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FULL-LENGTH ORIGINAL RESEARCH

Meta-analysis of the association between cysticercosis and epilepsy in Africa

***Fabrice Quet, *Maëlenn Guerchet, *†Sebastien D. S. Pion, *‡Edgard B. Ngoungou, §Alessandra Nicoletti, and *Pierre-Marie Preux**

***Université de Limoges, IFR 145 GEIST, Institut d'Epidémiologie Neurologique et de Neurologie Tropicale, EA 3174 NeuroEpidémiologie Tropicale et Comparée, Limoges, France; †Unité Mixte de Recherche 145, Institut de Recherche pour le Développement; Université Montpellier 1, Montpellier, France; ‡Département de Parasitologie – Mycologie et de Médicine Tropicale, Faculté de Médecine, Université des Sciences de la Santé, Libreville, Gabon; and §Department of Neurosciences, University of Catania, Catania, Italia**

Summary

Purpose: The association between cysticercosis and epilepsy has been widely studied in Latin America and Asia and has proven to be one of the main causes of epilepsy. Despite high prevalences of both diseases in Africa, their association remains unclear. In this article we quantified the strength of the association between epilepsy and cysticercosis in Africa and we proposed some guidelines for future studies.

Methods: We performed a systematic review of literature on cysticercosis (considered as exposure) and epilepsy (considered as the disease) and collected data from both cross-sectional and case–control studies. A common odds ratio was estimated using a random-effects meta-analysis model of aggregate published data.

Results: Among 21 retrieved documents, 11 studies located in 8 African countries were included in the meta-analysis. Odds ratio of developing epilepsy when presenting cysticercosis (defined as *Taenia solium* seropositivity) ranged from 1.3–6.1. Overall, association between cysticercosis and epilepsy was found significant with a common odds ratio of 3.4 [95% confidence interval (CI) 2.7–4.3; p < 0.001].

Discussion: The variability of the association found between the studies could be due to differences in study design or in pathogenesis of cysticercosis. Further studies should overcome identified problems by following some guidelines to improve epidemiologic and clinical assessment of the association. Better understanding of the relation between cysticercosis and epilepsy is a key issue in improving prevention of epilepsy in Africa.

KEY WORDS: Cysticercosis, Epilepsy, Meta-analysis, Africa.

Cysticercosis (CC) is a parasitic infection caused by the larval stage (*Cysticercus cellulosae*), of the tapeworm *Taenia solium* for which pigs are generally the intermediate host. Humans could also be intermediate hosts by ingesting eggs of *T. solium* in food or water contaminated by feces of individuals who harbor the adult parasite in their small intestines. Although CC and taeniasis could be encountered worldwide, the prevalence of these infections is highest in developing countries where multiple factors such as conditions of hygiene, breeding, and slaughtering of pigs; cooking habits; and absence or poor efficiency of wastewater network maintain the cycle of contamination. When the central nervous system (CNS) is invaded by *C. cellulosae* causing neurocysticercosis (NCC), this leads to severe pathogenic conditions. NCC is considered an important cause of neurologic diseases in Latin America, Africa, and Asia (Preux et al., 1996; White, 1997; Pal et al., 2000; Singh et al., 2000; Druet-Cabanac et al., 2002; Del Brutto et al., 2005) and has a broad spectrum of clinical manifestations, with seizures being the most frequent. In Latin America, NCC has proven to be a major cause of epilepsy (Garcia et al., 1993; Del Brutto, 2005; Montano et al. 2005, Nicoletti et al., 2005), even if some methodologic limitations have been highlighted in etiologic surveys (Carpio et al., 1998). The epidemiology of CC and NCC has been studied extensively in Latin America and Asia, but much less in Africa. Three types of biologic assays are currently used to determine exposure to CC. The first detects antibodies against *C. cellulosae* by enzyme-linked immunosorbent assay (designated here by Ab-ELISA), the second detects also antibodies but by enzyme-linked

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Address correspondence to Pierre-Marie Preux, Institut d'Epidémiologie neurologique et de Neurologie Tropicale, EA3174, Faculté de Médecine, 2 Avenue du Docteur Marcland, 87025 Limoges, France. E-mail: preux@unilim.fr

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immunoelectrotransfer blot (EITB), whereas the third detects circulating antigens of *C. cellulosae* by enzyme-linked immunosorbent assay (designated here by Ag-ELISA). These three types of assays can be employed in sera as well as in cerebrospinal fluid (CSF). Sensitivity and specificity were, respectively, close to 85% and 92% for Ab-ELISA (Bouteille et al., 1994), 98% and 100% for EITB (Carpio et al., 1998), and 94% and 100% for Ag-ELISA (Erhart et al., 2002).

New interrogations on pathogenesis appeared from the analysis of *T. solium* DNA sequences, as two strains were identified worldwide, one mainly located in Asia and the other in Latin America. *T. solium* encountered in Africa seems more similar to the latter (Nakao et al., 2002). However, clinical manifestations of CC seem to differ between continents and could correlate with this genetic difference (Singh, 1997). In Asia, patients with NCC commonly present subcutaneous cysticercosis. In Latin America such a presentation is very rare. In Africa patients with NCC could present either subcutaneous cysticercosis or not (Ito et al., 2003), but literature is scarce to draw a definitive picture. The doubt about a specific pathogenesis of CC in Africa remains.

We performed a critical review of studies on CC and NCC and epilepsy in Africa. The aim of this work was to specify the risk of developing epilepsy during the course of infection with CC in Africa and to highlight some methodologic points to be taken into account for the elaboration of future surveys. With this objective we attempted to collect all available data on the association between CC and epilepsy in Africa (published and nonpublished aggregated data) and to perform a meta-analysis on the relationship between CC and epilepsy.

Methods

Literature search

We performed an extensive literature search in the following online databases as MEDLINE, IngentaConnect (ex UnCover), ScienceDirect (Elsevier), ArticleScience (from INIST/CNRS), and the African Neurology database from the Institute of Neuroepidemiology and Tropical Neurology of the University of Limoges (http://www-ient.unilim.fr/). This last database contains more than 6,000 references of medical dissertations, theses, and articles dealing with tropical neurology and parasitology. In all databases we searched for the associated terms ''cysticercosis,'' ''epilepsy,'' and ''epidemiology.'' Moreover, we tried to identify and acquire unpublished materials by searching for communications and by contacting researchers in the field, in particular members of the RERENT French-speaking Network for research in tropical neurology. The research was restricted to documents dealing with Africa and human health and those reporting results from neuroepidemiologic surveys without language restriction. An attention was also brought to the references found in each publication. The systematic search was realized up to June 2009.

Data extraction

Eligibility of each study was assessed independently by two reviewers (FQ and MG). Considering epilepsy as the disease and CC as the exposure, an eligible study should fit the following inclusion criteria: (1) the presence of a control group (people without epilepsy, PWOE); (2) the possibility to determine the sample size of each of the following four groups in aggregated data—people with epilepsy affected by CC (PWE CC+), people with epilepsy not affected by CC (PWE CC−), people without epilepsy affected by CC (PWOE CC+), and people without epilepsy not affected by CC (PWOE CC−); (3) details of the techniques used to assess CC or NCC (i.e., any serologic assay or imaging technique); (4) detailed methods for case-finding and control selection; and (5) means used for epilepsy confirmation (questionnaire, physicians, or neurologist).

The main characteristics of these studies have been considered such as the overall study design, sources of both PWE and PWOE, and matching criteria and techniques employed for ascertaining epilepsy, CC, and/or NCC. For each survey, statistical power was calculated as a priori and a posteriori statistical power. A priori statistical powers were calculated, following the hypothesis that the objective of the survey was to identify a minimum odds ratio of 2 (i.e., CC exposure leads to twice more epilepsy), with one control per case, based on the number of PWE and the percentage of CC in PWOE. The a posteriori statistical powers were calculated upon the results of the surveys.

Meta-analysis

A meta-analysis was used to estimate the risk to develop epilepsy when exposed to CC in Africa, applying a random-effects model to account for the variance of each included study (Cucherat et al., 1997). Odds ratios (OR) and 95% confidence intervals (95% CIs) have been determined. A common risk was subsequently estimated as a common OR from all studies taken altogether. The homogeneity was tested by the Cochran Q test of heterogeneity. Because EITB is the most sensitive and specific assay to detect antibodies in sera, the same analysis was then restricted to studies ascertaining CC by EITB assays.

Results

Literature search

The result of the literature search is detailed in Fig. 1. A total of 462 publications were identified using the specified keywords, from which 84 documents dealt with Africa and human health. Among them 42 reported epidemiologic surveys. The elimination of multiple occurrences permitted to isolate 21 documents. Eight of them were excluded for not fulfilling the inclusion criteria: seven studies were excluded

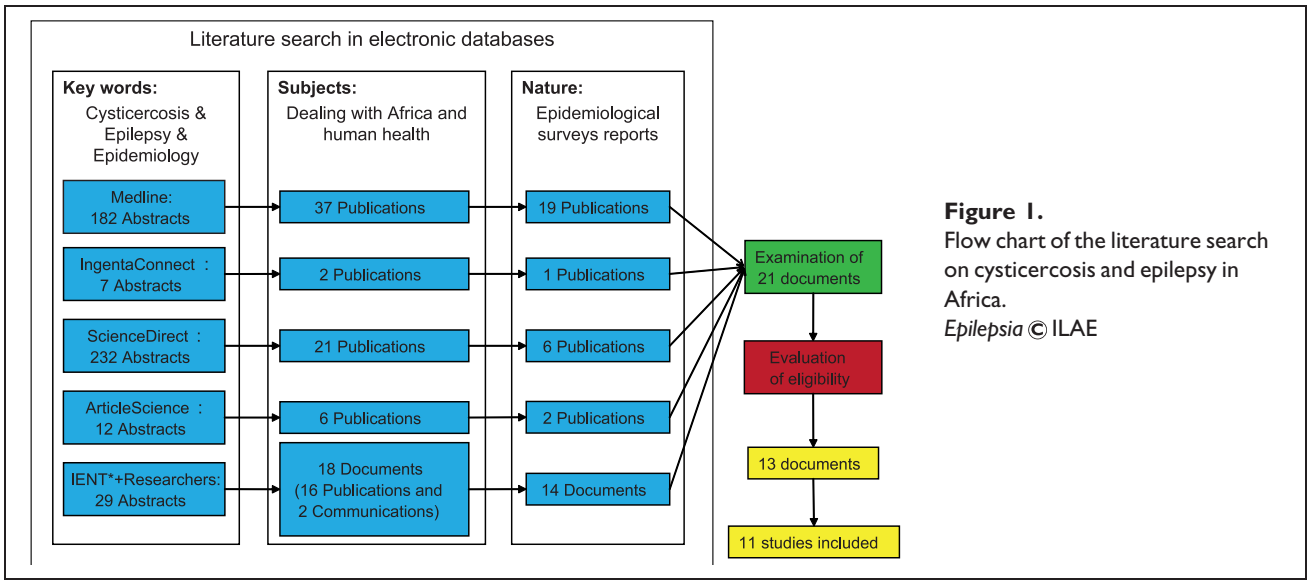

Figure 1.
Flow chart of the literature search on cysticercosis and epilepsy in Africa.
Epilepsia © ILAE

because CC infection (as *T. solium* seropositivity) was exclusively assessed in a sample of people with epilepsy (PWE) without control group (Heinz & Klintworth, 1965; Van As & Joubert, 1991; Powell et al., 1966; Zoli et al., 2003), or because aggregated data were not available (Grunitzky et al., 1995; Adjidé et al., 1996; Avodé et al., 1998). The last study (Nzisabira et al., 1992), in which 98 PWE (28 of whom presented antibodies anti *T. solium*) were compared with only 30 unmatched controls was excluded due to the low number of controls.

From 13 remaining documents, one was an oral communication (Bouteille et al., 1994) providing results from two different study sites: the first, located in Togo, investigated in 1987; the second, in Benin, was investigated in 1993. Results obtained in Togo were reported previously in Dumas et al. (1989) and were considered once. From Bouteille et al. (1994), only the data from Benin were included in the present study.

Results for the same survey were found in several publications: It is the case for the survey of Nsengiyumva et al. (2003) whose data were completed in Prado-Jean et al. (2007). Similarly the results reported in Winkler et al. (2008) have been detailed in Winkler et al. (2009). The samples of these studies were taken into account once, but the methodologic aspects have been discussed considering these four publications.

Included studies

A total of 11 epidemiologic studies were included from eight countries, providing a total number of 7,586 subjects (1,658 PWE and 5,928 PWOE). The localization of these surveys is presented in Fig. 2, and their main characteristics are shown in Table 1. Three were cross-sectional studies, and their objective was to estimate the prevalences of both epilepsy and CC (Dumas et al., 1989; Bouteille et al., 1994; Balogou et al., 2000), and the eight others were case–control studies (Mignard et al., 1986; Grill et al., 1996; Andriantsimahavandy et al., 1997; Newell et al., 1997; Waruingi et al., 2002; Nsengiyumva et al., 2003; Dongmo et al., 2004; Winkler et al., 2009). Half of them were matched case–control studies using different matching criteria. Among them age was the only common criteria. Four surveys were done in general population, whereas the remaining was hospital based.

The definition used for epilepsy was specified in only seven studies, among them five studies followed the

Figure 2.
Location in Africa of the included surveys.
Epilepsia © ILAE

Table 1. Description of methods used in studies looking for an association between cysticercosis and epilepsy in Africa, sorted by date of publication

			PWE ascertainment			PWOE		Exposure ascertainment		
References	Country	Study design	Sources	Definition used for epilepsy	Confirmation	Sources	Matching criteria	Examinations	Criteria for CC	Criteria for NCC
Mignard et al. (1986)	Reunion island	Case–control	Hospital-based population	Not specified	Cases known by local health centers	Hospitalized controls	None	CT scan, Sera Ab-ELISA.	Ab-ELISA positive	CT scan positive
Dumas et al. (1989)	Togo	Cross-sectional (assessment of prevalence of CC and epilepsy)	General population randomly selected samples. Age >15 years	Not specified	Neurologist	General population	Same household or neighbours	Biopsy of nodule, Skull, upper and lower limb radiography in nodules carriers, Sera Ab-ELISA, Stool examinations.	Histology of nodules Calcified cysts Ab-ELISA positive	Calcified cyst in skull radiography
Bouteille et al. (1994)	Benin	Cross-sectional (assessment of prevalence of CC and epilepsy)	General population Randomly selected samples >5 years	ILAE 1993	Neurologist	General population	None	Biopsy of nodule, Sera Ab-ELISA.	Histology of nodules Ab-ELISA positive	None
Grill et al. (1996)	Madagascar	Case–control	Hospital-based population. Children >1 year with unexplained seizures	Not specified	Neurologist	Hospitalized children	None	Sera Ab-ELISA, Sera EITB, CT scan, (CSF Ab-ELISA, CSF EITB for children presenting cysts).	Sera Ab-ELISA or Sera EITB positive	CT scan and CSF Ab-ELISA or CSF EITB positive
Andriantsima havandy et al. (1997)	Madagascar	Matched Case–control	Hospital-based population. Age >15 years	WHO neuroscience research protocol WHO, (1981)	Cases known by local health centers	Hospitalized controls	Same province Decennial age group Income group	Sera EITB, CSF EITB.	Sera EITB positive	CSF EITB positive
Newell et al. (1997)	Burundi	Case–control	PWE identified by local health centers	Not specified	Medical practitioner	Relatives	Same household	Sera Ag-ELISA, Sera EITB, Stool samples.	Sera Ag-Elisa or EITB positive	None
Balogou et al. (2000)	Togo	Cross-sectional (assessment of prevalence of CC and epilepsy)	General population randomly selected samples	ILAE (1993)	Neurologist	General population	None	Biopsy of nodule, Skull, upper and lower limb radiography, Sera Ab-ELISA.	Histology of nodules Calcified cysts Ab-ELISA positive (Del Brutto et al., 1996)	Calcified cyst in skull radiography
Waruingi et al. (2002)	Kenya	Matched Case–control	Hospital-based population	ILAE (1993)	Cases known by epilepsy health centers	Hospitalized controls	Same province Age Sex	Sera Ab-ELISA.	Sera Ab-ELISA positive	None
Nsengiyumva et al. (2003) and Prado-Jean et al. (2007)	Burundi	Matched Case–control	PWE identified by local health centers	ILAE (1993)	Neurologist	Control coming to hospital for vaccination	Same province Age ±5 years No blood relationship	Sera Ab-ELISA, Sera Ag-ELISA.	Sera Ag-Elisa or EITB positive	None
Dongmo et al. (2004)	Cameroon	Matched Case–control	General population Age >5 years	ILAE (1993)	Neurologist	General population	Age ±5 years	Sera Ab-ELISA.	Sera Ab-ELISA positive	None
Winkler et al. (2009)	Tanzania	Case–control	PWE identified by local health centers. Age >10 years	Winkler et al. (2007);	Neurologist	Hospitalized controls	None	CT-Scan, Sera Ab-ELISA, CSF Ab-ELISA.	Sera Ab-ELISA	CT scan and CSF Ab-ELISA positive (Del Brutto et al., 2001)

Ab-ELISA, antibodies enzyme-linked immunosorbent assay; Ag-ELISA, antigenes enzyme-linked immunosorbent assay; Ab-EITB, Antibodies enzyme-linked immunoelectrotransfer blot assay; Ag-EITB, Antignes enzyme-linked immunoelectrotransfer blot assay; CSF, cerebrospinal fluid; ILAE, International League Against Epilepsy; CC, Cysticercosis; CT-Scan, computed tomography.

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diagnosis criteria recommended by the International League Against Epilepsy (ILAE) (Commission on Epidemiology, Prognosis of the International League Against Epilepsy, 1993) (Bouteille et al., 1994; Balogou et al., 2000; Waruingi et al., 2002; Nsengiyumva et al., 2003; Dongmo et al., 2004), one study (Andriantsimahavandy et al., 1997) followed the definition proposed by the World Health Organization (WHO) for neuroscience research protocol (WHO, 1981) and the last used a definition proposed for resource-poor countries (Winkler et al., 2007). None of the study mentioned clearly what type of epilepsy was considered: only active epilepsy or epilepsy considered at any time post diagnosis, which is the most probable. The controls were originating from the same location than PWE in five studies and even from the same household in two studies, whereas one study selected controls closed to PWE without blood relationship (Nsengiyumva et al., 2003). The means used to ascertain exposure to cysticercosis show a great variability in medical facilities, from clinical examination of subcutaneous nodules to computed tomography (CT) scan as well as biologic assays in blood or CSF. Physical examinations, and in particular examination of subcutaneous nodules, have been described in 10 of the 11 surveys. Histology of the cysts was performed in only three surveys.

The majority of studies (10 of 11) first ascertained exposure to CC by detection of antibodies in sera using Ab-ELISA (Mignard et al., 1986; Dumas et al., 1989; Bouteille et al., 1994; Grill et al., 1996; Balogou et al., 2000; Waruingi et al., 2002; Nsengiyumva et al., 2003; Dongmo et al., 2004), and/or EITB (Grill et al., 1996; Andriantsimahavandy et al., 1997; Newell et al., 1997). Ascertainment for NCC was made a second time by assays in CSF (Grill et al., 1996; Andriantsimahavandy et al., 1997). Winkler et al. (2009), first ascertain exposure to NCC by imaging technique (CT scan) and then detected antibodies in a sample of 20 persons from subjects with radiologic signs of NCC.

Imaging techniques employed to assess CC and/or NCC comprised radiographs or CT scans. Radiographs of skull, upper, and lower limbs were used in two studies (Dumas et al., 1989; Balogou et al., 2000) detecting only calcified cysts. Brain CT scans were used in only two studies (Mignard et al., 1986; Winkler et al., 2009).

Association between CC and epilepsy

The results of the surveys are presented in Table 2. The prevalence of CC in the control group ranged from 2.4–31.5%. The association between CC and epilepsy was significant in 7 of the 11 selected studies (Mignard et al., 1986; Dumas et al., 1989; Grill et al., 1996; Andriantsimahavandy et al., 1997; Balogou et al., 2000; Nsengiyumva et al.,2003; Winkler et al., 2009) and was near significance for Newell et al. (1997). Significant ORs ranged between 2.5 and 6.1. A priori statistical power ranged from 7.4–99.0%, and a posteriori statistical power from 9.3–100.0%.

Meta-analysis

A meta-analysis was first performed on all 11 studies based on CC antibody detection in sera (Ab-ELISA or EITB). Results are presented in Fig. 3. A significant ($p < 0.001$) common OR of 3.4 (95% CI 2.7–4.3) was estimated. The test of heterogeneity was not significant ($p = 0.43$), indicating homogeneity of the studies included. Meta-analysis was then restricted to the three studies using EITB (Grill et al., 1996; Andriantsimahavandy et al., 1997; Newell et al., 1997) as shown in Fig. 4 and leads to an OR of 3.8 (95% CI 2.6–5.5; $p < 0.001$). The test for heterogeneity was also not significant ($p = 0.74$).

Table 2. Description of results obtained from studies searching an association between cysticercosis and epilepsy in Africa, sorted by date of publication

References	PWE (n)	PWOE (n)	Cysticercosis in PWE (n)	Cysticercosis in PWOE (n)	Cysticercosis in PWOE (%)	A priori statistical power (%)[a]	A posteriori statistical power (%)	Odds ratio (95% CI)	p-Value
Mignard et al. (1986)	242	385	45	32	8.3	66.8	96.6	2.5 (1.6–4.1)	<0.001
Dumas et al. (1989)	88	1,439	27	98	6.8	26.3	100.0	6.1 (3.7–10.0)	<0.001
Bouteille et al. (1994)	22	1,421	2	55	3.9	7.4	21.2	2.5 (0.6– 10.9)	0.490
Grill et al. (1996)	256	113	153	30	26.5	95.7	100.0	4.1 (2.5–6.7)	<0.001
Andriantsimahavandy et al. (1997)	104	104	33	14	13.5	47.8	88.6	3.0 (1.5–6.0)	0.002
Newell et al. (1997)	103	72	12	2	2.8	15.8	56.8	4.6 (1.0–21.3)	0.060
Balogou et al. (2000)	115	1,343	12	37	2.8	17.1	99.1	4.1 (2.1–8.1)	<0.001
Waruingi et al. (2002)	99	124	5	3	2.4	13.8	19.1	2.2 (0.5–9.2)	0.490
Nsengiyumva et al. (2003)	324	648	193	204	31.5	99.0	100.0	3.2 (2.4–4.2)	<0.001
Dongmo et al. (2004)	93	81	17	12	14.8	46.1	9.3	1.3 (0.6–2.9)	0.680
Winkler et al. (2009)	212	198	38	10	5.1	44.1	98.2	4.1 (2.0–8.5)	<0.0001

[a]Statistical power assuming an odds ratio equal to two with a type I error equal to 5%.
PWE, people with epilepsy as cases; PWOE, people without epilepsy as controls; 95% CI, 95% confidence interval.

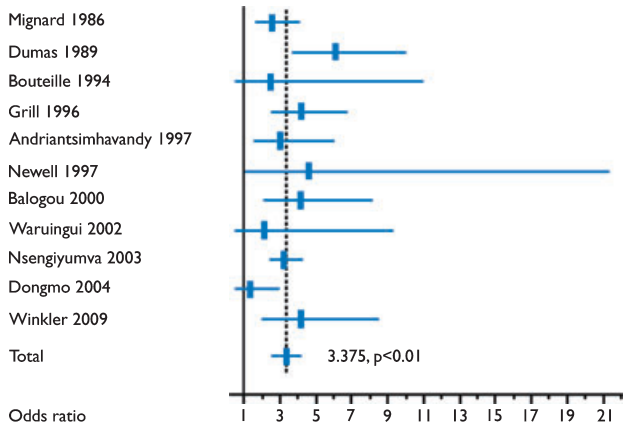

Figure 3.
Meta-analysis of studies on association between cysticercosis and epilepsy in Africa: ORs (Odds ratios) from each study and common OR estimated using a random-effects model.

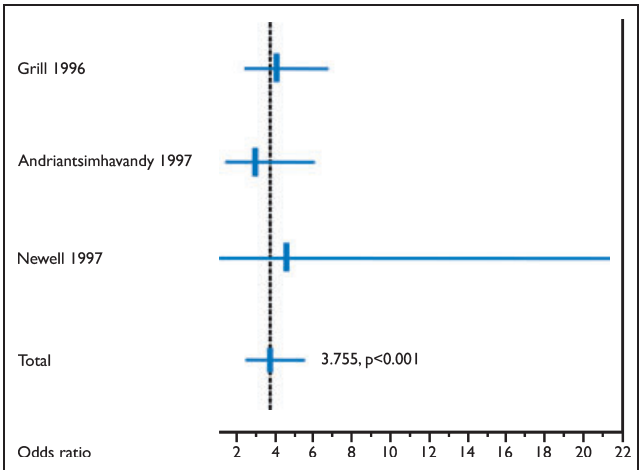

Figure 4.
Meta-analysis of studies on association between cysticercosis and epilepsy in Africa: ORs (Odds ratios) from each study and common OR estimated using a random-effects model. Restricted to studies using EITB.

Discussion

Based on our literature search, the association between CC and epilepsy in Africa has been evaluated in 11 studies. We are confident that this review reaches the exhaustiveness on the studies in this field, since we used several databases and also a specific database of literature on neurology in Africa as theses and memos, unpublished in international or electronic databases.

The evaluations of both CC and epilepsy were cross-sectional; the use of ''prevalent'' rather than ''incident'' cases, in fact, does not allow verification of the precedence of the exposure (*T. solium* infection) before the outcome (epilepsy). The immune markers, used here as a proxy for NCC, are likely associated with lower socioeconomic status, which can result in epilepsy and can also occur as a result of epilepsy. This may constitute limitations of this work.

Furthermore, we cannot exclude a survival bias related to a possible shorter survival time among PWE affected by a more severe form of disease (Kamgno et al., 2003; Diop et al., 2005), as well as for subjects affected by severe forms of CC. Only a prospective cohort follow-up study could avoid these biases. However, such a design leaving subjects exposed to CC or NCC (i.e., confirmed infection of the subjects) for a time and without intervention is ethically not acceptable.

Most of the studies included in the analysis were hospital-based. This may constitute a probable recruitment bias, as people receiving care in Africa are not representative of the general population. Beside this, an additional selection bias may occur for epilepsy, as some PWE in Africa are not aware of or do not report their disease because of fear of social exclusion (Jacoby & Austin, 2007). Prevention of such a bias has been taken into account in the studies performed in the general population, which intended to be representative of the population, ascertaining epilepsy and CC in randomly selected samples. The matching criteria are also important to consider. At least two criteria should be taken into account: (1) age (with a maximum interval of 5 years) because the prevalence of both epilepsy and CC vary with age, and (2) the geographical proximity between PWE and control to reflect the same level of exposure. Regarding the epilepsy definition, it should be stressed that it is important to consider occurrence of epilepsy at any time postdiagnosis and not only active epilepsy. Indeed mechanisms leading to seizures and epilepsy from one or more CC cysts are not clearly explained, and time between infection and symptoms depends on number, size, type, status, site of the cysts in the brain, and the presence of an eventual perilesional edema (Pal et al., 2000; Nash et al. 2008).

Concerning the assessment of CC infection, detection of anti-*T. solium* antibodies in sera reflects an exposition regardless of the localization, the conditions, and the number of the cysts. This detection was done using two different serologic assays (Ab-ELISA or EITB) and critically depends on cost and availability of these methods. However, the formulation ''Ab-ELISA test'' mentioned in studies represents a possible heterogeneous group of tests by the utilization of extracts obtained from the whole parasite or specific parts of the *C. cellulosae* to detect antibodies. This assay has shown also a risk of cross-reaction with other endemic parasites such as *Schistosoma* spp. or other *Taenia* spp. (Diwan et al., 1982; Grill et al., 1996). Therefore, evaluating the sensitivity and specificity of this assay seems important and has been done in only one included survey (Bouteille et al., 1994) and was, respectively, 85% and 92%. By contrast EITB assays are considered to have a sensitivity

of 98% and a specificity of 100%, but show a dramatic decline of sensitivity to 28% in cases with a single cyst in the brain (Wilson et al., 1991). Considering that sensitivity and specificity of assay have an impact on evaluation of exposure and by consequence on the statistical power of the study, the most efficient assay (EITB) should be used for detecting antibodies in sera. When restricted to the three studies that used antibodies detection by EITB, we found a significant common OR of 3.8, a close and even higher value than the OR obtained considering all studies, showing that the heterogeneity of assays was smaller than expected.

Absence of significant results was systematically associated with a lack of statistical power. The a priori statistical powers (i.e., before the realization of the elaboration of the study) was lower than 15.8% in three studies (Bouteille et al.,1994; Newell et al., 1997; Waruingi et al., 2002). The first way to improve the statistical power of a study is to perform surveys in areas with high level of exposure to CC assessed with the most sensitive sera assay. But once the area is selected, and the estimated number of potentially included PWE known, another way to improve statistical power is to match more than one control with each case, as done by Nsengiyumva et al. (2003). Even if matching more than two controls for a case is possible (up to four), it became difficult to recruit adequate controls. For Dongmo et al. (2004) the a posteriori power was very low (9.3%) due to a lower number of controls than cases, highlighting the fact that the elaboration of the control group is of first importance.

The relation between the status of the cysts (living, degenerating, or calcified) and the occurrence of epilepsy was studied in only two studies performed in Burundi, which ascertained the presence of living cysts by detecting circulating antigens by Ag-ELISA (Newell et al., 1997; Prado-Jean et al., 2007). In one study only (Prado-Jean et al., 2007) occurrence of epilepsy and CC were independently significant for both assessment of exposure by antigens and antibody detection. Further surveys are necessary to answer to this question, in other areas and in the general population.

The definitive diagnosis of NCC is provided only by the demonstration of the parasite in the CNS. This can be done by the same biologic assays described previously, but in CSF. Considering the risk associated with performing an extraction of CSF, these examinations should be reserved for patients where NCC is strongly suspected. Imaging techniques of brain can provide strong support for performing assays in CSF and should be done first when CC exposition (Ab or Ag) has been acknowledged. It is important that such imaging techniques provide results for the whole group considered and not only for those patients who can afford this exam. CT scan is the most efficient and can precisely identify what types of cysts are present (single or multiple rings, nodular enhancing lesion, or parenchymal brain calcifications).

Some interrogations that were not addressed in existing works still remain: (1) Does a particular genotype of *T. solium* exist in Africa? and (2) Do the genotypes of *T. solium* affect pathogenesis of CC with regard to epilepsy?

Conclusion

This review suggests that further studies have to be done in Africa. To overcome identified problems they should follow some guidelines: population-based case–control study, with a high and previously determined level of exposure to CC, with a good statistical power (a priori calculation of a number of needed subjects, sufficient number of PWE and controls included), controls matched for age and location, brain CT scan for all included subjects, and serologic assays (EITB and Ag-ELISA).

To our knowledge this is the first meta-analysis carried out to evaluate the common risk of CC with respect to epilepsy. In Africa, people with CC have a 3.4 to 3.8-fold increased risk for developing epilepsy. It could be interesting to specify the common risk in other parts of the world as a primary step to evaluate the difference of pathogenesis. This question remains of importance as CC has shown to be a preventable disease. This is a key issue in improving the strategies of prevention in development, such as vaccination (Lightowlers, 2006; Morales et al., 2008).

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We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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