Effects of maternal multiple micronutrient supplementation on mothers' cognition and children's development

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Abstract

Background: Examining the potential benefits of maternal multiple micronutrient (MMN) supplementation is important to inform policy decisions concerning maternal and child health programs. Two outcomes that may be improved by maternal MMN supplementation are maternal cognition and child development, since micronutrients are necessary for brain maintenance and function in adulthood as well as for foetal and infant development.

Aims: To examine the effects of the Supplementation with Multiple Micronutrients Intervention Trial (SUMMIT) on concurrent maternal cognition and on subsequent child development, particularly in women who were undernourished (mid-upper arm circumference < 23.5 cm) or anaemic (haemoglobin < 110 g/L) at enrolment.

Methods: SUMMIT was a double-blind cluster-randomized trial in Indonesia comparing the effects of a maternal MMN supplement to an iron and folic acid (IFA) supplement.[1] A battery of cognitive tests was administered to 640 SUMMIT participants after an average of 25 weeks of supplementation. A developmental test battery was administered to 487 children of SUMMIT participants at age 42 months.

Results: Mothers who received MMN scored significantly higher compared to IFA in overall cognition and reading performance in particular. The benefit of MMN supplementation on both scores was found particularly in undernourished and anaemic women. Children whose mothers received MMN scored significantly higher in motor development. In undernourished women, children of mothers who received MMN scored higher than IFA in overall development, particularly in motor development and aspects of non-verbal cognitive development.

Conclusions: These data suggest that MMN supplementation can improve maternal cognition and children's motor development. Maternal MMN supplementation seems to be especially important for anaemic women, to improve cognition, and for undernourished women, to improve their cognitive function as well as the cognitive and motor development of their children. This evidence supports maternal MMN supplementation as a beneficial program for pregnant women and their children.

Background

Micronutrients play important roles in the biological processes that underlie

1) cognitive function in adulthood
2) development during gestation and infancy

Acute deficiencies in some micronutrients result in cognitive impairment in adults, for example

- thiamine deficiency can cause memory loss and confusion[2]
- vitamin B12 deficiency is associated with mental problems and dementia[3]

Acute maternal deficiencies in some micronutrients have severe detrimental effects on foetal and child development, for example

1) folic acid deficiency can lead to birth defects such as spina bifida[4]
2) iodine deficiency can lead to cretinism in the child[4]

The extent to which milder (non-clinical) forms of micronutrient deficiencies during pregnancy impair maternal cognition and subsequent child development at pre-school age is not yet fully clarified. Trials of maternal multiple micronutrient supplementation have not yet measured either outcome.

Objectives

To measure the relative effect of MMN versus IFA on

1) maternal cognition, including
   - Overall cognitive performance
   - Cognitive performance in various specific domains
2) subsequent child development, including
   - Overall developmental levels
   - Developmental levels in various specific domains

To test whether any observed benefits are particularly found for

1) women who are anaemic: haemoglobin < 110 g/L
2) women who are undernourished: mid upper arm circumference (MUAC) < 23.5 cm

Methods: Supplementation with Multiple Micronutrients Intervention (SUMMIT)[1]

SUMMIT was carried out on the Indonesian island of Lombok by the University of Mataram, the Government of Nusa Tenggara Barat Province, the Ministry of Health of Indonesia, and Helen Keller International. Government-employed midwives were randomly assigned to distribute one of two types of supplements:

IFA:	MMN:	
Iron	Iron	
Folic Acid	Folic Acid	Niacin
	Vitamin A	Vitamin B6
	Vitamin D	Vitamin B12
	Vitamin E	Zinc
	Vitamin C	Copper
	Vitamin B1	Selenium
	Vitamin B2	Iodine

Participants (N = 31,290) were provided with a daily tablet:

First visit to local pre-natal care clinic — birth — 3 months post-partum

640 mothers (344 MMN, 246 IFA) participated in cognitive, motor, and mood assessment after an average of 25 weeks of supplementation (10% in the 1st or 2nd trimester, 39% in the 3rd trimester, 51% after birth).

487 children (246 MMN, 241 IFA; 256 boys, 231 girls) participated in developmental assessment at age 42 months (all were tested within three weeks of the day they reached 42 months of age).

Analysis

All tests (see next two panels) were adapted to the local context and evaluated for reliability and validity on the local population in Lombok.[5] For each test score *z*-scores were computed based on the distribution of our sample.

Analyses on overall cognitive and developmental performance:

- Overall cognitive performance: included all cognitive test scores (i.e., excluding tests of motor dexterity and mood)
- Overall development: included all tests of motor, language, and non-verbal cognitive development, all of which inter-correlated, but not socio-emotional development, which did not correlate as strongly with the other scores.
- For each analysis, all test *z*-scores from every participant were entered as the dependent variable in a mixed effects model using SAS PROC MIXED with a fixed effect of supplement type and random effects of midwife code (to account for clustered randomization) and participant on intercept. Specification of a random effect of participant is an alternative to averaging scores for each participant which preserves information that is lost when averaging.

Analyses on performance in individual domains:

- The effect of MMN on each domain (the individual test *z*-score or average of test *z*-scores representing that domain; see tables in next two panels) was estimated and adjusted for clustered randomization using SAS PROC MIXED by specifying a fixed effect of supplement type and a random effect of midwife code.

Covariates:

- All analyses on the maternal scores included fixed effects of four covariates that significantly predicted overall cognitive performance: maternal education, maternal age, whether or not the family owned a house, and the set of tests she was given (each participant was tested on a subset of the full battery).
- All analyses on the child scores included fixed effects of two covariates that significantly predicted overall developmental levels: the child's haemoglobin level, and a measure of the amount and quality of stimulation that children receive from their environment (HOME Inventory score).

Maternal Tests

Domain	Test
Verbal Declarative Memory	Word List Memory Test
Attention, Verbal Short-Term Memory, and Working Memory	Digit Span Forward Test Digit Span Backward Test
Semantic Memory and Executive Function	Category Fluency Test
Visuospatial Ability and Dynamic Mental Imagery	Mental Rotation Test
Lexical Retrieval	Speeded Picture Naming Test
Reading	Speeded (Real) Word Naming Test Speeded Pseudoword Naming Test
Motor Dexterity	Coin Rotation Test
Mood	Mood Scale

Results: Maternal Cognition, Motor, and Mood

Figure 1. Effects of MMN on overall cognitive performance (all scores except motor and mood) in all participants and subgroups of participants:

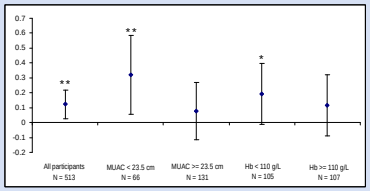
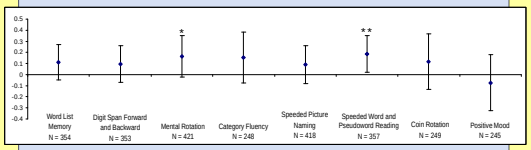


Figure 2. Effects of MMN on cognitive performance in various domains in all participants:



The analyses on cognitive performance in various domains in undernourished participants (analogous to Figure 5) yielded a similar pattern to Figure 2: the effect of MMN on reading was significant ($p < .05$);the effect on category fluency yielded a trend ($p < .1$); all other $ps > .4$.

**$p < .05$, *$p < .1$; all figures report the estimated effect of supplement type in mixed effects models; error bars show 95% confidence intervals

References

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Acknowledgments

The maternal cognitive testing was carried out under a Fulbright Grant from the US State Department. The child testing was carried out with funds provided by the Allen Foundation. Funding was also provided from a US National Science Foundation Graduate Research Fellowship and a Universities UK Overseas Research Studentship Award. SUMMIT was carried out with funding from the Turner Foundation, UNICEF, the Centre for Health and Human Development, and the United States Agency for International Development-Indonesia (grant no 497-G-00-01-00001-00).

Child Tests

Domain	Test
Motor Development	Fine Motor Development Scale Gross Motor Development Scale
Language Development	Picture Vocabulary Test Sentence Complexity Scale
Non-Verbal Cognitive Development	
Attention	Visual Search Test
Visuospatial Ability	Block Design Test
Executive Function	Snack Delay Test Windows Test
Socio-emotional Development	Socio-emotional Development Scale

Results: Child Development

Figure 3. Effects of MMN on overall developmental levels (all scores except socio-emotional scale) in all participants and subgroups of participants:

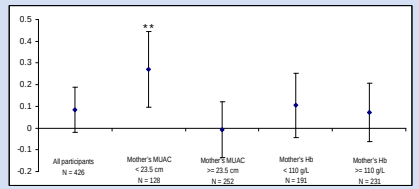


Figure 4. Effects of MMN on developmental levels in various domains in all participants:

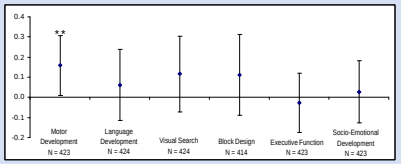
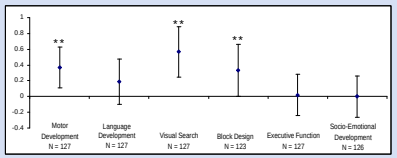


Figure 5. Effects of MMN on developmental levels in various domains in undernourished mothers (MUAC < 23.5 cm):



Summary and Conclusions

Compared to IFA, maternal MMN supplementation improved

- Overall maternal cognition (particularly reading performance)
- Children's motor development

In undernourished women, MMN supplementation also improved

- Overall developmental levels (particularly motor development and aspects of non-verbal cognitive development)

This evidence supports maternal MMN supplementation as a beneficial program for pregnant women and their children.