



MAKERERE UNIVERSITY



**Karolinska
Institutet**

Department of Public Health Sciences (Karolinska Institutet)

Department of Psychiatry (Makerere University)

Computerized rehabilitation for cognitive deficits after central nervous system malaria in Ugandan children

Academic Thesis

The public defence for the degree of Doctor of Philosophy at Karolinska Institutet and Makerere University will be held at Karolinska Institutet, Norrbacka, Social Medicine, Large Conference Room.

Tuesday, 1st February 2011, at 0900 hours

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Stockholm and Kampala 2011

Abstract

Background: Malaria infecting the central nervous system affects over 575,000 children annually in sub-Saharan Africa leading to cognitive deficits. The effect of this form of malaria on everyday behaviour and academic achievement has not been investigated in Uganda. In addition, no interventions have been carried out for children whose cognitive functioning has been affected by central nervous system malaria.

Main objective: To investigate the effectiveness of a rehabilitation program for cognitive deficits in Ugandan children after central nervous system malaria.

Methods: Five studies were carried out (I-V). Study I investigated the long-term cognitive outcomes of central nervous system (CNS) malaria. Children were given cognitive assessments 24 months after an episode of malaria. In study II, this same cohort of children were followed up and randomly assigned to receive either computerised cognitive rehabilitation training or treatment as usual, approximately four years after the CNS malaria episode. Pre- and post-intervention cognitive and behavioural assessments were done. The construct validity of a new cognitive test battery, the Kaufman Assessment Battery for Children second edition (KABC-II), was validated in Study III using assessments done during Study II. The effect of CNS malaria on cognition, behaviour and academic achievement was investigated in study IV. Study V investigated the effect of immediate computerised cognitive rehabilitation on cognition, behaviour and academic skills after an episode of CNS malaria. Chi-square and multiple linear regression analyses were used in Study I, analysis of covariance in studies II, IV, V and factor analysis in Study III.

Results: There was a 26.3% prevalence of cognitive impairment two years after CNS malaria with attention most affected (18.4%). Central nervous system malaria was associated with a 3.67 increased risk for impairment (Study I). At three months assessment, children with malaria had lower attention scores (estimated mean difference = 0.32, 95% confidence interval (CI) = 0.01 to 0.63) and more Internalising Problems (0.31, CI = 0.05 to 0.56) than the community controls (Study IV). Cognitive rehabilitation initiated four years after the illness resulted in improvement in visuospatial processing speed, on a working memory and learning task, psychomotor speed and internalising behaviour (Study II) while cognitive rehabilitation initiated three months after the malaria episode improved Learning only (mean difference in adjusted scores between intervention and control groups (standard error), 12.46 (6.05) (Study V). Factor analysis of the KABC-II resulted in five factors measuring Working Memory, Visuospatial skills, Learning and Planning. The fifth factor was composed of items that did not measure a specific cognitive ability (Study III).

Conclusion: Both delayed and immediate computerised cognitive rehabilitation result in improvement in cognition and behaviour after central nervous system malaria in Ugandan children.

Keywords: malaria, cognition, cognitive rehabilitation, child health