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

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7th International Conference on FASD Vancouver, Canada 2017

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Marulu
The Lililwan Project

Soft Neurological Signs (SNS)

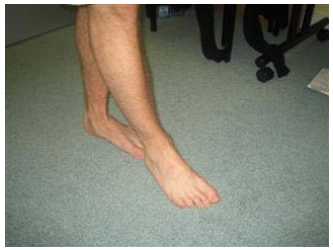
- mild dysfunction in regulation of muscle tone, choreiform dyskinesia, disdiadochokinesis, difficulties in balance, fine manipulative disability, and difficulties in co-ordination *(Gustafsson 2010)*









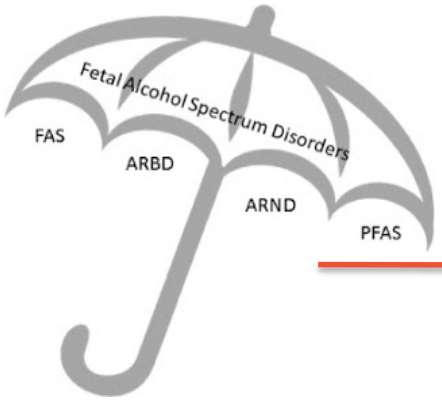



SNS and Diagnostic Promise

SNS

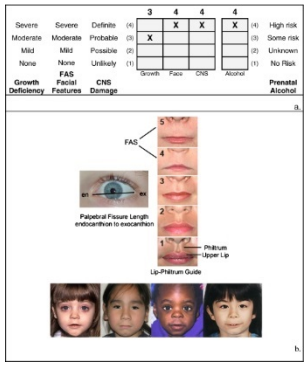
Alcohol can cause brain dysfunction

SNS and Prenatal Alcohol Exposure



Neuro-developmental Impairment

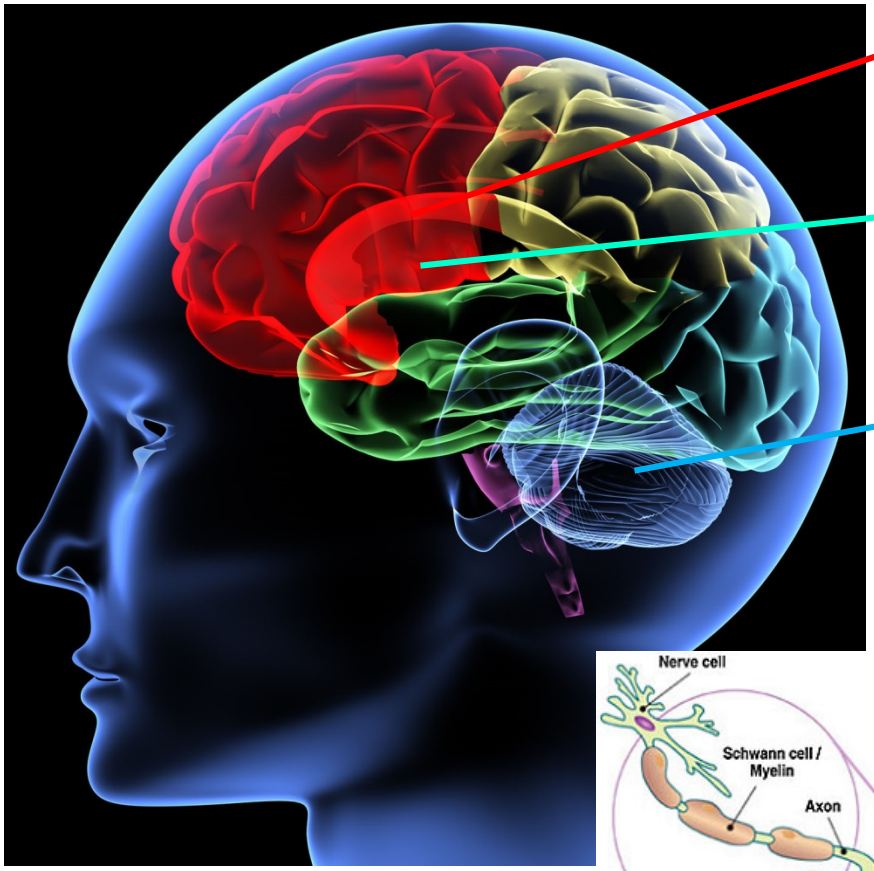
- Cognition
- Executive function
- Attention & learning
- Motor skills
- Memory



SNS Assessment

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

Biological plausibility



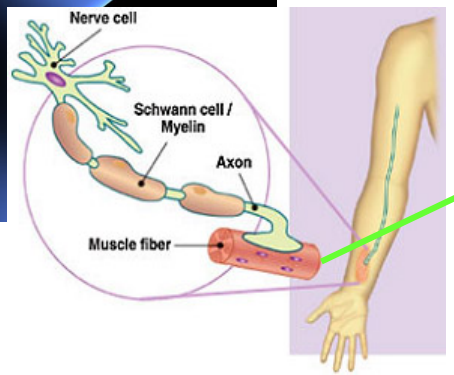
Corpus Callosum
Bimanual Coordination

Basal Ganglia
Bimanual Coordination and maintains motor cortex connections

Cerebellum
Balance and coordination

Other
Executive Function

CNS



PNS
Slower conductivity in peripheral nerves

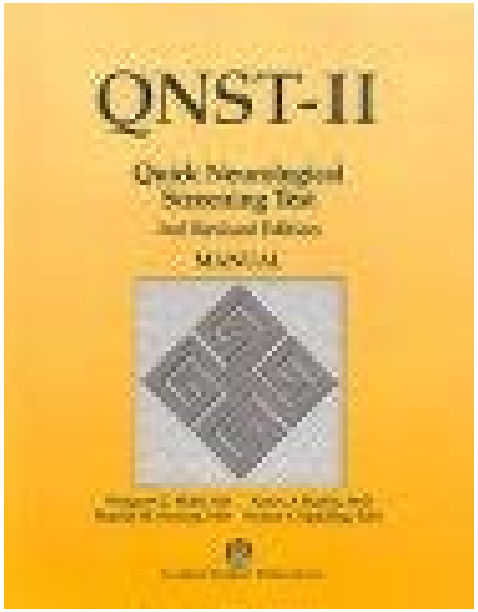
Evaluation of SNS

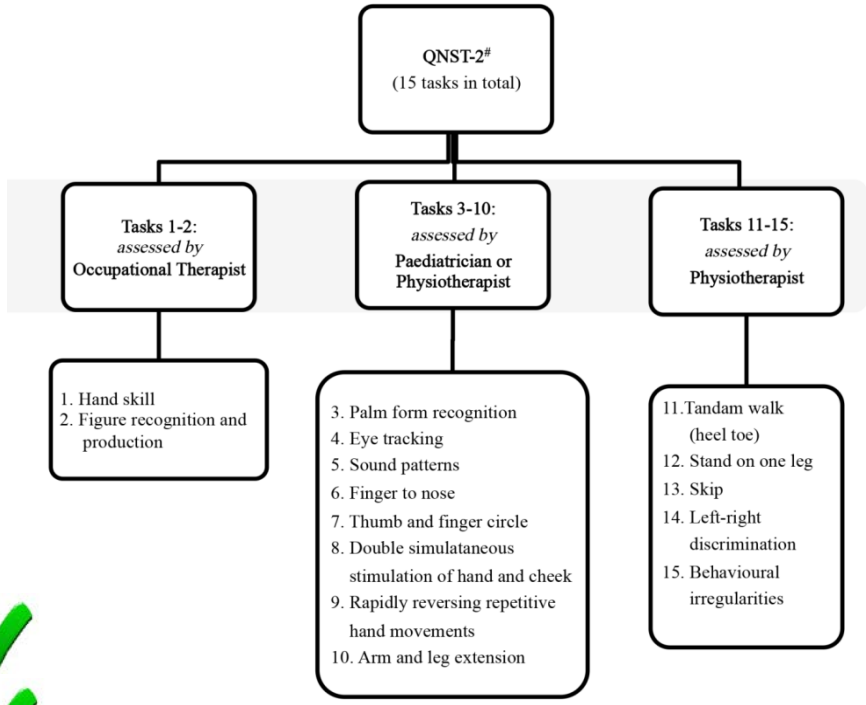
FASD Guideline Recommendations

FASD Guideline	Assessment recommendation	Cut-off for impairment	SNS Assessment Recommended
The Canadian FASD Diagnostic Guidelines[12, 13]	"motor skills"	2SD below the mean (2^{nd} centile)	
The 4-Digit Diagnostic Code – University of Washington[14]	"motor/sensory integration"	2SD below the mean (2^{nd} centile)	
Institute of Medicine (IOM)[15]	"motor dysfunction"	None provided	
Centers for Disease Control and Prevention[16]	"motor functioning" including gross and fine motor skills	1SD below the mean (16^{th} centile)	

- **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 ($\alpha = 0.05$)

Results

Child Characteristics

Child Characteristics	Result
Participants (%)	108/134 (81%)
Mean age	8.7 years
Males	53%
Aboriginality	98%
Living in very remote communities	70%
“Risky” and “high risk” PAE (AUDIT-C)	51.5%
FASD diagnosis	19.4%

Results

Study Aims

Aims	QNST-2 Total score median (range)	
1. Total Cohort	19.0 (4 – 66); **Normal range: 73.3%**	
2. FASD and no FASD	FASD: 22.0 (11 - 66)	No FASD: 18.0 (4 - 40)
	r=0.3*, p=0.004	
3. PAE and no PAE	PAE: 20.0 (4 – 66)	No PAE: 16.5 (4 – 66)
	r= 0.2*, p=0.045	

- 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

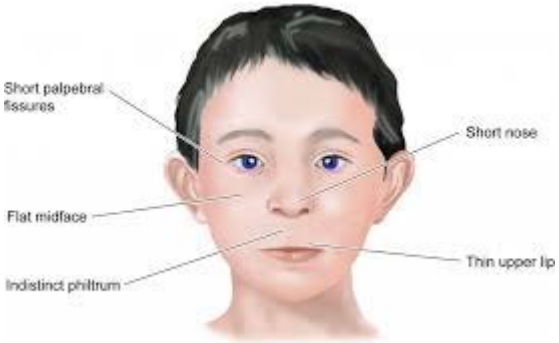
Prevalence of Severe SNS

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

Normal: ≥ 25th percentile, Score range: 0 – 28
Moderate Discrepancy: 6th to 24th percentile, Score range: 29 to 44
Severe Discrepancy: ≤ 5th percentile, Score range: + 45

Results

SNS and CNS Domains of Impairment



≥ 3 domains of impairment

QNST-2 Score	Percentile (score range)	Frequency ≥ 3 domains CNS impairment	Mean (SD)
Normal	≥ 25th (0-28)	29.2% (26/89)	1.65 (1.97)
Moderate discrepancy	6th – 24th (29 to 44)	50% (8/16)	2.94 (2.51)
Severe discrepancy	≤ 5th (+ 45)	100% (2/2)	

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; Jirikowic 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 $\leq 5^{th}$ 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.**

Acknowledgements

Co-authors

- **Prof Jane Latimer**
- Robyn Doney
- Dr Rochelle Watkins
- Dr Tracey Tsang
- Prof Tracy Jirikowic
- Prof Heather Carmichael Olson
- Dr James P Fitzpatrick
- June Oscar
- Maureen Carter
- **Prof Elizabeth J Elliott**

Support

- Sharon Eadie
- Hannah Parker
- Gary Rolls
- Trish Evans

Lililwan Collaborators

- The George Institute for Global Health
- The University of Sydney
- Marninwarntikura Women's Resource Centre
- Nindilingarri Cultural Health Services

Funders

- National Health and Medical Research Council (NHMRC)
- Department of Families, Housing, Community Services and Indigenous Affairs (FaHCSIA)
- Department of Health and Ageing (DoHA)
- Poche Centre for Indigenous Health, The University of Sydney
- Save the Children