Introducing Biological & Environmental Measures of Early Life Stress into the SPRING Home Visits Intervention Trial: Challenges & Solutions

Sunil Bhopal
Wellcome Trust Research Training Fellow | LSHTM
Paediatric Specialty Registrar | North East England

Outline

• From Child Survival to Child Development
• SPRING home visits intervention trial in rural India: promoting early growth & development
• Role of Early Life Stress in Child Development
• SPRING-ELS: Assessing role of stress in causal pathway

From Child Survival to Child Development

Major successes in child survival: now urgent need to ensure all children can thrive

“the time is right to recognise that investment in early child development is essential, not only for good health but also for sustainable development”

Three Lancet Series since 2007

Child development in developing countries 1

Developmental potential in the first 5 years for children in developing countries

250 million children (43%) in low & middle income countries at high risk of not reaching their developmental potential

Advancing Early Childhood Development: from Science to Scale 1

Early childhood development coming of age: science through the life course

SPRING cluster randomised controlled trial: promoting early child growth & development

Counselling approach informed by cognitive behavioural therapy: through pregnancy & first two years of child’s life
SPRING Monthly Home Visits

SPRING Cluster Randomised Controlled Trial

- **Rewari district**: Haryana, India
- **24 clusters**: 12 intervention | 12 control
- **Cluster**: population served by sub-centre

- **Total population**: 96,000
- **5000 mother-child dyads enrolled & followed up
- **Detailed outcome assessments** with 2000 children

SPRING Conceptual Framework

**Outcome Assessments: Length**

**SPRING Implementation: Inputs & Processes**

**Outcome Assessments: Bayley Scales of Infant Development**
Healthy child development can be derailed by adversity & its impact on the stress response systems

Damage impact of stress on learning, behaviour & health throughout the lifespan

Cortisol: end product of the hypothalamic-pituitary-adrenal axis

Diurnal rhythm matures from 3 months of age

Linear decrease through day. Small peaks post daytime nap

Measuring HPA Axis in SPRING

- Cortisol diurnal rhythm: Saliva
  - Reflects systemic concentration from 20 minutes previous
  - Multiple samples: 8am, 12noon & 4pm on two days
  - Diurnal slope of decrease: mean of two days
  - Non-invasive
  - Widely used but minimally in low & middle income countries

- Chronic cortisol exposure: Hair
  - 1cm=approx 1 month exposure
  - Assessing 3cm hair (15-75mg)

Saliva & Hair Sampling: Feasibility

- In-depth interviews
  - (5 mothers, 2 barbers)
- Focus group discussions with mothers
  - (2 groups)
- Piloting techniques
  - (13 children aged 11-13 months)

SPRING Conceptual Framework

+ Early Life Stress contribution

1. Impact of SPRING on stress
2. Determinants of biological stress

Additional stress risk factors

Intermediate outcomes
Impact outcomes
Saliva sampling: Variety of techniques

Saliva: Findings

- No cultural barriers found
- Practical findings:
  - Mothers know the waking times of their children and can tell our assessors
  - Mothers wanted workers to take sample
  - Large range of time taken to sample: 10 – 120 seconds
  - Staying in household all day for sampling: households welcoming but need to consider other tasks for workers to keep them busy

Hair: Posterior Vertex

Hair: 1-3cm

Hair

- Many cultural barriers to sampling
- Association with evil eye
- Usually cannot sample before ceremonial first haircut (up to three set times per year)
- Usually may not sample if mother is pregnant
- Usually may not cut hair on:
  - Tuesdays, often not on Thursday or Saturday
  - Festival days
  - Fasting days (approx. 10 individual days)
- Many children have very short hair/shaved head
- Suspicion from family – need to involve all household members

Hair: solutions

- Involvement of whole family at consenting visit, appointment visit & during assessment
- If cannot cut on day 1 of assessment– attempt to do on day 2
- Increase sample size to account for consent refusals, first haircut not done & short hair
Explanatory Framework for Stress

Exploring local understanding of infant stress to develop a questionnaire to measure risk-factors for ELS

Perceived causes of stress

- Household violence
- Poverty
- Poor hygiene
- Neglect
- Inadequate care
- Maternal stress
- Sibling abuse/violence
- Carer alcoholism

Incorporated into an environmental stress questionnaire to complement other SPRING measures

Impacts of adversity

- Difficult to predict: some children seem more resilient than others
- Negative impact on growth, development
- Leads to fear, behavioural problems
- Deficits can be reversed – but becomes more difficult over time
- Lesser impact on non-verbal young infants: too young to ‘understand’

Prevention & Treatment through extra love & improved caregiving

Summary

- Taking saliva & hair: feasible & acceptable
- To date: 4000 saliva | 800 hair | 1200 questionnaires
- First large integrated nutrition & development trial to include biological measures of stress
- Hair cortisol: first time in young children in South Asia

Thanks & Acknowledgements

SPRING Team
Prof Betty Kirkwood (PI & Supervisor)
Gauri Divan Sangath
Reetabrata Roy LSHTM
Bilal Avan LSHTM
Deepali Verma Sangath
Divya Kumar Sangath
Zelee Hill UCL

Collaborators
Bushra Khan, University of Karachi
Matt Bristow, Anglia Ruskin University
Jane Barlow, Oxford University

Funding
Wellcome Trust Research Training Fellowship 2015-2018
SPRING funded by Wellcome Trust Programme Grant

Contact
http://spring.lshtm.ac.uk
Sunil.Bhopal@lshtm.ac.uk
Twitter: @sunilbhop

Collaborators
Bushra Khan, University of Karachi
Matt Bristow, Anglia Ruskin University
Jane Barlow, Oxford University

Funding
Wellcome Trust Research Training Fellowship 2015-2018
SPRING funded by Wellcome Trust Programme Grant

Contact
http://spring.lshtm.ac.uk
Sunil.Bhopal@lshtm.ac.uk
Twitter: @sunilbhop