What is Motor Neurone Disease and why should I know more about it?

Session 1

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Learning Objectives

- Be aware of different types of presentation of MND and why this is important in relation to intervention and outcomes
- Be aware of the considerations around diagnosis and prognosis
- Be familiar with signs and symptoms of different types of presentation of MND
- Have an understanding of the role of Genetics in MND

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Spectrum of MND

- Different presentations of MND
- Different progression rates
- Different sites of onset
- Different physical presentations

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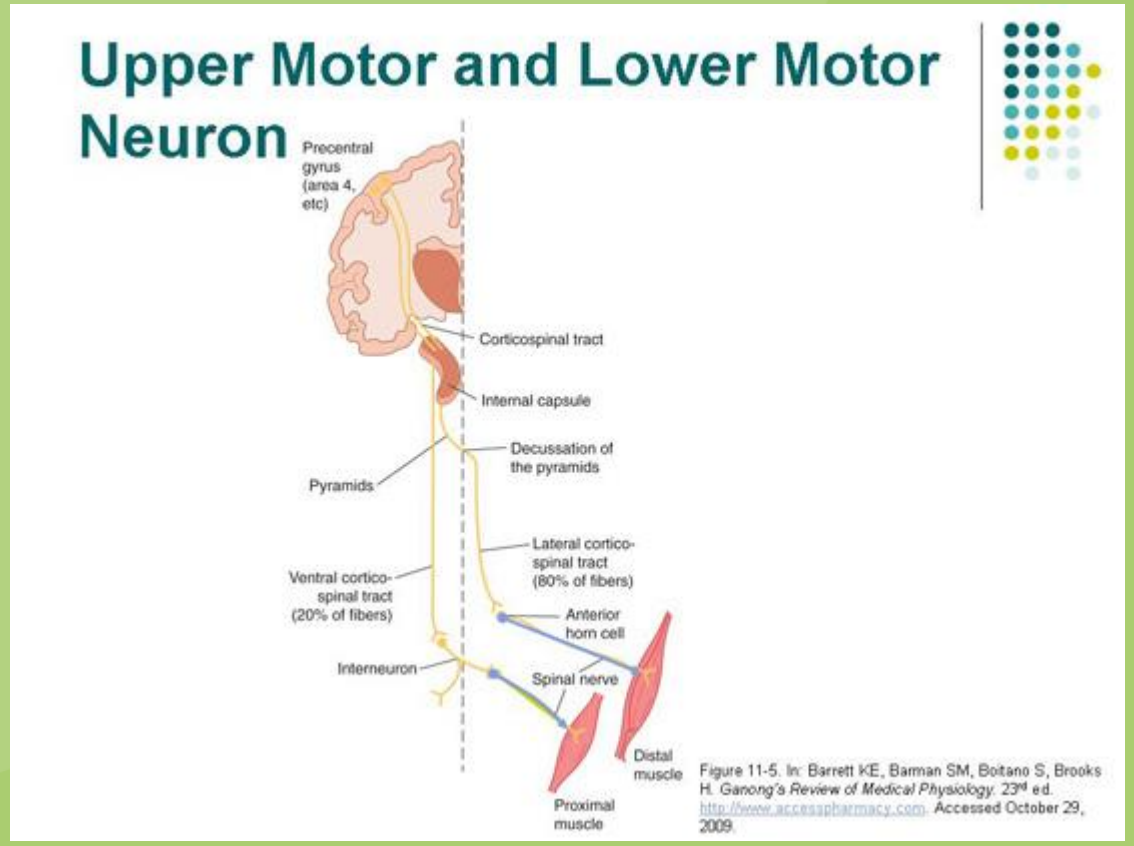
Spectrum of MND

- Onset Sites: Limb or spinal (66%), Bulbar (33%), Respiratory (3%) FTD (5-15%)
- Phenotypes:
  - ALS: Amyotrophic Lateral Sclerosis (upper and lower motor neurons)
  - PLS: Primary Lateral Sclerosis (mainly upper motor neuron)
  - PMA: Progressive Muscular Atrophy (mainly lower neuron)
  - Regional Phenotype – Flail Arm / Flail Leg



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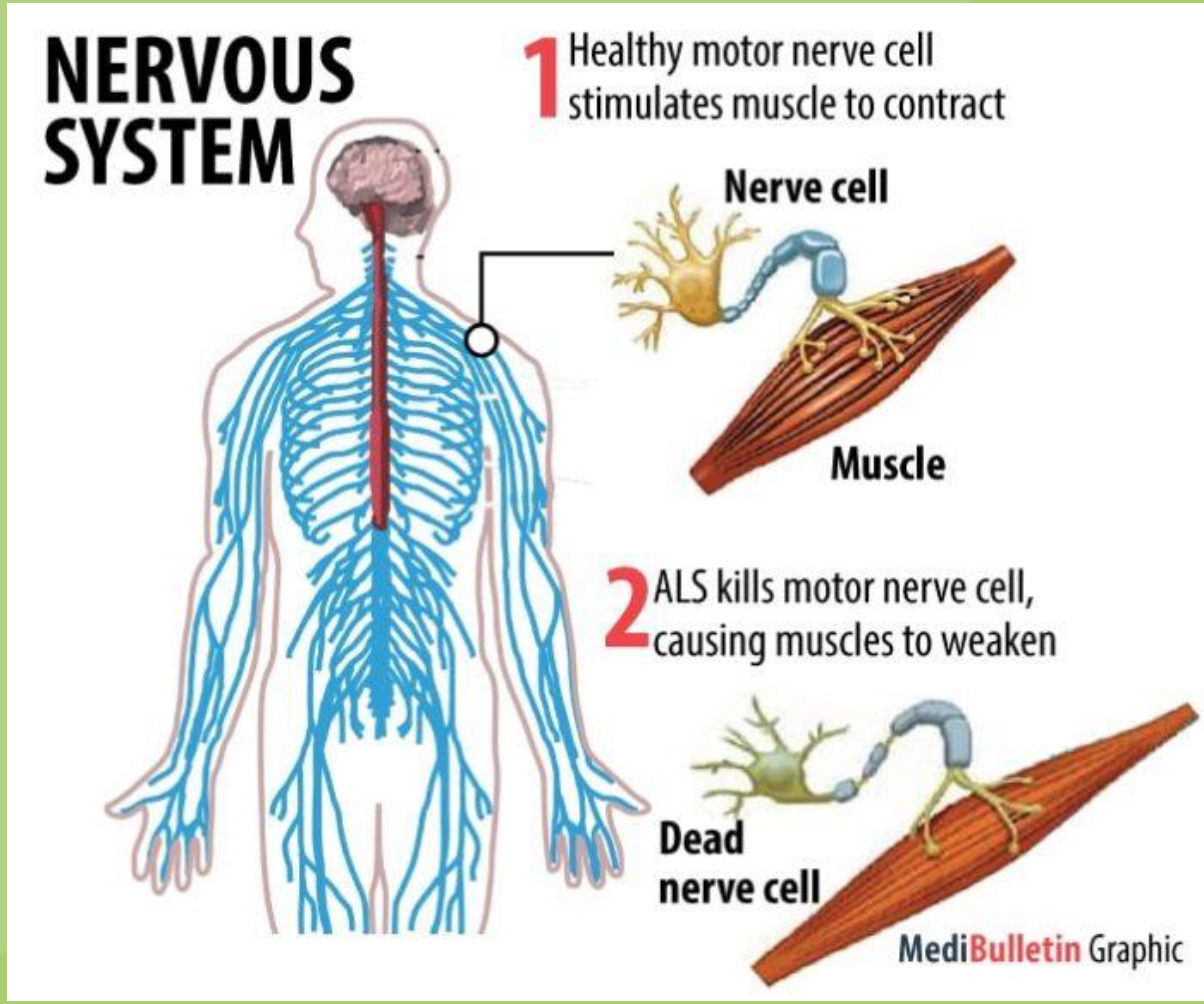
ALS Amytrophic Lateral Sclerosis:
Muscle wasting – Lower Motor Neurons (LMN)
Stiffness / spasticity – Upper Motor Neurons (UMN)
85% of people LWMND
Spinal or Bulbar onset
Variable rate of progression
Pattern of progression

PMA: Progressive Muscular Atrophy:
No UMN involvement (LMN predominant)
10% of people LWMND
Variable rate of progression

PLS: Primary Lateral Sclerosis:
LMN largely unaffected (UMN predominant)
1% of people LWMND
Normal lifespan
Slow progression



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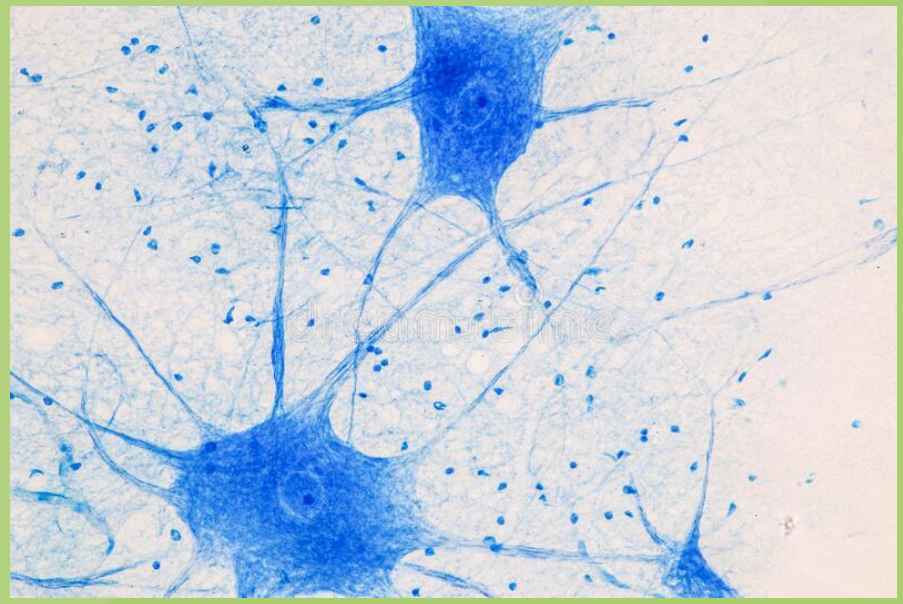
Diagnosis

No definitive test – or scan can confirm (as like with stroke or heart attack)

<u>Clinical diagnostics:</u>
Rule out other conditions (various tests):
History
Bloods
MRI
Neuro exam
EMG (electromyography)
LP



<u>Causes:</u>
Neurodegeneration related to aging
No known causes (other than genetic – see later)
Links to environment – unproven
Links to exercise – more related to genetics (see later)

The way a client receive the diagnosis will remain with them for the remainder of their life

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Diagnosis

Diagnostic delay – can be positive but not necessarily in eyes of person and their families

Pavey et al 2013, identified people found process stressful, upsetting and distressing. Identified need for more training for Dr's to be more holistic, not just considering physical health but mental psychological wellbeing as well.

Auon et al 2016, rated physicians in how they delivered diagnosis and identified the following associated with positive experiences:

- Empathy
- Sharing information willingly
- Exploring expectations
- Suggesting realistic goals
- Planning
- Delivering on agreed plans
- Holistic
- Considering needs of family and person

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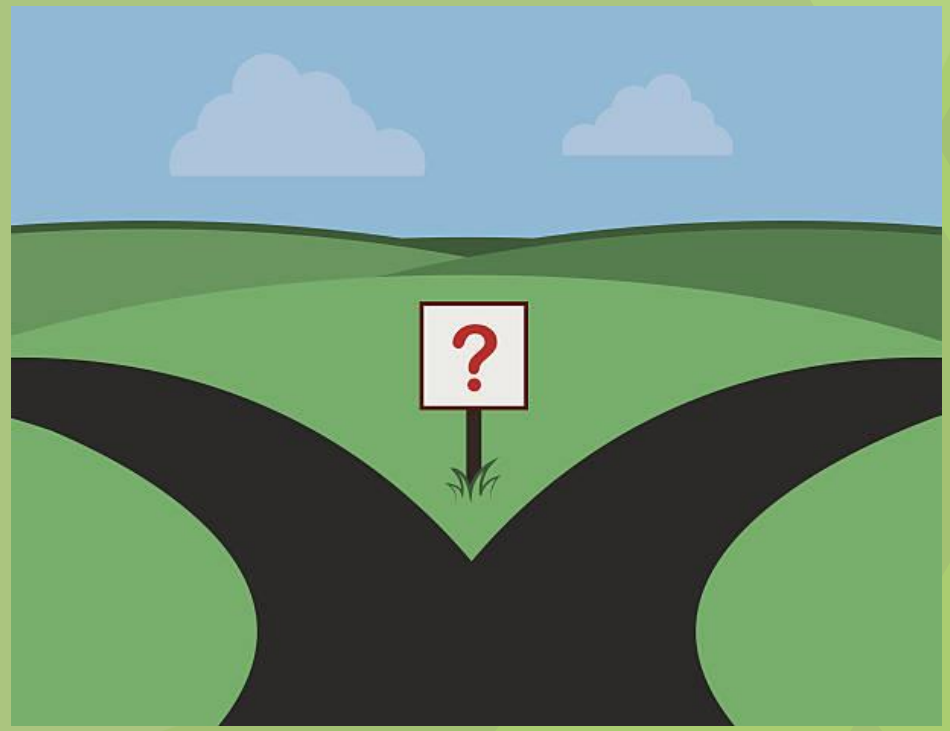
PROGNOSTIC INDICATORS

<u>Long Survival:</u>

- Flail Arm
- UMN Predominant
- LMN Predominant
- Longer time to diagnosis
- Younger onset age

<u>Short Survival:</u>

- UMN and LMN
- Respiratory onset
- Bulbar onset
- FTD
- Short time to diagnosis
- Older age at diagnosis



Van Es et al (2017)

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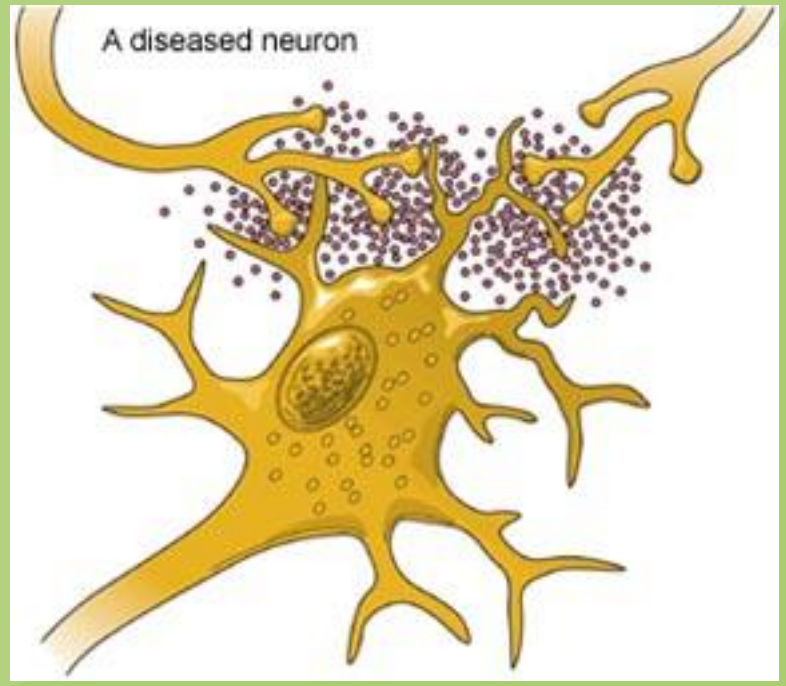
Cell Death

Motor neurone dies……

Release Glutamate……

Glutamate is toxic in excess……

Accelerates other cells death……..



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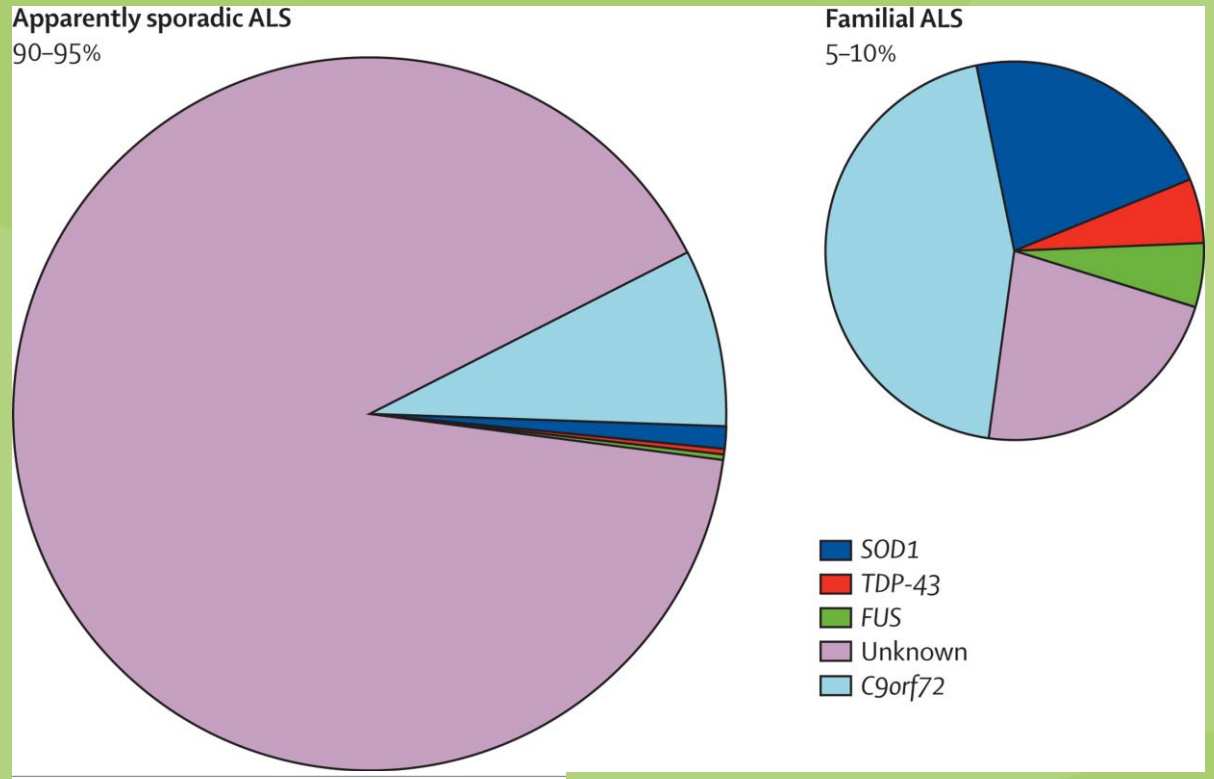
Genetics and MND




THE LANCET
Neurology
Volume 12, Issue 3, March 2013, Pages 310-322

Review

Controversies and priorities in amyotrophic lateral sclerosis

Martin R Turner PhD [a], Prof Orla Hardiman MD [b], Michael Benatar DPhil [c], Prof Benjamin R Brooks MD [d], Prof Adriano Chio MD [e], Prof Mamede de Carvalho MD [f], Prof Paul G Ince MD [g], Cindy Lin PhD [h], Robert G Miller MD [i], Prof Hiroshi Mitsumoto MD [j], Prof Garth Nicholson MD [k], Prof John Ravits MD [l], Prof Pamela J Shaw MD [g], Prof Michael Swash MD [m,n], Prof Kevin Talbot DPhil [a], Bryan J Traynor MD [o], Prof Leonard H Van den Berg MD [p], Jan H Veldink MD [p], Steve Vucic PhD [q], Prof Matthew C Kiernan DSc [r]

5-10 % have family history of MND
90-95% is sporadic

Tends not to skip generations
Links with genes affected in FTD – family background information is key

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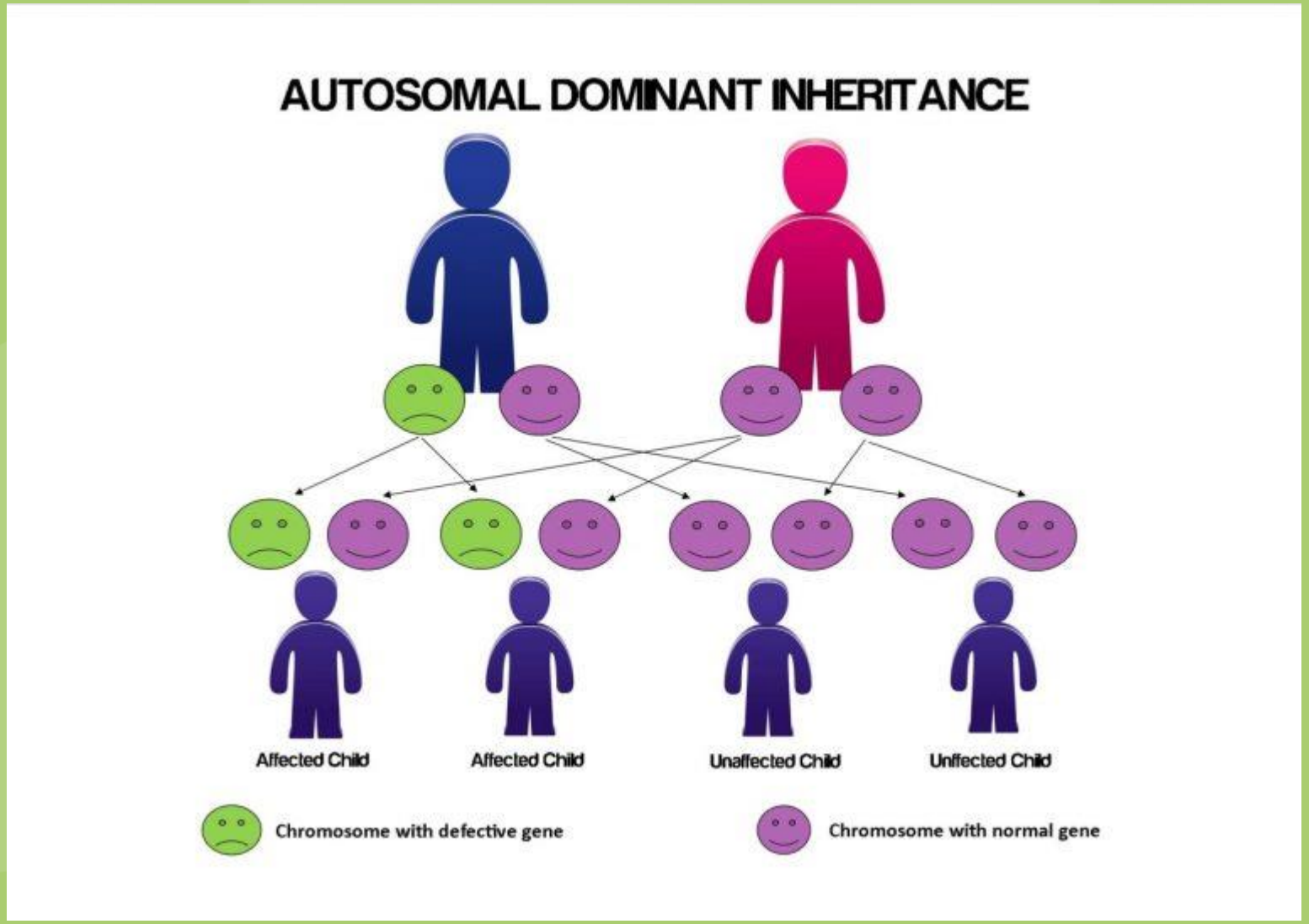
Genetics and MND

MND usually follows dominant pathway of inheritance (only needing 1 faulty gene)

If you have the gene you may not develop MND

Different members of family may develop at different ages and present differently….

Genetic counselling.



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Genetics and MND

- C9ORF72, discovered in 2011, which is responsible for around 40 in 100 cases
- SOD1, discovered in 1993, which is responsible for 20 in 100 cases
- TARDBP (TDP-43), discovered in 2008, which is responsible for up to 5 in 100 cases
- FUS, discovered in 2009, which is responsible for up to 5 in 100 cases

https://www.mndassociation.org/about-mnd/inherited-mnd/

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Medical Treatments

There is no cure for MND….currently

There are some drugs which can be used to help slow the progression of the condition or manage symptoms of the condition.

Riluzole:

This is the only widely available drug (although some areas of NHS are reluctant to prescribe due to cost) which has been shown to have an impact on the length of life in people with MND.

The drug acts to reduce the amount of excess glutamate so helps slow down cell death and consequently slows progression and can lengthen life. Evidence shows extension of life by months not years.

There are side effects to the drug and many people find it is not tolerable.

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Drug Trials

- There are multiple drug trials being conducted across the world all the time to help manage symptoms and ultimately identify a cure.
- Some drugs are targeting symptom management and others are aiming to stop the disease process in its tracks.
- Some drugs have shown some positive results in early studies but for very small populations of people living with very specific types of MND.
- There is a high interest amongst people living with MND to try alternative treatments and drugs which can be costly financially and to their health.

If there was a wonder drug out there which has been proven to be safe and effective everyone would be having it…

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Signs and Symptoms

(Rapid) Progressive weakness
Limb movement – reducing mobility reducing arm and hand function
Bulbar – speech and swallowing difficulties
Respiratory –cough and breathing difficulty

- Fatigue
- Constipation
- Pain
- Postural problems

- Loss of roles
- Grief
- Impact on family

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Cognition and MND

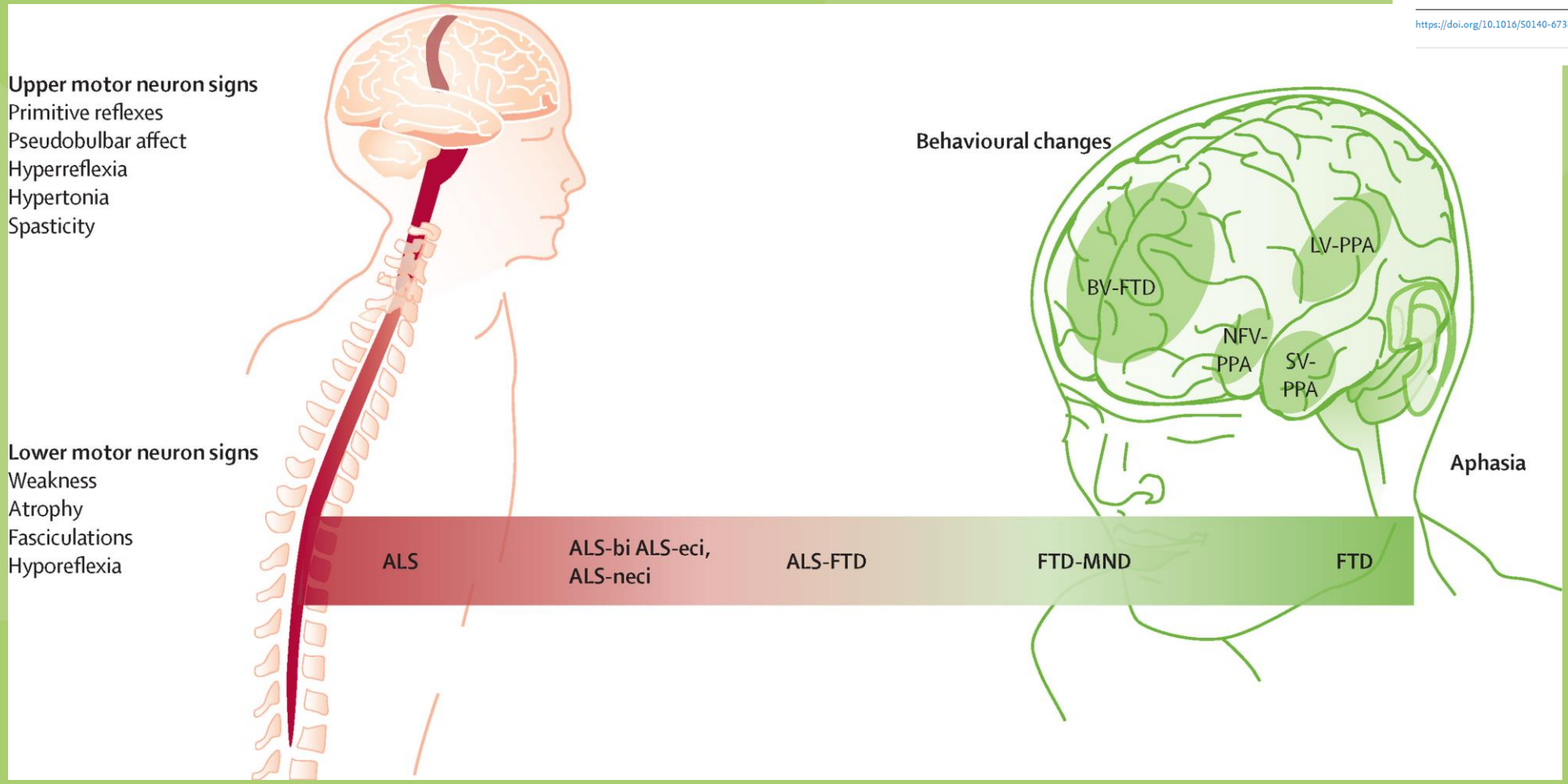
THE LANCET
Volume 390, Issue 10107, 4–10 November 2017, Pages 2084-2098

Seminar

Amyotrophic lateral sclerosis

Michael A van Es MD [a], Prof Orla Hardiman MD [c, d], Prof Adriano Chio MD [e, f, g], Prof Ammar Al-Chalabi MD [h, i], Prof R Jeroen Pasterkamp PhD [b], Prof Jan H Veldink MD [a], Prof Leonard H van den Berg MD [a]

https://doi.org/10.1016/S0140-6736(17)31287-4



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Cognitive change on a spectrum

- 50% of MND have some cognitive or behavioural change
- 5-10% of MND have FTD
- In cases where no dementia – decline in cognitive function is slow
- In cases where no dementia – executive dysfunction identified early on in diagnosis (Abrahams et al 2005)
- ALS Specific cognitive impairment (Crockford et al 2018)
- 10% of MND have some Behavioural issues – Emotional blunting, apathy & loss of sympathy (theory of mind) (Van Es et al 2017)

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Theory of Mind

‘the ability to infer and understand the mental states of self and others’

Found to be predominant in MND with cognitive impairment
Linked with other ALS specific impairments – Verbal fluency and apathy *(*Siciliano et al 2017)

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Summary

- MND has different presentations rates of progression
- Diagnosis is key to setting relationships for the future
- No cure but some medications to slow progression
- Genetic involvement
- Cognitive considerations

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References

Abrahams S, Leigh PN, Goldstein LH. 2005. Cognitive change in ALS: a prospective study. *Neurology*. Apr 12;64(7):1222-6. doi: 10.1212/01.WNL.0000156519.41681.27. PMID: 15824350.

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Rooney J, Byrne S, Heverin M*, et al* (2015) A multidisciplinary clinic approach improves survival in ALS: a comparative study of ALS in Ireland and Northern Ireland *Journal of Neurology, Neurosurgery & Psychiatry* ;86:496-501.

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Samar M Aoun, Lauren J Breen, Denise Howting, Robert Edis, David Oliver, Robert Henderson, Margaret O'Connor, Rodney Harris & Carol Birks (2016) Receiving the news of a diagnosis of motor neuron disease: What does it take to make it better?, Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration, 17:3-4, 168-178, DOI: 10.3109/21678421.2015.1111907

Resources

https://imnda.ie/

https://www.mndassociation.org/professionals/community-of-practice/

https://ecas.psy.ed.ac.uk/

https://jnnp.bmj.com/content/jnnp/86/5/496.full.pdf

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