NIDCAP – Promise to Protect the Preterm Brain

David Schiff Memorial Lecture
Grand Rounds, Department of Pediatrics
University of Alberta Faculty of Medicine and Dentistry,
Royal Alexandra Hospital, Edmonton, Alberta Canada
19 October 2017

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Conflict of Interest Disclosure

I, Heidelise Als, PhD have no financial relationship with any commercial entity producing healthcare-related products and/or services.

I am a volunteer member of Board of Directors of the non-profit NIDCAP Federation International (NFI) and a Senior NIDCAP Master Trainer.

Key Collaborators

Neurology: FH Duffy, MD
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Harris Foundation Chicago, H Als, PhD
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Many Other Collaborators Over the Years

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Nikk Conneman, MD
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Elsa Sell, MD
Kathy Vandenberg, PhD
Petra Hüppi, MD and Linda Gilkerson, PhD

The Challenge

- World-wide increase in prematurity rates:
- Thirteen million infants are born prematurely each year, i.e. 10% of all births.
- More than 50% of children born preterm show later learning disabilities, attention deficits, behavior problems, emotional issues, and school failure.

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Behavior

- Continuous expression of brain function
- Always available to be observed
- Guide for environment, interaction and care

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Synactive Model of Developmental Care
- NIDCAP
Newborn Individualized Developmental Care and Assessment Program

Affectionate and Gentle Care

Peaceful and Assuring Intimacy

Collaborative Care, Parents and Professionals
Photos: S. Butler, with permission 2014

Pleasurable Feeding, Nutrition and Nurturance

Safeguarding a quiet soothing environment for infant and family - growing security and trust

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Goal: Continuous Assurance of Protection
Predictability
Restfulness
Intimate Contact
Pleasure and Contentment


Results of 15 NIDCAP Studies (10 RCTs)

- Ventilator Days
- Extra Oxygen Days
- Gavage Feeding Days
- Severity of BPD
- Incidence of IHV
- Weight Gain Problems
- Growth Problems
- Length of Hospital Stay
- Age at Discharge

Ohlsson and Jacobs, Pediatrics, 2013; 131:3 e881-e893.

Bayley Mental Developmental Index at 9 or 12 mCA

Ohlsson A, Jacobs SE. NIDCAP: A Systematic Review and Meta-analyses of Randomized Controlled Trials. Pediatrics, 2013; 131:3 e881-e893. Fig. 3

Bayley Psychomotor Developmental Index at 9 or 12 mCA

Ohlsson A, Jacobs SE. NIDCAP: A Systematic Review and Meta-analyses of Randomized Controlled Trial. Pediatrics, 2013; 131:3 e881-e893. Fig. 4

Peters KL et al. The Edmonton NIDCAP Trial

Pediatrics 2009;124:1009-1020

Significantly fewer days of mechanical ventilation

Significantly better neurodevelopment at 18mCA

Very High Risk Preterm Infants
< 29wGA, Ventilated > 24h/first 48h
Newborn Period to Age Eight Years CA
Health, Neurobehavior and EEG
n = 107 (51C; 56E)

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Very High Risk Preterm Infants <29wGA; N=107
Medical Outcome Variables, 2wCA (1)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control (n=53)</th>
<th>Experimental (n=56)</th>
<th>F*</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventilator Days</td>
<td>(n=53)</td>
<td>(n=56)</td>
<td>4.18</td>
<td>0.005</td>
</tr>
<tr>
<td>Oxygen Days</td>
<td>(n=51)</td>
<td>(n=56)</td>
<td>0.37</td>
<td>0.23</td>
</tr>
<tr>
<td>Caffeine Days</td>
<td>(n=53)</td>
<td>(n=56)</td>
<td>0.25</td>
<td>0.005</td>
</tr>
<tr>
<td>Hospital Days</td>
<td>(n=53)</td>
<td>(n=56)</td>
<td>5.21</td>
<td>0.03</td>
</tr>
<tr>
<td>Discharge Age (w, LMP)</td>
<td>(n=53)</td>
<td>(n=56)</td>
<td>4.42</td>
<td>0.005</td>
</tr>
<tr>
<td>Daily wt. gain to 2w CA (g)</td>
<td>(n=53)</td>
<td>(n=56)</td>
<td>0.39</td>
<td>0.005</td>
</tr>
<tr>
<td>Weight at 2w CA (kg)</td>
<td>(n=53)</td>
<td>(n=56)</td>
<td>4.32</td>
<td>0.03</td>
</tr>
<tr>
<td>Length at 2w CA (cm)</td>
<td>(n=53)</td>
<td>(n=56)</td>
<td>0.73</td>
<td>0.24</td>
</tr>
</tbody>
</table>


Very High Risk Preterm Infants <29wGA; N=107
Medical Outcome Variables, 2wCA (2)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control (n=51)</th>
<th>Experimental (n=56)</th>
<th>χ²</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumothorax</td>
<td>(n=53)</td>
<td>(n=56)</td>
<td>3.47</td>
<td>0.03</td>
</tr>
<tr>
<td>Intraventricular Hemorrhage None, Grade I/II/III/IV</td>
<td>(n=51)</td>
<td>(n=56)</td>
<td>2.98</td>
<td>0.05</td>
</tr>
<tr>
<td>Bronchopulmonary Dysplasia None/Stage I/II/III/IV</td>
<td>(n=53)</td>
<td>(n=56)</td>
<td>2.98</td>
<td>0.05</td>
</tr>
<tr>
<td>Retinopathy of Prematurity None/Stage I/II/III/IV</td>
<td>(n=52)</td>
<td>(n=56)</td>
<td>1.00</td>
<td>0.80</td>
</tr>
</tbody>
</table>

Chi Square Test: χ², 2-tailed. Note: p (probability) in bold ≤ .05 level.


Very High Risk Preterm Infants <29wGA; N = 107
APIB System Scores, 2wCA

<table>
<thead>
<tr>
<th>Variable</th>
<th>C</th>
<th>E</th>
<th>F*</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autonomic system</td>
<td>(n=53)</td>
<td>(n=56)</td>
<td>6.67</td>
<td>0.0001</td>
</tr>
<tr>
<td>Motor system</td>
<td>(n=53)</td>
<td>(n=56)</td>
<td>6.62</td>
<td>0.0001</td>
</tr>
<tr>
<td>State system</td>
<td>(n=53)</td>
<td>(n=56)</td>
<td>5.87</td>
<td>0.0001</td>
</tr>
<tr>
<td>Attention system</td>
<td>(n=53)</td>
<td>(n=56)</td>
<td>7.19</td>
<td>0.0001</td>
</tr>
<tr>
<td>Self-regulation system</td>
<td>(n=53)</td>
<td>(n=56)</td>
<td>6.66</td>
<td>0.0001</td>
</tr>
<tr>
<td>Examiner facilitation</td>
<td>(n=53)</td>
<td>(n=56)</td>
<td>7.03</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Means (SD). Corrected Age (CA). Brown-Forsythe One-Way Analysis of Variance: F*, 2-tailed; Note: p (probability) in bold ≤ .05 level.


Very High Risk Preterm Infants <29wGA; N = 92
Bayley Scales of Infant Development, 9mCA

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control (n=42)</th>
<th>Experimental (n=50)</th>
<th>F*</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDI</td>
<td>(n=42)</td>
<td>(n=50)</td>
<td>6.65</td>
<td>0.0001</td>
</tr>
<tr>
<td>PDI</td>
<td>(n=42)</td>
<td>(n=50)</td>
<td>8.49</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Corrected Age (CA). Mental Developmental Index (MDI), Psychomotor Developmental Index (PDI). Results Means (SD) MDI and PDI: Mean = 100; SD = 15. Brown-Forsythe One-Way Analysis of Variance: F*, 2-tailed. Chi Square Test: χ², 2-tailed. Note: p (probability) in bold ≤ .05 level.


Neuropsychological Factors at 8 YCA < 29wGA High-Risk; C=11; E=11

<table>
<thead>
<tr>
<th>Factors</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor 1: Verbal and Language Abilities</td>
<td>0.40</td>
</tr>
<tr>
<td>Factor 2: Visual and Spatial EF Abilities</td>
<td>0.01</td>
</tr>
<tr>
<td>Factor 3: Automated Verbal Abilities</td>
<td>0.60</td>
</tr>
<tr>
<td>Factor 4: Perceptual Organization and Visual Memory</td>
<td>0.68</td>
</tr>
<tr>
<td>Factor 5: Verbal Expression and Memory</td>
<td>0.14</td>
</tr>
<tr>
<td>Factor 6: School Achievement</td>
<td>0.31</td>
</tr>
</tbody>
</table>

MANOVA, F* = 2.52; df = 6, 15; P < .05
MANOVA, multivariate analysis of variance; df, degrees of freedom.


EEG Coherence Factors, <29wGA, at 8yCA. C=9; E=10

- Head in vertex view, nose above, left ear to left.
- Index electrode at lower left; frequency at lower right.
- Background color is loading on PCA: Blue=Decreased; Red-orange=Increased.
- Arrow color is E-group coherence: Green=decreased; Red=Increased.
- Index electrode at lower left; frequency lower right.

Family Outcome: Parenting Stress Index (PSI) and Mother’s View of the Child (MVC) (n=77)
Very High Risk < 29wGA Preterm Infants at 2wCA
Control – Experimental: BWH 14-14; CHO 17-14; CHB 7-10

PSI Child Domain
PSI Parent Domain
PSI Total Stress
PSI Life Stress
MVC Overall Score

MANCOVA: Group: F=2.41; df=5,66; p<.05. Site: F=1.48; df=10,132; p<.15. G x S: F=0.57; df=10,132; p<.83; (* p<.05  ** p<.01  *** p<.001)

AGA Low-Risk Preterm-Born Infants (29-33wGA)

n = 30 (14 C; 16 E)
Newborn Period to Age Eight Years CA
Neurobehavior, EEG and MRI

EEG Coherence Measures 2wCA AGA Preterm Infants

Wilks’ Lambda=0.45; F=7.69; df=4,25; P ≤ .0001
Coherence factor background: blue – negative / orange - positive;
Arrow Color E-Group: green - decreased / red - increased

Bayley Scales of Infant Development, 2nd Edition
Low-Risk AGA Infants, 28-33wGA, 9mCA

Variable
Control (n=13) Experimental (n=11)
PDI
MDI
19.14 0.0002
94.89 (9.22) 109.55 (7.23)
107.00 (9.28)
89.23 (14.85)

Orientation/Engagement
Emotional Regulation
Motor Quality
BRS Total Score
56.92 (7.97) 70.55 (21.62)
39.51 (27.42)
56.64 (31.05)
38.69 (23.04) 72.64 (61.13)
1.81 0.19
7.22 0.01
9.38 0.007
17.87 0.0004

MDI-Mental Developmental Index, PDI-Psychomotor Developmental Index, BRS-Behavior Rating Scales. Results: Means (SD). Brown-Forsythe One-Way Analysis of Variance: F*, 2-tailed. Chi Square Test: \( \chi^2 \), 2-tailed. Note: p (probability) in bold \( \leq .05 \) level.

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School Age (8-10yCA) Effectiveness of NIDCAP
Neuropsychological Functioning
Rey-Osterrieth Complex Figure

ROCFT: Copy
Immediate Recall       Delayed Recall
Control 9y3m21d
Experimental 8y4m22d

Low-Risk Preterm, 29-33wGA, School Age Outcome,

EEG Spectral Coherence, Low-Risk Preterms, 29-33wGA, at School Age
Control (8) Experimental (15)

Head in vertex view, nose above, left ear to left.
Arrow color illustrates experimental group coherence:
green - decreased, red - increased.

Mean Diffusivity (MD) in Cortico-Spinal Tract - School Age
Low-Risk AGA 29-33wGA
Two Controls
L: 8y1m10d
R: 8y3m0d

Two Experiments
L: 8y3m21d
R: 9y6m20d

Color code: red (low) to yellow (high). Lighter yellow and orange:
higher measure of MD; darker orange and red: lower measure of MD

Severely IUGR High-Risk Preterm-Born Infants
(29-33wGA) n = 30 (18 C; 12 E)
Newborn Period to Age Eight Years CA
Neurobehavior, EEG and MRI

APIB System Scores 2wCA – IUGR Preterm Infants (JPerinat, 2011)

<table>
<thead>
<tr>
<th>Variable</th>
<th>C (n = 18)</th>
<th>E (n = 12)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autonomic System</td>
<td>6.86</td>
<td>5.54</td>
<td>0.0003</td>
</tr>
<tr>
<td>Motor System</td>
<td>6.93</td>
<td>5.89</td>
<td>0.02</td>
</tr>
<tr>
<td>State System</td>
<td>5.77</td>
<td>5.32</td>
<td>0.22</td>
</tr>
<tr>
<td>Attention System</td>
<td>7.61</td>
<td>7.36</td>
<td>0.55</td>
</tr>
<tr>
<td>Self-Regulation</td>
<td>6.90</td>
<td>6.01</td>
<td>0.004</td>
</tr>
<tr>
<td>Examiner Facilit.</td>
<td>7.81</td>
<td>6.79</td>
<td>0.07</td>
</tr>
</tbody>
</table>

MANOVA, F=6.95, df=6,22; p=0.0007 Brown-Forsythe ANOVA: F*.
p = probability, two-tailed. (Higher scores, poorer performance.)

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IUGR Preterm Infants (Study 2), J. Perinatology, 2012 Epub PubMed PMID: 22301525I

Bayley Scales-II, IUGR, 9mCA (JPerinat, 2011)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control (n = 18)</th>
<th>Experimental (n = 12)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDI</td>
<td>90.06 (11.33)</td>
<td>102.83 (10.99)</td>
<td>0.005</td>
</tr>
<tr>
<td>PDI</td>
<td>82.48 (20.56)</td>
<td>92.25 (20.33)</td>
<td>0.21</td>
</tr>
<tr>
<td>BRS Total Score</td>
<td>21.26 (19.95)</td>
<td>34.08 (25.63)</td>
<td>0.17</td>
</tr>
<tr>
<td>WNL/Question/Non-Opt.</td>
<td>3 / 10 / 5</td>
<td>7 / 1 / 4</td>
<td>0.02</td>
</tr>
</tbody>
</table>

MDI, PDI and BRS Total Score, MANOVA, F = 3.11, df = 3,26, p = 0.04.
Brown-Forsythe ANOVA: F*; Fisher Exact Test; Pearson’s Chi Square Test: \( \chi^2 \)

| p = probability, two-tailed. |

Mean diffusivity (MD) in corticospinal tract (internal capsule) at 42 wks PMA. Color coded from Red (Low MD → More mature fiber tracts) to Yellow (High MD → Less mature fiber tracts).

IUGR Preterm, 29-33wGA, School Age Outcome

ROCF: Control (9y6m1d), Copy
Immediate Recall
Delayed Recall

Experimental (9y10m18d)

Cerebellar Volume as Percent of Parenchyma

NIDCAP – Promise to Protect the Developing Brain

- Enhancement in experience mediated calmness and comfort (Protection of the NMDA N-methyl-d-aspartate axis, reduced toxic glutamate and free radical release, cell death).
- Assurance of steady blood flow (fewer hypoxemic events; reduction in intraventricular hemorrhage).
- Enhanced intimate contact and parenting (protective hormonal release – oxytocin) - enhanced social-emotional development.
- Assurance of darkness (enhanced melatonin release) – enhanced sleep and cognitive development.

System-Wide Paradigm Shift, Culture Change, and Professional Role Transformation

Accountability and Excellence in the Care of
The Infant
The Family
The Staff & Professionals
The Environment.

NIDCAP Nursery Assessment and Certification Program (NNACP)
NFI - 2011

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Summary Thoughts

- One brain for life – all experience matters. 
  *(Claudine Amiel-Tison)*
- It matters how we listen to the voice of each newborn and how we care for each newborn and each family.
- It matters how we care for one another and for ourselves.

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