional Abilities: Normal performance on the Facial Recognition Test (Benton) and the Visual Discrimination Test (Benton).
Performance discretely below average on the Picture Completion, Picture Arrangement and Object Assembly tests (WAIS-R). Normal performance on the Block Design test (WAIS-R).

Visual-Motor Dexterity: Impaired performance on the Digit-Symbol test (WAIS-R)

The first neuropsychological examination revealed a moderate to severe dysmnesic disorder without impairment of other higher mental functions, such as abstraction or language. Attention was normal. Although MS could not learn a list of paired words after 3 repetitions, she was able to learn 11 out of 12 words of a list in a different occasion (a couple of days later). Also, MS was able to recognize the whole test list when presented to a multiple choice list after some time, a finding that indicates preserved retention. The marked difficulty in remembering the verbal and visual items of the WMS-R supported some of her memory complaints in daily life. However, this results could be due to an impaired recall, since retention seemed preserved.

The preliminary diagnosis at that time was pseudo dementia and the patient was then initiated on citalopram.

She was seen on the 15th, 30th, 60th and 90th days after the beginning of treatment. On her third visit (day 30), she reported feeling less depressed. Her insomnia got better and she did not cry anymore. However, a slight diurnal variation was still present, as well as some mild symptoms of anxiety and restlessness. Her score on Hamilton Depression Scale was now 12, suggesting that some depressive symptoms were still present (it should be noted that this scale may not be suitable when using serotoninergic drugs). She still complained of memory problems but did not put much emphasis on them.

On her last visit (day 90) the clinical impression was that depressive symptoms improved in a significant way from the index visit, but still had a mild to moderate dysmnesic disorder. She did not report any depressive symptoms and spontaneously declared that she got better. When asked about her memory problems (she did not give any spontaneous report) she said "*it still needed some help*".

SECOND NEUROPSYCHOLOGICAL EXAMINATION (last visit, 3 months after beginning of treatment)

Attention:

- Digit Span Forward (WAIS-R): normal
- Digit Span Backwards (WAIS-R): normal
- Word Span (Rey Auditory Verbal Learning Test): normal
- Alphabet, regressive counting and successive additions of 3 (WMS-R): normal
- Visual Memory Span (WMS-R): normal

Memory :

- Short-Term Verbal Memory: MS could not recall most of a long paragraph immediately after it was read aloud by the examiner (Logical Memory, WMS-R).
- Short-Term Visual Memory: MS could recall part of 4 different drawings that were displayed to her, one at a time, for 10 seconds, obtaining a normal score for her age (Visual Reproduction, WMS-R)
- Long-Term Verbal Memory (30 minutes): MS recalled only a little amount of information (very few isolated facts about the original story)
- Long-Term Visual Memory (30 minutes): MS did not recall anything from the first presentation.

The scores are presented below:

	Raw Score	Percentile
Logical Memory I	8	5%
Logical Memory II	2	6%
Visual Reproduction	22	42%
Visual Reproduction II	0	4%

- Remote Memory: MS was now able to state the date of her marriage and the birthday of all her sons.
- Verbal Learning: MS was able to learn a list of six paired words after 3 repetitions of the same list by the examiner (Verbal Paired Associates, WMS-R).

This time we used the Rey Auditory Verbal Learning Test, very similar to the List Acquisition (MAS), notwithstanding this list has 15 words (instead of 12) and there are no logical groups (which usually improves the performance, specially in depressed patients). Before the free recall of the list, a second list is used as a distracter. The results are presented below :

List	I	II	III	IV	V	Recall
15	6	8	8	9	7	7

These results were considered below expected for her age[5].

MS seemed to improve a little on formal testing of her memory. However, it was clear that a significant dysmnesic disorder persisted besides the remission of the depressive symptoms. It was noteworthy that she did not emphasize her memory problems as before, even when asked directly. The impairment first seen on her remote memory had remitted.

COMMENTS AND CONCLUSION

The dichotomy "reversible" versus "irreversible" dementia cannot be supported in clinical practice in many instances. Depressive pseudo dementia is very often associated with irreversible symptoms; this case is portrayed as a typical example. The initial diagnosis of depressive pseudo dementia seemed adequate because of her clinical picture and the results of the first neuropsychological evaluation.

The following table plots some of her symptoms in two different sets as suggested by Wells[12] according to a presumed depressive or dementing nature.

a) History and evolution:

	Pseudo Dementia	Dementia
Onset	Dated with some precision	
Family is aware	Yes	
Duration before medical help is sought	Short	
Progression of symptoms		Slow
Previous psychiatric dysfunction	Yes	

b) Clinical symptoms

	Pseudo Dementia	Dementia
Cognitive complaints	Much	
Cognitive complaints	Detailed	
Cognitive complaints	Emphasis on Disability	
Performance	Highlight failures	
Effort to perform		Much
Affective change	Pervasive	
Social Skills		Retained
Behavior		Compatible with severity of cognitive dysfunction (?)
Diurnal Variation	Worse in the morning	

It seems that, at least in this case, such a clear-cut distinction between dementia and depression (pseudo dementia) is not possible if based on such criteria. However, MS has more symptoms of a depressive disorder than of a dementing one.

On her first neuropsychological evaluation, some aspects were considered suggestive of a depressive disorder :

a) The marked variability of her performance seen throughout the tests, which were administered in different days.This is commonly seen in depressive states but is very rare in dementia, except when it is associated with *delirium*, which was not the case.

b) Her attention was normal. Although some demented patients have normal scores on formal testing of attention[5], this aspect is considered more characteristic of depression.

c) Her cognitive impairment seemed restricted to memory systems, a result that suggests depression. It must be remembered that although many dementia begin clinically with a dysmnesic syndrome, neuropsychological evaluation often discloses impairment in other areas as well. It is noteworthy that besides revealing a severe deficit in memory testing (it was not even possible to calculate her Memory Quotient) the patient obtained normal scores for her age in almost all other tests, a neuropsychological profile not seen in dementia. In the former stages, demented patients usually show only a mild to moderate impairment of memory.

d) Recognition was normal, suggesting the deficit was one of recall and but retention. Although some demented patients show this profile in the beginning of their illness, this aspect strongly suggests depression, specially in the absence of other deficits.

e) The patient revealed some degree of learning of new material.This ability is usually lost or severely impaired in dementia, even in the former stages.

f) Impairment of remote memory does not occur in primary dementia, except in the late stages.Some dementia (like the one that occurs in Huntington's chorea) may show this "flat" dysmnesic profile (without temporal gradient) but this was obviously not the case.

g) Her visual-motor dexterity was impaired, and this result is commonly seen in depression and also dementia.

h) Her normal scores in abstraction problems posed against dementia.

After being properly treated for the depressive disorder, the patient improved her memory but still revealed some impairment. It is noticeable that she did not spontaneously complain of memory problems any further after the remission of depression. The deficit after the remission of depressive symptoms suggested a mild dementing disorder, probably of a primary degenerative type.

The continuum viewpoint discourages the dichotomy that considers some patients "treatable" and others not and also helps establish more realistic expectations.

It must be said that some authors, like Murphy[7] have *not* found consistent relationships between pseudo dementia and the appearance of true dementia on follow-up. The present author suggests some reasons for this interesting aspect :

a) It is possible that *some* patients diagnosed as pseudo demented do not have true cognitive impairment. At present the prevalence of these "pure" cases is unknown. However, a great number of studies point to the other direction.

b) Some patients considered not having cognitive impairment have *not* been evaluated through neuropsychological examination, which is more sensitive than commonly used instruments like the MMSE. It is not rare to see a patient with normal scores on the MMSE having a profile characteristic of mild cognitive impairment on neuropsychological examinations.

c) Follow-up studies vary greatly in respect of their length. Emery and Oxman[2] suggested that shorter follow-ups may not reveal impairments that may show on longer follow-ups.

d) There is no single accepted definition or characterization symptom pattern of pseudo dementia. This must be taken into account when consulting the literature.

e) Depression is common in most dementia; a "pseudo dementia" diagnosis may miss the underlying dementia.

f) Studies only rarely state the psychiatric examination of the patient. It is well established that many non-depressive states may mimic depression. The present author has seen personality disorders and factitious disorders, sometimes associated with depressive symptoms, presenting as dementia-like cases.

Appropriate treatment of depression improves patient's quality of life and also improves to some degree the memory impairment seen on formal testing. An empirical trial of adequate antidepressants should be done in those patients with cognitive impairment and clear depressive symptoms even though not qualifying for major depression.

This last aspect is noteworthy because elderly patients are prone to be undermedicated or even not medicated at all for the following reasons:

- minor depressive symptoms are still considered "secondary" (reactive) or "psychological" in many cultures where physicians relate them to the losses (social, professional, familiar and financial) that often occur in old age.
- besides the new drugs available in the market, some physicians still advocate that the use of antidepressant drugs in this population often brings more clinical problems than benefits (what may be probably true for some specific classes of drugs, but not all of them).

The term "pseudo dementia" may not be proper in face of our current knowledge and some authors question if it should be retained in medical literature[11]. On the other hand, the concept of "excess disability" seems more adequate since it precludes the superficial distinction between functional and organic impairment.

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