Chapter 17: Amyotrophic lateral sclerosis

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Abstract:

Amyotrophic lateral sclerosis (ALS) is a complex multisystem disease characterized by the neurodegeneration of peripheral and central motor neurons. Nowadays, it is widely acknowledged that ALS not only affects motor abilities but also comes with a range of neuropsychological impairments including language, in a strict relation with fronto-temporal dementia. Although pragmatic aspects are still largely unexplored, the available literature consistently points to the presence of pragmatic language disorder in ALS. The most documented feature of pragmatic impairment in ALS is the disruption of narrative language and discourse effectiveness. A few studies have also reported impairment in understanding non-literal language, including figurative expressions and sarcasm. These difficulties cannot be fully accounted for in terms of executive function deficits or social cognition impairment and call for specific consideration. In line with this evidence, the most recent consensus criteria for the diagnosis of fronto-temporal dysfunction in ALS include pragmatics in the description of the possible profiles of cognitive impairment. Yet, ALS remains an underserved population in terms of pragmatic language disorder. We encourage future research to consider pragmatics and social communication in ALS in order to provide better clinical assessment and improved treatment for patients with the condition and their caregivers.

Keywords: amyotrophic lateral sclerosis; Assessment of Pragmatic Abilities and Cognitive Substrates (APACS); discourse; figurative language; non-literal language; pragmatics; social communication

17.1 Introduction

Amyotrophic lateral sclerosis (ALS) owes its name to the major clinical and neuropathological findings indicating neurodegeneration of, respectively, the peripheral and the central motor neurons. The disease shows a spectrum of clinical patterns: variable duration (from 1 to 15 years), variable onset (spinal or bulbar), extremely variable involvement of the peripheral and the central motor neurons, from Primary Lateral Sclerosis to Progressive Muscular Atrophy, making almost each case unique. For many years, neurologists believed that people with ALS would be completely lucid even as their body experienced progressive, and eventually total paralysis. It is now well recognized, however, that a number of cognitive, behavioral, social, and pragmatic deficits may be observed in 50% of ALS patients, and 15% of cases reach criteria for a diagnosis of fronto-temporal dementia (FTD) (Crockford et al. 2018; Goldstein and Abrahams 2013).

This chapter reviews findings that have contributed to our understanding of pragmatic impairment in ALS. But first, it examines in section 17.2 the epidemiology and aetiology of ALS as well as criteria that are used to diagnose cognitive and linguistic impairment in ALS. Section 17.3 reviews structural aspects of language in ALS, including speech, grammar and the lexicon. This section provides an overview of the general linguistic profile of patients with ALS, highlighting the linguistic domains that are most impaired, and considering also the specific domain of action/verb semantics. Section 17.4 focuses on pragmatics. Although the literature is modest, it can be grouped into two domains: one dealing with difficulties in producing pragmatically appropriate discourse, and the other dealing with difficulties in comprehending implicit meanings. Studies in these two domains are reviewed in sections 17.4.1 and 17.4.2, respectively, with emphasis placed on tasks and assessment tools and examples of patients' communicative behavior. Section 17.5 deals with the broader issue of communication and conversation in everyday life. A summary of the chapter's contents is offered in section 17.6, together with some recommendations for future studies.

17.2 ALS: some background

The epidemiology of ALS has been the focus of several studies. An epidemiological meta-analysis of studies published between 1995 and 2011 reported that in Europe the median prevalence and incidence of ALS were 5.40 and 2.08 per 100,000 person-years, respectively (Chiò et al. 2013). Although studies from outside of Europe are scant, it seems that prevalence and incidence figures are lower in populations of mixed ancestral origin compared to European populations, with further

differences in age of onset (Zaldivar et al. 2009; van Es et al. 2017). Granted these differences, studies reported a worldwide median prevalence of 4.48 and a standardized incidence rate of 1.68 per 100,000 person-years (GBD 2016 Motor Neuron Disease Collaborators 2018; Marin et al. 2017). Median age of onset is 65 years in populations of European ancestry, whereas onset is approximately 10 years earlier in genetically heterogeneous populations (van Es et al. 2017). The male to female ratio is estimated to be around 1.5:1 (Manjaly et al. 2010), while the lifetime risk of ALS is 1 in 472 in women and 1 in 350 in men (Alonso et al. 2009). According to some studies, however, sex ratios might change with age and across countries, as well as over time (Logroscino et al. 2010; Longinetti and Fang 2019; Manjaly et al. 2010).

The genetic basis of ALS and its relationship to FTD is the focus of an increasing number of studies. Investigators have discovered more than 30 different genes linked to familial ALS (Renton et al. 2014), which indicate that ALS is a clinically and genetically heterogeneous multidomain neurodegenerative disease. Moreover, investigators have discovered gene mutations that give rise to ALS as well as to FTD and to combinations of both, namely TARDP, C9orf, FUS and other rarer genes (Saber et al. 2015). This underlines the relationship between ALS and FTD and confirms the idea that these conditions are the extremes on the phenotypic spectrum of a single disease (Burrell et al. 2016; Ferrari et al. 2011). The spectrum includes individuals with ALS with cognitive impairment who nevertheless do not meet the criteria for dementia (ALS-ci), individuals with behavioral impairment who nevertheless do not meet the criteria for dementia (ALS-bi), individuals with both cognitive and behavioral impairment without dementia (ALS-cbi), and individuals with features of both ALS and FTD (ALS-FTD) (Woolley and Rush 2017).

The complexity and heterogeneity of ALS profiles makes neuropsychological assessment in this population especially important, as reflected in the most recent consensus criteria for the diagnosis of fronto-temporal dysfunction in ALS (Strong et al. 2017). This new version of the consensus criteria expands on a previous version (Strong et al. 2009), by incorporating more fine-grained distinctions of cognitive domains and the idea of a fronto-temporal spectrum disorder of ALS. While the old version focused especially on executive dysfunction, the new version acknowledges the importance of also considering impairments in social cognition, language and pragmatics. Based on the 2017 consensus criteria, a diagnosis of ALS-ci is to be made when there is evidence of either executive

impairment (which could include social cognition) or language impairment (which could include pragmatics) or a combination of the two. More specifically, citing from Strong et al. (2017):

A diagnosis of ALS-ci depends on evidence of either executive dysfunction (including social cognition) or language dysfunction or a combination of the two.

Executive impairment is defined as:

(1) Impaired verbal fluency (letter). Verbal fluency deficits must control for motor and/or speech impairments to be valid.

OR

(2) Impairment on two other non-overlapping measures of executive functions (which may include social cognition).

Language impairment is defined as:

(1) Impairment on two non-overlapping tests (which could include pragmatic function).

What is relevant for this chapter is the definition of language impairment as impairment in two non-overlapping tests, *which could include pragmatic function*. This is important for two reasons: (1) it shows that the presence of pragmatic impairment in ALS is now fully acknowledged; and (2) it classifies pragmatic impairment as part of language impairment, which in turn is classified as part cognitive impairment. This does not imply that pragmatic impairment depends on impairment in other cognitive domains, but rather that pragmatic impairment is one of the forms in which cognitive impairment can appear in the highly heterogeneous ALS population. Indeed, the relationship between language, pragmatics, and executive problems has been one of the most investigated topics in the literature, along with the relationship with motor symptoms.

17.3 Speech, grammar, and lexical semantics in ALS

The most prominent language-related problem in ALS is speech production (Orange and Hillis 2012). Although speech is considered a ‘peripheral’ component of the faculty of language, as it lies at the interface with motor and sensory domains (Hauser et al. 2002), speech problems impact other language aspects, such as discourse productivity and conversation management, and in turn affect communication effectiveness and quality of life (Felgoise et al. 2016). Any study of language in ALS should thus start by considering speech, and should control for speech production impairments and motor deficits in assessing other linguistic aspects (Strong et al. 2017). Concerning ‘core’ language

aspects, the systematic review of the literature conducted by Pinto and colleagues (Pinto-Grau et al. 2018) identified 57 studies on ALS and language conducted between January 1975 and August 2017. Seven domains of linguistic abilities were considered in the review: (a) verbal expressive language (i.e. discourse productivity); (b) verbal fluency (i.e. word generation); (c) confrontation naming; (d) semantic processing; (e) auditory comprehension; (f) action verb processing vs. object noun processing; and (g) reading and writing. Overall, the review pointed to expressive problems at the level of both grammar and semantics and suggested that there might be linguistic difficulties in ALS that are independent of speech impairment and impairment in executive functions.

17.3.1 Speech and dysarthria

Dysarthria indicates the condition where, due to damage to the central and/or peripheral nervous system, speech movements are impaired in speed, force, range, direction and timing (Orange 2009). It is estimated that 80-95% of patients with ALS exhibit severe dysarthria during disease progression (Linse et al. 2018; Tomik and Guilloff 2010). Studies have also documented the co-occurrence of dysarthria and apraxia of speech, a condition where there are impairments in the ability to plan or program commands that direct speech movements (Duffy et al. 2007).

Dysarthria in ALS usually results from the involvement of both upper and lower motor neurons and is described as mixed spastic-flaccid dysarthria. Typical features of speech in ALS are imprecise consonants (i.e. slurred speech sounds), hypernasality, harsh voice quality, slow speaking rate, monopitch and short phrases (Orange and Hillis 2012). Assessment of speech includes sound error profiles (in tasks such as single and multiple sound production and repetition, single and multiple syllable word repetition, etc.), rate of speech, and intelligibility scores.

Many patients exhibit loss of adequate speech even at the onset of the illness (Linse et al. 2018). A longitudinal study showed that speech remained adequate for 18 months from the first bulbar symptoms, but speech quality rapidly declines during the course of the illness (Makkonen et al. 2018). Speech deteriorates more in the bulbar group compared with the spinal group and the difference remains significant at follow-up. In some cases, dysarthria might lead to complete speechlessness, i.e. anarthria (Orange and Hillis 2012). Because of these problems, 60% of patients need augmentative and alternative communication methods (Makkonen et al. 2018), such as eye-tracking-based computer devices and brain-computer interfaces. These technologies offer the

possibility of maintaining independent communication even in advanced stages of ALS (Linse et al. 2018).

17.3.2 Grammar and the lexicon

To sketch a global profile of the linguistic domains of grammar and the lexicon in ALS, it is useful to start from the study of Taylor and colleagues, who ran an extensive language assessment in 51 patients with ALS and matched controls (Taylor et al. 2013). They created a composite measure of language skills, based on a series of tests assessing fluency, grammar, and lexical/semantic knowledge, among which were the Cookie Theft Picture (from the Boston Diagnostic Aphasia Examination; Goodglass and Kaplan 1972), the Test of Reception of Grammar 2 (Bishop 2003), the British Picture Vocabulary Scale II (Dunn et al. 1997), and the Pyramid and Palm Trees Test (Howard and Patterson 1992). Using the 5% cut-off obtained from the control sample, the authors showed that 43% of the patients were classified as impaired in the composite language measure. Among the tests where patients mostly failed were the Test of Reception of Grammar (35%) and the British Picture Vocabulary Scale (49%). In parallel with the language assessment, the authors also ran an extensive assessment of executive functions, reporting that 31% of patients were impaired. Interestingly, although there was a significant correlation between language impairment and executive impairment, and executive scores accounted for 44% of variance in language scores, the two domains were to some degree distinct. The authors concluded that language and executive deficits do not always co-occur in ALS (see also Goldstein and Abrahams 2013).

Another study performing a broad language assessment is the one by Tsermenteli and colleagues, where a sample of 26 patients with ALS and controls was evaluated using syntactic and semantic tests as well as an examination of connected speech (Tsermentseli et al. 2016). Results indicated that patients' performance in some semantic tests was spared, such as single-word naming, but there were major deficits in other semantic tests (such as action/verb semantics) and in syntactic measures. They also found that syntactic measures discriminated between patients and controls and argued that syntactic difficulties are the predominant feature of the linguistic profile of ALS.

While some studies argue that syntactic impairment is predominant, the literature offers robust evidence of impairment in the semantic domain too. Studies focusing on lexical/semantic aspects showed that problems can affect naming, but also extend to semantic knowledge. For instance,

Leslie and colleagues evaluated lexical/semantic skills through a variety of tests (Leslie et al. 2014), and showed that approximately one third of a sample of 17 patients with ALS were impaired in the naming scores. The same frequency of impairment was also reported in semantic knowledge, which was calculated using non-verbal test scores (i.e. scores that required pointing responses) such as word comprehension and semantic association, thus minimizing the impact of dysarthria. These data indicate that semantic deficits are also common in ALS, and they are relatively independent of the severity of motor impairment. Interestingly, the study of Leslie et al. also included patients with ALS-FTD and with semantic dementia (SD), which allowed them to identify the following gradation of impairment: controls > ALS > ALS-FTD > SD. In all clinical groups, semantic deficits were associated with atrophy of the anterior temporal lobe, which is a region known for its pivotal role in semantic processes (Lambon Ralph et al. 2016).

17.3.3 Action Language

Because of the motor nature of the dysfunction in ALS, the literature has paid considerable attention to the domain of action language. The aim of studies in this area is to investigate whether patients with ALS are impaired in processing language that expresses actions, and whether this impairment is related to alterations of the motor cortex (Bak and Chandran 2012; Grossman et al. 2008). A series of studies of Bak and colleagues demonstrated that patients with ALS have more pronounced difficulties when dealing with action verbs than when dealing with objects nouns, as revealed through different tasks such as word-picture matching, naming from drawings, and picture-picture matching (Bak and Hodges 1997, 2004; Bak et al. 2001). Grossman et al. also offered neuroanatomical data, showing that the impairment in action words correlated with atrophy in the motor cortex (Grossman et al. 2008). Difficulties with verbs were reported also in production. For instance, Cousins and colleagues (2018) tested 28 patients with ALS in the Cookie Theft Picture description task and showed that, compared with matched controls, individuals with ALS produced less agent body verbs, i.e. verbs where the body is the agent of the action (e.g. “the boy is *stealing* the cookies”), but an equal amount of theme verbs, i.e. verbs where the body is the recipient of the action (e.g. “the boy is *falling*”). Moreover, this dissociation correlated with grey matter atrophy of the premotor cortex.

Papeo and colleagues, however, placed less significance on the claim of a specific problem in representing actions (Papeo et al. 2015). Indeed, Papeo et al. remarked that studies on nouns vs.

verbs have often confused grammatical and semantic aspects: by comparing nouns referring to objects and verbs referring to actions, what the literature showed might simply be a higher difficulty of verbs as a grammatical class, rather than of actions as a semantic domain. They argued that, if there is a specific difficulty in action representation in ALS, then the problem should arise not only with verbs but also with manipulable object nouns (e.g. *pen*). They tested 21 patients with ALS in a series of tasks involving action verbs and manipulable-object nouns and found that patients performed better with nouns than verbs. This speaks against a problem in action representation *per se*. Moreover, the noun-verb asymmetry was in the range observed in the normal population. Based on additional tests, the authors argue that the higher difficulty with verbs might be explained in terms of difficulty with the representation of the logical/temporal sequence of motor events, which belongs to the domain of executive functions. The debate on these aspects is of course still open, as it relates to the broader issue of grounded cognition, and the link between action and language.

17.4 Pragmatics in amyotrophic lateral sclerosis

Pragmatics in ALS has received very little attention from researchers to date. A search on Pubmed conducted in March 2019 using the keywords “amyotrophic lateral sclerosis” and “pragmatics” returned only two results. One is a paper by Bambini and colleagues (Bambini et al. 2016a). In this study, the authors performed a comprehensive assessment of pragmatic skills in ALS, using the Assessment of Pragmatic Abilities and Cognitive Substrates (APACS) test, a standardized tool for the evaluation of expressive and receptive pragmatics in Italian (Arcara and Bambini 2016). The other is a paper by Fisher and colleagues (Fisher et al. 2017), which deals with pragmatics in everyday communication and evaluated perceived communicative skills as assessed through the La Trobe Communication Questionnaire (see section 17.5). Searching for “amyotrophic lateral sclerosis” and a more specific pragmatic aspect, i.e. “figurative language”, returned again just one paper, the article by Bambini et al. (2016a). When we used “amyotrophic lateral sclerosis” and “discourse” as keywords, the search returned two other papers: Ash et al. (2014) and Roberts-South et al. (2012). Although these studies were not explicitly framed in a pragmatic perspective, they focused on expressive abilities in producing discourse, taking into account aspects that are often included in the pragmatic domain, such as measures of discourse coherence and informativity. The same searches with “motor neuron disease” did not return any other relevant paper. A search through other sources highlighted two other papers dealing with pragmatics: a paper by Strong et al. (1999) was retrieved in review articles on language in ALS (Orange and Hillis 2012; Pinto-Grau et al. 2018)

and includes the evaluation of discourse production; a paper by Staios et al. (2013) was found while examining the literature on social cognition in ALS (e.g. Strong et al. 2017) and is a study of sarcasm comprehension.

As is evident from the outcome of the search described above, i.e. six articles in total, the literature on pragmatics in ALS is still in its infancy and is more concerned with difficulties in production than in comprehension. Studies on production mostly applied discourse analysis to structured production tasks, often employing the Cookie Theft Picture description task (on the role of this task in identifying pragmatic markers of neurodegenerative diseases, see Cummings 2019), whereas comprehension was assessed through different types of comprehension questions. Moreover, the assessment of pragmatics was often accompanied by the evaluation of other linguistic and cognitive aspects. Albeit limited in number, these few studies consistently indicate that ALS is associated with impaired narrative expression and comprehension of non-literal meanings, possibly with an overall frequency of impairment – 36% based on Bambini et al. (2016a) – that is comparable to the one observed for language problems. Also, the available evidence suggests that pragmatic problems are dissociable from impairment in cognitive or socio-cognitive skills, and that they are to some extent distinct from impairment in structural language aspects (vocabulary and grammar).

17.4.1 The pragmatics of narrative and other discourse

In the study by Strong et al. (1999) – probably the first to consider pragmatics in ALS – a sample of 13 patients was evaluated at two different time points in order to characterize the neuropsychological profile of ALS longitudinally. Among the tests, patients were administered an interview task and the Cookie Theft Picture description task. The outcome of these tasks was evaluated in terms of discourse units, fluency, repetitions, self-corrections, and other conversational aspects. The study showed that, at the second time point, individuals with ALS produced significantly fewer self-corrective utterances compared with controls. Although not fully discussed by the authors and not considered in terms of pragmatics, this suggests altered discourse communication over time. Indeed, reduced self-correction and thus an increased presence of uncorrected errors has also been reported in other clinical conditions such as Alzheimer's disease and Parkinson's disease (McNamara et al. 1992).

More recently, a study by Roberts-South et al. (2012) assessed the description of the Cookie Theft

Picture over a period of 24 months in 16 non-demented patients with ALS and a group of matched controls. Several discourse measures were used, including discourse productivity measures (such as number of words and utterances), discourse efficiency measures (such as the number of correct information units, i.e. words that were intelligible in context, accurate in terms of picture/ topic content, and relevant to picture/topic content), and content units (different novel concepts used to describe the picture). Results showed that discourse efficiency was more vulnerable than discourse productivity. Although there were no differences between patients and controls in total words or total utterances, there were subtle differences in discourse content, with patients being less effective than controls in conveying content. The authors argued that a possible reason might be found in the high presence of revisions and reformulations (e.g. [He is] [she was climbing] she was reaching for a cookie), which was also compromised in the study by Strong et al. (1999), or the presence of "empty words" (e.g. The [thing] it is somewhat a [you know thing]), which did not contribute to content. Reduced discourse efficiency was observed at all time points, while there was no impairment in a range of standardized language measures (like vocabulary and grammar).

Difficulties in the pragmatics of narrative discourse also emerged in the Frog Story task, where participants are asked to tell the story in the children's picture book "Frog, where are you?" (Mayer 1969; see also Ash et al. 2006). Ash and colleagues showed the Frog Story to 26 patients with ALS and a sample of controls (Ash et al. 2014). The narratives were scored for local connectedness (paying attention to adverbials, referential expressions such as pronouns and determiners, and statements of cause and effect), global connectedness (whether the speaker acknowledges the point of the story, namely, that the frog found at the end is the frog that was present in the boy's room at the beginning), and maintenance of the story theme (i.e. searching for the frog). Differences between patients and controls were observed for local connectedness and for the maintenance of the story theme, but not for global connectedness. Although there was an association between narrative measures and executive scores, these differences were also observed in a subset of patients who did not have executive deficits. Moreover, the impairment was also observed in the subset of patients with no dysarthria. Thus, as shown in other studies, difficulties in discourse cannot be fully accounted for in terms of executive measures or motor impairments. The authors also investigated the neuroanatomical basis of discourse disruption. Local connectedness was associated with gray matter atrophy in right dorsolateral prefrontal and bilateral inferior frontal regions and with reduced fractional anisotropy in white matter tracts, specifically tracts mediating projections

between prefrontal regions. These data suggest that difficulties in discourse might be related to a disruption of the networks in the frontal lobes that are likely to support narrative abilities.

A later study by Ash et al. (2015) of the same sample of participants and with the same task (the Frog Story) focused on fluency and grammar rather than discourse. It showed that patients were less fluent (in terms of quantity of speech, speech rate, and speech articulation errors) and committed more grammatical errors compared with controls. Speech rate and articulation errors were related to motor impairment, while grammatical errors were independent of motor difficulty. The investigation of neuroanatomical aspects revealed that grammatical problems were related to gray matter atrophy in left inferior frontal and anterior temporal regions and to reduced fractional anisotropy in white matter tracts (superior longitudinal and inferior frontal-occipital fasciculi). These networks do not fully overlap with those reported in the Ash et al. (2014) study, thus pointing to some degree of segregation between the brain structures supporting structural language and those supporting pragmatics.

The data from the study by Bambini et al. (2016a) confirmed and extended findings of problems in the pragmatics of discourse in ALS, by offering evidence from other discourse tasks, namely the autobiographical interview and the description of everyday scenes. More specifically, Bambini and colleagues used the APACS test, which consists of one section devoted to the assessment of the production of pragmatics and one to the assessment of the comprehension of pragmatics (Arcara and Bambini 2016). Here, we will consider the outcome of the production section (see section 17.4.2 for the outcome of the comprehension part of the APACS).

The APACS production section includes an interview task and a description task. In the interview task, patients are asked to talk about autobiographical topics (family, house, job, daily routine) for a duration of 5-10 minutes, and then the outcome is annotated for the frequency of occurrence of several communicative difficulties. These difficulties mainly affect the pragmatic level of language, specifically informativity and information flow. As measures of informativity, the APACS considers instances of over- and under-informativity, i.e. inability to offer the appropriate amount of information and to adhere to the Gricean Maxim of Quantity. Measures of information flow include topic shifts, i.e. abrupt change of topic indicative of difficulties with the Gricean Maxim of Relevance and altered order of elements in the discourse. Measures of discourse cohesion (such as lack of

discourse referents) are also included. The frequency of communicative difficulties is then converted into a score. While the interview task aims at assessing the pragmatics of discourse, the description task aims at assessing communicative effectiveness more broadly, by measuring the ability to convey salient information. In the description task, patients are shown pictures of everyday situations and are asked to name the main elements, i.e. the agents, the actions, and the location, with the aim of evaluating the ability to identify and communicate salient information. For instance, one of the description items depicts a situation at the playground with children playing, and participants' descriptions are considered appropriate when the location (the playground), the main characters (the children), and the main action (playing) are spontaneously communicated. Scores focus on communicative effectiveness rather than on formal aspects (i.e. paraphasias are not counted as errors). Finally, a Pragmatic Production composite score is derived from the two production tasks (interview and description).

Bambini and colleagues reported data from 30 patients with ALS (after excluding three patients with dysarthria from the complete sample). They found that 12 patients (40%) were impaired in the Pragmatic Production score compared with the control sample: specifically, 14 patients (47%) were impaired in the interview task and 10 patients (33%) were impaired in the description task. Among all APACS tasks, the interview task was the one associated with the highest effect size in the group difference between patients and controls. Patients' speech was poorer than controls' speech in terms of informativity and information flow: patients were often over-informative, thus reducing thematic cohesion, and their narrative often lacked cohesion, with referents frequently missing. Table 17.1 shows an extract from an interview between an examiner (E) and A.S., a 61-year-old male participant (P) with ALS (A.S. is case 21 in Table 1 in Bambini et al. 2016a). A.S. has 11 years of education. He has limb onset, is 13 months post onset, and is rated 40/48 on the ALS Functional Rating Scale-revised form (Cedarbaum et al. 1999). Over-informativity and tangentiality are evident in turns 4, 10, and 12. Examples of missing referents are displayed in turn 10, with repetitive use of null-subject pronouns, not preceded by prominent discourse referents.

1	E: Com'è fatta la sua casa?	E: How is your house?
2	P: Ma io c'ho una casetta piccola eh. Due locali...	P: Well I have a small house eh. Two rooms...
3	E: Un appartamento?	E: An apartment?
4	P: Sì, due locali. Infatti nel bagno ho messo la doccia, che è più comoda eh. E poi l'ho personalizzata. Ah non c'ho... [cerca il telefono	P: Yes, two rooms. And in the bathroom I put the shower, which is more comfortable eh. Then I personalized it. Ah I don't have... [A.S. looks for

	nelle tasche, per mostrare una fotografia] se no le facevo vedere.	<i>the cell phone in the pocket, to show a picture] otherwise I would show.</i>
5	E: Non importa. Quante stanze ha?	E: It doesn't matter. How many rooms does it have?
6	P: Ma allora c'è la sala e la cucina. Sai che ho fatto il muretto per dividere. Poi c'è la camera da letto e il bagno. Saranno to'... sui cinquanta metri quadri, più o meno.	P: Well, there is the living room and the kitchen. You know I built a little wall to separate. Then there is the bedroom and the bathroom. It's probably... about fifty square meters, more or less.
7	E: Vive in un condominio?	E: Do you live in a condo?
8	P: Sì, è un condominio, brava, che non è grande eh, siamo noi e quelli..., si sta bene.	P: Yes, it is a condo, correct, which is not big eh, it's us and those... it's good.
9	E: A che piano è?	E: What floor is it?
10	P: Io? Piano terra, anzi menomale piano terra lì hanno sbagliato, mi han fregato eh. Han detto che mi facevano un pezzo di giardino. Sì me l'han fatto ma piccolo. Sarà... [si alza e mima lo spazio del giardino] Qui c'è la casa. Il giardino è così. Invece sulla mappa sai cos'era? Era due volte di più. E poi lì hanno detto che hanno sbagliato e ho dovuto accettar lo stesso... perché avevo firmato... va be'. Poi io...	P: Me? Ground floor, indeed thank goodness, ground floor, there they* made a mistake, they* fooled me eh. They* said that they* would do a piece of garden for me. Yes they* did it but small. It must be... [A.S. stands up and mimics the extension of the garden] Here's the house. The garden is like this. But do you know how it was on the map? Twice as big. And then they* said that they* made a mistake and I had to accept anyway because I had signed... whatever. Then I... <i>* indicates the use of null-subject pronouns in original Italian</i>
11	E: Eh... dica?	E: Yes... what?
12	P: Poi io essendo grafico così, io in un centimetro ci faccio stare un casino di sopra, perché io sfrutto veramente... Essendo grafico faccio le cose giuste. Se guardi quelli di sopra che c'hanno la casa come la mia...	P: Then since I am a graphic designer so, in a centimeter I fit lots of things because I exploit it really... Being a graphic designer I do the right things. If you look at the people upstairs who have the apartment like mine...
13	E: Non c'è paragone?	E: There is no comparison?
14	P: Si vede proprio la differenza	P: Yes, you really see the difference.

Table 17.1: Extract from the APACS interview task showing the discourse production of a patient with ALS

As in previous studies, Bambini and colleagues also explored the relationship between impairment in the pragmatics of discourse and executive functions. The latter were assessed with a battery of tasks including Phonemic Fluency (Carlesimo et al. 1995), Semantic Fluency (Novelli et al. 1986), the Wisconsin Card Sorting Test (Laiacina et al. 2000) and the Frontal Assessment Battery (Appollonio et al. 2005). Moreover, the authors also took into account the role of social cognition. This was evaluated with the Social Intelligence Battery (Prior et al. 2003), including measures of Theory of Mind, Normative Situations, Violations of Norms, and Appropriateness. A regression analysis

showed that 27% of variance in the Pragmatic Production composite score was explained by executive scores, whereas in another regression social cognition scores accounted for 20% of variance in the Pragmatic Production score. A combined analysis including both executive functions and social cognition showed that both predicted variance in Pragmatic Production (49% of variance in total), with a slightly higher effect size for executive functions than for social cognition. However, when looking at co-occurrence of deficits in different domains, no systematic association was found between pragmatic deficits and deficits in social cognition or executive functions. Specifically, only some of the patients with a deficit in Pragmatic Production were classified as impaired in executive functions or in social cognition. These findings suggest that executive function and social cognition skills are indeed linked to the ability to provide appropriate discourse in conversation. Executive functions possibly support aspects such as topic management (including avoiding repetitions and signaling topic shifts) and turn taking, whereas social cognition skills might help in understanding the interlocutor's perspective and informational needs. Yet, at least in ALS, pragmatic difficulties cannot be equated with dysexecutive behavior or social cognition impairment.

17.4.2 Inferring non-literal meanings and from texts

Information on receptive pragmatic abilities comes mainly from the study of Bambini et al. (2016a), and is based on the outcome of the comprehension section of the APACS test administered to 33 non-demented patients with ALS. This section of APACS includes four tasks: Narratives, which evaluates the ability to understand explicit and implicit aspects of narrative discourse; Figurative Language 1, which evaluates the ability to understand figurative expressions (idioms, metaphors, and proverbs) presented in a minimal context through multiple-choice questions; Humor, which also uses multiple-choice questions to assess the ability to understand humorous utterances; and Figurative Language 2, which differs from Figurative Language 1 in that the figurative expressions are presented out of context and the task is based on an open response format, asking participants to explain the meaning of the expressions. Finally, a composite score is derived from the four comprehension tasks, which is named Pragmatic Comprehension.

The study showed that patients with ALS performed worse than controls in all comprehension tasks. Focusing on figurative language understanding, patients were impaired both when assessed with the multiple-choice response format (Figurative Language 1 task) and when assessed with the verbal explanation response format (Figurative Language 2 task). The Figurative Language 2 task was more

difficult than the Figurative Language 1 task, as reflected in the higher effect size and higher frequency of the deficit: 9/22 (41%) patients impaired in Figurative Language 2 vs. 9/33 (27%) patients impaired in Figurative Language 1, based on the 5th percentile cut-off derived from the control sample (note that in Figurative Language 2 the N = 33 sample was reduced to N = 22 due to the exclusion of some patients for dysarthria or fatigue). The greater difficulty of the open response format has been observed in other clinical populations too (Arcara et al. 2019). It is probably due to the costs of planning and producing the response to the interlocutor, which increases the difficulty of inferring figurative meanings (Kalandadze et al. 2019).

The inspection of the responses given in Figurative Language 2 clearly shows the struggle of patients with ALS in organizing their responses and expressing abstract aspects of figurative meanings (see Table 17.2). Patients often repeated the target expressions and offered wrong (see example 1) or vague responses (see example 2) or used concrete examples to explain the figurative meaning of a proverb (example 3). The examples in Table 17.2 are taken from the responses of two participants with ALS. P.S. is a 70-year-old male participant with ALS (P.S. is case 26 in Table 1 in Bambini et al. 2016a). P.S. has 5 years of schooling. He has bulbar onset, 15 months of disease, and is rated 37/48 on the ALS Functional Rating Scale. Z.V. is a 72-year-old female participant with ALS (Z.V. is case 24 in Table 1 in Bambini et al. 2016a). Z.V. has 5 years of schooling. She has bulbar onset, 6 months of disease and is rated 43/48 on the ALS Functional Rating Scale.

Example 1, patient P.S.	E: "Certi ricordi sono spine".	E: "Some memories are thorns".
	P: Certi ricordi sono spine...	P: Some memories are thorns...
	E: Mhmmh	E: Mhmmh
	P: Perché... (tossisce)... la pace...	P: Because... [coughing]... the peace...
	E: Mi può ripetere, scusi?	E: Can you repeat please?
	P: Certi ricordi sono spine.	P: Some memories are thorns.
	E: Cosa vuol dire?	E: What does it mean?
	P: Sono falsi.	P: They are false.
	E: Sono falsi?	E: They are false?
	P: Mh sono spine.	P: Mh they are thorns.
Example 2, patient P.S.	E: "Certe voci sono trombe".	E: "Some voices are trumpets".
	P: Certe volte?	P: Some times? <i>[P.S. probably mistook the word 'voci' ('voices' in English) for 'volte' ('times' in English), as they both start with vo-]</i>
	E: "Certe voci sono trombe", cosa vuol dire?	E: "Some voices are trumpets", what does it mean?
	P: Eeh	P: Eeh
	E: Quando si dice quello è un	E: When one says "that guy is a big

	trombone...che cosa vuol dire?	trumpet"... what does it mean?
	P: Vuol dire che... ha un problema.	P: It means that... he* has a problem.
	E: Ok.	E: Ok.
Example 3, patient Z.V.	E: Allora, "L'abito non fa il monaco", cosa vuol dire?	E: So, "The vest does not make the monk", what does it mean?
	P: Per me sì.	P: For me yes.
	E: Che cosa vuol dire?	E: What does it mean?
	P: Eh il vestito fa il monaco... per esempio... le persone vestite bene.	P: Eh the vest makes the monk... for instance... well-dressed people.
	E: Cosa vuol dire in generale "L'abito non fa il monaco"?	E: What does it mean, in general, "The vest does not make the monk"?
	P: Se una persona è... giusta... messa bene, sta anche bene	P: If a person is... right... well dressed, also looks good.
	E: Ok.	E: Ok.
	P: Per me!	P: For me!

Table 17.2: Examples of responses of patients with ALS in the APACS Figurative Language 2 task

Other preliminary data by the same group (Bambini et al. 2018) showed that patients have more difficulties in understanding and explaining metaphors expressing mental characteristics (e.g. "Grandparents are pillars") than physical or behavioral characteristics (e.g. "Lifeguards are lizards"), which suggests that greater difficulties are experienced when dealing with more abstract contents. It is interesting to note that difficulties in ALS have also been reported in the domain of logical metonymy or aspectual coercion (Baggio et al. 2016), i.e. when linguistic elements trigger a shift in meaning, as in the case of temporal modifiers that change the meaning of a verb (for instance, the modifier "for two hours" in a sentence like "She repaired the TV for two hours" indicates an event which continued for two hours without conclusion). In a task where participants were asked to accept or reject sentences that involved aspectual coercion, patients with ALS exhibited an abnormally high acceptance rate compared with controls, i.e. patients accepted more instances of coercion than controls, likely due to a problem in representing the semantic and contextual constraints that govern the application of coercion. Although aspectual coercion does not strictly classify as pragmatic, these findings are indicative of difficulties in the broader domain of meaning shift and contextual adjustment that are not limited to figurative language.

Returning to the study by Bambini et al. (2016a), patients also failed in the Narratives task included in APACS. In this task, participants are orally presented with short stories that are similar to everyday news (e.g. about a robbery of a jewelry store or about commuters' protest at delayed train service). They are then asked questions about main or more detailed aspects of the texts, either explicit or

implicit. The frequency of impairment was 45% (15/33), indicating a widespread problem in text-based inferences. These difficulties in comprehending narrative discourse seem to correspond to difficulties in dealing with the production of conversationally appropriate discourse. This suggests that impairment of discourse is not linked to a specific modality but is 'overarching' (Grodzinsky et al. 1985), i.e. involving both expressive and receptive language.

Finally, patients exhibited difficulties in understanding humor, as assessed through the Humor task in APACS. This task includes seven items, each presenting a brief story that requires respondents to select the funny ending among three options: one humorous; one straightforward; and one a non-sequitur. For instance:

A man goes into an umbrella shop and sees that the price of an umbrella is 10 pounds. So he asks the shopkeeper: "What could I get for less?" And the shopkeeper replies:

Humorous ending: *"Wet."*

Straightforward ending: *"We don't have any umbrellas for less than that."*

Non-sequitur ending: *"It's nearly lunch time."*

In this task, A.S. (whose interview is reported in Table 17.1) selected the non-sequitur ending. He did the same for two of the other seven items. At group level, patients performed significantly worse than controls, with 7/33 (21%) showing impairment based on the 5th percentile cut-off derived from the control sample.

Sarcasm, which is considered a more aggressive form of ironic communication, is also a challenge for patients with ALS. In a study by Staios et al. (2013), participants were presented with the Social Inference-Minimal subtest of The Awareness of Social Inference Test (TASIT; McDonald et al. 2007). This consisted of video vignettes of actors producing sincere, sarcastic, or paradoxically sarcastic statements, followed by a series of yes/no questions about what the actor was doing, saying, thinking, and feeling. For instance, in one video the two actors have the following conversational exchange:

Michael: "Well, congratulate me!"

Gary: "What for?"

Michael: "I've got a date with Anne."

Gary: "Anne!"

Michael: "Come on, don't be jealous."

Gary: "Sure, I'm jealous"

And then the questions were presented, for instance, asking whether Gary thinks that dating Anne is a good thing. Patients with ALS did not differ from controls in answering questions about sincere statements, but they were impaired in answering questions about sarcastic and paradoxically sarcastic statements, with no differences between patients with bulbar and limb onset. The difference remained significant after controlling for executive skills. Interestingly, this study is framed in the context of social cognition, a domain which has been described as largely impaired in ALS (Bora 2017; Cerami et al. 2014). Indeed, the ability to understand humor, irony, and sarcasm is considered by some in pragmatic terms and by others in social cognition terms (Bischetti et al. 2019; Martin and McDonald 2003), which leads us to the next point, i.e. the relationship between pragmatics and other cognitive domains.

The study by Bambini et al. (2016a) also addressed the relationship between impairment in the domain of pragmatic comprehension and impairment in other cognitive domains. As observed for the pragmatics of discourse production (see section 17.4.1), results confirmed that several cognitive dimensions are related to impaired pragmatic comprehension but that these dimensions do not fully explain pragmatic comprehension difficulties. Regressions showed that 40% of variance in the Pragmatic Comprehension composite score was explained by executive scores, whereas social cognition (together with age) explained 63% of variance in pragmatic scores. A combined analysis including both executive functions and social cognition showed that only social cognition was a significant predictor of Pragmatic Comprehension. When examining co-occurrence of deficits in the different domains, no systematic association was found between deficits in Pragmatic Comprehension and deficits in social cognition or executive functions. These data are indicative of a strict relationship between pragmatic inferential skills and social cognition skills, although the two domains cannot be viewed as overlapping (see also Bosco et al. 2018), at least when considering a comprehensive pragmatic comprehension measure such as in APACS. Conversely, the role of executive skills in comprehending pragmatic aspects of language seems limited. Executive functions are less central for pragmatic comprehension compared to the role that they play in the domain of

pragmatic production.

17.5 From pragmatics to use: social communication and conversational patterns

The current section adopts a more ‘applied’ perspective, moving from the pragmatics of language – intended as the ability to produce adequate discourse and to infer implicit meanings – to the use of language in social communication by people living with ALS. While studies on the pragmatics of discourse described in earlier sections focused on linguistic characteristics such as informativity and coherence of speech, another relevant issue is how people with ALS use their pragmatic skills in everyday contexts and whether difficulties in pragmatics compromise daily communication. One tool that captures pragmatic skills as used in daily life and social communication is the La Trobe Communication Questionnaire (Douglas et al. 2000), a 30-item questionnaire of perceived verbal communicative abilities via self- and informant (e.g. a spouse) report. The La Trobe Communication Questionnaire assesses communicative behaviours and aspects related to the Gricean maxims, such as initiation/conversational flow (speak too slowly), disinhibition/impulsivity (speak too quickly), conversational effectiveness (give completely accurate information, in accordance with the Gricean Maxim of Quality), and partner sensitivity (hesitate, pause, or repeat yourself, thus contravening the Maxim of Manner).

Using this tool, Fisher and colleagues evaluated communicative skills in a sample of 32 patients with ALS without significant cognitive impairment and 24 healthy controls (Fisher et al. 2017). In addition, each participant nominated a close other (generally spouse, child or sibling) as informant. Self-reports did not reveal any difference between patients with ALS and controls. Within patients, results were similar for bulbar and limb onset subgroups and there was no effect of clinical variables. However, informants rated patients with ALS significantly lower than controls in communicative abilities, specifically in initiation, effectiveness and partner sensitivity (but not disinhibition). This indicates that patients with ALS do have difficulties in social communication related to pragmatic skills, and that they are mostly unaware of such difficulties.

Other studies have adopted a broader approach to communication, considering how people with ALS participate in a conversation and acknowledging aspects related to dysarthria and augmentative and alternative communication (AAC) strategies and technologies. As pointed out in Bloch and Tuomainen (2017), we cannot assume that unintelligibility automatically results in limited

interaction: despite poor speech sound intelligibility, some people with ALS remain interactive and participative in conversation thanks to AAC. Fruitful insights come from the use of conversation analysis, a qualitative approach that focuses on features of interaction (e.g. turn taking) and problems in talk (Bloch and Wilkinson 2009). For instance, by using conversation analysis to study the video-recorded natural conversation of two dyads with ALS over a period of 18 months, Bloch and Wilkinson (2009) were able to describe the main problems that recipients of dysarthric turns experience in everyday conversation with people with ALS. In some cases, recipients of dysarthric speech managed to identify the problem in a specific word in a prior turn and to fix it through repair in subsequent turns. In other cases, the problem was more complex, and the recipient could not identify the specific aspect in the dysarthric speaker's turn that was the source of the problem, which resulted in a longer repair sequence. Overall, these studies indicate that conversation in dysarthria is not simply a matter of intelligibility of single words, but rather it involves a fragile understandability, which must be closely monitored and negotiated between the conversational partners. Indeed, evidence also indicates that speech intelligibility does not predict the level of impairment in the interaction in a systematic way, suggesting that conversation contains elements that are not directly related to speech intelligibility but rather concern the patterns of the interaction (Bloch and Tuomainen 2017).

After seeing a range of pragmatic impairments and how these impairments affect everyday language and conversation, one should ask if all this in turn impacts patients' quality of life. There is indeed evidence, coming from a range of different clinical populations, that pragmatic language disorder and functional communication difficulties affect quality of life (Cummings 2014). For instance, the APACS total score is one of the predictors of quality of life scores in schizophrenia (Bambini et al. 2016b). Studies on more specific aspects of pragmatic competence also highlight a link between quality of life and discourse productivity (Bowie and Harvey 2008) and between quality of life and metaphor comprehension (Adamczyk et al. 2016; Bambini et al. 2019). Unfortunately, there are currently no studies of how pragmatics impacts quality of life in ALS. The only evidence of a relationship between language and quality of life concerns speech (Felgoise et al. 2016). By using the speech items of the ALS Functional Rating Scale, a popular measure of ALS severity that includes, among several other domains, the evaluation of speech in a range from 4 (normal speech) to 0 (loss of useful speech), the authors showed that there is a relationship between functional abilities for speech and quality of life (assessed with the ALS-Specific Quality of Life Questionnaire; Simmons et

al. 2006). Notably, not only individuals with complete loss of speech but also individuals with early symptoms of speech impairment rated their quality of life as significantly lower than individuals with no speech impairment, indicating that the impact of communicative difficulties on quality of life occurs early in the disease course.

17.6 Future research priorities

Several priorities for future research are suggested by this discussion. The first priority is there is a pressing need to undertake more research on pragmatics in ALS and to conduct studies of larger samples of participants. This research should attempt to define more clearly the pragmatic profile of people with ALS, the incidence of pragmatic language disorder in ALS, the progression of pragmatic disorder and the presence of co-morbid symptoms. Further studies are also needed to define the role of pragmatic impairment in the ALS-FTD spectrum. Most studies considered in this review included individuals with ALS who did not meet criteria for dementia. However, there is also evidence of pragmatic difficulties in FTD (especially the behavioral variant), including the domains of discourse (Ash et al. 2006; Rousseaux et al. 2010), non-literal language (Orange and Hillis 2012), pragmatic inference from scalar terms (Spotorno et al. 2015), humor (Clark et al. 2015) and sarcasm (Rankin et al. 2009). Research is needed to compare the profile of pragmatic language disorder in ALS (distinguishing also its sub-phenotypes) to that of ALS-FTD and pure FTD. This is consistent with the view of Roberts et al. (2017) who argue that “there is a growing imperative to develop cohesive and comprehensive profiles of pragmatic performances in non-AD dementia” which has for a long time been “plagued by disease heterogeneity, complexity of symptoms, as well as a myriad of diagnostic assessment protocols” (p. 348).

To better clarify patterns of pragmatic decline in ALS and in the ALS-FTD spectrum, the use of standardized tools for pragmatic evaluation is desirable. The diagnostic criteria of Strong et al. (2017) recommend a series of tests including the Pragmatic Protocol (Prutting and Kirchner 1987), the Lille Communication Test (Rousseaux et al. 2001), various picture description tasks such as the Picnic Scene from the Western Aphasia Battery (Kertesz 1982), as well as the APACS test. We support the recommendation to adopt standardized tests and we also highlight that the use of APACS has several advantages. First, it allows for comparisons with other clinical populations, since the test has been used to describe pragmatic language disorder across a wide range of conditions (Arcara et al. 2019; Bambini et al. 2016b; Carotenuto et al. 2018a). Second, the choice of APACS

allows for cross-linguistic and cross-national studies and comparisons – a highly relevant issue in the field of aphasia (Beveridge and Bak 2011; Menn et al. 1996) and pragmatic disorder (Ferr et al. 2012). Indeed, the APACS test, originally developed in Italian, has been adapted and validated in other languages, such as Russian (Tomas et al. in preparation) and Flemish (Schaeken et al. in preparation), and projects involving other languages are in progress.

The second priority for future research is that studies of pragmatics in ALS should also assess the impact that pragmatic impairment might have on quality of life. This would make it possible to devise strategies to help patients cope with those pragmatic difficulties that have the most adverse impact on daily functioning and social life. Communicative difficulties in ALS are not just speech difficulties (Bloch and Tuomainen 2017) and, although we know very little about them, pragmatic difficulties are likely to play a prominent role in the quality of communication and social relationships of people with ALS. Conversation analysis, which provides a naturalistic evaluation of conversation, could nicely complement other assessment tools and help provide a more accurate description of pragmatic symptoms in daily life in order to direct intervention (Bloch and Wilkinson 2009). We know that the relationship between communication difficulties and quality of life is not linear in ALS and that the early phases of disease have the greatest impact on well-being (Felgoise et al. 2016). It is thus key that communication intervention is provided as early as possible in the course of disease (Woolley and Rush 2017), that it anticipates, prepares for, and adapts to communicative changes (Judge et al. 2018), and that it includes family members and care providers. Technological aids such as augmentative and alternative communication should be considered too, as part of a complex support process (Judge et al. 2018) that extends beyond unintelligible speech to pragmatic difficulties.

A third priority for future research is that pragmatics in ALS should also be linked with theory. Research in this field not only allows for better clinical assessment and improved treatment for patients and their caregivers, but also sheds light on theoretical issues such as the connections between motor systems (especially pyramidal) and cognitive and language skills that were once considered to be unrelated to motor function. Studies on communication in ALS can thus generate new perspectives in research into human brain evolution and the relationship between motor function and social life in human beings.

17.7 Summary

Today, it is well established that there are language difficulties in ALS, affecting especially grammar and lexical/semantic knowledge. Additionally, there is initial evidence that language difficulties in ALS might also affect pragmatics. Pragmatic language disorder in ALS includes deficits in the content and organization of narrative and other discourse, and impaired comprehension of non-literal meanings, with these difficulties extending to social communication and daily conversation. While data for ALS are limited, it seems that pragmatic language disorder cannot be fully accounted for in terms of executive function and social cognition impairments, although these cognitive domains do show some association with pragmatics. As pointed out in the consensus criteria (Strong et al. 2017), it is possible that language impairment, including pragmatic impairment, 'may both contribute to the profile of ALS and also occur as part of a mixed cognitive profile that includes executive function impairments or social cognition impairments' (p. 7). As for neural substrates, the available evidence indicates that disruption of networks in the frontal lobes, specifically the dorsolateral prefrontal cortex and inferior frontal cortex bilaterally, might underlie difficulties in discourse production in ALS. There are no studies investigating the neural underpinnings of pragmatic comprehension difficulties in ALS. Based on what has been reported for other neurodegenerative diseases (Carotenuto et al. 2018b), it is likely that global pragmatic impairment in ALS is associated with damage to large-scale connections involving both hemispheres and extending beyond frontal to temporo-parietal regions.

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BIOGRAPHICAL NOTES

Valentina Bambini is Associate Professor of Linguistics at the University School for Advanced Studies IUSS Pavia, Italy. She earned her PhD at Scuola Normale Superiore of Pisa with a dissertation investigating the neural basis of metaphor comprehension. Her research interests lie in the fields of experimental pragmatics and neuropragmatics, focusing on the cognitive and neural underpinnings of communicative abilities, both in healthy individuals and in individuals with pathological conditions. Among her works, she has developed the Assessment of Pragmatic Abilities and Cognitive Substrates (APACS), a test of pragmatic language disorder in clinical populations. She is currently working on novel training programs to promote pragmatics across the lifespan and in patients.

Mauro Ceroni is Associate Professor of Neurology at the University of Pavia in Italy and head of the General Neurology Department at the National Neurological Institute Mondino Foundation of Pavia. Following four years of research in the field of prion diseases at the Nobel Prize Gajdusek Laboratory at the National Institutes of Health in Bethesda, USA, he started in the nineties the experimental Neurobiology Laboratory at the Mondino Foundation. In the last 10 years, he established the ALS out-patient center at Mondino Foundation, which provides full assessment and care for about 100 patients with ALS.

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Assessment of Pragmatic Abilities and Cognitive Substrates (APACS)

conversation

discourse

dysarthria

figurative language

fronto-temporal dementia (FTD)

non-literal language