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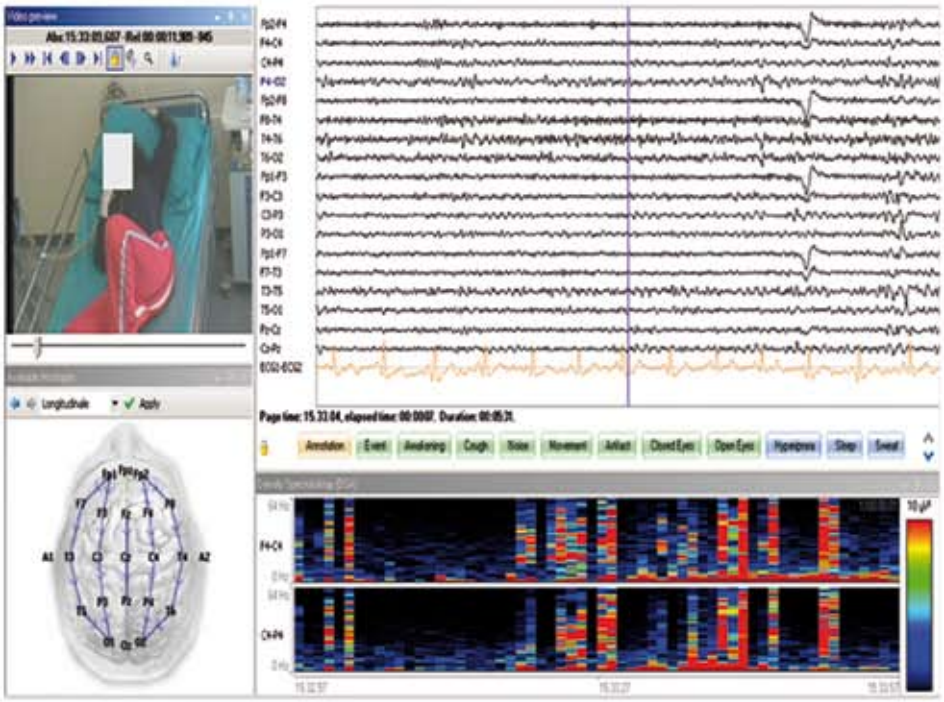

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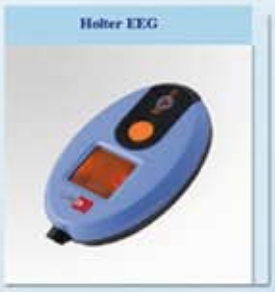

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INSTRUCTIONS AUX AUTEURS

Le Journal de l'épilepsie de l'Afrique du Nord et Moyen-Orient publie des articles originaux cliniques, scientifiques ou médico-sociaux sur l'épilepsie dans les pays d'Afrique du Nord et le Moyen-Orient, ou d'autres pays. Il publie également des éditoriaux, des articles de revue, des cas cliniques, des lettres à l'éditeur, des aperçus historiques sur l'épilepsie dans le monde et les histoires vécues par les patients atteints d'épilepsie, les médecins ou autres professionnels concerbés par cette maladie.

Il publie également des rapports des séances de travail des Sociétés, ligues et associations de l'épilepsie en Afrique du Nord et Moyen-Orient.

CONDITIONS DE PUBLICATION

Les articles ne doivent avoir fait l'objet d'aucune publication antérieure ni être simultanément soumis pour publication à une autre revue. Les textes sont rédigés en français ou en anglais. Les articles sont adressés, par le Comité de Rédaction, pour avis à des lecteurs qui restent anonymes pour les auteurs. En aucun cas la responsabilité de la Revue n'est engagée vis-à-vis des manuscrits qui lui sont adressés, avant la décision finale du Comité de Rédaction.

Les articles originaux ne doivent avoir fait l'objet d'aucune publication antérieure (à l'exception d'un résumé de moins de 400 mots), ni être simultanément soumis pour publication à une autre revue.

La mise en page des articles y compris résumés, références, tableaux et figures ne doit pas dépasser :

• 10 pages dactylographiées pour les mises au point, • 8 pour les articles originaux,
• 5 pour les éditoriaux, • 4 pour les cas cliniques, • 4 pour les activités associatives,
• 3 pour les aperçus historiques • 3 pour les lettres à l'éditeur • Et 2 pour les témoignages de patients épileptiques.

Les manuscrits doivent être sous format Word ou RTF (avec en 3 fichiers, 1-comportant le texte, les figures et les tableaux, 2-Comportant les photos et toute autre illustration Et 3-Attestation cédant les droits d'auteur à l'éditeur, attestant que le manuscrit n'est pas accepté ailleurs ou en cours de soumission, que tous les auteurs ont lu et approuvé la version finale et que les aspects éthiques sont respectés) ; tous les fichiers doivent être envoyés ensemble par email à l'adresse suivante : je.submission@gmail.com

RECOMMANDATIONS GENERALES POUR LA PRESENTATION DES MANUSCRITS:

Liste des recommandations (à vérifier avant l'envoi du manuscrit) :

Manuscrit

• Le manuscrit est dactylographié en double interligne avec une marge de 2,5 cm sur chaque bord, y compris la page de titre, le résumé, les remerciements, les références, les tableaux et les légendes des figures.
• Il est conseillé d'utiliser le minimum d'abréviations. Le terme en entier précède l'abréviation lors de sa première apparition dans le texte.
• La hiérarchie des titres et sous-titres est bien mise en évidence par une numérotation.
• La disposition des articles originaux doit suivre le plan suivant : page de titre, résumés et mots-clés, résumés en anglais et ses mots-clés, texte (avec introduction, matériel et méthodes, résultats, discussion), références, tableaux, figures et légendes.
• Les pages sont numérotées, en chiffres arabes en commençant par la page de titre.

Pour accélérer la publication des manuscrits soumis, il est demandé de se conformer strictement aux recommandations ci-dessous.

Les recommandations suivantes sont conformes aux normes dites de Vancouver pour la préparation des manuscrits soumis aux journaux biomédicaux.

Page de titre

La page de titre comporte :

• Le titre précis et concis mais informatif (en français et en anglais).
• Le nom de chaque auteur suivi de son prénom.
• Le nom des services et des institutions responsables du travail.
• Le nom et l'adresse de l'auteur responsable de la correspondance pour le manuscrit avec son adresse e-mail (impératif).
• les remerciements, les sources de financements et les conflits d'intérêts éventuels.

Résumés et mots-clés

• Un résumé en anglais, en français et en arabe (facultatif) de moins de 250 mots chacun sont inclus pour les articles originaux.
• Les résumés sont structurés avec 4 paragraphes (introduction, participants et méthodes, résultats, conclusion).
• Les mots-clés doivent être indiqués (entre 3 et 6 séparés par des tirets).
• Il n'y a pas d'abréviations ni de référence bibliographique dans les résumés.

Tableaux, figures

Les documents iconographiques – figures et tableaux – sont obligatoirement appelés dans le texte et conformes aux recommandations suivantes :

• Les figures sont numérotées en chiffres arabes, par ordre d'apparition dans le texte où elles sont appelées (figure 1).
• Les tableaux sont numérotés en chiffres romains, par ordre d'apparition dans le texte :
(tableau I).
• Les légendes des figures sont portées les unes à la suite des autres en fin d'article, sur une feuille séparée.
• Les figures doivent être présentées chacune sur un feuillet séparé, et fournies en fichiers séparés à raison d'un fichier par figure ; elles sont toutes accompagnées d'une légende.
• Des explications ou notes diverses nécessaires à la compréhension figurent au-dessous de chaque tableau.
• La reproduction de documents déjà publiés doit être accompagnée de l'autorisation de l'éditeur ou de l'auteur possesseur du copyright.
• Les abréviations sont à éviter. Si la figure et/ou le tableau comporte des abréviations, il faut les expliciter dans la légende.
• Les médicaments doivent être mentionnés selon leur dénomination commune internationale ou leur nom chimique. Les noms commerciaux doivent être mentionnés entre parenthèses après la DCI.
• Les symboles, chiffres et textes des figures sont clairs et de taille suffisante pour que chaque élément soit parfaitement lisible.
• En aucun cas les figures ne doivent être intégrées directement dans le corps du texte.
• La publication d'illustrations en couleur est recommandée.

Références

Les références bibliographiques, limitées selon la rubrique retenue, sont portées en fin d'article, numérotées selon l'ordre d'apparition dans le texte.

Le nombre de références :

• Ne doit pas dépasser 40 pour les articles originaux et 60 pour les mises au point,
• Doit être entre 5 et 10 pour les cas cliniques et entre 4 et 6our les lettres à l'éditeur,

Toutes les références doivent être appelées dans le texte (y compris celles appelées dans les figures et tableaux) : le numéro de la référence bibliographique citée est mentionné entre crochets.

Les références d'articles parus dans un périodique doivent comporter le nom des 6 premiers auteurs avec les initiales des prénoms (suivis de "et al." à partir du 7e auteur), le titre complet de l'article dans la langue originale, le nom de la revue selon les abréviations de l'Index Medicus, l'année, le numéro du tome, la première et la dernière page abrégée du texte.

La présentation – style et ponctuation – suit scrupuleusement les 3 exemples suivants :

1- Clark AM, Hartling L, Vandermeer B, McAlister FA. Meta-analysis: secondary preven¬tion programs for patients with coronary artery disease. Ann Intern Med 2005; 143: 659-72.
2- Champault A, Dagher I, Vons C, Franco D. Laparoscopic hepatic resection for hepatocel¬lular carcinoma. Retrospective study of 12 patients. Gastroenterol Clin Biol 2005; 29: 969-73.
3- Guilpain P, Chanseaud Y, Tamby MC, Mahr A, Servettaz A, Guillevin L et al. Pathogénie des vascularites systémiques primitives (l) : vascularites ANCA-positives. Presse Med 2005; 34: 1023-33.

• Les citations de livres doivent comporter les noms des auteurs, le titre du livre, la ville, le nom de la maison d'édition et l'année de publication.

La présentation – style et ponctuation – suit scrupuleusement les 2 exemples suivants :

3- Danowski RG, Chanussot JC. Traumatologie du sport. 7e ed. Paris: Masson; 2005.

Le Comité de Rédaction se réserve le droit de renvoyer aux auteurs les manuscrits qui ne seraient pas conformes aux recommandations exposées ci-dessus avant de les soumettre aux lecteurs.

INSTRUCTIONS TO AUTHORS

The review of epilepsy in northern Africa and the Middle East publishes original clinical, scientific or medical social on epilepsy in the countries of northern Africa and the Middle East, or any other the world. It also publishes editorials, general reviews, clinical cases, historical overviews on epilepsy in the world and stories experienced by patients with epilepsy, physicians or other other professionals involved in epilepsy.

It also publishes the minutes of the sessions of Societies, leagues and associations against epilepsy in northern Africa and Middle East.

Condition of Publication:

The articles must not have been published nor simultaneously submitted for publication in another journal. The texts are written in French or English. The articles are addressed by the Drafting Committee for its opinion to readers who remain anonymous to the authors. In no event shall the review is undertaken vis-à-vis the manuscripts sent to him before the final decision of the Editorial Board.

Original articles should have been no previous publication (with the exception of an abstract under 400 words), nor be simultaneously submitted for publication in another journal.

The layout of articles including abstracts, references, tables and figures must not exceed:

• 10 for general reviews, • 8 for original articles, • 5 for editorials, • 4 for case reports,
• 4 for association activities, • 3 for historical overviews • 3 for letters to the editor
• And for the testimony of two epileptic patients.

Manuscripts should be in Word or RTF format (including 3 files, 1-with the text, figures and tables, 2-Including photographs and other illustrations and 3-yielding certificate of copyright to the publisher stating that the manuscript is not accepted elsewhere or under submission, all authors read and approved the final version and the ethical aspects are met), all files must be sent together by email to: **je.submission@gmail.com**

GENERAL RECOMMENDATIONS FOR MANUSCRIPTS SUBMISSION:

List of Recommendations (check before sending the manuscript):

• The manuscript is typed double-spaced with a margin of 2,5 cm on each side, including the title page, abstract, acknowledgments, references, tables and figure legends.
• It is advisable to use as few abbreviations. The full term precedes the abbreviation at its first appearance in the text.
• The hierarchy of titles and subtitles is highlighted by a dial.
• The layout of the original articles should follow the following plan: title page, abstract and keywords, text (with introduction, materials and methods, results, discussion), references, tables, figures and legends.
• Pages are numbered in Arabic numerals, beginning with the title page.
• To expedite the publication of submitted manuscripts are asked to adhere strictly to the recommendations below.
• The following recommendations are consistent with standards of Vancouver called for the preparation of manuscripts submitted to biomedical journals.

Title page

The title page includes:

• The title clear and concise but informative (in French and English).
• The name of each author followed by his first name.
• Name of services and institutions responsible for the work.
• The name and address of the author responsible for correspondence for the manuscript with his e-mail address (mandatory).
• Acknowledgments, sources of funding and potential conflicts of interest.

Abstracts and Keywords

• A summary in English, French and Arabic (optional) with fewer than 250 words for each is included in the original articles.
• Abstracts are structured with four paragraphs (introduction, participants and methods, results, conclusion).
• The key words must be given (between 3 and 6 separated by dashes).
• No abbreviations or references in literature abstracts.

Tables, figures

• The Graphic - figures and tables - are necessarily called in the text and in accordance with the following recommendations:
• The figures are numbered in Arabic numerals, in order of appearance in the text where they are called (Figure 1).
• Tables are numbered in Roman numerals, in order of appearance in the text: (Table I).
• The figure legends are made one after the other end of the article, on a separate sheet.
• The figures must be submitted each on a separate sheet, and provided as separate files in a file its reasons for figure and are all accompanied by a caption.
• Different explanations or notes are required to understand below each table.
• The reproduction of previously published material must be accompanied by permission of the publisher or the author's copyright holder.
• Abbreviations should be avoided. If the figure and / or table contain abbreviations, they should explain in the legend.

Drugs should be referred by their international name or chemical name. Trade names must be listed in parentheses after the DCI.

• Symbols, figures and text figures are clear and large enough so that each element is perfectly readable.
• In any case the figures should be integrated directly into the text.
• The publication of color illustrations is recommended.

References

References, limited depending on the item selected, are brought to the end of the article, numbered in order of appearance in the text.

The number of references:

• Must not exceed 40 for original articles and 60 for general reviews
• Must be between 5 and 10 clinical cases and between 4 and 6 for letters to the editor

All references must be cited in the text (including those referred to in the figures and tables):
the number of the references cited is mentioned in brackets.

• References to articles in a journal should include the name of the first 6 authors with the initials of the first name (followed by «et al.» From the seventh author), the full title of the article in original language, the name of the journal abbreviations as cited in the Index Medicus, the year the number of the volume, the first and last page.

The presentation - style and punctuation - closely follows the three following examples:

[1] Clark AM, Hartling L, Vandermeer B, McAlister FA. Meta-analysis: secondary prevention Programs for patients with coronary artery disease. Ann Intern Med 2005; 143:659-72.
[2] Champault A, Dagher I, Vons C, Franco D. Laparoscopic hepatic resection for hepatocellular carcinoma lular. Retrospective study of 12 patients. Gastroenterol Clin Biol 2005, 29:969-73.
[3] Guilpain P Chanseaud Y, Tamby MC, Mahr A, Servettaz A, Guillevin L et al. Pathogenesis of systemic vasculitis primitives (l): ANCA-positive vasculitis. Presse Med 2005; 34:1023-33.

• Citations of books should include authors' names, book title, city, name of publisher and year of publication.

The presentation - style and punctuation - closely follows the two following examples:

[3] RG Danowski, JC Chanussot. Sports traumatology. 7th ed. Paris: Masson, 2005.

• The Editorial Board reserves the right to return manuscripts to authors who do not comply with the recommendations outlined above before submitting them to the readers.

Editorial

Epilepsy in MENA region VS developed countries different etiologies and big gap in surgery of epilepsy

Pr. Najib Kissani
Editor in Chief of Nameej
&Head of Neurology department, Marrakech University Hopistal.

If etiologies are dominated by Neoplastic, and cerebrovascular causes in developed countries, in our Middle East and North African region, Except few rich but still developing countries (e.g Saudi Arabia, Arab Emirates, Qatar, Kuwait), nearly all others are suffering from many various avoidable epilepsies, like infectious, antenatal and post-traumatic causes. This has been detailed by J. Katchanov & GL. Birbeck (BMC Med. 2012) in his overview about Epilepsy care guidelines for low- and middle- income countries: From WHO mental health GAP to national programs. In this report a very nice comparison is made regarding, 1-Access to health care, 2- Healthcare funding, 3- Common epilepsy etiologies, 4- Cultural perception of seizures, and 5- Socio-cultural attitudes towards epilepsy; with huge discrepancies between high-income versus low-income and middle-income countries (see Table1).

Now taking into account, epilepsy surgery; indicated for a better control of refracory seizures, for reducing neurological morbidity, preventing adverse effects of medications and improving quality of life of epileptic patients. Nowadays, this well known efficient procedure in refractory epilepsy is in use in very limited number of countries.
Focusing on our large region of 23 countries, sophisticated centers emerged, and epilepsy surgery is now in use in six countries: Lebanon and Saudi Arabia since 1995, Jordan (1996), Iran (2000), Tunisia (2002) and Morocco & Arab Emirates (2004).
We have to understand why such simple procedure is not widely used in our region (only 6 countries within 23!). The dominant candidates for epilepsy surgery are mesial temporal lobe epilepsies, which undergo easily and efficiently this kind of surgery, and are most of the time intractable; and last but not least for epilepsy surgery many cases can be selected and operated without all specialized and heavy techniques, like stereoEEG, PET & SPECT. The courageous countries who already started surgery in our region, are dealing with typical cases, with concordant data from clinical, EEG, VideoEEG, MRI and psychology testings, and the first results are very encouraging, this will allow other centers in the same country to go ahead in the surgery of epilepsy. By example in Morocco, where it started in 2004, actually this specialized surgery is in use in 4 big cities (Rabat, where it started firstly, than Casablanca and recently Fes and Marrakech).

	High-income countries	Low-income and middle-income countries
Gross national income per capita	High to US$9,386; upper middle US$3,036 to $9,385	Low to US$765 or lower; middle US$766 to $3,035
Access to health care	Initial access usually through primary care with established referral networks, which may include high indirect costs	Limited to very basic primary care especially in rural areas and/or established referral networks, which invariably include high indirect costs
Healthcare funding	National programs, private insurance, out-of-pocket expenses	Often ill-funded, may rely on donors/volunteering services. Indirect costs and informal payments can represent major barriers to care
Common epilepsy etiologies	Neoplastic, cerebrovascular	(Post) infectious, antenatal, post-traumatic
HIV prevalence	Low	Can be moderate to high
Cultural perception of seizures	Biomedical model	Traditional medicine, spiritual approach; contagion beliefs common
Socio-cultural attitudes towards epilepsy	Neutral public perception or at least social presentation of neutrality	Overt negative public perception, stigmatization, and discrimination common

J. Katchanov & GL. Birbeck (BMC Med. 2012)

If mesial temporal lobe epilepsies are the good condidates for a nearly guaranteed good result, other forms are also candidates but with fewer benefits, such neocortical temporal lobe epilepsy, premotor and central lobe epilepsy, mesial frontal epilepsy, basi-frontal lobe epilepsy, parieto-occipital lobe epilepsy, insular epilepsy, cingulate epilepsy, dysembryoplastic tumors, hypothalamic hamartomas, Rasmussen syndrome, and Landau–Kleffner syndrome. Other severe forms are relatively good candidates to reduce seizures frequency and improve quality of life, (e.g The Lennox–Gastaut syndrome post anoxic encephalitis...) they can benefit from palliative surgery (callosotomy, hemispherectomy, subpial transection and vagus nerve stimulation).

About the 17 countries in our region, where this surgery is not on the agenda for the coming years, we encourage the specialists involved (neurologist, neurosurgeon, neuroradiologist, neuropsychologist and neuropathologist) to share their efforts and to focus on the urgent need for initiating starting such procedures in order to 1-start this kind of surgery because of its efficacy and simplicity, 2-deal with intractable cases, which represent around 20% of all epileptic cases, 3-improve quality of life of the patients suffering from intractable epilepsies, 4-saving money because of the high cost of this group of epilepsies and the huge amount of money spent abroad when patients decide to travel to Europe or North America for benefiting of this surgery missing in their countries.

The steps to follow for epilepsy surgery are well known; 1-good selection of patients, through multidisciplinary meetings, where neurologist is the crucial element, this selection should pay good attention to all factors of contraindication (progressive systemic diseases, serious medical problems, limited cooperation, active psychological diseases and in patients who have deficits in contra lateral memory functions as revealed by a WADA (intracarotid amobarbital) test, which is now being replaced by functional MRI; 2- appropriate preoperative evaluation (exhaustive clinical analysis, EEG and especially Ictal video-EEG, Neuropyschology, Neuro-imaging investigations (simply brain MRI with epilepsy protocol) and in some cases medication titration; 3-than surgery can be performed, by qualified neurosurgeon with minimum expertise in this kind of surgery, and in our region centers of functional neurosurgery, rather than general neurosurgery are to be initiated; 4-an appropriate follow up by combined team of the referring neurologist and the neurosurgeon is not to be trivialized, and patients have to be aware of possible full continuation of medications.

In conclusion, no delay is acceptable in our region for starting epilepsy surgery, at least in countries where sophisticated centres for managing epilepsy are established since past decade, big efforts should be done not only by neurologists, neurosurgeons and all other specialists involved but also by governments and political deciders, who have to put epilepsy as health priority, because of high costs related to epilepsy, impairment of quality of life and by the huge amount of school and work abandon.

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(*) Including shipping expenses (**) World Bank Standards

The Association for Care of Epileptic People in Lebanon (ECAL)
Side by side with epileptic patients
L'Association pour les soins des personnes épileptiques au Liban (ECAL)
Côte à côte avec les patients épileptiques

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No disclosure to be declared

The Association for Care of Epileptic People in Lebanon (ECAL) is an association that was established in 2001, it is run by a dynamic team, including patients, family members, professionals (Figure 1).

Figure 1: Logo of ECAL (Association for Care of Epileptic People in Lebanon).

ECAL was acknowledged by the Ministry of Interior and Municipalities on 20 November 2000 and since then, its center was located in Sidon, the capital of South Lebanon (Figure 2a and 2b).

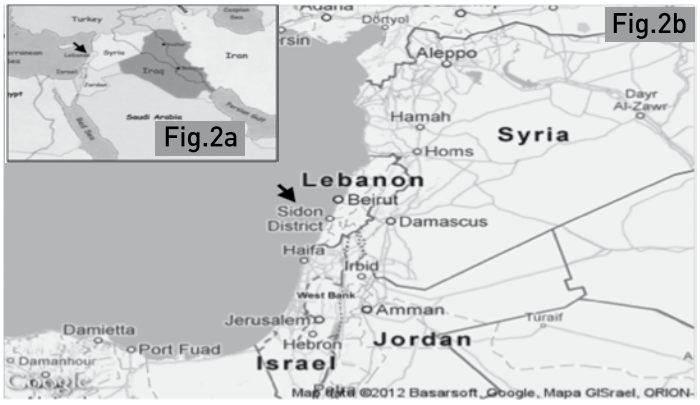

Figure 2a: Map of Lebanon and its situation in Asia.
2b: Map of Lebanon and situation of Sidon.

At its onset, ECAL's purposes were to follow up with the concerned government authorities to:

1. Fund a well-equipped rehabilitation and education center to provide epileptic people with these two main services as well as supported medication.
2. Support and help epileptic people and defend their rights.
3. Educate and enlighten citizens about the symptoms of epilepsy through seminars and conferences.
4. Do field research to get statistical figures about the rate and distribution of epileptic people in Lebanon, and keep up with the latest research findings and treatments.
5. Participate in local, regional, and international conferences and seminars that are directly related to the above mentioned articles, pursuant to the laws and regulation in effect, and after the approval of the relevant authorities.

Though formally acknowledged by the Ministry of Interior and Municipalities, ECAL was not listed as one of the beneficiaries of the annual budget of the Ministry of Social Affairs. As a result, ECAL team had to take action at a time when epileptic people were stigmatized and most of whom kicked out of schools when their conditions were declared. For this specific reason:

1. The ECAL team volunteered to provide all the needed support,
2. They started a campaign to collect donations so they would support epileptic people medically and make sure that with the needed support those people would use their medicaments without interruption and thus avoid possible risks,
3. ECAL president signed an agreement with a pharmacy so the latter would sell epilepsy medicaments at a reduced prices to epileptic people that ECAL transfers to them and,
4. ECAL started field work; using a survey questionnaire, ECAL team chose the old city of Sidon, where a lot of poor people lived, as the first place to start field visits, and it worked.

Obviously, poor people that needed the support did not mind reporting the real situation about their epileptic family member(s).

Those first responders:

1. Were the first visitors of the center; they came when they needed medicaments,
2. They reported epileptic cases they knew, thus helped ECAL start the snowball sampling and scheduling of visits.

Having known the size of the problem, ECAL had to work along three parallel lines: follow the set schedule of visits to families of epileptic people to tell them about the services ECAL would offer them; follow another schedule of visits to well known business people in the area to start collecting donations, and start an awareness campaign to raise people's awareness about epilepsy to reduce the stigma against epileptic people.

Based on the donations collected at the beginning, ECAL took the first decision: supporting poor epileptic people by paying 30% of the price of the needed medicament no matter what it was or how much it cost. Only in rare cases did

ECAL offer a higher percentage of support, and that was based on assessing epileptic people's socio-economic statuses. Doing this, ECAL could gain credibility and started receiving more epileptic people. Unfortunately, of the total amount of the collected donations, ECAL could support all incoming people till September of every year for three years in a row. Though ECAL was moving at a slow pace, the steps were steady and fruitful compared to the embryonic experience of the association. And for this, ECAL did not insist on contacting families that could afford medication expenses of their children especially that those parents were in denial and did not want the ECAL team to discuss the issue with them. They even deprived their epileptic children of the normal social life.

After all, to be able to support epileptic people all year round, ECAL had to come up with projects that are income generating and at the same time do not cost the Association much money nor do they lead to reduced support for epileptic people.

Project 1: Making and Selling Accessories

In the absence of financial resources other than donations, ECAL team studied the market needs and found accessories a good project for which ECAL would use some of its money for a good turnover without losses. And since the president is talented, she started making designs that would compete with what was in the market. The president announced that epileptic people were invited to ECAL center to receive training and work side by side with ECAL team, those who could devote some of their time to the Association, to produce accessories. She also announced that she would train parents of epileptic people on how to do the work, and thus make it easier for them to accompany their children and be paid for the work they did. Of course, this project has been running ever since the Association was established. However, selling accessories has always been a seasonal activity.

The produce of this project and all the projects that followed has been displayed in two fixed places all year round. The first place is ECAL center and the second is Khan Al Efranj, a touristic site that is located in the old city of Sidon, the capital of South Lebanon, where a number of other Associations each has a designated area for its exposition. ECAL's produce has also been sold in schools in two main seasonal occasions: Christmas and Mother's Day. Sadly enough, when the economic situation is deteriorating, the amount of selling deteriorates, and this year, 2013, some schools apologized for not being able to welcome the event. And since the projects that might work are seasonal, ECAL had to come up with all the other possible projects.

Project 2: The Loom Project

ECAL had on mind a project that aimed at training epileptic patients to do some manual work that would lead to their financial independence in the future. Based on field visits and some small scale research, and since there was a donor who offered ECAL two looms and an amount of threads, ECAL started the loom project. The project was effective in the sense that those patients succeeded to a great extent in making good produce and thus gained some income. As a result, ECAL could accommodate a bigger number of patients. Though ECAL had to pay for the training, ECAL was aware that some trainees were potentially future trainers for new visitors to use the looms and be able to manually knit carpets and similar produce.

In fact, ECAL team along with epileptic people succeeded in making good produce and motivating parents to participate, the thing that led to their interest in promoting this project. Two problems led to stopping the loom project. The first was the cost of thread. When the cost of the needed amounts of thread was not covered from donors, ECAL could not assign big budgets and wait for the produce to be sold to liquidate the cost. The second problem was that not all people were interested in paying for quality work, nor would big expos collaborate and promote some of the produce. However, from this experience, the Association could hit more than one target: getting to know how big the problem is when people are ignorant about epilepsy (1), the level of social awareness about epilepsy and the impact of the stigma on epileptic people (2), and consequently the amount of work needed to address the issue at a bigger scale (3); that is, across the whole country. With the growing number of epileptic people visiting the center, ECAL could spread the notion that reporting a case was not contingent upon the need for medicaments at reduced prices; rather, an act for a bigger and more important cause.

As mentioned earlier, this Loom Project was expected to upgrade the work and increase ECAL's income to be able to sustain epileptic people's medical support. Though the set objectives were not attained, it was after this project that ECAL team thought of making the Association more transparent to the wider community by designing a website through which the Association's produce would be displayed. Updating the website in a routine manner, ECAL promoted people's knowledge background and opened the door for new donors to provide more support to epileptic people. In addition, documenting the project, ECAL paved the way for other interested associations to replicate the project in the future. To this end, ECAL recommended that if another Association would adopt the idea, they should learn from ECAL's experience and thus take into account the fact that :

a. Good quality produce requires training and this should not be at the expense of the Association's main goals.

b. If the process is to be sustained, the Association should guarantee that the cost of material resources be paid from donors,

c. The loom project is a good project for epileptic people to be trained to perform in a risk free environment and to earn money from,

d. Pricing the produce is an issue of concern and is to be studied carefully,

e. Knowing where to promote the produce would help speed up the selling and thus turnover,

As mentioned earlier, income generating projects were a necessity. With this on mind, ECAL formed a team of all the talented people, including ECAL's president along with

some ECAL active members and epileptic people's parents. The team set a list of projects that would be run all year round and agreed on who will belong in each task force. The growing team started the following concurrent projects.

-Carving on copper,
-Cocoon patchwork,
-Canvas and embroidering (Figure 3),
-Carving on soap,
-Drawing on glass pottery
-Preserving seasonal vegetables and fruits
-Painting on carpets and cushions,
-The Chocolate project, and
-Making baskets from straw, filling them with chocolate and wrapping them for sale (Figure 4).

Figure 3: Making Canvas by epileptic patients' members of ECAL.

Figure 4: Making baskets from straw by epileptic patients' members of ECAL.

ECAL started implementing the projects one at a time in the sequence shown above (Also see the attached figures). To succeed, ECAL followed the same steps in each project: training the interested group, the thing that was paid most of the times, assigning a task force and paying them for their produce, setting deadlines for submitting produce and collecting it, and displaying the produce in the center AND Khan Al Efranj. Along with this, the amount of sale, accounting and customers' feedback were documented and consequently recommendations written as to the timing and amount of production of each item. Of course, this depended highly (1) on the seasonal activities being held and (2) on the market demand.

With these projects sustained, ECAL could support a big number of epileptic people. Of the total number of epileptic people the association has researched, 500 receive support in the form of medical check-ups, lab tests, provision of medicaments OR health and social support services ONLY when needed, yet they receive 30% discount on medicaments that they buy from pharmacies that ECAL transfers them to. Only 21 epileptic people receive free monthly medical check-ups, medicaments and lab tests that amount to USD 1350 monthly which is equivalent to 16000 annually. On the other hand, ECAL also provides some patients' families with substantial support, yet the support is sustained or halted on the basis of the association's budget and on setting priorities based on new research findings.

The ECAL team is satisfied with the above figures. More importantly, ECAL is content about:

- Having 12 trained mothers of epileptic patients working with ECAL to increase the produce of the different handcraft items,
- Having 30 active volunteer members and only four staff members; that is, little expenses,
- Having more visitors to ECAL center to buy not only handcrafts but also chocolate,
- Starting the Epilepsy group project in schools and colleges,
- Fixing a schedule for annual events.

To do more, ECAL team has been considering a number of research topics, considering the possibility to launch epilepsy campaigns, and reaching epileptic people outside the proximal zone of its center.

Obviously, ECAL has not and cannot attain all of its set goals, namely establish a well-equipped rehabilitation and education center, unless it is listed as one of the beneficiaries from the Ministry of Social Affairs or without sponsors that find in Epilepsy a really good cause. Interestingly, there was once a possible donor who wanted to buy a piece of land with a building erected, but then changed his mind because of the risky situation in Lebanon.

Though ECAL is determined and dedicated to a good cause, it is no until the situation settles that ECAL will be able to set a short-term strategic plan.

Meanwhile, the Association is content about the accomplishments:

1. Supporting the visiting epileptic people to make sure that they: a. Use the required medicaments, b. Acquire skills that would enable them to be financially independent,
2. Increasing the number of epileptic patients who will join the workshop,
3. Editing and developing the existing survey questionnaire and reactivating field research with the help of volunteers,
4. Setting scheduled seminars aimed at spreading knowledge about epilepsy to a wider range of social groups,
5. Participating in national, regional and international confe-

rences to be updated about the latest research findings and new directions,
6. Contacting more NGOs, business and social entities that are interested in supporting the project,
7. Participating in workshops where all civil community associations participate to set annual plans for new events.

The Association's long term objectives have been expanded to include:
- Improving the quality of life of epileptic patients by establishing:
• an infirmary specialized for epileptic patients and would provide their medical needs,
• an academy specialized in implementing a special curriculum for epileptic patients' academic progress,
• a technical and vocational center (TVE) for epileptic patients,
• a language center, the income of which will be utilized to support epileptic people.
- Fostering a culture of public health practice,
- Finding more solutions to make epileptic people more secure in jobs that are less risky and require minimal physical effort,
-Mainstreaming epileptic people with other people in a small scale career domain.

ECAL will always abide by the basic rights and legal principles that were inspired by the Regional Declarations on Epilepsy, and thus will be working so epileptic people are entitled to:
1. Assessment, access to treatment, and health and social care,
2. Welfare benefits,
3. Be ensured that people with epilepsy and their families are fully informed about the condition,
4. Involvement in the decisions affecting care and treatment,
5. Be ensured quality and standard of care,
6. Privacy and dignity,
7. Least restrictive legal constraints,
8. Reintegration/inclusion into the community,
9. Rehabilitation,
10. Enjoy all freedoms and privileges afforded to other citizens,
11. Protection against discrimination in law or otherwise or abuse in any form because of the condition.

Le Syndrome cérébello-vestibulaire sous doses pharmacologiques de Phénytoïne-A propos d'un cas
Cerebellovestibular syndrome under pharmacological doses of Phénytoin-About one case

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Mots clés : Epilepsie- Phénytoïne- Maladies du cervelet.
Keuwords : Epilepsy- Phenytoin- Cerebellar disorders.

Introduction

La phénytoïne (PHT) est un antiépileptique efficace, mais connu par divers effets indésirables, aigus ou chroniques. Si la dose de PHT est augmentée, sa concentration dans le sang monte d'une façon disproportionnelle, ainsi la concentration de plasma peut monter du niveau subthérapeutique à un niveau toxique même avec des petites augmentations des doses [1]. L'intoxication aiguë au PHT mène aux symptômes cérébelleux comprenant le nystagmus, la diplopie, la dysarthrie et l'ataxie [2-4]. Les signes cliniques du dysfonctionnement cérébelleux disparaissent habituellement à la réduction ou au retrait du médicament [4].

Les auteurs rapportent un cas de syndrome cérébello-vestibulaire réversible chez un enfant de 4 ans et demi, après administration d'une dose pharmacologique de PHT.

Observation

Cet enfant âgé de 4 ½ ans, avait comme antécédent un épisode de convulsion fébrile sévère à l'âge de 2½ ans, sans notion de cas similaire familiale, il n'avait pas de souffrance néonatale, et le développement psychomoteur était normal. Il présentait depuis l'âge de 3 ans (début 2002) des phénomènes critiques répétés, à type de chute atonique de la tête, mouvements tonico-cloniques généralisés avec fuite urinaires et parfois morsure de la langue. L'enfant est suivi à la consultation de neurologie depuis mars 2003. L'examen clinique était normal, et l'électroencéphalogramme (EEG) a confirmé le diagnostic de l'épilepsie partielle bifrontale. Le scanner cérébral et l'IRM encéphalique ne montraient pas d'anomalies. L'enfant a été mis sous Valproate de sodium, puis Carbamazépine; mais les crises n'ont que faiblement baissé de fréquence. Le 3 décembre 2003, le traitement par PHT fut commencé à dose de 200 mg/j (5 mg/kg/j) ; ce qui a pu stabiliser les crises. Deux semaines après l'enfant fut hospitalisé pour vertiges et gros troubles de l'équilibre, il ne pouvait ni marcher ni se tenir debout seul, et avait une grosse maladresse des extrémités. L'examen clinique avait trouvé un syndrome cérébello-vestibulaire, une latérodéviation, des oscillations dans tous les sens à la manœuvre du Romberg, une hypotonie généralisée, des troubles de coordination motrice et nystagmus multidirectionnel. Sur le plan biologique, il n'y avait aucun signe d'hépatotoxicité selon la GGT, la GOT, l'ASAT, et l'ALAT, et le reste du bilan paraclinique était normal. La PHT fut incriminée et arrêtée immédiatement et remplacé par le lévétiracetam, une semaine après, les troubles ont commencé à régresser. Et il a fallu attendre trois semaines pour voir une disparition totale des singes cliniques avec un examen clinique qui s'est normalisé.

Discussion

Rares sont les rapports qui incriminent la PHT comme responsable d'une atteinte cérébelleuse, c'est soit l'intoxication aiguë, ou rarement l'intoxication chronique. Ces atteintes provoquent une ataxie, une dysarthrie, un nystagmus typiquement multidirectionnel, la diplopie et l'encéphalopathie cérébelleuse avec des niveaux plus élevés dans le sang, qui sont habituellement réversibles à l'arrêt du médicament; par opposition à l'atteinte chronique qui tarde à récupérer, et qui laisse volontiers une atteinte cérébelleuse [4]. Chez notre patient, le syndrome cérébello-vestibulaire n'est vraisemblablement pas lié au surdosage de PHT, surtout que les posologies administrées étaient correctes et c'était toujours la mère qui donnait le médicament à l'enfant. Le rôle de la PHT dans l'atrophie cérébelleuse démontrée chez certains épileptiques chroniques a donné lieu à de nombreuses controverses. Quelques auteurs pensent que l'hypoxie répétée liée aux crises épileptiques est la cause principale de la dégénération cérébelleuse, néanmoins, certains cas d'atrophie sont observés sous PHT sans aucune crise épileptique [5].

En plus de données cliniques, des études expérimentales suggèrent que la PHT peut être toxique pour les cellules du cervelet, particulièrement les cellules de Purkinje [2, 3].

Si les travaux expérimentaux, suggèrent que les cellules du cortex cérébelleux sont vulnérables lorsqu'elles sont soumises à l'action de la PHT à dose élevée et/ou pendant une période prolongée. Notre observation montre que même à dose pharmacologique, sans aucun surdosage, les cellules cérébelleuses peuvent en souffrir ; et elles ne sont pas les seules, car même les structures vestibulaires peuvent aussi être affectées, comme en témoigne la présence des latérodéviations et du nystagmus chez notre patient.

Conclusion

Les auteurs soulignent à travers cette observation, la gravité des effets secondaires potentiels de la PHT, qui peuvent survenir même à de posologies non toxiques, que ces signes peuvent durer jusqu'à trois semaines après l'arrêt total du traitement, vu la longue demi vie du produit. Et de ce fait, et en connaissant les gros risques en cas de surdosage aigu ou d'exposition chronique, la PHT doit être évitée chez les enfants.

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Lennox Gastaut syndrome: about 27 cases
Le syndrome de Lennox Gastaut: à propos de 27 cas

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Abstract

Introduction: The Lennox-Gastaut syndrome (SLG) is a severe epileptic encephalopathy of childhood. The aim of our study is to identify the clinical, electroencephalographical, etiological and therapeutical aspects of this disease and to determine its outcome.

Patients and methods: Authors report 27 cases of children with the SLG compiled in neuro-pediatric unit of Paediatrics IIA, Children's Hospital of Rabat Morocco, over 10 years (January 2001 – January 2011).

Results: The average age was 6 years old, 81% were male. The clinical manifestations included, atypical absences (29.6%), tonic seizures (29.6%), tonic-clonic seizures (26.9%), atonic seizures (26.9%) and myoclonic ones 7.4%. Mental retardation, autistic features and behavioral problems were noticed in all patients. The cryptogenic and the idiopathic forms represented 66.5% while symptomatic forms represented 33.5% and were associated with preexisting brain damage such as perinatal asphyxia (7cases), tuberous sclerosis (1case), meningoencephalitis sequelea (1case). The diagnosis was based on clinical and EEG specific criteria of SLG. The most commonly used drug combination in our study was based on Sodium valproate, Clobazam & Lamotrigine (81.5%). Monotherapy was used in 18.5% of patients were treated. We noticed that 60% of patients responded to treatment with relative stabilization of seizures, while 40% remained refractory to anti-epileptics with severe mental retardation. An electrical stimulation of the vagus nerve is expected for these children.

Conclusion: The SLG is a severe epileptic encephalopathy requiring early diagnosis and appropriate management to improve the prognosis.

Keywords: Epileptic encephalopathy- Infant- Lennox Gastaut- EEG- Treatment- Prognosis.

Résumé

Introduction: Le syndrome de Lennox-Gastaut est une encéphalopathie épileptique de l'enfant fréquemment associée à un retard mental. Il représente 1 à 2% de toutes les épilepsies de l'enfant. Le but de notre étude est de dégager les aspects cliniques, électro-encéphalographiques, étiologiques, thérapeutiques et évolutifs de cette pathologie.

Patients et Méthodes : 27 enfants porteurs du SLG colligés à l'unité de neuro-pédiatrie du service P IIA de l'Hôpital d'Enfants de Rabat sur une période de 10 ans (2001-2011).

résultats : La moyenne d'âge : 6ans, 81% de sexe masculin. Les manifestations cliniques retrouvées : les absences atypiques 29.6%, les crises toniques 29.6%, les crises tonico-cloniques 26.9%, les crises atoniques 26.9% et les myoclonies 7.4%. Un retard mental, des traits autistiques et des troubles du comportement ont été notés chez tous les patients. 66.5% des formes du SLG étaient cryptogéniques et idiopathiques et 33.5% symptomatiques associées à une asphyxie périnatale (7 cas), une sclérose tubéreuse de Bourneville (1 cas) et des séquelles de méningo-encéphalite (1 cas). Le diagnostic était clinique et électro-encéphalographique répondant aux critères du SLG. L'association médicamenteuse la plus utilisée était Valproate de sodium- Clobazam- Lamotrigine. 18.5% des patients étaient traités par une monothérapie, et 81.5% des patients étaient traités par une polythérapie. 60% des patients ont relativement répondu au traitement avec une stabilisation des crises, 40% sont restés réfractaires aux anti-épileptiques avec un retard mental sévère. Ces derniers seront programmés pour une stimulation du nerf vague.

Conclusion : Le SLG est une encéphalopathie épileptique sévère nécessitant un diagnostic précoce et une prise en charge adéquate afin d'améliorer le pronostic.

Mots-clé: Encéphalopathie épileptique- Enfant- Lennox Gastaut- EEG - Traitement- Pronostic.

Introduction

Lennox Gastaut Syndrome (LGS) is a cryptogenic or symptomatic generalized epilepsy according to the international classification of epilepsy, epileptic syndromes and related seizure disorders of 1989. Based upon the contribution of Lennox and col. in 1950 and Gastaut in 1966, who were the first to correlate the slow spike-and-waves discharges on the EEG pattern with a distinctive group of clinical manifestations, the term of Lennox Gastaut Syndrome wad adopted in 1969 [1]. The LGS is defined by the majority of authors by three characteristics : 1- a multiple and drug resistant seizure types, mainly tonic, atonic and atypical absences, with tonic seizures during sleep as a constant feature, 2- slow spike-and-wave discharges at 1.5-2.5Hz on the EEG pattern during wakefulness specific of atypical absences and burst of diffuse fast rhythm at 10-20Hz during sleep specific of tonic seizures,3- some authors associate a progressive mental deterioration and a behavior disorder to the syndrome.

Aim of the study

-To Identify the clinical, electro-encephalographical (EEG), etiological and therapeutical aspects of this disease
-To determine its outcomes.

Patients and Methods

Authors performed a retrospective study of 27 cases compiled in the neuro-pediatric unit of Pediatrics 2a at the Children's Hospital of Rabat in Morocco, from January 2003 to May 2011. The diagnosis was based on the triad mentioned previously; we only included patients retaining all the clinical and electro-encephalographical features of LGS. We collected information from our patients that are saved as a back up records to examine both the history and the evolution of the syndrome. The statistical analysis was performed by SPSS 10.0.

Results

LGS syndrome represents 3% of all childhood epilepsy's cases followed in our neuro-pediatric unit. Eighty one percent of patients were male. The average age of the first seizure was 3 years and 1 month (1-6years) and the average age of diagnosis was 3 years and 9 months (2-7years), thus the period of diagnosis was 8 months. The average of hindsight was 5 years. 45% of cases had antecedents constituted by: psychomotor retardation 66.5%, a pre-existent West syndrome 40%, a history of perinatal asphyxia 33.5%, a history of familial epilepsy 17%, a tuberous sclerosis complex 8.5% and a meningo-encephalitis 8.5%. The majority of the patients had the first seizure between 2 and 4 years as tonic seizures 29.6%; atypical absences 29.6%, atonic seizures 26.9%, tonico-clonic seizures 26.9% and myoclonus seizures 7.4%. 18.5% of cases had 2 seizure types at the onset of the disease, mainly tonic, atonic and atypical absences. In the meanwhile of the evolution of the syndrome, all our patients had an association of tonic seizures, atonic seizures and atypical absences, and 30% of them developed a nonconvulsive status epilepticus, defined as a confusional state due to atypical absence status. All our patients performed and EEG and a CT. the EEG pattern was typical of LGS and the 26% of abnormalities discovered on the CT were confirmed by the MRI. The CT results showed 4 cases o f cortical atrophy sequelea of perinatal asphyxia and 2 cases of cerebral calcifications. 55.6% of our patients belong to the idiopathic group, 11.1% of them belong to the cryptogenic group and 33.3% to the symptomatic group (9 patients). The polytherapy was used in 81.5% of cases, the most commonly drug combination used was Valproic acid, Clobazam and Lamotrigine, the Phenobarbitone was prescribed when the Lamotrigine wasn't available. Corticosteroids were tried in the LGS not responding to therapy, 5 patients had receive 10 to 15mg/kg/day for 15-20 days in ambulatory, no one shows side effects, therefore a transient improvement in seizure frequency was observed with a re-establishment of the previous state 5 to 6 months later. We used helmet for all ambulatory patients to prevent head injury related to the repeated falls due to tonic, atonic and myoclonus seizures. The vagus nerve stimulation is expected for 4 of our patients. We chose to classify the clinical and EEG evolution of patients into 3 sections: we considered that the evolution was remarkable at the epileptic level if there was almost a total decrease of seizure's frequency and an improvement of the EEG pattern, the evolution was partial if there was a decrease by half of seizure's frequency, and resistant if there was a persistence or an increase of seizure's frequency. We found that the evolution was remarkable in 22% of cases, 66% of them belong to idiopathic form and 83% of them were under monotherapy (valproic acid), furthermore 37% of patients had a partial evolution and 40% of them had a resistant one, all of them were under polytherapy. At the cognitive level, all patients had a cognitive regress, a language regress and motion difficulties at different stages, and 18.5% had an autistic regression.

Discussion

LGS represents 3 to 10% of all childhood epilepsies and begins between 1 and 8 years, with a peaking age between 3 to 5 years [2]. The first typical seizures appear at 3 years (range 1 to 7 years). Mainly male, the majority of patients is normal or near normal before the onset of LGS as in our study (70%) [3]. In the literature the tonic seizures form the core of the syndrome (17-92%) then come the atypical absences (20-65%) and the atonic seizures (26-56%). The nonconvulsive status epilepticus (NCSE) has been reported in two-third of patients, yet because it's subtle and hardly noticeable by the parents, the NCSE was only reported in 30% of cases in our study. The LGS is symptomatic in 66.5% of cases, and 17-30% of patients have a history of infantile spasms (West syndrome) prior to its onset [1].

In the majority of cases, we find multiple etiologic factors associated to the syndrome such as perinatal asphyxia, meningo-encephalitis, a history of head trauma and the tuberous sclerosis. A family history of epilepsy is sometimes ascertained in children with LGS, in our study 2 idiopathic cases under polytherapy (17%) have a family story of epilepsy, one of them had a partial evolution and the second had a resistant one. The LGS, one of the most severe epileptic syndromes in childhood, is refractory to treatment, more than 80% of children with LGS continue to have seizures and develop a cognitive regress [3]. The mortality rate is around 5%, it's rarely bound to the evolution of the syndrome itself, as death is often related to accidents or episodes of tonic status epilepticus. Some authors associate the occurrence of tonic seizures, the pre-existent West syndrome, the LGS onset before 2 years and the frequent seizures with a poor prognosis for mental development [2]. It seems that children with an idiopathic etiology and better seizure control are less impaired [2]. In our study, only polytherapy was statistically related to a poor prognosis ($p< 0.001$), and only monotherapy is related to a good one ($p<0.001$). LGS is intractable childhood epilepsy, as such; it presents the largest treatment challenge in epilepsy. Therapy must be individualized in light of the clinical heterogeneity. Valproic acid VPA remains the drug of first choice in treatment [1]; Lamotrigine became the second drug of choice helping to reduce 50% of seizure frequency in 32% of cases [4]. Benzodiazepines such as Clonazepam, Nitrazepam and Clobazam are often added as a first line therapy [1]. Felbamate controls 8% of seizures and decreases 50% of all seizures type in 50% of patients [3]. In addition to these drugs other treatments may be considered, such as the use of ACTH which remains a short-term treatment with the potential to increase the frequency or intensity of seizures

potential to increase the frequency or intensity of seizures [5], the corticosteroids and intraveinous immunoglobulins which allow a transient improvement in seizure frequency with high risk to return to baseline after 5-6 months [5].

In our study, the first line therapy was VPA at the dose of 20-30mg/kg/day, used in 18.5% of our patients and within 80% has an idiopathic form and all of them have a remarkable evolution. Our second line therapy was the association between VPA and clobazam at the dose of 0.5– 1mg/kg/day, used for 15% of our patients whose 75% have an idiopathic form with 75% of remarkable evolution. The third line therapy was either the combination of VPA & Clobazam or Clobazepam & Lamotrigin, used in 37% of cases or VPA, Clobazam & Phenobarbitone association used in 30% of cases.

In addition to the pharmalogical therapy, a non pharmacological strategy can be adopted such as the ketogenic diet proposed for the drug resistant epilepsy cases. Studies showed that 38% of children assigned to the diet had greater than 50% seizure reduction and 7% of them had greater than 90% of seizure reduction [6]. VNS had shown effective long-term results (over 5 years) with 24% reduction of seizures [7], but the effectiveness is limited in epileptic encephalopathy. The repeated falls experienced by children with LGS constitutes a special problem requiring the use of helmet.

Limits of the study

Our results can't be generalized because of:

- The small size of the sample,
- The retrospective design of the study,
- The selection bias,
- Some patients lost at the follow up.

Conclusion

LGS is a severe childhood epileptic encephalopathy, the treatment still disappointing and the prognosis severe. The ketogenic diet and the vagal nerve stimulation are interesting options, but largest studies must be initiated to improve new anti-epileptics more efficient with fewer side effects.

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Epilepsy and Schizophrenia: Association or Antagonism?
Epilepsie et shizophrénie: association ou antagonisme?

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Abstract

The relationship between epilepsy and schizophrenia is complex. In 1934, von Meduna proposed camphor-induced convulsions in the treatment of schizophrenia and concluded that there was a biological antagonism between epilepsy and schizophrenia. From the1950s on, the prevalence of psychosis in epileptic patients has been studied repeatedly. The work of Slater et al. (1969) had a profound impact. Over a few years, they collected 69 cases of inter-ictal psychosis (schizophrenia-like psychosis) among epileptics. The onset of seizures preceded the development of mental deterioration by an interval of several years. Temporal lobe epilepsy was over-represented. Although the patients exhibited at times all the cardinal features of schizophrenia, the psychoses observed deviated from schizophrenic norms in some respects. Conversely, the occurrence of seizures and/or epilepsy in schizophrenics was documented many years ago and was not considered a major problem. Using modern diagnostic criteria of schizophrenia and epilepsy, Gelisse et al. (1999) confirmed that the prevalence of epilepsy and acute symptomatic seizures was low in schizophrenics, which points to a possible relative " resistance " to factors of epileptic seizures. In this article, we discuss the relationship between epilepsy and schizophrenia and hypothesize that there is an antagonism between seizures (not epilepsy) and schizophrenia. However, there is a link between longstanding and drug-resistant epilepsy and interictal psychosis, so epilepsy and schizophrenia-like psychosis can be associated.
Keywords: Epilepsy- Schizophrenia- Psychosis.

Résumé

Les relations entre épilepsie et psychoses ont été le sujet de nombreuses discussions et controverses. En 1934, von Meduna proposa le camphre pour induire des crises convulsives dans le traitement de la schizophrénie et conclut qu'il y avait un antagonisme biologique entre l'épilepsie et la schizophrénie. Cependant, une association entre épilepsie et psychoses a été évoquée au début du siècle mais avec de considérables incertitudes. A partir des années 1950, de nombreux travaux ont été consacrés a à ce sujet. Les psychoses schizophréniformes de l'épilepsie (schizophrenia-like psychosis des auteurs anglo-saxons) se développeraient au bout de plusieurs années d'évolution d'une épilepsie temporale mal contrôlée. La prévalence s'échelonne de 0,74 % à 9,25 %. Des différences culturelles et d'époque quant à la définition de la schizophrénie et de l'épilepsie temporale explique en partie la variabilité des résultats. Beaucoup d'études ont fait l'objet de biais méthodologiques en considérant l'épilepsie temporale comme un syndrome homogène décrit à l'époque comme épilepsie « psychomotrice » mais aussi en présélectionnant des populations de malades épileptiques graves consultant des centres spécialisés. C'est ainsi que Slater et al. (1969) concluaient à une relation en trouvant une fréquence de survenue d'une psychose schizophréniforme supérieure à celle de la population générale. Le début des crises précédait le développement d'une psychose de plusieurs années. Les épilepsies temporales « psychomotrices » étaient surreprésentées. Slater et al. (1963) avaient remarqué que si tous leurs patients avaient présenté à un moment ou à un autre, un des signes cardinaux de la schizophrénie, leur tableau ne correspondait pas à une vraie schizophrénie. Une histoire familiale de schizophrénie et une personnalité schizoïde prémorbide étaient relativement rares dans leur population. Cette opinion que ces patients ne présentent pas une schizophrénie typique est partagée par d'autres auteurs. Inversement, la survenue de crises ou d'une épilepsie chez des patients schizophrènes n'a jamais été considérée comme un véritable problème. En utilisant des critères modernes de diagnostic de schizophrénie et d'épilepsie, Gélisse et al. (1999) ont confirmé que la prévalence de l'épilepsie et des crises symptomatiques aiguës étaient rares chez ces patients et ceux malgré l'utilisation de psychotropes. Dans cet article, nous discutons les relations entre épilepsie et schizophrénie. Nous émettons l'hypothèse qu'il y a un antagonisme entre les crises d'épilepsie et la schizophrénie. Cependant, il y a un lien entre une épilepsie pharmacorésistante évoluant depuis de nombreuses années et une psychose shizophréniforme intercritique, ainsi schizophrénie (shizophrénie like-psychosis) et épilepsie peuvent être associées.
Mots clés : Epilepsie- Schizophrénie- Psychose.

Introduction

Epilepsy is a condition characterized by the recurrence of unprovoked seizures. Schizophrenia is a serious mental illness in which a person may lose contact with reality and experience hallucinations and delusions among other symptoms. Both epilepsy and schizophrenia are chronic disorders. The relationship between these two diseases is still controversial. In 1934, von Meduna proposed camphor-induced convulsions in the treatment of schizophrenia: as convulsions appeared to alleviate

the symptoms of psychosis, he concluded that there was a biological antagonism between the two conditions [1]. Conversely, patients with long-standing epilepsy develop schizophrenia-like psychosis at a rate exceeding that expected if the two disorders were independent [2]. Schizophrenia-like psychosis means that patients do not show a typical schizophrenic deterioration. It can be differentiated from schizophrenia in term of phenomenology, course, and outcome [3]. This is possibly the core of the controversy between antagonism or association between epilepsy and schizophrenia. We will here discuss the problem of epilepsy occurring in patients with schizophrenia and the reverse problem, i. e. epilepsy preceding and/or causing schizophrenia.

Epilepsy in Schizophrenia

The occurrence of seizures and/or epilepsy in patients with a chronic schizophrenia was documented many years ago and was not considered a major problem. In 1931, Glaus found only eight cases of epilepsy among 6,000 schizophrenic patients and stated that "schizophrenia has but a very slight pathogenetic significance for the outbreak of epileptic attacks" [4]. In 1932, Steiner and Strauss found 20 patients with seizures among 6,000 schizophrenics [5]. They wrote: "we find in only 20 cases anything regarding seizures either in the history, or during clinical observation, or in the follow-up. Typical epileptiform seizures are, if they occur at all, so very rare in true schizophrenia, that they immediately raise doubts about the correctness of the psychiatric diagnosis". Other epidemiological studies confirmed theses results. They were summarized by Davison and Bagley (1969) (Table I) [6].

Table I: Prevalence of epilepsy in patients with schizophrenia, literature data (adapted from Davison and Bagley, 1969) [6] - SE for confidence interval 95 %.

Authors	Year published	No. of Schizophrenic Patients	No. with Epilepsy	‰ ± SE
Urstein	1909	200 (females) 100 (males) 2700	39 14 95	195 ± 28 80 ± 27 35 ± 3.5
Giese	1914	347	30	86 ± 15
Vorkastner	1918	217	10	46 ± 14
Krapf	1928	1506	18	12 ± 3
Glaus	1931	6000	8	1.3 ± 0.5
Seiner & Straus	1932	6000	20	3 ± 0.7
Kat	1937	50 000	145-165	3 ± 0.2
Esser	1938	552	11	20 ± 13.3
Yde et al.	1941	715	20	27 ± 6
Hoch	1943	500	2	4 ± 3
de Boor	1948	3242	2	0.6 ± 0.4
Smorto and Sciortra	1955	537	3	3 ± 3
Persic	1956	1827	14	7.7 ± 2
Ballerini and Laszlo	1964	665	13	20 ± 5
Mäkikyrö et al.	1998	89	4	45 ± 22

The early German figures are probably an over-estimation, because they probably included non-epileptic attacks [7-9]. From the 1920s, prevalence figures have repeatedly been reported as low, ranging between 0.06 and 2.7 percent [4, 5, 10-18]. These earlier studies were done prior to the current classification systems of psychiatric disorders and of epilepsies. They may have taken into account only the "convulsive" forms of epilepsy. They were generally based on institutionalized patients, and performed before the era of neuroleptic drugs. Mäkikyrö et al. (1998) reported a prevalence of epilepsy of 4.5 percent among chronically hospitalized schizophrenics, but the population studied was very small (89 patients) [19].

We performed an epidemiological study to assess the prevalence of seizure and epilepsy in a population-based group of patients diagnosed with schizophrenia or paranoid disorders according to DSM III-R (American Psychiatric Association, 1987) (DSM III-R 295 and 297.1, respectively) [20]. In France, mental health care has been organized by geographical zones called " sectors ". In a well-defined territory and for a population of approximately 60,000 to 70,000 inhabitants, one single health team is in charge of the totality of the mentally ill. This team has the obligation to treat patients domiciled in its geographical zone. A patient can however freely choose a physician or a private psychiatric institution outside the sector if his mental state allows him to decide. Concerning chronic and serious psychiatric conditions, the psychiatric sector collects the essentials of such patients. A survey in a urban sector of Marseilles (France) that includes 56,910 inhabitants, collected 1,154 cases treated for psychiatric disorders, including 460 for schizophrenia or paranoid disorder. All 460 patients were on chronic neuroleptic treatment. Five had epilepsy (prevalence: 10.8 per thousand): cryptogenic temporal lobe epilepsy (2 cases), cryptogenic frontal lobe epilepsy (1 case), idiopathic generalized epilepsy (1 case) and chronic alcohol-induced epilepsy (1 case). Five were diagnosed with acute symptomatic seizures (prevalence: 10.8 per thousand), which appears as very few, given the accumulation of risk factors in schizophrenics: neuroleptic treatment, misuse of psychotropic drugs and repeated withdrawals, use of illicit drugs or alcohol. We wrote that "there is apparently no relationship between schizophrenia and paranoid disorders (DSM III-R 295 and 297.1) and epilepsy, and their occurrence together in a given patient is probably due to a coincidence". We also concluded that schizophrenia may be protective against seizure: « acute symptomatic seizure are not common is this population, in spite of multiple risk factors: their rarity in patients with schizophrenia may point to a possible, relative "resistance" to factors of epileptic seizures in patients with schizophrenia ».

Schizophrenia in Epilepsy

Epileptic patients with temporal lobe epilepsy may develop schizophrenia. The occurrence of psychosis and/or schizophrenia has been studied repeatedly from the 1950s on. Most series suggest that the prevalence of schizophrenia-like psychosis in epileptic patients is higher than the general population. However, there is

a fundamental controversy in the literature about the frequency of schizophrenia in epileptics: between 0.74 to 9.25 percent [6, 21-29]. Table II summarized the main studies. Cultural and time differences explain in part the variability of the results.

Table II: Prevalence of schizophrenia-like psychosis in epilepsy .

Authors	Year published	No. with epilepsy	Prevalence
Alström	1950	897	0.8%
Bartlett	1957	1073	0.74%
Asuni & Pillutla	1967	42	26%
Davison & Bagley	1969	8572	0.7%
Bruens	1971	720	2.4%
Standage	1972	53	11.3%
Shukla	1979	132	10.6%
Edeh & Toone	1987	88	1.1%
Mendez et al.	1993	1611	9.25%
David et al.	1995	151	0%

Many studies were limited by both their methodology and their imprecise terminology. Many studies were performed in patients with serious epileptic conditions or consulting specialized centers for epilepsy or mental hospitals. Thus, over a period of eleven years, Slater et al. (1963) collected 69 cases of inter-ictal psychosis among epileptics in an English mental hospital [2]. For them, schizophrenia-like psychosis occurs more commonly than chance would predict. Their work had a profound impact. However, it was criticized for drawing conclusions on the basis of insufficient statistics [30].

Mendez et al. (1993) performed a study using the DSM III-R criteria for schizophrenia (American Psychiatric Association, 1987) [28]. Interictal psychosis occurred in 149 of 1,611 epilepsy outpatients (9.25 percent), but in only 23 of 2,167 (1.06 percent) outpatient migraine sufferers of a university medical center. This study has been criticized because it would have been better to compare epileptic subjects with a group of CNS-damaged patients, such as in multiple sclerosis [31]. David et al. (1995) investigated the incidence of schizophrenia in a cohort of 50 087 male Swedish conscripts [29]. At the time of conscription, there were 151 epileptic patients. The Swedish National Register of Psychiatric Care detected over 13 years 203 subjects admitted for schizophrenia and 197 for another type of psychosis. Of the 151 epileptic patients, two became psychotic (1.32 percent) but no schizophrenia was detected. This study can be criticized because of the small number of epileptic subjects. However, on the basis of the findings of Mendez et al., a greater number of schizophrenics should have been detected. Another criticism is that about three percent of the male population had been excluded of conscription because of physical or mental deficiencies, thus patients with serious epilepsy, those precisely at risk for psychosis, may have been missed. Thus, in spite of modern studies, major doubts about the true prevalence of psychosis in patients with epilepsy do persist.

Schizophrenia-like psychosis observed in patients with epilepsy tends to have a relatively short and benign course [32]. Paranoid personality and schizotypical personality disorders are the most usual whereas negative symptoms are rare. Paranoid persons are suspicious. They present auditory hallucinations with interpretative ideas. They think that others want to harm, to poison them. As there is no systematization of the delirium in the majority of cases, this is not a paranoid disorder. Schizotypical personality corresponds to schizophrenia-like psychosis. Affective responsiveness tends to be preserved. Patients have a high frequency of delusions or hallucinations and religious mystical experiences. They have no formal thought disorder. Pond gave a precise description of the different clinical features in 1957: "they include paranoid ideas which may become systematised, ideas of influence, auditory hallucinations often of a menacing quality, and occasional frank thought disorders with neologism, condensed words and inconsequential sentences...a religiose colouring of the paranoid ideas is common. The affect tends to remain warm and appropriate, which is sometime in contrast to 'true schizophrenia', nor is there typical 'schizophrenic' deterioration to the empty hebephrenic state" [33]. Indeed, the schizophrenia-like psychosis of epilepsy substantially differs from true schizophrenia. In their population of schizophrenic epileptic patients, Slater et al. noted that if the subjects have shown at times all cardinal features of schizophrenia, the psychoses observed deviate from schizophrenic norms in some interesting respects."In summary one may say that there is not one of the cardinal symptoms of schizophrenia which has not been at some time exhibited by these patients. However, the combination of symptoms shown by individuals differs slightly from the most usual schizophrenic patterns. Although they are seen, catatonic phenomena of any gross degree are unusual, and loss of affective response does not occur so early or become so marked in the great majority of these patients as in the typical schizophrenic. By and large they are friendlier and more co-operative, and less suspicious of hospital staffs, so that only very rarely do they cause a serious nursing problem" [2]. A family history of schizophrenia and prepsychotic personalities was relatively rare in their population. The point of view that epileptic patients do not present a typical schizophrenia is shared by Bruens (1974) [34].

Seizures start in adolescence. Onset of epilepsy precedes the development of mental deterioration by an interval of several years (10-15 years). Drugs resistance, a history of status epilepticus, complex partial seizures, several types of seizures appear as risk factors for psychosis [35]. Most series report a higher frequency of psychosis in patients with focal than with generalized epilepsy [2, 26,

34]. Gibbs et al. (1948) wrote that " a patient bearing the diagnosis 'epileptic with psychosis' is almost invariably a psychomotor epileptic" [36]. However, earlier studies were performed at a time where anatomical correlations were not well known. When a patient experienced loss of consciousness, it was labeled a psychomotor epilepsy. Nevertheless, there is a consensus that temporal lobe epilepsy is over-represented.

Flor-Henry (1969) and latter Sherwin (1981) found that epileptic patients with schizophrenia-like psychosis were more likely to have dominant hemisphere temporal lobe foci [37, 38]. This opinion is very controversial. Controlled studies did not find evidence of lateral predominance of the epileptogenic zone [26, 28, 39, 40]. Mendez et al. (1993) reported in their population 34 patients with an interictal focus on the left side, 29 on the right and 29 with a bitemporal interictal focus [28]. They then compared 62 epilepsy-with-schizophrenia patients with 62 epileptic patients without schizophrenia. They found no difference in the laterality of the epilepsy and on the anticonvulsant treatment. There were significant differences in age at onset of epilepsy (it was later in the first group), there were more complex partial seizures, more "auras" and more seizures. For these authors, the repetition of seizures in the temporo-limbic structures is one of the main elements provoking schizophrenia-like psychosis. Adachi et al. (2000) compared 246 patients with epilepsy and interictal psychosis and 658 control epileptic patients [41]. For these authors an earlier age at onset of epilepsy, complex partial seizures or generalized tonic clonic seizures, and borderline intellectual functioning were the most important predictors of interictal psychosis. In contrast to the opinion expressed by Slater et al.', they also found a high frequency of family history of psychosis. Sex, a family history of epilepsy and the lateralization of epileptiform discharge did not correlated with psychosis.

The frequency of seizures is a controversial element. Seizure activity is reported to be lower in psychotic patients than in non-psychotic patients, which is coherent with the hypothesis of alternance between psychosis and epilepsy. From his extensive review of the medical literature, Trimble (1991) wrote "while acknowledging assessment of seizure frequency is difficult, particularly retrospectively,..., the controlled studies both suggest a diminished frequency of psychomotor temporal lobe seizures in patients developing psychosis...This may be viewed as a form of antagonism between seizures and psychosis, a variant of the phenomena described by Landolt, as in some cases the EEG is shown to normalise" [35].

Conclusion

Electroconvulsive therapy appeared in the past as an effective treatment of schizophrenia. Schizophrenic patients are not particularly prone to seizures. Schizophrenia may be protective against seizure. Schizophrenia-like psychosis appears when epileptic activity diminishes. It can thus be stated that there is apparently an antagonism between seizures (not epilepsy) and schizophrenia. However, there is a significant association between longstanding and drug-resistant epilepsy and interictal psychosis: this, on the other hand, shows that epilepsy and schizophrenia (schizophrenia-like psychosis) are linked to some degree.

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Management of medically resistant epilepsies
Prise en charge des épilepsies pharmaco-résistantes

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Abstract
Approximately 30% of the patients with the diagnosis of epilepsy will not go into remission despite appropriate therapy with antiepileptic drugs (AED). According to the consensus definition of the ILAE Commission on Therapeutic Strategies, drug-resistant epilepsy is defined as failure of adequate trials of two tolerated, appropriately chosen and used AED schedules (whether as monotherapies or in combination). The clinician should be concerned with the possibility of pseudo-resistance during the assessment of drug-resistance. Diagnostic and therapeutic errors, poor compliance, external factors and combination of these are the factors determining pseudoresistance. Although the mechanisms of medical intractability of epilepsy are not completely understood, current interest is focused on two hypothesis: multidrug-transporter hypothesis and drug-target hypothesis. The first step in the evaluation of the patients with intractable epilepsy is the reassessment of diagnosis and the treatment. Epilepsy surgery is the frequently applied treatment modality in order to improve quality of life. Diagnosing drug-resistant epilepsy will facilitate referral for early consideration of epilepsy surgery. Thus, patients will have opportunity for seizure freedom and for improvement of psychosocial impairments of drug resistant epilepsy.
Keywords: Epilepsy- Antiepileptic drugs- Drug resistance- Surgery.

Résumé
Environ 30% des patients avec le diagnostic de l'épilepsie ne sera pas en rémission malgré un traitement approprié avec des médicaments antiépileptiques (MAE). Selon la définition consensuelle de la Commission sur la LICE stratégies thérapeutiques, résistante aux médicaments épilepsie est définie comme l'échec des essais adéquats de deux MAE bien tolérés, convenablement choisis et utilisés (que ce soit en monothérapie ou en association). Le clinicien doit être préoccupé par la possibilité de pseudo-résistance au cours de l'évaluation de la résistance aux médicaments. Les erreurs diagnostiques et thérapeutiques, la mauvaise observance, certains facteurs externes et la combinaison de ceux-ci sont des facteurs déterminants de pseudoresistance. Bien que les mécanismes pharmacorésistance de l'épilepsie ne sont pas complètement compris, l'intérêt actuel est axé sur deux hypothèses: l' hypothèse multitransporteur et celle de la cible thérapeutique. La première étape dans l'évaluation des patients atteints d'épilepsie réfractaire est la réévaluation du diagnostic et du traitement. La chirurgie de l'épilepsie est la modalité de traitement fréquemment utilisé dans le but d'améliorer la qualité de vie. Le diagnostic d'épilepsie pharmaco-résistante facilitera le choix de l'indication de la chirurgie de l'épilepsie. Ainsi, les patients auront l'opportunité de voir leurs crises cesser et ainsi l'amélioration des troubles psychosociaux de l'épilepsie pharmacorésistante.
Mots-clés: Epilepsie- Médicaments antiepileptiques- Résistance aux médicaments- Chirurgie.

Introduction
Most of the patients with the diagnosis of epilepsy are responsive to the treatment with antiepileptic drugs (AED) and 70% of the patients have adequate control of the seizures. This percentage varies according to the etiology and the syndromes. Some patients' response to medical treatment may change without any reason in the course of time and may continue in complex patterns. Nonetheless, approximately 30% of the patients do not go into remission. In the recent years, studies on the concepts and mechanisms of drug resistance have become important. These studies contribute to the improvement of treatment modalities for the patients with the diagnosis of epilepsy and also help to understand the pathophysiology, natural progress and the prognostic factors of epilepsy [1].

Definition of "drug-resistant epilepsy"
Drug-resistant epilepsy may be defined in various ways by different researchers and clinicians. Variations in definition result in difficulties to compare the findings of different studies and to make practical recommendations [2-4]. In response to this situation, the International League Against Epilepsy (ILAE) appointed a Task Force under the Commission on Therapeutic Strategies to formulate a proposal for a consensus definition of drug resistant epilepsy in 2010. The aim of this proposal was to enhance an approach to patients and to support the clinical trials [5]. According to the Commission, drug-responsive epilepsy was defined as epilepsy in which the patient receiving the current AED regimen had been seizure free for a minimum of three times the longest preintervention interseizure interval or 12 months, whichever was longer. Drug resistant epilepsy was defined as failure of adequate trials of two tolerated and appropriately chosen and used AED schedules (whether as monotherapies or in

combination) to achieve sustained seizure freedom. These definitions could be used for the selection of appropriate candidates for epilepsy surgery immediately and for the referral of patients to the specialized centers for detailed evaluation. Also the development of the proposed definition was driven by the growing need among medical practitioners and clinical researchers to adopt a common language in recognizing drug resistant epilepsy in the face of rapidly expanding therapeutic options [5].

Pseudoresistance

While evaluating the insufficiency of AED treatment, the concept of "pseudoresistance" should always be concerned [6]. In the situation of pseudoresistance, the factors triggering the seizures are the ones other than the factors related with epilepsy and seizures may be controlled by re-evaluating the diagnosis and treatment. Patients with pseudoresistance can be seen in the centers in which epilepsy surgery is performed.

In the study in which 191 patients with the diagnosis of drug-resistant epilepsy were evaluated retrospectively, it was found that 20% of the patients had pseudorefractory epilepsy [7]. The reasons for pseudoresistance in this population were reported as diagnostic and therapeutic errors, poor compliance, external factors and a combination of these.

Incorrect classification of seizures and syndromes leads to failure in diagnosis and treatment. Administration of inappropriate treatment schedules may cause an increase in seizure frequency.

During treatment, an appropriate drug should be chosen and the dose of the drug should be increased up to the maximal tolerated dose. Response to the first administered AED has an important effect on prognosis [8]. Moreover, inappropriate combinations of AEDs are also the reasons for pharmacologic resistance.

Situations that may be mistaken for epileptic seizures, presenting with paroxysmal symptoms or changes in consciousness, should be considered in differential diagnosis. Nonepileptic psychogenic seizures are present in 10 to 45 percent of patients with refractory epilepsy [9]. On the other hand, movement disorders, migraine, syncope, parasomnias, transient ischemic attacks etc. may mimic epileptic seizures.

Insufficient education of patients and their parents, unfavorable life styles and poor compliance to treatment are common problems in patients wit refractory epilepsy. For these reasons, patients and their parents should be educated about epilepsy.

Mechanisms and factors related with drug-resistance

Although it was found that there was a significant correlation between drug resistance and early onset of epileptic seizures, there has been other studies showing similar prevalences in both pediatric and adolescent age groups [2,10]. Some researchers pointed out that it had been difficult to evaluate drug resistance in children. Berg et.al. proposed that response to treatment could not be predicted in 40% of the children in a 2-year- follow up period [11].

In pediatric age group, West, Lennox-Gastaut, Dravet, Ohtahara Syndromes and other myoclonic encephalopathies are known to be medically resistant disorders [12]. Organic brain insult, presence of multipl seizure types, increased seizure frequency, mental retardation, long duration of epilepsy are related with poor prognosis.

Etiology and the related seizure zone are important for focal epilepsies. Mesial temporal lobe is probably the most epileptogenic area of the brain. It is followed by occipital cortex, parts of motor cortex related with hands and face and supplementary sensorial-motor cortices. From etiologic point of view, mesial temporal sclerosis, cortical dysplasias, hemorrhagic lesions, multifocal and progressive lesions are the most common lesions found in intractable epilepsies [13-16].

Factors related with drug resistance in generalized epilepsies may be listed as onset of epilepsy in infancy and early childhood, high frequency of seizures at onset, inappropriate drug administration at onset, presence of abnormal basic bioelectric activity and frequent multifocal spikes in EEG and progressive disorders.

Although the mechanisms of medical refractoriness of seizures has not been totally understood, currently two major hypotheses are emphasized: Multi-drug transporter hypothesis and drug-target hypothesis [17]. According to multidrug-transporter hypothesis, a markedly enhanced expression of multidrug resistance-1 (MDR1) and P-glycoprotein (P-gp) in blood brain barrier (BBB) endothelial cells of epileptogenic brain tissue resected from patients with intractable epilepsy may explain drug-resistance. This hypothesis was first reported by Tishler et.al in 1995 [18]. Later, several members of multidrug resistance proteins (MRP) transporter family, including MRP1 and MRP2, were found to be overexpressed in such tissue [19]. It was proposed that overexpression of multidrug transporters in perivascular astroglia might represent a second barrier for AED penetration into the brain. Another hypothesis to explain AED resistance in epilepsy is the drug-target hypothesis which is principally based on studies with carbamazepine (CBZ) on voltage-gated sodium channels in hippocampal neurons. This hypothesis assumes that intrinsic or acquired loss of brain-target sensitivity is critically involved in resistance to AEDs. In addition to the loss of use-dependent inhibition of Na+ channels by CBZ, the fast recovery from inactivation of the fast Na+ current is CBZ insensitive in pharmacoresistant patients. The authors suggested that a loss of Na+ channel drug sensitivity might explain the development of drug-resistant epilepsy [17].

Approach to medically resistant patients

The first step in the evaluation of medically resistant patients is the reassessment of the diagnosis and the treatment. Correct classification of seizures and syndromes affects treatment options. Second step is to control the appropriateness of the administered AED. If the seizures continue in spite of the increased AED dose up to maximally tolerated dose, then a second rational AED with a different mechanism should be tried. If seizure

control could not be achieved despite the second AED, then polytherapy should be considered. Rational polytherapy is defined as the combinations of AEDs with different mechanisms and which are thought to have additive and potentially sinergistic effects on each other.

The response to the first AED is a powerful prognostic factor [20]. Kwan and Brodie reported that among patients in whom treatment with the first drug was ineffective, only 11% of such patients subsequently became seizure-free. They concluded that some patients with refractory epilepsy could be identified early in the course of the disease and could be targetted for rational combination of therapy or surgery. In another study, the authors stated that intractable epilepsy might be delayed, especially in focal epilepsy and that referral to surgery might take 20 years or longer due to quiescent periods followed by further remissions [21].

The importance of the choice of the drug that is appropriate for the seizure and syndrome type has been reported in various studies. While deciding the appropriate drug for the patient with a new diagnosis of epilepsy, the diagnostic scheme proposed by ILAE in 2001 may be a useful tool [22]. Most of the variables efficacious in the decision whether to start an AED treatment or not, were pointed out in this guideline. If the seizures are not controlled with the first AED or the alternative monotherapy, combination of AEDs is considered but polytherapy may cause drug interactions, increased risk for adverse effects, increased cost of treatment, poor compliance to therapy and as a result of all these impaired quality of life.

Epilepsy surgery is a treatment modality used in patients with intractable epilepsy in order to improve quality of life. The aim of epilepsy surgery is to control the seizures totally or reduce the frequency of seizures, to reduce neurologic morbidity, to prevent the adverse effects of AEDs and to improve the quality of life. Diagnosing refractory epilepsy would facilitate early consideration of epilepsy surgery [23]. Thus, the chance of seizure freedom for the patients with intractable epilepsy would increase and the development of interictal behavioral disturbances and psychosocial side effects of epilepsy would be prevented. The patient population who is thought to benefit mostly from epilepsy surgery is the population who has mesial temporal lobe epilepsy and who has well-defined, potentially epileptogenic lesions on MRI (Magnetic Resonance Imaging). Epilepsy surgery is not performed in patients who has idiopathic generalized epilepsy and who has minor seizures that does not impair the quality of life. Also epilepsy surgery is relatively contraindicated in patients with progressive systemic diseases or serious medical problems, limited cooperation, active psychological diseases and in patients who have deficits in contralateral memory functions in WADA(intracarotid amobarbital) test [24]. There are studies stating that surgery may be performed in all age groups.

Preoperative Evaluation

During preoperative evaluation, neuro-imaging investigations and electrophysiologic tests are performed. Noninvasive investigations are preferred first. Scalp EEG and cranial MRI (appropriate for epilepsy protocol) are done routinely. Ictal video-EEG serves for the determination of ictal semiologic features and for electro-clinic correlation. Clinical features of the seizures contribute to the determination of lateralization and localization of seizure activity.

Functional imaging techniques are useful for defining functional deficit zone and ictal onset zone, if the imaging technique suitable. Hypometabolism which is detected in interictal PET (Positron Emission Tomography) is regional in temporal lobe epilepsy. It was reported that the hypometabolism area was related with the propogation area of the last seizure [25]. The sensitivity of interictal SPECT (Single Photon Emission Tomography) is less than that of PET for mesial temporal sclerosis (MTS). The localization value of ictal SPECT is high. Functional MRI (fMRI) shows the localized perfusion defects in focal epilepsies and is used in the lateralization and localization of language functions and also in the detection of motor and sensorial areas in preoperative stage. There is an ipsilateral decrease in NAA/Cr ratio in the 90 percent of the patients with MTS in MR Spectroscopy and it is related with the side of ictal activity in EEG and the deficits of memory [26-28].

Neuropsychologic tests are used to evaluate the basal cognitive, language and other higher cortical functions of the patients. Neuropsychologic evaluation of language and memory functions contributes to the lateralization of temporal lobe dysfunction.

WADA test is performed in order to determine the hemispheric dominance and to evaluate the contribution of both hemispheres to memory function.

If noninvasive tests do not provide enough information about the lateralization and localization of epileptogenic zone, intracranial recordings are used in the patients for whom the resective epilepsy surgery has been planned.

Surgical Procedures and Vagal Nerve Stimulation (VNS)

Anterior temporal lobectomy (ATL) and selective amygdalohyppocampectomy (SAH) are the surgical procedures that are performed in mesial temporal lobe epilepsy (MTLE) [29, 30]. Seizure control is achieved 70 percent of the patients in which ATL is performed. Currently, it is known that patients with MTLE do not represent a homogenous group and that MTLE has some subgroups. Thus, the concept of standart surgical procedure is an important issue in this patient group [31].

Frontal lobectomy is the second most frequent surgical procedure in epilepsy surgery and seizure freedom is seen in 30-50% of the operated patients [32].

Parietal and occipital lobectomies are generally performed in patients who have structural lesions.

Corpus callosotomy is preferred in patients who have multifocal, bilateral lesions or localized lesions which can not be operated.

Hemispherectomy is performed in patients, especially children, whose seizures are originated from one hemisphere and whose seizures are severe.

Multiple transpial transsection and partial

hemispherectomy are the other surgical procedures used in epilepsy surgery.

Currently, VNS is used in patients with intractable epilepsy who are not suitable for standardized surgical procedures. Studies reveal that among patients in whom VNS was applied, one third of the patients had seizure control over 50%, one third of the patients had seizure control below 50% and the remainder had total remission [33].

As a conclusion, patients with medically resistant epilepsies should be diagnosed and evaluated in an accurate way. Evaluation of medically resistant epilepsies requires a multidisciplinary approach. This approach facilitates referral of patients for early consideration of epilepsy surgery and thereby gives opportunity of seizure freedom and improvement of quality of life.

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Psychogenic non epileptic seizures semiology: is it an international language? Sémiologie des crises psychogène non épileptique: est-elle d'un language universel?

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Abstract

Introduction: Psychogenic nonepileptic seizures (PNES) are prevalent in neurology and specialty epilepsy centers. They are categorized as a manifestation of dissociative or somatoform disorder. Video- Electroencephalography (VEEG) is the accepted diagnostic 'gold standard', and PNES semiology. Authors aimed at analyzing different semiologic elements of non epileptic events in an Egyptian sample and comparing them to other semiologies published in other countries.

Participants and methods: Retrospectively, authors reviewed the video EEG of patients examined in a 3 years period.

Results: The 24 subjects studied showed heterogeneous clinical seizure semiology. The most 3 frequently recorded abnormal movement 1-were eye closure more than 50% of the event (70.8%), 2-head shaking, and upper limb clonus like (or shaking) movements (each occurring 33.3%), 3-and pelvic thrusting (29.2%).

Conclusions: The semiologies recorded in the few discussed studies, as well as the results of the current study, share a lot, although they don't share the time or place. The "eyes closure sign" was noticeable.

Keywords: Psychogenic nonepileptic seizures- Semiology- Video EEG- Ictal eye closure- Dissociative Disorders.

Résumé

Introduction: Les crises non épileptiques psychogènes (CNEP) sont répandues dans les centres de neurologie et d'épileptologie. Elles sont classées en tant que manifestation d'un trouble dissociatif ou somatoforme. Vidéo-électroencéphalographie (VEEG) est l'outil 'gold standard' accepté ainsi que la sémiologie des CNEP. Les auteurs ont étudié et analysé les différents éléments sémiologiques des événements non épileptiques dans un échantillon égyptien et les en comparé à d'autres sémiologies publiés dans d'autres pays.

Les participants et méthodes: Rétrospectivement, les auteurs ont revu la vidéo EEG des patients examinés sur un délai de 3 ans.

Résultats: Les 24 patients étudiés ont présenté une sémiologie clinique hétérogène. Les 3 mouvements les plus fréquemment enregistrés étaient 1-la fermeture des yeux dans plus de 50% des cas (70,8%), 2-les secousses de la tête, 3-et clonus des membres supérieurs (chacun survenant 33,3%), et allongeant du pelvis (29,2%).

Conclusions: Les sémiologies enregistrées dans les quelques études discutées, ainsi que les résultats de l'étude actuelle partagent beaucoup d'éléments, mais ils ne partagent pas le temps ou le lieu. Le 'signe la fermeture des yeux' était très perceptible.

Mots-clés: Les crises non épileptiques psychogènes - Sémiologie- Vidéo EEG- Fermeture des yeux critique- Désordres dissociatifs.

Introduction

Psychogenic nonepileptic seizures (PNES) are prevalent in neurology settings and [1]. They are commonly mistaken for epilepsy, resulting in diagnostic delay for 7 to 10 years [2]. They are categorized as a manifestation of dissociative or somatoform (conversion) disorder [3]. They have no known definitive biomarker [4], and the differential diagnosis of PNES and epilepsy can be difficult [5].

Thus, video- Electroencephalography (VEEG) is the accepted diagnostic 'gold standard', as well as their semiologies [6]. Details of the episodes often include characteristics that are inconsistent with epileptic seizures [7]. However, the frequency of epilepsy in patients with PNES reached 50% [8].

The principle two aims of the current study are 1) Analysis of different semiologic elements of non epileptic events in an Egyptian sample and 2) Comparing semiologic elements of PNES in this study to other semiologies mentioned in literature published in other countries.

Methodology

The study is a retrospective study, reviewing the video EEG of 24 patients (12 females and 13 above the age of 18 years) examined in the period between May 2009 to May 2012 (with an approximate rate of "one video EEG case recorded per day"; on a "six working days per week" basis). All patients consented performing the VEEG, to diagnose the nature of their paroxysmal seizure like event. The recording was carried out for a duration ranged between one and twenty three hours.

Two electroencephalographers (EEGers; EEGer 1 and EEGer 2) contributed in this study. The EEGer 1, the originally referred to physician, visualized the whole length of the video EEG and determined the EEG is capturing a psychogenic non epileptic event (PNEE). While EEGer 2 only visualized video recordings (blinded to EEG tracings, seizure classification, subject identifiers and diagnosis), analyzing different semiologic elements recorded.

Results

The following semiologic elements occurred:

Eye closure more than 50 % of the event in 17 patients; eye opening in 5 patients; eye fluttering in 2 patients; squin-

ting in 1 patient; starring in 1 patient; frothing in 4 patients; mouth opening in 2 patients; teeth clenching in 1 patient; tongue protrusion in 2 patients; facial deviation in 2 patients; grimacing in 1 patient; facial myoclonia like movement in 3 patients; Head nodding in 2 patients; head shaking in 8 patients; Neck extension in 2 patients; back arching in 4 patients; pelvic thrusting (or spasms) in 7 patients; anteroposterior body shaking in 3 patients; Side to side body shaking in 3 patients; anteroposterior myoclonic like axial movements in 5 patients; shivering like movements in 5 patients; sitting attempts in 3 patients; upper limb clonus like (or shaking) movement in 8 patients; upper limb dystonic like posturing in 6 patients; Elbow flexion in 1 patient; fisting in 3 patients; touching gentalia in 2 patients; lower limb clonus like (or shaking) movement in 6 patients; lower limb dystonic like posturing in 2 patients; pedaling in 2 patients; hip inwards outwards movements in 3 patients; hyperventilation in 2 patients; non responsiveness in 2 patients ; crying in 2 patients. The events duration varied from 5 seconds to 30 minutes (mean of 9.13 minutes).

It is to be mentioned that The EEGs recorded were essentially normal apart from three patients (12.5%) showing interictal epileptiform discharges.

Table 1: Summary of the clinical signs encountered during the non epileptic events recorded during this study (number of subjects= 24).

Eye signs	rate of occurance (n=24)	Oral signs	rate of occurance (n=24)	Facial signs	rate of occurance (n=24)
Eye closure 50% of the event	17	Frothing	4	Grimacing	1
Eye opening	6	Mouth opening	2	deviation	2
Lid fluttering	2	Jaw clenching	1	Facial myocloni	3
Squinting	1	Tongue protrusion	2		
Head and neck signs	rate of occurance (n=24)	Axial movements	rate of occurance (n=24)	Limbs movements	rate of occurance (n=24)
Nodding	2	Back arching	4	Upper Limb clonia	8
Shaking	8	Pelvic movements	7	Upper Limb dystonia	6
Neck extension	2	Antroposterior movements	3	Elbow flexion	1
Others	rate of occurance (n=24)	Side to side movements	3	fisting	3
Touching genetalia	2	Myoclonia	5	pedaling	2
Hyperventilation	2	Shivering	5	Hip movements	3
Non responsiveness	2	Sitting attempts	3	Lower Limb clonia	6
crying	2			Lower Limb dystonia	2

Discussion

Psychogenic non-epileptic seizures are seen in 20–30% of patients referred to epilepsy centers for refractory seizures [9]. In the current study, all the patients were previously diagnosed as intractable epileptics.

In a study performed in Seattle, Washington U.S.A., Behaviors or signs strongly suggestive of PNES included: very gradual onset or termination; pseudosleep; and discontinuous (stop-and-go), irregular, or asynchronous (out-of phase) activity including side-to-side head movement, pelvic thrusting, opisthotonic posturing, stuttering, and weeping [10].

In a study carried in Prague, Czech Republic, the seizure semiology (frequency of individual symptoms) in PNES patients were ; closed eyelids resistant to lid opening (67.6%); rapid tremor, trembling (upper, lower extremities) (47.7%); asynchronous 'hyper-motor' limb movements, out-of-phase (37.8%); preictal 'pseudosleep' (33.3%); side-to-side head movement (32.4%); opisthotonus (25.2%); pelvic trusting, rhythmic pelvic movements (20.7%); 'aura', preceding other symptoms (23.2%); clonic limb movements (13.5%); unresponsiveness, nonreactivity, 'staring', without any motor symptoms (13.5%); tongue (tip), lip or buccal biting (11.7%); atonia with unresponsiveness (9.9%); sounds, screams, vocalization, or crying (9%). The five most typical symptoms were: initially closed eyelids, rapid tremor, asynchronous limb movement, preictal pseudosleep and side-to-side head movement [11].

Syed and colleagues in the U.S.A in 2011, documented preserved awareness, eye flutter, others can intensify or alleviate, postictal whispering, stuttering course, forced eye closure, eye respond to environment, ictal fighting, pelvic thrusting, arched back, side to side head movement, ictal crying/weeping, ictal avoidance, turn onto belly, postictal muscle soreness, postictal headache, postictal vomiting, postictal shallow, breathing, intelligible speech, ictal whispering, immediate return to baseline, non synchronous movements and seizures duration longer than 2 minutes, as 23 video documented signs for identification of PNES. Only 3 signs (''preserved awareness,'' ''eye flutter,'' and ''bystanders can intensify or alleviate'') were significant and reliable indicators of PNES [12].

A recent study, carried on children (subjects less than 18 years of age) in Budapest, Hungary showed the following semiology elements; Aura 54.7%; eyes closed during attack 21.9%; eyes closed at start of attack14.7%; abrupt start 80%; abrupt end 68%; responsibility (responsiveness) 65.6%; vegetative symptoms 9.3%; special eye movement 22.7%; sensory sign 41.3% ; hyperventilation 18.7% ; vocalization 16%; emotion 42.7%; eyewitness 89.3%; type of movement; tonus16%; clonus 9.3%; myoclonus 10.7%; tremor 25.3%; rhythmic 58.8%; symmetric 36.7%; intensity change 56.7%; upper limb involvement 35.1% (42% bilateral; lower limb involvement 21.6% (43.7% bilateral; trunk 21.6%; pelvis 2.7%; head 25.7%; axial arching 9.5%; pelvic trusting 2.7% [13].

As noticed, the semiologies recorded in the few above mentioned studies, as well as the results of the current study, share a lot of their semiologic elements, although they don't share the time (2002 till present time) or place (3 continents). Yet, the major semiologic elements of PNES are shared worldwide.

In this study, inter-ictal epileptiform discharges together with PNES were present in 12.5% of patients. Clinically coexisting epilepsy in PNES subjects was (34.9%) [14], 6.3% [11] and wide [15] ranged in the pediatric community 15–72% .

This lead to another wonder "Is there any specific brain dysfunction and/or genetic disorder related to the presentation of the PNES?". La France and colleagues, in 2010, suggested that serum brain-derived neurotrophic factor (BDNF) might represent a trait marker of PNES. In PVES, the decreased serum BDNF may be related to stress which has been shown to lower BDNF [4].

Eye closure for greater than 5% of the episode duration was most sensitive for PNES episode identification, while closure for the entire duration of the episode was most specific for PNES [14]. In our study the most 3 frequently recorded abnormal movement were eye closure more than 50% of the event (in 70.83% of patients), followed by head shaking, and upper limb clonus like (or shaking) movements (each occurring 33.33%), and finally pelvic thrusting (in 29.17% of patients).

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The epic history of epilepsy surgery
L'histoire épique de la chirurgie de l'épilepsie

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Abstract
At present day, the mainstay of epilepsy treatments is antiepileptics, surgery is only considered for intractable epilepsy. Many epileptic syndromes are remediable by surgery after the failure of antiepileptics. These epileptic syndromes are generally focal and pharmacoresistant and involves mesial temporal sclerosis, neocortical temporal lobe epilepsy, premotor and central lobe epilepsy, mesial frontal epilepsy, basi-frontal lobe epilepsy, parieto-occipital lobe epilepsy, insular epilepsy, cingulate epilepsy, hypothalamic hamartomas, Rasmussen syndrome, and Landau–Kleffner syndrome. However, not only focal pharmacoresistant Epilepsy can be remediable by surgery. The Lennox–Gastaut syndrome is an example of generalised epilepsy that can benefit from palliative surgery (callosotomy, vagal nerve stimulation or radiosurgery).
However, if epilepsy surgery has proved certain effectiveness, many surgical techniques were developed during the epilepsy history with unequal efficacy. The concept of epilepsy aetiology has remained for centuries dominated by supernatural views, considering seizure attacks as a religious or a superstitious concept. The "middle ages" in epilepsy surgery has unfortunately persisted until the twentieth century, based on wrong theories and illusory wisdom of curing epilepsy by numerous surgical procedures that gave no chance of any kind of improvement. Running parallel with these wrong theories, there were many bright spirits for more than 3000 years who gave considerable advances in the fields of medical and surgical treatment of epilepsy surgery.
Keywords: Epilepsy- Surgery- History-Treatment-Temporal lobectomy.

Résumé
De nos jours, la pierre angulaire du traitement de l'épilepsie reste le traitement médical. La chirurgie n'est indiquée qu'en cas d'épilepsie pharmacorésistante. Plusieurs syndromes épileptiques sont traités chirurgicalement après l'échec des antiepileptiques. Ces syndromes épileptiques sont généralement focaux et pharmacorésistants à l'instar de la sclérose mésiotemporale, de l'épilepsie basifrontale, mésiofrontale, pariétale, insulaire ou cingulaire, des hamartomes hypothalamiques, du syndrome de Rasmussen et du syndrome de Landau-Kleffner. En revanche, Le syndrome de Lennox-Gastaut est un exemple de l'épilepsie généralisée qui peut tirer bénéfice d'une chirurgie palliative telle que la callosotomie, la stimulation du nerf vague ou la radiochirurgie. Si actuellement l'efficacité de la chirurgie de l'épilepsie est reconnue, plusieurs techniques chirurgicales développées au cours de l'histoire n'ont pas connu le même succès.
Le concept même d'étiologie de l'épilepsie a été dominé par le caractère surnaturel considérant la crise d'épilepsie comme un phénomène religieux ou superstitieux. Le «moyen âge» de la chirurgie de l'épilepsie a malencontreusement persisté jusqu'au vingtième siècle basé sur des théories fallacieuses et de faux espoirs n'ayant amené aucune amélioration. Parallèlement à ces faux pas de la chirurgie, plusieurs grands esprits de la science ont apporté durant trois millénaires des avancées considérables dans le traitement médical et chirurgical de l'épilepsie.
Mots-clés : Epilepsie- Chirurgie- Histoire-Traitement-Lobectomie temporale.

Introduction

Etymology of Epilepsy comes from the greek word "Epilambanein" which signifies seize, attack by surprise. Epilepsy is a frequent neurological disease. Its incidence is about 50/100000 per year and its prevalence is 0,5%. Almost 60% of epileptic patients have focal epilepsy which is more suitable to surgery. From 30 to 50% of these focal epilepsies are medically intractable and among them 1/3 are potentially candidates for surgery [1, 2]. Nevertheless, until now there is an imbalance between candidates for surgery and number of operations every year. For example in USA among 5000 new patients only 500 are operated every year. In France among 2000 to 3000 new patients only 250 are operated. In the developing world Epilepsy prevalence and candidates for surgery is many fold that found in developed countries [4, 5].
This situation is also amplified in developing countries. Anamorphic maps of public health in the word shows the inequality in health spending, number of working physicians which are inversely proportional to epilepsy deaths in the world (Figures 1, 2, 3).
Of course developing countries are fighting other challenging pathologies like infectious and parasitic disease.
Not only focal epilepsy can be improved by surgery. Palliative surgery can be an interesting option for generalized epilepsy, where a dramatic decrease of catastrophic seizures would be expected [5]. However, the mainstay of epilepsy treatments is nowadays antiepileptics, surgery is only considered for intractable epilepsy.

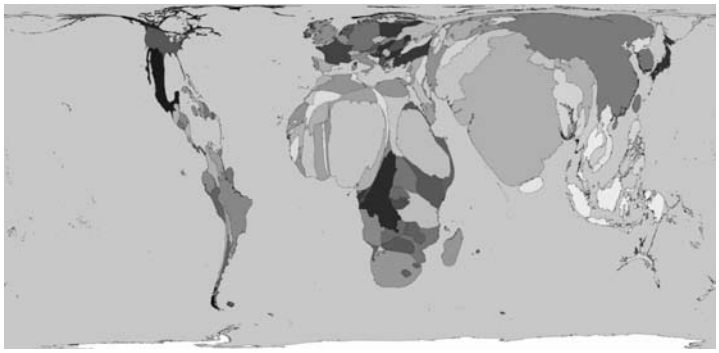

Figure 1: anamorphic map where the area of each country is scaled in proportion to the epilepsy deaths in the world.

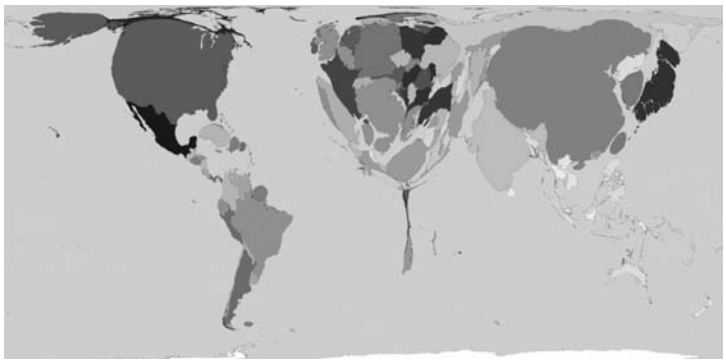

Figure 2: anamorphic map where the area of each country is scaled in proportion to number of physicians working.

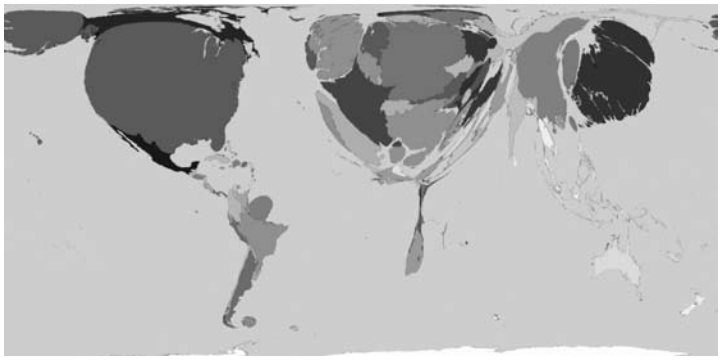

Figure 3: anamorphic map where the area is scaled in proportion to the health spending.

Medical intractability

The clinical goal of anticonvulsant therapy is to make patients seizure-free with minimal or no side effects. The anticonvulsant dose in controlling seizures is also very individualized [6].

The initial response to anticonvulsant drug therapy is highly predictive of long-term outcome. Almost two-thirds of patients respond to anticonvulsant therapy. Approximately 47% respond on one drug alone; about 13% respond to two drugs and 4% respond to three drugs or more [7].

Medical intractability is also known as multidrug resistant (MDR) or pharmacoresistant epilepsy. There is no general consensus on the definition of medical intractability. Generally, it has been observed that the chance of achieving seizure control beyond three drugs is 5 to 10% [8-10].In recently published studies, the minimum number of anticonvulsant drug failures to qualify for medical intractability is two or three [11-15]. If the minimum two-drug criteria is use to classify medical intractability, the percentage meeting this criteria ranges from 31 to 37.5% [12].

The current hypothesis of drug intractability is probably due to low drug penetration in the blood brain barrier, drug target insensitivity, or impaired reuptake of glutamate in epileptogenic brain tissue [6].

Epilepsies remediable by epilepsy surgery

At present days, many epileptic syndromes are remediable by surgery after the failure of antiepileptics. These epileptic syndromes are generally focal and pharmacoresistant and involves mesial temporal sclerosis, neocortical temporal lobe epilepsy, premotor and central lobe epilepsy, mesial frontal epilepsy, basi-frontal lobe epilepsy, parieto-occipital lobe epilepsy, insular epilepsy, cingulate epilepsy, hypothalamic hamartomas, Rasmussen syndrome, and Landau–Kleffner syndrome. In all these syndromes the first step is to define the precise and reliable diagnosis of the epileptogenic zone on the basis of a good assessment of clinical semiology and clinical neurophysiology, and with the help of many technological advances. However, not only focal pharmacoresistant Epilepsy can be remediable by surgery. The Lennox–Gastaut syndrome is an example of generalised epilepsy that can benefit from palliative surgery (callosotomy, vagal nerve stimulation or radiosurgery) [5]. Currently, if epilepsy surgery has proved a certain effectiveness, many surgical techniques were developed during the epilepsy history with unequal efficacy.

Epilepsy surgery from past to present era.

The history of epilepsy surgery was marked by the coexistence of clear theories that led to current knowledge, in parallel with fallacious theories that survived until the twentieth century.

Dark side history of epilepsy surgery:

For many centuries physicians and scientists were on the wrong way in the understanding and treating epilepsy. Despite the precise descriptions of epileptic attacks in early Babylonian texts of medicine (1000 BC), the concept of epilepsy aetiology has remained for centuries dominated by supernatural views, considering seizure attacks as a religious concept (divine visitation), or a superstitious concept (invasion of the body by evil spirits) [16]. As elegantly summarized by Temkin, the competing view held over many centuries was that epilepsy is a demonical disorder, and seizures were frequently interpreted as evidence of spiritual possession [17, 18].

The "middle ages" in epilepsy surgery has unfortunately persisted until the twentieth century, based on wrong theories and illusory wisdom of curing epilepsy by numerous surgical procedures that gave no chance of any kind of improvement.

In many civilisations, trepanation without any traumatic context was performed in order to treat probable epilepsy. The earliest form of brain surgery known is trepanation of the skull. It is the removal of a piece of calvarium without damage to the underlying vessels, meninges and brain, to

let out evil spirits stuck in the brain. The operation can also include cutting out the part of the brain that had been 'infected' with these evil spirits. Incredibly, people are known to have survived operations similar to these as skulls have been found which show bone growth around the hole cut by a surgeon [19-29].

Trepanation of the skull is recovered from a French archaeological site, carbon dated to 5100 BC, from a patient who survived trepanation (based on evidence of healing around the surgical site) represents the oldest example of a successful surgical procedure [22]. The evidence for trepanation begins in the Neolithic, and extends to the present, and comes from every corner of the world. It is also well known that during the pharaonic era, neurosurgical procedures like trepanations were widely used in many civilisations around the world, practiced and taught by healers [23].

Probably the first trepanations were performed for removing depressed skull pieces that was responsible of epilepsy with improvement of epilepsy. After this finding ancient practitioners would have generalised the procedure to every epilepsy and convulsion. It was believed that those who survived the dangerous procedure acquired a holy status and a removed piece of skull was worn as an amulet.

The "middle ages" was a period dominated by obscurantism and obsession of demonic possession during the Inquisition. Thus, many epileptics are regarded as possessed or witches and then tortured or burned alive. The bloodletting and other scarring remain normal to evacuate «the moods and pathogenic fumes responsible of epilepsy»[24]. Cauterization was considered a form of treatment used in the Middle Ages and perhaps before, when trepanation had failed to control the seizures (Figure 4 and 5).

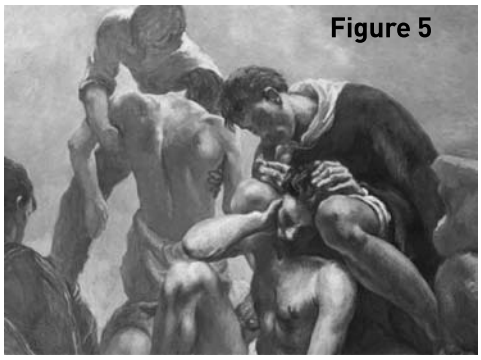

Figure 4: Painting from the Sloane manuscript, a collection of medical manuscripts at the end of the 12th century, showing a person with epilepsy ('epilepticus') is undergoing both trepanation and cauterization (British museum).

Figure 5: Painting of a medieval trephining of a patient with probable epilepsy. Treatment is meant to release the demons possessing the person or in later years to restore the balance of "humours." (Museum of Surgical Science, Chicago, Illinois, USA).

This was a relatively enlightened treatment in comparison to stoning and hanging [25].

In Australia in the late 18th century, medical treatments of epilepsy included: quiet rest, the feet placed in hot water and mustard bath, shaving of the scalp, mustard plaster to the back of the head, cooling of the head by a mixture of spirit of vinegar and water, bleeding in letting five fluid ounces of blood at a time, leeches to the temples, blister to the nape of the neck, use of prolonged chloroform anaesthesia, bromides introduced by Dr. Smith in 1873, and blistering where local limb auras occurred. At this time the treatment for epilepsy in the USA included bromides, arsenic, quinine, cod liver oil, iron, and hysterectomies [26, 27].

Gowers is often quoted as having said about epilepsy that "The tendency of the disease is toward self-perpetuation; each attack facilitates the occurrence of another by increasing the instability of the nerve elements. The spontaneous cessation of the disease is an event too rare to be reasonably anticipated". This remarkable description of epilepsy progression in the ninetieth century was unfortunately out clouded by the fact that Gowers himself did advocate circumcision and castration as a treatment of epilepsy. At the same time some of his contemporaneous practitioners performed burning of the shaking limb and nerve sectioning in cases of partial motor seizures [28].

If the development of Neurosurgery for epilepsy actually took his flight during the twentieth century, it is surprising to note the proliferation of various primarily peripheral indirect surgical approaches based on fallacious theories. Endocrinian theory led to perform partial resection of adrenalectomy in 1920 and partial pancreas resection in 1952. The vascular theory led to perform sigmoid and transverse sinus decompression, middle meningeal artery cauterization in 1950, carotido-jugular anastomosis and bilateral external carotids ligation in 1952. Other wrong way theories concerned neurovegetatif system with cervical sympathectomy or superior lymph node resection [29, 30].

Running parallel with theses wrong theories, there were many bright spirits for more than three millenniums who gave considerable advances in the fields of medical and surgical treatment of epilepsy surgery.

Bright history of epilepsy surgery

Seizures have been documented for more than 3000 years in Babylonian writings. Since then, abundant descriptions and explanation models can be found in the literature [31]. Al Razi, 'Rhazes' (830–923) and Hussein Ibn Sina, 'Avicenna' (980–1037) gave a remarkable description of epilepsy in the work entitled 'Alkanun Fi Tib', Rules of Medicine. They described different types of epileptic syndromes, like tonico-clonic seizures, absence, auras, post-ictal phenomenon and focal seizures, particularly the motor ones, 800 years before the description of Jackson [32]. Avicenna elaborates the concept that epilepsy is a brain disease resulting from an invasion by a noxious substance which then propagates towards the posterior part of the brain and later to the spinal cord and the peripheral nerves. This propagation engenders generalized seizures. He considered these seizures of the body as resulting from a contraction of the brain which is mandatory for the expulsion of noxious substances, and comparing also these contractions of the brain to the contractions of the stomach during hiccup or vomiting [32].

Later on in Europe during the Middle Ages, some surgeons as Ambroise Paré, Valsalva or De Chauliac operate few children with epilepsy related to depressed skull fracture at distance from the initial trauma. After 1770, Tissot in his treatise on epilepsy refers to «a predisposition of the brain to be in contraction more easily with a cause of irritation which activates it"[24].

In 1861, Pierre-Paul Broca (1824-1880) discovered the language motor site and engages in 1876 in the removal of an extra-dural empyema responsible of aphasia with a poor result. Shortly later, John Hughlings Jackson (1820-1903) between 1864 and 1870, 50 years before the rise of electrophysiology, described with precision seizure as a sudden temporary excessive discharge of unstable cells of a part of the brain grey matter. Thus he proposed the resection of irritative foci responsible of focal epilepsy [24].

The separation of both the actual attacks and epilepsy as a disease dates back to John Hughlings Jackson. Jackson's definition of a seizure still provides the basis for the understanding of seizures to the present day. According to him, a convulsion is a symptom, and implies only that there is an occasional, excessive, and disorderly discharge of nerve tissue on muscles. This discharge occurs in all degrees; it occurs with all conditions of ill health, at all ages, and under innumerable circumstances [33]. This definition has not changed much in the last 130 years. According to the International League Against Epilepsy (ILAE) an epileptic seizure "is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain"[34, 35].

The second half of the 19th century was the era of rising of many concepts in epileptology and remarkable progress in surgery as the means of asepsis and anesthesia that led to the development of Epilepsy Surgery. Hitzig and Fritsch were accountable in 1870 of the electrical excitability of the cerebral cortex. At the same time, Bartholom (Cincinnati USA) described in 1874 the first effects of cortical electrical stimulation on motor cortex but he is quickly forbidden to exercise because of his experiments on one of his servants who has a cancer related scalp and vault defect. William MacEwen (1848-1904) presented in Glasgow in 1879 the removal of a frontal Meningioma revealed by crises bravais-Jacksonian, what constitutes the first lesion surgery based solely on preoperative ictal events. The first epilepsy surgery was performed in 1886, by Victor Horsley on a 22-year-old patient with focal motor seizures, due to a scar caused 15 years earlier by a depressed skull fracture. He also reported 8 similar cases in the British Medical Journal in 1886 [24, 36].

At this time without available imaging, surgery was only planned on the bases of clinical semiology, and performed according to the in situ appearance of the brain tissue. Intraoperative cortical stimulation was firstly used by Krause to guide surgery, particularly to identify central sulcus in cases of motor epilepsy [37].

The 20th century was marked by several innovations in diagnostic and therapeutic fields. Phenobarbital was discovered in 1912 by Hauptmann and allows a new medical control of epilepsy. Imaging develops with radiography and its variants such as the pneumencephalography and angiography. In 1928, Hans Berger develops the electroencephalography, allowing a fundamental understanding of epilepsy. Wilder Penfield (1891-1976), proposed the concept of cerebral cortex "screaming" exerting a deleterious effect on the rest of the brain. He was the first who performs a temporal corticectomy in Montreal in 1928, and who describes in 1958 with Baldwin the resection of medial part of the temporal lobe (Figure 6) [38-40].

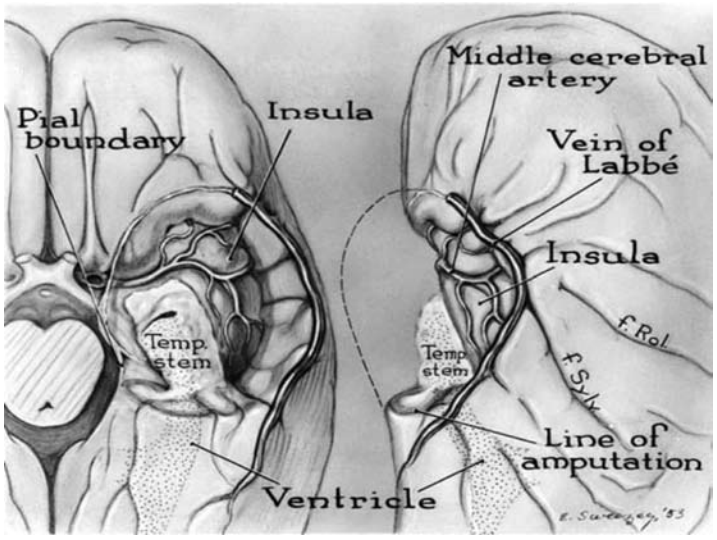

Figure 6: Drawing to show subtotal temporal lobectomy that includes the amygdala and up to 4 cm of the hippocampus as well as the antero-lateral temporal cortex, as described by Penfield and Baldwin in 1952 [40].

Erna Gibbs (1904-1988) et Frederick Gibbs (1903-1992) convinced Percival Bailey (1892-1973) to conduct an anterior temporal lobectomy in 1947 on the basis of anterior temporal spikes in the EEG [41, 42].

Stereotaxy was early implicated in the surgical treatment of pharmaco-resistant epilepsy. Spiegel and Wycis advocated the thermocoagulation of the dorso-medial nucleus of the thalamus. In France, Jean Talairach and Jean Bancaud used Stereotactic methods to insert deep brain electrodes in order to collect the origin and propagation of seizures: Stereo-Electro-Encephalography (SEEG). In addition, he performed an amygdaloid lesion by Yttrium90 under the same conditions in temporomesial epilepsy [43-45].

However, lobectomies carried out by North American school are considered until now as the best treatment for pharmaco-resistant focal epilepsy especially at the temporomesial area. Falconer described in 1953 «en bloc» removal of the uncus, anterior and lateral parts of hippocampus, T2 - T3, T4 - T5 gyri, and anterior (2 cm) T1. In 1958, Niemayer introduces the concept of selective resection of temporo-mesial structures. After a period of development of the medical treatment, H.G.Wieser and G.Yasargil in Zurich relaunched this surgery by development of the selective amygdalohippocampectomy [46-48].

During the twentieth century, other palliative surgical procedures were proposed for generalized epilepsy. Hemispherectomy was first utilized for epilepsy surgery in Toronto by McKenzie in 1938 and advocated for infantile hemiplegia.

Krynauw popularized the procedure in 1951 after reporting hemispherectomy on 12 children with infantile hemiplegia resulting in good seizure control [49, 50].
Other palliative surgery was corpus callosotomy for medically intractable epilepsies, and was based on the diminution of interhemispheric propagation of epileptic discharge, in order to decrease bilateral synchrony of cortical epileptiform activity and thus interrupt secondary seizure generalization. In 1940, Van Wagenen and Herren reported the first series of callosotomies for seizure control in humans. It is noteworthy that rationale for the surgery was based on the observation that patients with tumors of the corpus callosum would have decreasing seizure frequency as the callosum was destroyed by the tumor [51].
Among palliative surgical techniques, vagus nerve stimulation (VNS) is a worldwide applied technique for the treatment of intractable epilepsy that cannot benefit from resective surgery, even if the mechanism of action is not fully understood. Procedure consists to insert an electrode of stimulation around the left vagus nerve, all attached to a programmable generator buried in subclavicular subcutaneous space. Recent clinically-controlled trials of VNS have reported a 50% seizure control rate in about 30% of patients [52, 53].
Lars Leksell conceptualized radiosurgical treatment for neurologic disorders and progressively extended its utility. Differing from standard dose-fractionated radiotherapy, radiosurgery allows the neurosurgeon to deliver precise and accurate radiation to a smaller volume in a unique procedure without effecting large portions of normal parenchyma leading to a powerful radiobiological effect on the chosen targeted volume.
Patients with drug resistant focal epilepsy may potentially be managed by surgery. Among them, approximately one half may not fulfil the conditions for microsurgical approach of their seizure focus, or refuse microsurgery and its complication risks. Some of these patients can expect a clinical improvement after radiosurgical treatment [54].

Future

Experimental evidence for the involvement of the basal ganglia in the control of epilepsy have been discovered. Recently, the role of the basal ganglia (BG) among the circuitry involved in the genesis and propagation of different types of discharges has been widely studied in animal models. High level of evidence accumulated over the past 3 decades does support the theory that a system involving the substancia nigra reticulta and the BG may control the generation and spread of different kinds of seizures in animals (reviewed in Depaulis et al. in 1994). Although it is clear that the BG circuit cannot generate seizures and are unlikely to be involved in their initiation, numerous experimental data have revealed that thalamo-cortical connectivity influence the occurrence and/or cessation of epileptic seizures. Thalamus is suspected to be involved in temporal lobe epilepsy. Thalamic participation during seizure with impaired consciousness is required but cortex is probably leader [55, 56].
These experimental data have already led to initial clinical trials using high-frequency stimulation of the subthalmic nucleus in epileptic patients. Further researches will allow identification of the optimal target structures and the forms of epilepsy likely to benefit from this new therapeutic approach [57, 58].

Conclusion

Since prehistory, mankind was impressed by the clinical manifestations of Epilepsy due to its dramatic semiology. Thinkers of any time and any culture have tried to solve diagnostic, etiologic and therapeutic challenges. Unfortunately, they often fell into the meanders of the supernatural and fallacious scientific theories.
At each era, insightful minds did develop effective diagnostic and therapeutic methods. Today a majority of patients may benefit from multiple therapeutic options. For the others, the preliminary results of fundamental research in the field of epilepsy in general and the cortico basal coupling in particular will lead to new surgical and pharmacological treatments in a near future.

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Epilepsy Calendar events

American Clinical Neurophysiology Society 2013 Annual Meeting and Courses (ACNS 2013)
Du : 05 Février 2013 Au : 10 Février 2013
Lieu : Miami - Etats-Unis

International Stroke Conference 2013
Du : 06 Février 2013 Au : 08 Février 2013
Lieu : Honolulu - Hawaii

46th Annual Recent Advances in Neurology
Du : 13 Février 2013 Au : 15 Février 2013
Lieu : San Francisco, Californie - Etats-Unis

13th Congress of the Pan Arab Union of Neurological Societies
Du : 14 Février 2013 Au : 17 Février 2013
Lieu : Sharm El Sheikh – Egypte

Electromyography (EMG), Electroencephalography (EEG), and Neurophysiology in Clinical Practice
Du : 24 Février 2013 Au : 02 Mars 2013
Lieu : Amelia Island, FL - Etats-Unis

The 7th World Congress on Controversies in Neurology (CONy)
Du : 11 Avril 2013 Au : 14 Avril 2013
Lieu : Istunbul - Turquie

30th International Epilepsy Congress
Du : 23 Juin 2013 Au : 27 Juin 2013
Lieu : Montréal - canada

XXI World Congress of Neurology
Du : 21 Septembre 2013 Au : 26 Septembre 2013
Lieu : Vienne - Autriche

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