

Studi sperimentali

Linguistic analysis in the differential diagnosis between cognitive impairment and functional cognitive impairment (depression): a pilot study

Analisi linguistica nella diagnosi differenziale tra decadimento cognitivo e decadimento cognitivo funzionale (depressione): uno studio pilota

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SUMMARY. The differential diagnosis between cognitive impairment and functional cognitive impairment (depression) is complex and difficult, especially in the early stages of the disease. The aim of our study was to test linguistic analysis as a diagnostic tool to support clinical, and test-based diagnoses for this differential diagnosis. We enrolled 13 patients, requesting a diagnostic consultation in a Alzheimer Evaluation Unit. A provisional diagnosis through a neuropsychological evaluation (interview and neuropsychological tests) was made at baseline, while a definitive diagnosis was provided after six months, or, if not possible, after 12 months. The linguistic analysis was performed at T0 in blind by a linguist. Patients' language was studied at linguistic (morphological, syntactical, lexical literal and textual) and conversational (verbiage and humor) level. The correspondence rate between the linguistic analysis at T0 and the definitive diagnosis was 76.9%, compared to 58.4% between the neuropsychological équipe analyses at T0 and definitive diagnosis. There is no single pathognomonic phenomenon for cognitive impairment or depression, but rather a linguistic cluster can lead to a diagnosis with a fairly good reliability.

KEY WORDS: dementia, pseudodementia, conversation analysis, elderly.

RIASSUNTO. La diagnosi differenziale tra decadimento cognitivo e decadimento cognitivo funzionale (depressione) è complesso e difficile, specie nelle fasi precoci del disturbo. Lo scopo del nostro studio è di testare l'analisi linguistica come strumento diagnostico per supportare la diagnosi clinica e testale di questa diagnosi differenziale. Abbiamo arruolato 13 pazienti che hanno richiesto una consultazione diagnostica in un'unità di valutazione Alzheimer. È stata effettuata all'ingresso una diagnosi provvisoria attraverso una valutazione neuropsicologica con colloquio e test neuropsicologici, mentre è stata fornita una diagnosi definitiva a sei mesi o, se non possibile a 12 mesi. L'analisi linguistica è stata effettuata al T0 in cieco da una linguista. Il linguaggio del paziente è stato studiato a livello linguistico (morfologico, sintattico, lessicale, letterale e testuale) e conversazionale (verbiaggi e umorismo). Il tasso di corrispondenza tra l'analisi linguistica al T0 e la diagnosi definitiva è risultato del 76,9%, comparato al 58,4% tra la diagnosi effettuata dall'équipe neuropsicologica al T0 e la diagnosi definitiva. Non esiste un singolo fenomeno patognomonic per decadimento cognitivo o depressione, ma piuttosto un cluster linguistico può condurre alla diagnosi con un buon livello di affidabilità.

PAROLE CHIAVE: demenza, pseudodemenza, analisi della conversazione, anziano

INTRODUCTION

In neurology, the differential diagnosis between cognitive impairment and depression or some other psychiatric framework that mimics dementia, that we call "functional cognitive impairment"^{1,2}, is one of the most complex and difficult, especially in the early stages of the disease. The two clinical pictures can in fact overlap, as both entail significant mood decline, a real or subjective loss of memory, lowered perform-

ance, and social withdrawal^{3,4}. Clinical data and neuropsychological tests are not considered diagnostic⁵. An early diagnosis of cognitive impairment is important not only to give patients and their families useful information and a horizon of future changes, but also to undertake specific early treatment according to the recent therapeutic developments⁶⁻⁸.

Roark et al.⁹ studied pause frequency and duration, and many linguistic complexity measures, calculated from manually annotated time alignments (Syntactic Annotation, Pause

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Annotations From Time Alignments, Approaches to Linguistic Complexity, Alternative Tree Analyses, idea and content density, speech duration) of the transcript with the audio of 74 neuropsychological examinations either diagnosed as healthy or with mild cognitive impairment. The verbosity and intensity of speech often associated with cognitive impairment¹⁰ does not correspond to correctly structured speech. In fact, quite often the verbigeration characterizes oral production, often accompanied by a total lack of deictic components. Even at a lexical, syntactical, morphological, and phonetic level, there are clear deformations due mainly to patients' inability to monitor errors: they involuntarily deform words and sentences without showing the typical forms of auto-correction.

A case control study¹¹ comparing elderly participants with mild Alzheimer disease with patients with depression and controls without psychiatric or neurological diagnosis, found that patients with AD produce less-informative samples in quantitative, syntactic, and informative aspects of the discourse than patients with depression and controls, who did not significantly differ between them on any discourse variable. All this data show a growing interest in language for the differential diagnosis. Linguistic analysis (LA) is an approach to the study of social interaction, embracing both verbal and non-verbal conduct, in situations of everyday life¹², used in different clinical situations, both in children and in adults^{13,14}.

Two studies^{15,16} tried to study linguistic differences between functional cognitive impairment and cognitive impairment in 25 patients: the authors found that people with cognitive impairment were more likely to be accompanied by other persons, were less concerned than their caregivers about their memory problems, less able to display working

memory in interaction, less able to answer questions about personal information. They were also less likely to recall recent memory failure, and to answer to compound questions and to discover their repetitions, giving less importance to details. They also take more time to answer questions.

However, a blind validation study on the efficacy of this tool to support clinical, and test-based diagnoses for the differential diagnosis between cognitive impairment and psychiatric diagnosis resembling dementia is lacking. The aim of this pilot study is to test linguistic analysis in a sample of people referring to an Italian Alzheimer Evaluation Unit (AEU).

METHODS

We performed a validation longitudinal prospective conversation analysis study, with a 6-12 months follow-up.

Population

We enrolled a consecutive sample of patients requesting an initial consultation in an AEU at the Cliniche Zucchi in Carate Brianza, Italy, in order to obtain a diagnostic evaluation regarding the possible onset of a process of cognitive impairment.

For all the subjects involved in the study, a clear differential diagnosis based on clinical elements and testing was not possible. The sample consisted of 13 patients (10 females and three males) with a mean age of 75.8 (ranging from 65 to 85) (Table 1).

Table 1. Demographic and clinical variables of the sample.

N	Sex	Age	MS	Edu (years)	Previous occupation	Psychological symptoms	Neurological symptoms
1	F	69	Wi	8	Laborer	Depression	Amnesiac deficit
2	F	79	Wi	13	Teacher	Anxiety reportedly due to loneliness	Amnesiac deficit
3	F	80	Wi	5	Laborer	Social withdrawal, loss of appetite, loss of motivation	Amnesiac deficit
4	F	79	Ma	5	Laborer	Asthenia/ mood decline	Mental confusion
5	F	69	Ma	8	Office worker	Anxiety, emotional fragility	Anomie
6	F	85	Wi	5	Housewife	Anxiety, mood decline, insomnia	Difficulty handling daily tasks
7	F	83	Wi	5	Housewife	Melancholy, touchiness	Amnesiac deficit, social withdrawal
8	F	79	Ma	4	Laborer	Depression	Amnesia
9	M	82	Ma	8	Laborer	Somatization, depression	Amnesiac loss
10	F	76	Ma	5	Shopkeeper	Anger, aggressiveness, perception of loneliness and incomprehension, diffidence towards others (dysthymia, reactivity)	Amnesiac difficulties
11	F	72	Wi	8	Laborer	Anxiety and somatization	Amnesiac deficit
12	M	67	Ma	8	Artisan	Anxiety, mood decline	Loss of cognitive performance
13	M	65	Ma	17	Teacher	Insomnia, bad mood	Some amnesia

Legenda: MS: marital status; Edu: education; M: male; F: female; Wi: widowed; Ma: married.

A specific consent was not obtained since all the tools used were part of the diagnostic process.

Neuropsychological diagnosis

In line with current international standards¹⁷, at baseline the subjects were clinically evaluated by a neurologist (CP) along with a neuropsychological assessment¹⁸ performed by a neuropsychologist (BV). The tests used were: the Milan Overall Dementia Assessment (MODA)¹⁹, a short, neuropsychologically oriented test for dementia assessment, Raven's progressive matrices test²⁰, a 60-item test used in measuring abstract reasoning and regarded as a non-verbal estimate of fluid intelligence, the digit span test (forward and backward)²¹, that is the longest list of items that a person can repeat back in correct order immediately after presentation on 50% of all trials (items may include words, numbers, or letters), the Efron test²², identification of the correct shape of a visual stimulus and a symbol-number association test. A provisional diagnosis was made at baseline (T0), while a definitive diagnosis was provided after six months (T1), or, if not possible, after 12 months (T2).

Linguistic diagnosis

The linguistic analysis was performed in blind by an external psychiatrist at the center (CMC) along with a linguist (MP) at T0.

The interviews were transcribed using the Jefferson system²³, the most important symbols of which are described in Table 2.

The objective of the linguistic analysis was to discover if the two distinct clinical pictures presented by any unique linguistic characteristic could help to make a distinction between them. The aim was to see if it was possible to identify two distinct groups on a linguistic level.

Starting mainly from a medical point of view, an initial draft of an interview was composed as follows:

“I would like to speak to you about how you spend your day, about your life, and about your memories:

1. What did you do today/yesterday?
2. What do you remember about when you were young?
3. What are the most difficult things you face in your current situation?
4. How would you explain/describe your current status?”

In particular, the initial analysis grouped some phenomena into hypothetical significant linguistic clusters, to either confirm or deny their existence. In this first phase, a wide-spread linguistic analysis was performed in order to record phenomena so as to make any significant examples emerge. At first, the following were monitored:

Linguistic level

Morphological level: identification of the choice of personal pronoun; identification of commonly used verb tenses.

Syntactical level: phrase length.

Table 2. Glossary of transcription conventions.

[]	Overlapping of two or more voices
=	Continuity of utterance between two expressions
(0.5)	The number indicates the duration of a silence in tenths of a second.
(.)	A micro-pause: i.e. an audible but unmeasurable silence lasting less than 2/10 of a second.
.	Falling intonation.
?	Rising intonation.
,	Level intonation.
: repeatable :::::	Prolongation/lengthening of the sound preceding the symbol, depending on duration.
-	Voluntary or involuntary interruption of a word.
TESTO	Text spoken loudly.
°testo°	The part of the text between the symbols is spoken more quietly than the words before and after it.
<u>Testo</u>	The underlined text is spoken with particular emphasis.
>testo<	Discourse pronounced rapidly.
<testo>	Discourse pronounced markedly slowly.
h repeatable hhhh	Audible exhalation that may be a breathe or laughter, depending on duration.
.h repeatable .hh	Inhalation, depending on duration.
((testo))	Comments of transcriber to indicate events or significant non-verbal acts.
(testo)	Indicates a hypothesis in the case of inaudible or incomprehensible words. If the brackets are empty, the words are indecipherable.

Lexical level: presence of incorrect words; presence of any neologisms.

Textual level: presence of deixes; check for coherence and cohesion.

Conversational level: check for any questions to the interviewer; calculation of the patient's response time; use of metaphors.

During the first stage of the study, some elements immediately emerged. The “obstacle” of the video recorder²⁴ seems to affect the patients significantly: they often felt uncomfortable and judged by their interviewer. For this reason, we decided to create a more relaxed (not taped) moment before the interview, in order to let the patients feel more comfortable. In this informal moment matters that would be discussed during the interview should not be approached, so that the patient would not omit important details during the observation session. In any case, in all interviews, the patients progressively disregarded the video recorder, leading to more neutral behavior.

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Many notes and considerations made by the interviewers provided some important details for a positive outcome of the conversation. The interviewer's tone of voice and general attitude had to be authoritative but not authoritarian: any sign of doubt or response to indecision by the patient could make the patient uncomfortable, compromising his/her linguistic production. For the same reason, it was necessary to avoid the verb "remember" or any words that even remotely referred to memory matters, since these were alarming signals for the patients. The questions had to be asked sequentially and clearly, keeping in mind any possible physical limitations (deafness) of the patients. Moreover, if the patients digressed, they had to be brought back to the topic on hand in order to verify their comprehension and coherence abilities. The fact that many of the interviewees were quite old and the exam-like environment they were experiencing often made the patients complacent; for this reason, it was necessary to avoid any hinting, judgment, or personal opinions or comments. Furthermore, it was important to avoid the temptation to jump to conclusions or to answer on behalf of the patient.

The interviewer had to think about everything patients said, in order to keep communication open, and had to avoid direct questions about anything the patients said.

The linguistic analysis showed that many of the phenomena were not pertinent in the sample studied. The resulting significant linguistic clusters for the above categories were:

Linguistic level

Phonetic level: phonetic lengthening is significant if used as a strategy to fill in gaps in the conversation due to hesitation during formulation. Otherwise, it can be considered as a normal way to fill gaps during the conversation. In the first case, this has been considered a sign of cognitive impairment.

Morphological level: identification of prevalent verb tenses. The ability to distinguish the past from the present, and the awareness of and correct use of alternating morphology most likely indicate functional cognitive impairment. In order to note these variations, it is necessary to be precise when formulating questions: elderly patients, in fact, are often habitual and repetitive and often use the present tense.

Syntactical level: the presence of questions to the other speaker or to themselves. If the patient repeatedly asks questions to him/herself or to the interviewer, he/she probably suffers from cognitive impairment. One must pay attention to rhetorical questions, which are statements and do not require an answer from the other speaker. Presence of negations: the direct expression of negation and the lack of collaboration can be attributed to speech of patients with functional cognitive impairment.

Lexical level

Verbosity: the formulation of sentences based on unrelated or incoherent words, especially when spoken with intensity, has been considered a signal of problems related to cognitive impairment. Repetitions: if the repetition is used to go into further detail or to highlight something previously said, it can point to functional cognitive impairment. On the contrary, repetitions can signal cognitive impairment if they are near to each other and serve no purpose in terms of expression or clarity.

Literal level: the presence of problems of syntactical coherence and cohesion have been considered signs of cognitive impairment.

Conversational level

Repetitive, disorganized verbiage is often considered a sign of cognitive impairment, but on the other hand coherent, cohesive verbiage can be a sign of functional cognitive impairment. Collaboration can often lead to cognitive impairment. Humor: humor, often with bitter tones, is a sign of functional cognitive impairment.

After taking into account these considerations, the outline of the interview was modified and administered to the 13 patients in this way:

1. What did you do yesterday? (And afterwards, if the patient only described routine activities, without giving any specific details, questions such as: What did you have to eat yesterday?)
2. Tell us something about your childhood, about where you were born, about your family
3. What is the reason why you have come to this clinic for testing? (if needed) Have you also had memory problems?
4. What has been then happening to you or around you?

The 13 interviews were performed and analyzed blindly by a linguist.

Statistical analysis

The final neuropsychiatric diagnosis done at T1 or T2 was considered the gold standard for the diagnostic tool; the final diagnosis was compared to the one made through linguistic analysis and to the provisional neuropsychological diagnosis at T0.

The validity of the linguistic analysis was tested calculating sensitivity, specificity, predictive values and misclassification rate. For the small sample, no other statistical test were performed.

RESULTS

Correspondence between the linguistic diagnosis and the neuropsychological diagnosis

Table 3 shows the results of the linguistic analysis, and the correspondence between the two diagnoses (linguistic and neuropsychological) made at T0 with the final diagnosis.

As shown in the table, linguistic analysis performed better than neuropsychological diagnosis. Sensitivity, specificity, positive and negative predictive values were respectively 80%, 75%, 67% and 86% while the corresponding values for neuropsychological analysis were 60%, 63%, 50% and 71%. The results of linguistic and neuropsychological diagnosis corresponded in 76.9% and in 58.4% of cases respectively.

More specifically, we studied the number of times a phenomenon occurred, and when its presence was in line with a correct diagnosis. The phenomena leading to a diagnosis of

Table 3. Correspondence between conversational analysis at T0 and conclusive neuropsychiatric diagnosis (at T1 or T2).

Patient	Linguistic diagnosis (T0)	Neuropsych diagnosis (T0)	Neuropsych diagnosis GS (T1)	Neuropsych diagnosis GS (T2)	CorrespondLinguistic (T0)-GS	Correspond Neuropsych (T0)-GS
1	CI	MCI	MCI	MCI	Yes	Yes
2	No CI	CI	No CI	-	Yes	No
3	CI	CI	No diagnosis	CI	Yes	Yes
4	No CI	No CI	No CI	-	Yes	Yes
5	No CI	No CI	No CI	-	Yes	Yes
6	CI	No CI	CI	-	Yes	No
7	No CI	CI	CI	-	No	Yes
8	CI	No diagnosis	No CI	-	No	No
9	CI	No diagnosis	CI	-	Yes	No
10	No CI	No CI	No CI	-	Yes	Yes
11	No CI	No CI	No CI	-	Yes	Yes
12	No CI	No CI	No CI	-	Yes	Yes
13	CI	No diagnosis	No CI	-	No	No

cognitive impairment were: repetitive, disorganized “long-windedness” (4/5), phonetic lengthening when attributable to filling gaps due to hesitations in formulation (4/7), the presence of questions to the interviewer or to the patients themselves (with the exception of rhetorical questions) (3/4), verbigeration, i.e. the formulation of sentences consisting of strings of disconnected and unrelated words (4/7), empty repetitions or repetitions in a short word span (3/3), lack of syntactical coherence and cohesion (2/3).

Phenomena pointing to a diagnosis of functional cognitive impairment, on the other hand, were: the ability to distinguish between the past and the present tense (4/7), coherent answers (5/7), distancing themselves from the interviewer (3/3), the presence of negations, i.e. explicit uses of negation and lack of collaboration (6/8), the use of metaphors (1/1), repetition in order to better explain or to underline a concept (1/1), coherent and cohesive verbosity (4/5), humor (2/3).

Lengthenings

P: Well, yesterday as the other days I em:: I am an housewife. I am alone. I have a small apartment: I do the:: () I do the:: ((she claps)) I clean the house, I do grocery shopping then in the afternoon >in the afternoon< I take home my nephew. **Cognitive impairment**

P: Yesterday it was Monday, thus ((he coughs)) you know: I woke up normally around 7 o'clock., I did my breakfast:: >I mean I have to:< [(.) tell] about exactly in, **Cognitive impairment**

Tenses

C: So madam, in our conversation, may I ask you what you did yesterday?

P: What did I do yesterday?

C: Yes.

P: Nothing. I did: I was at home.:

C: You were at home,

P: I do grocery shopping, (.) then:: in the afternoon I take my bike and go to the cemetery, and bike. (.) and then I go back home.

C: And in the afternoon?

P: In the afternoon I go back home. (.) I watch TV. (.) or I take my bike and go to the cemetery.

C: What was on TV yesterday?

P: °I don't remember.° **Cognitive impairment**

Yesterday it was Monday. Nothing special. I had some rest because then (.) on Sunday I went home, to my friend, because the night before she did to me:: late. We were there a bit to talk about “more or less” because we are two sorrowful persons. We talk each other about our husbands' events. We went with the past. To a re- review:: what we did, what we got, and what is left to do. Then I came home, and I don't: even – yes no. No I had dinner there and I went to bed. Nothing special. **Functional cognitive impairment**

Questions

And for the rest what can I say? °what can I tell you more?° ((she laughs)) I don't know? eh? guys? ((she turns around)) What can I tell you? () and:: unfortunately:: my head lacks a bit:: m:: ((tongue click)) I mean my memory, you know °because my head:: well° <is still on my neck.< ((she laughs)) but::, in fact I am here. fo::r trying to to improve therefore:: a bit. (.) and for the rest:: >I don't know< ((she turns)) what can I say guys? **Cognitive impairment**

I can because what do I have to do? ((she laughs)) **Cognitive impairment**

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>maybe she killed< the beasts. to- to make:: How can I say? ((she turns towards the audience)) how could you say in the past:? To to: sell: (.). **Cognitive impairment**

Verbigeration

Because I am bored even to read the newspapers there are always the same:: () things:: even bad: ((she laughs)) () but are the:: women and all that stuff. () and:: yeah m: I like reading the newspapers **Cognitive impairment**

P: I had three sons, (.) out out out outside outside ((she laughs) there was nothing. (.) yes. **Cognitive impairment**

Text organization

I: And today It was instead a bit:: different?

P: e:: Today it was a bit different. Usually on Sundays:: (.) they leave:: they leave me free because maybe the children don't go:: to school (.) they are more: stay more with mom and dad and:: (.)

I: m.

P: (.) Today I didn't go outside. (.) before I: (.) I went outside maybe I went to buy the newspaper. Something like that but:: to the bar °as I always say° **Cognitive impairment**

Verbiage

I: did you wash the bowl then?

P: yes.

I: and did you arrange the couches?

P: I arranged the couches °and that's it.° now and and it's cold outside I can't because then we also have a piece of garden and I have to: arrange the garden too, don't I? the leaves, the stuff:, now it's cold (.) who- does who go outside? **Cognitive impairment**

P: m:: no no:: It's enough I do my things but::: some sometimes they bother me, I am bored (.) that's it. **Functional cognitive impairment**

Lack of cooperation

I: what do you feel it's happening to you in this period. of your life?

P: I don't know. m::: I can't say that that that it's "evil eye" because:::, no. But I think I did well with other people. **Functional cognitive impairment**

I: listen. () tell us something about your childhood, where were you born, of your family,

P: quite [quite]

I: [tell us something]

P: I am pretty normal. I mean I've never had:: (.) there were dad mom my brother well, I didn't have any diseases, thus:, I mean I feel good. **Functional cognitive impairment**

Humor

On Saturdays and Sundays that that we used to go with – with girls and friends, or to the theatre or: to take a walk, thus. (.) it was fun we settled for everything. Then we engaged and that's it. **Functional cognitive impairment**

P: before I go doing the funeral then I die °I mean.° **Functional cognitive impairment**

DISCUSSION

The differential diagnosis between cognitive impairment and functional cognitive impairment is very complicated as there is no valid diagnostic instrument in the early stages of the disease.

Linguistic diagnosis reiterates the importance of listening, something that, for various reasons, had been put aside in favor of structured and semi-structured psychiatric and cognitive impairment tests (Structural Clinical Interview for DSM-I²⁵) and II²⁶, Hamilton Anxiety²⁷ and Depression²⁸ scales, Mini Mental State Examination²⁹, MODA¹⁹) tests. Conversation analysis places attention on both verbal and non-verbal communication.

In this light, the international literature has recently given a growing importance to language in all its features as a diagnostic tool for the diagnosis of cognitive decline, as explained by the literature available, but the majority of papers on this topic studied linguistic features of patients through video recording of patients' speech without use of a guided interview with standard questions like we did here (linguistic analysis).

Our findings highlight that linguistic analysis could be an important instrument for the differential diagnosis between cognitive impairment and functional cognitive impairment, especially because it is generally quick and quite cheap, with good positive and negative predictive values. Our results point out the importance of language, already underlined by previous reports. Our findings can integrate previous data^{15,16} to detect the linguistic profile of patients with cognitive impairment and patients with functional cognitive impairment. In fact we tried to evaluate other linguistic features (verbiage, phonetic lengthening, repetitive questions to the other speaker or to themselves for cognitive impairment, coherent verbosity, correct use of past or present tenses, humor for functional cognitive impairment) that are in keeping with those identified by those authors to complete the linguistic profiles of the two groups.

In line with previous findings^{9,11,15,16,30} difficulties in oral production are detectable in several language levels (semantic, syntactic and lexical level); therefore there is no one single pathognomonic phenomenon for cognitive impairment or functional cognitive impairment, but rather a linguistic cluster can lead to a diagnosis with a fairly good reliability.

However, it is very difficult to detect specific "linguistic" risk factors that could lead to cognitive impairment, to be included in a linguistic diagnostic questionnaire with a sufficient reliability, but rather the whole complexity of speech in all its levels must be considered and it is therefore necessary to collaborate with a trained linguist who knows how to interpret each single phenomenon and how to give the correct weight to a cluster.

The most surprising and promising result of our study was that the linguistic diagnosis was able to establish the presence of cognitive impairment earlier than the diagnosis made by the neuropsychological staff.

An explanation of this result is that language impairment, which is considered a specific element of cognitive impairment, is the main element upon which linguistic analysis is based.

LIMITS

The results of our study should be taken with caution: in fact, they come from a pilot study done on a small sample of the population of interest. Patients with cognitive impairment and patients with functional cognitive impairment are not homogeneous: cognitive impairment can include Alzheimer disease, multiinfarctual dementia, Levy body dementia, frontotemporal dementia, etc., while functional cognitive impairment can include depression, anxiety or behavioral disorders). The results of linguistic analysis may vary according to the patients' phenotype.

CONCLUSIONS

The results obtained in a blind context are extremely promising, justifying the extension of linguistic analysis to a larger population of patients, even though new studies using this methodology, especially if associated with previous findings (see before), and on larger and homogeneous patient populations are needed to confirm the use of this technique and, if necessary, to refine it with the addition of words linked to emotions.

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