Cognitive Impairment in Facial Onset Sensory and Motor Neuronopathy (FOSMN)

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Introduction Facial Onset Sensory and Motor Neuronopathy (FOSMN) is a rare neurodegenerative condition of uncertain pathogenesis which typically presents with a trigeminal distribution sensory disturbance progressively engulfing the head, neck and upper trunk bilaterally, and associated with facial, bulbar and respiratory motor impairment. A handful of reported neuropathological post-mortem analyses have demonstrated neuronal loss within the brainstem nuclei in addition to the cervical dorsal root ganglia and anterior horns. TDP-43 inclusion bodies have been demonstrated in several of these cases suggesting that FOSMN may represent an unusual manifestation of ALS. Hitherto, little attention has been paid to the presence of cognitive impairment in FOSMN and has even been considered an exclusion criterion for the condition. Here we report characteristics of cognitive difficulties in 3 male patients with FOSMN manifest 12-24 years after disease onset.

Case	Previously Described	Age at Onset	Disease Duration	Cognitive Symptom Onset	Cognitive Tests	RBD	SNHL	MRI Brain & Spinal Cord
1	Broad & Leigh[1]	42y	17y	17th year	ECAS (see text)	✓	✓	Normal
2	Broad & Leigh[1]	45y	14y	12th year	Neuropsychometry (Fig.1)	-	✓	Normal
3	No	47y	26y	24th year	-	✓ (Fig. 2)	-	Normal

***Table 1*. Summary of clinical features in three cases.**
ECAS = Edinburgh Cognitive and Behavioural ALS Screen; RBD = REM sleep behavioural disorder; *(Neuropsychological Assessment Battery), SNHL* = sensorineural hearing loss

Case 1 Bilateral facial sensory was followed by dry cough, loss of taste, nasal dysarthria, dysphagia, neck extension weakness, progressive lower limb distal weakness accompanied increasing difficulty with hearing, tinnitus and motion-induced vertigo. Aged 56, pure tone audiogram (**PTA**) revealed asymmetrical sensorineural hearing loss (**SNHL**) across the frequency spectrum on the right and high-frequency on the left, and grossly abnormal auditory evoked potentials. Sleep was increasingly fragmented with hypnopompic auditory hallucinations. Polysomnography (**PSG**) confirmed rapid eye movement (**REM**) sleep behavioural disorder (**RBD**) rather than obstructive sleep apnoea.

17 years into symptoms he began to notice deteriorating memory for recent events, difficulty planning activities and more apathy with blunted empathy or emotional response.

ECAS scored 108/136 with reduced verbal fluency [12/24], executive [39/48; particularly attenuated reverse digit span] and memory [18/24] domains, with preserved language [28/28] and visuospatial [11/12] abilities.

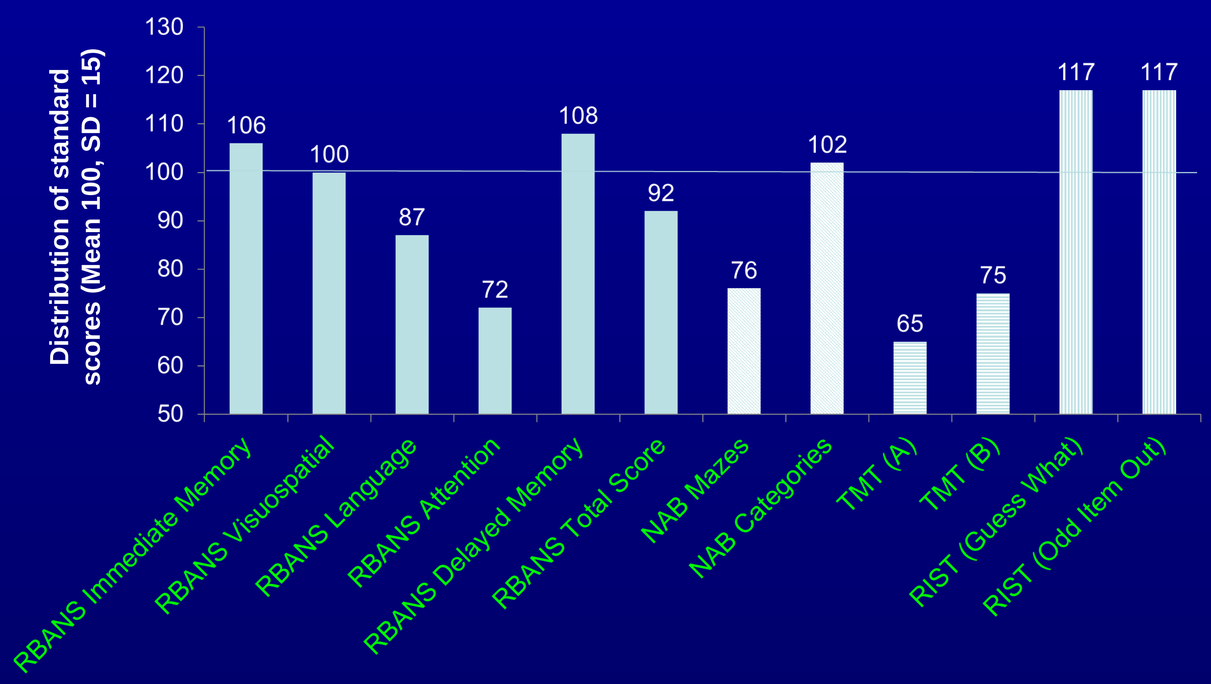

***Figure 1*. Psychometric profile for Case 2.** *Reynolds Intellectual Screening Test (RIST) revealed* superior range (92nd percentile) scores, but average range (30th percentile) on the *Repeatable Battery for the Assessment of Neuropsychological Status (RBANS)* with significant *Attention* domain impairment manifest as slowed processing & variable performance on executive tasks for planning (*NAB Mazes*) and switching (*Trails B*). Semantic word fluency task was poor (10th percentile).

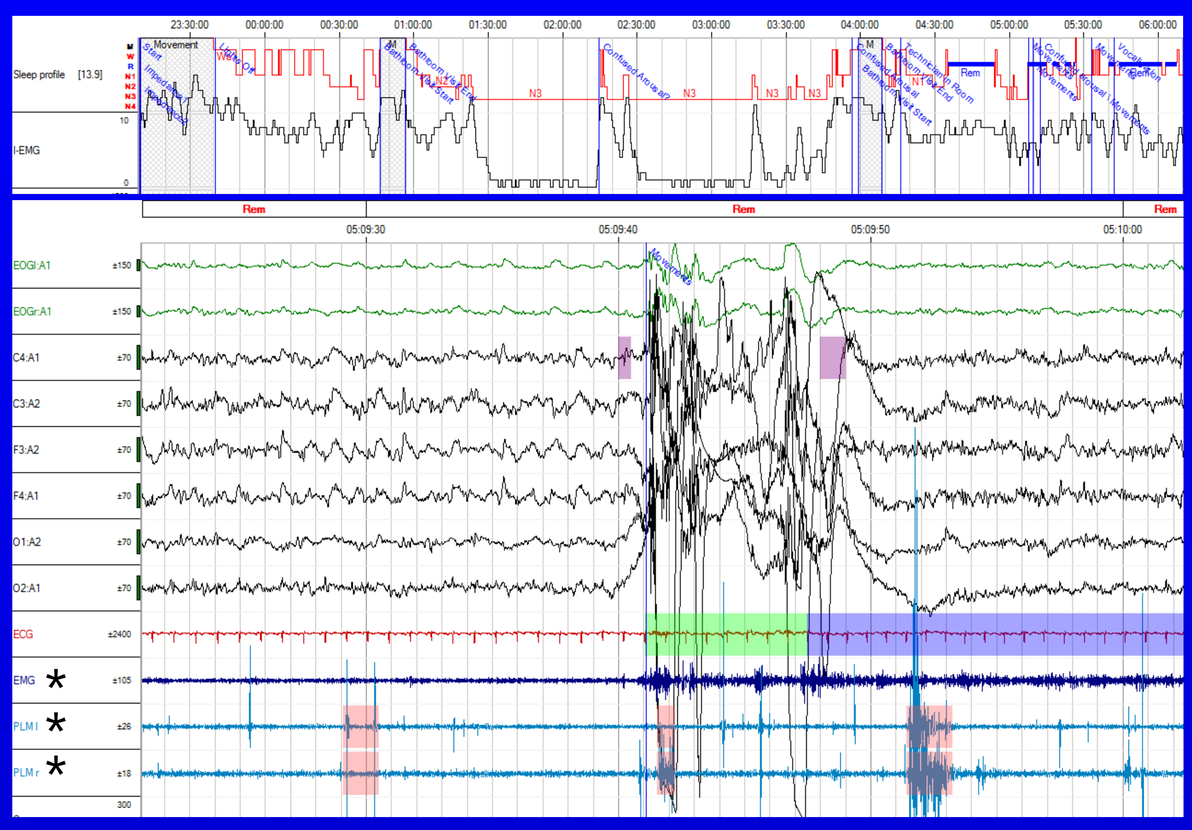

***Figure 2*. Polysomnography for Case 3.** Summary of sleep stages (A; red line) with 40s epoch containing evidence of RBD (in B) comprising tonic mentalis and phasic limb EMG activity (*) during REM sleep with movement artefact on EEG. *Thanks to Richard Knight, Queen Victoria Hospital.*

Case 2 Neck extension weakness followed by progressive weakness and wasting in the face and upper limbs, and abnormal two-point discrimination over the lips. PTA showed mild bilateral high frequency SNHL (aged 55). Swallowing difficulties accompanied a preference for sweeter foods. He became more irritable and socially withdrawn, more obsessional and mildly apathetic with diminished memory for recent events. Formal neuropsychometry was performed (see **Fig.1**).

Case 3 Nasal/perioral numbness slowly spread to involve the face, scalp, neck and arms with highly unpleasant paroxysmal nasal pain. Examination aged 57 revealed absent corneal and gag reflexes, and impaired lingual salt perception. MRI brain and cervical spine were normal but neurophysiology did show abnormal blink reflexes with absent R1 and delayed R2 responses bilaterally. From age 63 mild dysphagia developed and, by age 69, neck extension and proximal limb weakness along with confused nocturnal wandering soon after sleep onset (rocking on the bed rubbing his legs and muttering), with visual hallucinations, getting lost *en route* to the bathroom and urinating in inappropriate areas. He could become aggressive if challenged and would hold the delusion that his wife was an imposter. Donepezil partially resolved these symptoms. PSG indicated confusion from slow wave sleep and also demonstrated evidence of RBD. Anterograde memory and word-finding difficulties deteriorated, as did following written or spoken commands. The patient died before formal neuropsychometry could be achieved.

Discussion These three cases suggest that cognitive deficits consistent with a frontotemporal disorder appear to be an intrinsic, yet later onset, component of the FOSMN syndrome and expand the phenotypic spectrum.

- Two developed mild frontal dysexecutive features including apathy, reduced empathy, poor organisational skills, impaired task switching & verbal fluency, and poor anterograde memory; the 3rd experienced visual hallucinations and confused nocturnal wandering;
- Two patients had RBD on overnight sleep studies;
- Two patients developed high frequency SNHL from their mid-50s.

RBD may broadly correspond to the ponto-medullary region of degeneration in FOSMN but would classically herald one of the synucleinopathies rather than TDP-43 pathology. Whether sensorineural hearing loss implies involvement of central auditory circuitry or merely incidental presbyacusis is unclear.

Follow up of FOSMN cases is warranted to determine prevalence of cognitive deficits, SNHL and RBD, perhaps manifest only in latter stages, along with post-mortem analysis of the neuropathological basis, where possible.

References

1. Broad and Leigh. Pract Neurol (2015) 15: 293-297.
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