Hey Batter Batter Saccade Better: Abnormal Eye Movements May Be a Sensitive Indicator of Disease Severity and Disability in Patients with Multiple Sclerosis

Abstract:
Optometrists should employ tests of saccade and pursuit function along with conventional examination methods to diagnose oculomotor dysfunction in patients with Multiple Sclerosis. These findings correlate with brainstem and cerebellar disease as well as functionality.

I. CASE HISTORY
   - Demographic:
     o 35 year-old Caucasian male diagnosed with Relapsing Remitting Multiple Sclerosis (RRMS) in 2007
   - Chief Complaint:
     o The patient, an avid baseball player, reports that he can no longer follow or catch a baseball that is thrown to him. Even when watching a ballgame, he cannot follow the ball’s trajectory. The patient also reports occasional impairment of depth perception (eg. hitting the curb when parallel parking his car). The patient denies diplopia.
   - Ocular History:
     o Bilateral optic neuritis
     o Uhthoff’s phenomenon
     o Myopic astigmatism
   - Medical History:
     o Relapsing Remitting Multiple Sclerosis
     o Most recent clinical relapse occurred in August, 2015; confirmed by a new enhancing lesion on MRI.
   - Medications:
     o Dimethyl fumarate 240 mg
     o Gabapentin 600 mg
     o Modafinil 100 mg
     o Trazodone 10 mg
     o Oxybutynin chloride 10mg
     o IV Methylprednisolone infusions for clinical relapses
   - Other Salient Information:
     o Patient ambulates with a cane due to left lower extremity weakness, and uses a wheelchair when he is tired. The patient reports that his right foot has also become weaker.
     o Patient reports declining cognitive function, especially pertaining to his short-term memory.

II. PERTINENT FINDINGS
   - Entrance Testing
     o BCVA: 20/20 OD, 20/20 OS
     o Pupils: ERRL, trace APD OS
     o Color vision (Ishihara): 10/10 OD, 6/10 OS
Red cap desaturation: 100% OD, 50% OS
EOMs: full ranges with saccadic pursuit; bilateral end-gaze nystagmus which dampens; diplopia in extreme left gaze
Confrontation finger-counting fields: full OD, full OS
RANDOT2 Stereo: no appreciation for global and/or local stereo

Alignment Testing
Distance (cc): 1.5^ intermittent right exotropia (more evident after fatiguing)
Near (cc): 17^ intermittent right exotropia (high frequency)

Qualitative Oculomotor Testing following NSUCO guidelines
Saccades:
- Hypometric saccades worse in left gaze with overall reduced velocity as well as asymmetry (OS slower than OD)
- Mild left internuclear ophthalmoplegia (INO) was discernible when observing relative speed of saccades
- Able to complete all cycles with minimal head/body movement
Pursuits:
- Saccadic pursuits
- Able to complete clockwise and counterclockwise rotations with minimal head/body movement

Reading Assessment via ReadAlyzer (Grade 18)
Prolonged fixations with multiple regressions
- Average fixation: 0.48 seconds (Grade average: 0.22 seconds)
- Regressions/100 words: 16 (Grade average: 3)
Patient does not generate smooth return sweeps to the next line
Reading rate:
- 91 words/minute (Grade average: 605 words/minute)
Regression/Fixation ratio:
- 12% (Grade average: 7%)

Posterior Segment:
Optic nerve:
- OD: C/D 0.25, trace sectoral pallor at 9:00, margins distinct
- OS: C/D 0.25, trace diffuse pallor, margins distinct
Macula: flat and clear OD/OS

Imaging/Ancillary Testing
Fundus photography showing optic nerve rim pallor OS>OD
Humphrey Visual Field
- HVF 10-2
  - OD: reliable with clean field
  - OS: reliable with deep scotoma temporal to fixation (previously undetected with HVF 24-2)
Optical Coherence Tomography (OCT-RNFL)
• OS: G (82). Thinning temporal, superotemporal, and inferotemporal. Borderline thinning global.
  o Magnetic Resonance Imaging (MRI) of Brain
    • Extensive T2 hyperintense foci along the periventricular white matter, centrum semiiovale, and periatrial region of the lateral ventricles.
    • Scattered smaller lesions throughout the corpus callosum.
    • Large lesions are present involving the brainstem, the anterior pons, cerebellum, and middle cerebellar peduncles.

III. Differential Diagnosis
  - Primary/Leading:
    o Saccadic dysmetria is the primary contributor to the patient’s reported difficulties following a baseball that is thrown. Tracking a fast-moving visual target requires the eyes to make an accurate series of saccades.
    o The patient’s left INO in conjunction with an intermittent right exotropia are causing his occasional impairment of depth perception. Due to use-related fatigue and Uhthoff’s phenomenon, the symptoms of INO can fluctuate throughout the day and periodically interfere with the patient’s binocular status. This may be especially pronounced when the patient is parking his car and looking in right gaze, causing him to misjudge the distance between the car and the curb.
  - Others:
    o Impaired smooth pursuit
      • Although the patient demonstrates impaired smooth pursuit, it is unlikely the primary contributor because a baseball’s velocity during most of its path is too fast for pursuit eye movements. Accurate pursuits can be achieved for targets moving at less than 50 degrees/second, about ten times slower than for saccades.
    o Paracentral scotoma OS due to past optic neuritis
      • While a baseball can certainly fall within the patient’s scotoma in the left eye, the patient reports comparable difficulty following a ball moving either right or leftward. The scotoma exacerbates the patient’s ability to perform accurate eye movements, however is unlikely the main culprit.

IV. Diagnosis and Discussion
  - Our patient’s saccadic dysmetria, in particular hypometric saccades, correlates with his MRI showing large lesions in the brainstem and cerebellum.
  - The control of saccades comes from many integrated components of the central nervous system, especially those located in the brainstem and cerebellum. Some critical areas include the frontal eye fields, superior colliculus, paramedian pontine reticular formation (PPRF), medial longitudinal fasciculus (MLF), cerebellar vermis and fastigial nucleus. The cerebellar vermis and fastigial nuclei calibrate the size of the saccadic pulse, hence dysfunction of these pathways leads to saccadic dysmetria.
- The presence of brainstem and cerebellar disease not only affects eye movements, which can be visually disabling, but also impairs activities such as walking. Our patient has impaired gait due to left lower extremity weakness. His gait is improved with a Bioness device (knee brace which provides electrical nerve stimulation) and cane.
- Of particular interest is the fact that eye movement abnormalities often correlate with overall disease disability in patients with MS. Both cross-sectional and longitudinal analyses have found this correlation to be a reproducible finding.
- Servillo et al. found a positive association between the presence of oculomotor dysfunction (OMD) and the severity of disability quantified by the Expanded Disability Status Scale (EDSS).
- Serra et al. showed that MS patients with abnormal eye movements suffered more severe disability than those without OMDs, even though age and disease duration were similar between the two groups. A two-year follow up of the same cohort found that patients who presented with abnormal eye movements continued to suffer greater disability than patients without OMDs.
- Saccades are not routinely tested in patients with MS, however they are a sensitive test of brainstem and cerebellar function. It is important to realize that subtle INOs may only be clinically discernible during saccadic testing. During conventional tests of version (eg. “follow my light”), which is usually performed at a velocity of 70-90 degrees/second, the range of movement may seem “full” despite a diminished speed of the adducting eye.
- Our patient’s concomitant paracentral scotoma in the left eye, left INO, impaired smooth pursuit as well as an intermittent right exotropia further handicap his visual function.

V. TREATMENT AND MANAGEMENT
- We recommended for the patient Vision Therapy to assess techniques that may help him cope with his scotoma and improve visual tracking. Prospective approaches include:
  o Saccades:
    ▪ Loose prism jumps (monocular) from large to small looking at accuracy, speed, and the ability to detect movement changes
    ▪ Hart chart
    ▪ Michigan tracking
  o Pursuit/saccades:
    ▪ Groffman visual tracing (use pencil for pursuit; use only eyes for saccades)
    ▪ Peg board rotator
    ▪ VTS3 computer training program
  o Scanning techniques:
    ▪ Post-it notes (find all post-it notes in a given space)
    ▪ Pen and paper searches/puzzles
- The patient will also return to clinic to consider the benefits of prism correction in his spectacles to facilitate binocularity, especially at near/intermediate distances.
VI. CONCLUSION
- We need to look beyond optic neuritis and INOs when assessing the ocular health of a patient with MS.
- Oculomotor dysfunction (OMD) is common in patients with MS (prevalence ranges 32%-80% depending on the study), with saccadic dysmetria and impaired smooth pursuit being the most frequent OMDs.
- If symptoms are not reported by the patient, OMDs are often underestimated. Standard ocular motility testing that is limited to examining the range of movement without focusing on the dynamic properties of rapid eye movements may fail to reveal subtle abnormalities.
- Implementing an organized examination of saccade and pursuit function adds only a few minutes to the exam. We suggest following the protocol below (adapted from NSUCO):
  - Have the patient standing, with feet shoulder width apart, directly in front of the examiner at approximately 40 cm. Do not give instructions regarding head movement. Use small targets (1/2 cm in diameter) such as mounted sphere balls. Testing is performed binocularly. Observe and take notes regarding the patient’s accuracy, ability, and head/body movements (video recording may be helpful).
    - Saccades: Hold two targets approximately 20 cm apart, 10 cm on each side of the patient’s midline. Have the patient look at one target and then the other only when you instruct him or her to do so. Perform at least five round trips. Pay close attention to the relative velocity of each and both eyes.
    - Pursuit: Using one target, have the patient follow your target as it goes around. Move the target in a circular path approximately 20 cm in diameter. The upper and lower extent of the path should coincide with the patient’s midline. Perform in both clockwise and counterclockwise directions, at least two rotations in each direction.
- A precise examination of eye movements discloses not only pertinent information regarding disease location and disability in patients with MS, but may also have a substantial impact on the clinical management of MS patients. Our findings can suggest targeted symptomatic management and augment our ability to monitor disease progression, especially when subclinical lesions fall below the threshold for detection by MRI.

VII. REFERENCES


