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.
Studies of Oculomotor Function and Pathology in ALS (Chronologically)

<table>
<thead>
<tr>
<th>Study</th>
<th>Subjects</th>
<th>Assessment</th>
<th>Results</th>
</tr>
</thead>
</table>
| 1     | 24 ALS   | Bell phenomenon  
Voluntary gaze on command  
Pursuit movements  
Oculocephalic maneuvers | 15/24 Alteration of Bell phenomenon  
3/24 Impairment of conjugate ocular motility and upward gaze palsy |
| 2     | 1 BO ALS | Case report  
Postmortem pathology | Marked limitation of all extraocular movements progressing to complete ophthalmoplegia toward the time of death |
| 3     | 18 ALS   | EOG | 11/18 Defective pursuit eye movements  
7/16 Abnormally large SWJs  
Saccades largely found normal except in 3 patients who demonstrated OKN |
| 4     | 10 ALS   | Eye movements  
Saccadic velocities  
Smooth pursuit | 4/10 Decreased saccadic or smooth pursuit velocities (all rapidly progressive ALS)  
1/4 Unidirectional saccadic pursuit  
1/4 Progressively decreasing saccade velocity |
| 5     | 1 BO ALS  
1 LO ALS | Case report  
Postmortem pathology | 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 |
| 6     | 22 ALS   | Electronystagmography | Abnormalities of OKN, pursuit, and saccadic eye movements correlating with severity but not duration |
| 7     | 18 ALS   | Gaze on command in all planes  
Pursuit of examiner’s finger or face  
Bell phenomenon  
Corneal reflex | 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 |
| 8     | 37 Lytico-Bodig (ALS-PD-dementia complex) | Eye movements | 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) |
| 9     | 4 “Locked-in” ALS | Bedside assessment | Loss of voluntary ocular movements  
Loss of pursuit over time with slowing of saccades  
Nystagmus in 1 patient |
| 10    | 23 ALS  
7 Kennedy syndrome  
2 Unclassified | Bedside assessment  
EOG | 11/32 Incomplete convergence was observed in 11 cases  
6/32 Horizontal gaze nystagmus was observed in 6 cases |

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

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Inability to close eyes voluntarily, with retention of reflex activity
Saccadic pattern on smooth pursuit
Positive glabellar hyperreflexia

Marked reduction in pursuit gain in severely affected patients
Asymmetric pursuit (leftward gain lower than rightward)

External ophthalmoplegia (predominantly supranuclear)
Slow saccades leading to slow eye movements
Nuclear palsy as evidenced by loss of doll's eye phenomenon

Slow saccades and vertical gaze palsy suggestive of supranuclear ophthalmoplegia
Degeneration of substantia nigra

Impairment of saccade and pursuit eye movements seen only in patients with PD-ALS
Normal findings otherwise in patients without PD-ALS

Increased saccadic latencies
Decreased smooth pursuit gain
OKN (both mean and maximal velocity) unchanged

3/27 Ophthalmoplegia

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)

Moderately affected patients showed an acceleration but not velocity saturation
Severely affected patients’ performance decreased with increased velocity

Latency in the anti-saccade and remembered saccades
Elevated error rates (distractibility)
No abnormality of reflexive saccades

3/8 Progressive changes on EOG
3/8 Intermittent changes with normal EOG (1 patient) and progressive changes on EOG
2/8 Progressively pathologic

Slow vertical saccades, especially up-gaze
<table>
<thead>
<tr>
<th></th>
<th>Postmortem pathology</th>
<th>Cell loss in the rostral interstitial nucleus of the medial longitudinal fasciculus and substantia nigra</th>
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</thead>
<tbody>
<tr>
<td>25</td>
<td>1 BO ALS</td>
<td>Progressive supranuclear ophthalmoplegia</td>
</tr>
<tr>
<td>26</td>
<td>1 “Suspected” ALS</td>
<td>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>Slow saccades in both vertical and horizontal planes</td>
</tr>
<tr>
<td>28</td>
<td>1 LO ALS</td>
<td>Vertical saccades markedly impaired. Vertical eye movements severely limited</td>
</tr>
<tr>
<td>29</td>
<td>11 BO ALS</td>
<td>9/11 Vertical saccade impairment 5/6 Slowing of saccades</td>
</tr>
<tr>
<td>30</td>
<td>7 EE definite</td>
<td>Increased saccadic intrusion amplitude No difference in ocular fixation</td>
</tr>
<tr>
<td></td>
<td>19 EE probable</td>
<td></td>
</tr>
<tr>
<td></td>
<td>14 EE possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4 EE suspected</td>
<td></td>
</tr>
<tr>
<td>31</td>
<td>8 ALS 4 controls</td>
<td>Reduced proportion of MyHC slow tonic fibers in ALS</td>
</tr>
<tr>
<td></td>
<td>Immunohistochemical analysis of EOMs</td>
<td>Absent MyHC embryonic in ALS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>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>Reflexive saccades slower in BO compared with LO and controls</td>
</tr>
<tr>
<td></td>
<td>Infrared oculography</td>
<td>Antisaccade latency and antisaccade type 1 errors increased in ALS</td>
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<tr>
<td></td>
<td>(saccades, antisaccades, and pursuit) Neuropsychology</td>
<td>Antisaccade errors and velocity gain correlated with neuropsychology impairment</td>
</tr>
<tr>
<td>33</td>
<td>1 LO ALS</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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