Neurodevelopmental and mental health outcomes in a cohort of South African children: design and feasibility of the Safe Passage-BONO study

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The feasibility study showed that a multi-modal biomarker protocol can be applied to a lower socioeconomic South African context, and can be used to refine methods, define clinical cut-offs and develop the expertise of the research team

BACKGROUND

Children living in low- and middle-income countries are more frequently exposed to poverty-related adversities both pre-and postnatally which can impact their cognitive and socioemotional development. Longitudinal pregnancy cohorts are needed to track trajectories of neurodevelopmental, cognitive and mental health conditions in these children.

The South African Safe Passage Study (SASPS) originally enrolled 7,060 pregnant women at a community healthcare centre, Cape Town (2007-2015) to investigate the association between prenatal alcohol, multiple environmental risk factors and adverse pregnancy outcomes in a socioeconomically-disadvantaged community.

The Safe Passage-Biomarkers of Neurodevelopmental Outcomes (BONO) study aims to follow up 2,000 SASPS children, aged 4-16 years to assess the role of pre- and postnatal risk and protective factors in cognitive, neurodevelopmental and mental health outcomes.

Primary Objectives of the <u>feasibility study</u> were 1) to confirm recruitment capability and retention 2) select/translate/adapt measures 3) ensure visit was acceptable to participants, 4) establish criteria (cut-off scores) for the deep phenotyping phase in the main study.

METHODS

Between March and October 2019:

- 100 mother-child dyads from the SASPS assessed
- Attended 2 visits each within a 4-week interval at Tygerberg Hospital
- Age-groups: 3-4.9 years, 5-6.9 years, 7-8.9 years, 9-11.9 years
- Equal numbers in each age-group, 55% girls

Visit 1: Broad Phenotyping Phase (Screening)

Social Communication Questionnaire (SCQ) for autistic traits

Strengths & Difficulties Questionnaire (SDQ) for emotional/behavioral symptoms

Visit 2: Deep Phenotyping Phase (Diagnostic)

TABLE 2: Overview of Child and Maternal Measures

Phase	Visit 1 Broad Phenotyping	Visit 2 Deep Phenotyping
Clinical	Autism screener (SCQ) Emotional and behavioral symptoms (SDQ) Risk and Protective Factors	Autism Assessment: Childhood Autism Rating Scale Repetitive & sensory symptoms Psychopathology
Eye-tracking	Static and dynamic scenes	Static and dynamic scenes
Cognition	Intelligence Quotient Executive function Reward learning Emotion processing	Maternal Intelligence Quotient Social cognition Visual decision making
EEG	Task-related resting state Event-related potential task Sensory processing efficiency	Task-related resting state Event-related potential task Sensory processing efficiency

RESULTS

Recruitment, Enrolment and Participant Retention

50 initial letters delivered to potential participants informing them of study

25 participants responded telephonically and 24 enrolled in study within 48 hours.

76 participants heard about study from other participants (60) or research worker at a healthcare facility (16), and contacted SASPS research unit independently

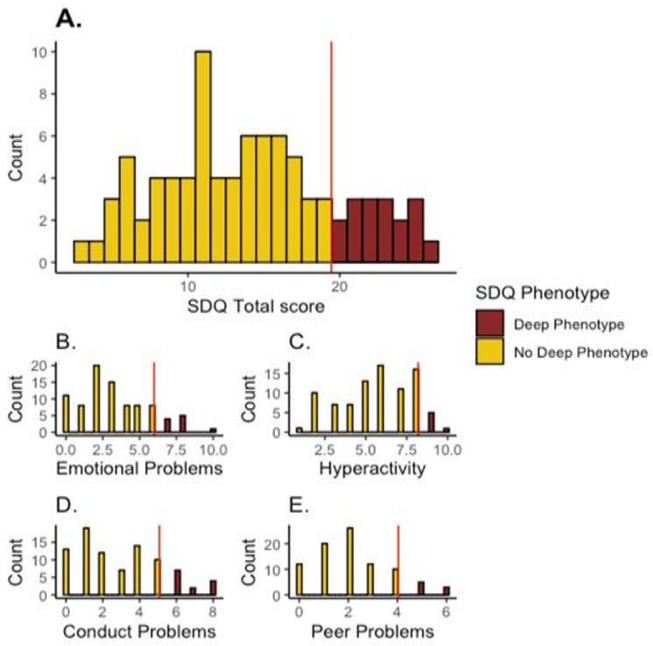
100 mother-child dyads attended and completed Broad Phenotype visit

96 dyads completed Deep Phenotyping visit (96% retention)

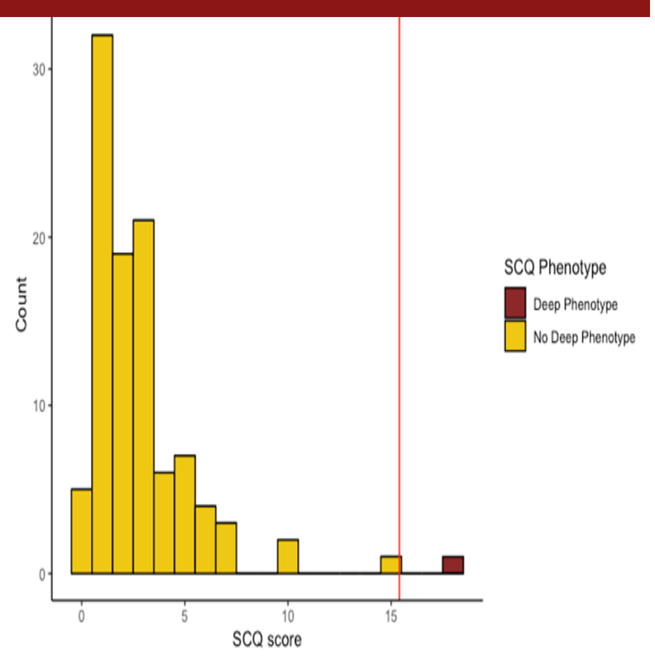
Feasibility study participants resembled larger SASPS cohort except for higher prenatal Edinburgh depression scores and household crowding indices (Table 1).

TABLE 1: Comparison of prenatal characteristics of Feasibility Cohort (N=100) with South African Safe Passage Study (SASPS) Cohort (N=6,874)

Variable/Study cohort	Feasibility cohort Mean (SD)	SA SPS cohort Mean (SD)	P-value
Maternal age (years)	25.1 (6.2)	24.8 (5.9)	0.78
Gravidity	2.5 (1.5)	2.3 (1.3)	0.16
Parity	1.3 (1.4)	1.1 (1.2)	0.31
Education (years)	9.7 (1.8)	10.0 (1.7)	0.13
Household crowding index	1.8 (0.9)	1.6 (0.9)	**0.005**
Household income (ZAR/month)	718 (425)	861 (589)	0.07
Edinburgh depression scale	14.1 (5.5)	12.9 (5.9)	**0.04**
Anxiety trait score	41.6 (11.1)	41.0 (10.8)	0.54
Total drinks in pregnancy	9.5 (20.4)	13.1 (33.7)	0.27
Cigarettes/ day in pregnancy	2.9 (3.4)	3.0 (3.7)	0.79
Gestation at delivery (days)	271.0 (16.2)	269.6 (23.0)	0.94
Birthweight (gram)	3027 (667)	2963 (618)	0.30
Birthweight z-scores	-0.2 (1.1)	-0.4 (1.0)	0.19



<u>Figure 1:</u> Distribution of SDQ with adjustment of cut-off scores: Total (A) and sub-scale scores (B) Emotional (C) Hyperactivity (D) Conduct (E) Peer Problems
Cut-off scores adjusted to include upper 10%



<u>Figure 2</u>: Distribution of SCQ scores with recommended cut-off score of 15. Two children had high scores classified as autism on CARS-2. Decision was made to reduce the SCQ cut-off score to 10, so as to include more children with autistic traits for the deep phenotyping visit.

Establishing citeria (cut-off scores) for the Deep Phenotyping visit

CONCLUSIONS

The feasibility study established and confirmed:

- **Adequate participant recruitment and retention capability**
- **Suitability and high acquisition rates of most measures**
- **Acceptability of the measures/visit duration to participants**
- **Cut-off scores limiting deep phenotyping to 30% of participants**

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