Randomised controlled trial of PREMM: Early somatosensory stimulation (massage) in preterm infants

M.M. Lai1,2, G. D’Acunto1, A. Guzzetta3, J. Fripp1, A. Chan1, S.E. Rose4, N. Ngenda2, K. Whittingham5, P.B. Colditz2, R.N. Boyd5

1Royal Brisbane & Women’s Hospital, Herston, Brisbane, Queensland, Australia.
2University of Queensland, Centre for Clinical Research, Brisbane, Australia.
3Stella Maris Scientific Institute, Department of Developmental Neuroscience, Pisa, Italy.
4The Australian E-Health Research Centre, Brisbane, Australia.
5Queensland Cerebral Palsy and Rehabilitation Research Centre, The University of Queensland, Brisbane, Australia.

Objectives:
Early interventions are designed to optimise preterm infant’s sensory experience and improve functional outcome. This study examines the efficacy of early somatosensory stimulation (massage) on neurobehavioural, neurological and visual development, and brain development in preterm infants at term equivalent age (TEA). Secondarily, whether massage delivered by the mother will enhance mother-infant attachment and maternal mental health.

Participants:
Low-risk very preterm infants (VPT; 28-32+6 weeks at birth) who were admitted to the Grantham Stable Neonatal Unit at the Royal Brisbane & Women’s Hospital were eligible for recruitment into the study.

Inclusion criteria: Birthweight between 10th and 90th percentile for gestational age and gender, clinically stable, off oxygen therapy and off respiratory support.

Exclusion criteria: The presence of abnormalities on brain ultrasound including severe intraventricular haemorrhage (grade III or IV), periventricular echogenicity or periventricular cysts. Infants with major genetic disorders and malformations were also excluded.

Ten healthy term born infants were recruited as a reference group (TC). These infants were born between 37 and 41 weeks with uncomplicated pregnancies and deliveries, and did not require special care admission.

Methods:
Mother-infant dyads were randomised to a massage group (PREMM) or care as usual group (CAU). Mothers in the PREMM group were taught to massage their babies from enrolment until TEA. The intervention protocol comprised both tactile and kinaesthetic phases for a total of 15 mins, 1-2 sessions/day. Mothers were provided with a structured diary to keep a record of the number and duration of each session. Infants in the CAU group received routine nursery care.

Outcomes assessed at TEA were Dubowitz Newborn Neurological Assessment (DNNA); Visual (Rici); and Neuroimaging with MRI (structural and diffusion tensor acquired without sedation on a 3T system using a MRI compatible incubator). Mothers’ mood, stress and anxiety was measured using Mother-to-infant Bonding Scale (MIBS), Edinburgh Postnatal Depression Scale (EPDS). Depression-Anxiety-Stress Scales (DASS) at baseline and at TEA.

Analysis was independent t-tests (2-tailed) post treatment or ANCOVA comparing pre-post intervention.

Results: Neurobehavioural
Thirty VPT infants were randomised to each study group. In the PREMM group, 23 infants received the intervention (2 withdrew, 1 unstable, 4 found it difficult). At TEA, 28 (93%) PREMM and 23 (77%) CAU infants returned for assessment. Birthweight was significantly greater in the CAU group (PREMM vs CAU, mean BW=1369±294 vs 1538±267, p=0.05). There were no significant differences between groups in DNNA and Visual scores at TEA, however both groups were significantly different to TC (Figures 1 & 2).

Results: MRI
For structural assessment, a T2 map series was acquired in the transverse plane (TR=10580ms, TEs 27, 122, 189 ms, slice thickness 2mm, FOV 144x180mm, voxel size = 0.7mm). Diffusion tensor images (n=30, b=1000s/m2) were acquired using a single shot echo planar multi-direction sequence (TR=9500ms, TE=130ms, slice thickness 2mm, FOV 224mm, voxel size=1.75mm). The structural MRI was segmented in gray matter (GM), white matter (WM) and corticospinal fluid (CSF), and labelled using the Albert Atlas (Miliaux). A population FA atlas was created and aligned to the John Hopkins Unit (JHU) neonatal Atlas. MRIs without significant motion artefact were analysed (24 PREMM, 16 CAU). Preterm measures can be seen in Figure 3.

MRI results:
Relationships between MRI and neurobehavioural exams were assessed using a general linear model with adjustments for GA at birth, PMA at scan, sex and BW. There was no significant differences in volumetry between CAU and PREMM groups.

A weak association was observed between visual scores and the mean diffusivity in the internal capsule (β=0.44, p = 0.002) and external capsule (β=0.37, p = 0.015) and thalamus (β=0.35, p = 0.03).

A weak association was observed between DNNA and the mean diffusivity in the corpus callosum (β=0.33, p = 0.02) and fornix (β=0.35, p = 0.03).

Maternal results:
The stress scale of the DASS was significant between groups (F=6.87, p<0.01, Partial Eta2=0.15) but no difference between groups for MIBS, EPDS or depression and anxiety scales of the DASS (Figure 5).

Conclusions:
Mothers randomised to massage their infants were less stressed after the intervention period compared to mothers whose infants received care as usual at TEA. Differences in volumetric changes and structural connectivity on MRI related to vision and social/emotional development were related to lower gestational age at birth in the PREMM group.

Acknowledgments:
QCPPRC funding project grant, Merchant Charitable Foundation RBWH Foundation Postgraduate Research Scholarship.