Patterns of ocular motor fatigue in Internuclear Ophthalmoparesis due to Multiple Sclerosis

CG Chisari [1,3], A. Serra [1-2], J. Jacobs [1-2], M. Matta [4], M. Skelly [1], M. Walker [1-2], M. Zappia [3], J. Cohen [5]

1 Cleveland VA Medical Center, 2 Case Western Reserve University, 3 University of Catania, Italy, 4 Ospedale San Luigi Gonzaga, Orbassano, Italy, 5 Cleveland Clinic Mellen Center

Background: Motor fatigue is a poorly understood yet highly disabling symptom in multiple sclerosis (MS). Internuclear ophthalmoparesis (INO) due to MS may worsen over time (ocular motor fatigue) and has been proposed as a model for motor fatigue in MS.1-3 We previously reported, in a very small population, that ocular motor fatigue could be characterized in two ways:

- Increased abducting-to-adducting-eye peak-velocity ratio **(pulse size ratio, PSR);**
- Increased delay of saccade onset in the affected eye **(pulse time delay, PTD).** PTD has to be confirmed as useful outcome measure for ocular motor fatigue in a larger INO population.

Aim: To study fatigue-induced changes in MS-related INO using measures of saccadic peak-velocity and onset.

Methods: We recorded saccades in 23 MS patients (median age 40, median EDSS 3) with INO (9 bilateral, total 32) using infrared or video oculography, using a 10-minute saccadic "fatigue test".1 Data were digitized at 500 Hz. We analyzed data from previously published results (13 patients, 19 INO), not originally studied using PTD, and from 10 new patients (13 INO). We measured PSR and PTD at first (time 1) and last 90 seconds (time 2) of the recordings. Onset of saccade was calculated using a 20 deg/sec velocity threshold. An average of 27±17.50 saccades were collected at each time per INO.

Mean and proportion differences were calculated with paired t- test and chi-square test respectively.

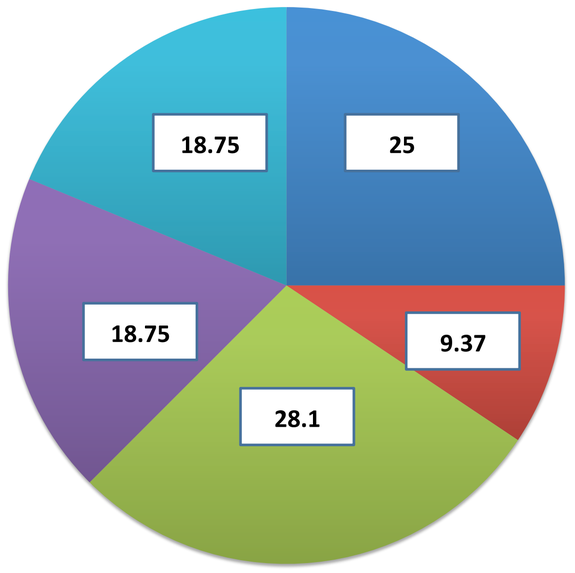
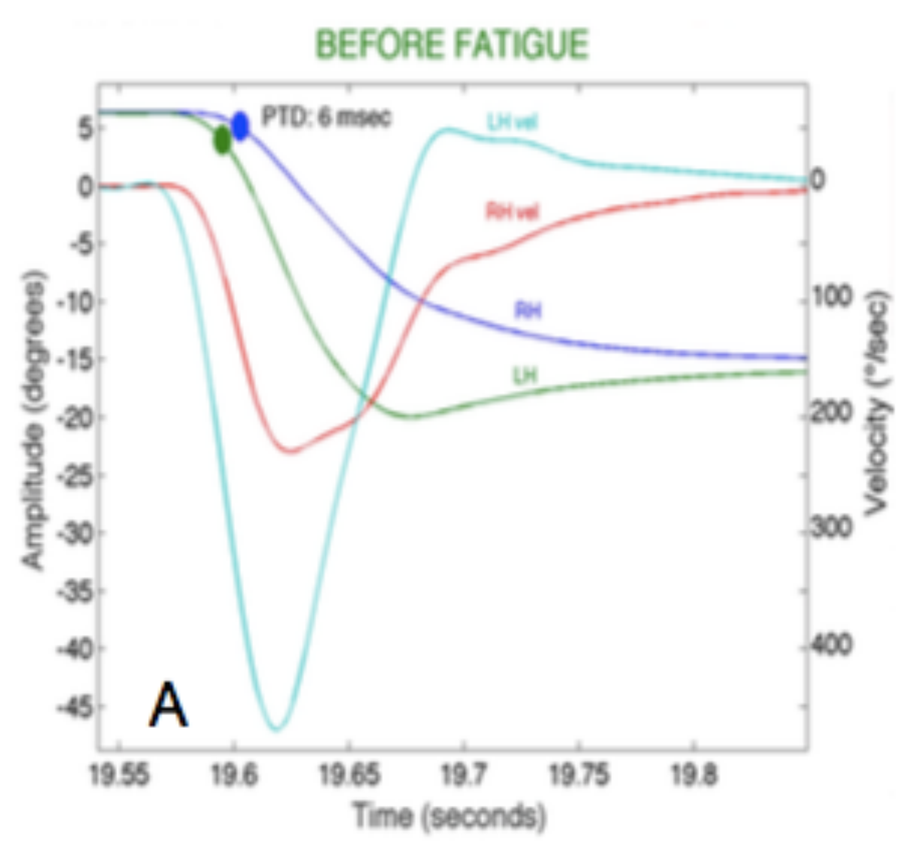


FIG. 2: INDIVIDUAL CHANGES
Percentages of INOs exhibiting different behaviors, as depicted. Threshold value for PSR changes was a difference of 0.1 between time 2 and time 1. Threshold value for PTD changes was a difference of ≥2 msec between time 2 and time 1. Total: 32 INOs.

Results: In our lab and in the literature,3 controls show pulse size ratio of ~1 and pulse time delay of < 2 msec.

- Overall, INO group showed **increased PSR** [average from 1.56 (range 1.01-2.77) at time 1 to 1.63 (range 1.11-3.3) at time 2), ***p=0.02***] and **increased PTD** [average from 0.015 sec (range 0.002-0.081) at time 1 to 0.019 sec (range 0.001-0.085) at time 2), ***p=0.004***]. See Figure 1.
- After fatigue, 25% of INOs showed increase of both PSR and PTD, **28% showed increased PTD and decreased PSR,** and 19% showed increased PSR and decreased PTD**.** See Figure 2.



A: Leftward Saccade of a patient with INO at baseline, at the beginning of the 10- minute fatigue test. Notice typical decreased velocity of the adducting eye (RH vel). The inter-ocular timing of saccade onset is 6 msec (PTD). **B:** Leftward Saccade of a patient with INO after fatigue, at the end of the 10-minute fatigue test. Notice typical decreased velocity of the adducting eye (RH vel). The inter-ocular timing of saccade onset has increased from baseline to 32 msec (PTD). RH: right eye horizontal position; LH: left eye horizontal position; RH vel: right eye horizontal velocity; LH vel: left eye horizontal velocity; PTD: pulse time delay; Green and blue dots: onset of saccade in the abducting and adducting eye, respectively.

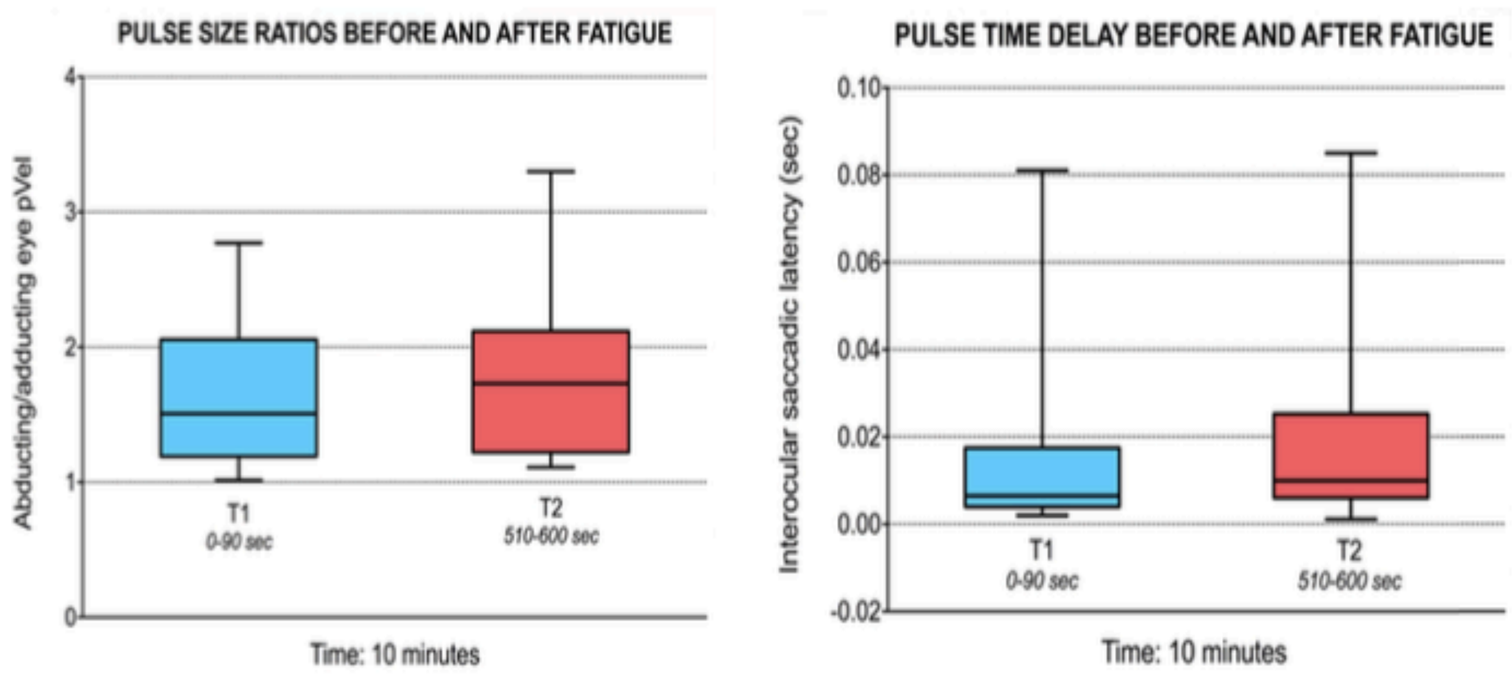


FIG. 1: GROUP OF CHANGE

Conclusions: Ocular motor fatigue in MS-related INO may be secondary to decreased size (increased PSR) and/or delayed delivery (increased PTD) of the saccadic "pulse" signal for the adducting eye.

Adding a measure of inter-ocular timing of saccade onset (PTD) may expand the ability to capture ocular motor fatigue in INO. Ocular motor fatigue may be due to compromised axonal transmission (slowing or block) in the MLF under high-demand ocular motor tasks. INO may represent an accessible model to understand motor fatigue in MS and test therapies intended to improve/repair axonal transmission.

We are currently conducting a phase II trial about effects of dalfampridine on INO and related ocular motor fatigue).

References

1. Matta et al, Neurology, 2009 2. Serra et al, Neurology, 2014 3. Leigh, Zee. The Neurology of Eye Movement, 5th Edition

Sin

XLVII CONGRESSO NAZIONALE
22-25 OTTOBRE 2016 – VENEZIA

WebPoster