SOMATOSENSORY DISCRIMINATION DEFICITS FOLLOWING PEDIATRIC CEREBRAL MALARIA

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Abstract. Pathologic studies of central nervous system damage in human falciparum malaria indicate primary localization in the cerebral white matter. We report a sensory-perceptual investigation of 20 Ghanaian children with a recent history of cerebral malaria who were age-, gender-, and education-matched with 20 healthy control subjects. Somatosensory examinations failed to show any evidence of hemianesthesia, pseudohemianesthesia, or extinction to double simultaneous tactile stimulation. While unilateral upper limb testing revealed intact unimanual tactile roughness discrimination, bimanual tactile discrimination, however, was significantly impaired in the cerebral malaria group. A strong negative correlation (r = −0.72) between coma duration and the bimanual tactile roughness discrimination test was also found. An inefficiency in the integrity of callosal fibers appear to account for our findings, although alternative subcortical mechanisms known to be involved in information transfer across the cerebral hemispheres may be compromised as well.

An estimated 40% of the world’s population is exposed to malaria.1 In Africa, children are at particular risk of developing the imminently lethal complications of Plasmodium falciparum infection, with 90% of all malaria deaths being pediatric cases.2 We are far from understanding why some children in malaria endemic areas who develop symptomatic manifestations of falciparum malaria progress to the more severe cerebral malaria while others do not.3 There is also scant, but increasing evidence of neurologic deficits in both uncomplicated falciparum malaria4±6 and cerebral malaria,7±9 with an estimated 5–10% of African children developing significant and neurologic sequelae following cerebral malaria. These include sensory (i.e., hearing deficits, cortical blindness, and other visual field defects) and motor (i.e., ataxic and paretic) disorders.

Recent advances in neuroradiologic imaging technologies have improved the diagnostic accuracy of detecting neuropathological changes in cerebral malaria10,11 over earlier, lower resolution methods.12 Unfortunately, however, neuropsychologic aspects of cerebral malaria have received very little clinical or research attention. Cerebral white matter lesions have been strongly associated with cerebral malaria,13, 14 with axonal demyelination15 and local cerebral hypoxic effects16 thought to be among its pathologic sequelae. The human corpus callosum is the largest neocortical fiber tract in the brain, and along with other forebrain commissures, facilitates efficient communication between the cerebral hemispheres. If indeed cerebral malaria shows a predilection for cerebral white matter, one can hypothesize interhemispheric transfer inefficiencies on neuropsychologic evaluation. To investigate this possibility, the efficiency in transmission of tactile somesthetic information across the cerebral hemispheres was studied in a sample of Ghanaian children.

MATERIALS AND METHODS

Study area and study population. Accra, the capital of Ghana where this study was conducted, is a coastal city (5°36′N, 0°6′W) with a population of more than 738,000 that has intense malaria transmission rates with strong seasonal variation, and maintains an overall pattern that is largely consistent with the savanna ecologic zone.16 About 8% of all annual deaths in Ghana are attributed to malaria.17

Between April and July of 1994, a sample of 40 Ghanaian children were assessed and administered a battery of standardized and experimental neuropsychologic tests. Suitable participants were selected from various local hospital and school sources in the city of Accra after informed parental consent and the subjects’ assent were obtained. Following an intake interview with each potential participant’s parent or legal custodial guardian, available medical records were reviewed to confirm eligibility for inclusion in this study. Of the total selected sample, 20 children who met the World Health Organization18 research diagnostic criteria for cerebral malaria were compared with 20 healthy age-, gender-, hand dominant-, and education-matched controls without a history of malaria. None of the subjects had a prior history of head injury, neurologic, medical or psychiatric disorder, perinatal birth complications, or a maternal history of malaria during pregnancy. Additional exclusion criteria were recent immigration from a non-malarious area (i.e., less than one year prior to the onset of this study), and use of antimalarial or other prescription medications for at least eight weeks before our assessment. This investigation was approved by the respective ethics committees of the University of Victoria and the University of Ghana Medical School.

Procedures and testing protocols. After consenting to the study that was explained verbally and in writing to each participant and their respective legal guardian, the participants were individually tested with the Sensory-Perceptual Examination19 and the Two-Point Discrimination Test,20 21 following standardized procedures. The Roughness Discrimination Test, an experimental measure, was also administered. Briefly, the full sensory-perceptual examination consists of subtests that assess integrity of the tactile, visual, and auditory sensory inputs via confrontation testing under both unilateral and bilateral stimulation modes. For our current study, however, only subtests measuring unilateral tactile perception, bilateral simultaneous tactile perception, finger-tip number writing perception, and unimanual tactile form recognition were considered. The unilateral and bilateral tactile perception subtests of the sensory-perceptual examination all use a predetermined confrontation format in

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determining whether the subject “is able to accurately recognize stimulation of the right hand, left hand, and both hands simultaneously” while blindfolded. The finger-tip number writing perception subtest “requires the subject to report numbers (3, 4, 5, or 6) written on the fingertips of each hand without the use of vision.” Scoring criteria for each of these subtests is based on number of errors produced (i.e., either a failure to respond, or the provision of an incorrect response to a presented stimulus). The tactile form recognition subtest evaluates the ability to identify four flat plastic shapes (circle, square, triangle, and cross) as they are individually placed in each hand without the benefit of vision. Scoring of the tactile form recognition subtest is based on the total time required to complete all eight trials for either hand, as well as the total number of incorrect identifications of the shapes.

The two-point discrimination test uses a pair of specially devised sharp-point calipers, calibrated in 0.0625-inch graduations to measure somatosensory thresholds following standard procedures. Central palmar assessments are taken for each hand, with the subject required to indicate without the benefit of visual cues whether one or two points of the calipers is presented. The test begins with a one inch span for the two-point discriminations, and this span is progressively narrowed at predetermined settings until discontinuation criteria are met (i.e., three errors on two consecutive trials). Any particular two-point span setting actually consists of presenting the one- and two-points five different times, and in a specific, standardized order. For instance, at the 0.5625-inch two-point setting, the presentation order is 1, 2, 1, 2, 1, 2, 1, 2, and 2. Then, assuming a subject makes less than three errors on this setting, but then goes on to make three or more errors on the next two successive settings (which each have different presentation orders), the test is discontinued and his/her somatosensory discrimination threshold becomes 0.5625 inches. The two-point span settings on this test range from 1.125 to 0.125 inches.

The roughness discrimination procedure was devised to assess efficiency of tactile interhemispheric perceptual discriminations using three different grades (220, P120, and P60) of sandpaper. Each of the three different grades of sandpaper was cut into two square strips, with an area of four square inches apiece. These six pieces were then each mounted in the center of a 6 × 6 inch smooth photographic paper. With the subject blindfolded, two randomly paired pieces of the sandpaper were then presented for a total of 15 paired trials. On each trial, and using the index fingerpad (digit 2) of each hand, the subject was required to rub the sandpaper and then indicate as quickly as possible whether the textures of these presented pairs of sandpaper were the same or different. Similar paradigms have been used in recent experimental somatosensory discrimination studies. Scoring is based on number of correct discriminations and total time taken to make the judgments for the 15 pairs of item presentations.

**Statistical analysis.** To assess differences between the cerebral malaria and matched control groups, the paired-sample t-test was used, with alpha levels set at 0.05. Pearson’s product moment correlation was also used to assess the relationship between coma duration and performance on the roughness discrimination test in the cerebral malaria group.

### RESULTS

The demographic and clinical characteristics of the children with a history of cerebral malaria and their healthy controls are presented in Table 1.

**Sensory-perceptual examination.** Assessment of the subjects’ unilateral tactile perception indicated no evidence for hypesthesia since none of the participants made any errors on either hand of this test. In the bilateral simultaneous tactile stimulation condition, there was likewise no evidence of imperception or extinction to double simultaneous tactile stimulation because no subject made any errors on this subtest. Also, finger-tip number writing perception was intact in individuals in both research groups, and tactile form recognition showed no evidence for astereognosis in either unilateral condition. The total time to recognition, which failed to reach significance, is shown in Table 2.

**Two-point discrimination test.** Results from this test, which are presented in Table 2, showed no significant differences in somatosensory discrimination thresholds between the cerebral malaria group and their matched controls on either the right (t = 1.73, P < 0.05) or left (t = 1.53, P < 0.05) hand.

**Roughness discrimination test.** The cerebral malaria group made significantly more errors under conditions requiring active bimanual tactile discrimination of textured
In the present study, findings from the sensory-perceptual examination and two-point discrimination tests show intact intrahemispheric processing of tactile information in children with a history of cerebral malaria. The lack of psychometric evidence for hemianesthesia, pseudoanesthesia, or astereognosis under conditions of tactile stimulation of either hand would imply generally intact contralateral cerebral somatosensory sites, localizable to the anterior regions of the postcentral parietal cortex. Recent neuroimaging investigations have reported somatosensory activation foci almost exclusively on the parietal operculum and insular cortices, with these areas known to receive their cutaneous afferents from textured surfaces with digit 2 \((t = -3.45, P < 0.01; \text{standard error of the mean} = 0.22)\). Among the cerebral malaria group, a strong negative correlation \((r = -0.72, \text{standard error of the estimate} = 0.97)\) was also found between coma duration and number of incorrect discriminations. Table 2 shows the mean number of error scores of the cerebral malaria and control groups on the roughness discrimination test. A more moderate and positive bivariate correlation between coma duration and response latency on the roughness discrimination test \((r = 0.42, P = 0.06)\) among the cerebral malaria group emerged. Of particular note, and also shown in Table 2, is the highly significant difference in response latency between the research groups \((t = 5.45, P < 0.001)\).

**DISCUSSION**

In the present study, findings from the sensory-perceptual examination and two-point discrimination tests show intact intrahemispheric processing of tactile information in children with a history of cerebral malaria. The lack of psychometric evidence for hemianesthesia, pseudoanesthesia, or astereognosis under conditions of tactile stimulation of either hand would imply generally intact contralateral cerebral somatosensory sites, localizable to the anterior regions of the postcentral parietal cortex. Recent neuroimaging investigations have reported somatosensory activation foci almost exclusively on the parietal operculum and insular cortices, with these areas known to receive their cutaneous afferents from textured surfaces with digit 2 (t = -3.45, P < 0.01; standard error of the mean = 0.22). Among the cerebral malaria group, a strong negative correlation (r = -0.72, standard error of the estimate = 0.97) was also found between coma duration and number of incorrect discriminations. Table 2 shows the mean number of error scores of the cerebral malaria and control groups on the roughness discrimination test. A more moderate and positive bivariate correlation between coma duration and response latency on the roughness discrimination test (r = 0.42, P = 0.06) among the cerebral malaria group emerged. Of particular note, and also shown in Table 2, is the highly significant difference in response latency between the research groups (t = 5.45, P < 0.001).

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