



# Impact of disease, cognitive and behavioural factors on caregiver outcome in amyotrophic lateral sclerosis

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## Abstract

Up to 50% of patients with amyotrophic lateral sclerosis (ALS) show mild to moderate cognitive-behavioural change alongside their progressive functional impairment. This study examines the relative impact of patients' disease symptoms, behavioural change and current executive function and social cognition abilities on psychosocial outcomes in spouse caregivers of people with ALS. Thirty-five spouse caregivers rated their own levels of depression and anxiety, subjective burden and marital satisfaction. Caregivers also rated their partner's everyday behaviour. The patients were assessed for disease severity and cognitive function, with composite scores derived for executive function and social cognition. Regression analyses revealed that caregiver burden was predicted by the severity of patients' limb involvement and behavioural problems. Depression was predicted by patients' limb involvement, while behavioural problems and patient age predicted caregiver anxiety. Current marital satisfaction was predicted by patient behavioural problems beyond the level of pre-illness marital satisfaction. In conclusion, the study highlights the potential impact of ALS patients' functional impairment and behavioural change on ALS caregivers' psychosocial functioning. Clinical communication with ALS families should emphasise both physical and psychological challenges presented by the disease.

**Key words:** *Cognitive-behavioural impairment, disease severity, anxiety, depression, caregiver burden*

## Introduction

While less marked than observed in frontotemporal dementia (FTD), up to 50% of non-demented patients with amyotrophic lateral sclerosis (ALS) may show behavioural symptoms (1) including apathy, disinhibition and/or egocentrism (2–4). In addition, non-demented people with ALS may also show impaired performance on standardized tasks of executive function (5) and social cognition (6–9). In informal family caregivers, mood and subjective burden is affected by the patients' functional impairment (10–12) and the presence of behavioural change (13–15). However, the contribution of cognitive impairment, as assessed by standardized tests, is unclear. The current study sought to explore the

relative impact of patient disease, objective cognitive function and behavioural change on four indicators of caregiver outcome: depression, anxiety, burden and marital satisfaction.

## Material and methods

### Participants

Spouse caregivers were recruited as part of a parallel study that explored cognitive and behavioural change in non-demented patients with ALS (for information about this study see Supplemental Appendix Table 1 available online at <http://informahealthcare.com/doi/abs/10.3109/21678421.2015.1051990>). Participants were recruited between January 2011 and May 2013

from five Motor Neurone Disease Care and Research Centres in the UK. The following exclusion criteria were applied for all participants: a diagnosis of a psychiatric condition; a formal diagnosis of dementia; a first language other than English. Patients were excluded from the parallel study on the basis of a formal diagnosis of another neurological condition or diabetes; aged > 75 years and evidence of respiratory insufficiency, as determined by the patients' clinical team; a forced vital capacity (FVC) < 70% (where available) and a score > 10 on the Epworth Sleepiness Scale (16). In total, 46 caregivers were approached with approval of the patient with ALS. Nine declined, and one was excluded due to dementia. One carer was excluded as they could not provide a report on their relationship prior to their spouse's illness. Informed written consent was obtained from the remaining 35 caregivers and their spouses. Ethics approval was obtained from the National Research Ethics South-East London Research Committee 4 (11/H0807/1).

### Measures

**Caregiver outcome.** The Hospital Anxiety and Depression Scale (HADS) (17) was used to measure caregiver anxiety (HADS A) and depression (HADS D). The Zarit Burden Inventory (ZBI) (18) measured caregivers' perceived burden associated with their partner's illness and their caregiving role. Caregivers' perceived marital satisfaction was measured using the Marital Intimacy Scale (MIS) (19), which assesses several dimensions of the marital relationship, such as affection, compatibility and autonomy. Caregivers completed this measure with respect to the time of the interview (MIS current) and a time approximately two years before the onset of their partner's ALS (MIS pre-illness).

**ALS measures.** Physical symptom severity was assessed using the revised Amyotrophic Lateral Sclerosis Scale (ALSFRS-R) (20). Patients' mood was measured using the revised HADS (HADS-R), which removes two items that may be confounded with the physical impairment of ALS (21). Cognitive function was assessed on a range of neuropsychological tests of executive function and social cognition. Table I provides descriptions and references (22–27) for these tasks. To reduce the number of variables used in the analyses, composite scores were created as follows: test scores were standardized by subtracting the mean score of the control group from each participant's score on an individual test and then dividing the difference by the corresponding standard deviation of the control group. The resulting standardized scores were then summed according to theorised function and divided by the number of component tests contributing to the composite. When participants did not complete all measures in the composite, the measures that were completed

were standardized and averaged as above. Where necessary, scores were reflected so that they shared the same direction; a higher score represented poorer performance. Internal consistency for these composites for the patient group (n=35) were satisfactory (Executive function composite  $\alpha = .79$ ; Social cognition composite  $\alpha = 5.89$ ). Caregivers rated their partner's current behaviour using the informant version of the Frontal Systems Behavioural Scale (FrSBe) (28) (apathy, disinhibition and everyday behavioural indications of executive dysfunction) and emotional lability using the Emotional Lability Questionnaire (ELQ) (29).

### Data analysis

Data were analysed using IBM SPSS for Windows version 21 (IBM SPSS Statistics Armonk, NY, USA). Demographic, clinical and cognitive characteristics were reported as percentages for categorical data and means for continuous variables. Categorical data were analysed using  $\chi^2$  tests. Outliers were identified and transformed by recoding the outlying value with a score one unit higher/lower than the next highest/lowest non-outlying score in the distribution. Pearson's correlations and multiple regression analyses were used to examine the relationships between parameter and caregiver outcome variables. All tests were two-tailed, and statistical significance was set at  $p < 0.05$ .

## Results

### ALS sample characteristics

Patients' demographics and disease information are shown in Table II. Limb-onset disease was observed in 77.1% and bulbar onset in the remainder. Most patients (80%) were receiving treatment with riluzole. Table III shows patients' mood scores, cognitive composite scores, mean group performance on individual cognitive tests and the percentage of patients whose performance was at or lower than the 5<sup>th</sup> percentile of an age-, education-, gender-matched control sample from a larger parallel study (see Supplemental Appendix Table 1 available online at <http://informahealthcare.com/doi/abs/10.3109/21678421.2015.1051990>). Table III also shows caregiver ratings of patient behavioural involvement and emotional lability. The percentage of patients being endorsed by their caregivers as demonstrating clinically relevant behaviour (a T-score > 65 on the FrSBe domains) is also shown. Figure 1 presents the proportion of patients by number of impaired scores on the cognitive tasks (as defined as a score at or lower than 5<sup>th</sup> percentile of controls' scores) and behaviour domains (as defined by T-score > 65). The number of patients meeting current cognitive impairment criteria (30) (impairments on two or more tests of executive function) was 3/35 (8.6%).

Table I. Descriptions of executive function and social cognition tasks.

Task	Description	Scoring
The verbal fluency index (22)	Participants write down/say as many words as possible in a given time limit and under conditions in which the response is specified by a particular restriction, such as a letter. In this study participants had to produce as many words beginning with S as they could in five minutes and as many 4-letter words beginning with C in four minutes. In a subsequent control condition the participant copies/reads out these words as quickly as they can.	An index is calculated by subtracting the time taken to copy/read aloud the words from the duration of the word generation condition and dividing this by the total number of words generated. This index represents the average time taken to generate each word; higher scores indicating longer thinking times and greater executive impairment.
The Card Sorting task from the Delis-Kaplan Executive Function Scale (23)	Participants sort cards into mutually exclusive categories based on the verbal or visual information of the cards with the goal of making as many sorts as possible. Participants are required to describe the conceptual relationships between cards within each created category.	The maximum possible scores (32 for number of sorts made; 64 for description scores) minus the participant's score served as a measure of 'errors' on these conditions; the higher these scores the worse the performance on these conditions.
The Brixton Spatial Anticipation Test (24)	Participants are presented with series of arrays containing 10 circles. Each array contains one coloured circle, the position of which varies from one array to the next according to implicit rules (which change abruptly). Participants indicate the likely position of the coloured circle in the following array.	The outcome measure was the total number of errors, with higher scores indicating worse performance (maximum possible errors were 56).
Three subtests of The Awareness of Social Inference Test (TASIT) (25)	These tasks use enacted scenes of everyday social interaction: Emotional Evaluation (EET, dynamic videos of basic emotion expression); Social Inference-minimal (SIM-M, dynamic videos portraying sincere and sarcastic social exchanges); Social Inference-enriched (SI-E, dynamic videos portraying sincere, sarcastic and deceptive social exchanges).	The maximum possible scores (EET: 28; SI-M: 60; SI-E: 64) minus the participant's scores on each subtask served as a measure of 'errors'; the higher the scores, the worse the performance.
Three subtests of the Happé Cartoon and Scenarios Task (26)	These tasks use humorous cartoons and vignettes depicting characters in social situations involving deception, belief and intention. In the experimental conditions, the targeted inference related to the mental states of these characters. In control conditions, the targeted inference related to physical causation or logical sequence.	The maximum possible scores (cartoon task 1: 32; cartoon task 2: 30; vignettes: 32) minus the participant's score served as a measure of 'errors'; the higher these scores the worse the performances.
The Reading in Mind in the Eyes (RME) task (27)	Participants are required to attribute complex mental or emotional states to facial images depicting only the eye region.	The maximum score (36) minus the participant's score served as a measure of 'errors'; the higher the score the worse the performance.

By extension, the number of impairments on two or more domains of social cognition was 4/35 (11.4%). The number of patients meeting criteria for impairment on two or more domains of the FrSBe was 8/33 (24.2%).

#### Caregiver sample characteristics

The mean age of the caregiver group was 57.7 years (SD = 10.5) and 71.4% were female. The mean duration of their marriage to the patient was 33.2 years (SD = 13). Table IV shows levels of caregiver anxiety, depression, burden and marital satisfaction (current and pre-illness). Pre-illness MIS ratings ( $M = 76.1$ ,  $SD = 15.4$ ) were significantly higher than current MIS ratings ( $M = 70.2$ ,  $SD = 18.4$ ),  $t(31) = 3.04$ ,  $p = 0.005$ ,  $d = 0.35$ . Current and pre-illness MIS scores were highly correlated ( $r = 0.81$ ,  $p < 0.001$ ).

#### Predictors of caregiver outcome

Potential predictor variables were selected on the basis of past research (10–15) and the objectives of the study and comprised ALSFRS-R subscale scores; months since diagnosis; Executive and Social Cognition composite scores; FrSBe Total and subscale T-scores; ELQ total severity score; caregivers' age; patients' age, patients' HADS-R scores and years of marriage. Variables that showed significant paired associations with the outcomes ( $p < 0.05$ ) were entered into forward selection multiple regressions (Table V). The correlations between outcome measures are shown in the Supplemental Appendix Table 2 available online at <http://informahealthcare.com/doi/abs/10.3109/21678421.2015.1051990>.

*Caregiver depression.* Significant correlates of caregiver HADS D were ALSFRS-R Limb ( $r = -0.48$ ,

Table II. Patient demographics and disease information.

	Mean	SD	Min – Max
Age	60.9	8.4	32.0 – 80.0
Education (years)	14.2	3.6	10.0 – 24.0
Months since symptom onset	30.4	14.3	10.0 – 75.0
Months since diagnosis	14.8	12.2	3.0 – 51.0
Age at symptom onset	58.6	8.5	34.0 – 72.0
ALSFERS-R total severity score (max 48)	34.1	8.2	9.0 – 48.0
ALSFRS-R bulbar severity score (max 12)	9.3	3.0	1.0 – 12.0
ALSFRS-R Limb severity score (max 12)	14.0	6.0	3.0 – 24.0
ALSFRS-R Respiratory severity score (max 12)	10.8	2.0	2.0 – 12.0
Epworth Sleepiness Scale Score (max 24)	3.3	2.9	0.0 – 10.0

Min: minimum; Max: maximum; ALSFRS-R: revised Amyotrophic Lateral Sclerosis Functional Rating Scale: bulbar=items 1–3; Limb=items 4–9; Respiratory=items 10–12, lower scores indicate greater functional impairment.

$p = 0.004$ ,  $n = 35$ ), FrSBe Apathy ( $r = 0.43$ ,  $p = 0.01$ ,  $n = 33$ ) and FrSBe Total ( $r = 0.37$ ,  $p = 0.04$ ,  $n = 33$ ). Only ALSFRS-R Limb entered the final model ( $F(1,31) = 8.07$ ,  $p = 0.08$ ) explaining 18% of the variance, with greater functional impairment (lower ALSFRS-R limb scores) associated with higher caregiver depression (higher HADS D scores).

**Caregiver anxiety.** Significant correlates of caregiver HADS A were FrSBe Total ( $r = 0.40$ ,  $p = 0.02$ ,  $n = 33$ ), ELQ Total ( $r = 0.36$ ,  $p = 0.03$ ,  $n = 34$ ), patients' age ( $r = -0.4$ ,  $p = 0.03$ ,  $n = 35$ ) and ALSFRS-R Limb ( $r = -0.38$ ,  $p = 0.03$ ,  $n = 35$ ). FrSBe Total and patients' age remained in the model ( $F(1,30) = 5.4$ ,  $p = 0.01$ ), explaining 22% of anxiety variance. Greater carer anxiety (higher HADS A scores) was predicted by greater behavioural impairment (higher FrSBe Total scores) and younger patient age.

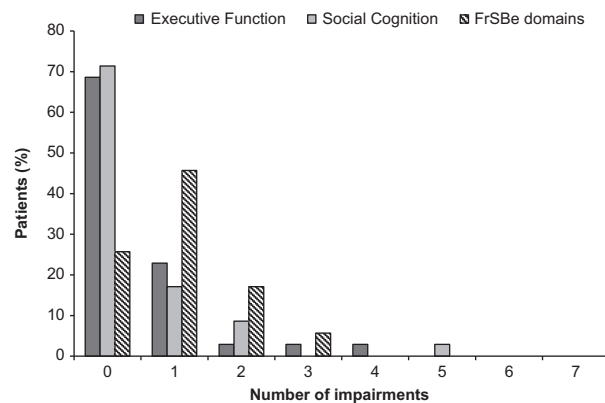


Figure 1. Proportion of patients by number of impairments on cognitive tests and behaviour domains. Executive function (max. 6 tests,  $n = 35$ ), social cognition (max. 7 tests,  $n = 35$ ), behaviour (max. 3 FrSBe domains,  $n = 33$ ). Impairment defined as performance at or below 5th percentile of control group (for cognitive tests) and a T-score  $> 65$  on the separate FrSBe domains (apathy, disinhibition, executive dysfunction).

**Caregiver burden.** Significant correlates of the ZBI score were ALSFRS-R Limb ( $r = -0.66$ ,  $p < 0.001$ ,  $n = 34$ ), FrSBe Apathy ( $r = 0.63$ ,  $p < 0.001$ ,  $n = 32$ ), FrSBe Disinhibition ( $r = 0.51$ ,  $p = 0.003$ ,  $n = 32$ ), FrSBe Executive Dysfunction ( $r = 0.51$ ,  $p = 0.003$ ,  $n = 32$ ), FrSBe Total ( $r = 0.69$ ,  $p < 0.001$ ,  $n = 32$ ) and patients' age ( $r = 0.35$ ,  $p = 0.04$ ,  $n = 34$ ). ALSFRS-R Limb and the FrSBe Total remained in the model ( $F(2,28) = 80.7$ ,  $p < 0.001$ ) and explained 84% of the variance in caregiver burden. Caregiver burden increased with worsening physical impairment (lower ALSFRS-R limb scores) and behavioural problems (higher FrSBe Total scores) in the person with ALS.

**Current caregiver marital satisfaction.** Significant correlates of current MIS scores were FrSBe Apathy ( $r = -0.37$ ,  $p < 0.04$ ,  $n = 31$ ), FrSBe Executive Dysfunction ( $r = -0.49$ ,  $p = 0.005$ ,  $n = 31$ ) and FrSBe Total ( $r = -0.54$ ,  $p = 0.002$ ,  $n = 31$ ). Only FrSBe Total entered the model,  $R^2 = 0.30$ , adjusted  $R^2 = 0.27$ ,  $F(1,29) = 12.12$ ,  $p = 0.002$ , standardized  $\beta = -0.54$ ,  $t(29) = -3.48$ ,  $p = 0.002$ . To control for the possible influence of pre-illness marital satisfaction, FrSBe Total scores were then entered into a hierarchical regression analysis, controlling for pre-illness MIS scores. The model explained 78% of the variance in caregivers' current marital satisfaction ( $F(2,27) = 52.7$ ,  $p < 0.001$ ) with FrSBe Total scores remaining a significant independent predictor.

### Selection bias

Caregivers were invited to participate in the study because their partner with ALS was taking part in a larger study (see Supplemental Appendix Table 1 available online at <http://informahealthcare.com/doi/abs/10.3109/21678421.2015.1051990>) and consented to their spouse being approached. Data for the nine spouses who declined invitation are not available; however, the demographic, disease and cognitive profiles of the nine patients ( $n = 2$  female) whose spouses declined participation are shown in Table S3 in the Supplemental Appendix available online at <http://informahealthcare.com/doi/abs/10.3109/21678421.2015.1051990>.

### Discussion

Previous studies have highlighted the impact of disease factors (10–12) and behavioural change (13–15) on caregivers of ALS, but the contribution of objectively measured patient cognitive function has not been established. The present results suggest that formal measures of executive function and social cognition do not independently predict any of the caregiver outcomes assessed. This is in contrast to previous studies of caregivers of patients with dementia (31), but similar to reports of caregivers of patients with Mild Cognitive Impairment (32). Together, such evidence suggests that for caregivers of non-

Table III. Mood, cognitive performance and behaviour of ALS participants.

Measure	Mean	SD	Min-Max	n	Cut-off	n (%) <sup>a</sup>
HADS-R Depression score	2.5	2.1	0.0–9.0	35	8	1 (2.9)
HADS-R Anxiety score	4.3	3.7	0.0–18.0	35	9	5 (14.3)
Executive Function Composite	0.5	0.4	–0.5–3.3	35	1.6	5 (14.3)
Social Cognition Composite	0.4	0.8	–0.9–2.9	35	1.7	4 (11.4)
VFI – S words	5.3	3.3	0.9–14.4	35	8.6	6 (17.1)
VFI – C words	16.2	12.0	0.04–39.3	35	20.7	3 (8.6)
DKEFS Card Sorting	6.3	2.1	2–10	33	12	2 (6.1)
DKEFS Card Sorting Description	28.5	11.3	8–54	33	47	3 (9.1)
Brixton errors	18.1	5.4	7–30	35	29.5	2 (5.7)
TASIT Emotion Evaluation Test	6.1	2.8	2–13	35	11	3 (8.6)
TASIT Social Inference Minimal	11.1	7.6	0–33	35	17	7 (20)
TASIT Social Inference Enriched	12.3	6.2	4–29	35	25	1 (2.9)
Happé Cartoons task 1	11.9	5.7	1–24	29	20.6	3 (10.3)
Happé Cartoons task 2	12.2	4.7	2–21	29	18.6	0 (0)
Happé Scenarios	9.2	4.1	1–17	25	19.1	0 (0)
RME	11.9	4.8	4–21	34	17	4 (11.8)
FrSBe Total	63.7	12.8	42–107	33	65	11 (33.3)
FrSBe Apathy	69.2	13.6	46–94	33	65	19 (57.6)
FrSBe Disinhibition	55.0	11.8	39–88	33	65	5 (15.2)
FrSBe Executive Dysfunction	60.0	13.3	41–102	33	65	10 (30.3)
ELQ Total	5.0 <sup>b</sup>	0.0–15.5 <sup>c</sup>	0.0–43.0	34	21	6 (17.6)

Higher scores indicate worse mood, cognitive performance and greater behavioural impairment and greater emotional lability.

<sup>a</sup>Number and percentage of patients meeting cut-off criteria for ‘caseness’ (HADS-R); performance at or below 5<sup>th</sup> percentile of controls (composites, cognitive tests scores and ELQ) and clinically relevant behaviour (FrSBe).

<sup>b</sup>Median.

<sup>c</sup>IQR.

demented patients (including ALS), the perceived severity of patients’ everyday behavioural impairment (as reflected in FrSBe ratings) have a greater effect on caregiver well-being than the objective level of cognitive impairment. However, the profile of cognitive impairments in the current patient sample may have influenced the results obtained. While impairments in performance on some measures of executive function and social cognition were noted in some patients, only a small proportion of patients qualified for cognitive impairment according to Strong et al.’s criteria. Thus, patients’ cognitive deficits might not have been severe enough to interfere with their everyday activities or create burden for their caregiver. With progression, and worsening of cognitive function in some patients, caregivers may become more aware of and affected by cognitive impairment and its impact on daily function.

Table IV. Caregivers’ self-ratings for outcomes.

Caregiver self-report measures	Scores	Mean	SD	n
The Hospital Anxiety and Depression Scale (HADS) (17)	HADS A	9.2	4.6	35
	HADS D	5.7	4.0	35
The Zarit Burden Interview (ZBI) (18)	ZBI Total	29.4	14.1	4
The Marital Intimacy Scale (MIS) (19)	MIS pre-ALS	76.1	5.4	32
	MIS current	70.2	18.4	32

Higher scores indicate worse symptoms except for the MIS measure in which higher scores indicate greater marital satisfaction.

Slightly different predictors emerged for caregiver burden, depression and anxiety, although the differences in the models should be interpreted with caution. Of the ALS symptoms, the severity of limb involvement was the best predictor of caregiver burden and depression, at least in the present sample of patients relatively early in their disease. Functional impairment may lead to increased physical dependence on the caregiver, imposing restrictions upon caregivers’ personal and social activities and needs (13,33). With disease progression and potential worsening of bulbar and respiratory impairments, these other symptoms may become more important for caregiver outcomes. Recent studies have emphasised the importance of the behavioural above the physical aspects of ALS on caregivers (14,15). In contrast, the current results suggest that both patients’ physical and behavioural symptoms may act in concert in their impact on caregivers. The disparity in these findings might reflect differences in the patient samples in terms of the severity of ALS and behavioural symptoms. For example, perhaps responding to acute behavioural symptoms eventually dominates caregivers’ priorities even alongside the progression of the patient’s disability.

As in previous studies, greater behavioural symptoms as measured by the FrSBe predicted poorer outcome in terms of burden, anxiety and marital satisfaction, even in spouses of patients in the first two years from diagnosis. This highlights the importance of detection of such problems early in the disease trajectory. The FrSBe Total score was a better

Table V. Predictors of caregivers' outcomes.

Outcome Predictor	Model 1				Model 2			
	R <sup>2</sup>	Adj. R <sup>2</sup>	$\beta$	<i>p</i>	R <sup>2</sup>	Adj. R <sup>2</sup>	$\beta$	<i>p</i>
Depression								
ALSFRS-R Limb	0.21	0.18	-0.45	<0.01				
Anxiety								
FrSBe Tot.	0.16	0.13	0.40	0.02	0.27	0.22	0.35	0.04
Patients' age (years)							-0.34	0.04
Burden								
FrSBe Tot.	0.60	0.59	0.78	<0.01	0.85	0.84	0.69	<0.01
ALSFRS-R Limb							-0.51	<0.01
Marital intimacy								
MIS pre-illness	0.63	0.62	0.80	<0.01	0.80	0.78	0.68	<0.01
FrSBe Tot.							-0.42	<0.01

Table V displays output for forward regression analyses except for Marital Intimacy which is a hierarchical regression analysis. Adj.: Adjusted;  $\beta$ : standardized beta; ALSFRS-RLimb: Amyotrophic Lateral Sclerosis Functional Rating Scale-revised Limb subscale; FrSBe Tot.: Frontal Systems Behaviour Scale Total T-score; MIS pre-illness: Marital Intimacy Scale score rated for period two years prior to ALS onset.

predictor of caregiver outcome than the subscale scores, suggesting that global behavioural change may be a more useful indicator than individual behavioural symptoms for caregivers of non-demented patients. This was true for the current sample despite more than half of the patients being endorsed for clinically relevant levels of apathy. Demographic characteristics did not emerge as independent predictors with the exception of patient age, with higher anxiety scores seen in the caregivers of younger patients. This may reflect concerns about the future in younger couples where the ALS may have greater economic and wider family impact.

Caregivers' levels of perceived marital satisfaction were significantly reduced compared to those reported for the period before their partners' illness, replicating previous findings (34). However, the quality of the marital relationship prior to the onset of ALS remained the most important determinant of current satisfaction. The significant association between marital satisfaction and burden suggests that a poor pre-illness relationship increases the risk of greater burden in caregivers after the onset of ALS, or conversely, that a strong relationship is protective against the negative effects on caregiver outcome.

Caregivers have reported that clinical services place disproportionate focus on the practical rather than emotional adjustments to the disease (35,36). The current findings suggest that routine monitoring of the patient's functional, cognitive and behavioural status may better prepare the clinical team to tailor their support for caregivers. Early interventions could include educating the caregiver about the possible interpersonal or behavioural changes that might accompany their partner's disability, so that caregivers do not misinterpret their partner's emerging disposition as resulting from inherent problems within their relationship (37). More formally, caregivers

might benefit from group or individual psychosocial interventions, although, to date, none has been evaluated for potential efficacy in improving the well-being of ALS caregivers.

This study is limited by its cross-sectional design; a longitudinal study of caregiver outcomes alongside patients' declining functional status and behavioural change would further clarify the causal relationships and interactions between the measures as the ALS progresses. Although objective measures of patients' neuropsychological performance were not predictive of caregiver outcomes here, there is merit in investigating whether changes in cognitive indices over time explain variability in caregiving outcomes at different stages of disease. As already mentioned, the relatively preserved cognitive status of the majority of patients in the sample may limit the inferences drawn regarding the influence of ALS-related cognitive impairment on caregivers' well-being. Future research would benefit from including a more cognitively heterogeneous sample and/or comparisons between caregivers of 'pure ALS' and ALS-FTD. The use of composite scores to measure patients' cognitive functions may have underestimated or masked correlations for individual measures; however, these were necessary to allow parsimonious analyses for the small sample size. The HADS is not diagnostic of mood disorder and caregivers' mean values for anxiety and depression did not suggest the presence of generally clinically significant dysthymia. Thus, the generalizability of these results to clinically depressed or anxious caregivers is restricted. The lack of objective FVC scores for some patients means that the study may underestimate the influence of subtle respiratory deficits (not noticeable to the patient or the clinical team) on patients' cognitive performance and/or caregivers' outcomes. The influence of recall bias on measures assessing retrospective outcomes cannot be excluded. Following ethics guidelines, the

study could not record data from the nine spouses who declined to consent to the research and thus we cannot exclude the possibility of selection bias. Finally, this study emphasised caregivers' experiences and precludes comment on the impact of ALS on patients and their spouses as a dyadic unit. Nonetheless, the current findings implicate the roles of both patients' functional impairment and behavioural dysfunction in caregivers' responses to ALS. Our findings suggest, therefore, that clinical communication with ALS families should emphasise both the physical and psychological challenges presented by the cognitive-behavioural features of ALS.

### Acknowledgements

We thank the patients with ALS and their caregivers who participated in the research. We also thank members of the research support team who assisted with participant recruitment for the study: Rachel Burman, Catherine Knights, Andrew Dougherty, Naomi Martin, Rachel Tuck, Jan Clarke, Christine Batts, Hazel Watts, Joanna Sasson, Helen Copesy, Trish Cutts.

This work was submitted in part fulfilment of a PhD project (for TJW) funded by the Medical Research Council, The National Institute of Health Research (NIHR) Dementias and Neurodegenerative Diseases Research Network and the Motor Neuron Disease Association. The work leading up to this publication was funded by the European Community's Health Seventh Framework Programme (AAC & CES grant number 259867). AAC and CES are involved in two EU Joint Programmes – Neurodegenerative Disease Research (JPND) projects (STRENGTH and ALS-CarE). These projects are supported through the following funding organizations under the aegis of JPND – [www.jpnd.eu](http://www.jpnd.eu): United Kingdom, Medical Research Council and Economic and Social Research Council. Some authors receive salary support from the NIHR Dementia Biomedical Research Unit (CES, AAC, RGB, LHG) and the NIHR Biomedical Research Centre for Mental Health (CES, AAC, RGB) at the South London and Maudsley NHS Foundation Trust and King's College London. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health.

**Declaration of interest:** The authors declare no conflicts of interest in this study.

### References

- Merrilees J, Klapper J, Murphy J, Lomen-Hoerth C, Miller BL. Cognitive and behavioural challenges in caring for patients with frontotemporal dementia and amyotrophic lateral sclerosis. *Amyotroph Lateral Scler.* 2010;11:298–302.
- Grossman AB, Woolley-Levine S, Bradley WG, Miller RG. Detecting neurobehavioural changes in amyotrophic lateral sclerosis. *Amyotroph Lateral Scler.* 2007;8:56–61.
- Gibbons Z, Richardson A, Neary D, Snowden JS. Behaviour in amyotrophic lateral sclerosis. *Amyotroph Lateral Scler.* 2008;9:67–74.
- Witgert M, Salamone AR, Strutt AM, Jawaid A, Massman PJ, Bradshaw M, et al. Frontal-lobe mediated behavioural dysfunction in amyotrophic lateral sclerosis. *Euro J Neurol.* 2010;17:103–10.
- Goldstein LH, Abrahams S. Changes in cognition and behaviour in amyotrophic lateral sclerosis: nature of impairment and implications for assessment. *Lancet Neurol.* 2013;12:368–80.
- Girardi A, MacPherson SE, Abrahams S. Deficits in emotional and social cognition in amyotrophic lateral sclerosis. *Neuropsychology.* 2011;25:53–65.
- Lillo P, Savage S, Mioshi E, Kiernan MC, Hodges JR. Amyotrophic lateral sclerosis and frontotemporal dementia: a behavioural and cognitive continuum. *Amyotroph Lateral Scler.* 2012;13:102–9.
- Gibbons Z, Snowden JS, Thompson JC, Happé F, Richardson A, Neary D. Inferring thought and action in motor neuron disease. *Neuropsychologia.* 2007;45:1196–1207.
- Staios M, Fisher F, Lindell AK, Ong B, Howe J, Reardon K. Exploring sarcasm detection in amyotrophic lateral sclerosis using ecologically valid measures. *Front Hum Neurosci.* 2013;7:178.
- Adelman EE, Albert SM, Rabkin JG, Del Bene ML, Tider T, O'Sullivan I. Disparities in perceptions of distress and burden in ALS patients and family caregivers. *Neurology.* 2004;62:1766–70.
- Gauthier A, Vignola A, Calvo A, Cavallo E, Moglia C, Sellitti L, et al. A longitudinal study on quality of life and depression in ALS patient-caregiver couples. *Neurology.* 2007;68: 923–6.
- Goldstein LH, Adamson M, Jeffrey L, Down K, Barby T, Wilson C, et al. The psychological impact of MND on patients and carers. *J Neurol Sci.* 1998;160:S114–121.
- Goldstein LH, Atkins L, Landau S, Brown R, Leigh PN. Predictors of psychological distress in carers of people with amyotrophic lateral sclerosis: a longitudinal study. *Psychol Med.* 2006;36:865–75.
- Chio A, Vignola A, Mastro E, Guidici AD, Iazzolino B, Calvo A, et al. Neurobehavioural symptoms in ALS are negatively related to caregivers' burden and quality of life. *Euro J Neurol.* 2010;17:1298–1303.
- Lillo P, Mioshi E, Hodges JR. Caregiver burden in amyotrophic lateral sclerosis is more dependent on patients' behavioural changes than physical disability: a comparative study. *BMC Neurol.* 2012;12:156.
- Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep.* 1991; 14:540–5.
- Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand.* 1983;67:361–70.
- Zarit SH, Zarit JM. Instructions for the Burden Interview. Pennsylvania: Pennsylvania State University, 1987.
- Morris LW, Morris RG, Britton PG. The relationship between marital intimacy, perceived strain and depression in spouse caregivers of dementia sufferers. *Br J Med Psychol.* 1988;61:231–6.
- Cedarbaum JM, Stambler N, Malta E, Fuller C, Hilt D, Thurmond B, et al. The ALSFRS-R: a revised ALS functional rating scale that incorporates assessments of respiratory function. *J Neurol Sci.* 1999;169:13–21.
- Gibbons C, Mills R, Thornton E, Ealing J, Mitchell JD, Shaw PJ, et al. Rasch analysis of the hospital anxiety and depression scale (HADS) for use in motor neuron disease. *Health Qual Life Outcomes.* 2011;9:1–8.
- Abrahams S, Leigh PN, Harvey A, Vythelingum GN, Grise D, Goldstein LH. Verbal fluency and executive dysfunction in amyotrophic lateral sclerosis (ALS). *Neuropsychologia.* 2000;38:734–47.

23. Delis D, Kaplan E, Krammer J. Delis-Kaplan Executive Function System. San Antonio, USA: Psychological Corporation, 2001.
24. Burgess PW, Shallice T. The Hayling and Brixton Tests. Bury St Edmonds, UK: Thames Valley Company, 1997.
25. McDonald S, Flanagan S, Rollins JB. The Awareness of Social Inference Test (TASIT). St Edmonds, UK: Thames Valley Test Company, 2002.
26. Happé F, Brownell H, Winner E. Acquired 'theory of mind' impairments following stroke. *Cognition*. 1999; 70:211–24.
27. Baron-Cohen S, Wheelwright S, Hill J, Raste Y, Plumb I. The "Reading the Mind in the Eyes" Test Revised Version: A Study with Normal Adults, and Adults with Asperger Syndrome or High-functioning Autism. *J Child Psychol Psychiatry*. 2001;42:241–51.
28. Grace J, Malloy P. The Frontal Systems Behavioural Scale (FrSBe). Florida: Psychological Assessment Resources Inc, 2001.
29. Newsom-Davis IC, Abrahams S, Goldstein LH, Leigh PN. The emotional lability questionnaire: a new measure of emotional lability in amyotrophic lateral sclerosis. *J Neurol Sci*. 1999;169:22–5.
30. Strong MJ, Grace GM, Freedman M, Lomen-Hoerth C, Woolley SC, Goldstein LH, et al. Consensus criteria for the diagnosis of frontotemporal cognitive and behavioural syndromes in amyotrophic lateral sclerosis. *Amyotroph Lateral Scler*. 2009;10:131–46.
31. Miller LA, Mioshi E, Savage S, Lah S, Hodges JR, Piguet O. Identifying cognitive and demographic variables that contribute to carer burden in dementia. *Dement Geriatr Cogn Disord* 2013;36:43–9.
32. Dean K, Wilcock G. Living with mild cognitive impairment: the patient's and carer's experience. *Int Psychogeriatr*. 2012;24:871–81.
33. Hecht MJ, Graesel E, Tigges S, Hillemacher T, Winterholler M, Hiltz MJ, et al. Burden of care in amyotrophic lateral sclerosis. *Palliat Med*. 2003;17:327–33.
34. Atkins L, Brown RG, Leigh PN, Goldstein LH. Marital relationships in amyotrophic lateral sclerosis. *Amyotroph Lateral Scler*. 2010;11:344–50.
35. Brown J. User, carer and professional experiences of care in motor neuron disease. *Primary Health Care Research and Development*. 2003;4:207–18.
36. Oyebo J, Smith H, Morrison K. The personal experience of partners of individuals with motor neuron disease. *Amyotroph Lateral Scler Frontotemporal Degener*. 2013; 14: 39–43.
37. Abrahams S. Social cognition in amyotrophic lateral sclerosis. *Neurodegener Dis Manag*. 2011;1:397–405.

### Supplementary material available online

Supplementary Tables 1–3 available online at <http://informahealthcare.com/doi/abs/10.3109/21678421.2015.1051990>