Cognitive Challenges in MND

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What do we mean by cognition.....

MEMORY Association CONCEPT FORMATION
LANGUAGE mental imagery attention
ACTION problem solving PERCEPTION

Research aims to create models to describe or explain specific behaviours.
What do we mean by cognition.....

The study of behaviour is divided into two broad categories:

- cognitive (how we know the world)
- affect (feelings and emotions)
Cognition v Emotion

• Traditionally, emotion was not thought of as a cognitive process

Now

• Seen as an artificial division, with research examining the cognitive psychology of emotion

• Depression is rare in MND (5–20%) v ~50% in multiple sclerosis and Parkinson's disease
There was once a recluse who never left his home. The only
time anyone ever visited him was when
his food and supplies were delivered,
but they never came inside.
Then, one stormy winter night when an icy gale was blowing,
he had a nervous breakdown.
He went upstairs, turned off all the lights
and went to bed.
Next morning, he had caused the deaths of several hundred people.

How?
Cognitive changes in MND

- Cognitive change is seen in up to 50% of patients.

- Approx 3% exhibit a form of frontotemporal dementia FTD

- A larger proportion (up to 50%) suffer from a milder version of cognitive change, known as executive function
Case examples: executive function

The ability to:

- initiate
- inhibit
- sustain
- switch attention
- Organise complex tasks
Variants of FrontoTemporal Dementia: clinical patterns

**Behaviour**
- disinhibited
- apathetic
- lack of social tact
- lack of empathy
- distractability
- loss of insight
- increased interest in sex
- changes in food preferences
- Decline in personal hygiene
- repetitive or compulsive behaviour

**Language**
- difficulty making or understanding speech, non fluent speech (progressive aphasia)
- impaired understanding of word meaning, fluent but empty spontaneous speech (semantic dementia)
Contrast with Alzheimer's Dementia
Key features of FTD in MND

- FTD in MND characterised by **behavioural abnormalities** such as disinhibition, apathy, and personality changes

- A small proportion of patients may also suffer from a **language difficulties**

- Recent laboratory studies show significant overlap between ALS and FTD in terms of the mechanisms of nerve cell degeneration
What is the relationship between MND and cognitive impairment? RECRUITING

- assessment of language and behaviour
- evidence of subclinical levels of FTD
- impact on the prognosis
- quality of life of the person with ALS and carer
- aid clinical management
- guidance for carers and health professionals

- Emotional Lability (EL) symptom of cortico-bulbar pathway dysfunction seen in 19-49% of patients

- This study of 41 pts incidence 71%

- Correlations between bulbar involvement and EL

- EL effects quality of life due to increased anxiety and emotional frailty for carers
ALS and FTLD: two faces of TDP-43 proteinopathy.

- TAR DNA-binding protein 43 (TDP-43), encoded by the TARDBP gene is the major pathological protein of FTLD, with ubiquitin-immunoreactive (ub-ir) inclusions (FTLD-U) seen in abnormal cells.

- Mutations in the TARDBP gene in familial and sporadic ALS show that abnormal TDP-43 alone can cause neurodegeneration.

- TDP-43 is found to be a component of the inclusions of an increasing number of neurodegenerative diseases.

- Spectrum of disorders called TDP-43 proteinopathies incl: FTLD-U, FTLD-U with ALS, ALS, and a spectrum of other disorders.

Neuropathology: more FINDINGS

- The microtubule-associated protein **tau** - key role in neurodegeneration

- Mutations in the **tau coding gene MAPT** are a cause of frontotemporal dementia, and the H1/H1 genotype of MAPT, gives rise to higher tau expression levels, is associated with progressive supranuclear palsy, corticobasal degeneration, and Parkinson disease (PD)

- **tau hyperphosphorylation** and aggregation is a hallmark of Alzheimer disease

- reducing endogenous tau has been reported to ameliorate cognitive impairment in a mouse model for AD

- Tau hyperphosphorylation and aggregation have also been described in amyotrophic lateral sclerosis (ALS), both in human patients and in the mutant SOD1 mouse model for this disease.

Identifying the genetic cause of MND and frontotemporal dementia: ONGOING trial

- affected family members are known to share a variation in their **genetic code** that can cause both MND and FTD.
- research has identified that the causative variation lies within a particular region of **chromosome 9**
- suggesting that the causative variation may lie in an area which holds instructions for **making proteins**
- this project aims to identify the causative variation by analysing the region within chromosome 9 and the message which is used to convert genes into protein.
- the identification will allowing **genetic testing**, for families with inherited form of MND
- understanding the genetic cause of MND/FTD will lead to the possibility of developing **new therapies**.
News

New £800 000 study sets out to discover what goes wrong in motor neurone disease

• Use **stem cells** from skin cells of a patient whose motor neurone disease is caused by a mutation on the TDP-43 gene. Although only about 1% of people with motor neurone disease have this mutation, the protein that the gene produces is present in 90% of cases and appears in clumps inside dying motor neurones.

• Induce stem cells to turn into two cells involved in the disease—the motor neurones which are destroyed, and other "support cells" called astrocytes, which have a role in neurone death.

• Once the cells have been generated, researchers will "mix and match" them with cells from healthy controls to discover how healthy neurones and diseased support cells affect one another and how diseased neurones and healthy support cells interplay.

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Where does that leave the patient
Patients’ perspectives:

Need cognition for:

- Decisions to be made
- Illness to adjust to and cope with
- Situations to be managed
- End of life care planning
SOCIAL COMMUNICATION SKILLS IN PATIENTS WITH MND: Findings

• evidence of a specific social cognition deficit

• difficulty in correctly interpreting social situations in which they must attribute a mental state to another person

• difficulties in interpreting and interacting in some social situations
The Future

NEXT EXIT
Clinical staging and disease progression in frontotemporal dementia.

42 patients followed up after 12 months. Assess change over time in the 3 main FTD variants: behavioural variant FTD [bvFTD]; progressive nonfluent aphasia [PNFA]; semantic dementia [SemD]).

RESULTS:
• Six severity stages (very mild to profound) using Frontotemporal Dementia Rating Scale
• Greater levels of impairment in behavioural variant FTD (bvFTD) than in the language variants
• Patients with bvFTD appear to move most quickly between stages
• SemD slowest, on average, 10 years to reach severe

CONCLUSIONS:
• Disease progression differs across frontotemporal dementia (FTD) variants
• Patients with behavioural variant FTD progress rapidly whereas those with semantic dementia progress more slowly.
• Staging dementia can help determining disease progression.

Impact of cognition on Advance Care Planning

Wants to know v prefer to not know
Knowing diagnosis
Knowing illness journey
Knowing lack tx options
Knowing about interventions:
  • Speech
  • Swallowing/ nutrition
  • Breathing/ NIV
Eol care
Place of death choices
Key learning points

- Multiple decisions about care are needed in MND
- Decisions necessary in advance of need
- Cognitive problems are common
- Frontotemporal dementia can occur
- Cognitive issues major cause of carer stress

Reference article:
Cognitive impairment in ALS Lancet Neurology 2007; 6:994-1003
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Case history

59 year old lady
Teacher
Recently widowed, husband had been 15yrs older
No children
History of bipolar disorder, needing medication and one admission to mental health care
Noticed to have problems with teaching with speech, attributed to overwork and stress
While on school trip unexplained fall, sprained ankle and injured shoulder
Pain problems due to restricted movement shoulder, referred for physio
Mental health deteriorated and became depressed, concern may need admission
Physio requested medical review and saw orthopaedic surgeon, appt in 3 mo
Referred on to neurology, further delay 3 mo
Diagnosis thought to be motor neurone disease

How and when should diagnosis be communicated?
Case History 2

Informed of diagnosis and main concern now relates to speech and swallowing problems

What information should be given about the illness journey?
and
What possible management issues should be discussed at this stage?
Case history 3

Accepted communication and mobility aids but declined to discuss PEG and NIV as discussion caused distress

Problems with care package due to carers unable to meet patients wishes re personal care, reliant on a niece who is now exhausted. Declining additional help and unable to accept HCP concern for her niece. Asking for measures to end life.

What end of life issues need to be discussed?
Advance care planning
Patient Preferences about information

Wants to know v prefer to not know
Knowing diagnosis
Knowing illness journey
Knowing no treatment to control illness
Knowing about interventions:
  • Speech
  • Swallowing/ nutrition
  • Breathing/ NIV
End of life care
Place of death
Aims for small groups ACP

Aims:

• To gain confidence in opening up discussions
• Identify what holds you back
• Identify what would help?
• Practical ideas for questions to ask
Questions for the small groups

• What are the key issues for this case?
• What are the challenges and barriers?

• Suggest a specific question that helps you to open up advance care planning discussions?