Potential impact of Kangaroo Mother Care on the neurobehavioral development of the ex-premature infant at middle and long term.

Dr Nathalie Charpak Pr Rejean Tessier
Laval, Quebec
Fundación Canguro, Bogota
THE PROBLEM

- 15 million children are born premature or LBW each year (10% of all deliveries in the world)
- Prematurity and LBW are a direct, or associated cause, of 50% of the 3,200,000 children’s deaths occurring annually in the world 'during the first month of life
- 90% of LBW infants are born in low and middle income countries
- Diffusion of KMC is too slow and coverage is not sufficient
- Mid-term and long term effects for survivors:
  - Cognitive deficits, poorer academic
  - Performance, attention problems,
  - less social competence and less secure attachment and relationship.
What is the KMC method?

Kangaroo Mother Care Method has three fundamental components:

1) **Kangaroo position (KP)** - Skin to skin contact on the mother's chest, in upright position 24 hours a day

2) **Kangaroo nutrition** Exclusive breastfeeding or almost exclusively

3) **Kangaroo discharge policy**: Timely (early) discharge in kangaroo position with close and strict outpatient follow-up up to 40 weeks of gestational age. In a second step high risk follow up during at least the first year of corrected age in a KMC program
KMC is a concept, a method of care targeted mainly at the baby/mother dyad

There is a logical progression in the implementation of KMC in a hospital facility

1-Skin to skin contact or kangaroo position
   - Intermittent
   - Continuous

2-Breastfeeding the premature infant or kangaroo nutrition
   - Empowerment of the mother and the family
   - Kangaroo rooms/ward

3-Home discharge in kangaroo position and Kangaroo discharge policies with strict follow up
KMC is a concept, a method of care targeted mainly at the baby/mother dyad.

1. Skin to skin contact (kangaroo position) intermittently or continuously.

2. Breastfeeding the premature infant or kangaroo nutrition.

3. Empowerment of the mother and the family.

Kangaroo rooms/ward or home discharge in kangaroo position or Kangaroo discharge policies with strict follow up.

There is a logical progression in the implementation of KMC in a hospital facility.

Macroscopic evolution of the brain between 24 and 40 weeks.

Maturation of the brain:
- Brain cerebral volume increase x 1.5
- Brain Cortex surface increase x 4

Cortesey Frédérique BERNE AUDEOUD
The main problem of prematurity?

Brain of a preterm infant at 40 weeks compared to a brain of a term infant (Rueckert 2003)
Early discharge with Ambulatory follow up

The life of the kangaroo mother and her baby at home
Bar Ilan U, KF

1994-2018: KMC knowledge transfer. 75 teams from 35 developing countries trained in Bogota. Training of trainers. South South cooperation
KF NGOs WorldLab, MinSalud PUJ APC

2003-2018: Quality KMC. Monitoring of indicators KF.

2012-2018 Long term follow up of the KMC infant GCC, Us

2005-2018 Neuro-psychomotor development of the KMC infants during the follow up. In the KMC program
KF U.Laval, PUJ

2004-2019: Research on pulmonary and neurological aspects of KMC impact
KF Colciencias, PUJ

2012-2018 Quality KMC. Monitoring of indicators KF.

1997 – 2018: Nutritional impact of the kangaroo nutrition (breastfeeding the premature infant)
Nestle Fundation, KF PUJ

1993 – 2018: Evaluation and enhancement of the emotional behavior with KMC and modification of the family environment
KF U.Laval, PUJ Colciencias

3 Centers of excellence in Teaching hospitals

Fundación Canguro or Kangaroo Foundation

Understanding resistances and solutions 1998-2018 KF, PUJ

3 Centers of excellence in Teaching hospitals
1993 – 1997: Cognitive development in a sub cohort in a RCT KMC versus traditional care

1993 – 2018: Evaluation and enhancement of the social and emotional behavior in a cohort of preterm and low birth weight infant with or without KMC and modification of the family environment

1999 – 2018: Short and long term Impact of KMC in the family environment of the premature infant

1996 – 1998: Longitudinal descriptive study between 2 cohorts of preterm infants who received or not KMC during the neonatal period and a term infant cohort from the same socio-economic level

2005: Ambulatory KMC and Brazelton scale

2013-2018: Comparison Griffiths/Bailey

2012-2018: Long term follow up of the KMC infant GCC, Us (5)

2010-2011 KMC and cerebral connectivity in a adolescent cohort U Laval

4. La prématurité : y survivre et s’en guérir. 2011 Rouen University, France
9. The long-term effects of the Kangaroo Mother Care intervention on cognitive functioning: Results from a longitudinal study. Stéfanie Ropars, Réjean Tessier, Natalie Charpak, Luis Felipe Uriza, Developmental Neuropsychology, Volume 43, 2018 - Issue 1, Pages 82-91 | Published online: 29 Jan 2018
Photos 1993-1996
Objective of the first RCT in 1993

- Given that effects of socioeconomic factors and perinatal conditions (including gestational age and birth weight) were controlled for, morbimortality at one year in infants with birth weights equal to or less than 2000 assigned to the kangaroo method, are at least as good as those observed in infants under "traditional" care.

- Eligibility for the intervention: thermal stability while in incubator, appropriate nutritional intake, absence of bradycardia and/or apnea episodes, no ambulatory oxygen no treatment evaluated by experienced nurse while the infant is still in the hospital.
Recruitment (delivery room, NCIU) Eligible (Randomization after stabilization) "Term or 40 weeks"

Ambulatory KMC program

No KMC

3 m 6 m 9 m 12 m

“A Randomized Controlled Trial on Kangaroo Mother Care: Results of follow-up at one year of corrected age”. Pediatrics 2001.
Psychological and medical results


Mother feels more competent. She is more sensitive to her baby, especially if he stayed in NCIU, baby will respond better to her mother.

Breast-feeding proportion was higher in KMC infants at 3 months.

KMC infants spent less time in hospital.

Less nosocomial infections in the KMC.

Our results suggest a 50% RR reduction in mortality.

Protective effect with regard to mortality and infectious morbidity for more fragile infants, protective effect when father’s level of education is very low, better Griffith quotients in infants with transient abnormalities in the INFANIB test and a mid-term impact (15 months) on mother-infant interactions where KMC mothers of infants with “transient” INFANIB were more sensitive and had more contingent responses.

Adequate Growth (HC)

KMC families had higher environmental scores, (appearing as greater stimulation for their KMC infants).

Kangaroo Foundation, Bogota, Colombie
2003: The KMC intervention can be viewed as developmentally supportive care, in which parents are guided in managing their biological parenting abilities and which provides “brain care” during a highly sensitive period of a preterm infant’s neurological development.

Kangaroo Mother Care: A method for protecting high-risk low-birth-weight and premature infants against developmental delay

Réjean Tessier a,*, Marta B. Crísto b, Stella Velez b, Martha Giron b, Line Nadeau a, Zita Figueroa de Calume b, Juan G. Ruiz-Paláez c, Nathalie Charpak b

a School of Psychology, Laval University, Laval, Québec, Canada G1K7P4
b Kangaroo Mother Care Program, Children’s Clinic, Colombian Social Security, Kangaroo Foundation, Bogotá, Colombia
c Clinical Epidemiology Unit, Faculty of Medicine, Javeriana University, Bogotá, Colombia

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Abstract

Aim: The purpose of this study was to examine the relationship between intervention with Kangaroo Mother Care (KMC) and the subsequent mental development of the infants. In this prospective study, 431 low-birth-weight and premature infants (≤ 1801 g) were assigned randomly to KMC or Traditional Care. Of these, 336 (78%) received the Griffiths test at 12 months of corrected age. Results: After control for the infant’s health at birth, family socioeconomic status and mother labor and delivery characteristics, the KMC infants had a higher IQ than those given traditional care (TC). The difference was most highly significant for infants who were more premature (30–32 weeks of gestational age), had required intensive care, and had a diagnosis of doubtful or abnormal neurological development at 6 months. The main impact of KMC was on the development of personal relations and on planning functions related to brain developmental stage at birth. Discussion: The KMC intervention can be viewed as a developmentally supportive care, in which parents are guided in managing their biological parenting abilities and which provides “brain care” during a highly sensitive period of a preterm infant’s neurological development.

Keywords: Kangaroo Mother Care; Low-birth-weight; Prematurity; Mental development; Developmental care

* Corresponding author. Tel.: +1-418-656-7180.
E-mail address: rtessier@psy.ulaval.ca (R. Tessier).
15 years later… What’s about brain development

“Sensorimotor impairment, poorer cognitive outcomes and behavioral disabilities observed in school-aged preterm children, have been related to a reduction in the volume of rapidly conducting myelinated nerve fibers, with a 13–35% thinning of the corpus callosum (interhemispheric connection)”

(Schneider et al, 2011)
Sensorial stimulations  Structure and functioning of the CNS

20 w  25w  36w  Connexion of 40,000 synapses per second

Neuronal migration

astrocitogénesis

oligodendrogénesis

axonal and dendritic development

sinaptogénesis

Programmed cellular death

A. Sola 2000
• KMC intervention could nurture the infant brain, with multiple sensory informations from the parents:
  – tactile
  – cutaneous
  – olfaction
  – audition
  – balance
  – proprioception
  – and visual

• KMC: optimal condition for cerebral integration of the body sensorimotor scheme

**Time window:** between 26 and 43 weeks of gestational age = last trimester of pregnancy = synaptogenesis and establishment of the intra and interhemispheric networks
KMC time window

Impact of KMC

Axonal growth
Synaptic connections

Biological risk = interrupted synaptogenesis and faulty networks (Ex.: CC)
What happened 20 years after?

1. The documented 1-year benefits persist up to 20 years?
2. Does the KMC intervention have a long-term protective effect against cognitive, social, and academic difficulties as reported in long-term follow-up?
3. ¿Hay modifications in the functioning of the brain or in volumes of anatomical brain structures related with psychological test and KMC intervention?
Randomized open controlled trial on Kangaroo Mother Care versus traditional Care for low birth weight infants. Patient-centered outcomes at the age of 20 years. 2014–2017

2012-2018
Long term impact of KMC

- Audiometric evaluation
- Optometric evaluation
- Pediatric evaluation
- Neuro-Psychological evaluation
- Magnetic Resonance Imaging, fRMI, DTI
- Transcranial Magnetic Stimulation
- Best Friend Interview (ABCL)
- Home Visit Interview and Home test
- Class Play Test
- Socioeconomic and education survey
Population and Sample

433 Original RCT Participants ≤ 1800 g

293 participants were located (71%)

119 participants could not be located

412 survivors at 1 year CA

264 participants (64%)

3 died

6 living outside Bogotá

20 refused to participate

6 living outside Bogotá
Outcome Variables

• Mortality and morbidity at 20 years
• General health at 20 years
  – Relevant medical history (diagnosed illnesses)
  – Clinical exam
  – Physical growth: height-for-age, weight-for-age, weight-for-height, head circumference; body mass index, lean body mass.
  – Metabolic profile
Outcome Variables

• Productivity and academic data
  – Preschool and school history
  – School achievement and performance (National Colombian Examination)
  – Labour force participation status and wages

• Sensory motor status
  – Fine motor skills, including visual motor integration.
Outcome Variables

• Cognition
  – General intelligence (Wechsler abbreviated scale of intelligence)
  – Memory (California Verbal Learning Test)
  – Attention (Test of attentional performance)

• Social and emotional behaviour
  – Behavioral and emotional problems (Conners Scal, ABCL)
  – Index of parent and peers attachment
  – Self-esteem and depressive mood
  – Stress and mental state (life habits)
Outcome Variables

• Family environment
  – HOME inventory during the domiciliary visit

• Sensorial acuity
  – Visual acuity: full optometric exam
  – Auditory acuity: tonal audiometry
Outcome Variables

• Neurophysiology and Imaging
  – Transcranial Magnetic Stimulation
  – Magnetic resonance imaging (MRI)
  – Functional MRI with five paradigms
  – Diffusion Tensor Imaging (DTI)
Innovative research for new tools to analyze neuroimages
Braviz (Grupo Imagine. U de los Andes)

Premature infant (Control=not KMC) of 900 gr at birth with 31 weeks of gestational age, IQ 78 (WISCR4) at 15 years

At term infant, male, 41 weeks of gestational age with a birth weight of 2855 gr. IQ 105 at 15 years

Kangaroo mother care helps premature babies thrive 20 years later

Los beneficios del método cangurro

Kangaroo Parenting Act to help improve the health and intelligence of premature children

El articulo fue reportado en más de 500 noticieros on-line, 18 idiomas, 50 países, más TV y prensa escrita!!!!!
Primary Finding

Cumulative Mortality at 20 years

<table>
<thead>
<tr>
<th>KMC (N/Total)</th>
<th>Control (N/Total)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8/229 (3.5%)</td>
<td>16/204 (7.7%)</td>
<td>0.42 (0.18 -1.02)</td>
</tr>
</tbody>
</table>

- After adjusting for weight and gestational age at birth:
  
  Protective effect of KMC OR 0.42 (0.16-0.94) $P=0.04$
Repeated measures of developmental and environmental outcomes at 6 months, 1 and 20 years according to neurological status at 6 months in the re-enrolled sample (≤ 1800 g)

<table>
<thead>
<tr>
<th>Measure</th>
<th>KMC</th>
<th>Controls</th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal (SD)</td>
<td>Normal (SD)</td>
<td>Transient or abnormal (SD)</td>
<td>Transient or abnormal (SD)</td>
<td>KMC vs controls</td>
<td>Neurological status</td>
<td>Interaction between neurological status and groups</td>
<td></td>
</tr>
<tr>
<td>IQ at 6 months, Mean (SD)</td>
<td>98.1 (10.0)</td>
<td>90.0 (13.4)</td>
<td>99.5 (9.2)</td>
<td>84.5 (12.6)</td>
<td>0.23</td>
<td>0.00</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td>IQ at 12 months, Mean (SD)</td>
<td>103.4 (6.6)</td>
<td>99.4 (8.8)</td>
<td>103.0 (6.7)</td>
<td>94.6 (10.2)</td>
<td>0.11</td>
<td>0.12</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>IQ at 20 years, Mean (SD)</td>
<td>87.2 (13.1)</td>
<td>90.2 (14.9)</td>
<td>89.9 (14.9)</td>
<td>87.0 (12.7)</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>HOME at 12 months, Mean (SD)</td>
<td>39.3 (6.8)</td>
<td>39.9 (5.5)</td>
<td>39.7 (7.5)</td>
<td>35.5 (8.0)</td>
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<td></td>
</tr>
<tr>
<td>HOME at 20 years, Mean (SD)</td>
<td>39.5 (7.3)</td>
<td>40.5 (6.0)</td>
<td>40.7 (6.6)</td>
<td>36.6 (5.4)</td>
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</tr>
</tbody>
</table>
Outcomes of the intervention observed at 12 months of corrected age on IQ at 20 years

<table>
<thead>
<tr>
<th>Outcome at 1 year</th>
<th>IQ at 20 years</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IQ &lt; 90</td>
<td>IQ ≥ 90</td>
</tr>
<tr>
<td>Factorial score* of weight during first year of corrected age (mean (SD))</td>
<td>−0.16 (0.96)</td>
<td>0.01 (0.89)</td>
</tr>
<tr>
<td>Factorial score* of height increase during first year of corrected age (mean (SD))</td>
<td>−0.24 (0.95)</td>
<td>0.07 (0.97)</td>
</tr>
<tr>
<td>Factorial score* of head circumference during first year of corrected age (mean (SD))</td>
<td>−0.12 (0.95)</td>
<td>0.15 (0.98)</td>
</tr>
<tr>
<td>Head circumference at 1 year of corrected age per 50th percentile of expected head circumference for age and gender x 100 (mean (SD))</td>
<td>97 (3.13)</td>
<td>98 (2.72)</td>
</tr>
<tr>
<td>Factorial score* of maternal feeling of stress (mean (SD))</td>
<td>0.12 (0.93)</td>
<td>−0.14 (1.15)</td>
</tr>
<tr>
<td>At 41 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At 1 year of corrected age</td>
<td>−0.13 (0.90)</td>
<td>0.28 (0.99)</td>
</tr>
<tr>
<td>HOME test at 1 year of corrected age (mean (SD))</td>
<td>37.5 (6.24)</td>
<td>40.4 (5.32)</td>
</tr>
<tr>
<td>All five subscales</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family cognitive stimulation subscale</td>
<td>4.4 (2.34)</td>
<td>5.6 (2.46)</td>
</tr>
<tr>
<td>Structured environment subscale</td>
<td>5.5 (1.49)</td>
<td>5.8 (1.26)</td>
</tr>
</tbody>
</table>

* Factorial score of weight, height and head circumference at 40 weeks, 3, 6, 9 and 12 months of CA.
Objective: to study the attachment differences at 20 years according to gender and exposure to KMC during the neonatal period.
Attachment’s gender difference and KMC

• Even when they are born at term, girls are 1.8 times more likely to have a secure attachment than boys (Gloger-Tippelt & Kappler, 2016). In a premature birth, boys are the more vulnerable, since their right brain (responsible for attachment functions) has a slower growth and is therefore more sensitive to social and environmental stressors (Schore, 2017).

• The structures involved are the right prefrontal cortex which regulates the limbic system and the right orbitofrontal system, with its cortical and subcortical connections (Schore, 2000, 2017).
There is a girl / boy difference (better in girls) in the control group ($p < .02$) and none in the KMC group.
Prematurity (<37 weeks' gestation) affects brain development in regions such as the hippocampus and executive functions such as the Working Memory.

KMC is a early intervention that could decrease the impact of prematurity through a reduction of stressful environmental factors.

KMC at birth favored Working Memory for both gender: F(1,238) = 3.73, p = 0.05.

However, girls make significantly fewer errors of omission than boys (F(1,238) = 6.33, p = 0.01), which is inversely proportional to the Working Memory score.


Paternal Support

• Paternal support had a positive impact on the home environment at 1 year of corrected age (CA).
• Paternal support at one year of CA depends on whether the father had carried the infant in the Kangaroo Position during the neonatal period.
• Clear relation between paternal support at 1 year and the stability of the family 20 years later (score for paternal support in families without separated parents, 15.3 versus 14.6 for separated families, $P = 0.01$).
<table>
<thead>
<tr>
<th>Mother’s level of education</th>
<th>KMC</th>
<th>Controls</th>
<th>P</th>
<th>Interaction mother’s level of education and intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low level</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Higher level, mean (SD)</td>
<td>62 (10)</td>
<td>65 (15)</td>
<td>74 (14)</td>
<td>60 (14)</td>
</tr>
<tr>
<td>Conners hyperactivity, mean (SD)</td>
<td>54 (12)</td>
<td>54 (11)</td>
<td>64 (15)</td>
<td>53 (11)</td>
</tr>
<tr>
<td>Conners aggressivity, mean (SD)</td>
<td>69 (16)</td>
<td>71 (14)</td>
<td>78 (14)</td>
<td>68 (16)</td>
</tr>
<tr>
<td>ABCL DSM antisocial, mean (SD)</td>
<td>72 (26)</td>
<td>74 (24)</td>
<td>82 (16)</td>
<td>74 (22)</td>
</tr>
<tr>
<td>ABCL DSM internalization, mean (SD)</td>
<td>63 (24)</td>
<td>64 (22)</td>
<td>79 (16)</td>
<td>62 (23)</td>
</tr>
</tbody>
</table>
The long-term effects of the Kangaroo Mother Care intervention on cognitive functioning: Results from a longitudinal study

Stephanie Ropars, R Tessier, N Charpak, L Uriza
Universite Laval, Quebec

ABSTRACT

Three hundred infants were randomly assigned at birth in one of two interventions, KMC or traditional care (TC), and completed cognitive tests at adulthood (19–21 years after recruitment).

The main results show that participants with a neurological vulnerability at 6 months had higher IQ and sustained attention scores at adulthood if they had received KMC than if they had received TC.
There is evidence of lower attachment quality and less control of emotions in patients who have been preterm.
Objective

- To evaluate aspects such as the quality of attachment, self-esteem, the environment and the antecedent of suicidal behavior in young adults with a history of prematurity and Kangaroo Mother Care (KMC) during the neonatal period compared with young adults born at term.
## Results

<table>
<thead>
<tr>
<th>Feature</th>
<th>Odds Ratio</th>
<th>Std. Err.</th>
<th>p</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>The participant has considered committing suicide</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Attachment Total Score</td>
<td>0.95</td>
<td>0.01</td>
<td>0.00</td>
<td>0.93</td>
</tr>
<tr>
<td>Self Esteem total Score</td>
<td>0.88</td>
<td>0.04</td>
<td>0.00</td>
<td>0.81</td>
</tr>
<tr>
<td>Preterm</td>
<td>2.50</td>
<td>1.28</td>
<td>0.08</td>
<td>0.91</td>
</tr>
<tr>
<td>Days of KP</td>
<td>0.89</td>
<td>0.06</td>
<td>0.09</td>
<td>0.79</td>
</tr>
<tr>
<td>HOME20y Accept</td>
<td>0.82</td>
<td>0.08</td>
<td>0.03</td>
<td>0.68</td>
</tr>
<tr>
<td>HOME20yAccept*Days of KP</td>
<td>1.01</td>
<td>0.01</td>
<td>0.08</td>
<td>0.99</td>
</tr>
<tr>
<td>_Cons</td>
<td>177.4</td>
<td>255.5</td>
<td>0.00</td>
<td>10.55</td>
</tr>
</tbody>
</table>

Logistic Regression
Number of Observations= 452
LR Chi2(6)= 51.3
p>Chi2= 0.0000
Pseudo R2= 0.18
## Schooling, productivity, academic record, and work history

<table>
<thead>
<tr>
<th>Variable</th>
<th>KMC (n=139)</th>
<th>Controls (n=125)</th>
<th>Difference</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Years of preschool, mean (SD)</td>
<td>2.52 (1.07)</td>
<td>2.05 (1.04)</td>
<td>0.47 (0.14)</td>
<td>0.00</td>
</tr>
<tr>
<td>School absenteeism, mean (SD)</td>
<td>0.07 (0.26)</td>
<td>0.17 (0.37)</td>
<td>-0.09 (0.04)</td>
<td>0.01</td>
</tr>
<tr>
<td>Years of school, mean (SD)</td>
<td>11.31 (1.34)</td>
<td>11.50 (1.61)</td>
<td>-0.19 (0.18)</td>
<td>0.15</td>
</tr>
<tr>
<td>School quality, mathematics score, mean (SD)</td>
<td>48.22 (4.72)</td>
<td>48.38 (4.26)</td>
<td>-0.16 (0.65)</td>
<td>0.40</td>
</tr>
<tr>
<td>Standardized mathematics score, mean (SD)</td>
<td>-0.17 (0.99)</td>
<td>0.17 (1.02)</td>
<td>-0.35 (0.14)</td>
<td>0.01</td>
</tr>
<tr>
<td>Standardized language score, mean (SD)</td>
<td>-0.12 (0.89)</td>
<td>0.13 (0.85)</td>
<td>-0.26 (0.13)</td>
<td>0.02</td>
</tr>
<tr>
<td>Wage per hour, mean (SD)</td>
<td>4.77 (6.65)</td>
<td>3.13 (2.29)</td>
<td>1.65 (0.78)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

School quality is the school average in the nationally standardized test score in mathematics.
Wage per hour is given in thousand Colombian pesos; 1000 pesos is equivalent to US$ 0.40.
Neurophysiology and neuroimages

– Transcranial Magnetic Stimulation (TMS)
– Nuclear Magnetic Resonance (NMR)
– Functional RMI with 5 paradigms: coordination, motor prehension, attention, memory, emotion
– Tractography (DTI)
Cerebral motor function in very premature-at-birth adolescents: a brain stimulation exploration of kangaroo mother care effects

Cyril Schneider (cyril.schneider@rea.ulaval.ca)¹,², Nathalie Charpak³, Juan G Ruiz-Peláez⁴, Réjean Tessier⁵

1. Clinical neuroscience and neurostimulation laboratory, Centre de recherche du CHUQ, Québec, QC, Canada
2. Department Rehabilitation, Faculty of Medicine, Université Laval, Québec, QC, Canada
3. Kangaroo Foundation, Bogotá, DC, Colombia
4. Department Clinical Epidemiology and Biostatistics, Faculty of Medicine, Javeriana University, Bogotá, DC, Colombia
5. School of Psychology, Centre de recherche du CHUQ et CIRRIIS Université Laval, Québec, QC, Canada

ABSTRACT

Aim: Given that prematurity has deleterious effects on brain networking development beyond childhood, the study explored whether an early intervention such as Kangaroo Mother Care (KMC) in very preterm preemies could have influenced brain motor function up to adolescence.

Methods: Transcranial magnetic stimulation (TMS) was applied over the primary motor cortex (MI) of 39 adolescents born very prematurely (<33 weeks’ gestational age, 21 having received KMC after birth, 18 Controls with no KMC) and nine adolescents born at term (>37 weeks’ gestational age, >2500 g) to assess the functional integrity of motor circuits in each hemisphere (motor planning) and between hemispheres (callosal function).

Results: All TMS outcomes were similar between KMC and term adolescents, with typical values as in healthy adults, and better than in Controls. KMC adolescents presented faster conduction times revealing more efficient MI cell synchronization (p < 0.05) and interhemispheric transfer time (p < 0.0001), more frequent inhibitory processes with a better control between hemispheres (p < 0.0001).

Conclusion: The enhanced synchronization, conduction times and connectivity of cerebral motor pathways in the KMC group suggests that the Kangaroo Mother Care positively influenced the premature brain networks and synaptic efficacy up to adolescence.
Neuroimages

• We have 214/264 (78%) sujets de ≤ 1,800 gr (target population) with a RMN, 195 were available for the classification of white matter lesions, there was no difference between the 2 groups (66% (N=78) versus 58% (N=54) p = 0,16).

• The main obstacle for the RMI has been the presence of “brackets”.
Caudate nucleus volume according to duration of the kangaroo position

Variables associated with left caudate nucleus volume at 20 years

<table>
<thead>
<tr>
<th>Time</th>
<th>Variable</th>
<th>Slope</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before intervention</td>
<td>Fragility index</td>
<td>– 0.29</td>
<td>0.00</td>
</tr>
<tr>
<td>During intervention</td>
<td>Duration of kangaroo position</td>
<td>+ 0.25</td>
<td>0.00</td>
</tr>
<tr>
<td>At 20 years</td>
<td>Nine-hole peg test</td>
<td>– 0.18</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Results of linear regression ($r^2 = 0.16$ $F(3.17) = 12.21$ $P=0.00$ calculated with Braviz software (25)
Brain amygdales and prematurity

• Brain amygdales play an important role in social development and neural control of emotions, especially fear.
• These structures are particularly vulnerable to injuries suffered by preterm labor.
<table>
<thead>
<tr>
<th>Group</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>KMC less than 2001g</td>
<td>104</td>
<td>44.8</td>
</tr>
<tr>
<td>Control less than 2001g</td>
<td>91</td>
<td>39.2</td>
</tr>
<tr>
<td>Reference population</td>
<td>37</td>
<td>15.9</td>
</tr>
<tr>
<td>(more than 2500g)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>232</td>
<td>100.0</td>
</tr>
</tbody>
</table>
Comparing preterm and at term patients, a smaller volume of both, left amygdale, with a difference of 102 mm³ (p = 0.02) and right amygdale, with a difference of 100 mm³ (p = 0.07) was evidenced.
Volume of the left amygdale

- more days in NICU, less volume
- more KP, more volume
- more internationalization, less volume
Volume of the right amygdale

- more WASI score, more volume
- male, more volume
- KP and hospitalized in NICU, more volume
Fear paradigm

- 113 fear paradigms in fRMI at 19-20 years
- Not yet analyzed
- Hypothesis: ex-Premature cared in KMC during the neonatal period are able to control better their emotions than ex premature infants who received traditional care.
Hippocampus volume and memory

- Especially sensible to hypoxia
- Less volumes in preterm infants compared with at term infants.
- Right hippocampus (or non dominant) is specially involved in visuospatial memory evaluated with VMI test while left hippocampus (or dominant) works in verbal memory processes evaluated with CVLT test.
- Left hippocampus
  - More days in NICU, less volume left hippocampus
  - Although being in NICU, more Kangaroo Position, more volume
  - Male, more volume
  - Less weight and NICU hospitalization, less volume
  - In spite of having less weight, more volume if Kangaroo Position
  - Less volume left hippocampus in fragile infants
  - Less intrusions in CVLT test, more volume
- Right hippocampus
  - More days in NICU, less volume
  - Although being in NICU, more Kangaroo Position, more volume
  - Male=more volume
  - In spite of having less weight and NICU hospitalization, more volume if Kangaroo Position
  - More volume, higher VMI visual standard score, controlling for fragility, NICU hospitalization, sex and Kangaroo Position
Food for thought

• At 20 years, KMC participants, especially in the **poorest and least educated families**:
  – Less aggressive drive
  – Less impulsive and hyperactive
  – Less antisocial behaviour

• KMC may change the behaviour of less well-educated mothers by increasing their sensitivity to the needs of their children

• We cannot separate the effects of stimulation by the family from a functional or anatomical impact of the intervention on the brain.
Family changes are an obvious effect of KMC.
Reduction of contextual disparities.
KMC mothers take their children to preschool earlier
   – Lower rate of school dropout.
KMC promotes paternal involvement in neonatal care, which affects the family structure.
   – In this long-term study, fathers’ involvement changed the young adults’ cognitive capacity.
Food for thought

• They had significantly larger cerebral volumes of total grey matter, and cerebral cortex and it seems that the duration of Kangaroo position has an impact on these volumes.

• The KMC (Kangaroo Mother Care) method is an intervention that allows shortening the separation from mother, and could stamp the stress and its consequences caused by the NICU on preterm infant. In 1994 the mother was not allowed to visit her infant in the NICU, the light, the noise and the pain were intense and a routine for these fragile infants. This situation is better now in developed countries but remains similar in a lot of neonatal units especially in the developing world were the challenge is the survival without considering the quality of the survival.
The moment at which KMC is administered is considered decisive since it is during the third trimester, a critical period for the development of the central nervous system, where interventions are most likely to have a significant and durable effect on cognitive functioning (Als et al, 2012; Kaffashi, Ludington-hoe et al, 2013.

Moreover, perinatal care depriving infants from physical proximity with their mothers could also cause other types of biophysiological alterations contributing to the emergence of cognitive difficulties:

1. First, maternal separation could increase apoptosis (e.g. programmed cell death), a phenomenon to which neurons are particularly vulnerable during the post-natal period (Bhutta et al. 2002).

2. Second, the experience of painful events (e.g. medical interventions, high exposure to lights and noises) could cause an excessive release of excitatory amino acids in premature infants leading to neuronal damage (Anand & Scalzo, 2000)

3. Finally, at the behavioral level, these events can lead to a disruption of the physiological activation cycle, to altered functioning of the hypothalamic-pituitary axis (HPA) and to difficulties in self-regulation.
Conclusion

• The detection of “minor” sequelae becomes important as neonatal technology becomes more accessible.
• Such “minor” effects can affect the lives of families but often go undetected, especially in developing countries.
• We hypothesize that the results obtained in our study at 18-20 years would be even more significant if KMC was introduced as soon as the infant could tolerate it, in the intensive care unit.
How is the intervention in 2018?

Delivery of a LBW Infant
Resuscitation is necessary (+KMC)
Evaluation of Extrauterine transition
Mother +KMC

Intensive Care +KMC
Intermediate Care+KMC
NCU

Hospital stay decrease around 10 days even without early discharge (Sweden, Spain, France)

KMC ward if necessary

Home discharge in KMC with a follow-up in a KMC program
KMC as soon as possible with the premature infant and its family
...at home during the ambulatory KMC program
It takes a long time to transform new idea into reality