Cross-sectional analysis of pro- and antisaccade development in retinopathy-confirmed cerebral malaria

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Introduction

Paediatric cerebral malaria (CM) causes death and disability, affecting about 500,000 children every year, primarily in sub-Saharan Africa. It has been reported that CM survivors are at increased risk of long term neurological sequelae including epilepsy⁵ and cognitive impairment⁵. However, diagnosis on the basis of standard clinical criteria missed CM in almost 25% of cases, and the interpretation of the results of neuropsychological tests which have been used is problematic: Tests are often not normed for the target population and the link between test performance and underlying cognitive and neurological function is often unclear. As part of a large ongoing prospective study CM survivors whose diagnosis had been confirmed by the presence of malarial retinopathy. Retinopathy is highly associated with pathologically confirmed CM, in contrast to current diagnostic criteria⁶. We investigated the execution of pro- and anti-saccades. Pro-saccade (PS) and anti-saccade (AS) tasks represent objective, biological measures of visuomotor reflexes related to the function of discrete brain circuits and cognitive processes such as attention, working memory and inhibitory control⁷. The developmental trajectory of several aspects of saccade performance is well established. In particular, AS directional error rate, closely related to frontal cortical function, falls rapidly between the ages of 8 and 12 years.

Figure 1. Tasks

Prosaccade task (PS) • Fixation: Randomised 1-2s • Direction: randomised 1-2s Antisaccade task (AS) • Fixation: Randomised 1-2s • Direction: randomised 1-2s Instruction: “Look at target” Instruction: “Look to mirror image position” Runs of 195 prosaccade and 100 antisaccade tasks were presented in separate blocks.

Methods

Participants: As part of the “Retinal Micronvasculature in Cerebral Malaria in African Children” study, based in the Queen Elizabeth Central Hospital, Blantyre, Malawi, we recruited 45 non-cerebral malaria survivors (CM; mean±SD age 110±24months; 64±120mos) and 43 control children (age 119±27mos; 72±120mos) who had been admitted to paediatric wards, but who had no fever, coma, parasitaemia or other disease. Many of the cases and controls had previously participated in the BMFES study.

Tasks and techniques: Horizontal eye movements were recorded binocularly with a miniaturized headmounted infrared saccadometer (Advanced Clinical Instrumentation, Cambridge, UK); the device incorporates two low-power red lasers projecting 10µm circular spots subtending approximately 0.1⁴. In a horizontal line, centrally, and at 10° to left and right of centre. As stimuli move with the head, participants were not head-fixed; they sat in a comfortable position approximately 1.5m in front of a white surface and completed 100 PS and 100 AS trials. In PS tasks they were instructed to look at the target when it appeared in an AS tasks they looked to the mirror image position of the target (Figure 1). Both tasks were synchronous in the target appearance. The fixation stimulus was extinguished. Tests were explained to children in the local language, and comprehension of instructions was checked before data collection.

Analysis: Median prosaccade latency and mean amplitude, mean AS directional error rate (expressed as a %), median error prosaccade and correct antisaccade latency were calculated for each participant.

Results

Prosaccade performance (amplitude and latency) was statistically indistinguishable between groups (Figure 3)

- Error prosaccade latency in the AS task also declined with age (Figure 5).
- Antisaccade directional error rate declined with age in both groups as expected (Figure 6).

Prosaccade latency was negatively correlated with age, as reported previously.

Conclusions

The data provide no evidence of a performance difference between cerebral malaria survivors and a locally recruited non-malaria control group for saccades or antisaccades. They are not consistent with CM survivors being at increased risk of gross longterm damage to the saccadic system. The age structure of the groups (Figure 1), longitudinal follow-up (which we are currently conducting) may reveal differences related to more cognitive aspects of saccade behaviour, particularly in the antisaccade task. It is possible that the (non-significant) difference in the slope of the regression of AS DERR on age (Figure 6; shallow slope in the CM group) is an early sign of this.

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References