



Research Round-up April 2022

Reference: Charpak, N., et al., *Kangaroo mother care had a protective effect on the volume of brain structures in young adults born preterm*. Acta Paediatr, 2022. **111**(5): p. 1004-1014.

url: <https://pubmed.ncbi.nlm.nih.gov/35067976/>

Welcome to the April 2022 Research Round-up. This month we will look at an article entitled "Kangaroo mother care had a protective effect on the volume of brain structures in young adults born preterm." This article was published in 2022 in Acta Paediatrica. I picked this because I love anything Kangaroo, and because this is a post-discharge outcome study. Click on the URL above to go to the full text. Remember to download the handouts "Critical Review of the Literature" and the Research Roundups definitions file if you need information on any of the abbreviations used. We will go through this article to better understand what was done and what we can draw from this study.

Title: The title accurately describes the study.

Abstract: The abstract summarizes aim, method, results, and conclusion of the study. This was part of a larger RCT on the effects of skin-to-skin or kangaroo-mother care (KMC). This original study was done decades ago – here they are looking at brain growth, maturation and pathway formations in the infants who are now 20 years old. They had 264 young adults who agreed to be part of this second study, they included 178. The ones excluded were excluded due to poor neuroimaging or because they had been born at term.

Background or Introduction: We once again start with looking at the references, with <2012, or published ≥ 2012 as our separation window. For the entire article, there are 30 references; of these, 17 references were published prior to 2012 and 13 published in 2012 or later. The ones that are earlier than 2012 include mostly papers on early KMC studies, on earlier follow-up studies of these same infants at earlier time periods, and references for tests and methods used in this follow-up study. In the background section, of the 11 articles cited, 5 were published prior to 2012. One of these was the original article on KMC; the current article follows these babies into adulthood.

The authors begin with a review of the known lasting effects of prematurity on neurodevelopmental outcomes, and the fact that the brain is growing at an incredibly fast rate in preterm infants while they are in the NICU. Prematurity affects the WAY brains develop – including growth, organization, and development even when there are no known injuries to the brain. They describe kangaroo mother care (KMC). Many of the benefits were published by the same study group as the authors who authored this article. They conclude with a statement of their aim which was to "assess the long-term impact of KMC on brain volume and its association with cognitive development." The study group was infants who have been followed since the original randomized controlled trial was done 20 years ago. These infants are now young adults.

Study Population: This study was originally done in Columbia between 1993 and 1996. They had 746 preterm and small for gestational age term infants, under 2000 grams. They stratified into 4 groups based on birth-weight categories and randomly assigned KMC. This study was of infants born under 1800 grams (the first three categories). In these categories, the original number of infants was 433, and 412 survived to one year. This study was done between 2012 and 2014 and included the 264 babies who were tracked down and agreed

to the study. They also had a group of infants who were full-term and healthy (n=37) that they used as a reference value for this study (e.g., they were not SGA or preterm, and therefore the “gold standard”).

Methodology: Interestingly, in the original study in 1993, infants were enrolled AFTER they were able to suck and swallow without treatment. Infants who were in the KMC group were exclusively or nearly exclusively breastfed, got continuous skin-to-skin contact and early home discharge in KMC with daily follow-up visits. Visits continued until they had proper weight gain and had reached 40 weeks PMA. Control infants were kept in incubators until they reached temperature regulation, discharged according to hospital practice at 1700 grams. All infants received standardized follow-up care until 1 year of age. There have been at least three articles published already on this population at younger ages.[1-3]

For this study, cerebral volumes of both grey and white matter, and organization of white matter, were assessed. They used neuroradiologists to measure size, thickness, and volumes of structures. They also did a series of neurological and neuropsychological tests; these included tests for cognitive performance, fine motor skills and coordination, and learning and memory. MRI and functional MRIs were completed. There is a great deal of detail about the imaging methods. The exposure (independent) variable was KMC, and they also looked at number of days of KMC to see if more days related to improved outcomes. Every researcher involved in the testing was blinded to the group of the participants. They controlled for potential confounders of parents’ demographics, education and SES. The participant’s weight at birth, GA at birth, APGAR score, and IUGR status, as well as any events that happened before they were enrolled were also included as control variables. Of note, more infants in the control group died during the 20-year follow-up period.

After taking out missing data and/or poor neuroimages, they had 97 infants from the KMC group and 81 infants that were controls. A higher proportion of the infants who were in the KMC group were male, had received ventilation, been hospitalized in an NICU, and had higher medical severity indexes. They also had shorter hospital stays and lower GA and weight at discharge.

Statistical Analysis: Data analysis was extremely complicated and thorough. Think about it – there are lots of things you are trying to look at, and several overlap. In general, they used Chi-square, t-tests, multilinear regressions, and ANOVAs.

Outcomes/Results: The primary outcomes related to brain size/volume showed the mean volumes for preterm infants compared to term infants were smaller in general and the white matter fibers were fewer and smaller. The cerebral amygdala was not smaller. Infants in the KMC group (now adults) had larger volumes of total grey matter and cortical grey matter, and subcortical grey matter in several areas. Infants in the KMC group had significantly higher volume of corticospinal tracts in the white matter. Key point: preterm brains are different than term brains – even as adults – and KMC improves brains of preterm babies.

Cognitive functioning showed an association between number of days of KMC and total brain grey matter as well as subcortical grey matter. These were also associated with better IQ scores, better memory/attention scores, and better fine motor skills and coordination.

Discussion/Conclusions: The authors begin their discussion by saying that their study shows KMC had significant independent effects on selected brain areas known to be associated with cognitive function. There was a dose-response relationship between number of KMC days and neuroprotective effects. They go on to say that another benefit of KMC is to allow infants in this study to go home sooner with their parents, and the family environment allows more active parenting. And discuss the benefits of reuniting quickly, as parents are

the primary environment in the first years of life. And parents who were in the KMC arm “knew their child better”. This is from one of the earlier studies. They reference a recent WHO study that shows immediate KMC at birth decreased neonatal mortality.[4-7]

The authors do an impressive job of describing the limitations of their study. These limitations primarily focused on the many possible influences on outcomes that could occur across the 20 years of this study. But they also describe how their statistical methods tried to control for these unknown variables.

Does this fit with your experience: Yes! Although I have not looked at the long-term data recently until this article came out. Parents ask me all the time about “how long”, “how much”, and benefits. This has helped with my answers – KMC should be done as early as possible, as much as possible, and at least this implies for well after discharge to home. And the benefits continue to grow – with every paper. This is exciting!

Other: The authors report conflicts of interest to disclose. The original article has the research approvals listed.

References use in this review:

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