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

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>
<th>Assessment</th>
<th>Results</th>
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<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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<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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<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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<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>
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<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 glabella 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 Post-mortem 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>
<table>
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<tr>
<th>Page</th>
<th>Case Study</th>
<th>Method</th>
<th>Description</th>
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<tbody>
<tr>
<td>1</td>
<td>LO ALS</td>
<td>Postmortem pathology</td>
<td>Cell loss in the rostral interstitial nucleus of the media longitudinal fasciculus and substantia nigra</td>
</tr>
<tr>
<td>25</td>
<td>1 BO ALS</td>
<td>Case report</td>
<td>Progressive supranuclear ophthalmoplegia</td>
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<tr>
<td>26</td>
<td>1 “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 &lt;br&gt; 19 EE probable &lt;br&gt; 14 EE possible &lt;br&gt; 4 EE suspected</td>
<td>Saccadic intrusion amplitude mean fixation period</td>
<td>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>Infrared oculography (saccades, antisaccades, and pursuit) 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-oculography; VOR, vestibulo-ocular reflex.
References

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