Tropical Medicine and International Health

VOLUME 7 NO 2 PP 104–117 FEBRUARY 2002

Heavy schistosomiasis associated with poor short-term memory and slower reaction times in Tanzanian schoolchildren

Partnership for Child Development*

Department for Infectious Disease Epidemiology, Imperial College School of Medicine, London, UK

Summary Cross-sectional studies of the relationship between helminth infection and cognitive function can be informative in ways that treatment studies cannot. However, interpretation of results of many previous studies has been complicated by the failure to control for many potentially confounding variables. We gave Tanzanian schoolchildren aged 9–14 a battery of 11 cognitive and three educational tests and assessed their level of helminth infection. We also took measurements of an extensive range of potentially confounding or mediating factors such as socioeconomic and educational factors, anthropometric and other biomedical measures. A total of 272 children were moderately or heavily infected with *Schistosoma haematobium*, hookworm or both helminth species and 117 were uninfected with either species. Multiple regression analyses, controlling for all confounding and mediating variables, revealed that children with a heavy *S. haematobium* infection had significantly lower scores than uninfected children on two tests of verbal short-term memory and two reaction time tasks. In one of these tests the effect was greatest for children with poor nutritional status. There was no association between infection and educational achievement, nor between moderate infection with either species of helminth and performance on the cognitive tests. We conclude that children with heavy worm burdens and poor nutritional status are most likely to suffer cognitive impairment, and the domains of verbal short-term memory and speed of information processing are those most likely to be affected.

keywords schistosomiasis, hookworm, cognitive function, educational achievement, schoolchildren, observational studies, Tanzania

correspondence Matthew Jukes, Partnership for Child Development, Department for Infectious Disease Epidemiology, Imperial College School of Medicine, Imperial College School of Medicine, Norfolk Place, London W2 1PG, UK. Fax: +44 20 7262 7912; E-mail: m.jukes@ic.ac.uk

Introduction

Two hundred million people worldwide are estimated to be infected with *Schistosoma haematobium* of which 70% live in sub-Saharan Africa. Around 1300 million people are estimated to be infected with hookworm (Chan 1997). These infections often occur concurrently (Lwambo *et al.* 1999) and it is school age children who are most likely to suffer the consequences of infection because they are generally more likely to harbour heavy infections (Savioli *et al.* 1992).

Severe and chronic helminth infection during this period in children's development could have consequences for their cognitive performance and ultimately their educational achievement. These effects on cognitive function may occur as a result of one or a combination of symptoms associated with infection. For example, one of the main consequences of infection with both parasites is iron deficiency anaemia[1] (IDA) (Farid 1993; Stoltzfus *et al.* 1997b; Olsen *et al.* 1998; Beasley *et al.* 1999) and there is much evidence that IDA is associated with impaired cognitive performance and development (Lozoff 1990;

*Individual authors of this document were M. C. H. Jukes, C. A. Nokes, K. J. Alcock, J. K. Lambo, C. Kihamia, N. Ngorosho, A. Mbise, W. Lorri, E. Yona, L. Mwanri, A. D. Baddeley, A. Hall and D. A. P. Bundy.

[1] Abbreviations used are: BMI, body mass index; epg, eggs per gram; IDA, iron deficiency anaemia; HAZ, height-for-age z-score; Hb, haemoglobin; NCHS, National Center for Health Statistics; MUAC, mid-upper arm circumference; SES, socioeconomic status; SEES, socioeconomic and educational status.

Grantham-McGregor & Ani 2000). Infection with hookworm and *S. haematobium* can also result in poorer growth rates (Stoltzfus *et al.* 1997a; Warren *et al.* 1993) and this may also be a route by which infection leads to impaired performance because undernutrition affects cognitive development and educational achievement (Simeon & Grantham-McGregor 1990; Mendez & Adair 1999).

Whilst these and other pathways provide the potential for helminth infection to impair cognitive function, evidence remains equivocal as to whether this impairment actually takes place (Dickson *et al.* 2000). Among the limited number of well-conducted treatment trials carried out to date, only two (Nokes *et al.* 1992; 1999) have found a main treatment effect on tests of cognitive function. Other studies have found improvements after anthelmintic treatment only for subgroups of the study population (Simeon *et al.* 1995a,b; Nokes *et al.* 1999) or no improvement at all (Gardner *et al.* 1996; Sternberg *et al.* 1997). In a review of these studies, Dickson *et al.* (2000) conclude that the evidence for a cognitive benefit of deworming is 'not convincing' (but see Michael *et al.* 2000). However, the failure of treatment to improve cognitive function does not imply that helminth infection has no effect on cognitive function in the first place. It is quite possible that the effect of helminth infection on cognitive function is irreversible, or that recovery may depend on children receiving remedial teaching in addition to medical treatment (Sternberg *et al.* 1997; Drake *et al.* 2000).

In such cases, treatment trials alone cannot give us a complete picture of the cognitive impairments caused by helminth infection. Ideally, randomised controlled trials of primary prevention of infection are needed to clarify this issue. However, such trials are often neither practical nor ethical and to our knowledge none has been conducted to assess the impact of helminth infection on cognitive function. In the absence of evidence from such preventive trials, the only way to measure the relationship between helminth infection and cognitive function without simultaneously altering that relationship is to conduct well controlled cross-sectional studies. Such studies cannot establish a causal relationship between infection and cognitive ability, but if sufficient care is taken to control for a wide range of possible confounders they may allow us to infer the likely profile of cognitive abilities that are affected by helminth infection in a way that treatment trials cannot.

The most likely confounding factor to affect studies of helminth infection and cognition is poverty (Seifer 2001) and yet the majority of cross-sectional studies have failed to control for socioeconomic status (SES) (Watkins & Pollitt 1997). Only six of more than 40 published studies have controlled for SES (Simeon *et al.* 1994; 1995b; Levav *et al.* 1995; Gardner *et al.* 1996; Sternberg *et al.* 1997; Sakti *et al.* 1999) and only one has controlled for nutritional status (Sakti *et al.* 1999) which may affect cognitive function either independently or as a further index of poverty. There is clearly a need for cross-sectional studies that make a comprehensive attempt to control for all candidate confounders in order to provide evidence to complement that from treatment trials.

Our research project in Bagamoyo, Tanzania addressed these research issues using a combination of cross-sectional methodology and a treatment trial. Here we report the results of the baseline cross-sectional study examining the association between moderate to heavy infections with hookworm and *S. haematobium*, cognitive function and educational achievement in schoolchildren. A major aim of the study was to improve on previous work in this area by including a large sample of children and by assessing a more comprehensive set of potentially confounding variables including SES, anthropometric variables, malaria parasite density, and levels of haemoglobin, ferritin and C-reactive protein.

Methods and subjects

Study population

The study took place in 10 schools in the coastal area of Bagamoyo District and Kibaha District, Tanzania, about 70 km north of Dar es Salaam. Children in these schools spoke Kiswahili at home and at school. School selection was made after giving a questionnaire to children on self-reported schistosomiasis and blood in urine. The questionnaire was based on that reported by Lengeler *et al.* (1991). Schools were asked to participate if they had a relatively high reported prevalence of schistosomiasis (lowest reported prevalence by a selected school was 22%), had more than 100 children enrolled in Grades 2–5, were accessible by road during the rainy season and had a rural catchment area.

In the 10 participating schools there were 2454 registered pupils. Of these, 1689 children met the age and grade criteria, being between 9 and 15 years of age, in Grades 2–5 inclusive, and within 2 years of the modal age for their grade. Children were also excluded if the child had notable severe clinical symptoms of infection with *S. haematobium,* if the child had severe mental handicap and/or severe physical handicap or if the child had chronic clinical disease other than *S. haematobium.* Ten children were excluded for such health reasons. Of the remaining 1679 children, 1476 returned signed consent forms and 906 of these were randomly selected for parasitological screening.

After completing the larger study of which the current investigation was a part, all children received anthelmintic treatment according to their infection status.[2] Children with haemoglobin levels (Hb) of < 80 g/l were given iron treatment. A local doctor was attached to the project throughout to monitor the health of children in participating schools. Any illnesses identified by the project nurse were treated or referred to the project doctor and district hospital.

Experimental design

Between May and August 1997, a comparison was made between children with moderate-heavy hookworm (≥ 400 epg)[3] and/or *S. haematobium* (≥ 50 eggs/10 ml)[3] infections and those without significant helminth infection on their performance on tests of cognitive and motor function and educational achievement.

As part of a larger study, half of the eligible children were randomly selected for parasitological screening after stratifying within school and grade. Of those who were screened, all children with moderate to heavy infection were recruited. For every second moderately to heavily infected child recruited in a class, an uninfected child in the same school grade and of the same sex was selected to serve as a control. If the ideal control was not available, a child of the opposite sex or from the grade above was selected. Where insufficient uninfected controls were available within the school, children with very light infections defined as those with < 50 epg hookworm and < 5 eggs/10 ml *S. haematobium* were also selected to participate in the study.

Approval for this study was obtained from the Tanzania Ministry of Health and Ministry of Education and Culture at national, regional, district and ward level and also by the schools and teachers participating in the study. Ethical clearance was obtained from the Institute of Child Health, London, UK, and the Tanzania Food and Nutrition Centre, Dar es Salaam, Tanzania. Children and parents had the study explained to them in Kiswahili and signed informed consent was obtained from all children and their parents before measurements began.

Psychometric tests

A battery of educational tests measuring reading, spelling and arithmetic skills (detailed in the Appendix) was given to all children by two testers. With the exception of oral arithmetic, which was administered individually, tests were given to groups of about 15 children in their classroom. The educational tests were completed before other psychometric tests were given. Half the children were also given tests measuring a range of cognitive and motor functions (see Appendix) by four testers. The test battery took 30–45 min per child to complete. Tests were presented in a fixed order to children and were organized so that tests placing the highest demands were administered towards the end of the battery when children were familiar with the testing situation. Testers were blind to children's infection status.

Both educational achievement tests and tests of cognitive function were developed over a period of 1 year prior to the start of the study to ensure face validity and content validity of the tests (correlations amongst tests and between school achievement and tests follow the predicted pattern), to ensure that children were familiar and comfortable with all testing materials and to ensure a test–retest reliability of at least 0.7 for each test (Table 1). A novel test of reading ability was developed as part of this study (Alcock *et al.* 2000). All other tests had been adapted and chosen because they measured a range of abilities, had been shown in previous studies to be sensitive to the effects of hunger, undernutrition, IDA, other chronic illnesses or helminth infection. Children were tested in Kiswahili by testers who were fluent in this language. Testers were blind to children's infection status. All children received a snack and a drink before testing to ensure they were not hungry during the test as short-term hunger has been shown to affect cognitive function (Pollitt & Mathews 1998).

Explanatory variables

Children's date of birth was recorded from the school register and from medical clinic cards. For 21% of children the full date of birth was available. For the remainder, only the year of birth was recorded, these children were assigned a birth date of 15th June. Children's sex, class and school attended were also recorded. Children were also given a structured interview individually at school to find out about their home environment and their educational opportunities – characteristics that might affect their cognitive function and educational achievement.

[2] Children received a 400-mg dose of albendazole (SmithKline Beecham, Brentford, UK) on approximately three consecutive days for the treatment of geohelminth infections and/or a single 40 mg/kg dose of praziquantel supplied by E. Merck Pharmaceutical Division (Darmstadt, Germany) for the treatment of *S. haematobium*. A triple dose was considered necessary as the efficacy of giving a single dose is not as high as a triple (Bennett & Guyatt 2000). Children with light infections who were not included in the study were also treated for their infection status and received a single 400 mg dose of albendazole and/or 40 mg/kg praziquantel. All treatment was supervised by a nurse.

[3] Cut-off points for schistosomiasis were determined from WHO (1985) recommendations. For hookworm, few children reached the accepted definition of moderate infection (Montresor *et al.* 1998). To provide a sufficient number of children for the treatment group, a cut-off point of around the 80th percentile was used.

Table 1 Test–retest reliabilities for tests of cognitive function, obtained by all four testers prior to the start of the study

Cognitive/motor test	Min. Max. test–retest reliability of four testers	Function measured
Fluency	0.54–0.93	Speed of scanning and retrieval from memory
Digit Span		
Forwards	0.76–0.92	Working memory – phonological
Backwards	0.65–0.88	Executive function
Spanish Learning	0.84–0.90	Paired associate learning/long-term memory
Corsi block	0.70–0.93	Working memory – visuospatial
Stroop		
Compatible	0.68–0.91	Speed of processing
Incompatible	0.71–0.86	Executive function
Pegboard		
Dominant hand	0.72–0.90	Psychomotor skills
Non-dominant hand	0.60–0.90	Psychomotor skills
Choice Reaction Time*	0.61	Speed of processing
Silly Sentences*	0.70	Speed of verbal processing

* Choice Reaction Time and Silly Centences were computer-based tests, and involved only minimal input from the testers. Thus an overall reliability coefficient was calculated for the test instead of a separate coefficient for each tester.

Biomedical variables

Three urine samples, taken on approximately consecutive days, and one stool sample were collected from each child. For the identification of *S. haematobium* infection, urine samples were sent to the laboratory for microscopic examination for eggs. A 10 ml sample was filtered through a 12 mm diameter polycarbonate membrane with a 12 μm pore size (Costar, UK) and the total number of eggs of *S. haematobium* was recorded as an indicator of the intensity of infection.

For the determination of hookworm and other geohelminth infection, stool samples were analysed in duplicate using the Kato-Katz technique. The total number of eggs of hookworm, *Ascaris lumbricoides, Trichuris trichiura* and any other helminth species seen on each slide was counted and the number of eggs per gram of faeces calculated. A random sample of 10% of urine and stool samples was screened a second time by the senior laboratory technician to check for accuracy of egg counts.

The following anthropometric measurements were taken for each child. Height was measured using a portable stadiometer (CMS Weighing Equipment, London, UK) to a precision of 1 mm. Weight was measured with a digital weighing scale (Soehnle, Germany) to a precision of ±50 g. Children were weighed barefoot, wearing the school uniform. Mid upper arm circumference (MUAC) was measured to a precision of 2 mm with a waxed paper insertion tape (TALC, St Albans, UK) and triceps skinfold thickness was assessed by the mean of three repeated measurements to a precision of ±0.1 mm with Holtain callipers (CMS Weighing Equipment, London, UK). Height-for-age *z*-scores (HAZ, calculated with reference to NCHS data) and BMI were calculated using Epi Info software (Dean *et al.* 1994).

A 2 ml venous blood sample was taken from each child by a nurse. Thick and thin blood slides stained with 3% Giemsa were prepared and examined for malaria parasites. The malaria parasite density was recorded as parasites per 200 white blood cells. The concentration of haemoglobin, an indicator of anaemia, was measured photometrically using a portable haemoglobinometer (Hemocue Ltd, Sheffield, UK). The machine was checked daily against its own standard (Bridges *et al.* 1987). Concentration of ferritin (an indicator of iron stores), and C-reactive protein (an indicator of an acute infection which may also lead to elevated ferritin levels independent of any increase in iron stores) were measured by ELISA using commercial antibodies and standards as described in Beesley *et al.* (2000).

Data analysis

The aim of the first analysis was to examine associations between infection with both hookworm and *S. haematobium* in Tanzanian schoolchildren and their cognitive abilities and educational achievement, controlling for confounding demographic and SES variables. A second analysis aimed to examine whether any associations found in the first analysis remained statistically significant once mediating nutritional and other biomedical variables were controlled for.

The distributions of all cognitive and education test scores were examined for normality and transformed where necessary. Scores for the Stroop test (compatible and incompatible) were log transformed. Reciprocal transformations were performed on both Pegboards scores (dominant and non-dominant hand), the Silly Sentences test and Choice Reaction Time. Reading and spelling tests both had bimodal distribution and were analysed as binary variables using logistic regression procedures. In order to reduce the SEES data and identify underlying constructs, factor analysis with varimax rotation was conducted with the socioeconomic variables and the resulting factors used in the analysis. This produced two factors related to economic wealth, including one related to quality of *house* and larger possessions (extracted from the following variables: type of walls, roof, floor, water source, fuel, toilet, and bed, and the ownership of a fridge, a sofa, a cupboard and cows) and one related to smaller *possessions* (ownership of a bicycle, a radio, tables and chairs) and also three school-related factors including *books* (number of books at home, number of exercise books and text books in the child's bag at time of interview), *uniform* (how complete uniform is, what state of repair uniform is in) and school *equipment* (number of pens and other miscellaneous items of school equipment). Intensity of helminth infection was coded into categorical variables representing intensity above and below certain thresholds. *S. haematobium* infection was coded into three categories: uninfected or lightly infected, moderately infected and heavily infected, with thresholds at 50 eggs/10 ml and 500 eggs/10 ml of urine. Hookworm infection was coded into a binary variable with infection above or below the threshold of 400 eggs/g of faeces. The category of heavy infection with hookworm (>4000 epg; Montresor *et al.* 1998) included only nine children (only five of whom did cognitive tests), which was considered insufficient to include in analyses as a separate group.

Multiple linear regressions were performed to analyse the effect of helminth infection on cognitive function controlling for possible confounding variables. Multilevel modelling using the MLWin program (Rasbash *et al.* 2000) was used to control for random effects at both child and school levels. Separate analyses were conducted for each cognitive and educational test score. In the first analysis, regression equations were constructed as follows: First, age and sex were entered into the regression equation. Second, three dummy variables were offered to control for the variation between the four testers who conducted the cognitive tests. The third step involved controlling for potentially confounding factors. Infection with *Plasmodium* spp. and all five SEES variables were offered. In this and all stepwise regression procedures used in the analysis, variables were admitted into the equation at the $P = 0.05$ level.

After all potentially confounding variables were offered in the regression equation, the categorical helminth infection variables were entered. Finally, interaction terms between all helminth infection variables and each of age, body mass index, and height-for-age were offered to the regression. (Previous studies have shown that both age, Sakti *et al.* 1999, and nutritional status, Simeon *et al.* 1995a,b, can moderate the effect of parasitic infection on cognitive function.)

The second analysis was conducted for each of the outcome variables to determine whether any associations found between infection status and psychological test scores were moderated by mediating variables. This involved a repeat of the first analysis with a fourth step included before parasitological variables were entered in the equation. In this extra step all potentially mediating variables (the nutrition and other health variables HAZ, BMI, Hb, MUAC, C-reactive protein concentration, ferritin concentration) were offered.

Given the large number of analyses performed, the overall error rate was controlled by the use of adjusted significance levels. Throughout cognitive test analyses a revised significance level ($\alpha = 0.010$) was used following Bonferroni corrections for multiple tests with correlated outcome measures (Sankoh *et al.* 1997).

Results

A total of 904 children were screened for their parasitological status; 272 children qualified for the moderately to heavily infected group (160 were infected with *S. haematobium* only, 69 with hookworm only and 43 with both parasites) and 117 for the uninfected control group. All of these 389 children were scheduled to take education achievement tests and 223 were scheduled to take tests of cognitive function. Complete records were available for 338 and 203 of children who did the educational and cognitive test batteries, respectively, representing an average loss of 13% resulting mostly from absenteeism on one or more of the days of testing.

Table 2 describes all measures taken in this study. Children are grouped by infection status: uninfected, moderately infected with either species (there were no species-specific differences for these children), and heavily infected with schistosomiasis. For moderately infected children no significant differences were found for any measure when children were grouped according to the species of parasite with which they were infected. Thus all moderately infected children are grouped together in Table 2 and their data are presented along with those of uninfected children and heavily infected children. These three groups were mutually exclusive.

Table 2 Description of all variables for children grouped by infection status. Arithmetic means (and ranges) are shown

	Uninfected	Moderate infection (hookworm or *S. haematobium*)	Heavy infection (*S. haematobium* only)
Total number	*n* = 97	*n* = 203	*n* = 38
Number of girls*	57 (58%)	99 (49%)	13 (34%)
Age (years)***	11.8 (9.6–14.2)	12.5 (9.6–14.3)	12.3 (9.7–14.2)
Biomedical data			
MUAC (mm)	192.7 (146–260)	191.9 (112–264)	193.9 (160–222)
Skinfold thickness (mm)	7.7 (3.6–22.1)	7.2 (3.6–17.5)	7.5 (4.9–14)
HAZ	−1.86 (−5.5–0.8)	−2.09 (−5.4–2.5)	−2.08 (−4.3–1.7)
BMI (kg/m^2)	16.3 (13.2–21.8)	16.3 (12.4–23.4)	16.4 (13.5–19.2)
CRProtein (mg/l)	2.4 (0.1–14.2)	1.9 (0.1–17.3)	2.2 (0.2–16.1)
Ferritin (μg/ml)**	39.1 (4–180)	28.6 (3–356)	24.6 (3.6–82)
Hb (g/l)***	119.0 (59–155)	113.7 (55–145)	110.6 (74–138)
Plasmodium spp. prevalence	37.1%	37.4%	34.2%
S. haematobium egg count (per 10 ml)	0 (0–5)	135 (0–494)	1036 (509–3291)
Hookworm egg count (per g)	5 (0–35)	709 (0–7193)	216 (0–1313)
Socioeconomic status indices			
Wealth (house)***	0.52 (−2.4–4.2)	−0.02 (−1.5–5.1)	−0.28 (−1.4–1.4)
Possessions*	0.28 (−1.9–2.0)	−0.00 (−2.5–2.1)	0.01 (−2.1–1.9)
School books	0.08 (−1.5–6.0)	0.01 (−1.6–5.3)	−0.26 (−1.6–1.9)
School equipment	−0.04 (−1.5–3.5)	0.03 (−1.5–3.6)	−0.03 (−1.3–3.5)
School uniform	0.14 (−4.6–1.7)	0.02 (−5.9–1.7)	−0.275 (−3.4–1.3)
Education tests			
Arithmetic	24.1 (10–38)	24.0 (13–53)	23.3 (12–33)
Reading	24.1 (−1–55)	25.6 (−2–60)	23.9 (−2–57)
Spelling	36.3 (1–59)	34.8 (5–58)	32.5 (8–58)
Cognitive tests	*n* = 62	*n* = 122	*n* = 19
Digit Span Forwards**	7.1 (4–11)	6.8 (2–14)	5.5 (3–8)
Digit Span Backwards**	4.6 (0–9)	4.2 (0–10)	3.0 (0–6)
Corsi Block	9.7 (5–16)	9.7 (5–14)	9.6 (6–13)
Spanish Learning	24.2 (9–62)	24.3 (12–46)	20.6 (12–30)
Stroop Compatible (s)	19.4 (12.5–36.1)	19.2 (11.7–34.3)	21.7 (14.4–36.5)
Stroop Incompatible (s)	21.7 (12.3–33.1)	22.1 (12.9–41.8)	23.2 (16.2–32.4)
Pegboard (dominant hand; min)	1.40 (0.89–7.35)	1.33 (0.83–4.51)	1.30 (0.88–2.2)
Pegboard (non-dominant hand; min)	1.69 (0.97–6.25)	1.64 (0.95–5)	1.54 (1.1–2.9)
Fluency**	25.2 (10–44)	29.0 (11–50)	28.9 (13–39)
Silly Sentences (s)	3.85 (3.31–4.47)	3.80 (3.22–4.92)	3.95 (3.4–4.6)
Choice Reaction Time (s)	0.704 (0.38–2.154)	0.670 (0.33–1.45)	0.981 (0.56–2.11)

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$; significance levels refer to results of one-way ANOVA of group differences.

Associations with parasitological status

Among cognitive tests, the most consistent pattern of results was observed for heavy infection with *S. haematobium* (Table 3). This was associated with lower scores in four of the 11 tests of cognitive function:[4] Digit Span Forwards ($P = 0.003$), Digit Span Backwards ($P = 0.004$), Silly Sentences ($P = 0.003$) and Choice Reaction Time ($P = 0.002$). For Silly Sentences, the relationship resulted from interactions between heavy schistosome infection and height-for-age ($P = 0.001$). This was because children who were both heavily infected with *S. haematobium* and stunted (HAZ < −2) had longer mean reaction times on the Silly Sentences test than other children (see Table 4). For one further cognitive test, Stroop Compatible ($P = 0.028$), the association between heavy schistosomiasis and poorer performance approached significance.

There were fewer and less consistent relationships between cognitive outcomes and moderate levels of infection. For *S. haematobium*, moderate infection was associated with higher cognitive test scores for the Verbal Fluency test ($P = 0.009$, diff. = 3.52 items or 0.46 SD).

[4] Note revised significance ($\alpha = 0.010$) used following Bonferroni corrections for multiple tests with correlated outcome measures (Sankoh *et al.* 1997).

Table 3 Results of regression analyses for each cognitive and educational achievement test with age, sex, SEES variables, all biomedical variables and categorical parasitological variables as independent measures. Note that because of the method of scoring and transforming dependent variables, a positive value of *b* represents a positive relationship with ability for all test scores except for the two Stroop tests (i.e. higher scores are better in all but these two tests)

	Digit span forwards		Digit span backwards		Corsi block		Spanish learning		Stroop compatible	
Fixed effects	*b*	*P*	*b*	*P*	*b*	*P*	*b*	*P*	*b*	*P*
Constant	**5.603**	**0.009**	**3.589**	**0.010**	**8.912**	**< 0.001**	**4.535**	**< 0.001**	**3.962**	**< 0.001**
Sex	−0.476	0.065	−0.457	0.076	−0.474	0.065	−0.127	0.256	−0.067	0.017
Age	−0.195	0.124	−0.006	0.962	0.054	0.671	0.010	0.849	**−0.052**	**0.001**
Grade	0.455	0.173	**0.543**	**0.001**	0.349	0.032	0.090	0.189	−0.034	0.052
Tester1					0.836	0.011				
Tester2							0.278	0.033		
Tester3										
House										
Possessions										
Books	1.753	0.073								
Equipment										
Uniform										
Malaria										
Ferritin					**−0.010**	**0.006**				
Haemoglobin										
HAZ									**−0.052**	**< 0.001**
BMI										
Skinfold										
MUAC										
Moderate *S. haematobium*	−0.018	0.947	−0.465	0.093	0.210	0.443	0.045	0.709	0.008	0.798
Heavy *S. haematobium*	**−1.476**	**0.003**	**−1.406**	**0.004**	−0.526	0.273	−0.388	0.066	0.115	0.028
Moderate Hookworm	−0.127	0.656	0.054	0.848	−0.552	0.062	0.017	0.889	−0.029	0.339
HAZ * Heavy *S. haematobium*										
HAZ * Moderate Hookworm										
BMI * Moderate *S. haematobium*										

Bold text denotes significant coefficient. Revised significance level ($\alpha = 0.010$) used following Bonferroni corrections for multiple tests with correlated outcome measures.

Table 3 (*Continued*)

	Stroop incompatible		Pegboard (dominant hand)		Pegboard (non dominant hand)		Verbal fluency		Silly sentences	
Fixed effects	*b*	*P*	*b*	*P*	*b*	*P*	*b*	*P*	*b*	*P*
Constant	**3.833**	**< 0.001**	0.330	0.111	0.371	0.065	**17.251**	**0.002**	**0.258**	**< 0.001**
Sex	**−0.113**	**0.001**	**−0.126**	**< 0.001**	**−0.107**	**< 0.001**	−0.356	0.721	−0.002	0.437
Age	−0.023	0.244	**0.033**	**0.009**	0.013	0.284	0.692	0.210	0.001	0.326
Grade			−0.006	0.723	−0.001	0.931	0.718	0.259	0.003	0.039
Tester 1									0.006	0.080
Tester 2							**4.054**	**0.001**	**0.015**	**< 0.001**
Tester 3			−0.064	0.027					**0.009**	**0.006**
House									**−0.039**	**0.006**
Possessions										
Books			0.179	0.053	0.184	0.041				
Equipment										
Uniform										
Malaria										
Ferritin										
Haemoglobin										
HAZ	**−0.060**	**< 0.001**					**1.275**	**0.008**	0.002	0.110
BMI										
Skinfold	**0.025**	**0.004**								
MUAC	−0.002	0.024								
Moderate *S. haematobium*	0.048	0.145	−0.024	0.374	−0.039	0.133	**2.800**	**0.009**	−0.002	0.489
Heavy *S. haematobium*	0.053	0.360	−0.027	0.572	0.007	0.875	0.095	0.960	**−0.020**	**0.003**
Moderate Hookworm	−0.021	0.534	0.022	0.425	0.030	0.266	1.631	0.141	0.002	0.500
HAZ * Heavy *S. haematobium*									**0.026**	**0.002**
HAZ * Moderate Hookworm										
BMI * Moderate *S. haematobium*										

Table 3 (*Continued*)

	Choice reaction time		Arithmetic		Reading		Spelling	
Fixed effects	*b*	*P*	*b*	*P*	exp(*b*)	*P*	exp(*b*)	*P*
Constant	**0.722**	**0.009**	2.840	0.590	**0.000**	**< 0.001**	**0.000**	**0.001**
Sex	0.017	0.734	**−1.580**	**0.003**	0.509	0.031	**0.384**	**0.001**
Age	0.038	0.139	0.196	0.495	1.000	0.998	0.774	0.072
Grade	0.053	0.101	**2.236**	**< 0.001**	6.515	**< 0.001**	**1.995**	**0.001**
Tester1	**0.227**	**0.003**					0.479	0.013
Tester2	**0.299**	**< 0.001**	N/A	N/A	N/A	N/A	N/A	N/A
Tester3	**0.232**	**0.001**	N/A	N/A	N/A	N/A	N/A	N/A
House								
Possessions								
Books			3.670	0.052			**20.548**	**0.007**
Equipment			**5.114**	**0.002**	**25.904**	**0.001**	**47.329**	**< 0.001**
Uniform					1.403	0.046	1.332	0.053
Malaria					1.006	0.048		
Ferritin								
Haemoglobin								
HAZ			0.557	0.025				
BMI								
Skinfold								
MUAC							1.020	0.011
Moderate *S. haematobium*	−0.858	0.048	−0.273	0.629	0.994	0.985	0.928	0.808
Heavy *S. haematobium*	**−0.307**	**0.002**	−1.079	0.220	0.561	0.285	0.630	0.313
Moderate Hookworm	−0.008	0.881	−0.113	0.846	1.098	0.781	1.003	0.993
HAZ * Heavy *S. haematobium*								
HAZ * Moderate Hookworm								
BMI * Moderate *S. haematobium*	0.051	0.050						

There was a relationship between moderate *S. haematobium* infection and higher scores in the Digit Span Backwards task ($P = 0.09$) which approached significance. Moderate hookworm infection was not significantly related to any of the cognitive tests. In addition, there were no significant associations between either worm infection and any of the three education tests.

Associations with other explanatory variables

Stunting (low HAZ) significantly predicted lower scores in three cognitive tests, strengthening evidence of the link between cognitive development and undernutrition (Simeon & Grantham-McGregor 1990; Mendez & Adair 1999). No other biomedical variable made a noteworthy contribution to the variance in test scores. Among SEES variables, the education-related factors had the greatest impact on results, particularly for the education tests. The *school equipment* factor predicted high scores on all three education tests. This adds validity to the procedures both for assessing SEES and for extracting relevant factors from the wealth of data.

Discussion

This study provides the strongest evidence to date that infection with *S. haematobium* is associated with impaired mental performance and, in doing so, contributes to a substantial literature implicating parasitic helminth infections as a cause of retarded cognitive development (Watkins & Pollitt 1997). Our results corroborate those from treatment studies (Nokes *et al.* 1992; 1999; Simeon *et al.* 1995a) in showing that cognitive function is impaired for the most heavily infected children. In addition, the associations found were independent of confounding factors, such as SES, age, sex, malaria infection and other chronic infections, and variables potentially responsible for mediating the effect of parasitic infection on cognitive function such as nutritional indices and iron status.

Problems with this interpretation of our findings arise from the cross-sectional design of the study. For example, we have concluded that mild infection does not impair cognitive function. However, there are a couple of alternative explanations for the lack of association between mild infection and cognitve impairment. First, helminth

Table 4 Breakdown of the interaction between height-for-age and heavy *S. haematobium* infection for the Silly Sentences test. Mean reaction time is shown in seconds

		Height-for-age *z* score	
		Below −2	Above −2
S. haematobium	< 500 eggs/10 ml	3.82	3.80
Infection	> 500 eggs/10 ml	4.11	3.80

infection is likely to have a cumulative effect on cognitive function over an extended period of time. Thus, associations found in the current study may represent the effects of infection levels over the past few years (for which current infection status is a proxy) in addition to the effects of the current parasitic load. Thus, those children with the heaviest current parasitic load may show the greatest impairment because they are also the children who have harboured a worm burden for the longest period of time. Second, there are known to be individual differences among children in exposure to schistosomiasis. More sociable and more active children are more likely to be infected (Kvalsvig & Becker 1988). It is possible that cognitive function is also linked with risk of exposure (for example there is a moderate relationship between curiosity and cognitive function (Alberti & Witryol 1994)) and that this positive correlation could cancel out the negative relationship between infection level and cognitive function at low levels of infection.

A further problem of interpretation arises from the fact that any association found in this study may have resulted from a codependence of cognitive function and helminth infection on a third variable. Our study was designed to minimize this problem by including a highly valid measure of SES (PCD, in preparation) and by sampling a wide range of other potential confounders, all of which were controlled for in final analyses. However, a more persuasive argument that there is a genuine causal relationship between cognitive function and helminth infection comes from the profile of cognitive abilities impaired by helminth infection. We found that having a heavy infection of schistosomiasis was associated with a drop in performance in the digit span forwards and backwards and with increased reaction time in the Silly Sentences and Choice Reaction Time tasks. No other tests were negatively affected by heavy schistosomiasis. There are two things to note in this pattern of results. First, there are large differences from one test to another in the relationship with helminth infection. In particular, the effect on the Choice Reaction Time task approaches 3 SDs, an extraordinarily large effect for a psychometric test, whilst other tests show more moderate or nonsignificant effects. This is not the pattern we would expect if the effect were based simply on the fact that poor performance in cognitive tests and high parasitic loads tend to co-occur in the poorest children. On the contrary, SES, the environmental factor having by far the largest influence on performance in psychometric tests, tends to have an equal effect on all domains of cognitive function (Seifer 2001). Second, the two domains showing the strongest relationship with helminth infection were verbal short-term memory (digit span forwards and backwards) and speed of information processing (choice reaction time and silly sentences). These domains have also been affected in most of the other cross-sectional studies that have controlled for SES in their analyses. Four of these five studies have found a relationship between helminth infection and speed of information processing (Nokes *et al.* 1992; Simeon *et al.* 1995a; Gardner *et al.* 1996; Sakti *et al.* 1999), three of the five have found a relationship with the verbal short-term memory (Nokes *et al.* 1992; Gardner *et al.* 1996; Sternberg *et al.* 1997; Sakti *et al.* 1999). Together these studies present an important pattern of results. As argued in the introduction, the cognitive functions that recover after anthelmintic treatment (if any) are not necessarily those that are affected in the first place, and so treatment trials are not in a position to, and so far have not been able to, inform us as to which cognitive functions are affected by helminth infection. By contrast, well controlled cross-sectional studies may present the best opportunity to understand the profile of cognitive functions affected by helminth infection. These studies are converging on the conclusion that speed of information processing and short-term memory are the domains most affected.

It is essential that serious attempts are made to identify the cognitive functions impaired by helminth infection – to look at the type and not just the number of tests affected – and consequently to formulate and test hypotheses concerning the mechanism for this effect. It is only when cognitive testing is used to address such specific hypotheses that we may hope for some clarity to emerge from the uncertain results that permeate this field.

One promising hypothesis may emerge from the substantial relationship between heavy schistosomiasis and reaction time found in the current study. This finding is common to cross-sectional studies in this field (as discussed above) and is consistent with the notion that children with heavy worm loads suffer from lassitude and show poor sustained attention. For example, Kvalsvig *et al.* 1991 found that heavily infected children performed more poorly than controls in a choice reaction time task (similar to the one used in the current study) but only in the latter 15 min of the 30-min test. It is interesting to note that our reaction time tasks were both administered at the end of potentially tiring battery of cognitive tests.[5] Previous studies have, on the whole, failed to measure children's attentional capacity directly and thus it is possible that attention deficits underpin poor performance in some cognitive tests. This hypothesis provides an interesting avenue for future research.

In conclusion, our study is the first to demonstrate a relationship between helminth infection and cognitive impairment that is independent of confounding biological and socioeconomic variables. In addition, a comparison of the results of this study with those of treatment studies points to the value of using a variety of methodologies in order to understand the link between helminth infection and cognitive function. Both cross-sectional and intervention studies have important and unique contributions to make in exploring the connection between helminth infection and cognitive function. Furthermore, the two methodologies map onto different practical solutions to the problems caused by helminth infections. Observational studies give us an indication of the (presumably cumulative) effect of infection whilst intervention studies tell us how much of this effect can be reversed by treatment. In other words, large effects found in cross-sectional studies highlight the need to prevent children from getting infected (or to treat their infection at an early age) whilst large treatment effects would suggest that a cure can be as effective as prevention. Put into this framework, the results of the current study strengthen the case for prevention and for giving all children the opportunity to learn and develop in the absence of helminth infection.

Acknowledgements

The MAKWAMI project was funded by the James S. McDonnell foundation.

We gratefully acknowledge the hard work of all the staff of the MAKWAMI Project: Chacha Musabi, Charles Deus, Christina Mwita, Erasto Tuntufye, Eliza Charles, Fausta Ngowi, Juliet Mdusi, Asnat Mchopa, Husna Tuli, Selemani Kungulilo, Zuhura Mfaume, Muhsin Iddi, Gordian Rwegasira. We would also like to thank the Primary School students who participated in the study, their teachers and the village leaders in participating villages, also the District Education Officers and District Medical Officers and District Health Management Teams of Bagamoyo and Kibaha Districts.

References

Alberti ET & Witryol SL (1994) The relationship between curiosity and cognitive-ability in 3rd-grade and 5th-grade children. *Journal of Genetic Psychology* **155**, 129–145.

Alcock KJN, Ngowi F, Musabi C *et al.* (2000) The development of reading tests for use in a regularly spelt language. *Applied Psycholinguistics* **21**, 525–555.

Baddeley A (1992) Is working memory working? The fifteenth Bartlett Lecture. *Quarterly Journal of Experimental Psychology: Human Experimental Psychology* **44a**, 1–31.

Baddeley A, Emslie H & Nimmo-Smith I (1992) *The Speed and Capacity of Language Processing (SCOLP) Test: Manual.* Thames Valley Test Company, Bury St Edmunds.

Baddeley A, Gardner JM & Grantham McGregor S (1995) Cross-cultural cognition: developing tests for developing countries. *Applied Cognitive Psychology* **9**, S173–S195.

Beasley NM, Tomkins AM, Hall A *et al.* (1999) The impact of population level deworming on the haemoglobin levels of schoolchildren in Tanga, Tanzania. *Tropical Medicine and International Health* **4**, 744–750.

Beesley R, Filteau S, Tomkins A *et al.* (2000) Impact of acute malaria on plasma concentrations of transferrin receptors. *Transactions of the Royal Society of Tropical Medicine and Hygiene* **94**, 295–298.

Bennett A & Guyatt H (2000) Reducing intestinal nematode infection: efficacy of albendazole and mebendazole. *Parasitology Today* **16**, 71–74.

Bridges M, Parvin R & Van Assesdelft O (1987) Evaluation of a new system for haemoglobin measurement. *American Clinical Product Reviews* **49**, 5–28.

Chan MS (1997) The global burden of intestinal nematode infections: 50 years on. *Parasitology Today* **13**, 438–443.

Dean A, Dean J, Coulombier D *et al.* (1994) *Epi Info, Version 6: a Word Processing Database and Statistics Program for Epidemiology on Microcomputers*. Centre for Disease Control and Prevention, Atlanta.

Dickson R, Awasthi S, Williamson P, Demellweek C & Garner P (2000) Effects of treatment for intestinal helminth infection on growth and cognitive performance in children: systematic review of randomised trials. *British Medical Journal* **320**, 1697–1701.

Drake LJ, Jukes MCH, Sternberg RJ & Bundy DAP (2000) Geohelminthiasis (*ascariasis trichuriasis* and hookworm): cognitive and developmental impact. *Seminars in Pediatric Infectious Disease* **11**, 245–251.

[5] As noted in the Methods section, there is good reason for administering cognitive tests in a fixed order even though order effects may confound results. The general principle is to administer more demanding tests at the end of the battery. Both reaction time tasks were conducted using a computer that was unfamiliar to many of the children. It was felt children would respond better to these tests at the end of the battery having become familiar with the testing situation. Nevertheless it would be interesting to vary the order of tests systematically in future studies, in the light of the hypothesis expounded in the text.

Farid Z (1993) Schistosomes with terminal-spined eggs: pathological and clinical aspects. In: *Human Schistosomiasis* (eds P Jordan, G Webb & R Sturrock). CAB International, Wallingford, pp. 159–193.

Gardner JM, Grantham McGregor S & Baddeley A (1996) *Trichuris trichiura* infection and cognitive function in Jamaican schoolchildren. *Annals of Tropical Medicine and Parasitology* **90**, 55–63.

Grantham-McGregor S & Ani C (2000) *A Review of Studies on the Effect Iron Deficiency on Cognitive Development in Children*. WHO, Geneva.

Kvalsvig JD & Becker PJ (1988) Selective exposure of active and sociable children to schistosomiasis. *Annals of Tropical Medicine and Parasitology* **82**, 471–474.

Kvalsvig JD, Cooppan RM & Connolly KJ (1991) The effects of parasite infections on cognitive processes in children. *Annals of Tropical Medicine and Parasitology* **85**, 551–568.

Lengeler C, Kilima P, Mshinda H, Morona D, Hatz C & Tanner M (1991) Rapid low-cost two-step method to screen for urinary schistosomiasis at the district level: the Kilosa experience. *Bulletin of the World Health Organization* **69**, 179–189.

Levav M, Mirsky AF, Schantz PM, Castro S & Cruz ME (1995) Parasitic infection in malnourished schoolchildren: effects on behaviour and EEG. *Parasitology* **110**, 103–111.

Lozoff B (1990) Has iron deficiency been shown to cause altered behaviour in infants? *Brain Behaviour and Iron in the Infant* (ed. J Dobbing). Springer-Verlag, London, pp. 107–131.

Lwambo NJ, Siza JE, Brooker S, Bundy DA & Guyatt H (1999) Patterns of concurrent hookworm infection and schistosomiasis in schoolchildren in Tanzania. *Transactions of Royal Society of Tropical Medicine and Hygiene* **93**, 497–502.

Mendez MA & Adair LS (1999) Severity and timing of stunting in the first two years of life affect performance on cognitive tests in late childhood. *Journal of Nutrition* **129**, 1555–1562.

Michael E, Bhargava A, Bundy D *et al.* (2000) Treatment for intestinal helminth infection. *British Medical Journal* **321**, 1224.

Montresor A, Crompton DWT, Bundy DAP, Hall A & Savioli L (1998) *Guidelines for the Evaluation of Soil-Transmitted Helminthiasis and Schistosomiasis at Community Level. A Guide for Managers of Control Programmes*. WHO, *Geneva* (WHO/CTD/SIP/98 1).

Nokes C, Grantham McGregor SM, Sawyer AW, Cooper ES & Bundy DA (1992) Parasitic helminth infection and cognitive function in schoolchildren. *Proceedings of the Royal Society London B Biological Sciences* **247**, 77–81.

Nokes C, McGarvey ST, Shiue L *et al.* (1999) Evidence for an improvement in cognitive function following treatment of *Schistosoma japonicum* infection in Chinese primary schoolchildren. *Americal Journal of Tropical Medicine and Hygiene* **60**, 556–565.

Olsen A, Magnussen P, Ouma JH, Andreassen J & Friis H (1998) The contribution of hookworm and other parasitic infections to haemoglobin and iron status among children and adults in western Kenya. *Transactions of Royal Society of Tropical Medicine and Hygiene* **92**, 643–649.

Pollitt E & Mathews R (1998) Breakfast and cognition: an integrative summary. *American Journal of Clinical Nutrition* **67**, 804s–813s.

Rasbash J, Browne W, Goldstein H *et al.* (2000) *A User's Guide to Mlwin V2, 1.* Multilevel Models Project Institute of Education, University of London.

Sakti H, Nokes C, Hertanto WS *et al.* (1999) Evidence for an association between hookworm infection and cognitive function in Indonesian schoolchildren. *Tropical Medicine and International Health* **4**, 322–334.

Sankoh A, Huque M & Dubey S (1997) Some comments on frequently used multiple endpoint adjustment methods in clinical trials. *Statistics in Medicine* **16**, 2529–2542.

Savioli L, Bundy D & Tomkins A (1992) Intestinal parasitic infections: a soluble public health problem [editorial]. *Transactions of Royal Society of Tropical Medicine and Hygiene* **86**, 353–354.

Seifer R (2001) Socioeconomic status multiple risks and development of intelligence. In: *Environmental Effects on Cognitive Abilities* (eds RJ Sternberg & EL Grigorenko). Lawrence Erlbaum Associates Inc, Mahwah, pp. 59–82.

Simeon D & Grantham-McGregor S (1990) Nutritional deficiencies and children's behaviour and mental development. *Nutrition Research Reviews* **3**, 1–24.

Simeon D, Callender J, Wong M, Grantham McGregor S & Ramdath DD (1994) School performance, nutritional status and trichuriasis in Jamaican schoolchildren. *Acta Paediatrica* **83**, 1188–1193.

Simeon DT, Grantham McGregor SM, Callender JE & Wong MS (1995a) Treatment of *Trichuris trichiura* infections improves growth spelling scores and school attendance in some children. *Journal of Nutrition* **125**, 1875–1883.

Simeon DT, Grantham McGregor SM & Wong MS (1995b) *Trichuris trichiura* infection and cognition in children: results of a randomized clinical trial. *Parasitology* **110**, 457–464.

Sternberg RJ, Powell C, McGrane P & Grantham McGregor S (1997) Effects of a parasitic infection on cognitive functioning. *Journal of Experimental Psychology: Applied* **3**, 67–76.

Stoltzfus RJ, Albonico M, Tielsch JM, Chwaya HM & Savioli L (1997a) School-based deworming program yields small improvement in growth of Zanzibari schoolchildren after one year. *Journal of Nutrition* **127**, 2187–2193.

Stoltzfus RJ, Chwaya HM, Tielsch JM, Schulze KJ, Albonico M & Savioli L (1997b) Epidemiology of iron deficiency anaemia in Zanzibari schoolchildren: the importance of hookworms. *American Journal of Clinical Nutrition* **65**, 153–159.

Warren K, Bundy D, Anderson R *et al.* (1993) Helminth Infection. In: *Disease Control Priorities in Developing Countries*. Oxford University Press, New York, pp. 131–160.

Watkins WE & Pollitt E (1997) 'Stupidity or worms': Do intestinal worms impair mental performance? *Psychological Bulletin* **121**, 171–191.

WHO (1985) *The Control of Schistosomiasis*. WHO Technical Report Series 728. WHO, Geneva.

Appendix

Cognitive and motor function tests

A brief description of the each of the tests used in the study, the function measured and the scoring procedure is given.

Digit span forwards and backwards

Children repeat increasingly longer strings of numbers immediately after the examiner has read them out. In the forwards test the numbers are repeated in the same order as they are read out, and in the backwards test, in the reverse order. For both tests there are three trials at each level, starting with three digits in the forward condition and two digits in the backwards condition. The test is discontinued if a child fails all three trials at one level. The score is the total number of correct answers. This is a test of verbal working memory. The backwards test is also thought to test executive function.

Grooved pegboard

The time taken for children to place 25 grooved pegs into a board is recorded. The first trial is completed with the dominant hand and the second with the nondominant hand. This is a test of psychomotor function.

Corsi block

The test is a visuo-spatial equivalent to the Digit Span Forwards test. There are nine blocks positioned on a board. The examiner points to the blocks in increasingly longer strings and the children have to replicate the pointing sequence. There are three trials at each level, starting with three blocks, and the test is discontinued if a child fails all three trials at one level. This is a test of visuo-spatial working memory.

Verbal fluency

This has two trials of one minute in which children name as many animals and then as many foods as they can. One point is given for each answer (disregarding duplicates) and totalled. The test is designed to measure the scanning and retrieval of long-term memory. There is also a speed of processing component.

Stroop

The test was an adaptation of the Stroop test. It consists of four trials each consisting of one page with 48 boxes containing either a tick (three) or a cross (eight). There are two trials with 'compatible' instructions, where children are asked to touch each box and say as quickly as possible whether it contains a tick or a cross. There are also two 'incompatible' trials where children do the reverse, saying, 'tick' if the box contains a cross and saying 'cross' if the box contains a tick. The time taken to complete each trial and the number of errors made were scored and from these the time taken to complete 48 boxes without error was calculated. (Where errors were made the time was divided by the proportion of correct answers.) The adjusted times were totalled and averaged separately for both trials on the compatible or the incompatible tests. The test is designed to measure executive function (Baddeley 1992).

Spanish vocabulary learning

Adapted from a French Vocabulary Learning test by Baddeley *et al.* (1995) designed for Jamaican children, this test consists of 16 familiar pictures whose names were to be learnt in Spanish. Spanish is not taught in school, is easy for testers to pronounce and is not spoken in East Africa so was considered equally unfamiliar to all children. Initially, children were told the names of four pictures and then asked to point to the correct pictures when the tester repeated the names. After two correct trials, four more pictures were named and they were then asked to point to the eight pictures in turn when they were named. This was repeated introducing four new pictures every time the child pointed correctly to all named pictures on two consecutive trials. A total of eight trials was given. The score was the total number of correct responses. It was designed to measure paired-associate learning.

Computerized tests

There were two computerized tests requiring the following equipment: Apple Mac portable computer, Psyscope software, a button box and speakers. Computers were unfamiliar to all the children in the study so the equipment was hidden prior to use and care was taken to introduce it in a sensitive and appropriate manner. Children were familiar with radios and audio speakers and most were comfortable with the set-up.

Auditory choice reaction time

Children's reaction time was measured when choosing which of two pictures matched an auditory stimulus. Above the red button on the button box was placed a picture of a dog and above the green button, a picture of a chick. Children were asked to press the red (dog) button as quickly as possible after hearing the sound of a dog ('woof woof') and the green (chick) button after hearing the sound of a chick ('cheep cheep'). The auditory stimuli (dog or chick) were presented in random order. The practice trial contained 10 stimuli and the main test 60 stimuli. The computer recorded each reaction time and calculated the mean reaction time for all responses excluding incorrect responses and those with reaction times greater than three standard deviations above or below the mean.

Silly sentences

The Silly Sentences test was computerized and based on the silly sentences task (Baddeley *et al.* 1992). Two lists of 40 questions requiring either a 'yes' or 'no' response, were presented to children over the speakers. Each child was randomly assigned one of the two lists. For example, children were required to answer the question as quickly as possible by pressing the appropriate button on the button box. There were two practice trials of 6 and 10 questions. In addition, to assist children, a tick symbol was placed above the green button for 'yes' and a cross symbol above the red button for 'no'. The test score was the mean reaction time for correct answers, excluding responses longer than three standard deviations above the mean response time. The test was designed to measure auditory speed of processing.

Educational achievement tests

Reading tests. These tests were developed specifically for the study. Traditional reading tests proved unsuitable because Kiswahili is a regularly spelt language which means that children can correctly read words out loud without understanding their meaning. Three tests were developed and presented in increasing order of difficulty. The letter reading and word reading tasks were given to all children. Sentence reading was given to all children scoring ≥ 9 (hits – false alarms) or ≥ 21 (total score) on the word reading task. The scores (hits –false alarms) for the letter, word and sentence reading tests were added together to produce a composite reading score. Note that a hit is when a real letter/word/sentence is correctly identified as real. A false alarm is when a false letter/word/sentence is incorrectly identified as real.

Letter reading. Children had to discriminate letters and non-letters by putting a tick or a cross next to the test item. There were 12 letters and 12 non-letters presented in random order. Letters that resembled Arabic letters were excluded during piloting as many children in the study also attended a Koran school. A standard guessing correction was applied by subtracting the number of false alarms from the number of hits. The maximum possible score was therefore 12 and a score of chance was 0.

Word reading. Children had to discriminate words from non-words in the same way as for the letter reading task. There were 12 words and 12 non-words. Words were taken from school reading books. A guessing correction was again used, hence the maximum possible score was 12 and a score of chance was 0. There were two parallel versions of this test and children were randomly assigned to receive either Version A or Version B.

Sentence reading. The test was based on the Silly Sentences task (Baddeley *et al.* 1992) and was intended to measure speeded comprehension for better readers. Children had to discriminate silly from true sentences, e.g. ('Do goats lay eggs?' or 'Is your hand attached to your arm?') The total number of sentences presented in the task was 125 and the time allotted was 5 min, which was designed to ensure no child would complete the task. Children were tested in groups of up to 10. Using a guessing correction based on hits minus false alarms, gave a maximum score of 63 and a chance score of 0.

Spelling. To test children's spelling, they were read out a total of 50 words and asked to spell the word on the sheet of paper they were given. The maximum score was 50.

Arithmetic. There were two arithmetic tests – one written and one oral. The oral arithmetic test was easier and given individually to all children in Grade 2 and those children in Grade 3 who scored ≤ 6 on the written arithmetic test. The test covered basic numerical understanding including number recognition, counting and simple addition and subtraction of numbers one or two digits long. The score was the total number correct and the maximum score was 15. The written arithmetic was given in groups and tested more advanced numerical skills of numbers two to six digits long. The score was the total number correct and the maximum score was 30. Children not qualifying to do the oral arithmetic test were awarded the maximum score on this test of 15. Scores on the two tests were added together to get an overall score on arithmetic of 45.

