Update on research in multiple system atrophy

Dr Christopher Kobylecki

Consultant Neurologist and Honorary Senior Lecturer

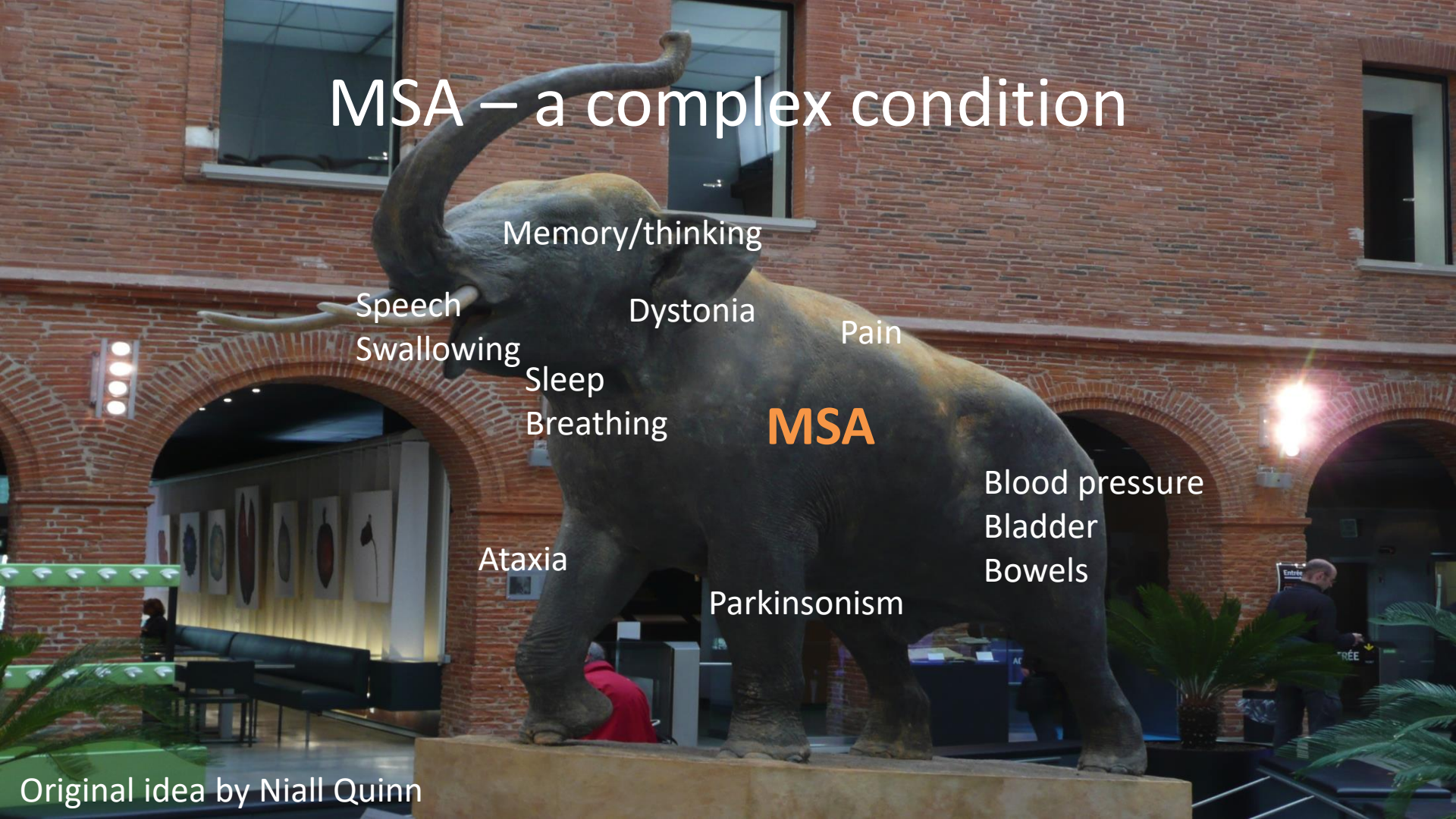
Chair, Scientific Advisory Panel MSAT

May 13th, 2023

Overview

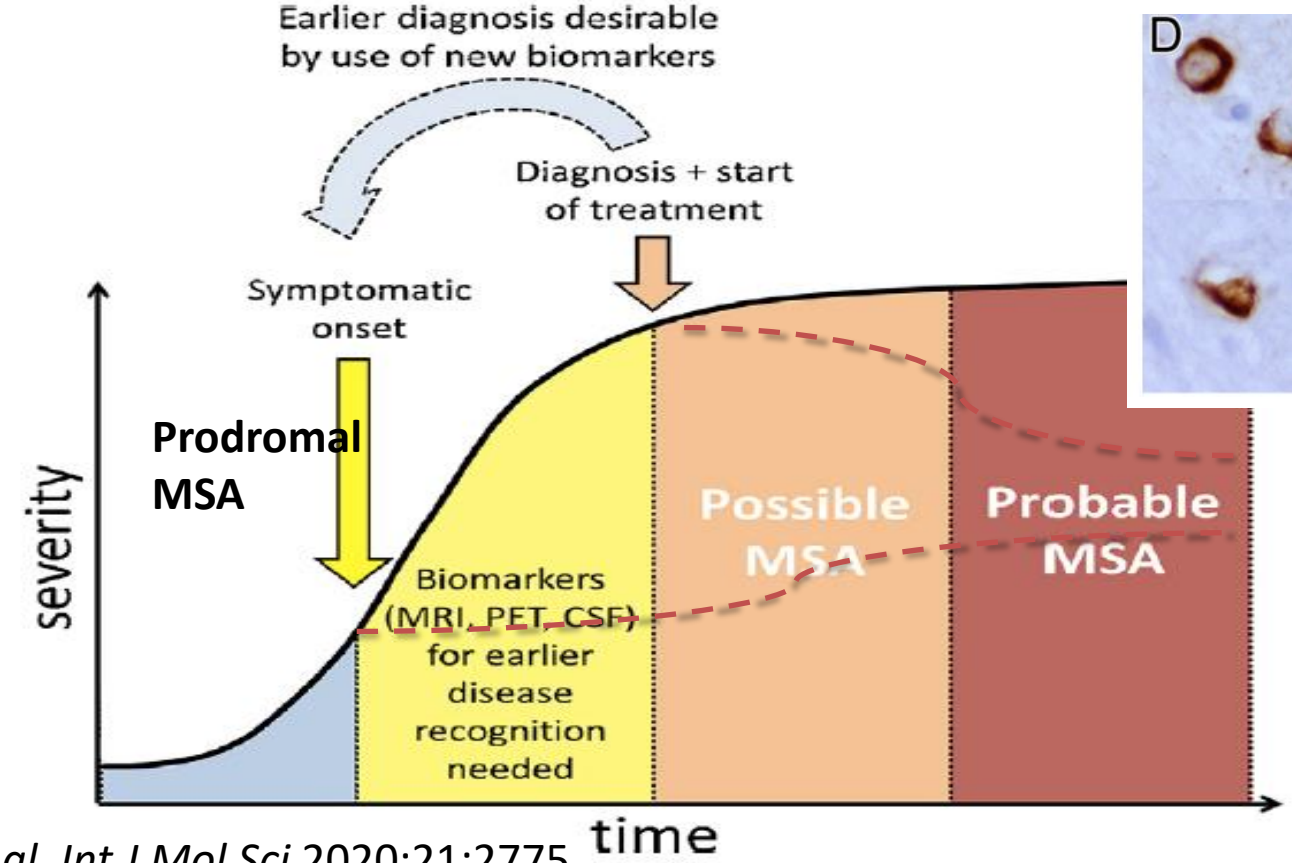
- MSA Trust priorities and funding for research
- Recent developments and ongoing trials in MSA

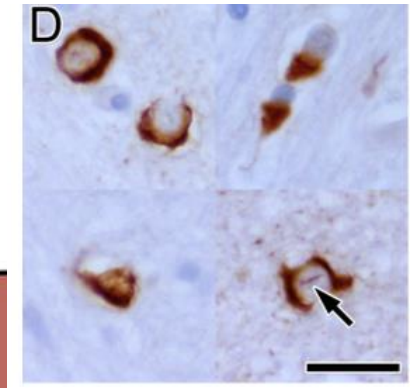
MSA – a complex condition



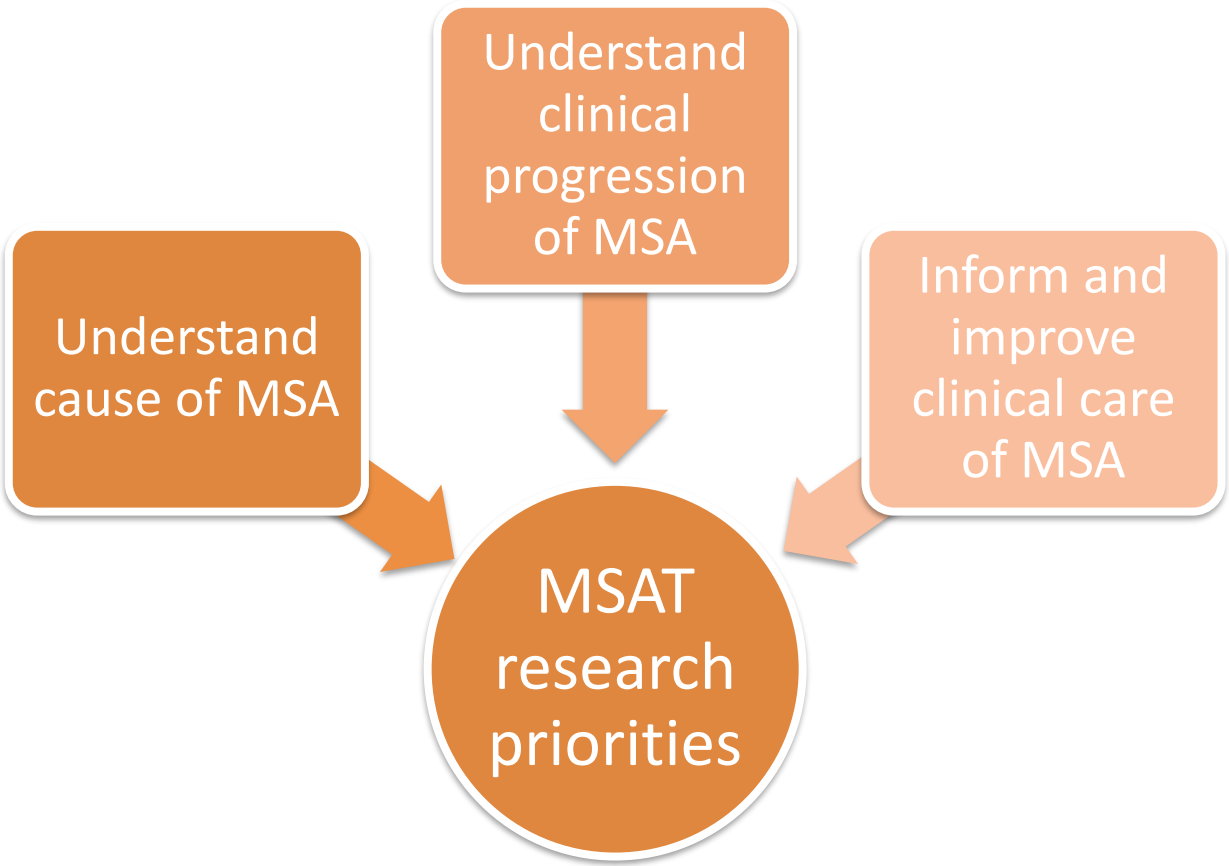
Original idea by Niall Quinn

Disease-modifying therapy in MSA





Mészáros L *et al. Int J Mol Sci* 2020;21:2775.


Understand clinical progression of MSA
Understand cause of MSA
Inform and improve clinical care of MSA
MSAT research priorities

Scientific advisory panel

MSAT research grants

£2.2 million
20 research grants since 2000

2 MSAT/ABN research training fellows since 2017

Research priorities

Links with pharma companies and other charities

Clinical research training

Collaborations

Current MSAT research grants 2022

Prof Anja Lowit, Strathclyde University, Glasgow

- Trial of group speech therapy in people with MSA-C
- Testing feasibility and effectiveness
- Potential to improve management of a major clinical problem in MSA

Prof Christos Proukakis, UCL, London

- Role of genetic changes in *SNCA* gene in MSA neurodegeneration
- Could help to better understand involvement of different brain areas
- Target for therapy in future?

Current MSAT research grants 2022

Prof Steve Gentleman, Imperial College London

- Identifying strains of alpha-synuclein using antibodies
- Help with diagnosis between MSA and Parkinson's
- Could help identify treatment targets

Dr Viorica Chelban, UCL, London

- A registry for MSA patients focused on swallow problems
- Better evidence for outcomes of feeding tube procedures
- Improved pathways of care
- Can be used to address other important clinical problems

ASSOCIATION OF BRITISH NEUROLOGISTS

Clinical fellows

MSA Trust

Dr Viorica Chelban (2017-2022)

https://doi.org/10.1093/brain/awac253

BRAIN
ORIGINAL ARTICLE

Neurofilament light levels predict clinical progression and death in multiple system atrophy

Viorica Chelban,[1,2] Elham Nikram,[3] Alexandra Perez-Soriano,[4,5,6] Carlo Wilke,[7,8] Alexandra Foubert-Samier,[9,10,11,12] Nirosen Vijiaratnam,[13] Tong Guo,[13] Edwin Jabbari,[13] Simisola Olufodun,[1] Mariel Gonzalez,[1] Konstantin Senkevich,[14,15,16,17] Brice Laurens,[9,10] Patrice Péran,[18] Olivier Rascol,[19,20,21] Anne Pavy Le Traon,[19,22] Emily G. Todd,[23] Alyssa A. Costantini,[13] Sondos Alikhwan,[1] Ambreen Tariq,[1] Bai Lin Ng,[24] Esteban Muñoz,[4,5,6] Celia Painous,[4,5,6] Yaroslau Compta,[4,5,6] Carme Junque,[5,6,25] Barbara Segura,[5,6,25] Kristina Zhelcheska,[1] Henny Wellington,[26] Ludger Schöls,[7,8] Zane Jaunmuktane,[27] Christopher Kobylecki,[28,29] Alistair Church,[30] Michele T. M. Hu,[31] James B. Rowe,[32,33,34] P. Nigel Leigh,[35] Luke Massey,[36] David J. Burn,[37] Nicola Pavese,[38] Tom Foltynie,[13] Sofya Pchelina,[16,17] Nicholas Wood,[13] Amanda J. Heslegrave,[26] Henrik Zetterberg,[26,38,39,40,41] Martina Bocchetta,[23] Jonathan D. Rohrer,[23] Maria J. Marti,[4,5,6] Matthis Synofzik,[7,8] Huw R. Morris,[13,†] Wassilios G. Meissner[9,10,42,43,†] and Henry Houlden[1,†]

Dr Yee Yen Goh (2021-)

Review

Multiple system atrophy

Yee Yen Goh,[1] Emma Saunders,[2] Samantha Pavey,[2] Emma Rushton,[2] Niall Quinn,[1] Henry Houlden ,[1] Viorica Chelban[1,3]

MSAT research symposium

Tel: 0333 323 4591

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27 Jan 2023 | 3 comments | Research

MSA Research Symposium- Morning Session

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On the 20th of January 2023 the MSA Trust, in partnership with the UCL Institute of Neurology, hosted its first MSA Research Symposium. Sessions focused on the latest basic science and clinical research into MSA. The event was also a unique opportunity for researchers to come together to learn and share knowledae.

PROSPECT-M-UK study

- Longitudinal study of conditions including MSA
- Better understanding of disease progression
- Biomarkers
  - Blood/CSF markers
  - Genetic modifiers
  - Imaging

MSA Trust PSP

Diagnostic criteria for MSA

Second consensus statement on the

REVIEW

The Movement Disorder Society Criteria for the Diagnosis of Multiple System Atrophy

Gregor K. Wenning, MD,PhD,[1*] Iva Stankovic, MD,PhD,[2*] Luca Vignatelli, MD,PhD,[3] Alessandra Fanciulli, MD,PhD,[1] Giovanna Calandra-Buonaura, MD,PhD,[3,4] Klaus Seppi, MD,PhD,[1] Jose-Alberto Palma, MD,PhD,[5] Wassilios G. Meissner, MD,PhD,[6,7] Florian Krismer, MD,PhD,[1] Daniela Berg, MD,PhD,[8,9] Pietro Cortelli, MD,PhD,[3,4] Roy Freeman, MD,[10] Glenda Halliday, MD,[11] Günter Höglinger, MD,PhD,[12,13] Anthony Lang, MD,[14] Helen Ling, MD,PhD,[15,16] Irene Litvan, MD,[17] Phillip Low, MD,[18] Yasuo Miki, MD,PhD,[15,19] Jalesh Panicker, MD,FRCP,[20,21] Maria Teresa Pellecchia, MD,PhD,[22] Niall Quinn, MD,FRCP,[20] Ryuji Sakakibara, MD,PhD,[23] Maria Stamelou, MD,PhD,[24,25] Eduardo Tolosa, MD,PhD,[26,27] Shoji Tsuji, MD,PhD,[28,29] Tom Warner, MD,PhD,[15] Werner Poewe, MD,[1] and Horacio Kaufmann, MD[5*]

T. Klockgether, MD, PhD
A. Lees, MD, FRCP
W. Poewe, MD
N. Quinn, MD, FRCP
T. Revesz, MD

responsive parkinsonism or cerebellar ataxia. Possible MSA requires a sporadic, progressive adult-onset disease including parkinsonism or cerebellar ataxia and at least one feature suggesting autonomic dysfunction plus one other feature that may be a clinical or a neuroimaging abnormality.

Conclusions: These new criteria have simplified the previous criteria, have incorporated current knowledge, and are expected to enhance future assessments of the disease.

Neurology® 2008;71:670-676

- Allows consistent diagnosis in clinical and research setting
- New criteria 2022

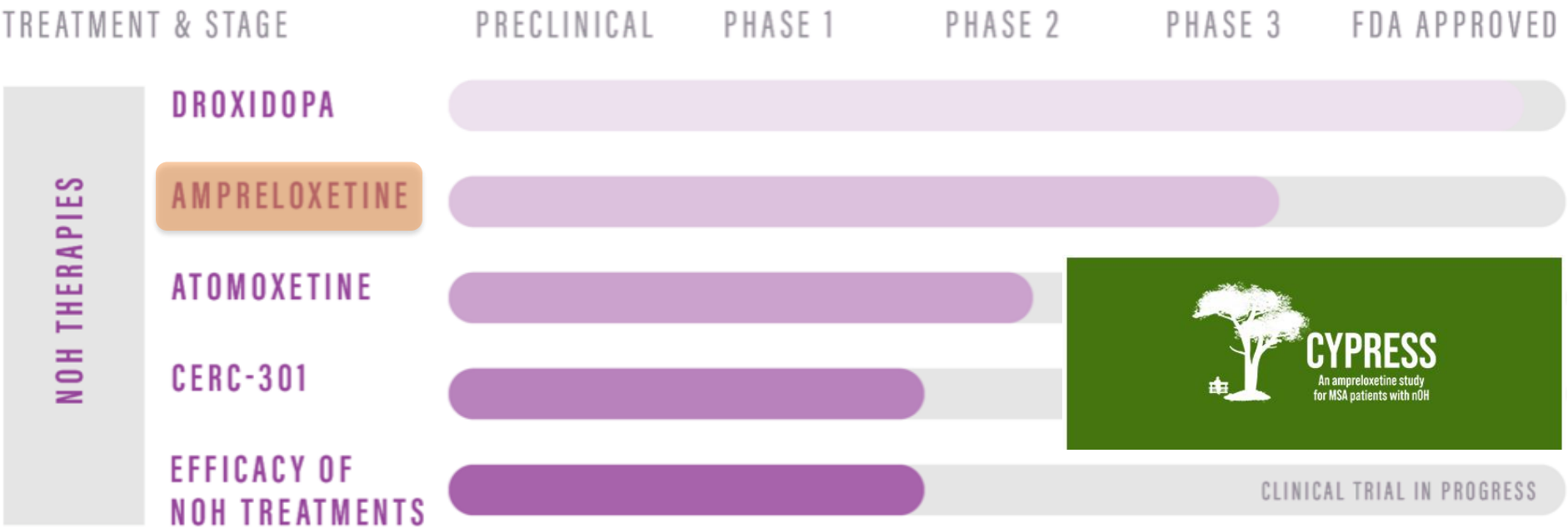
New diagnostic criteria

- Should allow more accurate early diagnosis
- Prodromal MSA
  - May present with sleep disturbance, bladder, BP problems before movement symptoms
  - Earlier diagnosis and better access to treatments?
  - Needs to be validated by further research

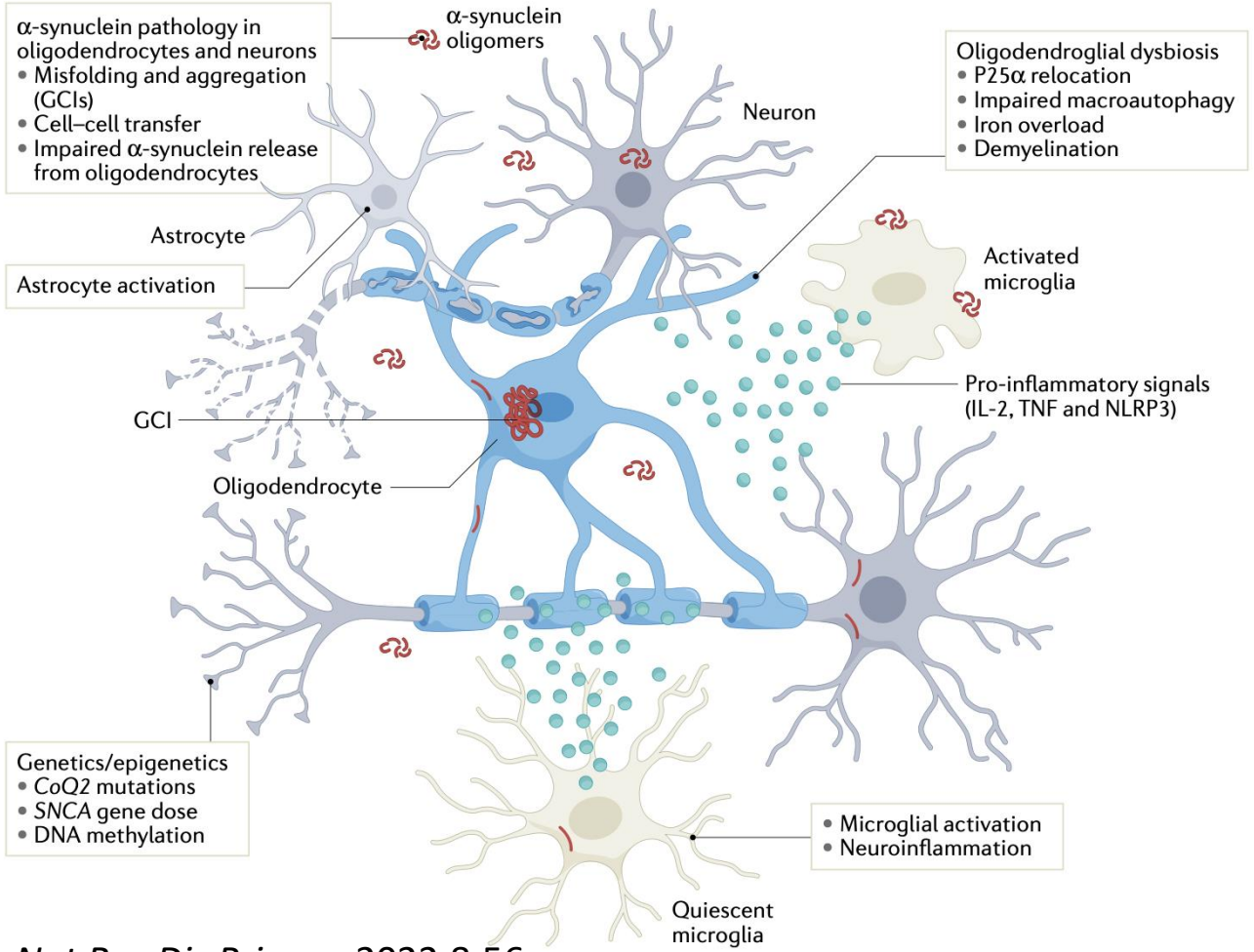
Trials in MSA

- Phase I –healthy volunteers or people with MSA, to check safety
- Phase II – larger numbers of people with MSA, looking at safety, dose required
- Phase III – larger study in people with MSA, compared to placebo (inactive treatment) or best current treatment, assess effectiveness and safety
- Phase IV – done once treatment is licensed in larger numbers

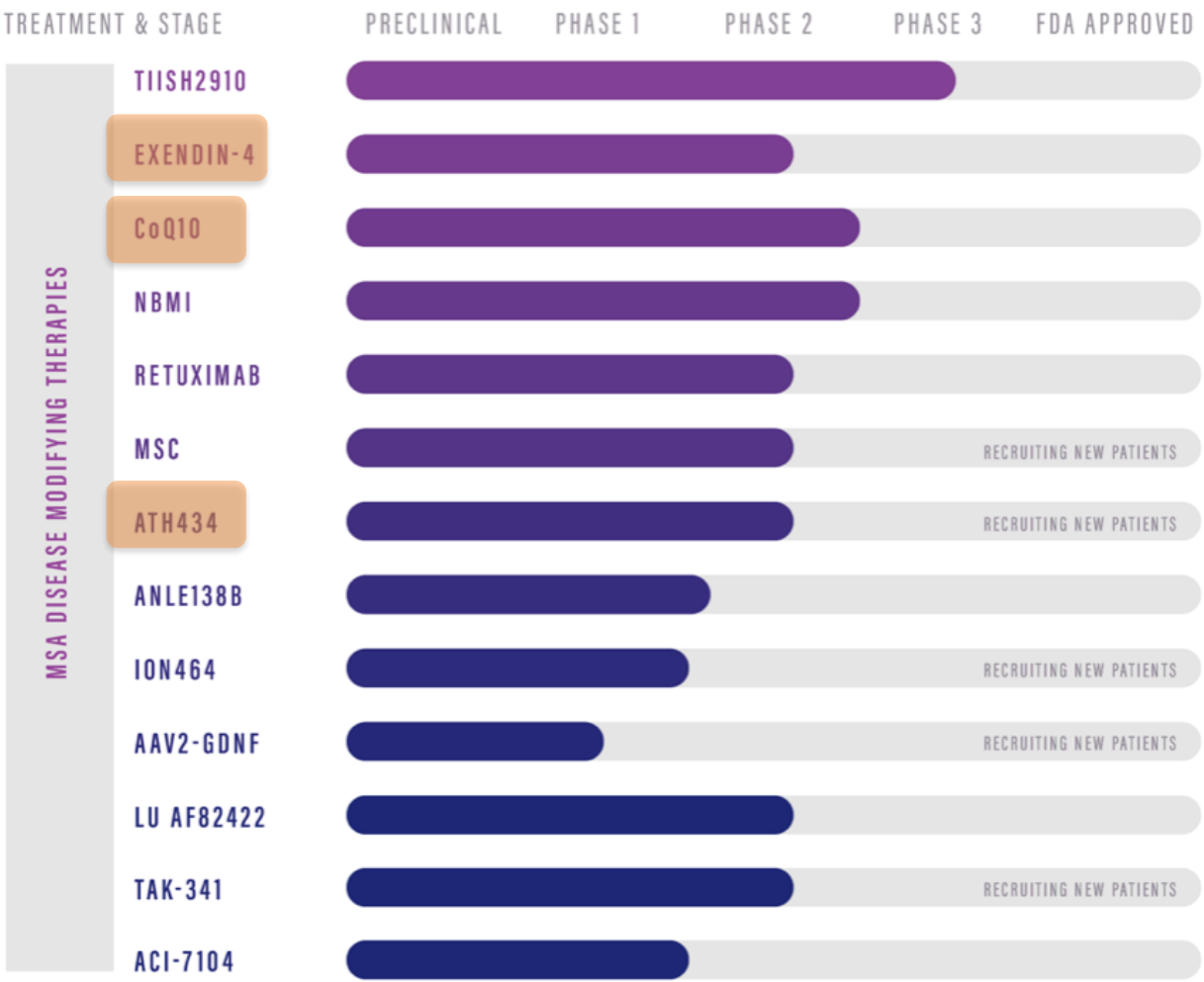
Treatments for low blood pressure



https://www.multiplesystematrophy.org/msa-research/msa-treatment-pipeline/ Accessed 09/05/2023



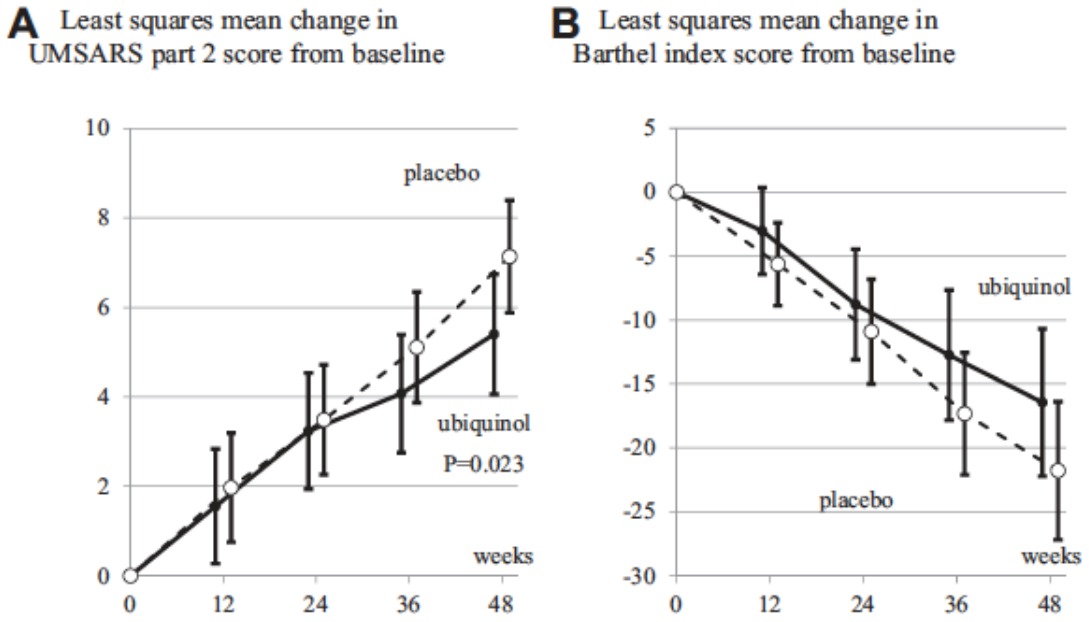
Poewe W *et al. Nat Rev Dis Primers* 2022;8:56.



https://www.multiplesystematrophy.org/msa-research/msa-treatment-pipeline/ Accessed 09/05/2023

Ubiquinol

- Genetic variants in *COQ2* gene linked to MSA
- Phase II trial in 139 Japanese MSA patients



Mitsui J *et al. eClinicalMedicine* 2023;101920.

Exenatide trial

Researchers begin trial of drug to slow progression of neurodegenerative condition Multiple System Atrophy

04 Nov 2019

Researchers at UCL Queen Square Institute of Neurology (IoN) and the UCLH National Hospital for Neurology and Neurosurgery (NHNN) are set to test whether a drug can slow progression of the devastating neurodegenerative condition Multiple System Atrophy (MSA).

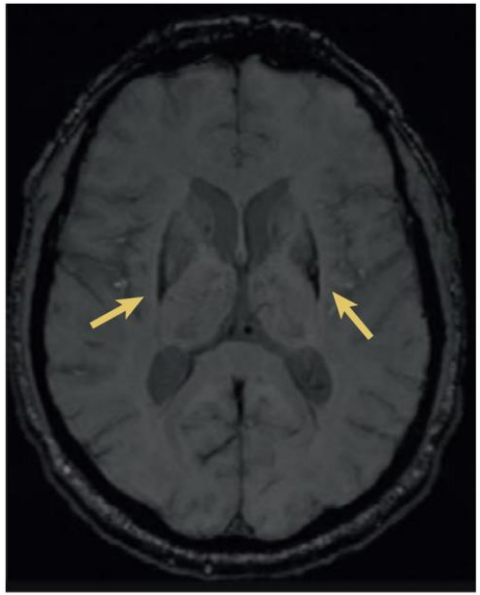
The National Hospital for Neurology and Neurosurgery (NHNN)

- 48 week phase II study
- People with MSA <3 years from diagnosis
- 50 participants Randomised to exenatide or usual care
- Aiming to detect differences in UMSARS (clinical score of MSA severity)

MSA Trust

ATH434

- Aim: reduce iron accumulation in brain
- Phase II trial ongoing
  - Recruiting at three centres in UK (Salford, UCL, Newcastle)



Summary

- MSAT are funding basic science and clinical research in MSA
- Next generation of clinical researchers
- Developments in diagnosis of MSA
- Several ongoing trials for symptoms and disease modification

Thank you

- MSA Trust board and staff
- Scientific advisory panel and peer reviewers
- Fundraisers for MSA
- Participants in research
- Any queries: fundraising@msatrust.org.uk

MSA Trust