Initial Disease Severity Predicts Executive Functioning in Children with Anti-NMDA Receptor Encephalitis (NMDARE)

Ilana Kahn, MD\textsuperscript{1,2}, Claire Semerjian, PsyD\textsuperscript{1,2}, William Suslovik, BS\textsuperscript{3}, Alyssa Doslea MS\textsuperscript{3}, Emily Matuska BS\textsuperscript{3}, Melissa Fleming MD\textsuperscript{1,2}, Elizabeth Wells MD\textsuperscript{1,2}, Leigh N. Sepeta, PhD\textsuperscript{1,2}

\textsuperscript{1}Children’s National Hospital, Washington, D.C. \textsuperscript{2}George Washington University School of Medicine

**Background**

Executive functioning (EF) and memory deficits are primary cognitive concerns following (NMDARE) in adults and children, although predictors of cognitive outcomes remain poorly understood.

Delay in treatment is predictive of worse outcomes for adults, but this has not been reported with children.

**Objective**: We aim to fill this gap by investigating predictors of memory and EF in children with anti-NMDARE encephalitis.

**Participants**

12 pediatric NMDARE patients with Neuropsychological evaluation.

**Measures**

**Executive functioning**: BRIEF-2, TOL-Dx

**Memory**: WRAML-II Stories

**Predictors**: premorbid developmental concerns; modified Rankin Scale (mRS, at admission); length of hospital stay (LOS), and other disease-related factors (i.e., presence of abnormal MRI and/or EEG on admission, seizures on admission, ICU stay, time to treatment from initial symptom presentation and admission)

**Analyses**:

Percentages of clinically significant (T>65) parent-reported concerns with daily executive functioning were calculated

Linear regression models examined several predictors of neurocognitive outcome in pediatric ANMDARE patients

**Results**

Approximately one-third of parents reported elevated daily EF concerns, while mean scores were broadly average across objective memory and EF measures

mRS predicted ratings of daily EF overall, accounting for 59.6% of the variance (p=0.01, n=10, Figure 1), as well as metacognitive skills at the trend level (p=0.056, R\textsuperscript{2}=0.43, n=10).

LOS predicted EF across objective and parent-report measures (BRIEF-2 ERI, p=0.02; TOL-Dx, Total Correct, p=0.04), accounting for 55-68.3% of variance respectively (Figure 2).

History of premorbid neurodevelopmental concerns also predicted higher-order executive planning (TOL-Dx Total Correct, p=0.03, R\textsuperscript{2}=0.63).

No variables predicted verbal memory performance.

**Conclusions**

Results highlighted the relative vulnerability of day-to-day executive functioning in this population.

Findings suggest that initial disease severity is helpful in predicting EF and self-regulation in children with NMDARE.

Further study with additional patients will be important to determine the clinical utility of disease severity and neurodevelopmental history in informing prognosis for neurocognitive functioning in this population.

**Figure 1**: mRS and BRIEF-2 GEC

**Figure 2**: LOS and Executive Functioning (BRIEF-2 ERI and TOL-DX Move Score)**

---

\*NOTE: On the BRIEF-2, higher scores indicate more significant concerns with daily executive functioning. Conversely, on the TOL-Dx, higher T-scores indicate better performance.

---

**Participant characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at evaluation</td>
<td>11.9 yr (7.4, 16.2)</td>
</tr>
<tr>
<td>Gender</td>
<td>Female: 7, Male: 5</td>
</tr>
<tr>
<td>Time from onset to evaluation</td>
<td>31.4 hr</td>
</tr>
<tr>
<td>Disease-related characteristics</td>
<td>55%</td>
</tr>
<tr>
<td>MRI, EEG</td>
<td>96%</td>
</tr>
<tr>
<td>Premorbid neurodevelopmental</td>
<td>75%</td>
</tr>
<tr>
<td>Time from symptom onset to admission</td>
<td>8 days (5-13)</td>
</tr>
</tbody>
</table>