



NEUROCOGNITIVE SUB-STUDY SUMMARY

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BACKGROUND

Moderate Acute Malnutrition (MAM) is a debilitating condition that compromises the development and function of multiple organ systems, including the brain. Evaluation of recovery from MAM in children should not be confined to anthropometric indicators, but should also include measures of neurocognitive, emotional, and social function. Our study uses a novel approach to examine neurocognitive function and recovery in children with MAM, and to evaluate the effects of various supplementary foods on neurocognitive function in children.

STUDY DESIGN

The study will use a case-control design (4:1) to compare neurocognitive function in children with MAM and well-nourished, age matched controls. Eligible subjects will be children with MAM enrolled in the four foods study or same-age children without MAM. All participants will be tested by eye-tracking and neuropsychological tests upon enrollment to the study (i.e., baseline), and again in up to four follow-up assessments to monitor changes in neurocognitive status over time.

The study will be piloted with 32 children with MAM and 32 well-nourished controls from two age groups (7-month-old and 18-month-old, total N = 128). For the principal study, our aim is to recruit 66 well-nourished controls and 264 MAM (66/group). Given preliminary data showing that a high proportion of children receiving treatment for MAM in the study area are under 12 months, the principal study will focus on younger infants and a more narrowly specified developmental window (7- to 11-month-old children).

Informed consent will be sought from the caretakers of all eligible children by a research assistant familiar with the study and fluent in the caretaker's native language. Duration of the study and participation requirements will be explained. Informed consent will be given verbally and in writing.



AIM 1

To conduct a pilot study to assess the feasibility, measurement properties, and utility of eye-tracking tests in monitoring neurocognitive changes in 7- and 18-month-old children over a 4-week period (i.e., the typical recovery period from MAM in supplementary feeding programs).

HYPOTHESIS 1A

Eye-tracking tests can be successfully performed and repeated in children with varying nutritional status in low-resource settings. Successful performance is indicated by moderate to high test trial success rates (i.e., >75%) and high overall test completion rates (>90%).

HYPOTHESIS 1B

Eye-tracking test scores have moderate to high stability (i.e., test-retest correlation) over a 4-week period in well-nourished controls with no expected changes in neurocognitive status.

HYPOTHESIS 1C

Factors reflecting infants' state at the measurement (e.g., fatigue level, irritability) and test success rates (i.e., number of successfully completed test items) are associated with the measurement properties of the eye tracking tests.

AIM 2

To examine the effects of MAM and 4 supplementary foods on neurocognitive function in 7-11 month-old children.

HYPOTHESIS 2A

Compared to well-nourished control children, children with MAM will have slower saccadic reaction time and higher incidence of missing saccades (i.e., reduced speed and accuracy of visual orienting) and shorter periods of fixation/attention hold on visual stimuli (i.e., reduced oculomotor/attention control) in brief eye-tracking-based and behavioral tests.

HYPOTHESIS 2B

Treatment with supplementary food will lead to a recovery of MAM after 4 weeks.

HYPOTHESIS 2C

There are differences in the effects of the 4 foods on measures of neurocognitive function in 7 to 11-month-old children with MAM after 4 weeks of supplementation.

HYPOTHESIS 2D

Eye-tracking-based measures of neurocognitive function correlate with conventional measures of cognitive function, particularly observation-based tests of visual reception and behavioral control.

MEASUREMENTS

The primary outcome measures will be i) measures of child nutritional status (tape measures of mid-upper arm circumference (MUAC), ii) eye-tracking measures of neurocognitive function, including *counts of saccades to high-contrast patterns* (consistency and accuracy of visual orienting), *mean saccadic reaction time* (speed of visual orienting), and *percentages of saccades to distracting stimuli* (attention control), as well as iii) observational tests of neuropsychological function (tests of visual reception and spatial cognition).

TECHNIQUE

In the eye tracking tests, infants will be seated in their parent's lap in front of a computer display equipped with an eye tracking camera. When the infant is correctly positioned, a battery of tests will be administered, including tests of the infant's visual fields (i.e., eye movements to patterns), saccadic reaction time (speed and accuracy of visual orienting), and inhibition of reflexive saccades to distracting stimuli (attention control). The pictures shown to the child will be drawings or photographs of everyday objects (for example, flowers, animals, or human faces). To help the infant to maintain interest on the screen and to obtain sufficient number of test trials, the test stimuli will be shown in short blocks, interrupted by presentations of dynamic infant-friendly videos. The testing sessions will last approximately 15 minutes. In the first (baseline) assessment and in the last follow-up assessment, the eye tracking tests will be followed by conventional tests of neuropsychological function, including tests of visual reception and spatial cognition (e.g., tests that require the child to fixate and track a visual object, or search for a toy hidden under one of two/three opaque cups), to assess global cognitive and social-cognitive development; and at 18 months of age, age-appropriate tests of cognitive and behavioral control (e.g., tests asking the child to wait before reaching for an attractive toy).²

IMPLICATIONS

The results from this study will contribute to the understanding of supplementary food product effectiveness in terms of recovering neurocognitive function. This study is operationally important because program implementers typically rely on weight, height, and MUAC as indicators for recovery, but there may be added value in assessing brain and cognitive function. If successful, the eye tracking tests we have designed for this study may provide a quick, easy, objective, and fully automated system for monitoring neurocognitive function and recovery in children with MAM in various points of child care and in food aid programs.

CONTACT

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¹ Forssman L, Ashorn P, Ashorn U, Maleta K, Matchado A, Kortekangas E, Leppänen JM. Eye-tracking-based assessment of cognitive function in low-resource settings. *Arch Dis Child*. 2016 Aug 22 (Epub ahead of print).

² Herrmann, E., Call, J., Hernandez-Lloreda, M. V., Hare, B., & Tomasello, M. (2007). Humans have evolved specialized skills of social cognition: The cultural intelligence hypothesis. *Science*, 317(5843), 1360-1366; Herrmann, E., Hare, B., Cissewski, J., & Tomasello, M. (2011). A comparison of temperament in nonhuman apes and human infants. *Developmental Science*, 14(6), 1393-1405. 10.1111/j.1467-7687.2011.01082.x