Soft neurological signs and prenatal alcohol exposure: a population-based study in remote Australia

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- Discipline of Paediatrics and Child Health
- George Institute for Global Health
- Poche Centre for Indigenous Health

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Soft Neurological Signs (SNS)

- mild dysfunction in regulation of muscle tone, choreiform dyskinesia, disdiadochokinesis, difficulties in balance, fine manipulative disability, and difficulties in co-ordination (Gustafsson 2010)
Alcohol can cause brain dysfunction
SNS and Prenatal Alcohol Exposure

Neuro-developmental Impairment
- Cognition
- Executive function
- Attention & learning
- Motor skills
- Memory

SNS Assessment
May provide additional information which increases the suspicion of brain dysfunction in children when PAE is known or suspected
Biological plausibility

- **Corpus Callosum**: Bimanual Coordination
- **Basal Ganglia**: Bimanual Coordination and maintains motor cortex connections
- **Cerebellum**: Balance and coordination
- **Other**: Executive Function
- **PNS**: Slower conductivity in peripheral nerves
### Evaluation of SNS

## FASD Guideline Recommendations

<table>
<thead>
<tr>
<th>FASD Guideline</th>
<th>Assessment recommendation</th>
<th>Cut-off for impairment</th>
<th>SNS Assessment Recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td>The Canadian FASD Diagnostic Guidelines(^{12,13})</td>
<td>“motor skills”</td>
<td>2SD below the mean (2(^{\text{nd}}) centile)</td>
<td>✔️</td>
</tr>
<tr>
<td>The 4-Digit Diagnostic Code – University of Washington(^{14})</td>
<td>“motor/sensory integration”</td>
<td>2SD below the mean (2(^{\text{nd}}) centile)</td>
<td>✔️</td>
</tr>
<tr>
<td>Institute of Medicine (IOM)(^{15})</td>
<td>“motor dysfunction”</td>
<td>None provided</td>
<td>✗</td>
</tr>
<tr>
<td>Centers for Disease Control and Prevention(^{16})</td>
<td>“motor functioning” including gross and fine motor skills</td>
<td>1SD below the mean (16(^{\text{th}}) centile)</td>
<td>✔️</td>
</tr>
</tbody>
</table>

- Few published FASD prevalence studies have reported using SNS as part of the diagnostic process (May 2006, 2007, 2011, 2013)
QNST-2 Assessment

Validated
Reliable
Inexpensive: < $200
Training: simple
Assessment: 15 mins & fun

# lower scores indicate better performance as each score indicates an error
❖ Normative data available for 5 to 80+ years
Background – Lililwan Project

What’s Known

❖ SNS are subtle indicators of brain dysfunction in a variety of disorders.
❖ The QNST-2 is a reliable and valid measure of SNS.

What’s Unknown

❖ QNST-2 has not previously been used in Aboriginal children living in remote Australian communities.
❖ QNST-2 utility for identifying SNS in children with known or suspected prenatal alcohol exposure (PAE) or Fetal Alcohol Spectrum Disorders (FASD).
Aims

1. To identify SNS in a population-based study of children aged 7-9 years living in very remote Aboriginal communities in the Fitzroy Valley where PAE was high

2. Compare children with and without
   (i) PAE or (ii) FASD.

Hypotheses

1. (i) In a cohort of predominantly Australian Aboriginal children living in remote communities the median QNST-2 scores will be higher than existing population norms.

2. (ii) QNST-2 scores and prevalence of SNS will be higher in children with PAE than without.

3. (iii) QNST-2 scores and prevalence of SNS will be higher in children with FASD than without.
Methods

- **Study Design:**
  Cross sectional study
  (Smaller study within population-based FASD prevalence study using active case ascertainment)

- **Setting:**
  Fitzroy Valley, Western Australia (population: 4,500; Aboriginal: 81% (Morphy 2010))

- **Participants:**
  All children born in 2002 and 2003

- **Standardised Assessments:**
  QNST-2 (Mutti et al 1998)
  - Significant SNS scores ≤ 5th percentile
  - Higher scores indicate more SNS
  AUDIT-C

- **Statistical Analysis:**
  SPSS (IBM 2012)
  Descriptive analyses, Independent t-tests (α = 0.05)
## Results

### Child Characteristics

<table>
<thead>
<tr>
<th>Child Characteristics</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants (%)</td>
<td>108/134 (81%)</td>
</tr>
<tr>
<td>Mean age</td>
<td>8.7 years</td>
</tr>
<tr>
<td>Males</td>
<td>53%</td>
</tr>
<tr>
<td>Aboriginality</td>
<td>98%</td>
</tr>
<tr>
<td>Living in very remote communities</td>
<td>70%</td>
</tr>
<tr>
<td>“Risky” and “high risk” PAE (AUDIT-C)</td>
<td>51.5%</td>
</tr>
<tr>
<td>FASD diagnosis</td>
<td>19.4%</td>
</tr>
</tbody>
</table>
## Study Aims

<table>
<thead>
<tr>
<th>Aims</th>
<th>QNST-2 Total score</th>
<th>Median (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Total Cohort</strong></td>
<td></td>
<td>19.0 (4 – 66);</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Normal range: 73.3%</strong></td>
</tr>
<tr>
<td><strong>2. FASD and no FASD</strong></td>
<td>FASD: 22.0 (11 - 66)</td>
<td>No FASD: 18.0 (4 - 40)</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em><em>r=0.3</em>, p=0.004</em>*</td>
</tr>
<tr>
<td><strong>3. PAE and no PAE</strong></td>
<td>PAE: 20.0 (4 – 66)</td>
<td>No PAE: 16.5 (4 – 66)</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em><em>r= 0.2</em>, p=0.045</em>*</td>
</tr>
</tbody>
</table>

- higher scores indicate more SNS
- each individual score indicates an error in motor task performance
- maximum Total Score = 140

**Size effects (r):** 0.1=small effect, 0.3=medium effect, 0.5=large effect *(Cohen 1998)*
## Results

### Prevalence of Severe SNS

<table>
<thead>
<tr>
<th>Score category</th>
<th>Total cohort (n=21) no. (%)</th>
<th>FASD (n=21) no. (%)</th>
<th>No FASD (n=86) no. (%)</th>
<th>PAE (n=60) no. (%)</th>
<th>No PAE (n=42) no. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>90 (83.2)</td>
<td>15 (71.4)</td>
<td>74 (86.0)</td>
<td>49 (81.7)</td>
<td>36 (85.7)</td>
</tr>
<tr>
<td>Moderate Discrepancy</td>
<td>16 (15.0)</td>
<td>4 (19.0)</td>
<td>12 (14.0)</td>
<td>9 (15.0)</td>
<td>6 (14.3)</td>
</tr>
<tr>
<td>Severe Discrepancy</td>
<td>2 (1.9)</td>
<td>2 (9.5)</td>
<td>0 (0.0)</td>
<td>2 (3.3)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

**Normal**: ≥ 25\(^{th}\) percentile, Score range: 0 – 28  
**Moderate Discrepancy**: 6\(^{th}\) to 24\(^{th}\) percentile, Score range: 29 to 44  
**Severe Discrepancy**: ≤ 5\(^{th}\) percentile, Score range: + 45
### Results

#### SNS and CNS Domains of Impairment

<table>
<thead>
<tr>
<th>QNST-2 Score</th>
<th>Percentile (score range)</th>
<th>Frequency of ≥ 3 domains CNS impairment</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>≥ 25&lt;sup&gt;th&lt;/sup&gt; (0-28)</td>
<td>29.2% (26/89)</td>
<td>1.65 (1.97)</td>
</tr>
<tr>
<td>Moderate discrepancy</td>
<td>6&lt;sup&gt;th&lt;/sup&gt; – 24&lt;sup&gt;th&lt;/sup&gt; (29 to 44)</td>
<td>50% (8/16)</td>
<td>2.94 (2.51)</td>
</tr>
<tr>
<td>Severe discrepancy</td>
<td>≤ 5&lt;sup&gt;th&lt;/sup&gt; (+ 45)</td>
<td>100% (2/2)</td>
<td></td>
</tr>
</tbody>
</table>
Findings are consistent with other studies

- SNS significantly more common in FASD children vs typically developing children ($p < 0.01$): QNST-2, $n=52$
  (Clinic based study University of Washington registry; 5-8 yo’s; Jirikovic 1998)

- QNST-2 scores were significantly higher in subjects with a FASD vs PAE but normal CNS
  (Clinic based study University of Washington registry; all ages; Astley 2010)

- Minor neurological anomalies (Touwen’s examination) higher in children with PAE vs no PAE; 4.5 yrs (Larroque 2000)

- QNST-2 discriminated between children with perceptual motor difficulties vs typically developing children (Parish 2002)

- DCD children had mean QNST-2 score ≤ 5th percentile (severe discrepancy) (O’Hare 2002)
Strengths & Limitations

**Strengths**

- Indigenous partnership
- Population-based study with high participation rates
- Blinding of assessors to PAE and FASD status
- Use of standardised assessment tools

**Limitations**

- Small sample size (unable to control for confounders)
- Absence of standardised norms for Aboriginal children
- Potential misclassification bias (assessment at one time point)
Conclusions

- Aboriginal children living in remote communities have similar SNS to population norms despite significant underperformance of some subgroups including children with PAE and FASD.
- High physical activity levels in children living in remote communities may be protective.
- SNS were more common in children with PAE or FASD, consistent with the known neurotoxic effect of PAE.
- Prevalence of SNS are 2 x higher in children with a FASD.
- The QNST-2 is a useful screen for detecting subtle neurological dysfunction and indicating the need for more comprehensive assessment in children with PAE or FASD.
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