THE EUAN MACDONALD CENTRE
FOR MOTOR NEURONE DISEASE RESEARCH

mnda
motor neurone disease association

Thomas H. Bak
*University of Edinburgh*

MND Scotland

# Cognitive & behavioural symptoms in ALS
## Why are they there
## and how to assess them?

# Samostojnost!

# Cognitive & Motor Symptoms in ALS: Why are they there?

- Because ALS is not a motor disorder
- Cognitive & behavioural symptoms are there not despite by because of ALS being a disease of the motor system

# Is it a new topic (since C9ORF72)?

The two narratives of ALS:

- ALS as a motor disorder
- Cognitive/behavioural symptoms only recently recognised

*But*

- Cognitive/behavioural symptoms documented since 19th C
- Explicit link between ALS and FTD made in 1932

# The nature of the deficits

- Intellectual impairment
  - "Merkfähigkeit" vs. "Gedächtnis", preserved visuo-spatial skills
- Language:
  - "Speechlessness", Spelling errors, Comprehension deficits
- Changes in personality & behaviour:
  - Suspiciousness, greed, tendency to hoard things
  - Apathy, irritability, emotional lability
- Psychotic symptoms:
  - Delusions & hallucinations

# Cognitive & behavioural symptoms in ALS: *dementia or mild cognitive dysfunction?*

Single case reports of overt Dementia

*Dornblüth 1889*

*Meyer 1929*

*von Braunmühl 1932*

*Teichmann 1935*

Subtle cognitive changes in non-demented patients

*Marie 1892*

*Raymond & Cestan 1905*

*Van Bogaert 1925*

***Ziegler 1930***

# How frequent?

- Marie (1892)
  - "psychic disturbances are fairly common"
- Raymond & Cestan (1905)
  - Half of 18 pathologically confirmed cases described as "psychologically feeble"
- Van Bogaert (1925)
  - "psychic alterations" in 13 out of 31 patients

# The tale of two traditions

*Dornblüth 1889*

*Marie 1892*

*Watanabe 1893*

*Raymond & Cestan 1905*

*Fragnito 1907*

*Westphal 1909*

*Gerbert & Naville 1921*

*Büscher 1922*

*van Bogaert 1925*

*Meyer 1929*

***Ziegler 1930***

***von Braunmühl 1932***

*Wechsler & Davison 1932*

*Teichmann 1935*

# Neurodegenerations as diseases of functional systems

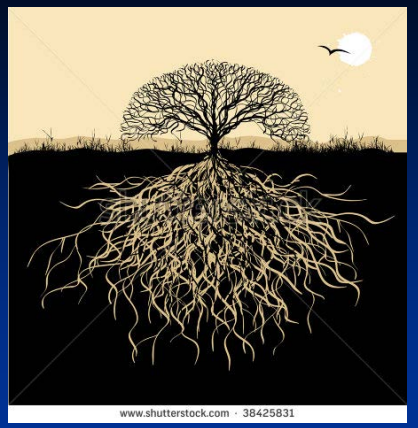
- Relatively focal onset (anatomically & clinically)
- A systematic spread of the disease (-> *John Ravits*)
- "What wires together, dies together"

  *(Bak & Chandran, Cortex 2012)*
- What is the motor system?

THE EUAN MACDONALD CENTRE
FOR MOTOR NEURONE DISEASE RESEARCH

# Namibia 2016

# Re-thinking the motor system




Before we execute any movement we have to:

- Have the intention to do it (initiative, generation)
- Select the correct motor pattern (action semantics)
- Suppress it if necessary (e.g. socially inappropriate)

All this could be referred to as "motor cognition"

*(Marc Jeannerod 2006)*

# Cognition/behavioural symptoms in MND

- Behaviour: Apathy & Desinhibition
- Generation of words, concepts etc
- Decision making, knowledge of actions, social cognition
- => Deficits in "Motor cognition"

- Distinct from (opposite to) the deficits seen in SD

- Extension of Hebb's Rule (*Bak & Chandran 2011*):
  - **What fires together wires together**
  - **What wires together dies together**

# FTD & ALS: one, two of three diseases (2010)

- 2001 - ALS and FTD:
  - Coincidence
  - Co-occurrance
  - Continuum

- 2010 -Specific features of ALS/FTD:
  - Psychotic features (*Bak, Lillo, Snowden*: particularly in C9ORF72)
  - Comprehension deficits (*Caselli, Rakowicz, Bak, Goldstein*)
  - Spelling errors (*Watanabe, Kawamura, Silani, Abrahams & Bak*)
  - Does not map neatly into bvFTD, NFPA and SD
- => Interaction rather than addition

# Why & how to assess cognition & behaviour in ALS?

- Heterogeneity of patients: "ALS patients" vs. "Normal controls" assumes homogeneity => subgroups
- Heterogeneity of functions: cognitive functions dissociate => selective deficits => multidimensionality
- Motor deficits confound cognitive performance:
  - Dysarthria, mutism – oral peerformance
  - Weakness, spasticity, apraxia – written performance
  - => tests minimising motor confounds

# Cognitive screening across the world

92% use regularely screening tools, often more than one:

- 62% MMSE
- 36% MoCA
- 20% ACE
- 14% CDR
- 5% Clock drawing
- 3.2% DRS
- 3% FAB

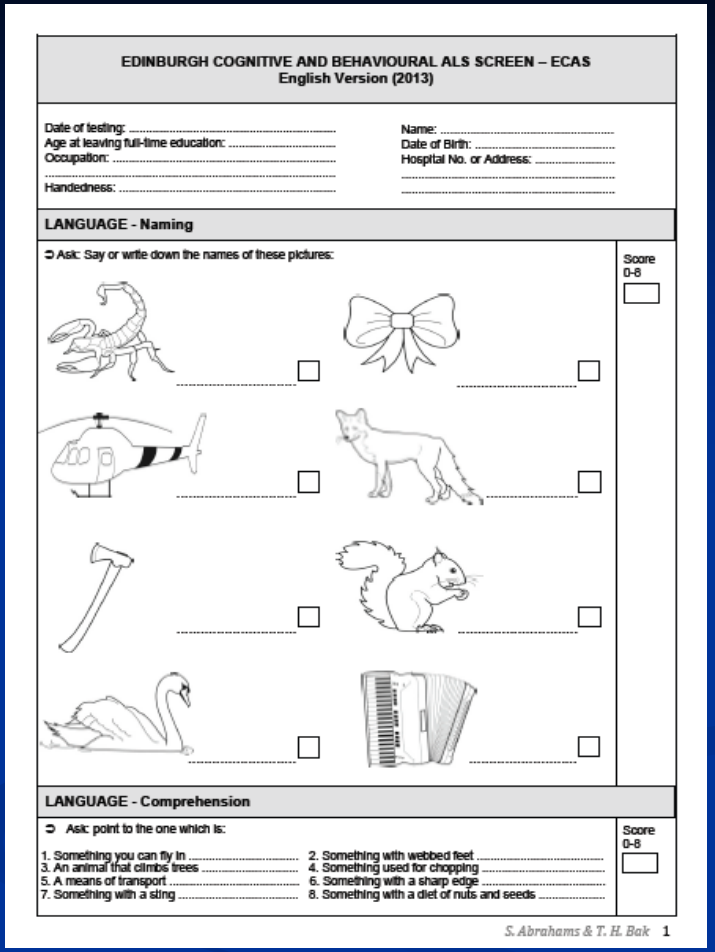
All these tests are substantially influenced by motor deficits.

# Edinburgh Cognitive Screen (ECAS)

- Cognitive assessment for patients with motor deficits
- Tries to minimise the influence of motor dysfunction (e.g. pointing tasks, yes/no answers etc)
- Parallel written and spoken versions
- Multi-dimensional
- First applied in ALS, currently piloted in PD & PSP

# ECAS – LANGUAGE

- Naming
- Comprehension:
  - nouns & verbs
- Spelling:
  - Irregular & regular
  - Compounds



EDINBURGH COGNITIVE AND BEHAVIOURAL ALS SCREEN – ECAS
English Version (2013)

Date of testing: .....
Age at leaving full-time education: .....
Occupation: .....
.....
Handedness: .....

Name: .....
Date of Birth: .....
Hospital No. or Address: .....
.....
.....

**LANGUAGE - Naming**

➲ Ask: Say or write down the names of these pictures:

Score 0-8

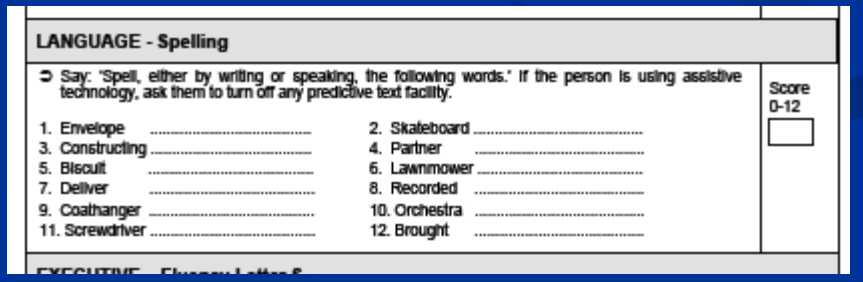
**LANGUAGE - Comprehension**

➲ Ask: point to the one which is:

1. Something you can fly in .....
2. Something with webbed feet .....
3. An animal that climbs trees .....
4. Something used for chopping .....
5. A means of transport .....
6. Something with a sharp edge .....
7. Something with a sting .....
8. Something with a diet of nuts and seeds .....

Score 0-8

S. Abrahams & T. H. Bak 1



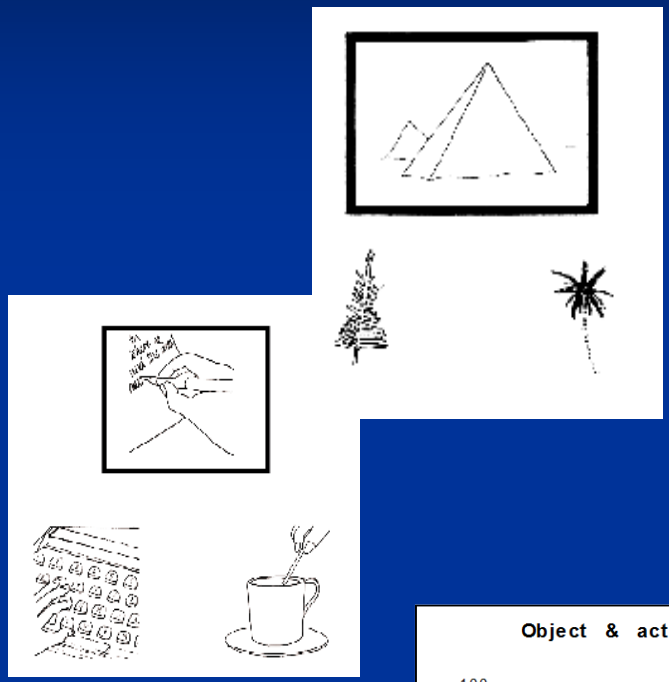
**LANGUAGE - Spelling**

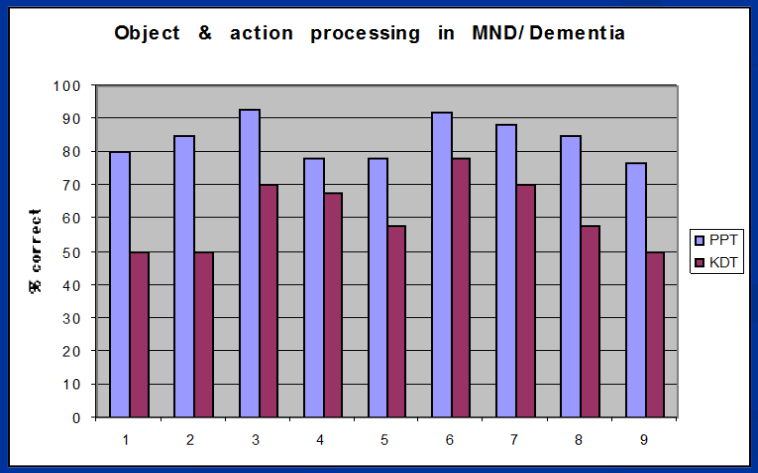
➲ Say: "Spell, either by writing or speaking, the following words." If the person is using assistive technology, ask them to turn off any predictive text facility.

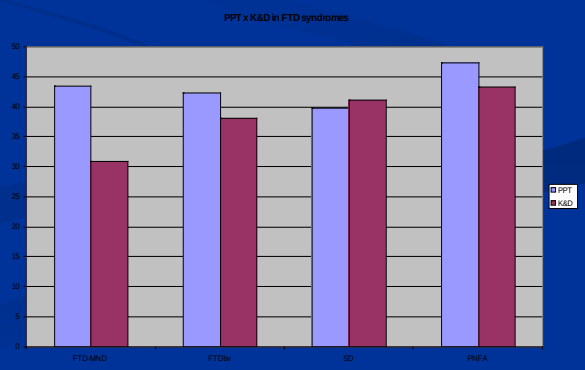
Score 0-12

1. Envelope .....
2. Skateboard .....
3. Constructing .....
4. Partner .....
5. Biscuit .....
6. Lawnmower .....
7. Deliver .....
8. Recorded .....
9. Coathanger .....
10. Orchestra .....
11. Screwdriver .....
12. Brought .....

# Nouns & verbs in ALS



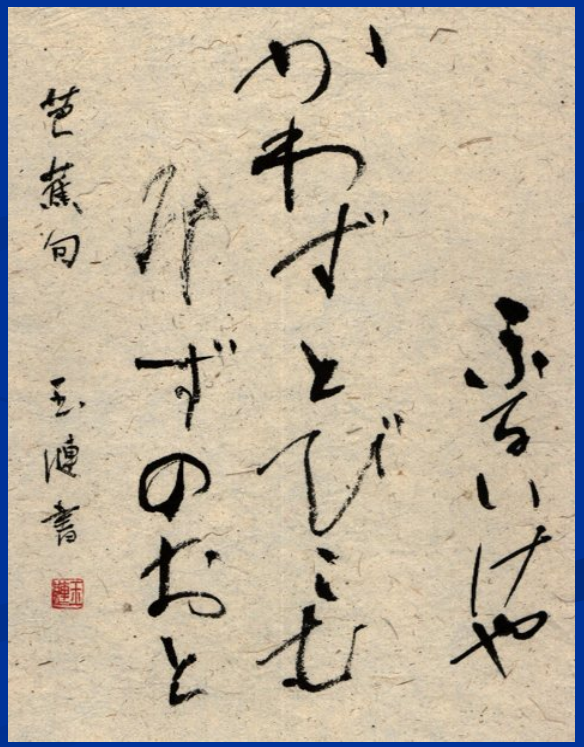


# Watanabe 1893

## *Journal of the Medical Society of Okayama*

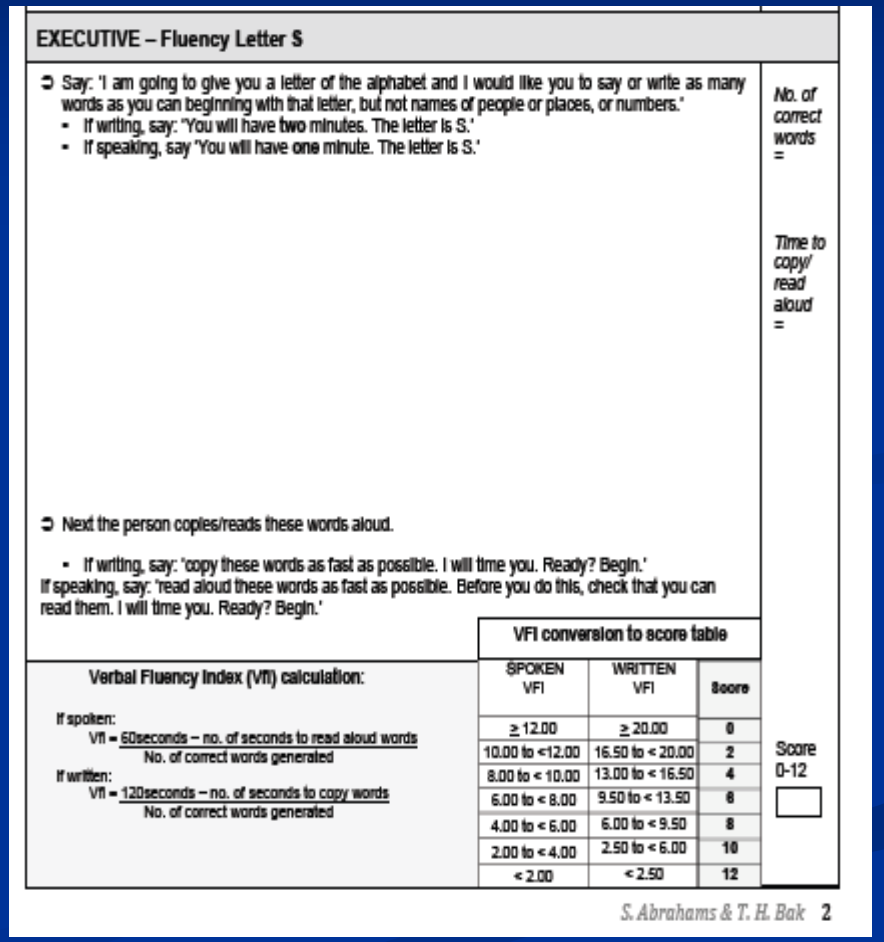
- Became available in English only recently (Ichikawa et al, European Neurology 2011)
- First aphasia description in Japan
- Aphasia in the context of MND
- Predominant impairment in kana
- (rather than kanji)



- Reports of errors in regular spelling
  - Italian, Spanish

# ECAS – VERBAL FLUENCY

- Spoken or written
- Verbal Fluency Index
- Letter Fluency:
  - Free
  - Constrained (4 letters)



**EXECUTIVE – Fluency Letter S**

➲ Say: 'I am going to give you a letter of the alphabet and I would like you to say or write as many words as you can beginning with that letter, but not names of people or places, or numbers.'
- If writing, say: 'You will have **two** minutes. The letter is S.'
- If speaking, say 'You will have **one** minute. The letter is S.'

*No. of correct words =*

*Time to copy/ read aloud =*

➲ Next the person copies/reads these words aloud.

- If writing, say: 'copy these words as fast as possible. I will time you. Ready? Begin.'

If speaking, say: 'read aloud these words as fast as possible. Before you do this, check that you can read them. I will time you. Ready? Begin.'

**Verbal Fluency Index (VFI) calculation:**

If spoken:
VFI = $\frac{60\text{seconds} - \text{no. of seconds to read aloud words}}{\text{No. of correct words generated}}$

If written:
VFI = $\frac{120\text{seconds} - \text{no. of seconds to copy words}}{\text{No. of correct words generated}}$

**VFI conversion to score table**

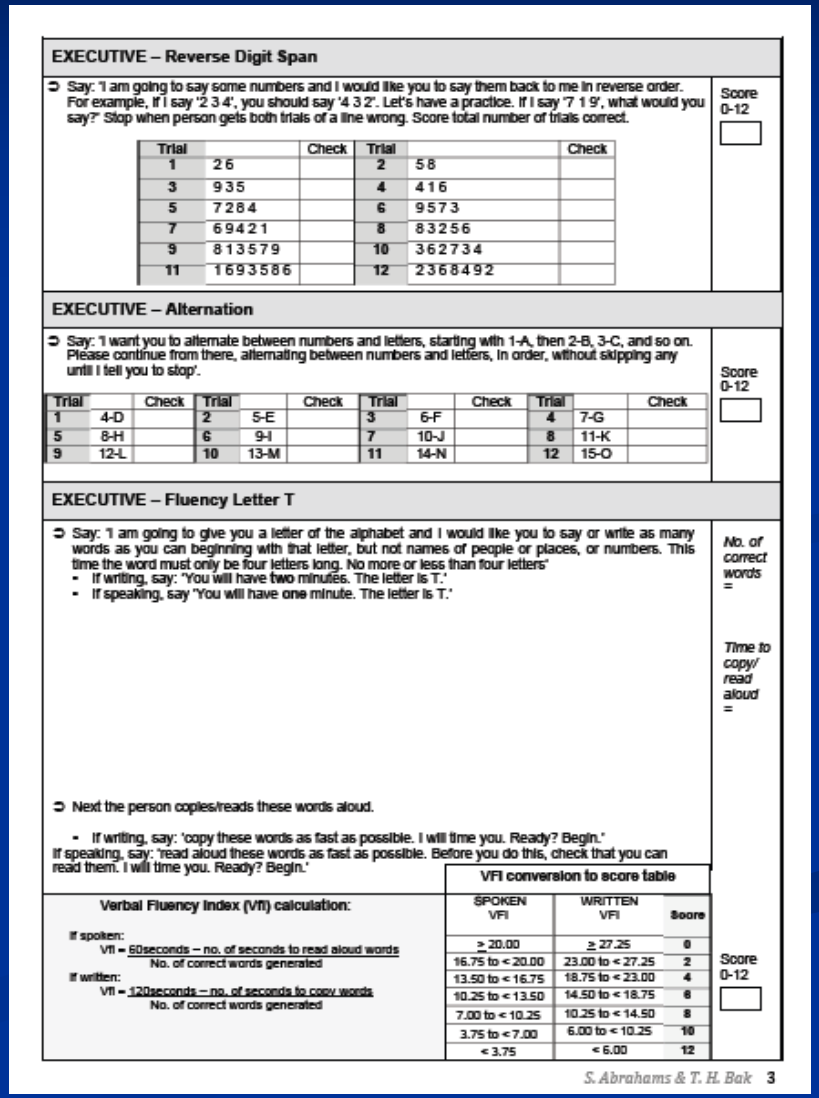
| SPOKEN VFI | WRITTEN VFI | Score |
|---|---|---|
| ≥ 12.00 | ≥ 20.00 | 0 |
| 10.00 to <12.00 | 16.50 to < 20.00 | 2 |
| 8.00 to < 10.00 | 13.00 to < 16.50 | 4 |
| 6.00 to < 8.00 | 9.50 to < 13.50 | 6 |
| 4.00 to < 6.00 | 6.00 to < 9.50 | 8 |
| 2.00 to < 4.00 | 2.50 to < 6.00 | 10 |
| < 2.00 | < 2.50 | 12 |

Score 0-12 ☐

*S. Abrahams & T. H. Bak* 2

# ECAS – EXECUTIVE FUNCTIONS

- Reverse Digit Span
- Alternation
- Inhibition (Hayling)



**EXECUTIVE – Reverse Digit Span**

➲ Say: 'I am going to say some numbers and I would like you to say them back to me in reverse order. For example, if I say '2 3 4', you should say '4 3 2'. Let's have a practice. If I say '7 1 9', what would you say?' Stop when person gets both trials of a line wrong. Score total number of trials correct.

Score 0-12 ☐

| Trial | | Check | Trial | | Check |
|---|---|---|---|---|---|
| 1 | 2 6 | | 2 | 5 8 | |
| 3 | 9 3 5 | | 4 | 4 1 6 | |
| 5 | 7 2 8 4 | | 6 | 9 5 7 3 | |
| 7 | 6 9 4 2 1 | | 8 | 8 3 2 5 6 | |
| 9 | 8 1 3 5 7 9 | | 10 | 3 6 2 7 3 4 | |
| 11 | 1 6 9 3 5 8 6 | | 12 | 2 3 6 8 4 9 2 | |

**EXECUTIVE – Alternation**

➲ Say: 'I want you to alternate between numbers and letters, starting with 1-A, then 2-B, 3-C, and so on. Please continue from there, alternating between numbers and letters, in order, without skipping any until I tell you to stop'.

Score 0-12 ☐

| Trial | | Check | Trial | | Check | Trial | | Check | Trial | | Check |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 4-D | | 2 | 5-E | | 3 | 6-F | | 4 | 7-G | |
| 5 | 8-H | | 6 | 9-I | | 7 | 10-J | | 8 | 11-K | |
| 9 | 12-L | | 10 | 13-M | | 11 | 14-N | | 12 | 15-O | |

**EXECUTIVE – Fluency Letter T**

➲ Say: 'I am going to give you a letter of the alphabet and I would like you to say or write as many words as you can beginning with that letter, but not names of people or places, or numbers. This time the word must only be four letters long. No more or less than four letters'
- If writing, say: 'You will have two minutes. The letter is T.'
- If speaking, say 'You will have one minute. The letter is T.'

*No. of correct words =*

*Time to copy/ read aloud =*

➲ Next the person copies/reads these words aloud.

- If writing, say: 'copy these words as fast as possible. I will time you. Ready? Begin.'

If speaking, say: 'read aloud these words as fast as possible. Before you do this, check that you can read them. I will time you. Ready? Begin.'

**Verbal Fluency Index (VFI) calculation:**

If spoken:
VFI = $\frac{60\text{seconds} - \text{no. of seconds to read aloud words}}{\text{No. of correct words generated}}$

If written:
VFI = $\frac{120\text{seconds} - \text{no. of seconds to copy words}}{\text{No. of correct words generated}}$

**VFI conversion to score table**

| SPOKEN VFI | WRITTEN VFI | Score |
|---|---|---|
| ≥ 20.00 | ≥ 27.25 | 0 |
| 16.75 to < 20.00 | 23.00 to < 27.25 | 2 |
| 13.50 to < 16.75 | 18.75 to < 23.00 | 4 |
| 10.25 to < 13.50 | 14.50 to < 18.75 | 6 |
| 7.00 to < 10.25 | 10.25 to < 14.50 | 8 |
| 3.75 to < 7.00 | 6.00 to < 10.25 | 10 |
| < 3.75 | < 6.00 | 12 |

Score 0-12 ☐

*S. Abrahams & T. H. Bak* 3

# ECAS – SOCIAL COGNITION

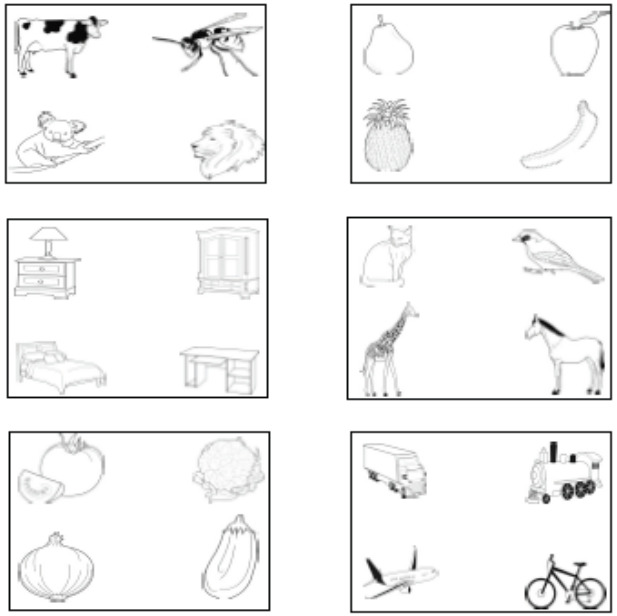
1. The postman knocked on the .....
2. He brought his umbrella with him in case of .....
3. Sally spread her toast with butter and .....
4. John went to the barbers to get his hair .....
5. She dived into the swimming .....
6. They all went to the local café for something to .....

Score 0-12

**Score 2 for different word, 1 for related word (e.g. associated or opposite meaning) or 0 for exact word.**

## SOCIAL COGNITION – Part A

➲ Say: 'You are going to see some pictures, one in each corner of a box. You have to choose **which picture you like best**. Either point to or say which picture you like best. Please respond as quickly as possible.' Circle participant's choice.

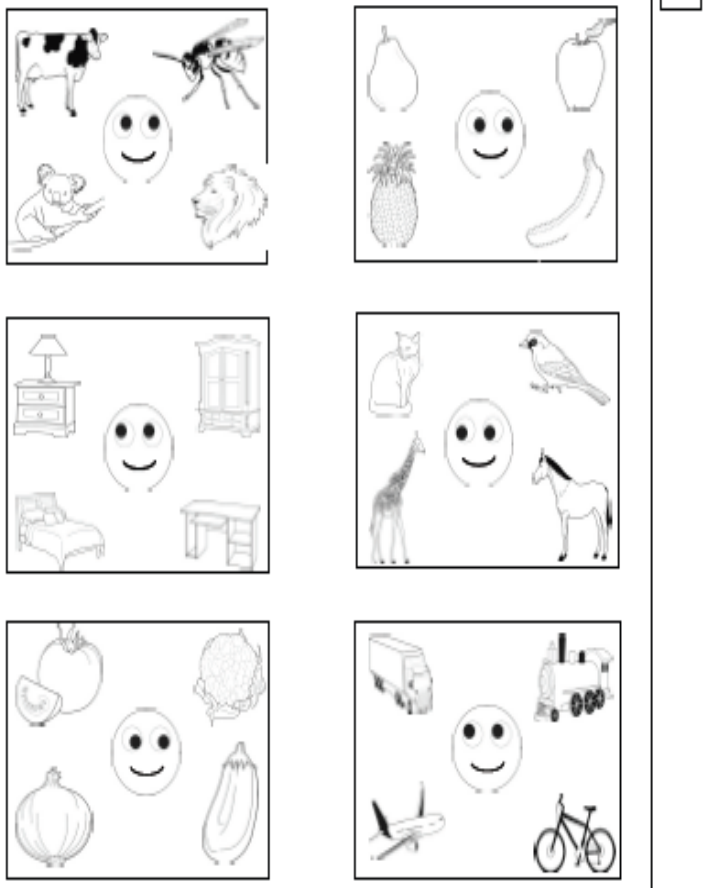




## SOCIAL COGNITION – Part B

➲ Say: 'You are going to see some pictures, one in each corner of a box. You have to choose **which picture does the face like best**. Either point to or say which picture **the face likes best**. Please respond as quickly as possible.' Circle participant's choice. Correct items = 2 points, error = 1 point, egocentric error = 0 points.

Score 0-12



# ECAS – MEMORY

- Encoding
- Recall (% retention)
- Recognition

**MEMORY – Immediate recall**

Score 0-10

➲ Say: 'I am going to read you a short story. Please listen carefully. When I am finished, say or write as much as you can remember'. Score 1 point for each (either entire or part of) underlined section recalled.

*Last Sunday, the annual litter collection took place in Primrose Woods. Forty two people joined in to remove old bicycles and shopping trolleys. Mr Douglas Watt from the woodland project told local reporters that he was very impressed and especially proud of the 17 children who came along.*

*Also use this score to calculate % retention later*

**MEMORY – Delayed Recognition**

If all items recalled, skip and score 4. Otherwise ask questions below.

Say: 'Lets see if you can remember anything more about that story. I will ask you some questions, please tell me if they are true or false'.

Circle responses (true or false) and score 1 point for each item recognised in this section. Use table below to calculate score.

Score 0-4

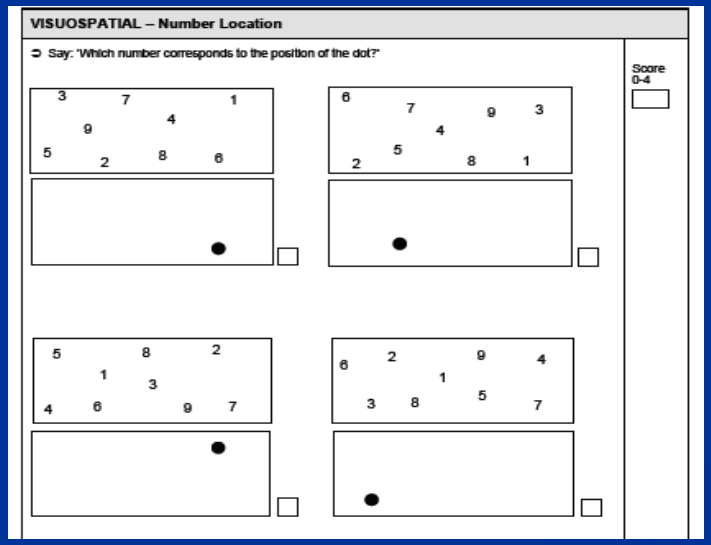
| | | | |
|---|---|---|---|
| Was the story about an event that occurred last Saturday? | T | F | 1 |
| Was the event the annual litter collection? | T | F | 1 |
| Did this take place in Primrose Woods? | T | F | 1 |
| Did they remove old drink cans and sweet wrappers? | T | F | 1 |
| Was the man in the story called Mr Watt? | T | F | 1 |
| Was his first name 'Thomas'? | T | F | 1 |
| Was he from the local council? | T | F | 1 |
| Was he especially proud of the children for coming along? | T | F | 1 |

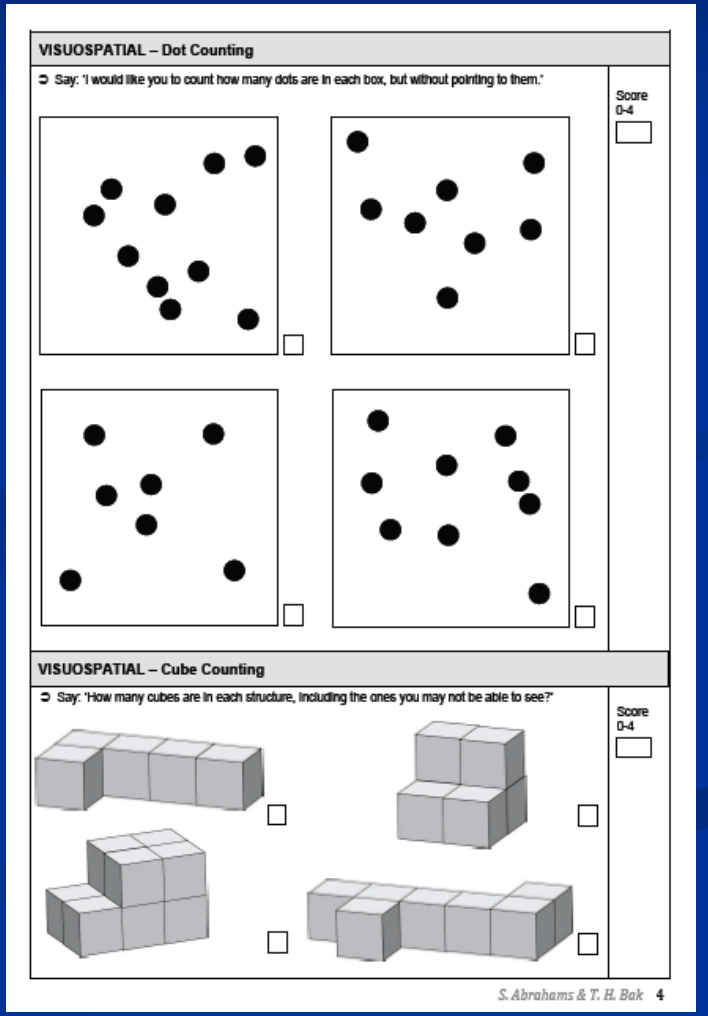
**Recognition to recognition score table**

| Number of correct answers | Converted Score |
|---|---|
| 0-4 | 0 |
| 5 | 1 |
| 6 | 2 |
| 7 | 3 |
| 8 | 4 |

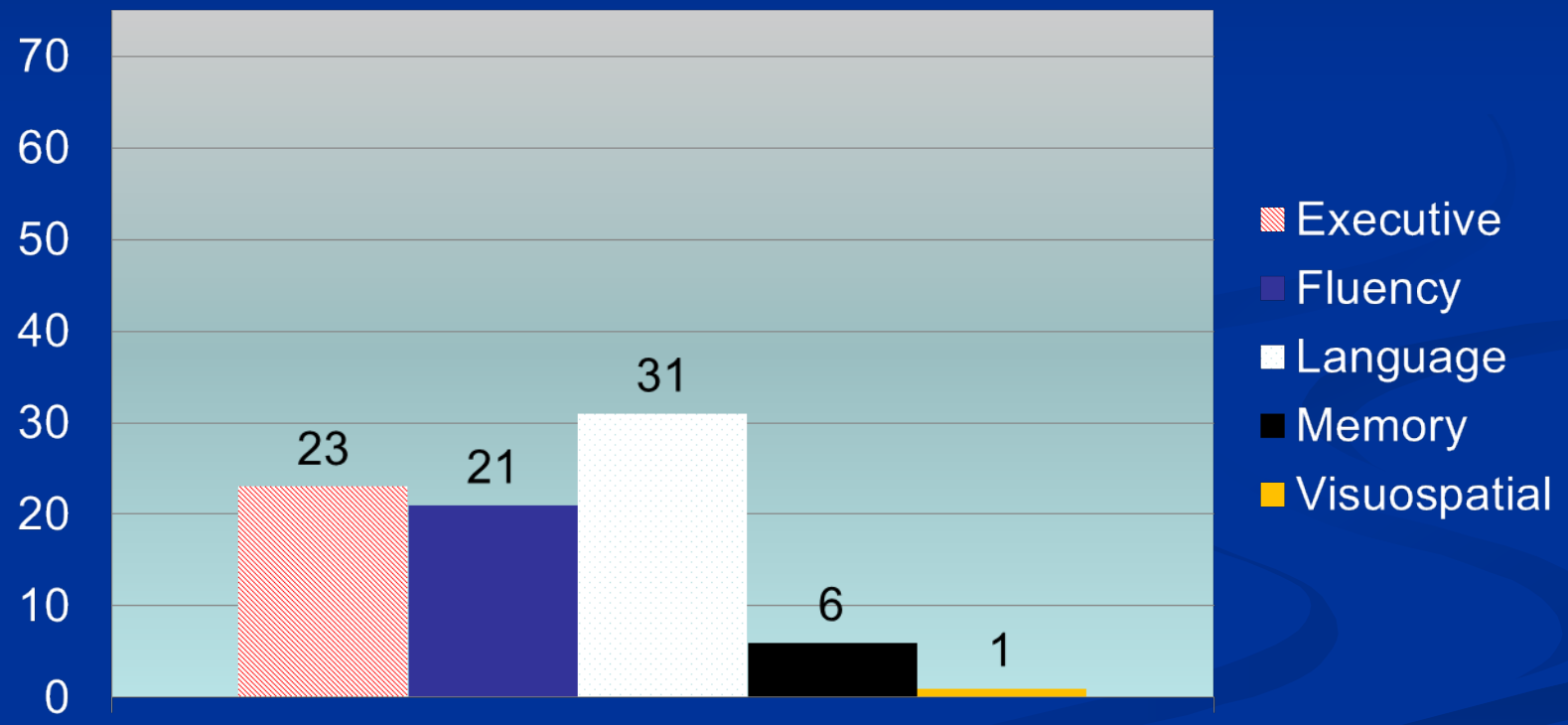
# ECAS – VISUOSPATIAL FUNCTIONS (WITHOUT DRAWING)

- Number location
- Dots
- Cubes

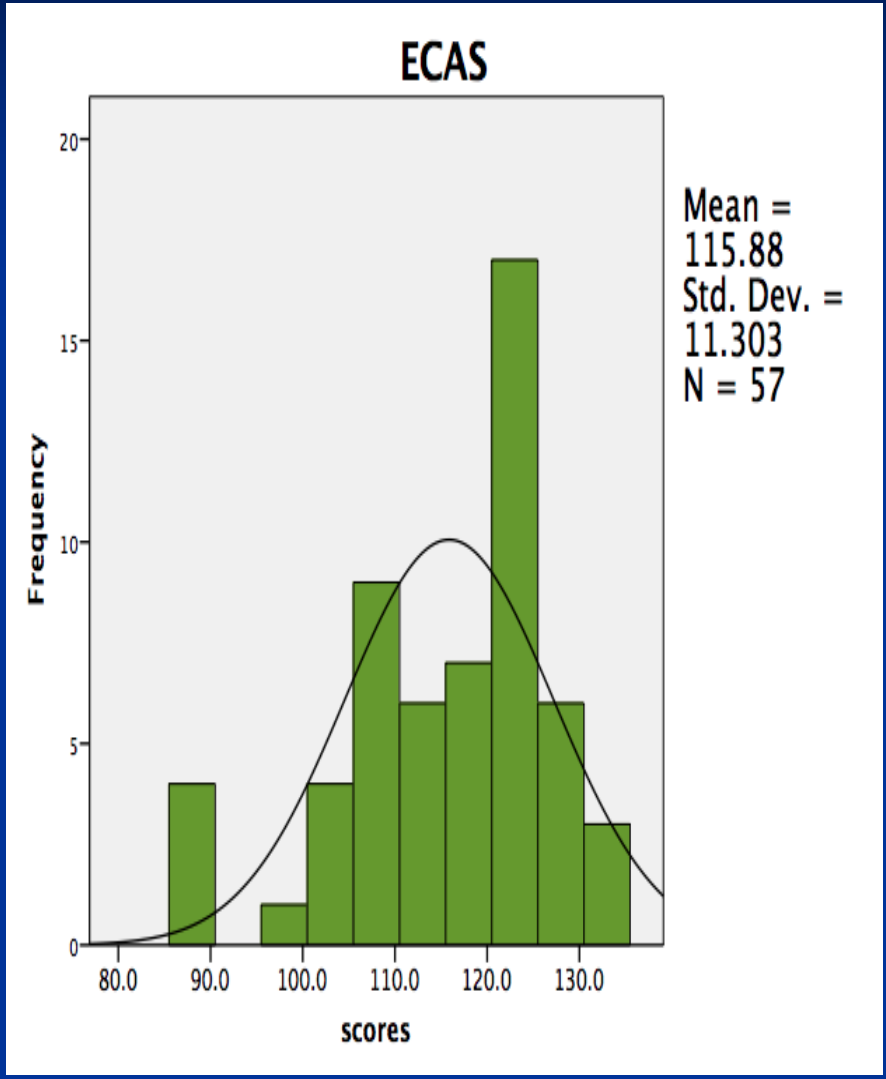


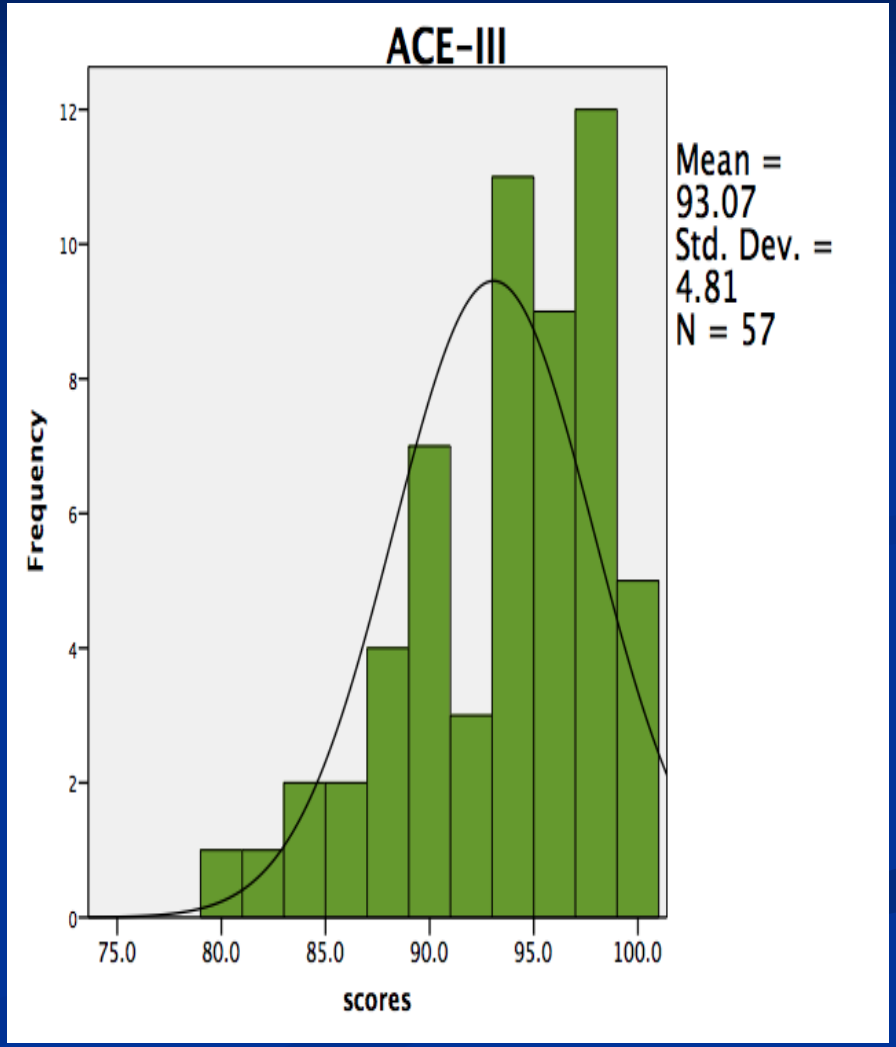



# ECAS Subdomains:
## Frequency of Abnormal Performance (75 ALS patients)

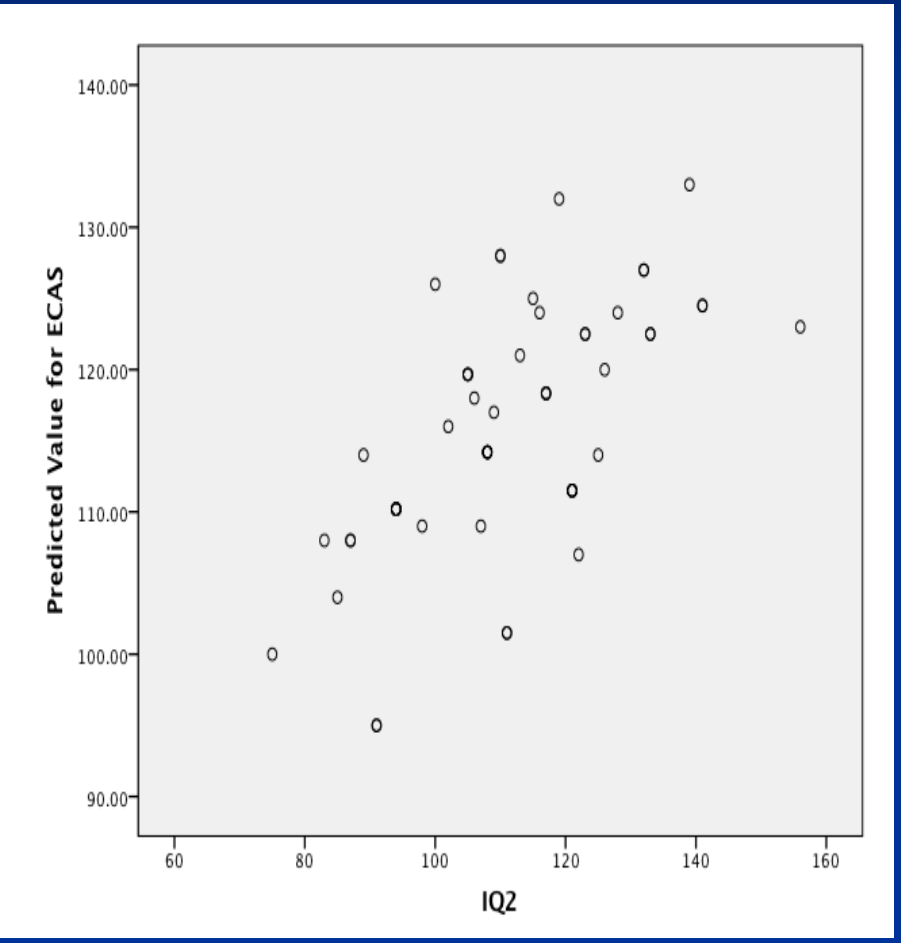


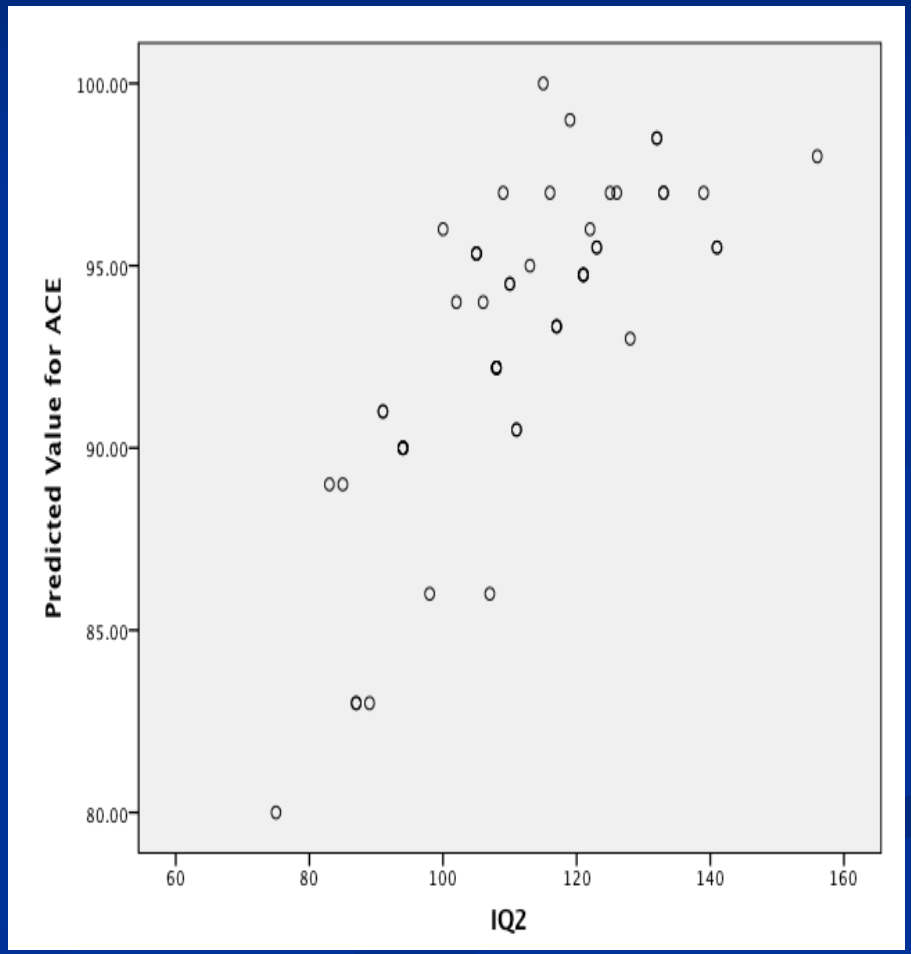
- *The ECAS had less ceiling effects than the ACE-III*



- *IQ predicts 23% of the variance of the total score of the ECAS vs 46% of the ACE-III*



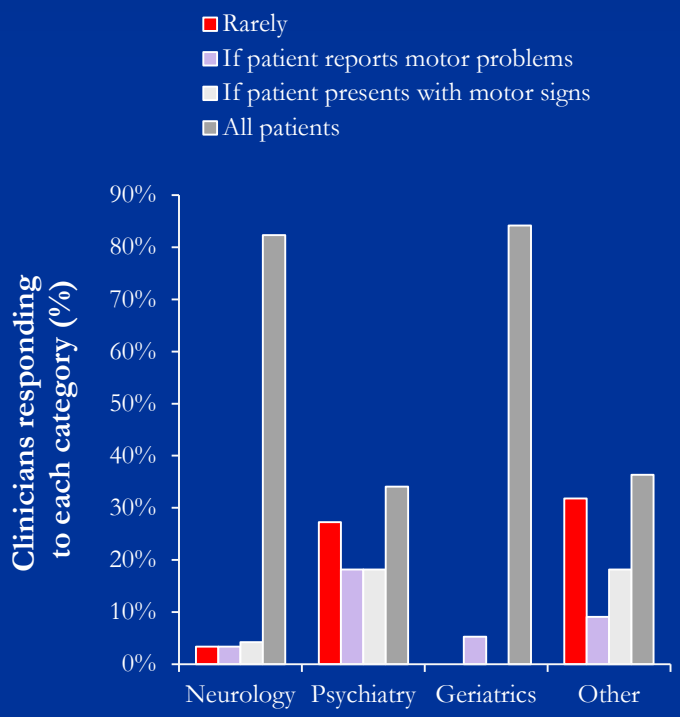



# Behaviour: don't ask, don't hear

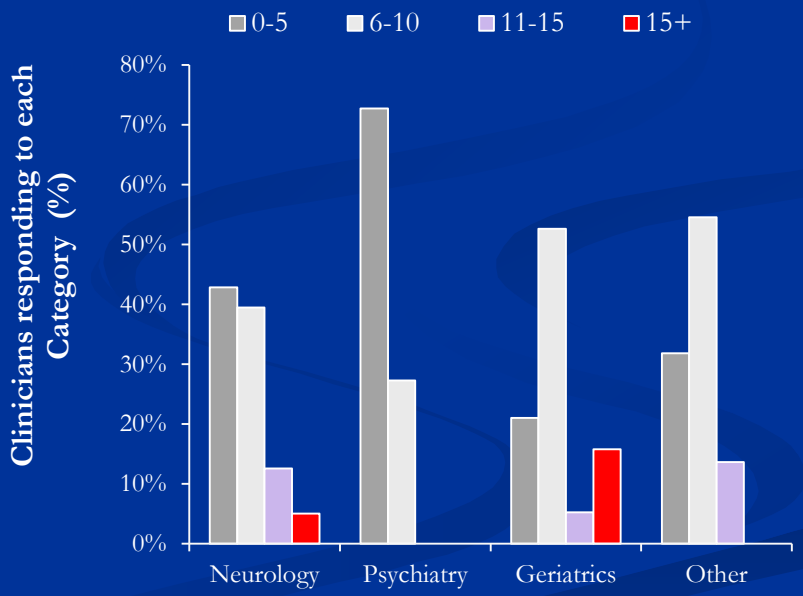
- The typical Natural course of behavioural & cognitive symptoms in ALS: psychosis -> dementia -> ALS
- Patients & carers unlikely to report apparently unrelated symptoms spontaneously
- Until recently, many continental (and Japanese) neurologists were also psychiatrists => seeing the same patients for psychiatric & neurological problems

# Motor examination in dementia: current practice

**Frequency with which a motor exam is conducted**




**Reported duration of motor examination (minutes)**



# Summary

- The motor system does not start at the motor cortex, it includes all aspects of motor cognition
- => Cognitive & behavioural symptoms are an integral part of the clinical picture of ALS
- Their assessment needs to be multidimensional and to control for motor dysfunction

Hvala za pozornost

@thbaketal