Supplementary Online Content


eTable. Studies of Oculomotor Function and Pathologic Abnormalities in ALS (Chronically)

eReferences

This supplementary material has been provided by the authors to give readers additional information about their work.
<table>
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<tr>
<th>Study</th>
<th>Subjects</th>
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<tr>
<td>1</td>
<td>24 ALS</td>
<td>Bell phenomenon Voluntary gaze on command Pursuit movements Oculocephalic maneuvers</td>
<td>15/24 Alteration of Bell phenomenon 3/24 Impairment of conjugate ocular motility and upward gaze palsy</td>
</tr>
<tr>
<td>2</td>
<td>1 BO ALS</td>
<td>Case report Postmortem pathology</td>
<td>Marked limitation of all extraocular movements progressing to complete ophthalmoplegia toward the time of death</td>
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<tr>
<td>3</td>
<td>18 ALS</td>
<td>EOG</td>
<td>11/18 Defective pursuit eye movements 7/16 Abnormally large SWJs Saccades largely found normal except in 3 patients who demonstrated OKN</td>
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<tr>
<td>4</td>
<td>10 ALS</td>
<td>Eye movements Saccadic velocities Smooth pursuit</td>
<td>4/10 Decreased saccadic or smooth pursuit velocities ( all rapidly progressive ALS) 1/4 Unidirectional saccadic pursuit 1/4 Progressively decreasing saccade velocity</td>
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<tr>
<td>5</td>
<td>1 BO ALS 1 LO ALS</td>
<td>Case report Postmortem pathology</td>
<td>BO: Gaze-evoked rotatory nystagmus, horizontal nystagmus in the primary position, supranuclear paresis of horizontal and up-gaze  LO: Rotatory nystagmus evoked by lateral gaze</td>
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<tr>
<td>6</td>
<td>22 ALS</td>
<td>Electronystagmography</td>
<td>Abnormalities of OKN, pursuit, and saccadic eye movements correlating with severity but not duration</td>
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<td>7</td>
<td>18 ALS</td>
<td>Gaze on command in all planes Pursuit of examiner’s finger or face Bell phenomenon Corneal reflex</td>
<td>5/9 Altered Bell phenomenon 3/18 Slow ocular and eyelid movements 2/18 Spasmodic gaze fixation 5/18 Impersistence of continuous eyelid closure 2/18 Dissociated movements of eyeballs and eyelids during corneal stimulation</td>
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<td>8</td>
<td>37 Lytico-Bodig (ALS-PD-dementia complex)</td>
<td>Eye movements</td>
<td>12/37 Conjugate gaze limitation 9/28 Slowing of saccades 21/31 Jerky saccadic pursuit 18/26 Abnormal cancellation of VOR 6/31 Interruption of fixation 9/36 Gaze-evoked horizontal nystagmus 13/33 Abnormal OKN, ranging from no response to varied horizontal and vertical OKN 15/27 Impaired/absent convergence 21/31 Glabellar hyperreflexia (Myerson sign)</td>
</tr>
<tr>
<td>9</td>
<td>4 “Locked-in” ALS</td>
<td>Bedside assessment</td>
<td>Loss of voluntary ocular movements Loss of pursuit over time with slowing of saccades Nystagmus in 1 patient</td>
</tr>
<tr>
<td>10</td>
<td>23 ALS 7 Kennedy syndrome 2 Unclassified</td>
<td>Bedside assessment EOG</td>
<td>Clinically: 11/32 Incomplete convergence was observed in 11 cases 6/32 Horizontal gaze nystagmus was observed in 6 cases EOG: SWJs were recorded in 3 cases Amplitude ratio of saccade significantly higher in MND The degree of ocular dysmetria significantly higher in MND</td>
</tr>
</tbody>
</table>
| 11 | 1 ALS | Case report  
Postmortem pathology | Inability to close eyes voluntarily, with retention of reflex activity.  
Saccadic pattern on smooth pursuit  
Positive glabellar hyperreflexia |
|---|---|---|---|
| 12 | 25 LO ALS  
5 BO ALS | Study to monitor progression of voluntary motor impairment | 5/30 Complete voluntary external ophthalmoplegia  
18/30 Incomplete external ophthalmoplegia  
11/30 Spasmodic gaze fixation |
| 13 | 17 ALS | Infrared oculography | Marked reduction in pursuit gain in severely affected patients  
Asymmetric pursuit (leftward gain lower than rightward) |
| 14 | 2 ALS | Case report  
Postmortem pathology | External ophthalmoplegia (predominantly supranuclear)  
Slow saccades leading to slow eye movements  
Nuclear palsy as evidenced by loss of doll’s eye phenomenon |
| 15 | 2 ALS | Case report  
Postmortem pathology | Slow saccades and vertical gaze palsy suggestive of supranuclear ophthalmoplegia  
Degeneration of substantia nigra |
| 16 | 22 LO ALS  
12 BO ALS  
(5 with PD features) | Ocular pursuit  
Slow phases of OKN  
Ability to suppress VOR | Impairment of saccade and pursuit eye movements seen only in patients with PD-ALS  
Normal findings otherwise in patients without PD-ALS |
| 17 | 13 ALS  
2 PMA  
1 PLS | Random and fixed saccades  
Smooth pursuit  
OKN (using EOG) | Increased saccadic latencies  
Decreased smooth pursuit gain  
OKN (both mean and maximal velocity) unchanged |
| 18 | 27 ALS | Bedside examination  
Postmortem immunohistology | Clinically:  
3/27 Ophthalmoplegia  
Histologically:  
Same changes seen as in anterior horn (Bunina bodies, ubiquitin-positive skeinlike lesions, Lewy-body-like inclusions, conglomerate inclusions and spheroids) |
| 19 | 1 LO ALS | Case report  
Postmortem pathology | Early onset ophthalmoplegia (5 mo after symptom onset)  
Oculocephalic reflexes abolished |
| 20 | 6 “Bulbar signs”  
3 “Limb-only signs” | Pursuit gain  
Optokinetic adaptation limit  
Peak velocity  
Percentage reduction of slow-phase velocity of vertical nystagmus | Decrease in saccade velocity  
Oculomotor abnormalities in those with bulbar signs |
| 21 | 9 ALS | Sinusoidal smooth pursuit eye movements | Moderately affected patients showed an acceleration but not velocity saturation  
Severely affected patients’ performance decreased with increased velocity |
| 22 | 13 LO ALS  
4 BO ALS | Reflexive, remembered, and antisaccades  
Smooth pursuit | Latency in the anti-saccade and remembered saccades  
Elevated error rates (distractibility)  
No abnormality of reflexive saccades |
| 23 | 8 ALS | EOG | 3/8 Progressive changes on EOG  
3/8 Intermittent changes with normal EOG (1 patient) and progressive changes on EOG  
2/8 Progressively pathologic |
<p>| 24 | 1 BO ALS | Eye movements | Slow vertical saccades, especially up-gaze |</p>
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<tr>
<td>25</td>
<td>1 BO ALS</td>
<td>Case report</td>
<td>Progressive supranuclear ophthalmoplegia</td>
</tr>
<tr>
<td>26</td>
<td>“Suspected” ALS</td>
<td>Case report</td>
<td>Vertical gaze palsy and impairment of saccades. Degenerative process severely affecting the lower motor neurons, and the neurons of the pars compacta of the substantia nigra among other structures</td>
</tr>
<tr>
<td>27</td>
<td>1 BO ALS</td>
<td>Case report</td>
<td>Slow saccades in both vertical and horizontal planes</td>
</tr>
<tr>
<td>28</td>
<td>1 LO ALS</td>
<td>Eye movements</td>
<td>Vertical saccades markedly impaired. Vertical eye movements severely limited</td>
</tr>
<tr>
<td>29</td>
<td>11 BO ALS</td>
<td>Eye movements</td>
<td>9/11 Vertical saccade impairment. 5/6 Slowing of saccades</td>
</tr>
<tr>
<td>30</td>
<td>7 EE definite 19 EE probable 14 EE possible 4 EE suspected</td>
<td>Immunohistochemical analysis of EOMs</td>
<td>Saccadic intrusion amplitude mean fixation period. Increased saccadic intrusion amplitude. No difference in ocular fixation</td>
</tr>
<tr>
<td>31</td>
<td>8 ALS 4 controls</td>
<td>Immunohistochemical analysis of EOMs</td>
<td>Reduced proportion of MyHC slow tonic fibers in ALS. Absent MyHC embryonic in ALS. EOMs notably preserved compared with the limb muscles in ALS</td>
</tr>
<tr>
<td>32</td>
<td>14 BO ALS 30 LO ALS 45 Controls</td>
<td>Neuropsychology</td>
<td>Reflexive saccades slower in BO compared with LO and controls. Antisaccade latency and antisaccade type 1 errors increased in ALS. Antisaccade errors and velocity gain correlated with neuropsychology impairment</td>
</tr>
<tr>
<td>33</td>
<td>1 LO ALS</td>
<td>Eye movements</td>
<td>Low-amplitude ocular flutter</td>
</tr>
</tbody>
</table>

**Abbreviations:** ALS, amyotrophic lateral sclerosis; BO, bulbar-onset; EE, el-escorial; EOG, electro-oculography; EOM, extraocular muscles; LO, limb-onset; MyHC, myosin heavy chain; MND, motor neuron disease; OKN, optokinetic nystagmus; PD, Parkinson disease; PLS, primary lateral sclerosis; PMA, progressive muscular atrophy; SWJ, square wave jerk; VOG, vestibulo-ocularography; VOR, vestibulo-ocular reflex.
References