Hot Topics in Neuromuscular Medicine: EDX and US

Ruple S. Laughlin MD
Financial Disclosure

Nothing to Disclose
Objectives

• To review themes in recent articles highlighting utilization or innovative applications of nerve conduction studies (NCS), needle electromyography (EMG) or ultrasonography (US) to neuromuscular diseases

• To identify important strengths and possible limitations of these studies

• To delineate take-home points that may be practice-changing or represent emerging science in electrodiagnostic studies (EDX)
Theme #1

Needle EMG correlation with muscle biopsy
EMG and muscle biopsy: Background and Significance

- Patients presenting with myalgia (with or without weakness) are often seen by a specialist.
- EMG study is a frequent tool used in the evaluation of these patients.
- These EDX findings, in turn, will guide therapy or further evaluations (i.e., muscle biopsy, genetics, and/or therapy or more blood work).

EMG and muscle biopsy: Background

- Typically, the focus of the EMG study is needle EMG data.
- Fibrillation potentials are generated from muscle fibers that have been separated from their endplate zone → Results in a functionally denervated muscle fiber.
  - Can occur due to various pathological mechanisms.
  - Purported to predict the presence of specific pathologic features on muscle biopsy.
- Motor unit potential changes can be identified by EMG in myopathic conditions affecting type 1 (large) muscle fibers.
  - Includes pathological changes resulting in loss of muscle fibers, muscle fiber size variation and regeneration or reinnervation of muscle fibers.

Myalgia with the presence of pathologic EMG correlates with perimysial inflammatory infiltrates

Kirsten Johannsen, MD, Nicholas Schwab, PhD, Carsten P. Wessig, MD, Karlheinz Reiners, MD, Heinz Wiendl, MD, and Claudia Sommer, MD

Neuroimmunol Neuroinflamm 2019;6:e549. doi:10.1212/NXI.0000000000000549

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Needle Electromyography and Histopathologic Correlation in Myopathies

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Muscle Biopsy and Electromyography Correlation

Elie Naddaf1*, Margherita Milone1, Michelle L. Mauermann1, Jayawnt Mandrekar2 and William J. Litchy1

Front. Neurol. 09 October 2018 | https://doi.org/10.3389/fneur.2018.00839
Myalgia with the presence of pathologic EMG correlates with perimysial inflammatory infiltrates

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Aim of study

- Identify normal T cell and macrophage count in muscle
- Evaluate the frequency of these markers in patients with myalgia or elevated CK who had abnormal EMG

Methods:

- Measured CD3+, CD4+, CD8+ and immunostaining to CD68+, MHC1, MRP8 in 71 biopsies
- Split into 4 groups
  - Group 1 = myalgia only (normal lab and clinical findings); n = 24
  - Group 2 = Asymptomatic elevation of CK; n = 26 (range 300-20,000 IU/L)
  - Group 3 = myalgia + “pathologic” EMG; n = 9; 6 with elevated CK (median 70 IU/L)
    - Concentric needle examination of the deltoid, biceps, AT, rectus femoris → abnormal if with short, small rapidly recruited fibers
  - Group 4 = Healthy control who had malignant hyperthermia testing; n = 12
## Synopsis of Patient Data

<table>
<thead>
<tr>
<th>Group 1 – myalgia</th>
<th>Group 2 – asymptomatic hyperCKemia</th>
<th>Group 3 – myalgia and pathologic EMG</th>
<th>Group 4 – normal (MH testing negative)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pts. (no.)</td>
<td>M</td>
<td>F</td>
<td>Age at biopsy (range, mean)</td>
<td>M</td>
</tr>
<tr>
<td>24</td>
<td>11</td>
<td>13</td>
<td>18-66 (40.2)</td>
<td>14</td>
</tr>
<tr>
<td>26</td>
<td>18</td>
<td>8</td>
<td>7-70 (27.1)</td>
<td>0</td>
</tr>
<tr>
<td>9</td>
<td>6</td>
<td>3</td>
<td>19-67 (45.8)</td>
<td>6</td>
</tr>
<tr>
<td>12</td>
<td>6</td>
<td>6</td>
<td>6-72 (38.8)</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>71</td>
<td>41</td>
<td>30</td>
<td>6-72 (36.0)</td>
</tr>
<tr>
<td>Positive controls</td>
<td>13</td>
<td>2</td>
<td>11</td>
<td>31-73 (60.8)</td>
</tr>
<tr>
<td>DM</td>
<td>5</td>
<td>1</td>
<td>4</td>
<td>63-73 (68.6)</td>
</tr>
<tr>
<td>PM</td>
<td>4</td>
<td>1</td>
<td>3</td>
<td>31-67 (46.3)</td>
</tr>
<tr>
<td>IBM</td>
<td>4</td>
<td>0</td>
<td>4</td>
<td>60-72 (65.5)</td>
</tr>
</tbody>
</table>

Abbreviations: CK = creatine kinase; DM = dermatomyositis; IBM = inclusion body myositis; MH = malignant hyperthermia; PM = polymyositis; R = symptoms at rest, E = symptoms at exercise.
Myalgia and Muscle Biopsy: Summary of Findings

Results

- Group 1, 2 and 4 had similar CD3 and CD68 concentrations
- Only group 3 (abnl EMG) had increased numbers of perimysial macrophages, perimysial CD3+ and CD8+ lymphocytes and all had MRP8 expression

Conclusions

- Normal muscle has large macrophage and T-lymphocyte numbers but not MHC1 or markers of macrophage activation (MRP8)
- Muscle biopsy is likely to be helpful in patient with myalgia or hyperCKemia ONLY if “pathologic “ EMG is present
Myalgia and Muscle Biopsy: Limitations

• Unclear if each muscle needled had to have ALL findings (short duration, small amplitude AND rapid recruitment)

• Unclear if only required findings in one muscle

• No comment made on relevance of abnormal spontaneous activity (fibrillation potentials, myotonic)
  ○ Acknowledged that 1 of 9 had positive sharp waves but did not identify if this biopsy was different in any way

• MHC1 can be very sensitive but not very specific in delineating inflammatory from non-inflammatory myopathies
Muscle Biopsy and Electromyography Correlation

Elie Naddaf1*, Margherita Milone1, Michelle L. Mauermann1, Jayawant Mandrekar2 and William J. Litchy1

1 Department of Neurology, Mayo Clinic, Rochester, MN, United States, 2 Department of Internal Medicine, Mayo Clinic, Rochester, MN, United States

Aims:

o To determine if there is correlation between EDX features and specific histopathological findings on muscle biopsy

Methods:

o Retrospective muscle biopsy re-review of 75 patients over 1 year who underwent EMG and had muscle biopsy of same muscle (typically contralateral)
  • Also reviewed 25 additional patients with rare biopsy findings
o Muscle pathologist blinded to EMG findings
  • Created new clinical muscle biopsy grading scale in order to be systematic
  • Graded 17 histopathological findings
o Correlated biopsy findings to the following electrophysiological features:
  • Fibrillations
  • Motor unit potential duration
  • Motor unit potential recruitment and complexity
<table>
<thead>
<tr>
<th>Grading Criteria</th>
<th>Histopathologic finding</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Quantitative</strong></td>
<td>Necrotic fibers; regenerating fibers; fiber splitting; fibers harboring vacuoles; ragged-red fibers; cytochrome c oxidase negative fibers; fibers with target formations; fibers with increased glycogen content; fibers over-reacting to non-specific esterase; fibers with congophilic inclusions</td>
<td>0: Normal</td>
</tr>
<tr>
<td></td>
<td>Atrophic fibers</td>
<td>1: or rare: 3 or less per biopsy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2: or mild: more than 3 per biopsy, less than 1 per 10X-power field</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3: or moderate: 1 or more per 10X-power field, less than 2 per 10X-power field</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4: or severe: 2 or more per 10X-power field</td>
</tr>
<tr>
<td><strong>Semi quantitative</strong></td>
<td>Inflammation:</td>
<td>0: Normal</td>
</tr>
<tr>
<td></td>
<td>1: or rare: Occasional atrophic fibers, less than 1 per 10X power field</td>
<td>1: or rare: Minimal scattered inflammation</td>
</tr>
<tr>
<td></td>
<td>2: or mild: scattered atrophic fibers occurring singly, or in pairs, about 1 fiber or pair per 10X power field</td>
<td>2: or mild: 1 small collection per 5X-power field</td>
</tr>
<tr>
<td></td>
<td>3: or moderate: atrophic fibers forming small groups of up to 5 fibers per group, about 1 small group per 10X power field</td>
<td>3: or moderate: 2 small collections per 5X-power field</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4: or severe: Atrophic fibers forming large groups (more than 5 fibers per group), about 1 large group per 10X power field</td>
</tr>
<tr>
<td><strong>Qualitative</strong></td>
<td>Type 1 fiber atrophy</td>
<td>0: Normal</td>
</tr>
<tr>
<td></td>
<td>2: mild (type 1 fibers have a mildly smaller diameter than type 2 fibers)</td>
<td>2: mild (type 2 fibers have a mildly smaller diameter than type 1 fibers)</td>
</tr>
<tr>
<td></td>
<td>4: severe (type 1 fibers have a markedly smaller diameter than type 2 fibers)</td>
<td>4: severe (type 2 fibers have a markedly smaller diameter than type 1 fibers)</td>
</tr>
<tr>
<td></td>
<td>Type 2 fiber atrophy</td>
<td>0: Normal</td>
</tr>
<tr>
<td></td>
<td>2: mild (type 2 fibers have a mildly smaller diameter than type 1 fibers)</td>
<td>1: mildly increased focally</td>
</tr>
<tr>
<td></td>
<td>4: severe (type 2 fibers have a markedly smaller diameter than type 1 fibers)</td>
<td>2: mildly increased</td>
</tr>
<tr>
<td></td>
<td>Endomysial connective tissue</td>
<td>3: moderately increased</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4: severely increased</td>
</tr>
<tr>
<td></td>
<td>Fiber type grouping</td>
<td>0: random distribution of histochemical fiber types</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1: or rare: One small group</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2: or mild: occasional grouping</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3: or moderate: frequent grouping</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4: or severe: Most fascicles display fiber type grouping</td>
</tr>
</tbody>
</table>
Muscle Biopsy and EMG Correlation: Summary of Findings

- Fibrillation potentials were not specific (seen in 68 (68%) of patient on EDX)
  - Seen in wide range of histopathology: atrophic fibers, necrotic, regenerating, splitting, NSE+, vacuoles, inclusion, increased endomysial or perimysial inflammation

- Short duration fibers seen in more patients (85%) within a narrower subset of histopathological changes
  - Atrophy, necrosis, decreased connective tissue and perimysial but no endomysial inflammation

- Also looked at correlations between complexity and recruitment

(Naddaf, Milone et al. 2018)
| FIGURE 3. Results summary. Histopathologic (rows) vs. electromyographic (columns) findings: statistically significant correlations are marked with a star. |
|---|---|---|---|---|---|---|
| **Fibrillation potentials** | **Short duration MUP** | **Long duration MUP** | **Increased Phases** | **Increased Turns** | **Rapid Recruitment** | **Myotonic Discharges** |
| Atrophic fibers | ⭐️ | ⭐️ | | | | |
| Necrotic fibers | ⭐️ | | | | | |
| Regenerating fibers | | ⭐️ | | | ⭐️ | |
| Fiber splitting | | | | | | |
| Vacuoles | | | | | | |
| Ragged-red fibers | | | | | | |
| CCO negative | | | | | | |
| Target formations | | | | ⭐️ | | |
| Increased glycogen | | | | | | |
| NSE positive | | ⭐️ | | ⭐️ | | |
| Congophilic inclusions | | ⭐️ | | | | |
| Increased endomysial connective tissue | | ⭐️ | | ⭐️ | ⭐️ | ⭐️ |
| Perimysial inflammation | | ⭐️ | | | | |
| Endomysial inflammation | | | | | | |
| Fiber type grouping | | | | ⭐️ | | |
| Type 1 fiber atrophy | | | | | | |
| Type fiber atrophy | | | | | | |

(Naddaf, Milone et al. 2018)
Aim:
- To assess whether specific voluntary or spontaneous needle EMG findings can predict certain pathological findings on muscle biopsy or types of myopathy

Methods:
- Reviewed muscle biopsy findings and EMG findings in 218 patients referred for muscle biopsy
  - Calculated sensitivity and specificity of specific EDX features as well as the PPV and NPV of individual and combined needle EMG features in having an abnormal biopsy
- EMG diagnosis = possible myopathy in 178 (82%)
  - Of these, 143 (80.3%) given final diagnosis of myopathy
- Final diagnosis of myopathy from all 218 after muscle biopsy =
  - Mismatch as some were metabolic myopathies (muscle fiber them

### Table 1. Number of patients with specific myopathic and nonmyopathic final diagnoses

<table>
<thead>
<tr>
<th>Condition</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammatory myopathies, n = 62</td>
<td>Dermatomyositis 14</td>
</tr>
<tr>
<td></td>
<td>Symptomatic CPT II carrier 3</td>
</tr>
<tr>
<td>Inclusion body myositis</td>
<td>McArdle disease 21</td>
</tr>
<tr>
<td></td>
<td>Amyloidosis 2</td>
</tr>
<tr>
<td>Mixed connective tissue disease</td>
<td>Polymyositis 9</td>
</tr>
<tr>
<td></td>
<td>Critical illness myopathy 3</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>Inclusion body myopathy 1</td>
</tr>
<tr>
<td>Scleroderma</td>
<td>Mitochondrial myopathy 2</td>
</tr>
<tr>
<td>Sjogren syndrome</td>
<td>Radiation induced 1</td>
</tr>
<tr>
<td>Not further classified</td>
<td>Other 12</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Muscular dystrophies, n = 19</th>
<th>Nonmyopathy diagnosis, n = 68</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calpainopathy</td>
<td>HyperCKemia 6</td>
</tr>
<tr>
<td>Dysferlinopathy</td>
<td>Denervation atrophy 5</td>
</tr>
<tr>
<td>Other limb girdle dystrophy</td>
<td>Type 2 fiber atrophy of unclear etiology 7</td>
</tr>
<tr>
<td>Dysferrochelatosis</td>
<td>Motor neuron disease 4</td>
</tr>
<tr>
<td>FSH dystrophy</td>
<td>Neuromuscular junction disorder 2</td>
</tr>
<tr>
<td>OPMD</td>
<td>Polyradiculopathy 2</td>
</tr>
<tr>
<td>Myotonic dystrophy</td>
<td>Other conditions 8</td>
</tr>
<tr>
<td></td>
<td>No clearly established diagnosis 37</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Congenital myopathies, n = 8</th>
<th>Myopathy of unknown etiology, n = 36</th>
</tr>
</thead>
<tbody>
<tr>
<td>Centronuclear</td>
<td>1</td>
</tr>
<tr>
<td>Multicore</td>
<td>1</td>
</tr>
<tr>
<td>Myofibrillar</td>
<td>2</td>
</tr>
<tr>
<td>Nemaline rod</td>
<td>2</td>
</tr>
<tr>
<td>Not further classified</td>
<td>2</td>
</tr>
</tbody>
</table>

CPT, carnitine palmityl transferase; FSH dystrophy, fascioscapulohumeral muscular dystrophy; OPMD, oculopharyngeal muscular dystrophy.
Needle EMG and Muscle Biopsy: Summary of Findings

• Overall sensitivity of EMG was 95.3% in confirming a pathologic myopathy diagnosis
  o Specificity was 48.5%
  o Other conditions: hyperCKemia, denervation atrophy, MND, NMJ, GBS, unknown (18)

• Presence of fibrillation potentials 65-74% sensitive and 55-81% specific for any pathological change
  o Similar sensitivity and specificity whether with or without Short MUPs

<table>
<thead>
<tr>
<th></th>
<th>Inflammation Sn/Sp (%)</th>
<th>Fiber necrosis Sn/Sp (%)</th>
<th>Fiber splitting Sn/Sp (%)</th>
<th>Vacuoles Sn/Sp (%)</th>
<th>Any abnormality Sn/Sp (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibs</td>
<td>73.1/67.9</td>
<td>71.4/73.3</td>
<td>74.2/57.8</td>
<td>67.3/59.9</td>
<td>65.4/80.7</td>
</tr>
<tr>
<td>Short-duration MUP</td>
<td>85.9/38.6</td>
<td>83.7/40.8</td>
<td>93.5/33.7</td>
<td>88.5/35.5</td>
<td>93.1/48.9</td>
</tr>
<tr>
<td>Fibs and short MUP</td>
<td>78.9/72.9</td>
<td>64.3/76.7</td>
<td>71.0/63.1</td>
<td>63.5/65.1</td>
<td>59.2/84.1</td>
</tr>
<tr>
<td>Myotonic discharges</td>
<td>3.8/93.6</td>
<td>6.1/95.0</td>
<td>19.4/96.8</td>
<td>9.6/95.8</td>
<td>6.9/96.6</td>
</tr>
</tbody>
</table>

(Sener, Martinez-Thompson et al. 2019)
Needle EMG and Muscle Biopsy: Summary of Findings

- Absence of fibrillation potentials had high NPV: **80% NPV**
  - No fibrillations = less likely there is a destructive process

### PPV and NPV of EMG Findings for Selected Pathological Changes on Biopsy

<table>
<thead>
<tr>
<th>Findings</th>
<th>Inflammation PPV/NPV (%)</th>
<th>Fiber necrosis PPV/NPV (%)</th>
<th>Fiber splitting PPV/NPV (%)</th>
<th>Vacuoles PPV/NPV (%)</th>
<th>Any abnormality PPV/NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibs</td>
<td>55.9/81.9</td>
<td>68.6/5.9</td>
<td>22.5/93.1</td>
<td>34.30/85.3</td>
<td><strong>83.3/61.2</strong></td>
</tr>
<tr>
<td>Short-duration MUP</td>
<td>43.8/83.1</td>
<td>53.6/75.4</td>
<td>19.0/96.9</td>
<td>30.1/90.8</td>
<td>70.6/66.2</td>
</tr>
<tr>
<td>Fibs and short MUP</td>
<td>58.2/80.3</td>
<td>69.2/72.4</td>
<td>24.2/92.9</td>
<td>36.3/85.0</td>
<td>84.6/58.3</td>
</tr>
<tr>
<td>Myotonic discharges</td>
<td>25.0/63.6</td>
<td>50.0/55.3</td>
<td>50.0/87.9</td>
<td>41.7/77.2</td>
<td>75.0/41.3</td>
</tr>
</tbody>
</table>

EMG, electromyography; Fibs, fibrillation potentials; MUP, motor unit potentials; NPV, negative predictive value; PPV, positive predicting value

- However, **PPV were low for SPECIFIC histopathological changes**
<table>
<thead>
<tr>
<th>Findings</th>
<th>Fibs, n (%)</th>
<th>Short-duration MUP, n (%)</th>
<th>Fibs and short MUP, n (%)</th>
<th>Myotonic discharges, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammatory (n=62)</td>
<td>45 (72.6)</td>
<td>60 (96.8)</td>
<td>44 (71.0)</td>
<td>1 (1.6)</td>
</tr>
<tr>
<td>Congenital myopathy (n=8)</td>
<td>4 (50.0)</td>
<td>6 (75.0)</td>
<td>4 (50.0)</td>
<td>2 (25.0)</td>
</tr>
<tr>
<td>Muscular dystrophy (n=19)</td>
<td>12 (63.2)</td>
<td>17 (89.5)</td>
<td>11 (57.9)</td>
<td>3 (15.8)</td>
</tr>
<tr>
<td>Mitochondrial (n=2)</td>
<td>1 (50.0)</td>
<td>1 (50.0)</td>
<td>1 (50.0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Other myopathy (n=23)</td>
<td>14 (60.9)</td>
<td>16 (69.6)</td>
<td>11 (47.8)</td>
<td>2 (8.7)</td>
</tr>
<tr>
<td>Unclear etiology (n=36)</td>
<td>14 (38.9)</td>
<td>29 (80.6)</td>
<td>11 (30.6)</td>
<td>3 (8.3)</td>
</tr>
<tr>
<td>Nonmyopathy (n=68)</td>
<td>13 (19.1)</td>
<td>24 (35.3)</td>
<td>9 (13.2)</td>
<td>1 (1.5)</td>
</tr>
</tbody>
</table>

EMG, electromyography; Fibs, fibrillation potentials; MUP, motor unit potentials
Needle EMG and Muscle Biopsy: Summary of Findings

- Short duration motor unit potentials *sensitive but not as specific* for “inflammatory” features
- Fibrillation potentials *less sensitive but more specific* for identifying an *inflammatory* myopathy
- ➔ *Both helpful to identify a myopathy is present, but not in subtyping the pathological process*

<table>
<thead>
<tr>
<th>Findings</th>
<th>Inflammation PPV/NPV (%)</th>
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EMG, electromyography; Fibs, fibrillation potentials; MUP, motor unit potentials; NPV, negative predictive value; PPV, positive predicting value
Muscle Biopsy and Needle EMG: Limitations of Study 2 and 3

• Both studies retrospective
• All patients “abnormal” in some way (all sent to EMG lab)
  o All patients ended up with biopsy, likely increasing the number of abnormal EMGs
• Needle examination semi-quantitative in all cases
• Myopathies can be patchy, therefore EMG or biopsy may be flawed
• Immune therapies not controlled for in either (although identified in #2)
• Any pathological processes affecting type 2 fibers would not have been identified
• Only small subset with myotonia (#2: n=8; #3: n=12)
  o Consider selection bias
  o If myotonia present diffusely, more likely to move to genetic testing
Needle EMG and Muscle Biopsy: Take Home Points

• These 3 papers elucidated the correlation between EDX findings and muscle biopsy findings in patients referred for myopathy

• Abnormal EMG features can help predict an abnormal muscle biopsy (Johannsen)

• Fibrillation potentials are highly sensitive as a predictor of muscle pathology (Sener) but not very specific as to the nature of the histopathologic change (Naddaf)
Theme #2

US as a diagnostic tool in Ulnar Neuropathy
UNE and US: Background

- US is being used increasingly in EDX studies
- US as an adjunct (and occasionally the only test) is quite common in CTS
  - Studies show a narrow range for median nerve cross-sectional area (CSA) at the wrist
- Ulnar neuropathy at the elbow (UNE) is second most common mononeuropathy
  - EDX not always abnormal, and when abnormal, not always localizing
- Sensitivity range of US for UNE is quite large
  - CSA of the ulnar nerve is influenced more prominently by height, BMI, age and sex than the median nerve; absolute measures/cutoffs difficult
  - Bilateralism (1/3 of cases) makes side-to-side evaluations difficult
Diagnostic sensitivity of electrophysiology and ultrasonography in ulnar neuropathies of different severity

Luciana Pelosi a,*, Eoin Mulroy b

• Aim:
  o To evaluate the accuracy of electrophysiological and ultrasound testing referred with neuropathic symptoms in the ulnar distribution of varying severity
  o Severity was graded on a 4 point scale of symptoms and physical findings:
    • 1- Very mild: Symptoms only
    • 2- Mild: Above plus reduced sensation in ulnar distribution or very mild weakness ADM>FDI (MRC>4)
    • 3- Moderate: Above plus ADM/FDI weakness or atrophy MRC 4
    • 4- Severe: Sensation reduced or absent, with ADM/FDI weakness MRC <

• Methods:
  o 135 consecutive patients (141 arms) NCS studies followed AANEM guidelines (included inching techniques as indicated)
  o Needle EMG of additional ulnar muscles was performed when NCS were non-localizing
  o EDX graded on 4 point scale
  o Ultrasound testing involved scanning from the wrist to mid-humerus with measurements of cross-sectional nerve area where the nerve was the thickest (CSA max) on the same day as EDX

1. Normal
2. Mild: reduced SNAP with nl CMAP
3. Moderate: reduced SNAP and CMAP or absent SNAP with nl or mildly reduced CMAP with abnormal EMG
4. Severe: absent SNAP and absent or markedly reduced CMAP
US in UNE of differing severity: Summary of Findings

<table>
<thead>
<tr>
<th>Clinical severity</th>
<th>V mild</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>All 4 Severity</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of nerves</td>
<td>54 (38%)</td>
<td>40 (28%)</td>
<td>24 (17%)</td>
<td>23 (16%)</td>
<td>141 (100%)</td>
<td>100</td>
</tr>
<tr>
<td>FDX &amp; US abnormal</td>
<td>1</td>
<td>18</td>
<td>23</td>
<td>23</td>
<td>65</td>
<td>46</td>
</tr>
<tr>
<td>EDX abnormal</td>
<td>2</td>
<td>19</td>
<td>23</td>
<td>23</td>
<td>67</td>
<td>47</td>
</tr>
<tr>
<td>US abnormal</td>
<td>11</td>
<td>25</td>
<td>24</td>
<td>23</td>
<td>83</td>
<td>58</td>
</tr>
<tr>
<td>Total abnormal</td>
<td>13</td>
<td>25</td>
<td>24</td>
<td>23</td>
<td>84</td>
<td>60</td>
</tr>
<tr>
<td>Total normal</td>
<td>41</td>
<td>15</td>
<td>0</td>
<td>0</td>
<td>57</td>
<td>40</td>
</tr>
<tr>
<td>(Sub) Luxation</td>
<td>14</td>
<td>6</td>
<td>2</td>
<td>2</td>
<td>24</td>
<td>17</td>
</tr>
</tbody>
</table>

- Overall, sensitivity was *slightly higher* for US 83/141 (58%) than EDX 67/141 (47%)
  - The difference was almost exclusively driven by testing of the clinically “very mild” group (20% for US; 3% for EDX) and the clinically “mild” group (62% vs. 47%, respectively)
  - **Both** techniques had extremely high sensitivity (100%) in clinically moderate and severe groups
- A combination of the two techniques resulted in a higher sensitivity
US in UNE of differing severity:
Summary of Findings

• Sensitivity improved greatly in both EDX and US groups when “very mild” or “mild” ulnar neuropathies were excluded:
  o Sensitivity of US 58% → 82%
  o Sensitivity of EDX 47% → 72%

• Important to keep nonetheless, as this group represented almost 40% of referrals to EDX
  o This data suggests utilizing US in these milder cases

• 25 of their patients did not have localizing studies by EDX
  o 17% of total referrals, over 1/3 of those with abnormal EDX
  o 18 were clinically moderate or severe
  o US abnormal in all 25 (increased CSA max at elbow in 22)

(Pelosi & Mulroy, 2019)
NEUROMUSCULAR ULTRASOUND IN ELECTRICALLY NON-LOCALIZABLE ULNAR NEUROPATHY

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Accepted 1 July 2018

• **Aim:**
  - Is there Value of high resolution ultrasound in non-localizable UN?

• **Methods:**
  - Prospectively studies 56 patients referred to EMG laboratory for UN
  - Sensory sx involving digit 5 and possibly 4
  - Used AAEM guidelines for UN in the EDX; minimum of 3 ulnar muscle sampled

• **12 had non-localizing studies and received US**
  - CSA measured and >10mm2 at any location considered abnormal
  - CSA elbow compared with CSA at mid forearm and mid-humerus
    - Ratio > 1.5= abnormal (this value is similar to earlier study)
UN in non-localizable UN: Summary of Findings

• HRUS able to localize abnormality in all 12:
  ○ 5 at retrocondylar groove
  ○ 2 cubital tunnel
  ○ 3 at both
  ○ 1 wrist
  ○ 1 RTC groove and tandem lesion more proximally

(Alrajeh & Preston, 2018)
US in UNE: Limitations:

- Main limitation in both studies is that the ultrasonagapher was not blinded
- Neither studied compared US directly to short incremental stimulation for localization
- Significant overlap in CSA max values in Pelosi study
  - Especially noted between mild and moderate clinical groups
  - CSA (nerve enlargement) without clinical and/or EDX correlate should NOT be used a measure of disease severity
UNE and US: Take Home Points

• US is a useful adjunct to EDX in the assessment of UNE
• US seemingly outperforms EDX in clinically very mild or mild cases of UN
• Conversely, CSA\text{max} should not be used in categorizing the severity of UN as there is overlap in nerve size in the milder clinical groups
• Major contribution of US in UN is in localization of abnormal but non-localizing EDX findings

(Terlemez, Yilmaz et al. 2018)
Theme #3

Machine Learning in needle EMG
AI Background

• 1956 John McCarthy coined “artificial intelligence”
  o Machines (now algorithms) that could perform “human” tasks such as learning and problem solving
• Currently, concept is one of “computational excellence”
  o In essence, pattern matching, image analysis or patterned decision making as a predictive tool
• AI in medicine is developing quickly
  o Does the concern need AI? Are their components of the image/discharge that are not accessible to the provider?
    • Arrhythmia monitors in watches, Devices to monitor movements; seizure detection
    • Google AI for lymph node analysis in BRCA
  o Can you integrate into existing workflow?
AI Background

• If yes, then generate AI algorithm
• First step: find structured data (label or annotation recognizable to an AI algorithm)

  CORE EFFORT OF ALL AI
  o Do we have enough data? Need large data sets to “train” machine algorithm
  o Is it Correct data? Biased data? (ethnic, age, etc….)
  o Is data presented in a way that it can be used? Legal issues?

• Second step: Test accuracy of algorithm “Validate model”
  o Usually done by using input data for which answers are known

• Third step: Optimize model
• Fourth step: Find way to implement easily into clinical work
Artificial Intelligence
Algorithms capable of demonstrating cognitive functions associated with the human mind, such as ‘learning’, ‘problem solving’, ‘adaptation’, ‘logic’, ‘if-then rules’, and/or decision trees

Machine Learning
A form of intelligence based on compilation of complex algorithms and software that mimics the human mind to decipher critical problems that include visual perception, speech recognition and decision making on exposure of more data over time

Deep Learning
Class of artificial neural networks that learn in a supervised and unsupervised manner

• Machine can learn or modify output based on new or increasing data (predicting a movie you might like from previously chosen movies)
• Deep learning algorithms
  o “Deep” = number of layers in the artificial neural (in this case, computer) network (ANN)
    • More layers → higher accuracy and ability to guide itself
• EMG waveforms are a potential area in which AI deep learning might be applied
Deep learning for waveform identification of resting needle electromyography signals

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CLASSIFICATION OF NEEDLE-EMG RESTING POTENTIALS BY MACHINE LEARNING

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Accepted 16 October 2018

• Authors published 2 separate papers looking at machine learning in the identification of resting needle EMG signals

• AIMS:
  
  o Assess the accuracy of machine learning algorithms in classifying resting needle EMG discharges
Deep Learning in Needle EMG: Methods

• In both studies, evaluated 6 different spontaneous potentials from video and audio recordings
  - Complex Repetitive Discharges
  - Endplate Potentials (noise and spikes)
  - Fasciculation potentials
  - Fibrillation Potentials/Positive Sharp Waves
  - Myotonic discharges
  - Technical artifacts (60 Hz, movement, etc.)

• Utilized recordings of up to 20 seconds in Study #1, and 10 Seconds in Study #2
• Resting activity was elicited in any of the following muscles in both studies:
  - Biceps brachii, first dorsal interosseous, vastus medialis or tibialis anterior
Deep learning for Spontaneous EMG: Methods: Study 1

- Discharge identified by lead electromyographer
- Video content extracted → only audio component utilized for analysis
  - EMG signal and audio data are interchangeable for machine learning, no loss or alteration of data occurs
- Divided audio files into 2 second segments yielding up to 4 files
  - Use mel-powered power spectrogram to create an image from each of the 2 sec snips
  - Deep learning algorithm applied using Python and MXNET

Diagram:
- Record EMG audio files
- Trim 2-second clips
- Normalize audio levels
- Divide into training/validation/test data
- Data augmentation for training data
- No data augmentation for training data
- Deep learning
- Calculate accuracy

(Nodera, Osaki et al. 2019)
Spectrogram used for signal visualization

Shows frequency content as a function of time

Representative Mel-spectrogram of six resting n-EMG discharges.

Scale magnitude is demonstrated by the following color order: Yellow > orange > purple.

CRD
Endplate potentials
Fasciculation potentials
Fibrillation/PSW
Myotonic discharges
Noise artifacts

1 sec
Deep learning for spontaneous EMG: Summary of Findings

RESULTS

• Total of 330 needle files from 83 patients with following diagnosis:
  o CRDs (62 files in ALS, radics)
  o Endplate (26 files)
  o Fasciculations (61)
  o Fibs or PSW (75)
  o Myotonic (55)
  o Noise (51)

• Data augmentation efforts increased sensitivity

• More complex deep learning networks (more layers) did not yield higher validation accuracy

(Nodera, Osaki et al. 2019)
Deep learning for spontaneous EMG: Methods: Study 2

- Again, extracted video content → only audio component utilized for analysis
- Divided in 2 second segments yielding up 3 files
- Extracted characteristic features (384 and 4367 features using 2 preselected audio feature sets)
- Tested the accuracy of classification by 5 different machine learning algorithms
Deep learning for spontaneous EMG: Summary of Findings Study #2

- Recordings obtained for 103 patients with a total of 389 files analyzed
  - CRDs (18)
  - Endplate (15)
  - Fasciculations (32)
  - Fibs or PSW (28)
  - Myotonic (17)
  - Noise (24)

- Smaller number of attributes yielded slightly higher accuracy
  - The best overall accuracy was 90.4%

<table>
<thead>
<tr>
<th>50 cases of CRD classified</th>
</tr>
</thead>
<tbody>
<tr>
<td>45 correct</td>
</tr>
<tr>
<td>5 incorrect</td>
</tr>
</tbody>
</table>
  - 1 endplate
  - 1 fibrillation
  - 3 myotonic

Table 2. Confusion matrices of classification, with classified classes by machine learning shown horizontally and true classes shown vertically

(A) Generalized linear modeling (GLM) (IS_09 feature set)
Accuracy = 0.904

```
A  B  C  D  E  F  >> Classified as
45 1  0  0  3  0  A = CRD
0  22 0  2  0  0  B = endplate potentials
0  0  59 1  0  1  C = fasciculation
0  0  2  69 0  4  D = fibrillation/PSW
2  0  0  2  46 0  E = myotonic discharges
0  0  4  6  1  40 F = noise artifact
```

(B) Generalized linear modeling (GLM) (IS_11 feature set)
Accuracy = 0.899

```
A  B  C  D  E  F  >> Classified as
52 0  0  0  3  0  A = CRD
1  23 0  0  1  0  B = endplate potentials
0  0  56 3  0  0  C = fasciculation
0  0  4  63 1  2  D = fibrillation/PSW
5  0  0  3  45 0  E = myotonic discharges
0  0  1  3  4  37 F = noise artifact
```

CRD = complex repetitive discharges; PSW = positive sharp wave.
Deep learning for spontaneous EMG: Take home points

• Machine learning with deep learning algorithms can be utilized in auditory classification of EMG signals as has been done in classification of chest auscultation and snoring detection

• The best accuracy seems to come with a lesser number of features
  ○ More layers did not enhance accuracy

• These findings should be tested in a clinical setting- best accuracy was 90.4%
  ○ Likely higher than interrater accuracy

• Different EMG machines and different filter settings will have different results → larger, prospective data is needed

(Nodera, Osaki et al. 2019)
Questions and Discussion at Break

Thank you!

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References


