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
<table>
<thead>
<tr>
<th>Cognitive &amp; behavioural symptoms in ALS: dementia or mild cognitive dysfunction?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Single case reports of overt Dementia</strong></td>
</tr>
<tr>
<td>Dornblüth 1889</td>
</tr>
<tr>
<td>Meyer 1929</td>
</tr>
<tr>
<td>von Braunmühl 1932</td>
</tr>
<tr>
<td>Teichmann 1935</td>
</tr>
<tr>
<td><strong>Subtle cognitive changes in non-demented patients</strong></td>
</tr>
<tr>
<td>Marie 1892</td>
</tr>
<tr>
<td>Raymond &amp; Cestan 1905</td>
</tr>
<tr>
<td>Van Bogaert 1925</td>
</tr>
<tr>
<td>Ziegler 1930</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Dornblüth 1889</th>
<th>Büscher 1922</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marie 1892</td>
<td>van Bogaert 1925</td>
</tr>
<tr>
<td>Watanabe 1893</td>
<td>Meyer 1929</td>
</tr>
<tr>
<td>Raymond &amp; Cestan 1905</td>
<td>Ziegler 1930</td>
</tr>
<tr>
<td>Fragnito 1907</td>
<td>von Braunmühl 1932</td>
</tr>
<tr>
<td>Westphal 1909</td>
<td>Wechsler &amp; Davison 1932</td>
</tr>
<tr>
<td>Gerbert &amp; Naville 1921</td>
<td>Teichmann 1935</td>
</tr>
</tbody>
</table>
Neurodegenerations as diseases of functional systems

- Relatively focal onset (anatomically & clinically)
- A systematic spread of the disease (-> John Ravits)
- “What wires together, dies together”
  \cite{Bak2012}
  \cite{Chandran2012}
- What is the motor system?
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-occurrence
- 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 performance
  - Weakness, spasticity, apraxia – written performance
  - => tests minimising motor confounds
Cognitive screening across the world

92% use regularly 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
Nouns & verbs in ALS

Object & action processing in MND/Dementia

Graph showing % correct for different conditions.
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)
ECAS – EXECUTIVE FUNCTIONS

- Reverse Digit Span
- Alternation
- Inhibition (Hayling)
ECAS – SOCIAL COGNITION

1. The postman knocked on the ____________________________ Score 0-12
2. He brought his umbrella with him in case of ____________________________
3. Sally spread her toast with butter and ____________________________
4. John went to the barber to get his hair ____________________________
5. She dived into the swimming ____________________________
6. They all went to the local café for something to ____________________________

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 does the face 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 you like best. Please respond as quickly as possible.” Circle participant’s choice.

Correct items – 2 points, error – 1 point, egocentric error – 0 points.
ECAS – MEMORY

- Encoding
- Recall (% retention)
- Recognition
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
- Rarely
- If patient reports motor problems
- If patient presents with motor signs
- All patients

Reported duration of motor examination (minutes)
- 0-5
- 6-10
- 11-15
- 15+

Clinicians responding to each category (%)
- Neurology
- Psychiatry
- Geriatrics
- Other
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