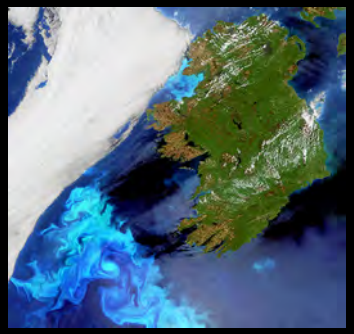
Young Onset Neurodegeneration study

The YON Project

2010/2013

The Dublin
Neurodegeneration Consortium



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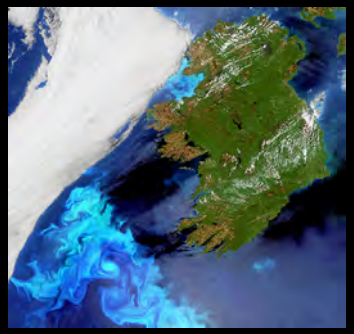
ST. JAMES'S HOSPITAL

Neurology at the Memory Clinic

Dr Thomas Monaghan
SpR in Neurology
Memory, Cognitive Studies and Behavioral Neurology Clinics at St James's
Dr Colin Doherty / Prof Brian Lawlor

The YON Project
2010/2013

The Dublin
Neurodegeneration Consortium



Disclosure:

YON project part funded by unrestricted educational grant from Lundbeck

Neurology at the Memory Clinic

- The Younger Patient and their Profile
- The Patient with Neurological Disease
- The Patient with Epilepsy
- The Rapidly Progressive Patient

Neurology at the Memory Clinic

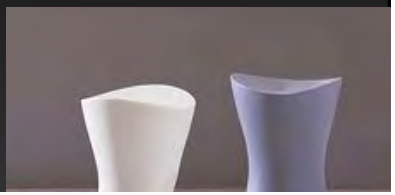
- The Younger Patient and their Profile
- The Patient with Neurological Disease

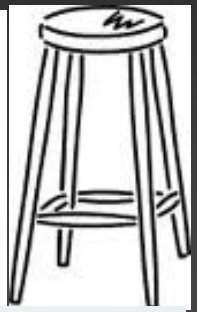
Neurology at the Memory Clinic

The Younger Pa

How do we define ?

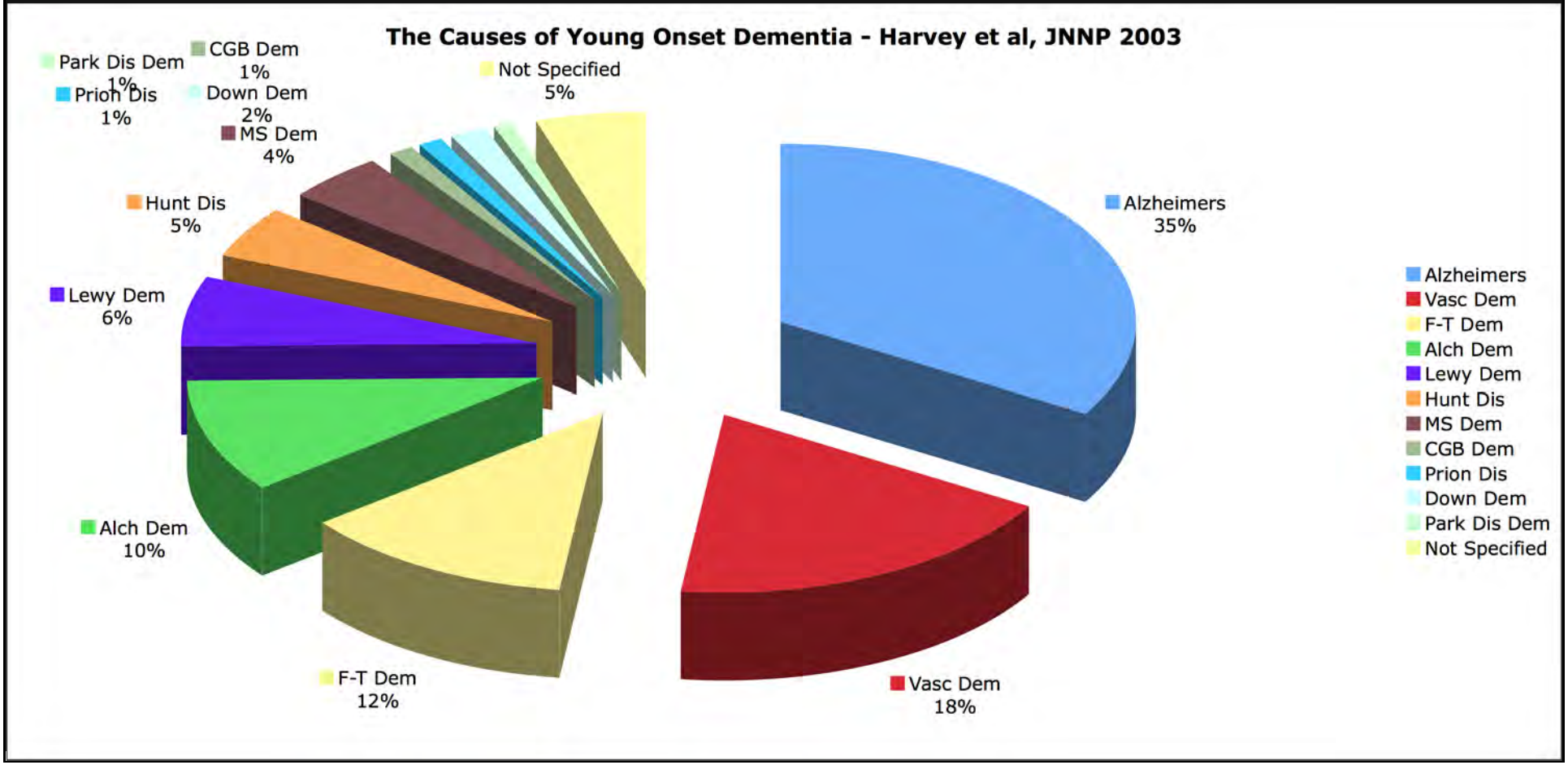
- as a matte cality - 65
- arbitrary based on social conventions





Neurology at the Memory Clinic

The Younger Patient



Neurology at the Memory Clinic

The Younger Patient
…example

- 56 yr old
- Returning to clinic.
- History of indolent decline x 5 years
- Heralded by decline in golf game, playing bridge and managing meals as well as minor RTCs.
- Evidence of an Amnestic deficit on Neuropsychology

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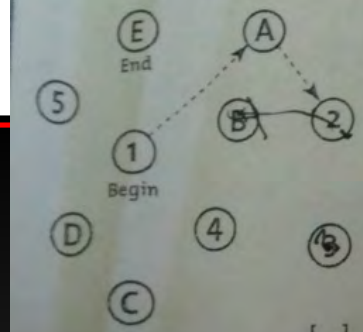
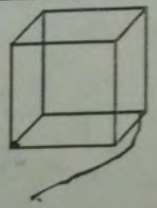
MONTREAL COGNITIVE ASSESSMENT (MOCA)

NAME
Education
Sex

VISUOSPATIAL / EXECUTIVE



Copy cube



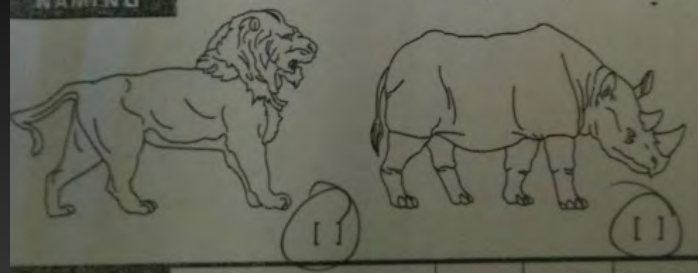
[ ] [ ]

Draw CLOCK (Ten past eleven) (3 points)

[ ] Contour [ ] Numbers [ ] Hands

1/5

NAMING



[ ] [ ]

1/3

MEMORY

Read list of words, subject must repeat them. Do 2 trials. Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1st trial					
2nd trial					

No points

ATTENTION

Read list of digits (1 digit/ sec.). Subject has to repeat them in the forward order [ ] 2 1 8 5 4

Subject has to repeat them in the backward order [ ] 7 4 2

2/2

ad list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors

[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B

/1

rial 7 subtraction starting at 100

[ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65

4 or 5 correct subtractions: 3 pts, 2 or 3 correct: 2 pts, 1 correct: 1 pt, 0 correct: 0 pt

/3

LANGUAGE

Repeat : I only know that John is the one to help today. [ ]

The cat always hid under the couch when dogs were in the room. [ ]

/2

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] (N ≥ 11 words)

/1

ABSTRACTION

Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler

/2

DELAYED RECALL

	Has to recall words	FACE	VELVET	CHURCH	DAISY	RED
	WITH NO CUE	[ ]	[ ]	[ ]	[ ]	[ ]
Optional	Category cue					
	Multiple choice cue					

Points for UNCUED recall only

/5

LANGUAGE - Reading

Ask the subject to read the following words: [Score 1 only if all correct] [Score 0-1] 0

sew "see" |0| "see" X

Query visual / misread these > pint "mint" |0| "mint, P.I.N.T" sc

soot "boot" |0| S.O.O.T ✓

dough ✓

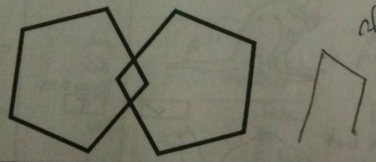
height ✓

(Color read and executed ~~to command~~ another) ✓

L [18/20]

VISUOSPATIAL ABILITIES

Overlapping pentagons: Ask the subject to copy this diagram: [Score 0-1] 0

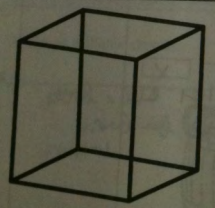


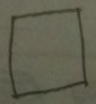
also hated ~~this~~ before

Very slow and laborious.

She doesn't know how to do this

Wire cube : Ask the subject to copy this drawing (for scoring, see instructions guide) [Score 0-2] 0





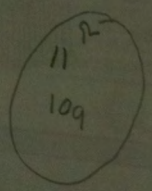
She can't do any more with this.

Clock: Ask the subject to draw a clock face with numbers and the hands at ten past five. (for scoring see instruction guide. circle = 1, numbers = 2, hands = 2 if all correct) [Score 0-5] 1

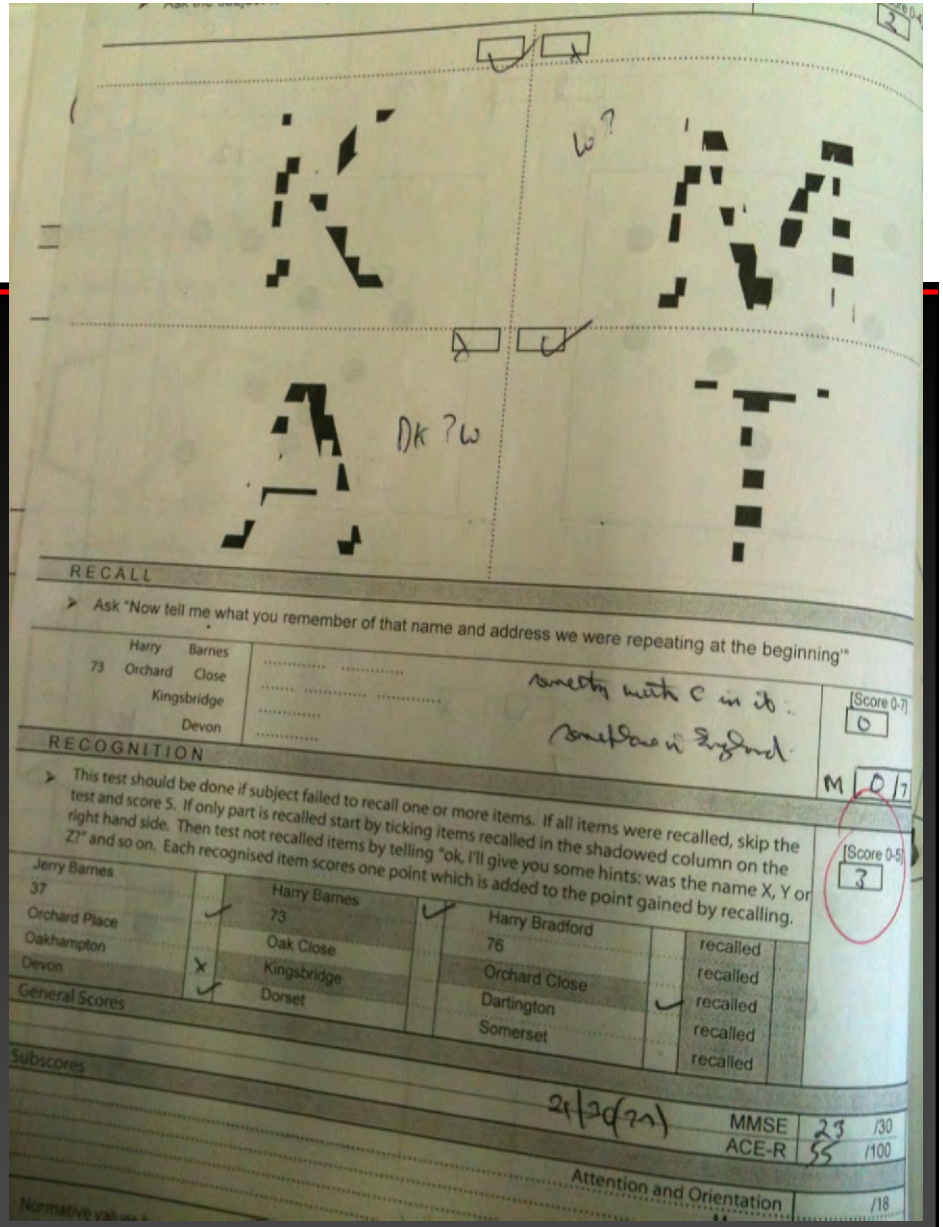
clock wrong for this

also ~~can't~~ writes "10" first "11" correctly but hand execution is poor.

receptacle check for 10 past 11.



She's answer that this is all wrong



RECALL

Ask "Now tell me what you remember of that name and address we were repeating at the beginning"

Harry Barnes
73 Orchard Close
Kingsbridge
Devon

something with C in it.

Something in England

[Score 0-7] 0

M [0/7]

RECOGNITION

This test should be done if subject failed to recall one or more items. If all items were recalled, skip the test and score 5. If only part is recalled start by ticking items recalled in the shadowed column on the right hand side. Then test not recalled items by telling "ok, I'll give you some hints: was the name X, Y or Z?" and so on. Each recognised item scores one point which is added to the point gained by recalling.

[Score 0-5] 3

Jerry Barnes		Harry Barnes	✓ Harry Bradford	recalled
37		73	76	recalled
Orchard Place		Oak Close	Orchard Close	✓ recalled
Oakhampton	X	Kingsbridge	Dartington	recalled
Devon	✓	Dorset	Somerset	recalled

General Scores

Subscores

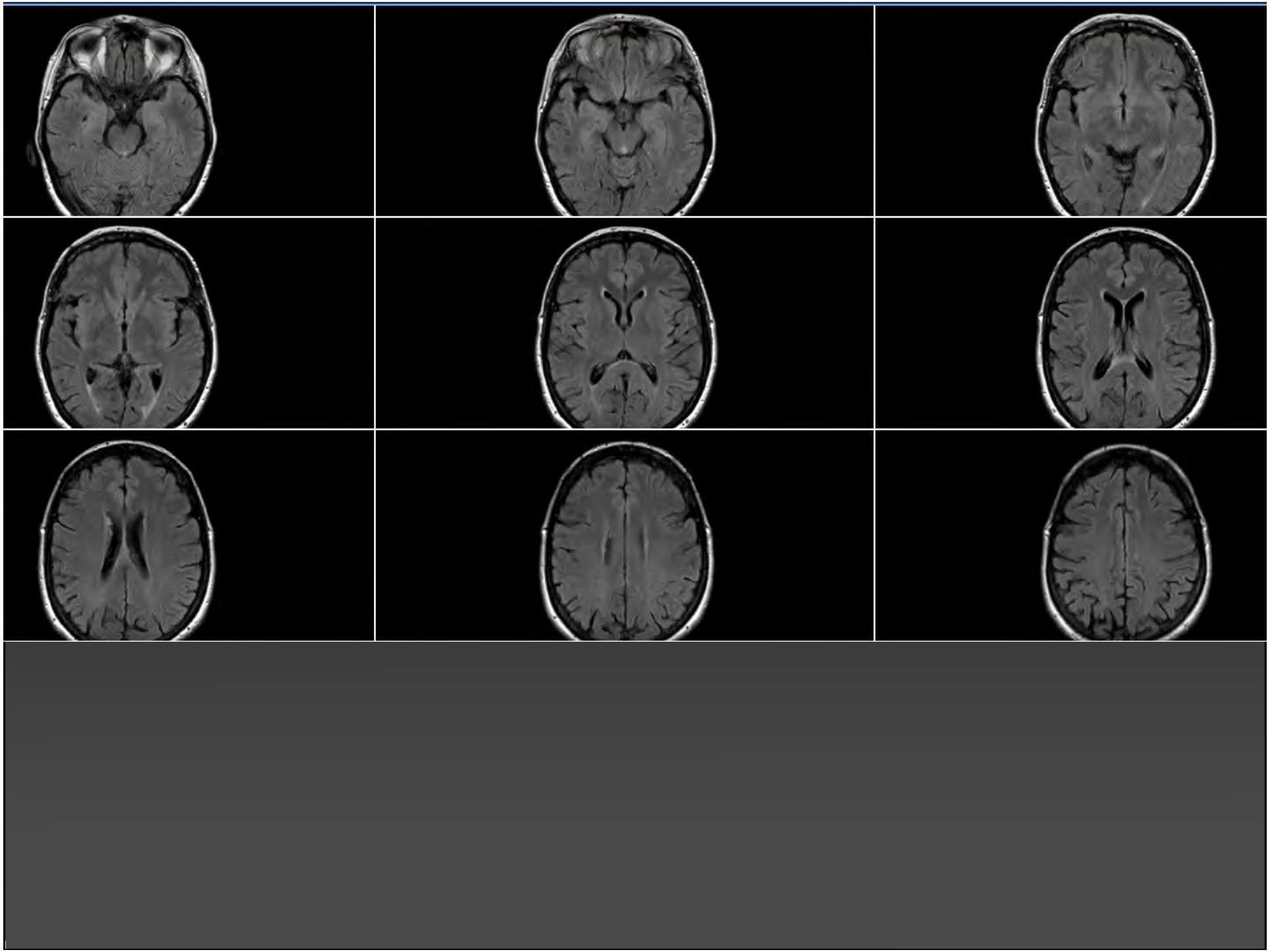
21/30(21)

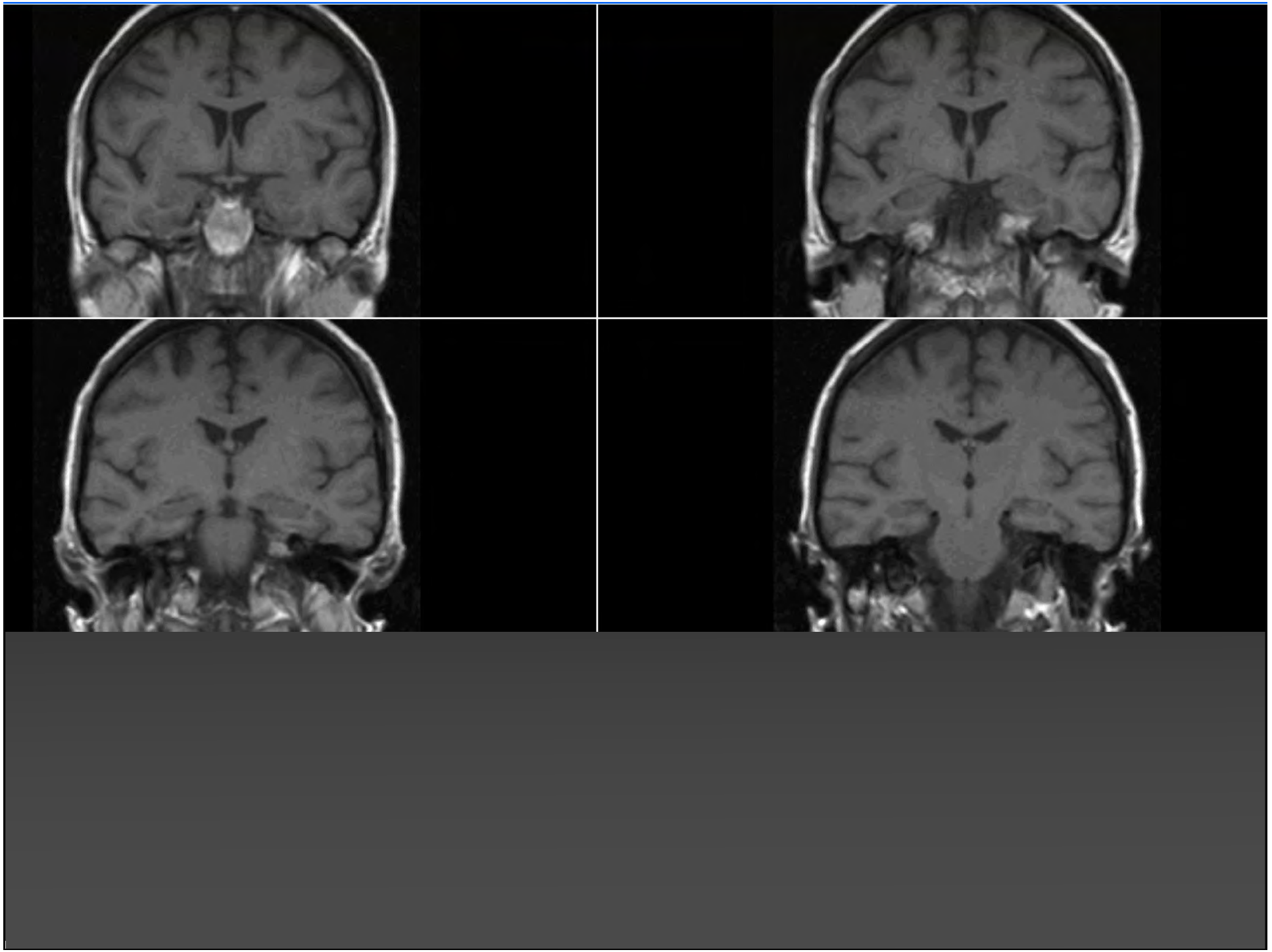
MMSE 23 /30

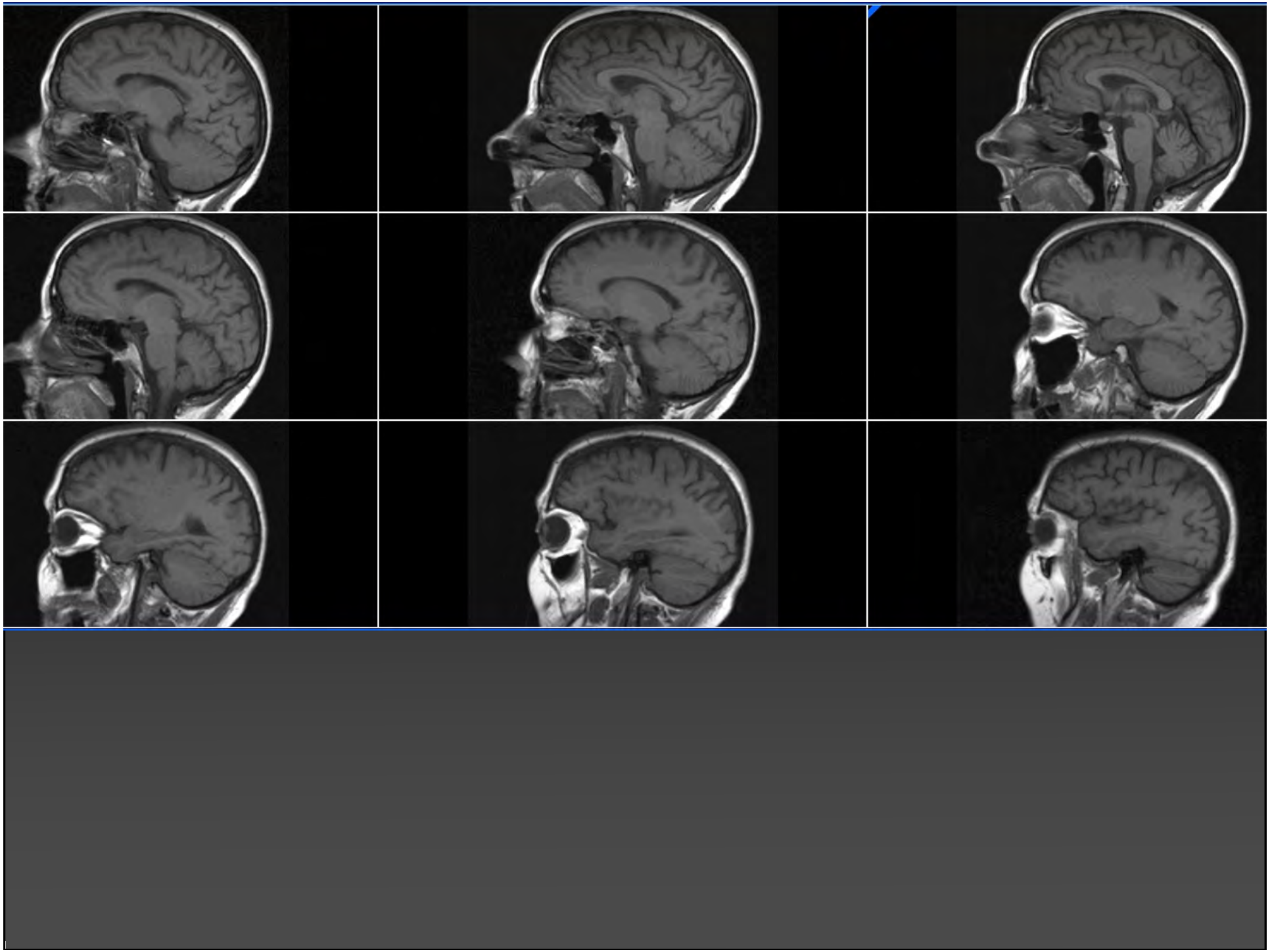
ACE-R 55 /100

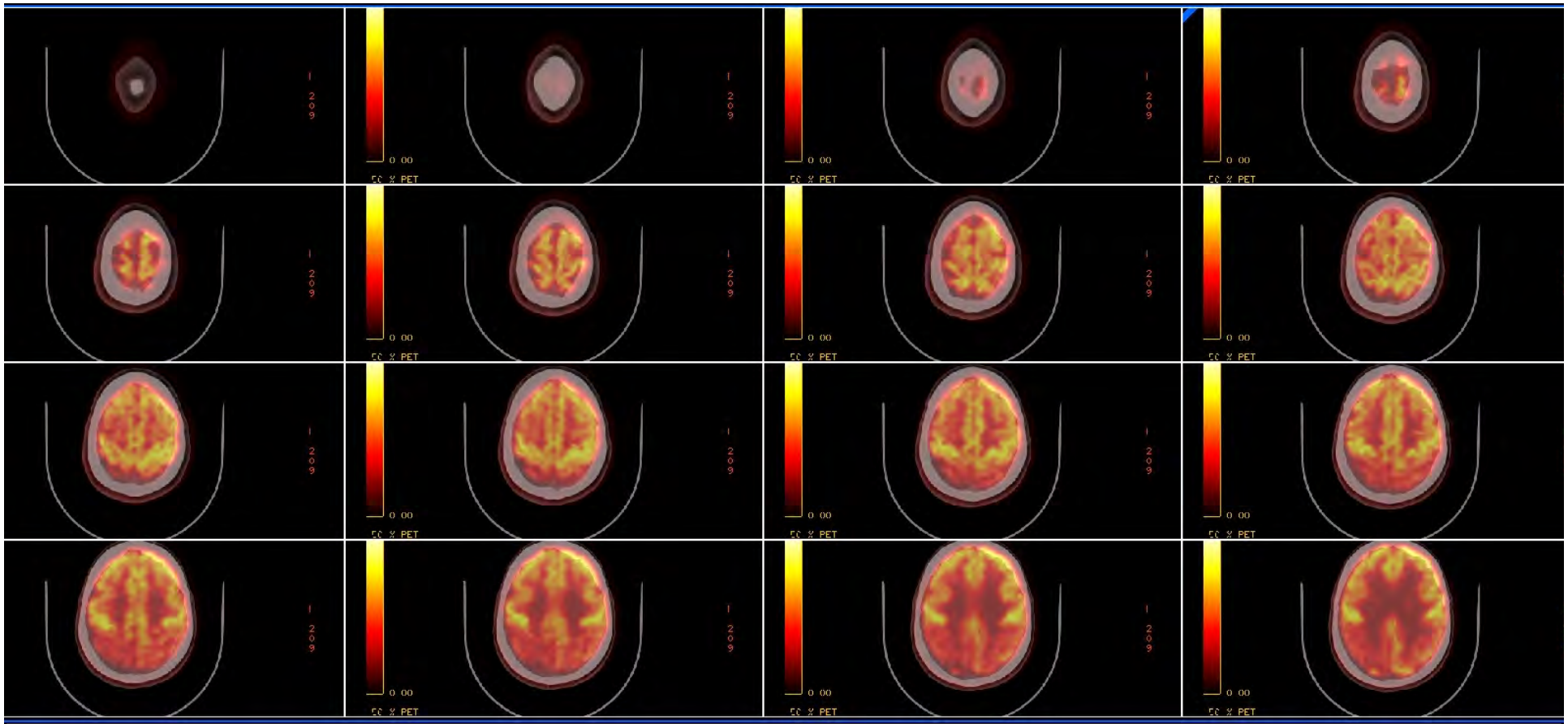
Attention and Orientation /18

Normative val

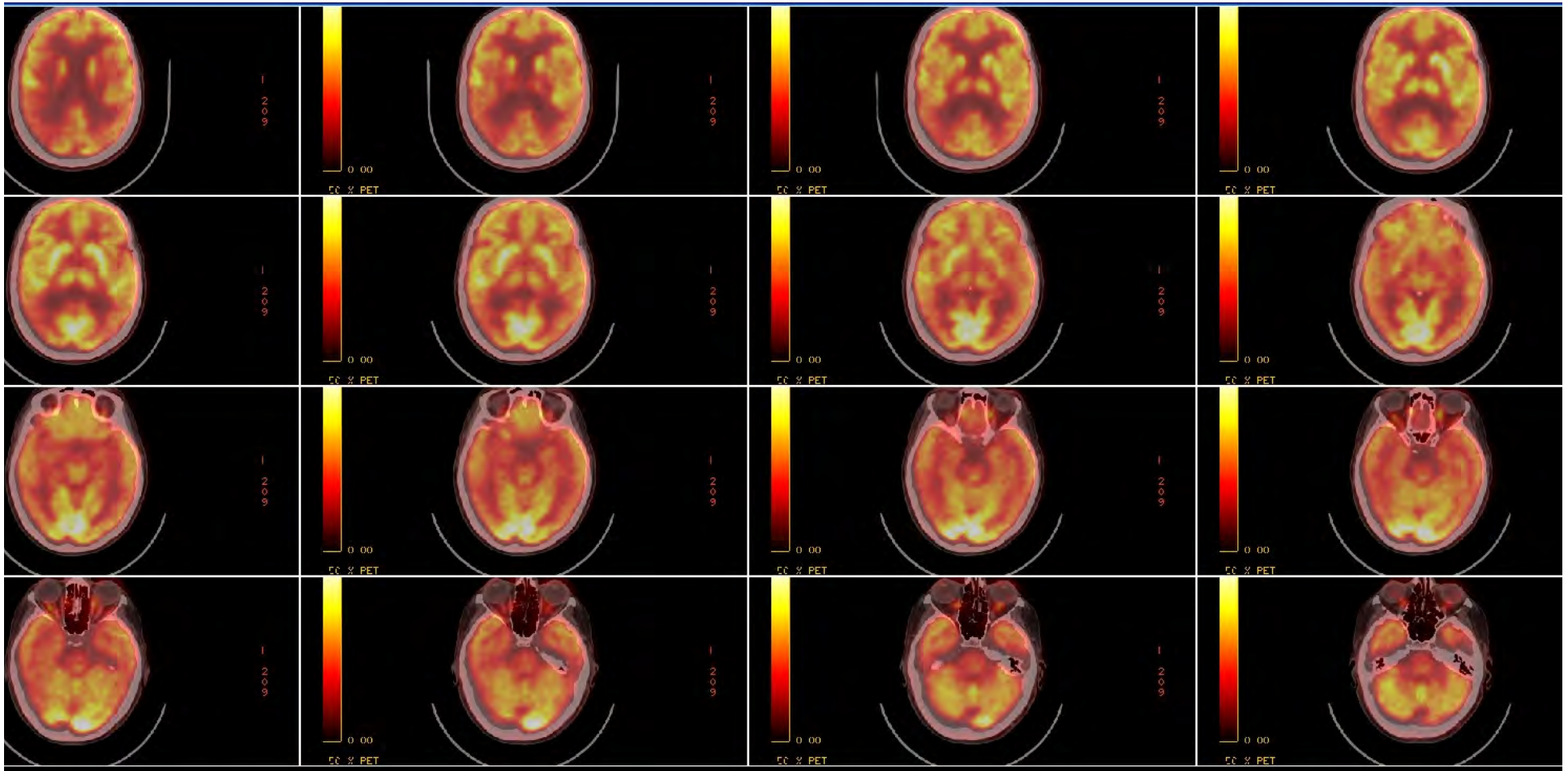








Abnormal study. Although there is diffuse hypometabolism involving the parietal and frontal lobes, the pattern is most prominent in the posterior cingulate cortex and the associated visual cortex. This would be more consistent with Alzheimer's disease and cortical basal degeneration or multiple infarct dementia. Note, there is sparing of the temporal lobe s.



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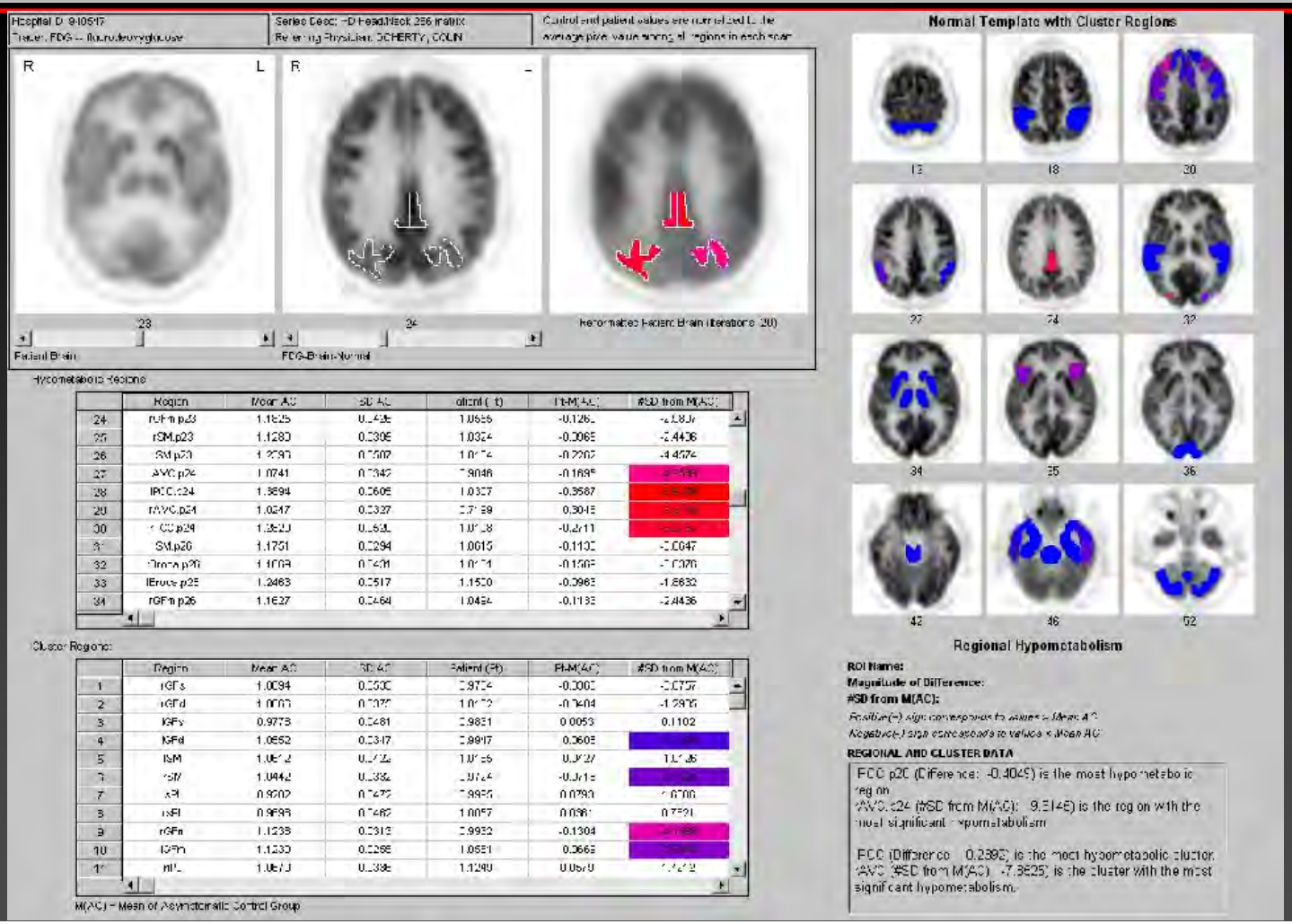

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Neurology at the Memory Clinic

The Younger Patient
…example

essential core diagnostic criteria were used: (1) asymmetrical presentation, (2) akinetic-rigid syndrome, (3) ideomotor apraxia, and (4) signs of frontal-executive dysfunction. Apraxia was systematically assessed by asking subjects to first copy a series of meaningless gestures, then to mime to command meaningful gestures and finally to copy the examiner performing transitive movements.[20] The supportive criteria included (1) insidious onset and gradual progression (2) lack of sustained response to dopaminergic treatment (3) myoclonus, (4) dystonia, (5) alien hand syndrome, (6) cortical sensory loss tested by two-point discrimination, graphaesia or tactile object recognition, (7) visuospatial deficits, and (8) progressive nonfluent aphasia.[20] The diagnosis of CBS was based on the presence of at least three essential and four supportive features.

Final Diagnosis:

The Corticobasal Syndrome

pathology ? Alzheimer's Disease

1/4 with be Alzheimer's Pathology
1/4 will be Progressive Supranuclear Palsy pathology
1/4 will be Cortico Basal Degeneration pathology
1/4 will be Fronto Temporal Degeneration pathology

Neurology at the Memory Clinic

- The Younger Patient and their Profile
- The Patient with Neurological Disease

Neurology at the Memory Clinic

The Patient with Neurological Disease

- *Who presents with memory disorder for management but comes with an established neurological diagnosis…*

- Second Opinion esp on legal matters - EPoAs

- MND
- Huntington's Disease
- Parkinson's / PSP
- Alcohol Dep Synd
- But there will be the rarer entities too - tremor and Fragile X Ataxia synd

- Multiple Sclerosis

Neurology at the Memory Clinic

The Patient with Neurological Disease -Multiple Sclerosis

- *1.57/1000 get Multiple Sclerosis*
- *Majority survive.*
- *Was thought to be a disorder of White Matter…*
- *However most of the Atrophic changes affect grey matter as well as white matter*
- *In more recent times known that Grey matter demyelination plays a significant role.*
- ***c50% will have cognitive impairment by c20 years in to diagnosis***

Neurology at the Memory Clinic

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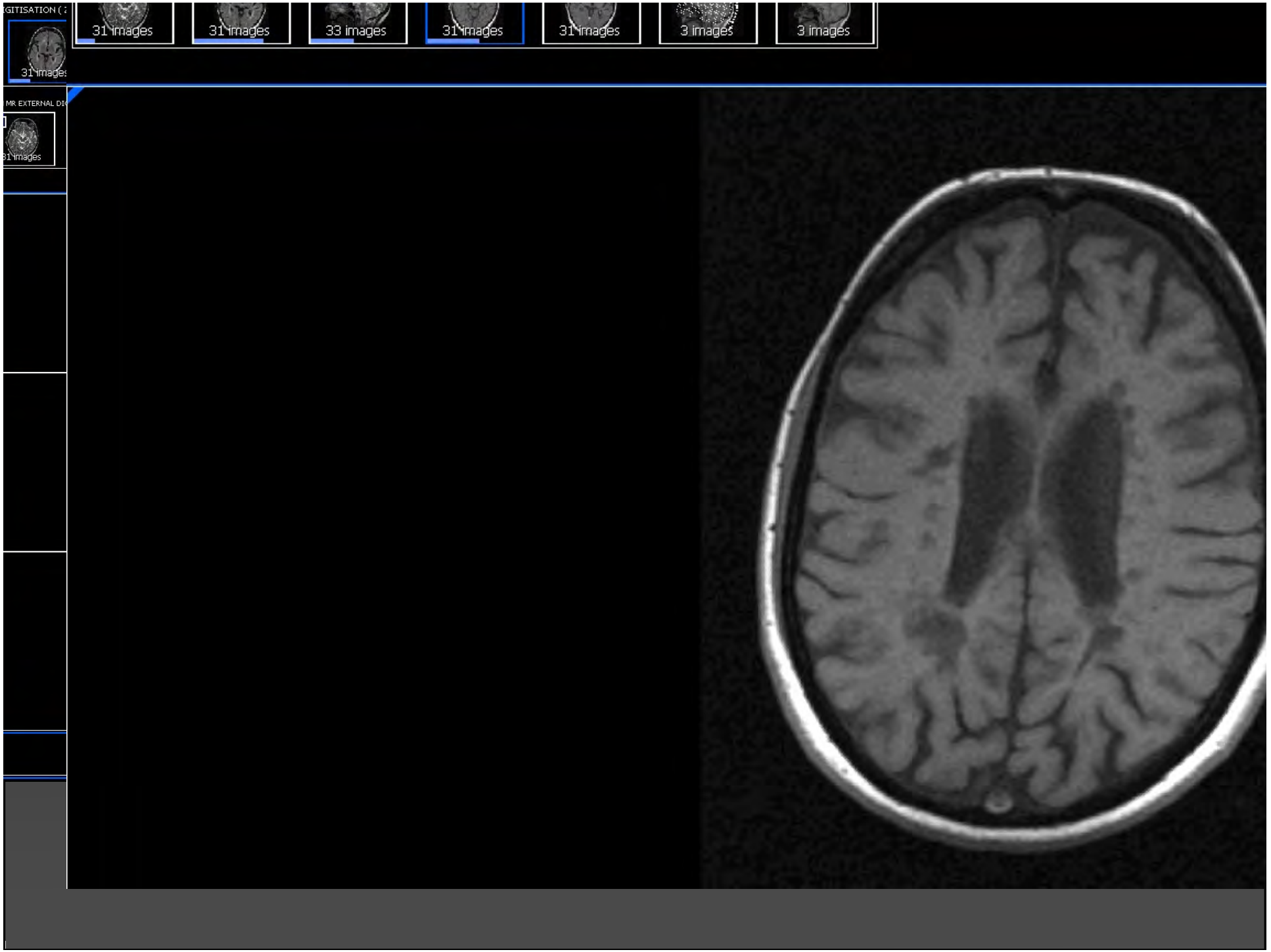
The Patient with Neurological Disease -Multiple Sclerosis

Table Lists of neuropsychological tests administered in the Rao Brief Repeatable Neuropsychological Battery (BRNB)[7] and the Minimal Assessment of Cognitive Function in Multiple Sclerosis (MACFIMS)[4,8]

Domain	BRNB	MACFIMS
Processing speed and working memory	Paced Auditory Serial Addition Test	Paced Auditory Serial Addition Test
	Symbol Digit Modalities Test	Symbol Digit Modalities Test
New learning and episodic memory	Selective Reminding Test	California Verbal Learning Test
	10/36 Spatial Recall Test	Brief Visuospatial Memory Test
Language	Controlled Oral Word Association Test	Controlled Oral Word Association Test
Spatial processing		Judgment of Line Orientation Test
Higher executive function		DKEFS Sorting Test

Views and Reviews
M. Filippi, M.A. Rocca, R.H.B. Benedict, J. DeLuca, J.J.G. Geurts, S.A.R.B. Rombouts, M. Ron, and G. Comi
The contribution of MRI in assessing cognitive impairment in multiple sclerosis
Neurology December 7, 2010 75:2121-2128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33 images
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MR EXTERNAL DI
31 images

Neurology at the Memory Clinic

The Patient with Neurological Disease -MS

Recent memory - information processing, speed, sustained attention

Lesions correlate to defects; frontal lesions - executive etc

Learning and memory are most common impairments

Neurology at the Memory Clinic

The Patient with Neurological Disease -MS

Rx:

Disease Modifying - do help

Symptomatic -

AChEi Donepezil - 4 done - 1 published

RCCT DB Krupp 2004: 69 improved memory on Selective Reminding -

The problem: repeated with 120 pt group….

AChEi Rivastigmine 3/12 n = 60 no difference on Wechsler Memory Scale

Glutaminergic Memantine 3/12 Multicentre DBPCCT n=126 Initially no difference but 1 yr DBRCCT - "reversible neurologic impairment" in moderate to severely affected patients ??? "Axonal blockage"

Neurology at the Memory Clinic

The Patient with Neurological Disease -MS

Rx:

Symptomatic -
Antiviral Dopaminergic Amantadine -
DRI - Pemoline
Attention, Verbal memory and Motor speed all improved - but no better than Placebo….
Ginkgo biloba slight but non-significant improvement
Fluoxetine ? Neuroprotective- fewer new lesions

Cognitive Impairment in MS. Chiarvalloti et al Lancet Neurology 2008
Treatment options of Cognitive Impairment in MS. Patti et al Neurol Sci 2010

Neurology at the Memory Clinic

The Patient with Neurological Disease -MS

How did we manage the patient -

Already on Donepezil- Limited evidence - but no strong indication to stop.

Exercise.

Cognitive Activity.

Heavy Smoker.

Cognitive Impairment in MS. Chiarvalloti et al Lancet Neurology 2008

Treatment options of Cognitive Impairment in MS. Patti et al Neurol Sci 2010

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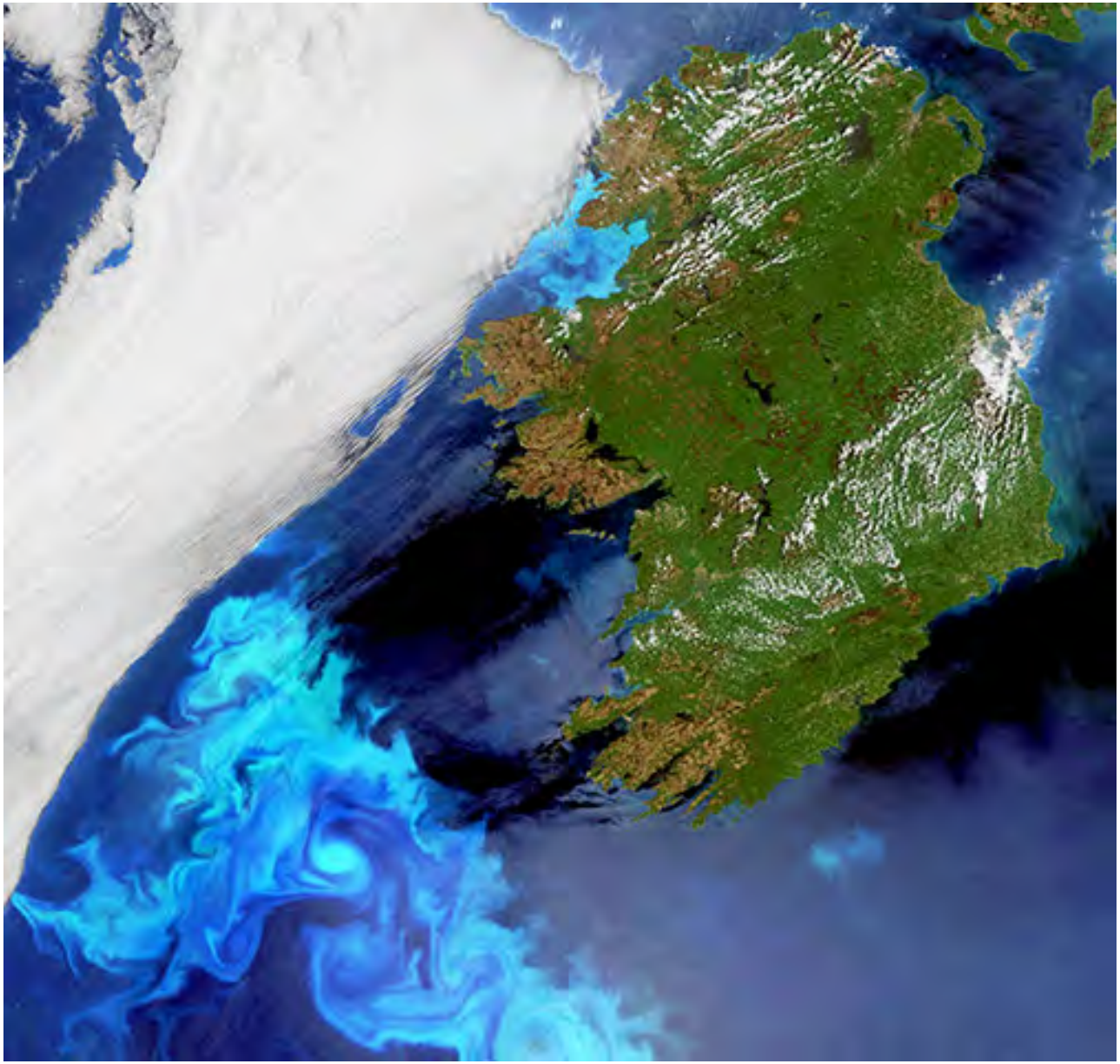

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The Dublin
Neurodegeneration Consortium

Young Onset Neurodegeneration

A longitudinal population-based study of young onset neurodegeneration piloting in Dublin, examining people under 65 with Parkinsons, Alzheimer's, ALS/MND, the FTDs and other primary causes of Neurodegeneration.

Young Onset Neurodegeneration

Dr Arun Bodke	Neuroimaging TCIN
Dr Roberty Coen	Neuropsychology, St James's
Dr Colin Doherty	Behavioural Neurology St James's
Prof Orla Hardiman	ALS/MND, Beaumont
Prof Dan Healy	Movement Disorders, Beaumont
Prof Brian Lawlor	Memory Clinic, St James's
Prof Tim Lynch	Parkinson's, Mater
Prof Jim Meaney	Neuroimaging St James's
Dr Fiona Molloy	Neurophysiology, Beaumont
Dr Niall Pender	Neuropsychology, Beaumont
Prof Richard Reilly	Neural Engineering, TCD

St. Vincent's University Hospital
TRINITY COLLEGE DUBLIN
HRB
TRINITY COLLEGE
Institute of Neuroscience
ST. JAMES'S HOSPITAL
UCD DUBLIN
Mater Misericordiae University Hospital Ltd.
The Dublin Neurological Institute
Beaumont Hospital
Molecular Medicine Ireland
wellcome trust
ST. JAMES'S HOSPITAL, DUBLIN
Centre for Advanced Medical Imaging
3T Magnetic Resonance Imaging Research Facility
THE ALZHEIMER SOCIETY of IRELAND
IHCN
SCHOOL OF MEDICINE
300 YEARS OF EXCELLENCE

The YON Project
2010/2013
The Dublin Neurodegeneration Consortium

Young Onset Neurodegeneration

-

Noticeboard Information Sheet

Inclusion Criteria :

- Patients aged 40-64.
- Resident in Dublin City/County.
- With a Primary Neurodegenerative Condition.
- In current workup or diagnosed within one year.

Conditions:
Any Primary Neurodegenerative Disorders.
e.g. :

- Alzheimer's
- Parkinson's, Progressive Supranuclear Palsy, Multiple Systems Atrophy.
- Frontotemporal Dementia
- Motor Neurone Disease

Referral pathway:

-Via your local hospital with a Neurology Service, as per your usual care or the patient's wishes.
-We would be grateful if you could make your patient aware of the study.

OR

-Alternatively the patient may be referred for usual care directly to the Neurology Services at **St James's Hospital (Dr Doherty)** or **Beaumont Hospital (Prof Hardiman) or Mater Hospital (Prof Lynch).** These hospitals have primary neurodegenerative interests.
-There, additional to their usual care and subject to consent/assent, they may be recruited into this study.

Further Information

For additional information now or any future time please contact:
Dr. Thomas Monaghan Research Fellow at
- Memory Clinic, Top Floor, Hospital 4, St James's Hospital, Dublin 8 or
- DCCR, Clinical Research Centre - Smurfit Building, Beaumont Hospital, Dublin 9 or
- Dublin Neurological Institute - MMUH, 57 Eccles Street, Dublin 7
Tel: 087 1 65 45 85
or
General enquiries by email to: yonstudyinfo@gmail.com *(no patient details please by email)*
c/o
Prof Orla Hardiman, Clinical Research Centre, Smurfit Building Beaumont Hospital, Dublin 9