OVERVIEW OF AUTONOMIC NERVOUS SYSTEM DEVELOPMENT IN THE FETUS AND INFANT

ANS: Focus on the Vagus Nerve
• Mammalian ANS developed beyond the reptilian survival function
  – Rapidly adapted to accommodate fight-flight events and social interactions
• High vagal tone via myelinated vagal pathways to the heart
  – Acts as a brake, slowing the heart, calming the person
  – Low vagal tone: no inhibition on the heart

Vagal Pathways in Infants
• Partially myelinated at birth
  – Myelination is necessary for effective nerve signal transmission
• Myelinated fibers increase from 24 weeks gestation through adolescence
• Greatest increase occurs between 32 and 34 weeks gestation to ~6 months of age
  – Vagal tone through myelinated fibers increases with gestational age

Three Subsystems (Circuits) of the Autonomic Nervous System (ANS)
1) Social communication—highest levels of communication
   1) Partially available at term gestation
2) Mobilization—tantrums, behavioral acting-out
3) Immobilization—oldest circuit associated with survival—possum feigning death, physiologic shutdown

(Porges & Furman, 2011)

Autonomic Nervous System Function and the Effect of Massage Therapy on Enhancing Parasympathetic Activity in Preterm Infants
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(Porges, Doussard-Roosevelt, et al., 1996)
Vagal Pathways in Infants

- Thus infants born prior to 30 weeks gestation lack the high vagal efferent and vagal brake activity on the heart
  - Myelination is not complete
  - Reactivity to stressors is exaggerated and recovery impaired
- Long term effects are unknown but may affect social and behavioral development

Preterm Infant ANS Function

- Preterm infants demonstrate a prolonged ANS dysfunction
  - Yiallourou et al. (2013): preterm infants have a persistent depressed parasympathetic activity at 5-6 months of age
  - Patural (2008): Preterm infants have depressed ANS activity at 1 year of age

Given the interruption of ANS development and the prolonged ANS dysfunction experienced by preterm infants, what treatments may enhance ANS development in this vulnerable group?

Effect of Massage Therapy on Preterm Infants

- Improved weight gain
- Increased IGF-1 expression (enhanced growth)
- Decreased length of hospital stay (~5 days)
- Increased gastric motility
- Improved bone mineral deposition
- Alterations in brain waves (sleep)
- No difference between massage and controls (Arora et al., 2005; Diego et al., 2003, 2007; Field et al., 2006, Guzzetta, 2011)

Methodological Concerns

- Massage treatment given 2 x/day for 5-10 days
- Variability in who delivered the massage
  - Mothers
  - Others (OT, PT)
  - LMTs
- Underpowered due to small sample sizes
- Lack of blinding by the researchers

Autonomic Nervous System Function and the Effect of Massage Therapy on Enhancing Parasympathetic Activity in Preterm Infants

Longitudinal, randomized controlled trial of 44 medically stable preterm infants born between 29 and 32 weeks gestation.
Hypotheticals

- In preterm infants, twice daily MT will
  - promote ANS function as measured by heart rate variability (HRV) and urine catecholamine
  - improve growth quality
  - improve bone accretion

Intervention and Testing Schema

- Medically stable 29-32 week preterms
- Randomized to group (MT or CTL)
- Masked to HCP and Parents
- LMTs provided intervention

Infant Characteristics
(Enrollment 7/08-5/11)

<table>
<thead>
<tr>
<th></th>
<th>MT</th>
<th>Control</th>
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<tbody>
<tr>
<td>Gender</td>
<td>12F/10M</td>
<td>12F/10M</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>36% Hispanic 64% White</td>
<td>32% Hispanic 68% White</td>
</tr>
<tr>
<td>Birth PMA (wk)</td>
<td>31.4 ± 0.8</td>
<td>31.0 ± 0.9</td>
</tr>
<tr>
<td>Entry PMA (wk)</td>
<td>32.5 ± 1.0</td>
<td>32.4 ± 0.9</td>
</tr>
<tr>
<td>Birth Weight (g)</td>
<td>1573 ± 231</td>
<td>1618 ± 289</td>
</tr>
<tr>
<td>Entry Weight (g)</td>
<td>1522 ± 238</td>
<td>1590 ± 272</td>
</tr>
</tbody>
</table>

Smith et al., J.Pregnatal, 2012
HRV

- ANS mediates physiological fluctuations in R-R interval
  - Interaction and adaptability of SNS and PNS
- Data were acquired continuously prior to, during, and post MT or CTL
  - Pre, during, and post session epochs were extracted for analysis
- Fast Fourier Transform (FFT) analysis
  - Estimates cardiac modulation by ANS
  - Regions are specific to the SNS and PNS

\[ \text{LF/HF Ratio (SEM)} \]

\[ \text{ wk 0 wk 1 wk 2 wk 3 wk 4} \]

\[ ^* p < 0.5 \text{ between MT & CTL at wk 3 and 4} \]
\[ ^\dagger p < 0.05 \text{ MT baseline to wk 4} \]


HRV Regions of ANS Activity

- Sympathetic nervous system (0.02-0.2 Hz)
- Parasympathetic nervous system (>0.2 – 2.0 Hz)

\[ \text{ LF/HF ratio} \]

\[ \text{ LF:HF Ratio (SEM)} \]

\[ \text{ wk 0 wk 1 wk 2 wk 3 wk 4} \]

\[ ^* p < 0.5 \text{ between MT & CTL at wk 3} \]


NS between groups by sex


HRV 6 HOURS POST SESSION WEEK 2

- Males (4 MT, 4 CONTROL)

\[ \text{ LF:HF Ratio (SEM)} \]

\[ \text{ wk 0 wk 1 wk 2 wk 3 wk 4} \]

HRV 6 HOURS POST SESSION WEEK 2
Females (6 MT, 7 CONTROL)

Urine Catecholamine Levels were
Decreased in MT infants

Back (Trunk) Fat Increase was Highest in
Control Male & MT Female Preterm Infants

Blood Markers Indicate Higher Abdominal Fat
In Control Male Preterm Infants

MT Attenuates the Decrease in Tibial
Speed of Sound seen in Preterm Infants

Hypotheses Revisited

- In preterm infants twice daily MT promoted improved ANS function as measured by HRV in preterm male infants
- Infants who received MT had lower urinary catecholamine, an indicator of decreased stress response, although not statistically significant

LF/HF Ratio (SEM)

Urine Catecholamine Levels were
Decreased in MT infants

Mean (SEM): MT = 8, CTL = 11

MT Attenuates the Decrease in Tibial
Speed of Sound seen in Preterm Infants

In preterm infants twice daily MT promoted improved ANS function as measured by HRV in preterm male infants

Infants who received MT had lower urinary catecholamine, an indicator of decreased stress response, although not statistically significant
Hypotheses Revisited

• Although males had increased adiponectin/leptin ratio suggestive of increased abdominal fat, we have insufficient data to support improved growth quality
• Twice daily MT improved bone strength in male and female preterm infants

Future Research

• Long term benefits of massage on ANS function in preterm infants
  – Is there a carry over effect after discharge?
  – What are the effects on neurobehavioral development?
• What are the mechanisms of massage in promoting ANS function in preterm infants

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