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Assessing Behaviour in ALS:

The importance of using disease-specific tools

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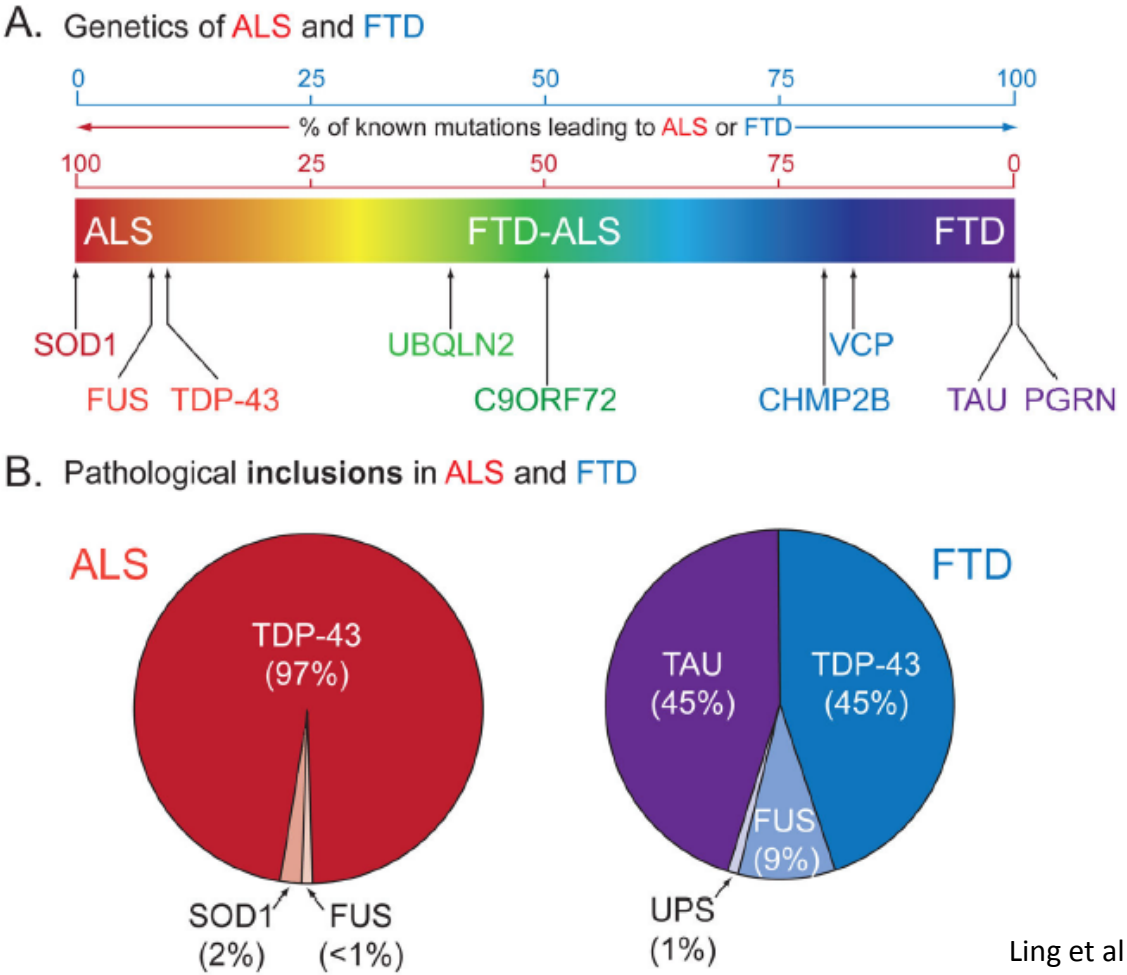
ENCALS Meeting 2017 - Ljubljana

The ALS-FTD Continuum



Ling et al., 2013, Neuron, 2013

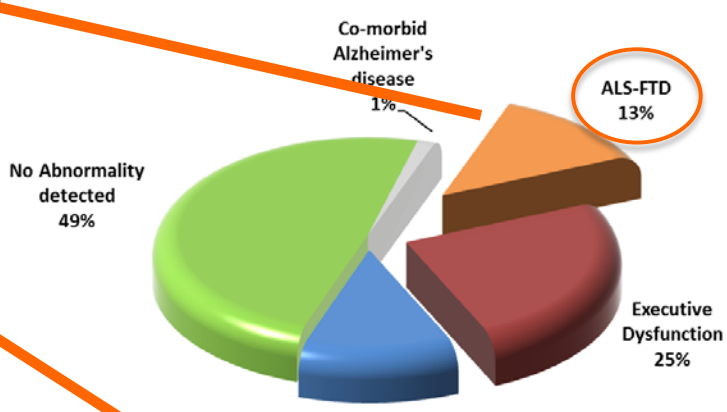
The ALS-FTD Clinical Overlap

Extremes of a spectrum of overlapping clinical symptoms.

RESEARCH PAPER

The syndrome of cognitive impairment in amyotrophic lateral sclerosis: a population-based study

Julie Phukan,[1] Marwa Elamin,[1] Peter Bede,[1] Norah Jordan,[2] Laura Gallagher,[2] Susan Byrne,[1] Catherine Lynch,[1] Niall Pender,[2] Orla Hardiman[1,3]



RESEARCH ARTICLE

A Cross-sectional population-based investigation into behavioral change in amyotrophic lateral sclerosis: subphenotypes, staging, cognitive predictors, and survival

Tom Burke[1,2], Marta Pinto-Grau[1,2], Katie Lonergan[1,2], Peter Bede[1,2], Meabhdh O'Sullivan[1], Mark Heverin[1], Alice Vajda[1], Russell L. McLaughlin[3], Niall Pender[1,2,a] & Orla Hardiman[1,2,a]

RESEARCH ARTICLE

Amyotrophic lateral sclerosis - frontotemporal spectrum disorder (ALS-FTSD): Revised diagnostic criteria

MICHAEL J. STRONG[1], SHARON ABRAHAMS[2], LAURA H. GOLDSTEIN[3], SUSAN WOOLLEY[4], PAULA MCLAUGHLIN[5], JULIE SNOWDEN[6], ENEIDA MIOSHI[7], ANGIE ROBERTS-SOUTH[8], MICHAEL BENATAR[9], TIBOR HORTOBÁGYI[10], JEFFREY ROSENFELD[11], VINCENZO SILANI[12], PAUL G INCE[13] & MARTIN R. TURNER[14]

Sensitivity of revised diagnostic criteria for the behavioural variant of frontotemporal dementia

Katya Rascovsky,[1] John R. Hodges,[2] David Knopman,[3] Mario F. Mendez,[4,5] Joel H. Kramer,[6] John Neuhaus,[7] John C. van Swieten,[8] Harro Seelaar,[8] Elise G. P. Dopper,[8] Chiadi U. Onyike,[9] Argye E. Hillis,[10] Keith A. Josephs,[3] Bradley F. Boeve,[3] Andrew Kertesz,[11] William W. Seeley,[6] Katherine P. Rankin,[6] Julene K. Johnson,[12] Maria-Luisa Gorno-Tempini,[6] Howard Rosen,[6] Caroline E. Prioleau-Latham,[6] Albert Lee,[6] Christopher M. Kipps,[13,14] Patricia Lillo,[2] Olivier Piguet,[2] Jonathan D. Rohrer,[15] Martin N. Rossor,[15] Jason D. Warren,[15] Nick C. Fox,[15] Douglas Galasko,[16,17] David P. Salmon,[16] Sandra E. Black,[18] Marsel Mesulam,[19] Sandra Weintraub,[19] Brad C. Dickerson,[20] Janine Diehl-Schmid,[21] Florence Pasquier,[22] Vincent Deramecourt,[22] Florence Lebert,[22] Yolande Pijnenburg,[23] Tiffany W. Chow,[24,25] Facundo Manes,[26] Jordan Grafman,[27] Stefano F. Cappa,[28,29] Morris Freedman,[24,30] Murray Grossman[1,*] and Bruce L. Miller[6,*]

ALS with behavioural impairment (ALSbi)

- Identification of APATHY, with or without other behaviour change,

OR

- The presence of two or more of the following symptoms:
  - Disinhibition
  - Loss of sympathy/empathy
  - Perseverative, stereotyped or compulsive behaviour
  - Hyperorality/dietary change
  - Loss of insight
  - Psychotic symptoms (somatic delusions, hallucinations, irrational beliefs)

The Assessment of Behaviour in ALS

- Behavioural assessments are fundamental in routine neuropsychological evaluations in ALS.
- Detailed family interviews are not always practicable in a multidisciplinary clinic setting; need for a self-explanatory proxy-report.
- Baseline/premorbid psychological and behavioural status determined, to assess if:
    1. new onset (not premorbid characteristics of the patient),
    2. associated with the time of onset of ALS,
    3. disabling or causing clear impairment.

    (Strong et al. 2017)
- Consider potential confounds.
- Important to use disease-specific tools.

The Beaumont Behaviour Inventory (BBI)

Code for Patient [ ] Informant's relationship to Patient [ ] **Date** -- /-- /----

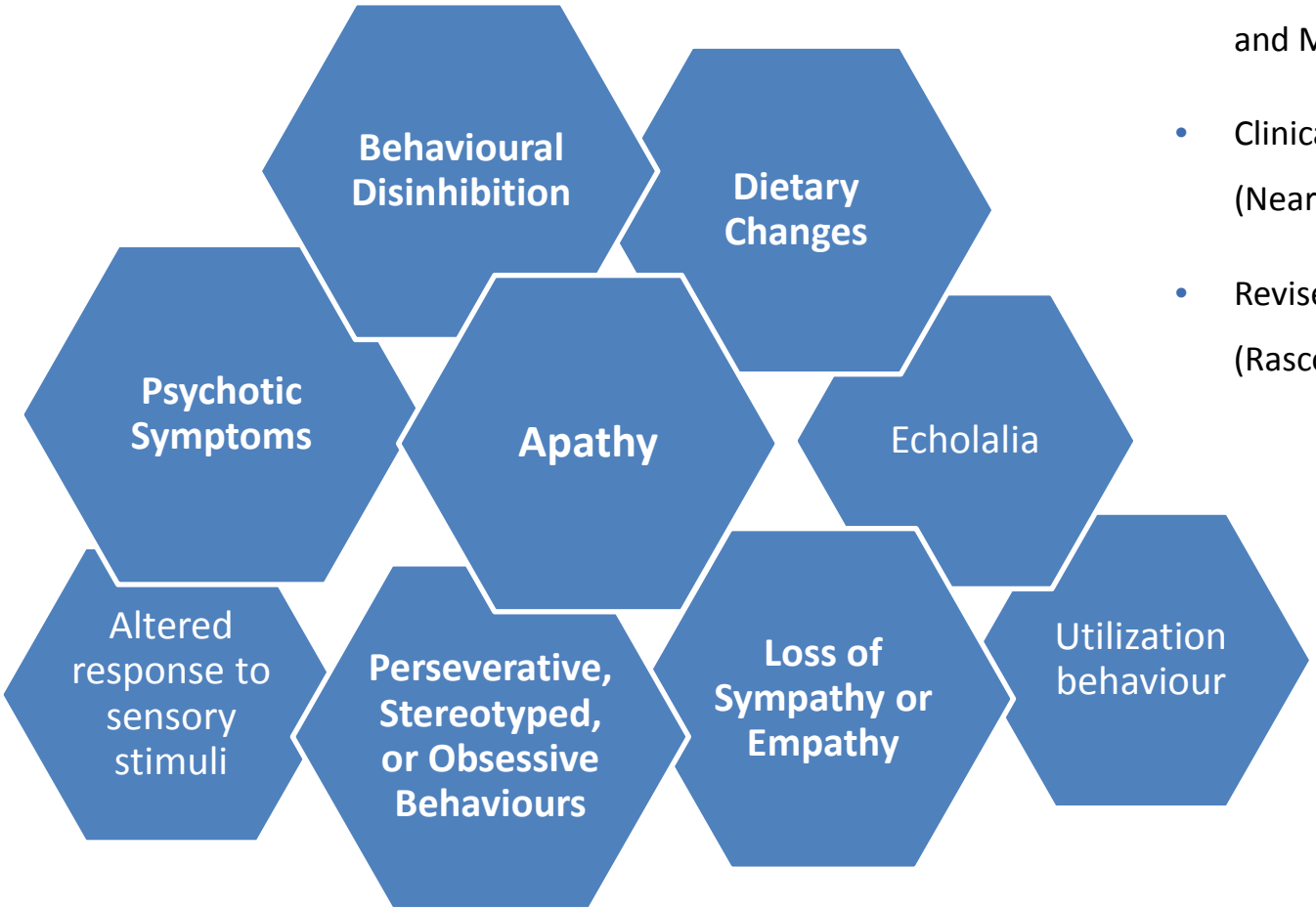
- Your view is very **important** so please read instructions carefully.
- We would like to ask you a number of questions about **changes in behaviour** that you may have noticed in the person
  (1) in last 10 years up to start of the motor neuron disease (MND)
  (2) since the start of the symptoms of the motor neuron disease (MND)
  In each case use a tick (√) to indicate your choice
- If the new behaviour described has been present, then please rate the change as mild, moderate or severe depending on how it has affected your life.
- If the person does <u>not</u> have this behaviour OR has <u>always</u> behaved this way, then select "No/No Change".

		<u>IN THE LAST 10 YEARS</u>	**<u>SINCE ONSET OF MND</u>**
1	Has become more irritable than before	No/No change □ Yes: Mild □ Moderate □ Severe □	No/No change □ Yes: Mild □ Moderate □ Severe □
2	Is much less aware of painful sensations such as hot things, sharp objects etc.	No/No change □ Yes: Mild □ Moderate □ Severe □	No/No change □ Yes: Mild □ Moderate □ Severe □
3	When talking, often makes more grammatical mistakes than before	No/No change □ Yes: Mild □ Moderate □ Severe □	No/No change □ Yes: Mild □ Moderate □ Severe □
4	Is generally not as aware of making mistakes as he/she used to be	No/No change □ Yes: Mild □ Moderate □ Severe □	No/No change □ Yes: Mild □ Moderate □ Severe □
5	Is less able to react to difficulties, plan or foresee problems	No/No change □ Yes: Mild □ Moderate □ Severe □	No/No change □ Yes: Mild □ Moderate □ Severe □
6	If has an idea to do something, he/she has to do it immediately, often without thinking it through	No/No change □ Yes: Mild □ Moderate □ Severe □	No/No change □ Yes: Mild □ Moderate □ Severe □
7	Shows much more emotion than before, cries or laughs too easily	No/No change □ Yes: Mild □ Moderate □ Severe □	No/No change □ Yes: Mild □ Moderate □ Severe □

The Beaumont Behaviour Inventory (BBI)

- ALS-specific 41-item, self-explanatory, proxy-report behavioural assessment.
- Presence of symptoms is graded on a scale from 0 to 3:
  - 0 = no changes
  - 1 = mild changes
  - 2 = moderate changes
  - 3 = severe changes
- Items phased to control for the effect of motor dysfunction on behaviour.
- Behavioural changes rated considering two different timelines.
- Takes 5-10min to complete.

The Beaumont Behaviour Inventory (BBI)



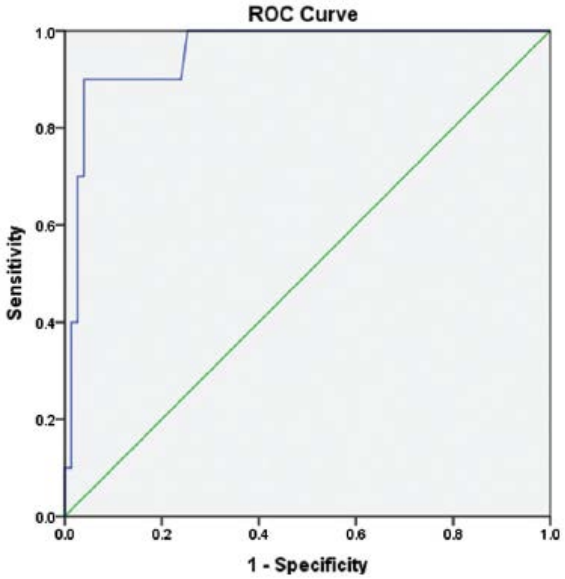
- Clinical Criteria for FTD - The Lund and Manchester Groups (1994)
- Clinical Diagnostic Criteria for FTLD (Neary et al., 1998)
- Revised Diagnostic Criteria for bvFTD (Rascovsky et al., 2011)

RESEARCH ARTICLE

Identifying behavioural changes in ALS: Validation of the Beaumont Behavioural Inventory (BBI)

MARWA ELAMIN[1]*, MARTA PINTO-GRAU[1,2]*, TOM BURKE[1,2], PETER BEDE[1], JAMES ROONEY[1], MEABHDH O'SULLIVAN[1], KATIE LONERGAN[1,2], EMMA KIRBY[1], EMMA QUINLAN[1], NADIA BREEN[1], ALICE VAJDA[1], MARK HEVERIN[1], NIALL PENDER[2] & ORLA HARDIMAN[1]

- Cronbach's α = 0.891 (n=85) // Cronbach's α = 0.906 (n=317).
- Proven Convergent and Discriminant Validity.
- **BBI** score of **≥7** as cut-off for abnormality:
  - Sensitivity of 88% and Specificity of 79%
- **BBI** score of **≥23** indicates severe changes:
  - AUC = 0.955
  - Sensitivity of 90% and Specificity of 96%



Cross-Validation of ALS-specific measures

- Comparison of the BBI to another ALS-specific tool, to explore their ability to capture the entire spectrum of behavioural changes in ALS.

The ALS-FTD-Q

- ALS-specific 25-item proxy-report questionnaire.
- Phrasing of items adjusted for motor and speech dysfunction.
- Cronbach's $\alpha = 0.92$
- Proven Convergent and Discriminant Validity.

Cross-Validation of ALS-specific measures

- 60 consecutive patients fulfilling El Escorial criteria for the diagnosis of ALS.
- Attending the MND National Clinic in Beaumont Hospital, Dublin.
- Exclusion criteria: history of other neurological, psychiatric or medical conditions that can cause cognitive and behavioural changes.
- 9% of participants met revised criteria for bvFTD.
- Carer accompanying the patient completed both the BBI and the ALS-FTD-Q during a clinic visit.
- The ALSFRS-R was also completed in a subset of patients (n=20)
- Demographic and clinical characteristics were acquired from the Irish ALS register.

Cross-Validation of ALS-specific measures

Demographic and Clinical Characteristics of the patient sample (n=60)		
Gender n(%)	**Males**	42 (**70%**)
	Females	18 (**30%**)
Age mean(sd)		**65.42** (9.72)
Years of Education mean(sd)		**13.2** (3.42)
Age at Onset mean(sd)		**63.42** (9.35)
Site of onset n(%)	**Spinal**	38 (**64%**)
	Bulbar	17 (**28%**)
	Thoracic/Respiratory	5 (**8%**)
Age at Diagnosis mean(sd)		**64.68** (9.51)
Diagnosis Delay, in months mean(sd)		**15.37** (11.69)

Cross-Validation of ALS-specific measures

Corroborated **Convergent and Discriminant Validity**:

- Significant large positive correlation between BBI - ALS-FTD-Q *(r=.807, p<.0001)*
- No significant correlations with most demographic and clinical measures:
  - Age *(r=-.074, p=.576)*
  - Education *(r=-.077, p=.558)*
  - Age at onset *(r=-.100, p=.450)*
  - Age at diagnosis *(r=-.066, p=.615)*
  - ALS-FRS-R *(r=-.014, p=.954)*
  - Diagnostic Delay *(r=.405, p=.001) // **(r=.197, p=.149)*

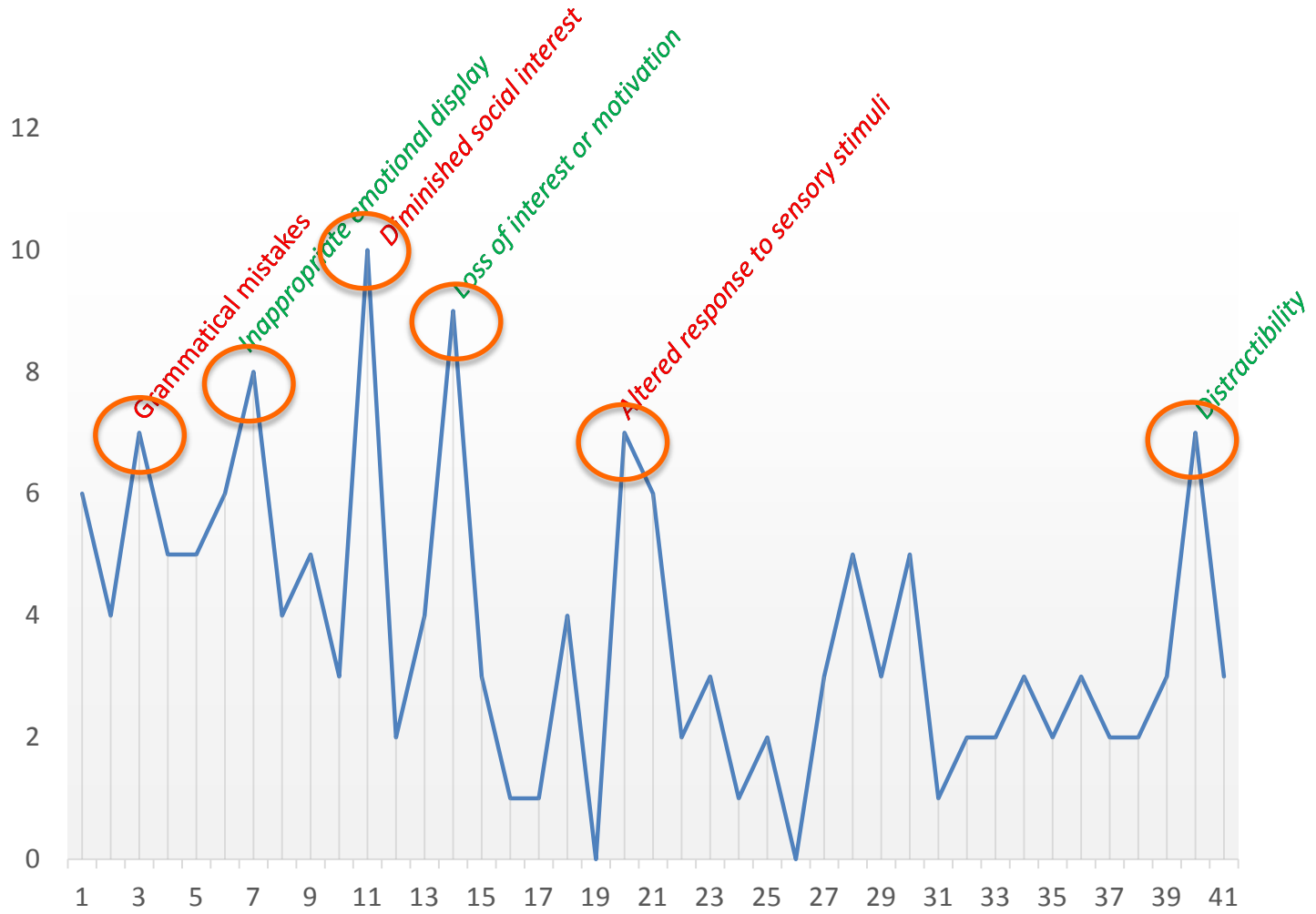
Cross-Validation of ALS-specific measures

		BBI		
		Normal	Abnormal	Total
ALS-FTD-Q	Normal	32	17	46
	Abnormal	0	14	14
	Total	32	28	60

80% Mild Behaviour Changes

Sensitivity	1
Specificity	0.65

Cross-Validation of ALS-specific measures



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A. Early* behavioural disinhibition [one of the following symptoms (A.1–A.3) must be present]:
   - A.1. Socially inappropriate behaviour
   - A.2. Loss of manners or decorum
   - A.3. Impulsive, rash or careless actions

B. Early apathy or inertia [one of the following symptoms (B.1–B.2) must be present]:
   - B.1. Apathy
   - B.2. Inertia

C. Early loss of sympathy or empathy [one of the following symptoms (C.1–C.2) must be present]:
   - C.1. Diminished response to other people's needs and feelings
   - C.2. Diminished social interest, interrelatedness or personal warmth

D. Early perseverative, stereotyped or compulsive/ritualistic behaviour [one of the following symptoms (D.1–D.3) must be present]:
   - D.1. Simple repetitive movements
   - D.2. Complex, compulsive or ritualistic behaviours
   - D.3. Stereotypy of speech

E. Hyperorality and dietary changes [one of the following symptoms (E.1–E.3) must be present]:
   - E.1. Altered food preferences
   - E.2. Binge eating, increased consumption of alcohol or cigarettes
   - E.3. Oral exploration or consumption of inedible objects

Conclusions

- General behavioural instruments that do not correct for motor disability tend to **overestimate** the presence of behavioural changes in ALS.
- Disease-specific instruments that do not include the whole spectrum of behaviours characteristic of ALS tend to **underestimate** its presence.
- These additional elements on the BBI **improve its discriminatory power for mild behavioural changes**.
- The BBI is a simple-to-administer

  ALS-specific behavioural proxy report,

  with proven adequate psychometric properties,

  which seems to overcome both limitations.

TRINITY COLLEGE DUBLIN

BEAUMONT HOSPITAL

rmn Research Motor Neurone

Acknowledgements

Professor Orla Hardiman

Professor Niall Pender

Dr. Marwa Elamin

Mr. Emmet Costello

Ms. Sarah O'Connor

Dr. Tom Burke

Mr. Mark Heverin