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Communication and pragmatic breakdowns in amyotrophic lateral sclerosis patients

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ABSTRACT

While there is increasing attention toward cognitive changes in amyotrophic lateral sclerosis (ALS), the domain of pragmatics, defined as the ability to integrate language and context to engage in successful communication, remains unexplored. Here we tested pragmatic abilities in 33 non-demented ALS patients and 33 healthy controls matched for age and education through 6 different tasks, ranging from discourse organization to the comprehension of figurative language, further grouped in three composite measures for pragmatic production, pragmatic comprehension and global pragmatic abilities. For a subgroup of patients, assessment included executive functions and social cognition skills. ALS patients were impaired on all pragmatic tasks relative to controls, with 45% of the patients performing below cut-off in at least one pragmatic task, and 36% impaired on the global pragmatic score. Pragmatic breakdowns were more common than executive deficit as defined by the consensus criteria, and approximately as prevalent as deficits in social cognition. Multiple regression analyses support the idea of an interplay of executive and social cognition abilities in determining the pragmatic performance, although all these domains show some degree of independence. These findings shed light on pragmatic impairment as a relevant dimension of ALS, which deserves further consideration in defining the cognitive profile of the disease, given its vital role for communication and social interaction in daily life.

1. Introduction

Research in the last decades has radically modified the traditional view of amyotrophic lateral sclerosis (ALS) as a pure motor neuron disease, leading to the recognition of cognitive and behavioral changes as an integral feature of the disease, in addition to motor manifestations (Goldstein & Abrahams, 2013; Phukan et al., 2012). Several studies indicated that cognitive impairments affect approximately 50% of the ALS population, with a spectrum ranging from pure motor disorders to dementia, most often of the fronto-temporal type (Bennion Callister & Pickering-Brown, 2014; Consonni et al., 2013; Montuschi et al., 2014). In this continuum, a large proportion of non-demented ALS patients (approximately 30%) have cognitive dysfunctions, predominantly dysexecutive syndrome, with the earliest and most commonly reported signs consisting in deficit in verbal fluency, followed by other features, such as disturbances in problem solving, attentional control and reasoning.

In addition to the executive deficit, impairments in social cognition are frequently reported in ALS (Abrahams, 2011). Patients perform poorly in processing emotions and in attributing emotional and cognitive states to others, as assessed through a variety of tasks of different complexity, from eye-gaze to cartoon stories and social decision making (Cecchetto et al., 2014; Cerami et al., 2014; Palmieri et al., 2010; van der Hulst, Bak, & Abrahams, 2014). Notably, impairments in social cognition seem to be more diffuse and possibly dissociated from executive dysfunction (Girardi, Macpherson, & Abrahams, 2011).

Other studies have investigated linguistic aspects, both in production and comprehension. Independently of speech articulation problems, patients might have impaired sentence grammar (Ash, Olm et al., 2014) and single word processing (Leslie et al., 2014), especially for verbs as compared to nouns (Bak & Hodges,

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2004; Papeo et al., 2015). Impaired performance in an extensive battery of tests assessing different aspects of language processing has been reported in about 40% of the non-demented ALS population (Taylor et al., 2013). Executive deficit does not fully account for these linguistic breakdowns, similarly to what observed for social cognition (Abrahams, 2013).

While deficits in executive functions, social cognition and selected aspects of language are well documented, one domain that is nearly unexplored in ALS is pragmatics, i.e. the ability of integrating language and context for the purpose of the communicative exchange (Bambini, 2010; Bambini & Bara, 2012). When used in naturalistic environments and social interaction, language is more than coding and decoding words and sentences, and involves the recognition of the speaker's communicative intention based on contextual clues, as well as engaging in contextually appropriate discourse and conversation (Grice, 1975; Sperber & Wilson, 1995). The complexity of these processes becomes especially evident in language uses that massively exploit context, such as non-literal language. A large amount of research in neuropragmatics has documented deficits in dealing with contextual aspects of language, first described in right-hemisphere brain damaged patients, and later observed in many clinical populations, including different forms of dementia, schizophrenia and autism (Bambini & Bara, 2012; Stemmer, 2008). Despite relatively intact abilities in formal aspects of language (i.e. word and sentence processing), these patients typically have difficulties in understanding metaphors and idioms, in deriving ironic and humoristic nuances, in producing discourse that stays on topic and is appropriate to the conversational context, all which makes communication with familiars and proxies especially difficult.

There are several reasons to hypothesize a pragmatic impairment in ALS. First, failures in organizing discourse (Ash et al., 2006; Roberts-South, Findlater, Strong, & Orange, 2012) and in comprehending non-literal expressions such as metaphors (Orange & Hillis, 2012) have been reported in fronto-temporal dementia (FTD). Given the notion of an FTD–ALS spectrum (Bennion Callister & Pickering-Brown, 2014), it is not surprising that discourse analysis has revealed similar modifications in the speech produced by ALS patients (Ash, Menaged et al., 2014), and impairment is likely to extend to other pragmatic domains.

Second, although to a degree that varies between different clinical populations, pragmatics seems to be connected to other cognitive abilities, especially social cognition and executive functions (Martin & McDonald, 2003), that are known to be impaired in ALS. For instance, the association between pragmatics and social cognition is especially evident in tasks that involve the interpretation of linguistic materials based primarily on intention attribution, such as sarcasm detection. In similar tasks, patients with behavioral variant of FTD perform poorly (Kipps, Nestor, Acosta-Cabronero, Arnold, & Hodges, 2009; Shany-Ur et al., 2011), and so do ALS patients (Staios et al., 2013). Impairments in ALS might extend also to other pragmatic tasks that capitalize on social cognition abilities. As for executive functions, they form a system that coordinates behavior and enables individuals to use their cognitive abilities in a flexible manner through different situations, which represents an important platform for adapting to the communicative context of the ongoing conversation (Martin & McDonald, 2003). The dysexecutive syndrome observed in ALS might thus be associated to pragmatic impairment as well.

Third, anatomical basis of pragmatics are also compatible with descriptions of structural and functional abnormalities in ALS. Pragmatic abilities are supported by frontal and temporal networks in both hemispheres. In addition, pragmatics engages mentalizing regions such as the medial prefrontal cortex and the temporo-parietal junction (Catani & Bambini, 2014; Hagoort & Levinson, 2014). Functional neuroimaging in ALS has frequently described frontotemporal dysfunction in relation to dysexecutive deficit (Tsermentseli, Leigh, & Goldstein, 2012), as well as malfunctioning in dorsolateral and medial prefrontal cortex (Girardi et al., 2011), including alteration of functional asymmetry (Palmieri et al., 2010), possibly related to emotional and social cognition deficits. Other studies have reported reduction of white matter integrity in the frontal, temporal and parietal lobes, including frontotemporal-limbic connections important for social cognition (Crespi et al., 2014). Given this pattern of impairment, the circuits underlying pragmatics may be affected as well.

The primary aim of this study was to explore for the first time the domain of pragmatic abilities in non-demented ALS patients, with the ultimate goal of contributing to the description of the cognitive profile of the disease in order to include this important domain of language and social interaction. Secondly, we aimed at investigating the relationship between pragmatic behavior and performance on executive functions and social cognition tasks. Based on previous evidence on pragmatic impairment in FTD and given the notion of ALS–FTD continuum, we hypothesized that pragmatic deficit might affect a large percentage of non-demented ALS population. Finally, we hypothesized that this impairment might be intertwined with social cognition and dysexecutive deficits.

2. Materials and methods

2.1. Participants

The patient group consisted of thirty-three non demented sporadic ALS patients (13 females; mean age, years ± standard deviation: 63.30 ± 9.64; mean education: 9.79 ± 4.61) recruited through the General Neurology Department of National Neurological Institute 'Casimiro Mondino', Pavia. All of them were native speakers of Italian and had a diagnosis of probable or definite ALS based on Revised El Escorial Criteria (Brooks, Miller, Swash, & Munsat, 2000) and electrodiagnostic criteria (de Carvalho et al., 2008). None of the patients met consensus criteria for diagnosis of frontotemporal dementia (Neary et al., 1998). Other exclusion criteria were major comorbid medical, neurological or psychiatric history. Patients scored 34.85 ± 8.83 (range 0–48) on the ALS Functional Rating Scale (Cedarbaum et al., 1999). Disease onset frequencies were as follows: bulbar ($n = 8$; 24.24%), limb ($n = 25$; 75.76%), consistent with typical phenotype frequencies. Mean disease duration, defined as $\text{date}_{\text{time examination}} - \text{date}_{\text{start ALS symptoms}}$ was 25.61 ± 18.99 months. See Table 1 for the population details.

The control group consisted of thirty-three neurologically healthy adults (18 females; mean age: 61.24 ± 6.66; mean education: 10.97 ± 4.34), all native speakers of Italian. The ALS patients and the controls did not significantly differ in terms of age ($p = 0.32$) or years of education ($p = 0.29$).

The study was approved by the local Ethics Committee. Informed consent was obtained from all participants in accordance with the principles of the Declaration of Helsinki.

2.2. Pragmatic assessment

Pragmatic abilities were assessed in ALS patients ($n = 33$) and in controls ($n = 33$) through a novel test (APACS, Assessment of Pragmatic Abilities and Cognitive Substrates) combining different pragmatic tasks that are widely used in the literature, with refined linguistic materials in Italian, and in a unified framework inspired by language pragmatics (Grice, 1989; Sperber & Wilson, 1995). Two pragmatic domains were targeted, namely discourse and non-literal meanings, as they are widely impaired in clinical conditions. Special care was taken to preserve the contextual validity of the linguistic materials, and to control for psycholinguistic

Table 1
Characteristics of patients in the ALS group.

Case	Sex	Age (ys)	Education (ys)	Onset site	Testing post onset (months)	ALS-FRSr scale
1	M	77	5	b	12	22
2	M	67	13	l	77	39
3	M	71	18	l	52	36
4	M	74	10	l	2	38
5	M	56	8	l	18	35
6	F	58	13	l	15	47
7	M	42	18	l	75	34
8	M	79	5	l	10	37
9	F	68	8	b	27	23
10	F	71	8	l	39	43
11	M	63	13	l	48	34
12	F	62	8	l	39	38
13	M	67	6	l	37	33
14	F	66	10	l	30	7
15	M	63	8	l	20	40
16	M	66	5	l	20	39
17	F	63	8	l	5	21
18	M	65	5	l	22	43
19	M	65	13	l	38	30
20	F	71	5	l	12	23
21	M	61	11	l	13	40
22	M	56	10	l	20	29
23	F	72	5	b	42	34
24	F	72	5	b	6	43
25	F	65	13	b	24	43
26	M	70	5	b	15	34
27	M	62	10	l	40	23
28	F	38	15	b	9	45
29	F	57	5	b	11	38
30	F	49	18	l	41	45
31	M	48	21	l	8	30
32	M	51	13	l	10	44
33	M	74	5	l	8	40

b = bulbar onset; l = limb onset.

variables. The test is divided into two main sections, devoted to production and comprehension, with further articulation, for a total of 6 tasks. The pragmatic test was administered to patients and healthy controls by trained clinicians or by research assistants, in a single session lasted approximately 40 min. Scores were assigned after consultations with the linguists of the teams for the most problematic cases.

Task 1: Interview (production section)

This task aims at assessing the ability of engaging in conversation though a semi-structured interview, organized around four autobiographical topics: family, home, work, organization of the day, known to be suitable topic to enhance speech (Borovsky, Saygin, Bates, & Dronkers, 2007). The discourse produced by the subject is assessed according to a checklist including the main parameters of discourse analysis, based on previous approaches to pathological speech (Marini, Andreetta, del Tin, & Carlomagno, 2011; Prutting & Kirchner, 1987). Several dimensions of discourse are rated for the presence of communication difficulties at the contextual–pragmatic level: speech (e.g., repetition, incomplete utterances, echolalia), informativeness (over- or under-informativeness, loss of verbal initiative), information flow (missing referents, wrong order of the discourse elements, abrupt topic shift), including the paralinguistic dimension (e.g., altered intonation, loss of eye-contact, fixed facial expression, abuse of gesture). Also errors in grammar and vocabulary are annotated, as they impact on the communicative effectiveness of the discourse. All these aspects are assessed on line during the interview. The frequency of each communication difficulty is annotated (always/sometimes/never) and then converted into scores (0/1/2). Maximal score: 44.

Task 2: Description (production section)

This task aims at assessing the ability of producing informative descriptions and sharing information about everyday life situations. Compared to the Interview task, here expressive abilities are measured through a more structured task, similar to traditional picture description task, but still with ecological validity. Ten photographs that depict scenes of everyday life (e.g. a woman waiting at the bus station, a man buying a newspaper in a shop) are presented one by one. The subject is asked to describe the photograph in relation to the main elements that characterize the scene (the location, i.e. the so-called "scene setting topic", the agent and the action performed). For each salient element in each picture, a score is assigned differentiating missed identification, partially correct identification, correct identification (0/1/2). Maximal score: 48.

Task 3: Narratives (comprehension section)

This task aims at assessing the ability to comprehend discourse and the main aspects of a narrative text. 6 stories were built, inspired by real newspaper and TV news, with increasing length (number of sentences ranging from 4 to 8), and complexity set on a medium difficulty level for subjects with 8 years of schooling, scoring on average 58.5 on the Gulpease readability index (range 0–100) (Lucisano & Piemontese, 1988). Each story includes two non-literal expressions. Stories are read to the subject at normal rate. Following each story, several question items are administered:

- an open question about the global topic of the story, rated 1 when correctly answered or 0;
- 2–4 yes/no questions on specific elements of the text, either main or detail, either stated or implied, as in previous story comprehension tasks (Ferstl, Walther, Guthke, & von Cramon, 2005), rated 1 when correctly answered or 0;
- 2 questions on the non-literal expressions embedded in the story, requiring a verbal explanation, rated 2, 1 or 0, based on the accuracy of the explanation, as described below for Figurative Language 2. Maximal score: 56.

Task 4: Figurative language 1 (comprehension section)

This task aims at assessing the ability to infer non-literal meanings through multiple choice questions, similarly to existing tests (Rinaldi, Marangolo, & Lauriola, 2004). Fifteen sentences are presented, selected from available databases, with different degrees of lexicalization, including: 5 highly familiar idioms, average familiarity 6.36 on a 7 point scale, based on existing norms (Tabossi, Arduino, & Fanari, 2011); 5 novel metaphors, average familiarity 3.78 on a 5 point scale, based on existing ratings (Bambini, Ghio, Moro, & Schumacher, 2013); 5 common proverbs extracted from a dictionary of Italian proverbs (Guazzotti & Oddera, 2006). All sentences are provided with a minimal context. For each sentence, three possible interpretations are presented and the subject is asked to choose the one that correctly expresses the figurative meaning. For metaphors (e.g. "Ho appena visto una corsa di formula uno. Certe automobili sono frecce", tr. "I have just seen a F1 match. Some cars are arrows"), the options include: a correct, figurative interpretation, which expresses a salient property of the metaphorical word (e.g. "Certe automobili sono veloci", tr. "Some cars are fast"); an incorrect, literal interpretation, which expresses a property of the metaphorical word yet not salient in the context (e.g. "Certe automobili sono appuntite", tr. "Some cars are pointy"); another incorrect interpretation expressing a property of the sentence subject (e.g. "Certe automobili sono lussuose", tr. "Some cars are luxurious"). Each item is scored either 1 or 0 according to the accuracy. Maximal score: 15.

Task 5: Humor (comprehension section)

This task aims at assessing the ability to comprehend verbal humor through multiple choice questions, inspired by the Joke and Story Completion Test (Brownell, Michel, Powelson, & Gardner, 1983). The materials consist of 7 items, each presenting a brief story. For each story, three possible endings are provided, including: a correct funny ending; an incorrect straightforward non-funny ending; an incorrect unrelated non-sequitur ending. Correct funny endings either play with literal and polysemous meanings, or require to derive non explicit, unexpected scenarios (Yus, 2008). The subject is asked to select the ending that best functions as punchline of the story. Each item is scored either 1 or 0 according to the accuracy. Maximal score: 7.

Task 6: Figurative Language 2 (comprehension section)

This task aims at assessing the ability to infer non-literal meanings through verbal explanation, similar to previous tests (Amanzio, Geminiani, Leotta, & Cappa, 2008; Papagno, Cappa, Forelli, Garavaglia, & Al, 1995). The materials were selected as for the Figurative Language 1 task, and consist of 15 sentence, including: 5 highly familiar idioms (average familiarity 6.52), 5 novel metaphors (average familiarity 3.88), and 5 common proverbs listed in the dictionary. The subject is asked to explain the meaning of each expression. Responses score 2 when the subject provides a good description of the actual meaning of the figurative expression, 1 when the subject provides an incomplete explanation, such as a concrete example, but fails in providing a general meaning, 0 when the subject paraphrases the figurative expression, provides a literal explanation, or ignores the expression. Maximal score: 30.

2.2.1. Composite pragmatic measures

Three composite pragmatic scores were computed from the pragmatic tasks. The Pragmatic Production score was calculated from Interview and Description tasks, whereas the Pragmatic Comprehension score was calculated from Narratives, Figurative Language 1, and Humor tasks.[1] Each composite score was obtained transforming the original task scores in proportion, and averaging these proportions. Hence, each task contributed with equal weight to the final composite score, which ranged from 0 to 1. Moreover, the APACS Total was calculated as average of Pragmatic Production and Pragmatic Comprehension scores, to provide a global measure of pragmatic ability. These composite scores can be useful to classify patients according to a general notion of pragmatic abilities as well as to describe the global status of pragmatic impairment for clinical purposes.

2.2.2. Additional linguistic assessment

In addition, to diagnose aphasic impairment in language comprehension, a shortened version of the *Token Test* (De Renzi & Faglioni, 1978) was administered, scored as in the Token Test section included in the Italian version of the Aachener Aphasie Test (Luzzatti, Willmes, & De Bleser, 1991) (score range: 0–32).

2.3. Assessment of executive functions

A subgroup of ALS patients ($n = 21$) underwent a battery of standard neuropsychological tests to provide background information about their cognitive and behavioral profile. Tests were administered by a trained neuropsychologist, blind to the purpose of the study. For the purpose of the present investigation, we followed the previous literature in selecting 4 measuring executive functioning, in their Italian version: *Phonemic Fluency* (Carlesimo et al., 1995); *Semantic Fluency* (Novelli et al., 1986); *Wisconsin Card Sorting Test* (WCST) (Laiacona, Inzaghi, De Tanti, & Capitani, 2000); *Frontal Assessment Battery* (FAB) (Appollonio et al., 2005).

2.4. Assessment of social cognition

A subgroup of ALS patients ($n = 19$) were also tested for social cognition abilities, by using tests included in the Italian version of the Social Intelligence Battery (Prior, Sartori, & Marchi, 2003), adapted from (Blair & Cipolotti, 2000). Specifically, the following tests were administered:

- *Theory of Mind Task*, which involves the participant reading 13 stories describing social situations and being asked about why the characters behaved as they did (maximal score:13);
- *Social Situations Task*, where 25 stories describing social situations incorporating a behavior that was either normative or a violation were read by the patient. At various points in each story the patient was asked to comment on how appropriate the behavior was. Three scores are obtained for this tasks: *Normative situations* (maximal score: 15), referring to the number of normative situations correctly identified; *Violations of norms* (maximal score: 25) referring to the number of violations correctly identified; *Appropriateness* (maximal score: 75), referring to the extent to which the patient judged the violations to be socially inappropriate.

3. Data analysis

The scores on each pragmatic task (Interview, Description, Narratives, Figurative Language 1, Humor, Figurative Language 2) and the three composite pragmatic scores (Pragmatic Production, Pragmatic Comprehension, APACS total) were compared between the ALS patients ($n = 33$) and the controls ($n = 33$) by means of separate independent sample *t*-tests. Cohen *d* was employed as effect size measure. The scores in each pragmatic task and the two composite pragmatic scores obtained by ALS patients with bulbar onset ($n = 8$) or limb onset ($n = 25$) were also contrasted. To account for variance inequality Welch *t*-tests were used. All *p*-values associated with the *t*-tests were corrected with Bonferroni method after grouping the comparisons in four groups: production tasks (Interview, Description), comprehension tasks (Narratives, Figurative Language 1, Humor, Figurative Language 2), and composite scores (Pragmatic Production, Pragmatic comprehension, APACS total). The Token Test was analyzed separately and was not corrected with Bonferroni method.[2]

To determine the prevalence of a pragmatic deficit in our ALS sample, individual data were compared to cut-off scores,

[1] The Figurative Language 2 task was not included in the computation of the Pragmatic Comprehension score because of the relatively high number of missing values in the ALS sample. There are two possible reasons for the missing data: first, 3 patients were excluded due to dysarthria (see Note 2) and second the administration of the APACS test was interrupted when fatigue became apparent. Importantly, the inclusion of available Figurative Language 2 data in the Pragmatic Comprehension composite score would presumably increase the difference between ALS patients and controls, given the very low scores obtained by the patients who completed the task (see Fig. 1, panel A) and the overall high number of patients performing below cut-off (see Fig. 1, panel B).

[2] As suggested in the consensus criteria (Strong et al., 2009), measures were controlled for motor dysfunctions (dysarthria) and motor weakness. Accordingly, the Interview and Description tasks were not administered to 3 patients with severe dysarthria. These patients were also not administered with Figurative Language 2, which, although testing comprehension of figurative expressions, requires a verbal explanation. For these patients, the Pragmatic Production composite score was not available. As for Figurative Language 2, this was excluded from the computation of the Pragmatic Comprehension composite score (see Note 1). The Token Test was not administered to 8 patients, due to the severity of motor impairment.

calculated as the 5th percentile of scores in the control sample. Separate cut-offs were calculated for each pragmatic task and for the three composite pragmatic scores.

Further analyses were run on the ALS patients group, considering their performance in both the pragmatic scores and other neuropsychological task scores, namely executive functions and social cognition. These analyses were run on subsample of the whole ALS group, according to the available data sample.

The association between executive functions and pragmatic abilities in ALS was investigated in a subsample of patients ($n = 21$) in two different ways. First, the co-occurrence of a deficit in executive functions and a deficit in pragmatic abilities was analyzed by means of Fisher's exact tests on contingency tables. Executive deficit was defined according to the consensus criteria (Strong et al., 2009), i.e. a performance below cut-off on at least two of the tests tapping on executive abilities (Phonemic Fluency, Semantic Fluency, Wisconsin Card Sorting Test, and Frontal Assessment Battery). Pragmatic deficit was defined as a performance below cut-off in the composite pragmatic scores (Pragmatic Production and Pragmatic Comprehension), considered separately.

Second, the relationship between executive abilities and pragmatic performance was explored by means of multiple regression modeling. In this analysis all the executive functions measures, together with age and education, were entered as predictors in a linear regression model with pragmatic scores as dependent variables. Two separate models were fit, one for the Pragmatic Production and one for the Pragmatic Comprehension composite scores. Predictors were standardized before entered in the analysis to improve fit procedure. Before running the regression analysis the potential presence of harmful collinearity across predictors was checked. The condition number k characterizing the collinearity across predictors was 4.23, widely below the threshold of 30, which indicates a harmful collinearity (Baayen, 2008). The preliminary analysis on collinearity ensured that none of the predictors was excessively correlated with the others, and thus that every predictor could be included in the regression. Starting from a null model including only an intercept, variables were added to the model by means of a stepwise forward method that took into account the Akaike Information Criterion (AIC). Predictors were added one at the time, starting from the one whose inclusion leads to the model with best AIC. We a priori decided to stop the predictor inclusion after the first two significant predictors, since with 22 participants we considered that the estimate of regression coefficients would be acceptable with two predictors at maximum. This choice was based on the rule-of-thumb of one predictor for each 10–20 participants (Harrel, 2015). However in no cases more than two predictors resulted significant in the forward selection. After this procedure, predictors whose p-values were above 0.05 were excluded, starting from the one with the highest p-value. Each final regression model included only the significant variables that best accounted for the dependent variable. The percentage of explained variance was calculate as adjusted R^2.

The association between social cognition and pragmatic abilities was analyzed in a subsample of patients ($n = 19$) in the same fashion as the analysis of executive functions. First, we investigated the co-occurrence of a deficit in social cognition abilities and a deficit in pragmatic abilities. Social cognition deficit was defined as a performance below cut-off in at least one of the obtained measures (Theory of Mind, Normative Situations, Violations of Norms, Appropriateness), whereas a pragmatic deficit was defined as a performance below cut-off in the Pragmatic Production and Pragmatic Comprehension composite scores, considered separately. Second, the relationship between scores in social cognition tests and the two composite pragmatic measures was analyzed by means of multiple regression. The collinearity across predictors was below the threshold of harmful collinearity ($k = 3.4$). All the scores in social cognition measures, together with age and education, were included as potential predictors and the same modeling procedure as for executive functions was adopted (see above).

Finally, we investigated the relative role of executive functions and social cognition in predicting pragmatic abilities with a regression analysis including both executive functions tests and social cognition tests as predictors and Pragmatic Production and Pragmatic Comprehension as dependent variables.

We did not perform statistical analyses on association and co-occurrence between APACS Total score and social cognition and executive function performance, because they would have been redundant, as APACS Total is a simple average between Pragmatic Production and Pragmatic Comprehension scores. All statistical analyses were performed with R, release 3.1.0 (R Core Team, 2014).

4. Results

4.1. Performance in the pragmatic tasks

The comparisons between the ALS and the control subjects showed significantly worse performance in ALS patients on all pragmatic tasks (all ps < 0.05). Detailed results are reported in Table 2. The highest effect size was observed for the Interview, i.e. in the production of pragmatically appropriate discourse in conversation. The second highest effect size is reported for Narratives, namely the comprehension of different aspects of stories. The three composite pragmatic scores were also significantly lower in patients than in controls, all with large effect size, and larger for Pragmatic Production than for Pragmatic Comprehension. Overall, 15/33 patients (45%) had a performance below cut-off in at least one pragmatic task. In the Pragmatic Production score, 15/30 patients (50%) had a performance below cut-off, whereas in the Pragmatic comprehension score 12/33 patients (36%) had a performance below cut-off. In the APACS total score, 12/33 patients (36%) performed below cut-off.

The comparisons between ALS with bulbar and limb onset showed a significant difference only in the Interview task ($p = 0.02$), which reflected also in the almost significant Pragmatic Production score ($p = 0.05$), while no significant differences were observed in the other tasks (all ps > 0.05). See Appendix A, Table A.1.

Fig. 1 depicts the results for each pragmatic task and the three composite pragmatic scores. Panel A shows the comparisons between ALS patients and healthy controls groups and Panel B shows the individual data of patients scoring below cut-off.

In the Token Test, no significant differences were observed between patients (mean score: 31.20, SD 1.47) and controls (mean score: 31.67, SD 1.64) ($t(56) = 1.65$, $p = 0.11$), nor in the comparison between bulbar onset (mean score: 30.14, SD 2.27) and limb onset patients (31.61, SD 0.77) ($t(5.56) = -1.67$, $p = 0.14$).

4.2. Co-occurrence of executive and pragmatic deficits

Mean scores and standard deviations for the tests of executive functions are shown in Table A.2 in Appendix A. Individual data of patients falling below cut-off in each executive test and the two composite pragmatic scores assessing Pragmatic Production and Pragmatic Comprehension are reported in Fig. 2, Panel A. From these data we calculated the pattern of co-occurrence of executive deficit and pragmatic deficit, considering Pragmatic Production and Pragmatic Comprehension scores separately. The observed co-occurrences are reported in the two 4×4 Tables represented in Fig. 2 (Panels B and C). Both the Fisher's exact tests on count data of these tables were not significant (ps > 0.05). This indicates that there is no statistically reliable association between the deficit in the executive domain and the deficit in the pragmatic domains.

Table 2
Performance in pragmatic tasks and composite scores in ALS patients and healthy controls.

	Healthy controls mean (SD) [proportion]	ALS patients mean (SD) [proportion]	*t*-value	*p*-value	*d* (effect size)
Interview	43.30 (1.28) [0.98]	39.70 (4.21) [0.90]	$t(61) = 4.67$	0.00005**	1.15
Description	47.85 (0.51) [0.99]	46.11 (3.35) [0.96]	$t(61) = 2.91$	0.01*	0.71
Narratives	52.61 (2.84) [0.94]	45.97 (8.70) [0.82]	$t(61) = 4.17$	0.004**	1.03
Figurative Language 1	13.88 (1.41) [0.92]	12.18 (3.17) [0.81]	$t(61) = 2.81$	0.03*	0.69
Humor	6.12 (1.11) [0.87]	5.06 (1.95) [0.72]	$t(61) = 2.71$	0.03*	0.67
Figurative Language 2	25.97 (3.20) [0.86]	21.09 (7.84) [0.70]	$t(61) = 3.21$	0.009*	0.78
Pragmatic Production	0.99 (0.01) –	0.93 (0.07) –	$t(61) = 4.44$	0.0001**	1.09
Pragmatic Comprehension	0.91 (0.08) –	0.78 (0.19) –	$t(64) = 3.53$	0.002**	0.87
APACS Total	0.95 (0.04) –	0.86 (0.13) –	$t(61) = 3.86$	0.0008**	0.95

This table reports the Mean and SD (enclosed in round brackets) on pragmatic tasks in the ALS group and in the Healthy Control group. Values enclosed in square brackets represent the mean values transformed to proportions (thus ranging from 0 to 1) of the maximum obtainable score. No proportions are reported for composite scores, which already ranged from zero to one (see Section 2). The *p*-values were corrected with Bonferroni method after grouping in production tasks, comprehension tasks, and composite scores. The last column reports the effect size, calculated as Cohen's *d*. * $p < 0.05$; ** $p < 0.005$.

According to the consensus criteria, only 3/21 patients (14%) of this subsample showed an executive deficit. An inspection of data on the different executive tests shows that indeed only few patients obtained a performance below cut-off even on one single executive test, and that patients mostly failed in WCST. Below cut-off performance was more frequent in the composite pragmatic scores, where 10/21 patients (46%) were classified as impaired in Pragmatic Production, and 5/21 (24%) were classified as impaired in Pragmatic Comprehension. All the patients who showed an executive deficit also showed a deficit in Pragmatic Production, and 2/3 patients with executive deficit also showed an impairment in Pragmatic Comprehension. Conversely, 7/10 patients with a Pragmatic Production impairment and 3/5 patients with a Pragmatic Comprehension impairment did not show an executive impairment.

4.3. Relationship between executive and composite pragmatic scores

In the multiple regression analysis investigating the relation between the Pragmatic Production score and the executive tests, FAB score resulted as the only significant predictor [*Intercept* = 0.00 (SE = 0.18), $t = 0$, $p = 1$; *FAB* = 0.55 (SE = 1.91), $t = 2.90$, $p = 0.009$]. The accounted variance in this model (R^2) was 27%. Results from this model indicate that, as the score on FAB increases, the expected Pragmatic Production score increases.

The multiple regression analysis investigating the relationship between the Pragmatic Comprehension score and the executive tests yielded to a model with Semantic Fluency score as the only significant predictor [*Intercept* = 0 (SE = 1.69), $t = 0$, $p = 1$, *Semantic Fluency* = 0.65 (SE = 1.73), $t = 3.76$, $p = 0.001$]. The explained variance of this model (R^2) was 40%. This model shows that as the Semantic Fluency increases, the predicted Pragmatic Comprehension score increases.

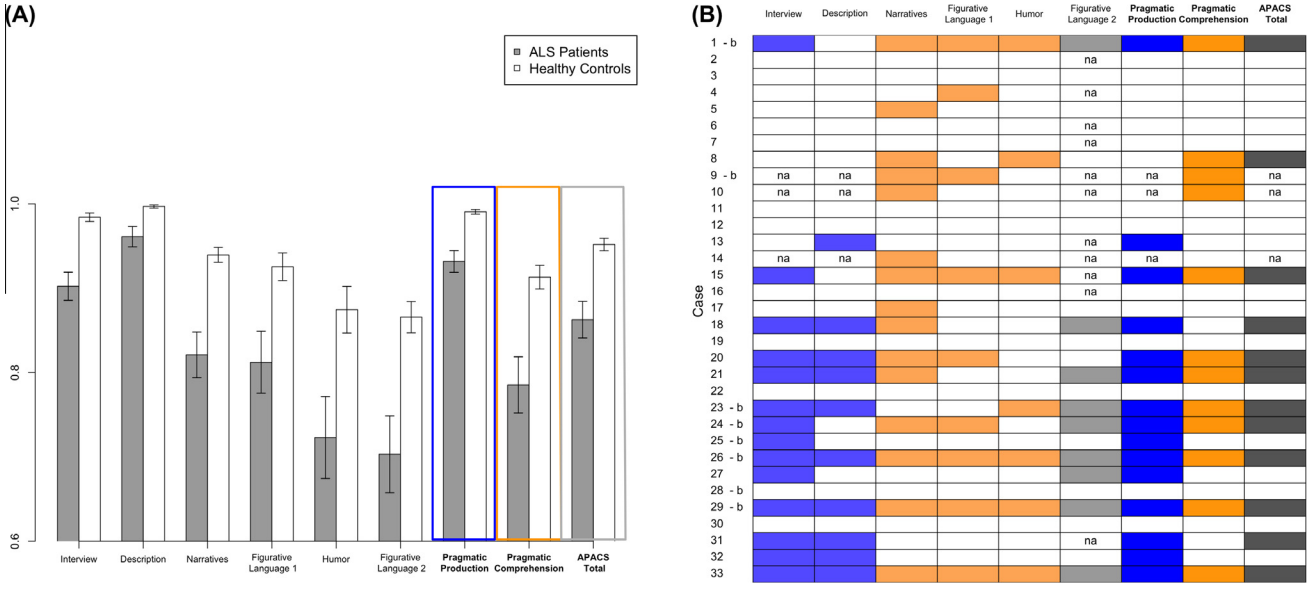

Fig. 1. Performance of ALS patients and healthy controls in pragmatic tasks and composite scores. The figure in panel (A) shows the performance of ALS patients and healthy control in the pragmatic tasks and in the three composite scores, i.e. Pragmatic Production, Pragmatic Comprehension and APACS Total (indicated by dark blue, dark orange and gray colors, respectively). Raw scores in the pragmatic tasks were transformed in proportion (relative to the maximum obtainable score) before plotting. Gray bars indicate the mean performance of ALS patients, whereas white bars indicate the mean performance of healthy controls. The figure in panel (B) shows the ALS patients who scored below cut-off (i.e. below 5° percentile of healthy control data) in the pragmatic tasks and in the three composite pragmatic scores. Each row denotes a patient, whose case number is reported in the left part of the figure, consistently with Table 1 ("b" denotes bulbar onset patients). Each column denotes a task or composite score. White cells indicate a performance equal to or above cut-off, whereas colored cells indicate a performance below cut-off. Light blue cells are used in the columns with the pragmatic tasks included in the Pragmatic Production score and dark blue cells in the column of the Pragmatic Production score. Light orange cells are used in the columns of the pragmatic tasks included in the Pragmatic Comprehension score, and dark orange cells the column of the Pragmatic Comprehension score. Dark gray is used for APACS Total. For the Figurative Language 2 task, performances below cut-off are denoted by light gray cells as this task was not included in the composite score due to the high number of missing data. A cell marked with 'na' (not available) indicates that the patient could not perform that test. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

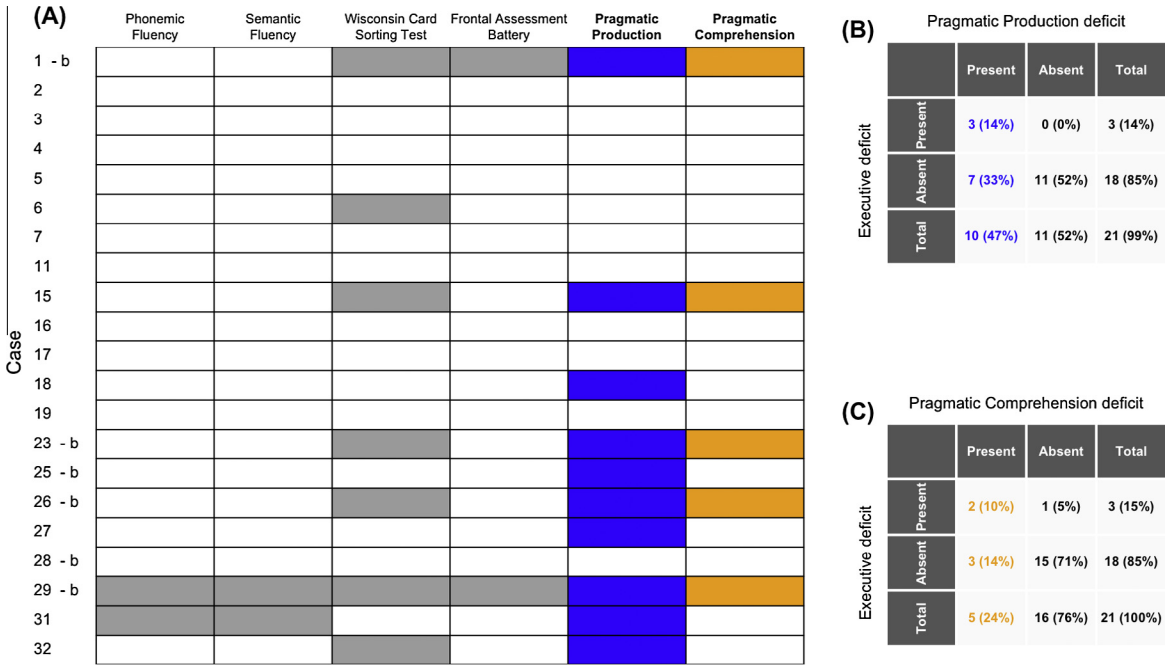

Fig. 2. Performance of ALS patients in executive tests and co-occurence of executive and pragmatic deficit. The figure in panel (A) shows the ALS patients who scored below cut-off on executive functions tests (i.e. below the 5th percentile as determined by normative data) and below cut-off in the two composite pragmatic scores (i.e. below 5th percentile of healthy control data). Each row denotes a patient, whose case number is reported in the left part of the figure, consistently with Table 1 ("b" denotes bulbar onset patients). Each column denotes a task or composite score. White cells indicate a performance equal to or above cut-off, whereas gray cells indicate a performance below cut-off. The table in panel (B) reports the total raw data (percentages enclosed in parentheses) of the co-occurrence of executive functions deficit (defined according to consensus criteria, Strong et al., 2009) and Pragmatic Production deficit. The table in panel (C) reports the total raw data (percentages enclosed in parentheses) of the co-occurrence of executive function deficit and Pragmatic Comprehension deficit.

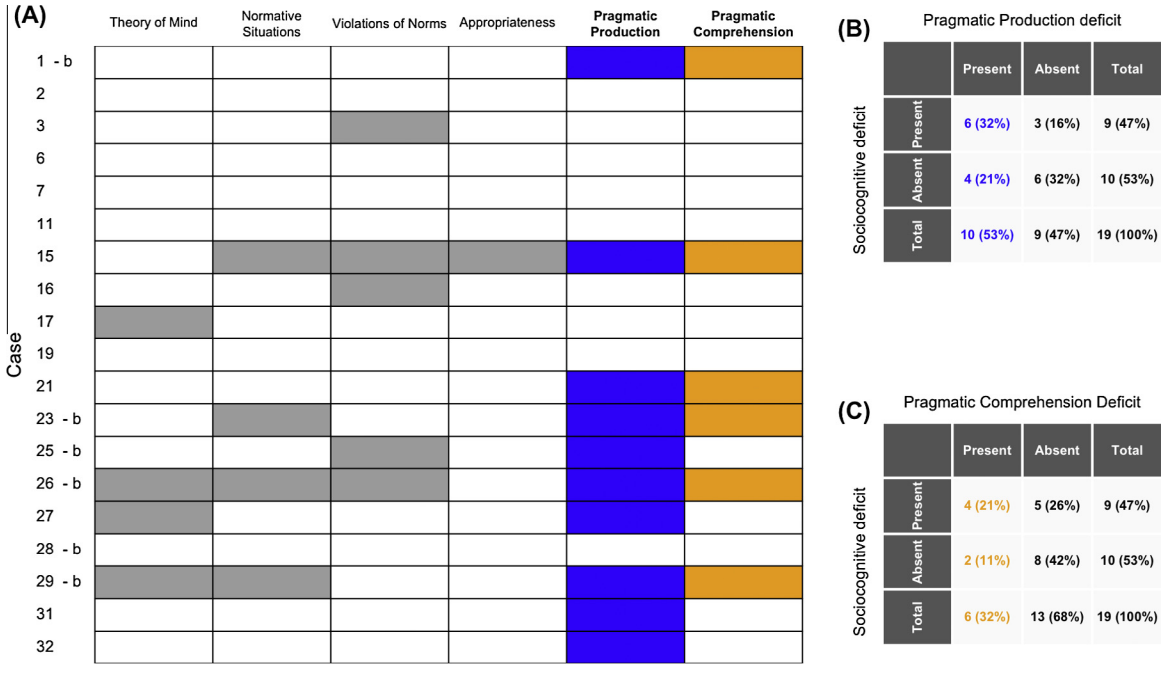

Fig. 3. Performance of ALS patients in social cognition tests and co-occurence of social cognition and pragmatic deficit. The figure in panel (A) shows the ALS patients who scored below cut-off on social cognition tests (i.e. below the 5th percentile as determined by normative data) and below cut-off in the two composite pragmatic scores (i.e. below 5th percentile of healthy control data). Each row denotes a patient, whose case number is reported in the left part of the figure, consistently with Table 1 ("b" denotes bulbar onset patients). Each column denotes a task or composite score. White cells indicate a performance equal to or above cut-off, whereas gray cells indicate a performance below cut-off. The table in panel (B) reports the total raw data (percentages enclosed in parentheses) of the co-occurrence of social cognition deficit and Pragmatic Production deficit. The table in panel (C) reports the total raw data (percentages enclosed in parentheses) of the co-occurrence of social cognition deficit and Pragmatic Comprehension deficit.

4.4. Co-occurrence of social cognition and pragmatic deficits

Mean scores and standard deviations for the tests of social cognition are shown in Table A.2 in Appendix A. Individual data of patients below cut-off in each social cognition test and in the two composite pragmatic scores assessing Pragmatic Production and Pragmatic Comprehension are displayed in Fig. 3, Panel A. The overall co-occurrence of a social cognition deficit

(i.e. a performance below cut-off in at least one social cognition test) and a pragmatic deficit is reported is reported in the two 4 × 4 Tables represented in Fig. 3 (Panel B and C). As in the case of executive deficit, both the Fisher's exact tests on count data of these tables were not significant ($p > 0.05$). This indicates that there is no strong association between a deficit in social cognition abilities and a deficit in either pragmatic production or pragmatic comprehension.

As visible from Fig. 3, performances below cut-off were diffuse both in social cognition tests and in pragmatic measures. In this subsample, 9/19 patients (47%) showed a deficit in social cognition abilities, 10/19 patients (53%) showed a deficit in Pragmatic Production, and 6/19 patients (32%) showed a deficit in Pragmatic Comprehension. There is, however, no clear pattern of co-occurrence. Among the patients with a Pragmatic Production deficit, 6/10 had also a deficit in social cognition, and among the patients with a Pragmatic Comprehension deficit, 4/6 showed a deficit in social cognition. Conversely, 6/9 patients with a social cognition deficit had also a Pragmatic Production deficit, and 4/9 patients with a social cognition deficit had also a Pragmatic Comprehension deficit.

4.5. Relationship between social cognition and composite pragmatic scores

In the multiple regression investigating the relationship between social cognition scores and Pragmatic Production score, the Normative Situations test was the only significant predictor [*Intercept* = 0 (SE = 0.24), $t = 0$, $p = 1$; *Normative Situations* = 0.50 (SE = 2.10), $t = 2.36$, $p = 0.03$]. This model had an explained variance of 20%. The model indicates that as the score at the Normative Situations test increases, the predicted Pragmatic Production score increases.

In the regression model with Pragmatic Comprehension score as dependent variable, two predictors were significant: the Normative Situations score and age [*Intercept* = 0 (SE = 0.1), $t = 0$, $p = 1$; *Normative Situations* = 0.73 (SE = 0.14), $t = 5.10$, $p = 0.0002$; *age* = −0.39 (SE = 1.43), $t = -2.71$, $p = 0.01$]. This model accounted for 63% of variance in the dependent variable. Results indicate that, as the score on Normative Situations increases, the predicted score increases. On the other side, as the age increases, the predicted score decreases.

4.6. Relationship between executive functions, social cognition and composite pragmatic scores

In the multiple regression investigating the relationship between executive functions tests, social cognition tests and Pragmatic Production score, the Semantic Fluency test and the Appropriateness test were significant predictors [*Intercept* = 0 (SE = 1.67), $t = 0$, $p = 1$; *Semantic Fluency* = 0.59 (SE = 1.72), $t = 3.45$, $p = 0.003$; *Appropriateness* = 0.51 (SE = 1.72), $t = 2.95$, $p = 0.01$]. This model accounted for 0.49% of the variance of the dependent variable. As an estimate of the effect size of the effect of each predictor, we used squared semi-partial correlations. The squared semi-partial correlation of a predictor and a dependent variable indicates the unique contribution of a predictor on the dependent variable, by controlling for the effect of the other predictors.[3] According to this approach, *Semantic Fluency* had an effect size of 0.43 while *Appropriateness* had an effect size of 0.36.

In the regression analysis including executive functions tests, social cognition tests and Pragmatic Comprehension score, *Normative Situation* test and Age were significant predictors [*Intercept* = 0 (SE = 0.1) $t = 0$, $p = 1$; *Normative Situations* = 0.73, (SE = 1.44), $t = 5.09$, $p = 0.0001$; Age = −0.39 (SE = 1.44), $t = -2.72$, $p = 0.02$]. Using squared semi-partial correlation as measure of effect size, we obtained that *Normative Situations* had an effect size of 0.63 and Age had an effect size of 0.33.

5. Discussion

This study explored pragmatic abilities in ALS employing a novel test that incorporates classic pragmatic tasks, from discourse production to the comprehension of non-literal meanings. The study also aimed to undertake the analysis of the relationship among pragmatics, executive functions and social cognition in ALS.

Our results revealed that, relative to controls, ALS patients performed poorly in all pragmatic tasks. Consistently, patients scored poorly also in the composite pragmatic measures, i.e. Pragmatic Production, Pragmatic Comprehension and APACS Total. Considering the 5th percentile cut-off, the pragmatic deficit was confirmed as widespread, with 45% of the patients performing below threshold in at least one of the six pragmatic tasks (Fig. 1). Based on the composite measures, 50% of the patients had a deficit in Pragmatic Production, 36% had a deficit in Pragmatic Comprehension, and 36% of the patients were found to be impaired in the APACS Total score. Although the investigated sample of 33 patients is relatively small and the results are therefore limited, the prevalence of pragmatic impairment appears to be considerable.

Some considerations can be drawn on the specific pragmatic tasks that seem to posit major difficulties for ALS patients. The highest effect size in the comparison between patients and controls was observed for the Interview task, i.e. the production of discourse in a conversational setting. Typically, patients failed in maintaining the discourse topic, and in providing the appropriate amount of information, being either over or under-informative. This reflected also in the Description task, where patients might fail in communicating the salient elements. The paralinguistic aspects of discourse might also be deviant, with loss of eye-contact and fixed facial expression. Not only the production but also the comprehension of discourse might be compromised, as assessed in the Narratives task, where patients showed difficulties in recalling aspects of the story, especially non-explicit information, and in interpreting non-literal meanings, despite rich contextual cues. Consistently, patients performed poorly in tasks specifically assessing the comprehension of figurative language. In Figurative Language 1 and Humor, patients might fail in selecting the correct interpretation or ending, and in Figurative Language 2 task paraphrases and concrete examples were often provided instead of generalized and abstract explanations of the figurative expressions.

Our findings are compatible with the few sparse evidence indicating difficulties in story telling (Ash, Menaged et al., 2014) and sarcasm detection in ALS (Staios et al., 2013), and in addition provide a broader picture of communicative and pragmatic breakdowns in ALS patients. To this purpose, the composite measures offer a glimpse into the general impact of the deficit. When considering a global notion of pragmatic abilities such as the one reflected in the APACS Total score, we can observe that patients are impaired compared to controls, with a large effect size. It is also interesting to consider the composite measures targeting production and comprehension. Although both measures show a significant impairment and a large effect size, Pragmatic Production was associated with a larger effect size and was more frequently impaired than Pragmatic Comprehension. On the one hand, this might reflect intrinsic differences separating the pragmatic tasks that contribute to the two measures, along with a truly major difficulty experienced by patients in organizing their discourse and behaving appropriately in a conversational context. On the other hand, it is important to note that controls have a ceiling performance in the two pragmatic production tasks (Interview and Description), which certainly affect

[3] Note that the sum of squared semi-partial correlations can lead to values higher than 1 and that this sum is not equivalent to *R*-squared value.

the effect sizes. Notably, a larger statistical effect in terms of effect size does not necessarily imply a larger impact in real life. Clinicians' informal, qualitative evaluations often emphasize the comprehension difficulties of ALS patients, above discourse organization difficulties. Only future studies adopting external criteria could establish which pragmatic domain has the highest impact on communication and social interaction.

Globally, the pragmatic profile of ALS patients closely mirrors the description of pragmatic breakdowns in behavioral variant of FTD (Orange & Hillis, 2012), as expected in the hypotheses of the study. This is of some importance in clinical terms, as it can contribute to define further the ALS–FTD continuum, and to clarify the heterogeneity of cognitive impairment in ALS. There is now extensive evidence of cognitive and behavioral changes, ranging from subclinical impairment to dementia, in a considerable proportion of patients with ALS. While the impact of motor dysfunction, psychological reaction to disability and social isolation in evaluating cognitive and behavioral performance should never be neglected, there is a general consensus that these modification reflect the pathological involvement of extra-motor cerebral structures. A recent meta-analysis of imaging studies demonstrated consistent gray matter atrophy compared to healthy controls in the precentral, postcentral and inferior frontal gyri, right temporal pole and bilateral superior temporal gyri (Sheng et al., 2015). These findings indicate a consistent overlap with the social cognition network (Kennedy & Adolphs, 2012) and with the pattern of brain involvement present in early stage behavioral variant of FTD (Seeley, 2008). They thus support the concept of a FTD–ALS continuum suggested by neuropathological and genetic studies (Thomas, Alegre-Abarrategui, & Wade-Martins, 2013).

Many important issues deserve further consideration, which could help in understanding the neural mechanisms affected in ALS. Among these, one revolves around the relation between impairments in formal aspects of language (word and sentence processing) and in pragmatics. Based on our sample, ALS patients have a normal performance in language comprehension, as assessed in the Token Test, supporting the idea of a distinction between pragmatics and sentence processing. This indicates that ALS patients do not exhibit the clinical profile of aphasia. The previously reported high prevalence of impairment on an extensive language test battery (Taylor et al., 2013) may be due to the use of test sensitive to subtle dysfunctions, or in which performance can be affected by executive abilities.

A second aspect concerns the relation between different onset sites and pragmatic abilities. In our study, a significant difference between bulbar onset and limb onset patients was observed only in the Interview task and reflected in the Pragmatic Production composite score, which suggests that the pattern of involvement becomes especially relevant in the activity of engaging in a pragmatically appropriate conversation. Note that dysarthric subjects were not tested in production tasks, indicating that the worse performance of bulbar patients in the Interview is related to cognitive aspects, for instance difficulties in planning the conversation and adapting to context, possibly linked to higher executive dysfunctions. We observed no differences between bulbar and limb onset patients in any other task. Although the literature agrees on the worse cognitive decline in bulbar patients, evidence on specific tasks is conflicting, with studies finding no differences (Staios et al., 2013; Taylor et al., 2013) and studies observing a preponderance of bulbar cases in the cognitively impaired subset (Girardi et al., 2011). Further investigations are in need to define possible differences in patterns of impairment, and the specific role of motor dysfunction in cognition, language (Schreiber et al., 2005), and specifically in pragmatics. This issue is indeed of major interest for the cognitive neuroscience of language as well, in light of the lively debate over the role of the action system in language (Moro, 2014; Tettamanti & Moro, 2012) and in ALS (Bak & Chandran, 2012; Papeo et al., 2015).

One important issue investigated in this paper is the relation of pragmatic abilities with executive function and social cognition. Here only a subsample of patients was assessed in both domains. In this group, we observed that, while 14% of patients were diagnosed with executive deficit according to the consensus criteria, 46% of the patients fell below cut-off in Pragmatic Production and 24% in Pragmatic Comprehension (Fig. 2). Of the patients with pragmatic impairment, only a limited number had executive deficit. The frequency of the dysexecutive syndrome observed here falls within the range reported in previous literature (Montuschi et al., 2014). The pragmatic deficit, both in comprehension and in production, appears thus to be more frequent than the executive deficit. While there is an effect of executive functions (especially Semantic Fluency) in determining the pragmatic performance, no more than 40% of variance in our composite scores is explained by executive performance. This indicates that the role of executive functions in accounting for pragmatic behavior is relatively modest, and it is similar to the role of executive functions in relation to language impairment (Taylor et al., 2013). These findings suggest that pragmatics shows some degree of independence on executive function impairment.

In applying the same approach to the domain of social cognition, we found that 47% of the patients in our subsample had a deficit in at least one of the available measures, which again confirms previous literature (van der Hulst et al., 2014). The prevalence of pragmatic deficits confirmed as widespread as in the above subsample (not equal, given the slightly different dimension of the sets), with 53% of the patients falling below cut-off in Pragmatic Production and 32% in Pragmatic Comprehension (Fig. 3). Although the prevalence of social cognition and pragmatic deficits is similar, no significant pattern of co-occurrence emerged. In terms of scores, performance in social cognition tests seems indeed to play some role in determining the pragmatic performance. This is especially evident for Pragmatic Comprehension, where Normative Situation scores accounted for 63% of variance.

Interestingly, a global analysis taking into consideration both executive functions and social cognition showed that the former has a major impact on production tasks, while the second has a major impact on comprehension tasks. In other words, abilities in task shifting and mental flexibility support our ability to engage in appropriate conversation (managing the discourse topic, taking turns appropriately, conveying salient information, avoiding repetition, etc.), while our skills in understanding and judging other people's behavior are closely connected to the comprehension of the speaker's communicative intention, especially when what is communicated departs from what is literally said, as in metaphor and humor.

These findings call for a more specific discussion upon of the cognitive substrates of pragmatic behavior. The relationship between pragmatic abilities and other cognitive domains is indeed an open issue in the literature (Martin & McDonald, 2003). Correlational evidence of the interplay between executive functions and pragmatic abilities have been reported in the literature, for instance in relation to the ability to produce a coherent discourse in traumatic brain patients (Marini, Zettin, & Galetto, 2014; Mozeiko, Le, Coelho, Krueger, & Grafman, 2011), or to the ability to understand novel metaphors in Alzheimer patients (Amanzio et al., 2008). For other populations, mainly autistic patients and schizophrenic patients, a strong interplay of social cognition (especially Theory of Mind abilities) and pragmatics has been emphasized (Bosco, Bono, & Bara, 2012; Brüne, 2005). Support in favor of the link between pragmatics, social cognition and Theory of Mind comes also from theoretical approaches such as Relevance Theory (Sperber & Wilson, 2002) and research on the healthy population (Holtgraves & Kashima, 2008; Spotorno, Koun, Prado, Van

Der Henst, & Noveck, 2012). The common view is that several cognitive abilities are in need to behave in a pragmatically appropriate fashion, yet these abilities represent a necessary but not sufficient cognitive base in pathological conditions (Stemmer, 2008) as well as in development (Blain-Brière, Bouchard, & Bigras, 2014). The conclusions that can reasonably be drawn from our data are along the lines expressed above: in ALS, executive and social cognition impairments seem to contribute to the pragmatic deficit, yet they neither necessarily co-occur with it, nor fully predict it. Moreover, our findings suggest that pragmatic abilities are not a monolithic component, but capitalize upon cognitive substrates with differences depending on the specific communicative task. When our attention switches from formal aspects of language to its communicative use, we are projected into social interaction, with an array of representations and retrieval of beliefs, intentions and other elements of context requiring flexible integration. Further research on the relation between ALS, pragmatics, social cognition and executive functions would be important both for the taxonomy of the ALS population, as it could further underscore the heterogeneity of possible cognitive impairment patterns, and for neuropragmatics as well, as it could provide neuropsychological evidence of the specific nature of pragmatic abilities.

6. Conclusions

Few years after Charcot described ALS as a motor disorder, Pierre Marie noted subtle intellectual and emotional modifications accompanying the disease, among which "childish" and "credulous" behavior (Marie, 1895). This clinical intuition probably captures what nowadays falls under the label of emotional and social cognition disruption, and may be related to the inability to communicate in a pragmatically appropriate fashion, taking utterances literally and accepting the concrete meaning of metaphors and jokes. In this study we provide the first systematic study of pragmatic abilities in ALS, spanning through different domains of language use in context. Through the analysis of co-occurrence and regression modeling, we found that this impairment cannot be solely explained as a consequence of executive dysfunction and social cognition impairment. The results of this study have important implications for the description of the cognitive profile al ALS and the definition of the neuroanatomical basis of pragmatic breakdowns in ALS. They also underline the possible role of assessment tools tapping into the patients' communicative disabilities, as one important aspect of their social interaction abilities.

Authors contribution

Design and construction of the pragmatic test: VB, GA. Data collection: IM, SB, EA. Data analysis and interpretation and manuscript writing: VB, GA, SFC. Supervision of clinical and formal linguistics aspects: MC, AM. All authors provided feedback on the draft and approved the final version of the manuscript.

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Appendix A

See Tables A.1 and A.2.

Table A.2
Mean scores of ALS patients on neuropsychological tests.

Executive functions		Social cognition	
Test	Mean (SD)	Test	Mean (SD)
Phonemic fluency	26.75 (13.28)	Theory of Mind	11.4 (1.54)
Semantic fluency	32.77 (10.65)	Normative situations	12.16 (3.62)
Wisconsin card sorting test	87.76 (34.39)	Violation of norms	22.26 (2.16)
Frontal assessment battery	14.83 (3.62)	Appropriateness	48.16 (11.54)

This table reports ALS score on neuropsychological tests. The leftmost part of the table reports mean values (standard deviations in parentheses) on executive functions tests, whereas the rightmost part of the table reports mean values (standard deviations in parentheses) on social cognition tests.

Table A.1
Performance in pragmatic tasks and composite scores in ALS patients with bulbar and limb onset forms.

	Bulbar ALS mean (SD) [proportion]	Limb ALS mean (SD) [proportion]	*t*-value (Welch *t*-test)	*p*-value	*d* (effect size)	Patients included
Interview	35.57 (3.99) [0.80]	40.96 (3.47) [0.93]	$t(8.94) = -3.22$	0.02*	−1.39	b = 7, l = 23
Description	45.00 (3.05) [0.94]	46.48 (3.42) [0.97]	$t(11.02) = -1.09$	0.60	−0.47	b = 7, l = 23
Narratives	41.25 (11.12) [0.73]	47.48 (7.41) [0.85]	$t(9.08) = -1.48$	0.69	−0.60	b = 8, l = 25
Figurative Language 1	9.75 (4.02) [0.65]	12.96 (2.46) [0.86]	$t(8.73) = -2.13$	0.25	−0.86	b = 8, l = 25
Humor	3.87 (2.03) [0.55]	5.44 (1.80) [0.78]	$t(10.78) = -1.95$	0.31	−0.79	b = 8, l = 25
Figurative Language 2	15.00 (7.46) [0.50]	23.93 (6.41) [0.80]	$t(10.32) = -2.73$	0.08	−1.25	b = 7, l = 15
Pragmatic Production	0.87 (0.06) –	0.94 (0.06) –	$t(11.09) = -2.79$	0.05	−1.21	b = 7, l = 23
Pragmatic Comprehension	0.65 (0.22) –	0.83 (0.16) –	$t(-2.16) = 9.51$	0.17	−0.87	b = 8, l = 25
APACS Total	0.76 (0.14) –	0.89 (0.11) –	$t(8.30) = -2.24$	0.16	−0.97	b = 7, l = 23
Age	64.87 (12.36) –	62.80 (8.85) –	$t(9.42) = 0.442$	0.67	0.18	b = 8, l = 25
Education	7.62 (4.10) –	10.48 (4.62) –	$t(13.22) = -1.66$	0.12	−0.67	b = 8, l = 25

This table reports the Mean and SD (enclosed in round brackets) on pragmatic tasks and composite scores in the ALS groups, divided according to the onset site. Values enclosed in square brackets represent the mean values transformed to proportions (ranging from 0 to 1) of the maximum obtainable score. No proportions are reported for the two composite scores, which already ranged from 0 to 1 (see Section 2). The *p*-values were corrected with Bonferroni method after grouping in production tasks, comprehension tasks, and composite scores (age and education are not corrected). Effect size measures were calculated as Cohen's *d*. The last column indicates the number of patients with available data included in the analyses (b = bulbar; l = limb). The last two rows report the mean values (SD) and statistics for age and education. * $p < 0.05$; ** $p < 0.005$.

References

Abrahams, S. (2011). Social cognition in amyotrophic lateral sclerosis. *Neurodegenerative Disease Management, 1*(5), 397–405. http://dx.doi.org/10.2217/nmt.11.54.

Abrahams, S. (2013). Executive dysfunction in ALS is not the whole story. *Journal of Neurology, Neurosurgery, and Psychiatry, 84*(5), 474–475. http://dx.doi.org/10.1136/jnnp-2012-303851.

Amanzio, M., Geminiani, G., Leotta, D., & Cappa, S. (2008). Metaphor comprehension in Alzheimer's disease: Novelty matters. *Brain and Language, 107*(1), 1–10. http://dx.doi.org/10.1016/j.bandl.2007.08.003.

Appollonio, I., Leone, M., Isella, V., Piamarta, F., Consoli, T., Villa, M. L., ... Nichelli, P. (2005). The Frontal Assessment Battery (FAB): Normative values in an Italian population sample. *Neurological Sciences: Official Journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology, 26*(2), 108–116. http://dx.doi.org/10.1007/s10072-005-0443-4.

Ash, S., Menaged, A., Olm, C., McMillan, C. T., Boller, A., Irwin, D. J., ... Grossman, M. (2014). Narrative discourse deficits in amyotrophic lateral sclerosis. *Neurology, 83*(6), 520–528. http://dx.doi.org/10.1212/WNL.0000000000000670.

Ash, S., Moore, P., Antani, S., McCawley, G., Work, M., & Grossman, M. (2006). Trying to tell a tale: Discourse impairments in progressive aphasia and frontotemporal dementia. *Neurology, 66*(9), 1405–1413. http://dx.doi.org/10.1212/01.wnl.0000210435.72614.38.

Ash, S., Olm, C., McMillan, C. T., Boller, A., Irwin, D. J., McCluskey, L., ... Grossman, M. (2014). Deficits in sentence expression in amyotrophic lateral sclerosis. *Amyotrophic Lateral Sclerosis & Frontotemporal Degeneration, 1–9*. http://dx.doi.org/10.3109/21678421.2014.974617.

Baayen, R. H. (2008). *Analyzing linguistic data a practical introduction to statistics using R*. Cambridge University Press.

Bak, T. H., & Chandran, S. (2012). What wires together dies together: Verbs, actions and neurodegeneration in motor neuron disease. *Cortex; a Journal Devoted to the Study of the Nervous System and Behavior, 48*(7), 936–944. http://dx.doi.org/10.1016/j.cortex.2011.07.008.

Bak, T. H., & Hodges, J. R. (2004). The effects of motor neurone disease on language: Further evidence. *Brain and Language, 89*(2), 354–361. http://dx.doi.org/10.1016/S0093-934X(03)00357-2.

Bambini, V. (2010). Neuropragmatics: A foreword. *Italian Journal of Linguistics, 22*(1), 1–20.

Bambini, V., & Bara, B. G. (2012). Neuropragmatics. In J.-O. Östman & J. Verschueren (Eds.), *Handbook of pragmatics* (pp. 1–21). Amsterdam: John Benjamins.

Bambini, V., Ghio, M., Moro, A., & Schumacher, P. B. (2013). Differentiating among pragmatic uses of words through timed sensicality judgments. *Frontiers in Psychology, 4*(December), 938. http://dx.doi.org/10.3389/fpsyg.2013.00938.

Bennion Callister, J., & Pickering-Brown, S. M. (2014). Pathogenesis/genetics of frontotemporal dementia and how it relates to ALS. *Experimental Neurology, 262 Pt B*, 84–90. http://dx.doi.org/10.1016/j.expneurol.2014.06.001.

Blain-Brière, B., Bouchard, C., & Bigras, N. (2014). The role of executive functions in the pragmatic skills of children age 4–5. *Frontiers in Psychology, 5*(March), 240. http://dx.doi.org/10.3389/fpsyg.2014.00240.

Blair, R. J., & Cipolotti, L. (2000). Impaired social response reversal. A case of "acquired sociopathy". *Brain: A Journal of Neurology, 123*(Pt 6), 1122–1141.

Borovsky, A., Saygin, A. P., Bates, E., & Dronkers, N. (2007). Lesion correlates of conversational speech production deficits. *Neuropsychologia, 45*(11), 2525–2533. http://dx.doi.org/10.1016/j.neuropsychologia.2007.03.023.

Bosco, F. M., Bono, A., & Bara, B. G. (2012). Recognition and repair of communicative failures: The interaction between Theory of Mind and cognitive complexity in schizophrenic patients. *Journal of Communication Disorders, 45*(3), 181–197. http://dx.doi.org/10.1016/j.jcomdis.2012.01.005.

Brooks, B. R., Miller, R. G., Swash, M., & Munsat, T. L. (2000). El Escorial revisited: Revised criteria for the diagnosis of amyotrophic lateral sclerosis. *Amyotrophic Lateral Sclerosis and Other Motor Neuron Disorders: Official Publication of the World Federation of Neurology, Research Group on Motor Neuron Diseases, 1*(5), 293–299.

Brownell, H. H., Michel, D., Powelson, J., & Gardner, H. (1983). Surprise but not coherence: Sensitivity to verbal humor in right-hemisphere patients. *Brain and Language, 18*(1), 20–27.

Brüne, M. (2005). "Theory of mind" in schizophrenia: A review of the literature. *Schizophrenia Bulletin, 31*(1), 21–42. http://dx.doi.org/10.1093/schbul/sbi002.

Carlesimo, G. A., Caltagirone, C., Fadda, L., Marfia, G., Gainotti, G., & Al, E. (1995). Batteria per la valutazione del Deterioramento Mentale (parte III): analisi dei profili qualitativi di compromissione cognitiva. *Archivio Di Psicologia, Neurologia E Psichiatria, 4*, 489–502.

Catani, M., & Bambini, V. (2014). A model for Social Communication and Language Evolution and Development (SCALED). *Current Opinion in Neurobiology, 28*, 165–171. http://dx.doi.org/10.1016/j.conb.2014.07.018.

Cecchetto, C., Aiello, M., D'Amico, D., Cutuli, D., Cargnelutti, D., Eleopra, R., & Rumiati, R. I. (2014). Facial and bodily emotion recognition in multiple sclerosis: The role of alexithymia and other characteristics of the disease. *Journal of the International Neuropsychological Society : JINS, 20*(10), 1004–1014. http://dx.doi.org/10.1017/S1355617714000939.

Cedarbaum, J. M., Stambler, N., Malta, E., Fuller, C., Hilt, D., Thurmond, B., & Nakanishi, A. (1999). The ALSFRS-R: A revised ALS functional rating scale that incorporates assessments of respiratory function. BDNF ALS Study Group (Phase III). *Journal of the Neurological Sciences, 169*(1–2), 13–21.

Cerami, C., Dodich, A., Canessa, N., Crespi, C., Iannaccone, S., Corbo, M., ... Cappa, S. F. (2014). Emotional empathy in amyotrophic lateral sclerosis: A behavioural and voxel-based morphometry study. *Amyotrophic Lateral Sclerosis & Frontotemporal Degeneration, 15*(1–2), 21–29. http://dx.doi.org/10.3109/21678421.2013.785568.

Consonni, M., Iannaccone, S., Cerami, C., Frasson, P., Lacerenza, M., Lunetta, C., ... Cappa, S. F. (2013). The cognitive and behavioural profile of amyotrophic lateral sclerosis: Application of the consensus criteria. *Behavioural Neurology, 27*(2), 143–153. http://dx.doi.org/10.3233/BEN-2012-110202.

Crespi, C., Cerami, C., Dodich, A., Canessa, N., Arpone, M., Iannaccone, S., ... Cappa, S. F. (2014). Microstructural white matter correlates of emotion recognition impairment in Amyotrophic Lateral Sclerosis. *Cortex; a Journal Devoted to the Study of the Nervous System and Behavior, 53*, 1–8. http://dx.doi.org/10.1016/j.cortex.2014.01.002.

de Carvalho, M., Dengler, R., Eisen, A., England, J. D., Kaji, R., Kimura, J., ... Swash, M. (2008). Electrodiagnostic criteria for diagnosis of ALS. *Clinical Neurophysiology: Official Journal of the International Federation of Clinical Neurophysiology, 119*(3), 497–503. http://dx.doi.org/10.1016/j.clinph.2007.09.143.

De Renzi, E., & Faglioni, P. (1978). Normative data and screening power of a shortened version of the Token Test. *Cortex; a Journal Devoted to the Study of the Nervous System and Behavior, 14*(1), 41–49.

Ferstl, E. C., Walther, K., Guthke, T., & von Cramon, D. Y. (2005). Assessment of story comprehension deficits after brain damage. *Journal of Clinical and Experimental Neuropsychology, 27*(3), 367–384. http://dx.doi.org/10.1080/13803390490515784.

Girardi, A., Macpherson, S. E., & Abrahams, S. (2011). Deficits in emotional and social cognition in amyotrophic lateral sclerosis. *Neuropsychology, 25*(1), 53–65. http://dx.doi.org/10.1037/a0020357.

Goldstein, L. H., & Abrahams, S. (2013). Changes in cognition and behaviour in amyotrophic lateral sclerosis: Nature of impairment and implications for assessment. *The Lancet. Neurology, 12*(4), 368–380. http://dx.doi.org/10.1016/S1474-4422(13)70026-7.

Grice, H. P. (1975). Logic and conversation. In P. Cole & J. L. Morgan (Eds.). *Syntax and semantics* (Vol. 3, pp. 41–58). Academic Press.

Grice, H. P. (1989). *Studies in the way of words*. Cambridge, Mass: Harvard University Press.

Guazzotti, P., & Oddera, M. F. (2006). Il Grande dizionario dei proverbi italiani. *Zanichelli*.

Hagoort, P., & Levinson, S. C. (2014). Neuropragmatics. In M. S. Gazzaniga (Ed.), *The cognitive neurosciences* (5th ed.. Cambridge, Mass: MIT Press.

Harrel, F. E. (2015). *Regression modeling strategies. With applications to linear models, logistic regression, and survival analysis* (2nd ed.). New York: Springer.

Holtgraves, T. M., & Kashima, Y. (2008). Language, meaning, and social cognition. *Personality and Social Psychology Review: An Official Journal of the Society for Personality and Social Psychology, Inc, 12*(1), 73–94. http://dx.doi.org/10.1177/1088868307309605.

Kennedy, D. P., & Adolphs, R. (2012). The social brain in psychiatric and neurological disorders. *Trends in Cognitive Sciences, 16*(11), 559–572. http://dx.doi.org/10.1016/j.tics.2012.09.006.

Kipps, C. M., Nestor, P. J., Acosta-Cabronero, J., Arnold, R., & Hodges, J. R. (2009). Understanding social dysfunction in the behavioural variant of frontotemporal dementia: The role of emotion and sarcasm processing. *Brain: A Journal of Neurology, 132*(Pt 3), 592–603. http://dx.doi.org/10.1093/brain/awn314.

Laiacona, M., Inzaghi, M. G., De Tanti, A., & Capitani, E. (2000). Wisconsin card sorting test: A new global score, with Italian norms, and its relationship with the Weigl sorting test. *Neurological Sciences: Official Journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology, 21*(5), 279–291.

Leslie, F. V. C., Hsieh, S., Caga, J., Savage, S. A., Mioshi, E., Hornberger, M., ... Burrell, J. R. (2014). Semantic deficits in amyotrophic lateral sclerosis. *Amyotrophic Lateral Sclerosis & Frontotemporal Degeneration, 1–8*. http://dx.doi.org/10.3109/21678421.2014.987301.

Lucisano, P., & Piemontese, M. E. (1988). GULPEASE: Una formula per la predizione della difficoltà dei testi in lingua italiana. *Scuola E Città, 34*, 110–124.

Luzzatti, C., Willmes, K., & De Bleser, R. (1991). *Aachener Aphasia test (AAT) – Versione Italiana*. Firenze: Organizzazioni Speciali.

Marie, P. (1895). *Lectures on diseases of the spinal cord*. London: New Sydenham Society.

Marini, A., Andreetta, S., del Tin, S., & Carlomagno, S. (2011). A multi-level approach to the analysis of narrative language in aphasia. *Aphasiology, 25*(11), 1372–1392. http://dx.doi.org/10.1080/02687038.2011.584690.

Marini, A., Zettin, M., & Galetto, V. (2014). Cognitive correlates of narrative impairment in moderate traumatic brain injury. *Neuropsychologia, 64C*, 282–288. http://dx.doi.org/10.1016/j.neuropsychologia.2014.09.042.

Martin, I., & McDonald, S. (2003). Weak coherence, no theory of mind, or executive dysfunction? Solving the puzzle of pragmatic language disorders. *Brain and Language, 85*(3), 451–466.

Montuschi, A., Iazzolino, B., Calvo, A., Moglia, C., Lopiano, L., Restagno, G., ... Chiò, A. (2014). Cognitive correlates in amyotrophic lateral sclerosis: A population-based study in Italy. *Journal of Neurology, Neurosurgery, and Psychiatry, 1–6*. http://dx.doi.org/10.1136/jnnp-2013-307223.

Moro, A. (2014). On the similarity between syntax and actions. *Trends in Cognitive Sciences, 18*(3), 109–110. http://dx.doi.org/10.1016/j.tics.2013.11.006.

Mozeiko, J., Le, K., Coelho, C., Krueger, F., & Grafman, J. (2011). The relationship of story grammar and executive function following TBI. *Aphasiology, 25*(6–7), 826–835. http://dx.doi.org/10.1080/02687038.2010.543983.

Neary, D., Snowden, J. S., Gustafson, L., Passant, U., Stuss, D., Black, S., ... Benson, D. F. (1998). Frontotemporal lobar degeneration: A consensus on clinical diagnostic criteria. *Neurology, 51*(6), 1546–1554.

Novelli, G., Papagno, C., Capitani, E., Laiacona, M., Vallar, G., & Cappa, S. F. (1986). Tre test clinici di ricerca e produzione lessicale. Taratura su soggetti normali. *Archivio Di Psicologia, Neurologia E Psichiatria, 47*(4), 477–506.

Orange, J. B., & Hillis, A. E. (2012). *Language profiles in amyotrophic lateral sclerosis. Amyotrophic Lateral Sclerosis and the Frontotemporal Dementias*. Oxford University Press (pp. 78–92). Oxford University Press.

Palmieri, A., Naccarato, M., Abrahams, S., Bonato, M., D'Ascenzo, C., Balestreri, S., ... Sorarù, G. (2010). Right hemisphere dysfunction and emotional processing in ALS: An fMRI study. *Journal of Neurology, 257*(12), 1970–1978. http://dx.doi.org/10.1007/s00415-010-5640-2.

Papagno, C., Cappa, S. F., Forelli, A., Garavaglia, G., & Al, E. (1995). La comprensione non letterale del linguaggio: taratura di un test di comprensione di metafore e di espressioni idiomatiche. *Archivio Di Psicologia Neurologia E Psichiatria, 4*, 402–420.

Papeo, L., Cecchetto, C., Mazzon, G., Granello, G., Cattaruzza, T., Verriello, L., ... Rumiati, R. I. (2015). The processing of actions and action-words in amyotrophic lateral sclerosis patients. *Cortex, 64*, 136–147. http://dx.doi.org/10.1016/j.cortex.2014.10.007.

Phukan, J., Elamin, M., Bede, P., Jordan, N., Gallagher, L., Byrne, S., ... Hardiman, O. (2012). The syndrome of cognitive impairment in amyotrophic lateral sclerosis: A population-based study. *Journal of Neurology, Neurosurgery, and Psychiatry, 83*(1), 102–108. http://dx.doi.org/10.1136/jnnp-2011-300188.

Prior, M., Sartori, G., & Marchi, S. (2003). *Cognizione sociale e comportamento: uno stumento per la misurazione*. Padova: Domeneghini Editore.

Prutting, C. A., & Kirchner, D. M. (1987). A clinical appraisal of the pragmatic aspects of language. *The Journal of Speech and Hearing Disorders, 52*(2), 105–119.

R Core Team (2014). R: A language and environment for statistical computing. R Foundation for Statistical Computing. Vienna, Austria.

Rinaldi, M. C., Marangolo, P., & Lauriola, M. (2004). *BLED SantaLucia. Batteria sul Linguaggio dell'Emisfero Destro SantaLucia*. Firenze: Giunti O.S.

Roberts-South, A., Findlater, K., Strong, M. J., & Orange, J. B. (2012). Longitudinal changes in discourse production in amyotrophic lateral sclerosis. *Seminars in Speech and Language, 33*(1), 79–94. http://dx.doi.org/10.1055/s-0031-1301165.

Schreiber, H., Gaigalat, T., Wiedemuth-Catrinescu, U., Graf, M., Uttner, I., Muche, R., & Ludolph, A. C. (2005). Cognitive function in bulbar- and spinal-onset amyotrophic lateral sclerosis. A longitudinal study in 52 patients. *Journal of Neurology, 252*(7), 772–781. http://dx.doi.org/10.1007/s00415-005-0739-6.

Seeley, W. W. (2008). Selective functional, regional, and neuronal vulnerability in frontotemporal dementia. *Current Opinion in Neurology, 21*(6), 701–707. http://dx.doi.org/10.1097/WCO.0b013e3283168e2d.

Shany-Ur, T., Poorzand, P., Grossman, S. N., Growdon, M. E., Jang, J. Y., Ketelle, R. S., ... Rankin, K. P. (2011). Comprehension of insincere communication in neurodegenerative disease: Lies, sarcasm, and theory of mind. *Cortex; a Journal Devoted to the Study of the Nervous System and Behavior, 48*(10), 1329–1341. http://dx.doi.org/10.1016/j.cortex.2011.08.003.

Sheng, L., Ma, H., Zhong, J., Shang, H., Shi, H., & Pan, P. (2015). Motor and extra-motor gray matter atrophy in amyotrophic lateral sclerosis: Quantitative meta-analyses of voxel-based morphometry studies. *Neurobiology of Aging, 36*(12), 3288–3299. http://dx.doi.org/10.1016/j.neurobiolaging.2015.08.018.

Sperber, D., & Wilson, D. (1995). *Relevance: communication and cognition* (2nd ed.). Oxford: Blackwell.

Sperber, D., & Wilson, D. (2002). Pragmatics, modularity and mind-reading. *Mind and Language, 17*, 3–23.

Spotorno, N., Koun, E., Prado, J., Van Der Henst, J.-B., & Noveck, I. a. (2012). Neural evidence that utterance-processing entails mentalizing: The case of irony. *NeuroImage, 63*(1), 25–39. http://dx.doi.org/10.1016/j.neuroimage.2012.06.046.

Staios, M., Fisher, F., Lindell, A. K., Ong, B., Howe, J., & Reardon, K. (2013). Exploring sarcasm detection in amyotrophic lateral sclerosis using ecologically valid measures. *Frontiers in Human Neuroscience, 7*(May), 178. http://dx.doi.org/10.3389/fnhum.2013.00178.

Stemmer, B. (2008). Neuropragmatics: Disorders and neural systems. In B. Stemmer & H. A. Whitacker (Eds.), *Handbook of the neuroscience of language*. New York: Elsevier.

Strong, M. J., Grace, G. M., Freedman, M., Lomen-Hoerth, C., Woolley, S., Goldstein, L. H., ... Figlewicz, D. (2009). Consensus criteria for the diagnosis of frontotemporal cognitive and behavioural syndromes in amyotrophic lateral sclerosis. *Amyotrophic Lateral Sclerosis, 10*(3), 131–146. http://dx.doi.org/10.1080/17482960802654364.

Tabossi, P., Arduino, L., & Fanari, R. (2011). Descriptive norms for 245 Italian idiomatic expressions. *Behavior Research Methods, 43*(1), 110–123. http://dx.doi.org/10.3758/s13428-010-0018-z.

Taylor, L. J., Brown, R. G., Tsermentseli, S., Al-Chalabi, A., Shaw, C. E., Ellis, C. M., ... Goldstein, L. H. (2013). Is language impairment more common than executive dysfunction in amyotrophic lateral sclerosis? *Journal of Neurology, Neurosurgery, and Psychiatry, 84*(5), 494–498. http://dx.doi.org/10.1136/jnnp-2012-303526.

Tettamanti, M., & Moro, A. (2012). Can syntax appear in a mirror (system)? *Cortex; a Journal Devoted to the Study of the Nervous System and Behavior, 48*(7), 923–935. http://dx.doi.org/10.1016/j.cortex.2011.05.020.

Thomas, M., Alegre-Abarrategui, J., & Wade-Martins, R. (2013). RNA dysfunction and aggrephagy at the centre of an amyotrophic lateral sclerosis/frontotemporal dementia disease continuum. *Brain: A Journal of Neurology, 136*(Pt 5), 1345–1360. http://dx.doi.org/10.1093/brain/awt030.

Tsermentseli, S., Leigh, P. N., & Goldstein, L. H. (2012). The anatomy of cognitive impairment in amyotrophic lateral sclerosis: More than frontal lobe dysfunction. *Cortex; a Journal Devoted to the Study of the Nervous System and Behavior, 48*(2), 166–182. http://dx.doi.org/10.1016/j.cortex.2011.02.004.

van der Hulst, E.-J., Bak, T. H., & Abrahams, S. (2014). Impaired affective and cognitive theory of mind and behavioural change in amyotrophic lateral sclerosis. *Journal of Neurology, Neurosurgery, and Psychiatry, 1–8*. http://dx.doi.org/10.1136/jnnp-2014-309290.

Yus, F. (2008). A relevance-theoretic classification of jokes. *Lodz Papers in Pragmatics, 4*(1), 131–157. http://dx.doi.org/10.2478/v10016-008-0004-4.