Neonatal Neurobehavior, Medical Risk, and 2-year Developmental Outcomes in Infants Born <30 Weeks> Gestation

Elizabeth McGowan
Marie Camerota
Julie A. Hofheimer
Michael O'Shea
Brian S. Carter

*See next page for additional authors*

Follow this and additional works at: https://scholarlyexchange.childrensmercy.org/presentations

Part of the Pediatrics Commons
Creators
Elizabeth McGowan, Marie Camerota, Julie A. Hofheimer, Michael O'Shea, Brian S. Carter, Howard Kilbride, Steven Pastynak, Charles R. Neal, Lynne Smith, Jennifer Helderman, Jennifer Check, Lynne Dansereau, Sheri A. DellaGrotta, and Barry Lester
Neonatal Neurobehavior, Medical Risk & 2 year Developmental Outcomes

Elisabeth C. McGowan, MD
Associate Professor of Pediatrics, Warren Alpert Medical School
Women & Infant’s Hospital, Providence, RI
emcgowan@wihri.org
Neonatal Neurobehavior, Medical Risk & 2 year Developmental Outcomes

Co-authors:

M Camerota, PhD; J Hofheimer PhD; M O'Shea, MD; Brian Carter, MD; H Kilbride, MD; S Pastynak PhD; C Neal, MD, PhD; L Smith MD; J Helderman MD, MS; J Check MD; L Dansereau MSPH; S DellaGrotta MPH; B Lester PhD

Dr. McGowan has no financial relationships to disclose or Conflicts of Interest (COIs) to resolve
Background

- Infants born preterm (PT) are at increased risk for neurodevelopmental and behavioral delays
- Medical morbidities ↑↑ this risk
- Socio-economic factors are linked to poor outcomes
  - Post-NICU home environment is a critical mediator of development & behavior
- NICU is a non-optimal environment for PT infant growth & development
- Infant neurobehavioral assessments can be completed while in the NICU
- Provide an early window into understanding the infant’s ability to respond to multisensory environment, prior to the influences of the home environment.
AIMS: To determine among infants born < 30wks gestation
1. Associations between medical risk, neurobehavior (at NICU discharge) & 2 year development
2. Relations between medical risk & neurobehavior
3. Role of the post-discharge environment in explaining associations between medical conditions, neurobehavior & 2 yr outcomes

Multi-center, prospective, observational cohort study (9 U.S. NICUs enrolled pts between 2014-2016)
**NOVI Study Flow**

- **Screening**
  - Enrollment
    - Maternal data
    - Infant medical data

- **Enrollment**
  - Infant neurobehavior assessment
    - NICU Network Neurobehavioral Scale (NNNS)
  - Depression & distress questionnaires
  - Cry acoustics
  - Buccal swab

- **Neurodevelopmental**
  - Bayley-3, Neuromotor Questionnaires
  - (Child Behavior Checklist CBCL)
  - Buccal swab

- **Birth**
- **Approximately 30 wks**
- **Discharge**
- **2 Year**

**Inclusion:**
- PMA <30wk, likely to survive to d/c, inborn + outborn, live w/in 3 hrs NICU & FU Clinic,
  Maternal Lang (English, Spanish, Japanese, Chinese)

**Exclusion:**
- Maternal death, age < 18y, cognitive impairment; infant congenital anomaly
**NOVI Study Flow**

- **Inclusion:** PMA <30wk, likely to survive to d/c, inborn + outborn, live w/in 3 hrs NICU & FU Clinic, Maternal Lang (English, Spanish, Japanese, Chinese)
- **Exclusion:** maternal death, age < 18y, cognitive impairment; infant congenital anomaly

**N = 704 → 689**

- **Enrollment**
  - Maternal data
  - Infant medical data

**Screening**

- Birth
- ≈ 30 wks

**N = 680/689**

- Infant neurobehavior assessment
  - NICU Network Neurobehavioral Scale (NNNS)
  - Depression & distress questionnaires
  - Cry acoustics
  - Buccal swab

**Discharge**

- 556/680 (82%)

- Neurodevelopmental
  - Bayley-3, Neuromotor Questionnaires (Child Behavior Checklist CBCL)
  - Buccal swab

- 2 year
Statistics

• **NNNS Profiles** (Latent Profile Analysis, LPA)
  
  Group infants in mutually exclusive, clinically unique subgroups → 12 NNNS summary scores
  
  6 distinct profiles were calculated
  
  Profiles 1-4 (most “typical”) vs profiles 5-6 (most “atypical”) were compared

• **Primary outcomes**: 2 year Bayley-3 composite scores & Child Behavior Checklist (CBCL) T-scores

• Generalized estimating equation (GEE) models* tested association between NNNS profiles 5-6, neonatal medical risk (≥ 2 major medical morbidities) & 2 year developmental & behavioral outcomes.

• Covariates included site, maternal SES**, race/ethnicity, maternal primary language, partner status, maternal distress, infant sex, PMA at birth

* Accounted for multiple births
** Hollingshead criteria
Total NOVI Cohort - 6 Behavioral Profiles

<table>
<thead>
<tr>
<th>Profile</th>
<th>Percentage</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>11.6%</td>
<td>79</td>
</tr>
<tr>
<td>2</td>
<td>30.7%</td>
<td>209</td>
</tr>
<tr>
<td>3</td>
<td>11.5%</td>
<td>78</td>
</tr>
<tr>
<td>4</td>
<td>15.9%</td>
<td>108</td>
</tr>
<tr>
<td>5</td>
<td>23.4%</td>
<td>159</td>
</tr>
<tr>
<td>6</td>
<td>6.9%</td>
<td>47</td>
</tr>
</tbody>
</table>
## Results – Maternal characteristics by NNNS Profiles

<table>
<thead>
<tr>
<th>N (%), mean (SD)</th>
<th>Profile 5-6 N = 135</th>
<th>Profile 1-4 N = 331</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-English Primary Language</td>
<td>27 %</td>
<td>17 %</td>
<td>&lt; .01</td>
</tr>
<tr>
<td>Low SES *</td>
<td>17 %</td>
<td>7 %</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Minority race/ethnicity</td>
<td>56 %</td>
<td>54 %</td>
<td>0.4</td>
</tr>
<tr>
<td>Single</td>
<td>27 %</td>
<td>27 %</td>
<td>0.9</td>
</tr>
<tr>
<td>Maternal Distress Screening **</td>
<td>0.3 (.4)</td>
<td>0.27 (.3)</td>
<td>0.5</td>
</tr>
</tbody>
</table>

* Hollingshead category 5  
** average total from discharge and 2 yrs
## Results – Infant characteristics by NNNS Profiles

<table>
<thead>
<tr>
<th>N (%) or mean (SD)</th>
<th>Profile 5-6 ( N = 157 )</th>
<th>Profile 1-4 ( N = 389 )</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PMA at birth</td>
<td>26.8 (2)</td>
<td>27.0 (2)</td>
<td>.2</td>
</tr>
<tr>
<td>Female</td>
<td>42 %</td>
<td>46 %</td>
<td>.4</td>
</tr>
<tr>
<td>Brain Injury *</td>
<td>17 %</td>
<td>10 %</td>
<td>.03</td>
</tr>
<tr>
<td>NEC/Sepsis</td>
<td>23 %</td>
<td>16 %</td>
<td>.05</td>
</tr>
<tr>
<td>CLD</td>
<td>51 %</td>
<td>51 %</td>
<td>.9</td>
</tr>
<tr>
<td>Severe ROP</td>
<td>6 %</td>
<td>6 %</td>
<td>.9</td>
</tr>
</tbody>
</table>

* (by ultrasound) parenchymal echodensity, cPVL, ventricular dilation (+/- hemorrhage)
## Results – 2y Neurodevelopmental outcomes by Medical Risk & NNNS Profiles

<table>
<thead>
<tr>
<th>Bayley-3</th>
<th>Medical Risk aOR (95% CI)</th>
<th>NNNS Profiles 5-6 aOR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cognitive comp &lt; 85</td>
<td>1.6 (1.2, 2.2)</td>
<td>1.8 (1.1, 3.1)</td>
</tr>
<tr>
<td>Motor comp &lt; 85</td>
<td>2.4 (1.7, 3.3)</td>
<td>2.3 (1.4, 4.0)</td>
</tr>
<tr>
<td>Language comp &lt; 85</td>
<td>1.4 (1.1, 1.8)</td>
<td>1.1 (0.7, 1.7)</td>
</tr>
<tr>
<td>Cognitive comp &lt; 70</td>
<td>3.0 (1.9, 4.5)</td>
<td>3.9 (1.7, 9.0)</td>
</tr>
<tr>
<td>Motor comp &lt; 70</td>
<td>4.4 (2.7, 7.1)</td>
<td>4.1 (1.7, 9.8)</td>
</tr>
<tr>
<td>Language comp &lt; 70</td>
<td>1.4 (0.9, 2.1)</td>
<td>1.7 (0.9, 3.2)</td>
</tr>
</tbody>
</table>

Adjusted for low SES, minority race/ethnicity, maternal primary language, single, BSI average, PMA, sex, study site
## Results – 2y Behavior outcomes by Medical Risk & NNNS Profiles

<table>
<thead>
<tr>
<th>Child Behavior Checklist (CBCL)</th>
<th>Medical Risk aOR (95% CI)</th>
<th>NNNS Profiles 5-6 aOR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Internalizing T-score &gt; 63</td>
<td>1.0 (0.6, 1.7)</td>
<td>2.7 (1.2, 5.8)</td>
</tr>
<tr>
<td>Externalizing T-score &gt; 63</td>
<td>0.7 (0.4, 1.0)</td>
<td>1.4 (0.7, 2.8)</td>
</tr>
<tr>
<td>Total Problem Score T-score &gt; 63</td>
<td>0.9 (0.6, 1.4)</td>
<td>2.6 (1.3, 5.5)</td>
</tr>
</tbody>
</table>

Adjusted for low SES, minority race/ethnicity, maternal primary language, single, BSI average, PMA, sex, study site.
Summary

• Among infants born < 30 weeks, clinically valid neurobehavioral patterns or “profiles” can be quantified with precision.

• Neonatal medical risk remains a consistent concern for poor cognitive, language and motor performance.

• After controlling for medical risks, atypical neonatal neurobehavioral patterns were significant predictors adverse cognitive and motor outcomes.

• Atypical neurobehavior at NICU discharge was associated with behavioral problems (clinical range for internalizing & total behavioral scores) at 2 years.

• NNNS assessment at NICU discharge suggests that the profiles are an early predictive clinical tool that can inform targeted interventions prior to discharge to the home environment.
Acknowledgements

PI’s
- Barry Lester, PhD *(Women & Infants Hospital, RI)*
- Michael O’Shea, MD, MPH *(UNC Chapel Hill, NC)*
- Julie Hofheimer PhD *(UNC Chapel Hill, NC)*
- Brian Carter, MD *(Children’s Mercy, MO)*
- Jennifer Helderman, MD, MS *(Wake Forest Univ, NC)*
- Jennifer Check, MD *(Wake Forest Univ, NC)*
- Charles Neal, MD, PhD *(Univ Hawaii, Honolulu, HI)*
- Steve Pastyrnak PhD *(Helen DeVos Hospital, MI)*
- Lynne Smith MD *(Harbor UCLA, CA)*
- Antoine Soliman MD *(Miller UCLA, CA)*

Brown Center/NOVI Data Center
- Lynne Danserau, MSPH
- Sheri DellaGrotta, MPH
- Linda LaGasse, PhD

Study Site Co-Investigators
- NNNS examiners
- Study coordinators
- Ultrasound Consultants
- NICU Staff
- Family participants

Funding
- NIH NICHD R01HD072267