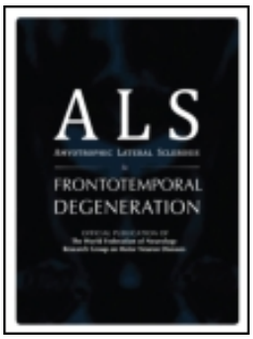


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# THEME 3 COGNITIVE AND PSYCHOLOGICAL ASSESSMENT AND SUPPORT

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# THEME 3 COGNITIVE AND PSYCHOLOGICAL ASSESSMENT AND SUPPORT

# THEME 3 COGNITIVE AND PSYCHOLOGICAL ASSESSMENT AND SUPPORT

## P59 FREQUENCY OF COGNITIVE IMPAIRMENT IN ALS PATIENTS

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*Keywords: FTD, cognitive evaluation, PET*

**Objective:** To determine the frequency of cognitive impairment in ALS patients.

**Methods:** We selected 40 patients with the diagnosis of ALS using the "El Escorial" criteria who came for a first appointment to the ALS Unit at Bellvitge University Hospital. They were evaluated both by this Unit and the Dementia Unit. A structured interview, a thorough general and neurological examination, a neuropsychological study, an analysis, a functional and structural neuroradiological study (MRI and PET-18FDG), and an electromyography were all performed. They were evaluated with ALS-CBS test too. We classified the patients according to their cognitive state in three categories: (a) Normal patients, (b) Mild cognitive impairment patients according to consensual criteria by the FTD in ALS workshop in London (Canada), and (c) FrontoTemporal Dementia patients according to Neary's criteria.

**Results:** The percentages for each diagnosis were as follows: ALS-bi (6.3%), ALS-ci (12.5%), ALS-cibi (43.8%), and ALS-FTD (3.1%). 34.4% of patients were cognitively normal. All the patients with ALS from bulbar onset suffer cognitive impairment. All the patients except those suffering from ALS-FTD had a normal PET-18FDG.

**Conclusions:** (1) Cognitive impairment is frequent at the moment of diagnosing ALS; (2) It is recommendable to include the cognitive evaluation in the initial approach to ALS patients; (3) The bulbar onset of ALS is more frequently associated with cognitive impairment; (4) PET-18FDG is probably useful in diagnosing ALS-FTD, but not ALS with mild cognitive impairment.

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## P60 THE COGNITIVE PROFILE OF ALS. UPDATE OF A META-ANALYSIS AS A BASIS FOR A COGNITIVE SCREEN

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*Keywords: cognitive impairment, meta-analysis, screen*

**Background:** In 2008, we performed a literature meta-analysis on the cognitive profile of amyotrophic lateral sclerosis (ALS) which showed significant effect sizes for fluency, executive function, language and memory. For some cognitive domains no firm conclusions could be reached. Since many neuropsychological studies have been published after 2008, we updated the meta-analysis. The results will be used to select tests for an ALS-specific cognitive screen.

**Objectives:** To update a literature meta-analysis on the cognitive profile of ALS, which is used as a basis for a cognitive screen.

**Methods:** Pubmed and PsycInfo were searched for articles published since 2008, in English, French, Dutch and German. Articles were selected if healthy volunteers (controls) and non-demented ALS patients, fulfilling El Escorial criteria, underwent at least one validated cognitive test. All tests were categorized in cognitive domains. Effect sizes, expressed as Hedges' g, were calculated per domain. Demographic and clinical data were extracted from the articles.

**Results:** Twenty-seven new articles were included, resulting in a total of 42 articles (n = 1251 patients and 1111 controls). The median number of neuropsychological (sub) tests administered to patients and controls was 8 (1–34). Patients (63% men, 33% bulbar onset) had a mean age of 58.6 years, a mean educational level of 11.6 years and mean disease duration of 27.8 months. Most patients had mild to moderate disability (mean ALSFRS-R 32.7). The following cognitive domains showed significant effect sizes compared to controls (Hedges' g): social cognition (0.78); delayed verbal memory (0.62); fluency (0.60); visuoconstructive functions (0.59); global cognition (0.59); language (0.57); immediate verbal memory (0.56); executive functions (0.46); attention (0.43); psychomotor speed (0.42); and visual memory (0.27).

**Discussion and conclusion:** A new cognitive domain, that is social cognition, showed the largest effect size. Although this finding should be interpreted with caution, as only three studies included social cognition measures, it highlights the

clinical overlap between ALS and frontotemporal dementia. The update further reinforces the view that the cognitive profile extends beyond executive dysfunction and includes language and memory impairment (verbal > visual). In the visuoconstructive and psychomotor domains bias due to motor impairment could not be ruled out. Based on these findings, we propose to cover social cognition, verbal memory, fluency and language in a cognitive screen, which will include the following tests: Faux Pas Recognition Test, Rey Auditory Verbal Learning Test, Verbal Fluency (Letter; fluency index), and the Boston Naming Test. These tests are readily available and can be adjusted to correct for motor impairment or dysarthria.

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## P61 THE VERBAL FLUENCY INDEX: NORMATIVE DATA BASED ON A SAMPLE OF HEALTHY DUTCH CONTROLS

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*Keywords: fluency, VFI, normative data*

**Background:** Cognitive changes have been demonstrated in 30% of ALS patients with verbal fluency being the most consistent deficit. For ALS patients, the verbal fluency index (VFI) has been developed which corrects for speech and motor impairment (1). The absence of normative data for the VFI hinders the interpretation of fluency deficits in individual patients and restricts the use of the VFI as a marker of cognitive performance.

**Objective:** To provide normative data for the 3-minute verbal fluency index based on a sample of age-matched healthy controls.

**Methods:** Three hundred and eighty-three native Dutch speaking volunteers were randomly selected by general practitioners who look after patients with ALS participating in a population-based study aiming at complete ascertainment of all patients with ALS in the Netherlands. The volunteers were age-matched with ALS patients and had no history of a neurological or psychiatric disorder or previous significant head injury. We recorded age, gender, education, medication, past medical history and use of toxic substances. The VFI, a 3-minute letter fluency task adjusted for motor impairment, was administered according to standard procedures. We used the letter "D" as this letter is comparable to the letter "S" in the English language, in terms of degrees of difficulty(2). Participants with more than five errors (perseverative errors, rule breaks and non-existing words) were excluded. To examine the effects of age, gender, education, medication, past medical history and use of toxic substances, a multiple stepwise linear regression was used.

**Results:** Three hundred and sixty-one participants (228 males and 133 females; mean age: 63; SD 9.5) were included. Educational level ranged from 'primary education' (4%) to 'academic/college degree' (27%) and was inversely correlated ($p < 10^{-7}$) to VFI performance. The VFI scores did not relate to the other variables. The regression formula to transform raw scores into a standardized Z-score was: $Z = (11, 37 - (0.86 * education)) - VFI/3.44$.

**Discussion and conclusion:** In this large cohort of healthy volunteers, VFI scores were dependent on the level of education with higher scores in higher educated subjects, which is in agreement with standardised fluency tests. The educational level of our volunteer sample was comparable to a large Dutch ALS cohort. This normative data can be used to quantify fluency impairment in individual Dutch ALS patients and thus serve as a marker of cognitive impairment in ALS. Validation of these findings warrants similar studies in other countries.

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## P62 BRAIN COMPUTER INTERFACE AND EYE-TRACKING FOR COGNITIVE ASSESSMENT IN AMYOTROPHIC LATERAL SCLEROSIS: THE EBRAIN PROJECT

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*Keywords: eye-tracking, brain computer interface, neuropsychological assessment*

**Background:** Many patients affected by amyotrophic lateral sclerosis (ALS) show cognitive alterations, especially regarding frontal executive functions, ranging from a mild cognitive impairment to frontotemporal dementia clinical profiles (1). Cognitive assessment is problematic in moderate-severe stages of ALS, due to the presence of motor-verbal impairment which makes the use of traditional paper and pencil tests poorly reliable or not feasible. Recently, Eye-tracking (ET) and Brain Computer Interface (BCI) have been preliminarily used in ALS to administrate cognitive testing (2–4). However, an extended motor-verbal free neuropsychological (NP) battery is not available for ALS longitudinal assessment.

**Objectives:** A recently funded project, 'eBrain: BCI-ET for ALS', aimed at evaluating the use of P300-based BCI and ET technologies to administrate cognitive tests in ALS.

**Methods:** Twenty-eight ALS patients (mean age: 62.6 ± 11.8; mean education: 9.6 ± 3.6) and 30 healthy subjects (mean age: 56.2 ± 11.9; mean education: 13.7 ± 4.2) underwent a traditional cognitive (*Frontal Assessment Battery – FAB*; *Montreal Cognitive Assessment – MOCA*) and psychological screening (*Beck Depression Inventory – BDI*; *State-Trait Anxiety Inventory – STAI –Y1,Y2*). Also behavioural features were recorded. Adapted versions of NP tests assessing verbal comprehension, frontal functioning, attentive and theory of mind abilities were administered with both BCI and ET. Furthermore, clinical data were collected (respiratory parameters and *ALS Functional Rating Scale – Revised – ALSFRS-R*) and usability of both devices was evaluated with an ad hoc questionnaire.

**Results:** Data showed significant differences between healthy subjects and ALS patients performances in BCI and ET adapted measures of frontal abilities ($p < 0.05$); furthermore, a correlation between traditional NP assessment and BCI-ET testing was found ($p < 0.05$), supporting the concurrent validity of the adapted measures. Finally, a better perceived usability was observed for ET overall, compared to BCI ($p < 0.05$); nevertheless, patients evaluated BCI as a more positive and useful tool in order to compensate the verbal limitation, in comparison to the evaluation given by controls.

**Discussion and conclusion:** These results support the good level of sensitivity of the BCI and ET-based NP assessment, offering promising insights into the use of such devices for the longitudinal cognitive testing in ALS. Besides, the high perceived usability not only of ET, but also of BCI system seems relevant, since BCI represents the only means to bypass verbal-motor deficit for patients in advanced stages of the disease, where ocular motility can also be damaged.

**Acknowledgements**: research support was provided by the *eBrain* project, funded by the Lombardy Region.

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## P63 USE OF FNIR TO EXAMINE HEMODYNAMIC CHANGES DURING COGNITIVE TASKS IN INDIVIDUALS WITH ALS

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*Keywords: functional near-infrared spectroscopy (fNIR), executive function*

**Background:** Evidence suggests that deficits in frontally mediated executive skills occur in up to 50% of ALS patients (1). Dysexecutive and behavioural impairments are most common, and likely related to frontal lobe alterations (2,3). Functional Near-Infrared Spectroscopy (fNIR) is a noninvasive optical neuroimaging technology that monitors hemodynamic changes in the brain, that is, blood oxygenation and volume, concurrently with cognitive tasks. Studies show that fNIR measures are sensitive to executive functions (4).

**Objective:** To examine and compare hemodynamic changes detected by fNIR during challenging cognitive tasks in ALS and healthy controls (HC).

**Methods:** Twenty-four subjects (11 ALS, ALSFRS-R: 36.8 ± 5.2) completed three neuropsychological tests: Philadelphia Brief Assessment of Cognition (PBAC), Mini Mental State Exam (MMSE), and Clock Drawing Test (CDT), and three fNIR-monitored tasks: 5-minute Psychomotor Vigilance Test (PVT), King-Devick Test (KD), and Number Interference Task (NIT). The PVT, a sustained-attention, visual-response task, and KD, a rapid number naming task, were used to obtain baseline fNIR measures. The NIT, a computerized adaptation of the Stroop Test, triggered working memory and maintenance of a complex mental set. Demographics, medical history, ALSFRS-R, and pulmonary function tests were collected as applicable. Between group differences were assessed by Welch ANOVAs ($p = 0.10$) to account for unequal sample sizes and variances. Analysis focused on the NIT, which progresses through three trials of increasing difficulty. Correlations between mean oxygenation (μmolar) and clinical parameters were also examined.

**Results:** ALS subjects had more years of education (HC = 13.3 ± 1.8, ALS = 16.1 ± 2.4, $p = 0.004$), but no differences in PBAC, MMSE or CDT scores. Significant differences in oxygenation were found during NIT Trials 2 and 3 in the Right Dorsolateral Prefrontal Cortex (DLPFC) (Trial 2: ($F_{(1,15.129)} = 4.03$, $p = 0.063$) (HC = 0.393 ± 0.385, ALS = 0.861 ± 0.687); Trial 3: ($F_{(1,15.596)}$4.141, $p = 0.059$) (HC = 0.272 ± 0.416, ALS = 0.766 ± 0.707)). Correlations were detected between oxygenation and PBAC subscales measuring Behavior/Comportment (Trial 2: Left DLPFC, Left/Right midPFC ($r = -0.367$ to $-0.465$, $p < 0.077$); Trial 3: Left midPFC, Right DLPFC ($r = -0.356$ to $-0.424$, $p < 0.088$)) and Executive functions (Trial 3: Right DLPFC ($r = 0.417$, $p = 0.043$)). Within the ALS group, ALSFRS Respiratory subscale correlated with oxygenation in the Left DLPFC and Right midPFC (Trial 3: $r = -0.591$ to $-0.601$, $p < 0.054$).

**Discussion and conclusion:** ALS subjects displayed higher oxygen utilization than HC to complete a challenging cognitive task, possibly indicating increased mental workload. Differences in oxygenation are noted despite lack of gross cognitive impairment, implying that fNIR may be more sensitive to early cognitive difficulties and frontal lobe involvement than neuropsychological testing alone. Furthermore, correlations between oxygenation and respiratory, executive and behavioral subscales imply that the fNIR is sensitive to changes in these at-risk areas.

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## P64 THE ITALIAN VERSION OF THE ALS-COGNITIVE BEHAVIORAL SCREEN (ALS-CBS): A MOTOR NEURON DISEASE DEDICATED TOOL

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*Keywords: screening test, cognitive dysfunction, ALS-CBS*

**Background:** Cognitive/behavioral dysfunction has been recognized as a consistent part of the ALS clinical phenotype, ranging from a mild impairment to a full blown dementia. Currently used neuropsychological tools for exploring this novel clinical dimension often do not take into account physical disabilities of ALS patients, undoubtedly introducing a source of bias in the interpretation of results. The ALS-Cognitive Behavioral Screen (ALS-CBS) is a recently proposed ALS-dedicated tool separated into two subscales: a cognitive one (patient, max score 20) and a behavioral one (caregiver, max score 45).

**Objectives:** To test our Italian version of the ALS-CBS in a consecutive series of ALS outpatients, assessing its value for the screening of cognitive dysfunction.

**Methods:** Fifty-seven consecutive ALS non-demented outpatients were recruited (age: $65.2 \pm 9.8$ years old (range: 42–80); ALSFRS-R score: $31.7 \pm 8.6$). Each patient underwent the ALS-Cognitive Behavioral Screen (ALS-CBS), the Frontal Assessment Battery (FAB) and, due to previously shown FAB limits (Tremolizzo *et al* 2013), the Weigl's Sorting Test (WST).

**Results:** Mean ALS-CBS cognitive subscore was $13.2 \pm 3.8$ and a correlation with both FAB and WST raw scores was present ($r = 0.697$ and $r = 0.616$, respectively, $p < 0.0001$). Originally proposed (Woolley *et al*. 2010) cut-off values are less than10 and less than 17 for dementia and mild cognitive impairment, respectively; however, most of our patients scored less than 17 (91.2%), and a consistent part less than 10 (17.5%). Possibly this data might in part be explained by the fact that mean education in our patients was $9.8 \pm 3.9$ years, lower with respect to the original ALS-CBS series, and both age and education correlated with the ALS-CBS cognitive subscore ($r = -0.400$ $p = 0.002$ and $r = 0.318$ $p = 0.016$, respectively). For this reason, we are currently testing healthy controls for producing opportune normative data.

The ALS-CBS behavioral subscores were obtained for 46 patients and mean value was $34.0 \pm 9.2$. With respect to original cut-off values, 16 patients (34.7%) scored less than 32, and 24 (47.8%) scored less than 36. Cognitive and behavioral score did not correlate between them or with the degree of motor impairment.

**Discussion and conclusion:** The ALS-CBS is a sensitive tool for screening cognitive and behavioral alterations in ALS. However, normative values are needed for improving its value.

**Acknowledgements:** Mrs. Sofia Rosso and the Italian association for ALS (AISLA) for allowing this project to be carried out.

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## P65 PRIMITIVE REFLEXES FOR THE SCREENING OF COGNITIVE DYSFUNCTION IN AMYOTROPHIC LATERAL SCLEROSIS

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*Keywords: primitive reflexes, cognitive dysfunction, frontal assessment battery*

**Background:** The presence of primitive reflexes (PRs) has been classically associated to cognitive dysfunction, albeit the role of these signs is highly debated since they are often present also in apparently healthy controls. Interestingly, the combination of more than one PR has been shown to have more discriminative value for the screening of cognitive dysfunction with respect to each single PR. Some PRs have been reported in amyotrophic lateral sclerosis (ALS) albeit never in relationship to the cognitive status; this question, however, might be of relevance since a continuum between ALS and frontotemporal dementia has already been postulated.

**Objectives:** Testing a battery of PRs including sucking, snout, grasping, Myerson's, palmomental and corneomandibular reflexes in ALS patients with respect to their cognitive status in an outpatient screening situation.

**Methods:** Fifty consecutive ALS outpatients were recruited (age: $65 \pm 1.5$ years old (range: 42–81); ALSFRS-R score: $29.7 \pm 1.5$); the putative presence of cognitive dysfunction was screened by the frontal assessment battery (FAB).

**Results:** The number of PR recorded in each patient (0–6) correlated with the FAB score ($r = -0.60$, $p < 0.0001$) and dichotomizing patients for presence versus absence of cognitive dysfunction (FAB score $< 13.4$) the number of PR was $2.8 \pm 0.3$ ($n = 14$) versus $1.3 \pm 0.1$ ($n = 36$), respectively ($p = 0.0003$). Only Myerson's, palmomental and corneomandibular reflexes were consistently prevalent in our population (45–65%), while the other three PR were under-represented.

**Discussion and conclusion:** According to our results, PR might give useful information regarding the frontal function of ALS patients in an outpatient setting. Albeit each single PR might lack of specificity, the added value of an array of PRs emerges. Hence, including a battery of selected PR in the neurological examination might be of value for the fast screening of cognitive dysfunction in ALS.

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## P66 CALLOSAL DYSFUNCTION AND COGNITIVE IMPAIRMENT IN ALS: IS THERE A LINK?

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*Keywords: corpus callosum, cognition, frontal lobe*

**Background:** In ALS, neuroimaging studies have demonstrated a prominent involvement of white matter, encompassing, as key structures, not only the corticospinal tract but and the corpus callosum(CC)(1). The observation of mirror movements was the first evidence of callosal impairment in interhemispheric inhibition (2). Although myelination breakdown of the callosal motor segment was found to be unrelated to the neuropsychological performance (3), cognitive decline psychiatric symptoms have been found in ALS patients showing substantial atrophy of the anterior fourth of the CC (4).

**Objectives:** We aimed to determine callosal dysfunction (CD) in ALS, on the basis of performances of task evaluating the integrity of the sensory-motor segment of the CC (s-mCD) and of novel tasks assessing bimanual motor control (BMC), and its correlations with clinical, cognitive and behavioural profiles.

**Methods:** Twenty-six non-demented ALS patients were enrolled after neurological evaluations. Integrity of s-mCD was quantified with tasks assessing the ability in interhemispheric transfer of motor-inhibitory input (3) and somesthetic information (5). Control of inhibition and interference during bimanual complex movements were assessed with newly developed tasks. An in-depth neuropsychological test battery was used to evaluate executive functions, social cognition, memory, attention, language and visual-spatial skills. Behavioural dysfunction was assessed through caregiver interviews. Cluster and correlations analyses between CD measures and neuropsychological data were computed.

**Results:** Patients with high s-mCD scores obtained lower performances on verbal fluency and verbal episodic memory tests. The novel CD measure was strongly related to executive functions (verbal fluency, control of inhibition and interference), frontally mediated aspects of memory (working memory, short-term memory and false recognitions) and social cognition (emotion recognition, interpersonal reactivity index). A cluster analysis considering as independent variable the new CD measure discriminated two groups of patients according to the degree of cognitive impairment quantified as the percentage of cognitive performances below the normal range. Overall CD measures did not correlate with clinical signs of ALS.

**Discussion and conclusion:** We demonstrated that higher CD values corresponded to lower neuropsychological performances, suggesting a correlation between CD and cognition in ALS. In particular, we developed novel tasks to assess BMC, which were strongly associated with frontal function. We speculate that correct performances in BMC tasks need the integrity of the anterior portion of the CC connecting dorsolateral prefrontal cortex and cingulate cortex in order to prevent interference from the opposite hemisphere. More generally, CC impairment might interfere with neuronal circuitry responsible of executive and behaviour control. Future studies are warranted to investigate if the involvement of the anterior portion of the CC can predict cognitive decline in ALS.

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## P67 PATTERN OF PERSONALITY CHANGES IN ALS: A PRELIMINARY LONGITUDINAL STUDY

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*Keywords: personality, neuropsychiatry, cognition*

**Background:** While personality is a complex and only partially understood construct, different theoretical models allow the inter-individual differences as well as intra-individual longitudinal changes in personality to be quantified. Currently, one of the more widely used models of personality is represented by the "five factors" personality model (1). According to this model, personality results from the stable balance of five key traits, extraversion, agreeableness, conscientiousness, neuroticism and openness to new experiences.

While pervasive personality changes represent one of the key features of different neurodegenerative conditions (2), the presence and extent of personality alterations in ALS are only partially understood.

**Aim:** Aim of the study was thus to longitudinally evaluate personality traits according to the five factor model in a group of ALS patients to explore the presence of personality changes over time and as well as the cognitive and behavioural correlates.

**Methods:** Twenty-two subjects with a diagnosis of definite or probable ALS were included in the study. A control group of age- and sex-matched healthy subjects was also included in the study. All patients underwent clinical, cognitive and behavioural evaluations at baseline and at follow-up after 6 months. In both ALS patients and controls, personality was evaluated at both time points with the Big Five Inventory (3) using self-report and observer-based questionnaires.

**Results:** Compared to controls, ALS subjects presented at baseline with reduced agreeableness and conscientiousness scores as evaluated with the observer-based questionnaire. Moreover at the follow-up evaluation, ALS subjects presented with a further reduction in both agreeableness and conscientiousness scores compared to baseline. Lastly agreeableness and conscientiousness scores at baseline were respectively associated with increased behavioural disturbances and cognitive impairment at follow-up.

**Discussion:** Here, we showed a reduction of agreeableness and conscientiousness scores in ALS subjects both compared to controls and over time. Moreover development of cognitive or behavioural disturbances over time was correlated with more pathological agreeableness and conscientiousness scores at baseline. Given the known relationship between prefrontal structural alterations and the two aforementioned personality traits (4) our observation is in line with the known involvement of prefrontal areas in ALS. Our data suggest expansion of the current construct of non-motor facets of ALS to include personality alterations and suggest that personality assessment could provide useful information to the plan of ALS patients.

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## P68 CHARACTERISTICS AND CLINICAL SIGNIFICANCE OF EXECUTIVE FUNCTIONING IN AMYOTROPHIC LATERAL SCLEROSIS (ALS) WITH AND WITHOUT FTD

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*Keywords: executive functioning, neuropsychology, cognition*

**Background:** Executive dysfunctions are a key indicator for a negative prognosis in ALS (Elamin, 2011). Symptoms closely related to executive functioning are interconnected with behavioural abnormalities, for example, apathy, disinhibiton, and disorganization. Both behavioural abnormalities and cognitive impairments are poorly reflected at the clinical level though they are highly prevalent when assessed by neuropsychological measurements.

**Objectives:** The aim was to investigate executive dysfunctions in relation to their relevance in everyday functioning.

**Methods:** We conducted a prospective neuropsychological study of 103 patients with ALS (including 11 ALS-FTD cases) and 71 age, education and intelligence matched healthy controls. We used a comprehensive neuropsychological test battery adapted to motor incapabilities, including a behavioural questionnaire. All executive test variables were assigned to their corresponding level of cognitive regulation (basic, complex, social and emotional). Previous criteria according to Strong (2009) and Phukan (2012) were modified, and all patients were categorized regarding cognitive and behavioural abnormalities. By analyzing frequency distributions, comparisons between cognitive subgroups at all levels of cognitive regulatory processes were performed.

**Results:** 19% of ALS patients without FTD and all ALS-FTD patients demonstrated executive function impairment. The extent of basic function disorders (eg shifting, updating, and fluency) ranged from 28% to 78% in patients without FTD, from 45% to 100% in ALS-FTD patients. In contrast, impairment of complex functioning (eg monitoring, problem solving) was not particularly prevalent regardless of FTD (27%). Difficulties in problem solving occurred even only in ALS-FTD cases. Behavioural disorders were apparent in 16% of ALS patients and 54% of ALS-FTD patients.

**Discussion and conclusion:** ALS patients with executive function impairment had a significantly higher frequency of impaired basal regulatory processes in contrast to more complex processes or rather impairments at the highest level of executive functioning (activity and social behaviour). Processes controlling behaviour, however, seem to be only affected in ALS-FTD. Basal executive functions are less relevant to everyday functioning than complex functions such as problem solving. This may explain the lack of relevant abnormalities in ALS patients based on our clinical observation. Our results indicate a pattern of executive impairment in ALS patients without FTD which appears to be not as severe to affect everyday's functioning.

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## P69 SEMANTIC IMPAIRMENT PROFILES OF THE FTD-MND CONTINUUM

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**Background:** Increasingly, cognitive and behavioural deficits are recognized in Motor Neuron Disease (MND), and a proportion of patients develop frank frontotemporal dementia (FTD-MND). Executive impairment is well characterized in MND, but non-executive deficits have not been investigated in detail. Aphasia is characteristic of some FTD phenotypes; for example, semantic deficits characterize the semantic dementia (SD) phenotype of FTD. Nonetheless, the nature and extent of semantic impairment in MND remains unexplored, even though recent studies have described SD-like anterior temporal lobe changes in the disease.

**Objectives:** The current study aimed to compare semantic deficits in MND and FTD-MND, compared to those seen in SD and controls.

**Method:** Semantics were evaluated using the Sydney Language Battery (SYDBAT), a test of single-word processing

comprising four subtests: three specifically designed to assess semantics (confrontational naming, comprehension, and semantic association).

**Results:** In total 112 participants were recruited from a multidisciplinary research clinic in Sydney (mean age = 64.9; male = 63.4%; mean years of education = 12.7); 24 patients with MND, 26 patients with FTD-MND, 33 patients with SD and 29 age- and education-matched healthy controls. Significant semantic impairments were observed in MND and FTD-MND, compared to controls. The MND cohort demonstrated the mildest impairment for both confrontational naming and word comprehension, although performed comparably to controls for semantic association. The FTD-MND group performed significantly below MND participants on all semantic subtests, but not as poorly as the SD group.

**Discussion:** The present study demonstrates that semantic impairment is present in MND and FTD-MND. The severity of this disturbance however differs, with a mild impairment being observed in MND patients and a significantly poorer performance by FTD-MND patients, albeit not as severe as in SD. The increasing severity of semantic impairment across the three patient groups supports the view of an FTD-MND continuum. Importantly, these findings implicate left anterior temporal lobe involvement, which is acknowledged as the semantic hub and critical in linking representations across cortical regions. This is consistent with imaging studies, which have reported changes to anterior temporal regions in both MND and particularly in FTD-MND.

**Conclusion:** Semantic deficits may be a feature of MND and FTD-MND, potentially reflecting left anterior temporal lobe involvement. These findings highlight the necessity for clinical assessment of semantic knowledge in MND, not only to ensure optimal patient communication, but also to detect non-executive cognitive impairment.

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## P70 CEREBROSPINAL FLUID PROGRANULIN LEVELS IN AMYOTROPHIC LATERAL SCLEROSIS ARE ASSOCIATED WITH FRONTO-EXECUTIVE DYSFUNCTION

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*Keywords: progranulin; cerebrospinal fluid; fronto-executive dysfunction*

**Background:** There is an overlap between fronto-temporal lobar degeneration (FTLD) and amyotrophic lateral sclerosis (ALS) clinically and genetically. Mutation of the progranulin (GRN) gene causes FTLD and less frequently ALS. GRN can be measured in serum and cerebrospinal fluid (CSF) and was found to be decreased in FTLD. In ALS patients CSF GRN showed an inverse correlation with disease duration.

**Methods:** CSF analysis including GRN and extensive neuropsychological examination was applied to healthy controls and ALS patients. Furthermore, the GRN levels in CSF of ALS patients were compared to FTLD and control subjects.

**Results:** Included were 19 healthy controls (age: 66.8 ± 6.8 years) and 30 ALS patients (age: 62.8 ± 12.6 years). For CSF analysis 38 patients with FTLD were examined (age: 68.6 ± 7.5). GRN in CSF was decreased in ALS ($p = 0.03$) and in FTLD ($p = 0.003$) compared to controls. In ALS subjects GRN was correlated to the MOCA as a summary score of cognition, to TMT-B and to verbal working memory, reflecting fronto-executive dysfunction.

**Conclusion:** In ALS patients we found abnormal levels of GRN in CSF. As in FLTD, GRN may serve as a biomarker indicating a cognitive impairment in ALS. Further study is necessary to determine the potential utility of GRN as a biomarker for frontal lobe degeneration in ALS.

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## P71 BEHAVIOURAL ASSESSMENT OF AMYOTROPHIC LATERAL SCLEROSIS

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*Keywords: behavioural assessment, FrSBe, cognitive impairment*

**Background:** Non-motor manifestations are subtly present in the vast majority of patients with amyothrophic lateral sclerosis (ALS), with a subgroup developing a frontotemporal dementia (FTD). The presence of behavioural or dysexecutive dysfunction is a negative prognostic indicator and patients with ALS-FTD have a shorter survival than those with classic ALS.

**Objectives:** To evaluate the frequency of neurobehavioral symptoms related to FTD, to determine the relevance of changes and to ascertain the relationship between cognitive and behavioural changes.

**Material and methods:** Two hundred and two ALS incident cases were assessed for the presence of cognitive and behavioural aspects. Different domains were considered (attention, memory, language and visuo-praxic abilities); behavioural abnormalities were assessed with the FrSBe. Cognitive impairment was defined when scores were equal or below the 5th percentile, compared to age- and education-matched norms. Binary correlation was evaluated with Pearson's coefficient. Differences between patients and caregivers were tested (paired *t*-test and Cohen's K coefficient). FrSBe scores were included as T-scores.

**Results:** A group of 183 patients (19 excluded): 177 Male and 77 Female; mean age of 67.3 (±9.7) years; mean educational level of 8.3 (±4.1) years; mean duration of the illness of 15.4 months (±13.5), was considered for statistical analysis.

In 23 cases (12.6%) a diagnosis of possible or probable dementia of the frontotemporal type was defined.

According to the cut-off, more than one-third exhibited behavioural impairment on the FrSBe "after" total scale rated by caregivers (41.5%) with a predominance of Apathy (51.8%), followed by Executive impairment (25.6%) and Disinhibition (25.6%). Neurobehavioral symptoms were not related to patients' age and gender, to the duration of the disease, to bulbar onset, or to the presence of bulbar symptoms at the time of the interview. They were instead significantly related to the physical status ($p < 0.05$). Considering delta scores, 13% of self-administered and 28% of caregivers' questionnaires reported relevant changes at the 'present time'.

For a group of 125 patients' and caregivers' coupled questionnaires were examined: in most cases (46.1%, n = 53) patients and caregivers shared the opinion about the absence of pathology (Cohen's K = 72); in nine cases (7.8%) patients agreed on the presence of a behavioural disturbance, in three cases (2.6%) having a score above the cut-off. Patients with impaired cognition had greater rates of behavioural impairment.

**Discussion:** Results at the FrSBe can be different when considering the 'after' scores (caregivers' forms T-scores) or distances resulting in comparing the pre-symptomatic and the disease phase, highlighting phenocopy cases. We observed a rating correspondence between patients and caregivers and a concordance regarding the overall condition of absence/presence of behavioural impairment. As expected, this correlation was not present in patients with high levels of cognitive/behavioural pathology.

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## P72 A NOVEL TOOL FOR DETECTION OF NEUROPSYCHIATRIC SYMPTOMS IN ALS – THE MIND-BEHAVIOURAL (MIND-B)

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*Keywords: neuropsychiatric symptoms; behavioural changes; assessment*

**Background:** There is great need for short, reliable and valid assessments of neuropsychiatric symptoms in ALS. Apathy is pervasive in ALS, but other challenging symptoms such as disinhibition and stereotypical behaviour have also been recognised. Crucially, neuropsychiatric symptoms have been shown to explain high levels of carer burden in ALS.

**Objective:** (1) To develop a novel tool to detect neuropsychiatric symptoms in ALS; (2) to compare levels of apathy, disinhibition and stereotypical behaviour in ALS; (3) to compare ALS and ALS plus patients in the novel tool.

**Methods:** One hundred and forty patients (Limb onset = 74.3%; bulbar onset = 25.7%) were included in the development of the novel tool, MiND-B, which is a reduced version of the Cambridge Behavioural Inventory (CBI-R). Rasch analysis was employed to identify the minimum amount of questions, and which were the best questions from the CBI-R that described the behavioural impairment in the ALS sample. The MiND-B contains 12 questions assessing neuropsychiatric symptoms, with Likert scores designed in a similar fashion to the ALSFRS-R to facilitate use and face validity; higher scores reflect normal behaviour. The MiND-B demonstrated construct validity (Mean infit and outfit statistics = 1.05; Z = 0.2, SD = 0.19); good reliability (Cronbach alpha = 0.97), and unidimensionality (raw variance explained was 44.4%). The MiND-B can be completed by the informant.

An independent sample of 79 patients was used for the validation analysis. Limb (70%) and bulbar onset patients (30%) were compared in their MiND-B scores. ALS plus and ALS patients (40/79), subcategorised according to the Strong criteria (2009), were also compared in their MiND-B scores. All patients were diagnosed following current criteria for ALS. Non-parametric tests were used for the comparison of symptoms and disease subgroups.

**Results:** Limb and bulbar onset patients did not differ in levels of apathy, disinhibition or stereotypical behaviour ($p > 0.05$). When comparing types of behaviour, however, apathy was the most marked neuropsychiatric symptom, followed by stereotypical behaviour and disinhibition ($p < 0.05$). Critically, the MiND-B could differentiate patients subcategorised into ALS or ALS plus on disinhibition and stereotypical behaviour ($p < 0.05$). Apathy was pervasive.

**Discussion:** The MiND-B has demonstrated all necessary psychometric properties as a valid, reliable and unidimensional tool to detect neuropsychiatric symptoms in ALS. It can differentiate types of behavioural symptoms, and more importantly, can also help in differentiating patients with ALS plus from those who present with pure motor symptoms.

**Conclusions:** The MiND-B is a useful, short, valid and reliable tool for use in ALS clinics and research studies. It is available from the authors and free of charge.

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## P73 DELAY IN DIAGNOSIS IS A MAIN RISK FACTOR FOR DEPRESSION IN MND

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*Keywords: depression, delay in diagnosis, psychological interventions*

**Background:** Despite severe physical impairment, patients with MND report satisfactory quality of life (1). Accordingly, the prevalence of major depression among these patients is relatively low contrary to what people may expect (2). This is likely to be due to unique risk factors underlying depression in this patient population, which remain unclear. Clarifying predisposing and precipitating factors related to depression in MND can help with identifying patients at risk of developing major depression and establish specific goals of psychological intervention.

**Objective:** To identify risk factors for depression in MND patients.

**Methods:** Forty-one patients with MND (61% female; 61% limb onset; mean age = 64.5 years, *SD* = 12) completed questionnaires on medical and psychological history, family background and depression (Depression, Anxiety, Stress Scale-21). Patients' level of functioning was assessed by the ALSFRS-R. Direct logistic regression was performed to assess the impact of various factors (physical function, time between symptom onset and diagnosis, family and personal history of mental illness) on the likelihood that patients would report a high level of depression.

**Results:** The average time between symptom onset and diagnosis was 15.8 months (*SD* = 13.7). ALSFRS-R scores between limb and bulbar onset patients were similar ($p = 0.54$). Depression scores did not vary across patients with limb or bulbar onset MND ($p = 0.49$). A similar proportion of patients reported a family (32%) or personal (29%) history of mental illness (12% had both family and personal history of mental illness). Most patients reported no depressive symptoms (66%). The logistic regression revealed that only delay between symptom onset and diagnosis predicted the likelihood of reporting high levels of depression ($p < 0.05$).

**Discussion:** The findings of this study suggest that delay between symptom onset and diagnosis is a key risk factor for depression in MND. Patients who experienced a longer delay in diagnosis were more likely to report depression and are at higher risk of developing more severe symptoms. These patients may be prime targets of psychological intervention. The findings also suggest that interventions focusing on helping patients cope with the process of differential diagnosis may be particularly useful, especially given that there are no specific tests for MND. Often, the remaining confirmatory factor for the diagnosis is symptom progression. Identifying and supporting patients at risk of developing major depression ensures cost-effective and evidence-based psychological intervention.

**Conclusion:** Understanding disease-specific risk factors for depression in MND is important for developing tailored psychological interventions. This study suggests that delay in diagnosis is a key precipitant of depression in MND. Specific psychological approaches are required to take into account patients' experiences from symptom onset to definitive diagnosis of MND.

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## P74 CONFOUNDERS OF DEPRESSION MEASUREMENT IN ALS/MND: META-REGRESSION ANALYSIS OF PUBLISHED LITERATURE

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*Keywords: depression, quality of life, clinical psychology*

**Objective:** To estimate measurement bias from popular questionnaire measures for depression using meta-regression.

**Methods:** A systematic review of the literature published on the following databases was conducted without time limits: PubMed (MEDLINE), PsycINFO, the Cochrane Central Register of Controlled Trials, CINAHL, Scopus and ISI Web of Science. Mean scores for depression questionnaires were separately meta-regressed on study-level mean times since onset of ALS/MND symptoms in order to test the significance of the slopes and assess the goodness of fit of the two conditional random models.

**Results:** Our literature search revealed 110 studies that reported depression scores from psychometric questionnaires. Data were included from 103 studies (3,190 patients). The most commonly used questionnaires were The Hospital Anxiety and Depression Scale (HADS) and the Beck Depression Inventory (both the BDI-I and the BDI-II).

Average scores on both questionnaires do not indicate a large number of patients with case-level depression and average scores for depression are similar to score from normal populations. Scores for depression increase with duration of illness. The BDI and the BDI-II were highly influenced (more than 50% of the variance in scores) by level of physical impairment. Scores from the HADS were also influenced by physical impairment, but to a lesser degree (19%).

**Discussion:** Meta-evidence from the published literature suggests that commonly used generic depression scales are overly influenced by the presence of impairment.

**Conclusion:** Widely used depression scales over-estimate severity of depression due to confounding with physical symptoms of the underlying physical symptoms in ALS/MND.

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## P75 GROUP INTERVENTION BASED ON MINDFULNESS FOR HOSPITAL HEALTH CARE PROVIDERS: TAKING CARE OF THOSE WHO CARE

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*Keywords: support for staff, mindfulness, psychological interventions*

**Background:** Stress and compassion fatigue is a common part of everyday life in neuromuscular clinics. These degenerative conditions are highly stressful not only for patients and caregivers but also for health care providers, usually living

with pain and death. The greatest risk for health care providers is to develop burn-out syndromes which imply reduced emotional involvement and respect for other people negatively affecting relationships (1). Meditative practice, based on Mindfulness Training developed by John Kabat Zinn (MBSR) is quickly spreading in the health field (2). This program has proven successful to reduce stress levels and promote skills inherent in the concept of resilience (3).

**Objective:** To promote group interventions to prevent burn-out and relieve the distress of healthcare professionals and also to provide useful tools to manage stressful situations and improve personal skills to manage stress and pain.

**Methods:** This group intervention consists of five session of one hour each. Five health care providers are involved in each group, starting with nurses and physiotherapists. By working with a meditative instructor and a psychologist health providers have the opportunity to cope with their feelings and exercise with some meditation practice at their workplace. Meditation practices combined with cognitive restructuring help to develop a new point of view that allows individuals to cope with negative and painful experience in a non-judgmental and accepting manner.

**Results:** We expect that the implementation of this group in the workplace can lead to: reduced burn-out symptoms, both physical and psychological; increase quality of life perception and life satisfaction, reduced levels of stress and negative thinking (rumination). These outcomes will be evaluated by structured and validated tests.

**Discussion and conclusion:** If Mindfulness combined with cognitive psychological approaches proves to reduce the risk of burn-out, we recommend that this intervention is included in clinical practice to enable health care providers to better manage their stress and develop their own coping strategies.

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## P76 ALS PATIENT'S DEATH: PSYCHOLOGICAL IMPACT ON THE CAREGIVER

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*Keywords: caregiver, complicated grief, attachment style*

**Background:** Caring for ALS patients during the disease proved to be very demanding in terms of anxiety, depression, and somatic symptomatology and to cause a poor quality of life. However, there is only little knowledge on the psychological impact of surviving the death of an ALS patient on family caregivers (1,2).

**Objectives:** The main objectives were to investigate the psychological impact of the death of patients with ALS on their caregivers, in terms of personality characteristics, mood tone, the implicit relational style (attachment style), quality of life and complicated grief disorder (CG) (3), as defined by new DSM-V manual criteria. Understanding the psychological consequences of ALS patients' death can help clinicians to identify those caregivers who are likely to experience more severe psychopathological consequences of bereavement.

**Methods:** Forty-six family caregivers of deceased ALS patients participated in the study. Participants underwent an in-depth telephonic interview about their experience and were asked to complete questionnaires orally proposed: the Relationship Questionnaire to assess adult attachment; the short-form revised Eysenck Personality Inventory, to measure personality traits; the Parental Bonding Instrument which measures subjectively perceived parental characteristics; the Inventory of Complicated Grief to assess symptoms of complicated grief; the Life satisfaction Index, short form to evaluate the mood tone and the quality and life satisfaction of caregivers.

**Results:** Main results revealed that 17 participants (39%) met the DSM-V criteria for CG. Furthermore only a minority of the caregivers showed a secure adult attachment (about 22% of the total); the great majority of participants were insecure (about 78%), with a prevalence of the dismissing attachment style (63%).

**Discussion and conclusion:** The preliminary results of the study showed that the loss of a familial ALS patient may have dramatic psychological consequences on their caregivers in terms of attachment relational representation and CG. Only a small percentage of the caregivers had a secure attachment style, a percentage significantly lower than the normative population. Since attachment relational style is considered a stable psychological trait negatively influenced only by catastrophic emotional events, this finding appears as particularly relevant. Analogously, a relevant proportion of the caregivers of deceased ALS patients met the new criteria for Complicated Grief such as feelings of disbelief, being stunned, avoidance, anger, shock, and separation distress (ie yearning and searching for the deceased, excessive loneliness, personal guilt, auditory and visual hallucinations). Further analysis is warranted to identify predictors of complicated grief.

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