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Applied Clinical Neuroscience

Experimental Basic Neuroscience

Neuroeducation

Neurotechnology

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Um **NOVO PASSO** para uma vida com **NOVAS POSSIBILIDADES**

AGORA no BRASIL

Keppra® levetiracetam

- ***Keppra®** é o **único FAE** considerado **nível A** de evidência para o **tratamento de crises focais**, em terapia adjuvante, pelos guidelines da **ILAE***, em pediatria[1]
- ***Keppra®** solução oral, em terapia adjuvante, se mostrou bem tolerado no tratamento **de crises focais em crianças a partir de 1 mês de idade, crises mioclônicas (incluindo epilepsia mioclônica juvenil) a partir de 12 anos** e em crises tônico-clônicas primariamente generalizadas a **partir dos 6 anos de idade**[2,3,4,5]*

**International League Against Epilepsy*

CONTRAINDICAÇÃO: Hipersensibilidade ao princípio ativo ou a outros derivados da pirrolidona ou a qualquer um dos excipientes. **INTERAÇÃO MEDICAMENTOSA:** Foram observados relatos isolados de diminuição de eficácia quando o laxante osmótico macrogol foi administrado concomitantemente a levetiracetam oral. Assim, a administração oral de macrogol não deve ser realizada dentro de 1 hora (antes ou após) da administração de levetiracetam.

Referência Bibliográfica: 1. Wilmshurst JM, Summary of recommendations for the management of infantile seizures: Task Force Report for the ILAE Commission of Pediatrics. - Epilepsia. 2015 Aug; 56(8): 1185-97. **2.** Berkovic; Placebo-controlled study of levetiracetam in idiopathic generalized epilepsy – Neurology 2007; 69: 1751–1760. **3.** Piña Garza; Adjunctive levetiracetam in infants and young children with refractory partial-onset seizures - Epilepsia, 50(5): 1141-1149, 2009. **4.** Noachtar et al.; Levetiracetam for the treatment of idiopathic generalized epilepsy with myoclonic seizures - Neurology. 2008 Feb 19; 70(8): 607-16. **5.** Glauser; Double-blind placebo-controlled trial of adjunctive levetiracetam in pediatric partial seizures - Neurology. 2006 Jun 13; 66(11): 1654-60.

Keppra® (levetiracetam). **Apresentação**: Frasco de vidro âmbar contendo 150 mL de solução oral (100 mg/mL), acompanhado de uma seringa de 3 mL para administração. **Indicações**: é indicado como monoterapia para o tratamento de crises parciais, com ou sem generalização secundária em pacientes a partir dos 16 anos com diagnóstico recente de epilepsia. Keppra® também é indicado como terapia adjuvante no tratamento de: - crises convulsivas parciais em adultos, crianças e bebês a partir de 1 mês de idade, com epilepsia; - crises convulsivas mioclônicas em adultos e adolescentes a partir dos 12 anos, com epilepsia mioclônica juvenil; - crises convulsivas tônico-clônicas primárias generalizadas em adultos e crianças com mais de 6 anos de idade, com epilepsia idiopática generalizada. **Contraindicações**: Hipersensibilidade ao princípio ativo ou a outros derivados da pirrolidona ou a qualquer um dos excipientes. **Cuidados e Advertências**: para informações completas de advertências, vide bula do produto. A administração de Keppra® em pacientes com comprometimento renal poderá necessitar de um ajuste da dose. Foram notificados suicídio, tentativa de suicídio e ideias e comportamento suicida em pacientes tratados com levetiracetam. *Gravidez*: categoria C de risco de gravidez. Este medicamento não deve ser utilizado por mulheres grávidas sem orientação médica ou do cirurgião-dentista. Levetiracetam é excretado no leite humano materno. **Keppra®** é um medicamento. Durante seu uso, não dirija veículos ou opere máquinas, pois sua agilidade e atenção podem estar prejudicadas. *Interações medicamentosas (vide bula completa do produto)*: Dados indicam que levetiracetam não influencia as concentrações séricas de medicamentos antiepilépticos existentes (fenitoína, carbamazepina, ácido valproico, fenobarbital, lamotrigina, gabapentina e primidona) e que estes medicamentos antiepilépticos não influenciam a farmacocinética de levetiracetam. A probenecida (500 mg quatro vezes ao dia), um agente bloqueador da secreção tubular renal, mostrou inibir a depuração renal do metabólito primário, mas não a do levetiracetam. Contudo, a concentração deste metabólito permanece baixa. Levetiracetam 1000 mg por dia não influenciou a farmacocinética dos contraceptivos orais (etinilestradiol e levonorgestrel). Foram observados relatos isolados de diminuição de eficácia quando o laxante osmótico macrogol foi administrado concomitantemente a levetiracetam oral. Assim, a administração oral de macrogol não deve ser realizada dentro de 1 hora (antes ou após) da administração de levetiracetam. A extensão de absorção do levetiracetam não sofreu qualquer alteração com a ingestão de alimentos, mas a taxa de absorção diminuiu ligeiramente. Não estão disponíveis dados sobre a interação do levetiracetam com o álcool. *Reações Adversas*: para informações completas de reações adversas, vide bula do produto. Os eventos adversos mais comumente reportados nos estudos clínicos foram astenia, fadiga, dor de cabeça e sonolência. Adicionalmente às reações adversas relatadas durante os estudos clínicos, as seguintes reações adversas foram reportadas na experiência pós-comercialização, além de outras mencionadas na bula completa do produto: comportamento anormal, raiva, ataque de pânico, ansiedade, estado de confusão, alucinação, distúrbios psicóticos, suicídio, tentativa de suicídio e ideação suicida, parestesia, coreoatetose, discinesia, letargia. **Posologia**: A dose inicial recomendada para monoterapia no tratamento de crises parciais, com ou sem generalização secundária em pacientes a partir dos 16 anos com diagnóstico recente de epilepsia, é de 250 mg (2,5 mL) duas vezes ao dia, a qual poderá ser aumentada para uma dose terapêutica inicial de 500 mg (5 mL) duas vezes ao dia, após duas semanas. A dose máxima é de 1500 mg (15 mL) duas vezes ao dia. Nos casos de terapia adjuvante, para adultos e crianças acima de 12 anos e com peso igual ou superior a 50 kg, a dose terapêutica inicial é de 500 mg/duas vezes ao dia (5 mL/duas vezes ao dia). Esta dose poderá ser iniciada no primeiro dia de tratamento, a dose diária poderá ser aumentada até o máximo de 1500 mg/duas vezes ao dia (15 mL/duas vezes ao dia). Ainda nos casos de terapia adjuvante, para adolescentes, crianças e bebês a partir dos 6 meses com peso inferior a 50 kg a dose terapêutica inicial é de 10 mg/kg (0,1 mL/kg) duas vezes ao dia, a dose pode ser aumentada até 30 mg/kg (0,3 mL/kg) duas vezes ao dia. A alteração das doses não deve exceder aumentos ou reduções de 10 mg/kg (0,1 mL/kg) duas vezes ao dia, a cada duas semanas. Deve ser utilizada a dose eficaz mais baixa. A posologia em crianças com peso igual ou superior a 50 kg é igual à dos adultos. Nos casos de terapia adjuvante para bebês com mais de 1 mês e menos de 6 meses de idade a dose terapêutica inicial é de 7 mg/kg (0,07 mL/kg) duas vezes ao dia, a dose pode ser aumentada para um máximo de 21 mg/kg (0,21 mL/kg) duas vezes ao dia. A alteração das doses não deve exceder aumentos ou reduções de 7 mg/kg (0,07 mL/kg) duas vezes ao dia a cada duas semanas. Deve ser utilizada a dose eficaz mais baixa. A solução oral é a forma farmacêutica ideal para uso em bebês. **USO ADULTO E PEDIATRICO ACIMA DE 01 MES DE IDADE. USO ORAL. VENDA SOB PRESCRIÇAO MEDICA – SO PODE SER VENDIDO COM RETENÇAO DA RECEITA. SE PERSISTIREM OS SINTOMAS, O MEDICO DEVERA SER CONSULTADO.** Para maiores informações, consulte a bula completa do produto. (0302040021R8 Rev. Agosto 2015). www.ucb-biopharma.com.br **Reg. MS – 1.2361.0083**

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JECN Journal of Epilepsy and Clinical Neurophysiology

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JECN Journal of Epilepsy and Clinical Neurophysiology

Instructions for authors / Instruções aos autores / Instrucciones para los autores

Most recent revision: March 2015

The Journal of Epilepsy and Clinical Neurophysiology (JECN) is the Official Body of the Brazilian Epilepsy League, whose purpose is to publish original scientific-technological articles about epilepsy and clinical neurophysiology, resulting from ethically developed and approved clinical and experimental research. Volumes are published annually, with quarterly editions, in March, June, September and December of each year. The articles submitted must be original and concise, written in English, Portuguese or Spanish. The text should be prepared in accordance with the technical standards, and sent via the publications management system. In order to be approved, the articles will be submitted for evaluation by a panel of reviewers (peer review), who will receive the text anonymously and decide on its publication, suggest changes, request clarification from the authors, and provide recommendations to the Editor-in-Chief. The concepts and statements contained in the work are the sole responsibility of the authors. The Journal Epilepsy and Clinical Neurophysiology follows, in full, the international trend of the Vancouver style, which is available at www.icmje.org.br. We thank the authors, in advance, for their collaboration in following the instructions.

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Type of Article	Abstract	Number of words	References	Figures	Tables
Original	Structured with up to 250 words	6.000 not including the abstract, references, tables and figures	45	10	6
Update / Review Case Report	It is not structured with up to 250 words	6.000 not including the abstract, references, tables and figures	60	3	2
Editorial	0	500	5	0	0

MANUSCRIPT PREPARATION: The Journal of Epilepsy and Clinical Neurophysiology receives the following types of manuscript for publication: Original Articles, Update and Reviews Articles, Case Report, Editorial. The manuscripts should be submitted in accordance with PC standard, in Word files, double spaced, with wide margins, and the author shall include a signed letter of authorization for publication, declaring that it is an original work, and that it has not been, or is not being submitted for publication in any other journal. Ensure that the manuscript is fully in accordance with the instructions.

CLINICAL TRIALS: The Journal of Epilepsy and Clinical Neurophysiology supports the policies for the recording of clinical trials of the World Health Organization (WHO) and the International Committee of Medical Journal Editors (ICMJE), recognizing the importance of these initiatives for the recording and international disclosure of information on clinical trials, in open access. Accordingly, only clinical research articles that have received an identification number in one of the Clinical Trial Records validated by the WHO and ICMJE criteria will be accepted for publication. The addresses for these records are available on the ICMJE website (www.icmje.org). The identification number should be declared in the text.

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ORGANIZATION OF THE ELECTRONIC FILE: All parts of the manuscript must be included in a single file, which must be organized with the cover page first, then the text, AND THE references followed by figures (with captions) and at the end, tables and charts (with captions).

COVER PAGE: The cover page must include:

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ABSTRACT: The Abstract must be structured in the case of original articles, and must clearly present the study objectives, with historical data, methods, results, and the main conclusions. It must be written Portuguese, English and Spanish, and should not exceed 200 words.

DESCRIPTORS: Must contain at least three key words in Portuguese based on the Health Sciences Descriptors (DeCS) -http://decs.bireme.br. In English, submit keywords based on the Medical Subject Headings (MeSH) - http://www.nlm.nih.gov/mesh/meshhome.html, at least three and at most six citations.

INTRODUCTION: Present the subject and purpose of the study, and provide citations, without giving an external review of the subject.

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CONCLUSION: Must be clear and concise and establish a connection between the conclusion and the study objectives. Avoid conclusions not based on data.

ACKNOWLEDGEMENT: Addressed to persons who have collaborated intellectually but whose contribution does not constitute co-authorship, or those who have provided material support.

REFERENCES: Quote up to about 20 references, restricted to the bibliography essential to the content of the article. Number references consecutively in the order in which they are mentioned in the text, using superscript Arabic numerals, in the following format: (Reduction of functions of the terminal plate.[1]) Give the names of the first three authors, followed by et al.

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b) Books: Author(s) or editor(s). Title of the book. Edition, if not the first. Translator(s), if applicable. Place of publication: publisher, year. E.g. Diener HC, Wilkinson M, editors. Drug-induced headache. 2nd ed. New York: Spriger-Verlag; 1996.

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d) Summaries: Author(s). Title, followed by (summary). Journal year; volume (supplement and its number, if applicable): page(s) E.g. Enzensberger W, Fisher PA. Metronome in Parkinson's Disease (abstract). Lancet. 1996 ;34:1337.

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Revisão mais recente: Março de 2015

A Revista Journal of Epilepsy and Clinical Neurophysiology (JECN) é o Órgão Oficial da Liga Brasileira de Epilepsia, cujo propósito é publicar artigos científico-tecnológicos originais sobre epilepsia e neurofisiologia clínica, resultante de pesquisas clínicas e experimentais, eticamente desenvolvidas e aprovadas. Os volumes são publicados anualmente, com edições trimestrais em março, junho, setembro e dezembro de cada ano. Os artigos submetidos devem ser inéditos e concisos, redigidos em inglês, português ou espanhol. O texto deverá ser preparado de acordo com as normas técnicas e enviados pelo sistema de gerenciamento de publicações. Os artigos para serem aprovados são submetidos à avaliação de uma comissão de revisores (peer review) que recebem o texto de forma anônima e decidem por sua publicação, sugerem modificações, requisitam esclarecimentos aos autores e efetuam recomendações ao Editor Chefe. Os conceitos e declarações contidos nos trabalhos são de total responsabilidade dos autores. A Journal of Epilepsy and Clinical Neurophysiology segue na íntegra a tendência internacional do estilo Vancouver, disponível (www.icmje.org.br). Desde já agradecemos a colaboração dos autores no atendimento às instruções citadas.

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Tipo de Artigo	Resumo	Número de Palavras	Referências	Figuras	Tabelas
Original	Estruturado com até 250 palavras	6.000 Excluindo o resumo, referências, tabelas e figuras	45	10	6
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Editorial	0	500	5	0	0

PREPARAÇÃO DE MANUSCRITO: A Journal of Epilepsy and Clinical Neurophysiology recebe para publicação os seguintes tipos de manuscritos: Artigo Original, Artigo de Atualização e Revisão, Relato de Caso. Os manuscritos enviados deverão estar em padrão PC com arquivos em *Word*, espaço duplo, com margem larga, devendo o autor inserir carta assinada, autorizando sua publicação, declarando que o mesmo é inédito e que não foi, ou está sendo submetido à publicação em outro periódico. Certifique-se de que o manuscrito se conforma inteiramente às instruções.

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PÁGINA DE ROSTO: A página de rosto deve conter:

a) o tipo do artigo (artigo original, de revisão ou atualização);

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c) o nome completo de cada autor (sem abreviações); e a instituição a que pertence cada um deles;

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RESUMO: O Resumo deve ser estruturado em caso de artigo original e deve apresentar os objetivos do estudo com clareza, dados históricos, métodos, resultados e as principais conclusões em português, inglês e espanhol, não devendo ultrapassar 200 palavras.

DESCRITORES: Deve conter no mínimo três palavras chaves baseadas nos Descritores de Ciências da Saúde (DeCS) -http://decs.bireme.br. No inglês, apresentar keywords baseados noMedical Subject Headings (MeSH) - http://www.nlm.nih.gov/mesh/meshhome.html, no mínimo três e no máximo seis citações.

INTRODUÇÃO: Deve apresentar o assunto e objetivo do estudo, oferecer citações sem fazer uma revisão externa da matéria.

MATERIAL E MÉTODO: Deve descrever o experimento (quantidade e qualidade) e os procedimentos em detalhes suficientes que permitam a outros pesquisadores reproduzirem os resultados ou darem continuidade ao estudo. Ao relatar experimentos sobre temas humanos e animais, indicar se os procedimentos seguiram as normas do Comitê Ético sobre Experiências Humanas da Instituição, na qual a pesquisa foi realizada ou de acordo com a declaração de Helsinki de 1995 e Animal Experimentation Ethics, respectivamente. Identificar precisamente todas as drogas e substâncias químicas usadas, incluindo os nomes genéricos, dosagens e formas de administração. Não usar nomes dos pacientes, iniciais, ou registros de hospitais. Oferecer referências para o estabelecimento de procedimentos estatísticos.

RESULTADOS: Apresentar os resultados em sequência lógica do texto, usando tabelas e ilustrações. Não repetir no texto todos os dados constantes das tabelas e ou ilustrações. No texto, enfatizar ou resumir somente as descobertas importantes.

DISCUSSÃO: Enfatizar novos e importantes aspectos do estudo. Os métodos publicados anteriormente devem ser comparados com o atual para que os resultados não sejam repetidos.

CONCLUSÃO: Deve ser clara e concisa e estabelecer uma ligação entre a conclusão e os objetivos do estudo. Evitar conclusões não baseadas em dados.

AGRADECIMENTOS: Dirigidos a pessoas que tenham colaborado intelectualmente, mas cuja contribuição não justifica coautoria, ou para aquelas que tenham provido apoio material.

REFERÊNCIAS: Citar até cerca de 20 referências, restritas á bibliografia essencial ao conteúdo do artigo. Numerar as referências de forma consecutiva de acordo com a ordem em que forem mencionadas pela primeira vez no texto, utilizando-se números arábicos sobrescritos, no seguinte formato: (Redução das funções da placa terminal.[1]) Incluir os três primeiros autores seguidos de et al.

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a) Artigos: Autor(es). Título do artigo. Título do Periódico. ano; volume: página inicial - final

Ex.: Campbell CJ. The healing of cartilage deffects. Clin Orthop Relat Res. 1969;(64):45-63.

b) Livros: Autor(es) ou editor(es). Título do livro. Edição, se não for a primeira. Tradutor(es), se for o caso. Local de publicação: editora; ano. Ex.: Diener HC, Wilkinson M, editors. Drug-induced headache. 2nd ed. New York: Spriger-Verlag; 1996.

c) Capítulos de livros: Autor(es) do capítulo. Título do capítulo Editor(es) do livro e demais dados sobre este, conforme o item anterior. Ex.: Chapman MW, Olson SA. Open fractures. In: Rockwood CA, Green DP. Fractures in adults. 4th ed. Philadelphia: Lippincott-Raven; 1996. p. 305-52.

d) Resumos: Autor(es). Título, seguido de [abstract]. Periódico ano; volume (suplemento e seu número, se for o caso): página(s) Ex.: Enzensberger W, Fisher PA. Metronome in Parkinson's disease [abstract]. Lancet. 1996;34:1337.

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g) Material eletrônico: Título do documento, endereço na internet, data do acesso. Ex: Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis. [online] 1995 Jan-Mar [cited 1996 Jun 5];1(1):[24 screens]. Available from:URL:http://www.cdc.gov/ncidod/EID/eid.htm

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Revisión más reciente: Marzo 2015

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Tipo de Artículo	Resumen	Número de Palabras	Referencias	Figuras	Tablas
Original	Estructurado con hasta 250 palabras	6.000 Excluyendo el resumen, referencias, tablas y figuras	45	10	6
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a) el tipo de artículo (artículo original, de revisión o actualización);

b) el título completo en portugués, inglés y español con hasta 120 caracteres debe ser conciso, aunque informativo;

c) el nombre completo de cada autor (sin abreviaciones); y la institución a la que pertenece cada uno de ellos;

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RESUMEN: El Resumen debe ser estructurado en caso de artículo original y debe presentar los objetivos del estudio con claridad, datos históricos, métodos, resultados y las principales conclusiones en portugués, inglés y español, no debiendo sobrepasar 200 palabras.

DESCRIPTORES: Debe contener como mínimo tres palabras llave basadas en los Descriptores de Ciencias de la Salud (DeCS) -http://decs.bireme.br. En inglés, presentar keywords basados en el Medical Subject Headings (MeSH) - http://www.nlm.nih.gov/mesh/meshhome.html, como mínimo tres y como máximo seis citaciones.

INTRODUCCIÓN: Debe presentar el asunto y objetivo del estudio, ofrecer citaciones sin hacer una revisión externa de la materia.

MATERIAL Y MÉTODO: Debe describir el experimento (cantidad y calidad) y los procedimientos en detalles suficientes que les permita a otros investigadores reproducir los resultados o darle continuidad al estudio. Al relatar experimentos sobre temas humanos y animales, indicar si los procedimientos siguieron las normas del Comité Ético sobre Experiencias Humanas de la Institución, en la que la investigación fue realizada o de acuerdo con la declaración de Helsinki de 1995 y Animal Experimentation Ethics, respectivamente. Identificar detalladamente todas las drogas y sustancias químicas usadas, incluyendo los nombres genéricos, dosajes y formas de administración. No usar nombres de los pacientes, iniciales, o registros de hospitales. Ofrecer referencias para el establecimiento de procedimientos estadísticos.

RESULTADOS: Presentar los resultados en secuencia lógica del texto, usando tablas e ilustraciones. No repetir en el texto todos los datos que constan en las tablas y o ilustraciones. En el texto, enfatizar o resumir solamente los descubrimientos importantes.

DISCUSIÓN: Enfatizar nuevos e importantes aspectos del estudio. Los métodos publicados anteriormente deben ser comparados con el actual para que los resultados no sean repetidos.

CONCLUSIÓN: Debe ser clara y concisa y establecer una conexión entre la conclusión y los objetivos del estudio. Evitar conclusiones no basadas en datos.

AGRADECIMIENTOS: Dirigidos a personas que hayan colaborado intelectualmente, pero cuya contribución no justifica coautoría, o para aquellas que hayan suministrado apoyo material.

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Los títulos de periódicos deberán ser abreviados de acuerdo con el Index Medicus.

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TABLAS: Las tablas deben ser numeradas por orden de aparición en el texto con números arábigos. Cada tabla debe tener un título y, si fuera necesario, un subtítulo explicativo. Los cuadros y tablas deberán ser enviados a través de los archivos originales (p.e. Excel).

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JECN Journal of Epilepsy and Clinical Neurophysiology

Contents/Sumário/Contenido

ABSTRACTS PRESENTED AT THE 3rd BRAINN CONGRESS BRAZILIAN INSTITUTE OF NEUROSCIENCE AND NEUROTECHNOLOGY (CEPID–FAPESP)

APRIL 11th TO 13th 2016

Abstracts/Resumo/Resumen

JECN Journal of Epilepsy and Clinical Neurophysiology

ABSTRACTS PRESENTED AT THE 3rd BRAINN CONGRESS BRAZILIAN INSTITUTE OF NEUROSCIENCE AND NEUROTECHNOLOGY (CEPID–FAPESP) - APRIL 11th TO 13th 2016

Applied Clinical Neuroscience

DTI ANALYSIS OF TEMPORAL STEM AFTER ANTERIOR LOBECTOMY

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Introduction: This present work consists on a study of temporal stem (TS) components after modified anterior temporal lobectomy (developed in our service) in patients with temporal lobe epilepsy (TLE). The aim of DTI analysis of TS is to evaluate the anatomical consequences of this non selective access to the integrity of white matter fibers. **Materials and Methods:** DTI analysis was done in both hemispheres of 26 patients who underwent modified anterior temporal lobectomy (MAL), also was performed in both hemispheres of 33 healthy controls (control group – CTR). The tracts analyzed were inferior fronto - occipital fasciculus (IFOF), uncinate fasciculus (UF) and optic radiation (OR) of TS. All data were measured using the analysis of variance with Turkey's post-test (SYSTAT 13 software), considering p< 0, 05 as a significant result. **Results:** This study found that TS analysis showed complete interruption of UF in 80,77% of MAL patients and 11,54% presented complete interruption of the IFOF. Utilizing controls, there was no significant difference comparing the fractional anisotropy (FA) from OR of CTR and MAL groups, while the comparisons of the UF and IFOF remaining fibers between the MAL and CTR groups showed significant diference (p<0,05) with lower FA for the surgical group. **Discussion:** The results found an important damage to the UF and IFOF fibers that are located at the anterior portion of the TS and implication on the integrity of remaining fibers. The most anterior fibers of the OR showed to be severed in some patients but the remaining fibers didn't show to be damaged. This suggests also involvement of function, which could lead to visual field deficit and neuropsychological loss, such as verbal memory. **Conclusion:** Despite MAL has been proposed to spare the temporal stem and its fibers we could find some anatomic damage to the anterior part of the TS, mainly the UF and IFOF. Further correlations between these findings and visual field exams and neuropsychological data are needed for better understanding the clinical value of these DTI abnormalities, allowing better understanding of the implications of the MAL in patients's quality of life.

INTRANETWORK AND INTERNETWORK CONNECTIVITIES IN ALZHEIMER'S DISEASE AND THE RELATIONSHIP WITH CSF BIOMARKER LEVELS

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Introduction: Many studies have reported abnormal functional connectivity (FC) within the default mode network (DMN) in Alzheimer's disease (AD) over the last decade. Few studies, however, have investigated other resting-state networks as well as their relationship with physiopathology. In this work we aimed to check for connectivity alterations within (intranetwork FC) and among RSNs (internetwork FC) in mild AD patients and amnestic mild cognitive impairment (aMCI) subjects; and investigate possible associations between AD physiopathology extracted from cerebrospinal fluid (CSF) and intra/internetwork FC. **Materials and Methods:** 30 mild AD patients, 24 aMCI patients, and 48 healthy controls had imaging acquired on a 3.0T MRI Philips Achieva® scanner. CSF samples were obtained only from aMCI subjects. We performed imaging analysis in UF²C (www.lni.hc.unicamp.br/app/uf2c), and regions of interest (ROIs) were obtained from http://findlab.stanford.edu/functional_ROIs.html (analyzed by adjacency matrices). We used a total of 70 ROIs of 12 networks: anterior and posterior Salience (antSAL and postSAL), Basal Ganglia (BG), dorsal and ventral DMN (dDMN and vDMN), left and right Executive Control (lECN and rECN), Auditory (AUD), Visual (VN), Language (LN), Sensorimotor (SMN), and Visuospatial (VSN). **Results:** aMCI subjects had weaker negative FC between areas of the LN, VN, VSN, left ECN, and dDMN. Connections involving other regions of the postSAL, LN, and left ECN were all positive in controls, while they were negative in aMCI subjects. AD patients also presented weaker FC in several regions belonging to many RSNs beyond the DMN (although mainly in the dDMN and vDMN). An inverted pattern of connectivity occurred between some ROIs of the dDMN and vDMN (positive correlation in controls and negative in patients). Regarding the relationship with CSF values, all proteins levels correlated with the FC of many RSNs, but tau levels, specifically, correlated the most with FC disruption. **Discussion:** In AD, the pairs that presented an inversion of correlation signal involved areas typically belonging to the DMN, a well-known disrupted network in the disease that accumulates amyloid-beta. In aMCI subjects, an inversion of the correlation signal involved the medial temporal regions, possibly reflecting atrophy in these structures. Another explanation could be that the temporal regions present extensive anatomical connections with posterior regions that are known to accumulate amyloid-beta. Elevated tau level is considered an indicator of neuronal degeneration, that seeds and spreads along the neuroanatomical connections, affecting the FC between brain areas. **Conclusion:** In conclusion, the functional alterations in AD and aMCI subjects extend beyond the connectivity within networks and also involve alterations among different networks (observed by both weaker connectivity and opposed correlation signal). In aMCI subjects, intra and internetwork alterations correlated to all protein physiopathological measures obtained from CSF. Subjects with higher tau levels, specifically, exhibited the highest network disruption, suggesting a crucial role between this protein and network dysfunction.

TWO DIFFERENT MENTAL MODELS REVEAL DISTINCT INTERACTIONS BETWEEN FUNCTIONAL NETWORKS

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Introduction: In response to the increasing number of medical errors, healthcare improvement initiatives have implemented a more standardized workplace to enhance patient safety and decrease professional workload [1]. According to Bressan [2], information from a workplace is received, processed and used differently by people with distinct mental models. In this sense, mental models can be divided into: 'operational' - those who receive information and make decisions based in a concrete plan, and 'strategic' - who organize information, identifying new possibilities to support decisions. Yet, there are no references of evidence concerning this classification and the brain response to different levels of organization. Within the field of Neuroscience applied to Management, functional Magnetic Ressonance Imaging (fMRI) laid the foundation to differentiate entrepreneurs behavior [3], as well as to understand brain activation and connectivity in task-based studies [4]. In this research, interactions between functional networks are analyzed to compare the two groups (operational and strategic) while searching for tools in a disorganized healthcare setting. **Methods:** fMRI images (TR=2s, voxel=3x3x3 mm^3, FOV=240x240x117mm^3) of 39 healthy volunteers classified as operational (n_a=24) and strategic (n_b=15) were acquired on a 3T MR

(Philips Achieva). Using UF²C (on a PC with Matlab and SPM8) we first ran a preprocessing pipeline and the Cross-Correlation modality with 70 ROIs from 12 functional networks. During the exam, volunteers were given 20s to mentally identify 5 units of four different healthcare items (syringes, scissors, bandages and a medicine) in a picture, which illustrated a disorganized set of medical and non-medical tools. This picture was developed by Prof. Earl Murmann (Massachusetts Institute of Technology), as part of a Master of Science research about functional organization of the workplace. **Results:** According to the *t* test, four functional modules presented intra-connectivity significant differences ($p<0.05$) between the groups: visuospatial, language, basal ganglia and post salience networks, while only two inter-connectivity alterations were observed: visuospatial and language networks. Considering these hubs, both overall and within-module connectivity were significantly greater among individuals classified as operational, revealing a more widely distributed pattern of functional connectivity in the globalizing group. **Discussion:** Previous findings refer to the *basal ganglia network* as involved in action selection, helping to determine which behavior to execute at any given time, while the *post salience network* is implicated in disparate cognitive, affective and regulatory functions, including interceptive awareness, emotional responses and empathic processes [5]. Nevertheless, *visuospatial* and *language* networks play an important role in the coordination of information flow. Results from this study suggest a lower specificity in the recruitment of those specific brain networks within the operational group. **Conclusion:** This work provides evidence of differences in functional connectivity between 'operational' and 'strategic' while receiving and processing disorganized information. Therefore, the results imply different patterns of brain activation corresponding to these two mental models.

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GENERALIZED EPILEPSIES AND PERSISTENT SEIZURES: CLINICAL AND NEUROIMAGING FEATURES

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Introduction: Idiopathic generalized epilepsies (IGE) are usually associated with good response to antiepileptic drugs and normal brain MRI. Recent studies have demonstrated structural and functional alterations in these patients, without noticing differences between seizure-free and patients with persistent seizures[1]. **Objective:** To compare clinical and MRI differences in IGE patients with and without seizure control. **Methods:** We consecutively recruited 40 IGE patients (25 women, 33± 10 years) and 118 healthy controls, paired for age and gender. Patients were classified as seizure free (SZ-free, 21 subjects) or refractory seizures (SZ-refr,19 subjects). All subjects underwent high-resolution T1 weighted images scan on 3T MR device. Images were automatically parcellated with Freesurfer 5.3. We compared cortical and subcortical volumes between patients and controls. In a subsequent analysis we searched for differences between patients with and without seizures. **Results:** After covarying MANOVA for intracranial volume, IGE group presented reduced volume of subcortical grey matter ($p<0.05$), but not of white matter or cortical GM volume. Cortical thickness was thinner in right precentral gyrus and left paracentral area. The thalamus volume is indicated in figure 1. Clinically, SZ-free and SZ-ref groups were balanced for gender, age, age of onset and occurrence of absence seizures. A preliminary analysis with logistic regression (SZ-free x SZ-refr) suggested that presence of myoclonus was associated with persistent seizures ($p=0.017$). **Discussion:** Our results indicate that some IGE patients persist with seizures despite medication, even with polytherapy. These preliminary analyses suggest that thalamic volume is reduced in controlled patients, who also present less myoclonus than patients with seizures. Further analyses with white matter and functional connectivity may add information about factors related to differences in seizure control.

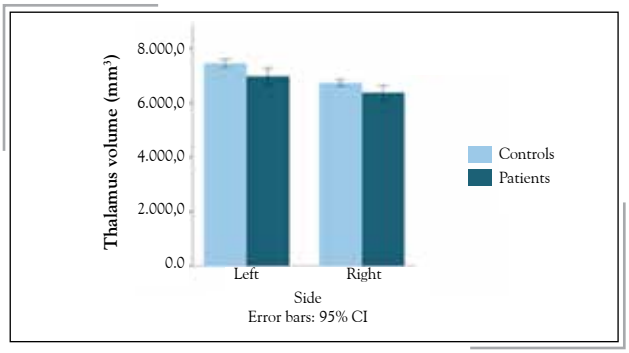
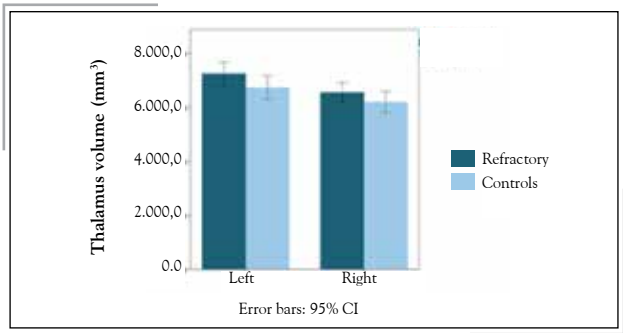


Figure 1. Controls and Patients Thalamic volumes.



Figuree 2. Controls and Refractory patients Thalamic volumes.

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GRAY MATTER ATROPHY IN PATIENTS WITH EPILEPTIC ENCEPHALOPATHY OF UNKNOWN CAUSE

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Introduction: Epileptic encephalopathies are characterized by epilepsies in which the epileptic activity alone can contribute to the poor outcome in terms of the seizures, as well as the cognitive and behavioral impairment[1,2]. Little is known about its pathophysiological mechanisms, in particular the pathological changes in structural neuronal networks[3]. The aim of this study is to evaluate the presence and distribution of gray matter (GM) atrophy in children with epileptic encephalopathies. **Materials and Methods:** We included six patients with clinical diagnosis of epileptic encephalopathy followed at Clinical Hospital of UNICAMP and 12 age and sex matched controls. Clinical data was collected through structured questionnaire. Cerebral T1-weithed volumetric images of patients and controls were acquired in a 3 Tesla MRI (Phillips Achieva, Netherlands). Voxel based morphometry (VBM) was used to evaluate GM volume with SPM8 software (Statistical Parametric Mapping - Welcome Department of Cognitive Neurology, http://www.fil.ion.ucl.ac.uk) (Two-sample T-test, $p<0.001$, minimum of 20 contiguous voxels). **Results:** There was no difference of age or sex distribution between patients and controls (patients: mean age 14 years (range 7 to 19), 67% women; controls: mean age 13 (range 8-18), 67% women). Mean age of seizure onset was 2.6 years (range 2 months to 10.6 years). All patients had history of focal seizures and 5 had concomitant primary generalized seizures. Two patients had history of status epilepticus. The most commonly used anti-epileptic drug was valproate and clobazam (100% of patients). VBM analysis showed GM atrophy in patients with epileptic encephalopathy, including the following areas: left pre and postcentral gyri and insula. **Discussion:** Our results show areas of GM atrophy exclusively localized in the left hemisphere of patients with epileptic encephalopathy. Few studies so far have tried to evaluate GM abnormalities in specific types of epileptic encephalopathies. One study showed increased GM in temporal lobe of patients with West Syndrome[4]. In contrast, a study in patients with Dravet Syndrome revealed no differences in GM volume[5]. The causes of these possible structural changes in children with epileptic encephalopathy also remain unknown, but the occurrence of seizures, especially status epilepticus, could contribute to it. Most importantly, efforts have to be made to understand if the structural abnormalities could contribute to the cognitive and behavior impairment of these children. **Conclusion:** Patients with epileptic encephalopathy present areas of gray matter atrophy localized in the frontal, parietal and insular regions of left hemisphere**.** Additional studies with larger sample sizes are necessary to confirm these findings.

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MANDALAS OF EMOTIONS FACILITATE PERCEPTION OF FEELINGS

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Introduction: Epilepsy is a chronic disease with a psychosocial impact on patient. Although there has been a significant progress for the development of novel treatments in epilepsy, there is still a great psycho-social burden associated with this condition [1]. In this sense, patients with epilepsy may find it difficult to talk about their feelings. The technique called 'Dialogue with the feelings through mandalas' consists of an integrative practice derived from the traditional Chinese medicine [2].

Its main goal is to facilitate the expression and awareness of emotions, through a greater connection between body and mind. **Materials and Methods:** Patients were recruited at the Epilepsy Outpatients Clinic of the Hospital of Clinics (University of Campinas), with the approval of Ethics Committee. Volunteers provided written informed consent to participate in the study and were randomly divided into two groups: 'Control' and 'Intervention'. Both groups received the same initial recommendations: 'please, lie down, relax and pay attention to your breath'. The intervention protocol is divided into two stages: first, the step 'harmonization' consists of placing five stones around the participant for five minutes, and after, the mandala is applied according to the emotion chosen by the participant, which lasts ten minutes. The total intervention time was fifteen minutes, the same for control. Then individual assessment was performed blinded to whom received intervention using a structured questionnaire and Likert-scales about the degree of relaxation and feelings after the experiment. Statistical analysis was conducted with MyStat using non-parametric tests (Mann-U-test, Wilcoxon) and Chi-square. **Results:** Forty-six volunteers participated of this study, divided into two groups: 20 participants in the 'control' group and 26 in the 'intervention' group. Groups did not differ for sex, age, years of schooling, onset of seizures, last seizure, frequency of seizures, use of monotherapy and seizure control. There is a significant difference between groups for perception of body changes (69.23% of patients in the intervention group perceived body changes, compared to 35% in the control group, p=0.02). Fifty percent of patients that were submitted to 'Mandalas of Emotions' reported being 'extremely relaxed', whereas only 25% reported this outcome in control group (p=0.037). The comparison between perception of emotion before and after the procedure showed a significant change in the intervention group (mean pre-procedure: 3.19 +/-1.41; mean post-procedure: 3.92+/-0.93, p=0.006) but not in the control group (mean pre-procedure: 3.45+/-0.88, mean post-procedure: 3.70+/-1.21, p=0.23). **Discussion:** Results of this study suggest the potential for awakening emotions and physical changes using this novel technique, in order to mediate the recognition and to work on emotions, enhancing coping with the conditions imposed by the disease. When facing internal conflicts, patients may develop a blockage in self ability, understanding of feelings and social withdrawal, implying directly in the way they express their emotions, desires and opinions. **Conclusion:** The present work suggests that 'Mandalas of Emotion' may facilitate the perception of feelings, since there was a significant difference between groups for body changes and also a significant change in perception of emotion pre and post intervention.

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WORSE COGNITIVE PERFORMANCE IS ASSOCIATED TO DEFAULT MODE NETWORK ABNORMALITIES IN ISCHEMIC STROKE

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Introduction: One-third of patients that suffered a stroke will face cognitive decline, which negatively impacts outcome[1]. Resting-state functional connectivity is defined as temporal correlation between spatially remote regions of brain[2]. The Default Mode Network (DMN) is one of most prominent resting-state functional network and it has been associated to cognitive and emotional processing. We aimed to investigate whether resting state functional connectivity of DMN was associated to cognitive performance in stroke patients. **Materials and Methods:** The present study was approved by ethics committee and all individuals gave written informed consent for their participation. Thirty-four subacute (less than one month from the ictus) stroke patients aged between 45-80 who had experienced their first-ever ischemia and without previous neurological history were submitted to: 1) neuropsychological evaluation through Montreal Cognitive Assessment (MoCA) and 2) functional Magnetic Resonance Imaging (fMRI) acquisition using a 3T scanner (Philips Achieva®). The image processing were based on realignment, segmentation, normalization (MNI-152) and smoothing, using UF^{2}C (User Friendly Functional Connectivity) toolbox. One-way analysis of variance was performed in SPM12 for MATLAB, adjusting for gender, age, educational level and Fazekas score and following the parameters of p<0.001 uncorrected and cluster size with at least 50 voxels. **Results:** We found a negative correlation between MoCA scores and DMN functional connectivity in left middle frontal gyrus and left inferior parietal gyrus (table 1 and figure 1), suggesting that worse cognitive performance is related to increased functional connectivity of DMN core areas.

Table 1. Coordinates and cluster size of negatively correlated area between MoCA scores and DMN functional connectivity (p<0.001, uncorrected).

		Stereotaxic coordinates (mm)				
Cluster size	Region	X	Y	Z	T value	Z value
67	Left middle frontal gyrus	-40	48	10	4.35	3.80
66	Left inferior parietal gyrus	-48	-52	56	4.20	3.69

Figure 1. Correlation results between MoCA scores and DMN functional connectivity (p<0.001, uncorrected).

Discussion: Previous studies indicate that DMN plays an important role in cognitive impairment[3]. Deactivation of key nodes of the DMN may be a prerequisite for focused attention and successful memory encoding[4]. However, the increased DMN functional connectivity suggests failure to suppress activity in some of the core DMN in cognition, which in turn is associated with worse performance in MoCA scores[5]. **Conclusion:** Abnormal DMN was associated with worse cognitive performance following stroke in subacute stage. Our findings may be helpful for facilitating further understanding of the potential mechanism underlying post stroke cognitive performance.

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DIFFUSION TENSOR IMAGING OF CORTICOSPINAL TRACT, CINGULUM AND CORPUS CALLOSUM IN PARKINSON'S DISEASE (PD) PATIENTS

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Introduction: Considering the variability of symptoms of Parkinson's disease (PD) and the still unclear etiology, MRI-based studies are important tools to better understand the mechanisms behind the disease [1]. Diffusion tensor imaging (DTI) is a valuable tool to assess abnormalities in PD [2], especially in early stages. Previous studies demonstrated fractional anisotropy (FA) reduction in substantia nigra, globus pallidus, thalamus, uncinate fasciculus, superior longitudinal fasciculus and thalamic radiation [3]. Our main objective was to evaluate white matter tractography of the corticospinal tract, cingulum and corpus callosum in PD. **Materials and Methods:** 58 patients with PD (42 men, mean age 60.3 years, SD 8.99; average disease duration 7.88, SD 6.29) and 33 healthy subjects (mean age 57.8 years, SD 10.59) underwent the same MRI protocol, and 46 patients were assessed by clinical scales and a complete neurological evaluation. We performed DTI analysis using the ExploreDTI software to compare PD patients and controls. After the initial analysis we divided patients into early PD, moderate PD and severe PD. For statistical analysis we used Stata 13.1 (http://www.stata.com). **Results:** We found higher FA and reduced medial (MD), radial (RD) and axial diffusivity (AD) in the corticospinal tract. Diffusion values from the mild PD group were also different than controls. There was no difference between patients and controls at cingulum, however we found reduced FA in severe PD in comparison to controls. At corpus callosum we found lower FA in PD when compared to controls. There was also an association between MD and RD values of the corticospinal tract and cingulum with SCOPA-COG scores, and between FA and RD values of the corpus callosum and UPDRS-III scores. **Discussion:** We assesses three tracts relevant to PD and found abnormalities in all of them, demonstrating important white matter involvement in the disease. We also found differences between groups, showing that more severe patients have more diffuse brain alterations. The association between diffusion values and scales scores also demonstrate a relation between motor and non-motor symptoms and cerebral abnormalities. **Conclusion:** Our data suggest that DTI analysis is a sensitive tool to asses microstructural abnormalities already in early stages of the disease and in areas beyond the substancia nigra, and the association with clinical scores indicate that these alterations might be measured indirectly by clinical evaluation.

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ENTORHINAL AND CINGULATE CORTICAL THICKNESS PREDICTS EPISODIC MEMORY AND GLOBAL COGNITION IN MILD ALZHEIMER'S DISEASE

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Introduction: Hippocampal atrophy is a potential biomarker for Alzheimer disease (AD). However, there are other atrophic areas during the development of this disease. Amnestic Mild Cognitive Impairment (aMCI) is a clinical condition where the patient presents a memory impairment but with normal daily activities. It is important to analyze what areas are impaired in AD and aMCI compared to controls, and also see if the atrophic areas could influence the cognitive performance of this population. Therefore, we aimed to analyze if cortical thickness may influence a global cognitive test (Mini Mental State Exam, MMSE) and verbal episodic memory (Rey Auditory Verbal learning test, RAVLT). **Materials and Methods:** 67 voluntaries were evaluated: 18 with mild AD, 22 with aMCI and 27 controls (CTL) matched for aged and education. We used MMSE for global cognitive status and RAVLT for verbal episodic memory. MRI data were acquired on a 3.0T MRI Philips Achieva scanner. FreeSurfer program (https://surfer.nmr.mgh.harvard.edu/fswiki) was used to analyze cortical thickness of the population. We compared cortical thickness between the groups and performed multiple regressions to check the possible associations between cortical thickness and the cognitive scores. **Results:** One-Way Anova, using age as covariant, showed that mild AD group had significant difference in cortical thickness compared to aMCI and CTL in the areas: entorhinal, fusiform, inferior parietal, inferior temporal, insula, isthmus cingulate, lateral occipital, lateral orbito frontal, lingual, medial temporal, posterior cingulate, precuneus, superior temporal and supramarginal ($p<0.05$, corrected for multiple comparisons.) Regression models revealed that entorhinal cortex thickness predicts MMSE scores ($R^2=0.32$) and isthmus cingulum thickness predicts RAVLT (immediate - $R^2=0.32$ - and delayed recall - $R^2=0.34$). **Discussion:** Our results are in accordance with the literature that says the early stages of AD are associated with atrophy the medial temporal lobe [1], but also revealed some significant differences in thickness from other areas less explored in AD. Studies have already indicating good relation between MMSE scores and hippocampal atrophy, suggesting MMSE is an efficient tool to investigate AD [2]. The same in the present study, entorhinal cortex, which is related to memory, had strong predicting power on MMSE. About our findings between isthmus cingulum and immediate and delayed recall of RAVLT, there should be further investigation, since isthmus is part of the limbic system, also relatedto memory. **Conclusion:** The present study shows only mild AD patients differed from controls in terms of cortical thickness. Entorhinal and isthmus cingulum cortex have a relative strong predicting power on MMSE and RAVLT, respectively.

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THALAMIC VOLUMES IN DIFFERENT AGE GROUPS

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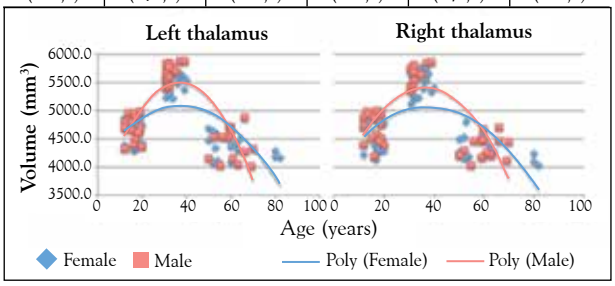
Introduction: The volumetric brain study may provide information about anatomy of underlying pathological processes. Therefore, proper study of thalamus, deep structure involved in reception and transmission of information in the brain is important to understand the clinical manifestation of diseases such epilepsy, stroke as well as neurodegenerative processes, which may occur in different ages. Thus, we performed the segmentation and volumetric measurement of thalamus on magnetic resonance images (MRI) of healthy subjects in three age groups, in order to identify an average volume for each age studied. **Materials and Methods:** Segmentation of thalami was manually performed using the MRIcron software on T1 volumetric isotropic 1mm voxel brain imaging acquired from healthy individuals in a 3T MRI (Phillips, Achieva, Holland) from a brain imaging data bank. We studied 90 subjects (45 women), equally divided into 3 age groups: Group A, mean age 16,5 (range from 12 to 20); Group B, mean age 33,7 (range from 30 to 40); and Group C, mean age 60,7 (range from 50 to 90). We used Atlas [1] as reference for thalamus segmentation. **Results:** The results for thalami segmentation for each group are shown in Table 1. **Discussion:** MRI studies demonstrated the changes undergone by the human brain during childhood and adolescence [2], so that lower volumes achieved in the Group A, compared to Group B, for example, can be explained by the age of the subjects. Similarly, Group C also showed a smaller volumes. It's known that normal aging reduces the volume of both grey matter and white matter of the brain, and this process is accelerated from the sixth decade of life [3], when the brain parenchyma shrinks as the ventricles increase [4]. The thalamus is associated with cognitive agility and is affected by atrophy more than other brain areas [2]. Full maturation of the brain has been described to take place after adolescence [2], which is supported by our finding. **Conclusion:** The volumetric analysis of healthy subjects MRI in different age groups plays an important role in the study of relevant concepts to normal brain development and aging effects on thalamic structure. This can be used to study cognitive decline, as well as in diagnosis, surgical planning and following of certain neurological diseases involving the thalamus. **Acknoledgement:** A.F.B. Camargo is recipient of FAPESP Scholarship 2015/04273-7.

Table 1. Thalamic volumes in mm^3 mean (SD) from manual segmentation for each group of control MRI.

Group A		Group B		Group C	
Left	Right	Left	Right	Left	Right
4646,3 (226,8)	4609,2 (278,1)	5585,7 (183,1)	5543,7 (203,1)	4372,1 (240,3)	4333,8 (203,8)



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METABOLIC ALTERATIONS AND INFLAMMATORY CYTOKINES IN MESIAL TEMPORAL LOBE EPILEPSY WITH OR WITHOUT HIPPOCAMPAL ATROPHY: A PRELIMINARY STUDY.

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Introduction: Mesial temporal lobe epilepsy (mTLE) is one of the most prevalent forms of focal epilepsy in adulthood and most of them become refractory to the pharmacological treatment. Proton magnetic resonance spectroscopy (^{1}H-MRS) is able to detect subtle changes in brain tissue and might be a useful tool to better understand mTLE [1]. The aim of the present work was to investigate changes in ^{1}H-MRS metabolites in relation to response to antiepileptic drugs (AED) and hippocampal atrophy (HA) in mTLE patients. We analyzed N-acetylaspartate+N-acetyl-aspartate-glutamate (NAA+NAAG/Cr) and glutamate (Glu/Cr). Moreover, we quantified preliminarily data on cytokines in order to better characterize inflammatory process inmTLE. **Materials and Methods:** We included 58 mTLE patients with poor AED response, 47 with good AED response and 47 healthy controls (mean values of metabolites from right+lef thippocampi). ^{1}H-MRS data was acquired in a 3T scanner (Philips Achieva) using a single voxel PRESS (Point Resolved Spectroscopy) sequence with repetition time (TR) = 2000msec and echo time (TE) = 35msec. Spectra were then quantified ipsi- and contralateral to the lesion using LCModel (MRI negative patients were lateralized according to EEG) [2]. We also performed a preliminary multiplex essay (xMap) of eight regulatory mediators: TNF-Alfa, BDNF and interleukins (IL) 1β, 4, 6, 10, 12 and 13 in patients (n = 57) and healthy controls (n = 29). We used SPSS (IBM, Version 22.0) for statistical analysis. Metabolic data was compared between groups using MANCOVA co-varying for age and the t Test was used to evaluate data on cytokines. **Results:** We found an ipsilateral decrease of NAA+NAAG/Cr in refractory group when compared to responders and controls ($p = 0.021$ and $p = 0.0001$, respectively). NAA+NAAG/Cr was also decreased in contralateral hippocampus of refractory group compared to controls ($p = 0.004$). Moreover, we observed a decrease in Glu/Cr in refractory patients ipsilateral to the lesion when compared to controls ($p = 0.008$). Regarding xMap analysis, only BDNF and IL-8 were quantified (the other cytokines were under the detection range of the essay kit). This analysis reached no significant difference between groups ($p > 0.05$). **Discussion:** The results found are probably due to pharmacological response than the presence of HA [1]. Cytokines data are preliminary and resulted from a pilot study to guide next analysis. Nonetheless, IL-8 might be expressed by microglia and reactive astrocyte [3] thus next step is evaluating the relationship between metabolic data measured by ^{1}H-MRS and cytokine levels. **Conclusion:** Metabolic alterations seems to be related to the pattern of AED response when ipsilateral to the lesion. However, alterations in NAA might go beyond the lesion and affect both hippocampi [1]. Further analysis is required to investigate whether there is or not an association between metabolic alterations and regulatory mediators levels.

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EFFECT OF PREVIOUS TREATMENT WITH ANTIPLATELET SEVERITY OF ISCHEMIC STROKE SUBTYPES

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Introduction: Several studies indicate that aspirin use prior to cerebrovascular event may be associated with mild deficits. To investigate whether prestroke antiplatelet agent use was associated with initial stroke severity and if this benefit may be attributed to the mechanism of stroke. **Materials and Methods:** prospective registry with patients hospitalized for ischemic stroke during 2014 in two referral hospitals in Campinas, Brazil. Baseline stroke severity was measured using the National Institutes of Health Stroke Scale (NIHSS) scores at presentation. The impact of previous antiplatelet use in admission NIHSS was verified through Multiple Linear Regression. This analysis was adjusted for age as well as other confounding variables. An interaction term was added to ckeck if the effect of antiplatelet use was dependent on the stroke etiology (TOAST). **Results:** A total of 287 were included. Patients' mean age was 67.2 (± 11.2) years and 177 were men (61.7%). A total of 91 (31.7%) patients had been taking aspirin prior 1 week of stroke onset. Antiplatelet users had a median admission NIHSS of 7 (interquartile range [IQR] 3 – 15) vs 6 (IQR 3 – 11) for the non users (p=0,036). The significance was maintained after multivariate adjusments, with the use of antiplatelets reducing the admission NIHSS in 2,4 points. Having the small vessels oclusion as the reference category, NIHSS at admission was higher for large artery atherosclerosis (B=3,2, p<0,001) and cardioembolism (B=5,7, p<0,001). Although the interaction term between antiplatelet use and TOAST subtype was not significant, there was absolute differences in the NIHSS relative reduction (RR). **Discussion:** Antiplatelet use independently reduced the initial stroke severity. Although a possible lack of power hindered the interaction analysis, this study suggests a difference in effect size dependent on the TOAST subtype. **Conclusion:** This study confirms the utilization of antiplatelet for the reduction of the severity of ischemic stroke.

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BRAIN MORPHOMETRIC ALTERATIONS DURING THE PROGRESSION OF DEMENTIA DUE TO ALZHEIMER'S DISEASE

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Introduction: Dementia caused by Alzheimer's disease (DAD) is a primary and progressive neurodegenerative disorder with a clear pattern of cognitive deterioration and memory commitment [1]. In the brain, the pathology is presented predominantly by neurofibrillary tangles mainly in hippocampus during the disease progression [2]. Most studies have evaluated pre-clinical and initial stages of the disease through clinical trials and its correlation to biomarkers. Most studies have evaluated pre-clinical and initial stages of the disease through clinical trials and its correlation to biomarkers. However, progression into advanced stages were not evaluated [3]. This work evaluated the brain morphometry of DAD patients in all disease stages, aiming at identifying the structural neuro-degeneration profile in every phase of disease progression. **Materials and Methods:** DAD patients above 60 years old (n=44) and age paired healthy controls (n=16) were recruited to compare with non-cognitively impaired subjects. Cognitive clinic stages were evaluated using clinical demential rate (CDR) and cognitive indexes Mini Mental State Examination (MMSE). Brain images were acquired in a 3T magnetic resonance scanner. Gradient eco 3D T1-weighted images were acquired without contrast injection. Volumetric and cortical thickness measurements were obtained by automatic segmentation in the Freesurfer® software using a Desikan-Destrieux parcellation atlas. The volume of each region was normalized considering whole brain volume to minimize inter-individual variation in head size [4]. **Results:** Brain regions targeted by the disease during the initial stages were found to be altered even in the later stages of the dementia (p<0.05) (Figure1). We found an association between volumetry and cortical thickness with cognitive indexes MMSE (R^2<0.47), Clinical Dementia Rating (CDR) (Figure 2) and disease duration in years (R^2<0.52) for individual regions as showed on Figure 2 in yellow color. No significant correlation was observed between regional brain volume or cortical thickness with age and years of education. The cortical thickness measurements were less sensible in differentiating the groups than volumetry measures (p>0.01). **Discussion and Conclusion:** We conclude that most affected brain regions suffer atrophy in a linear fashion until the later stages of the disease; it is in disagree with previous hypothesized model considering a faster degeneration rate in earlier stages [3]. But in agreement, with neuropathology founds of neuronal loss and gliosis [5]. About less sensibility to differentiate the groups with cortical thickness, the cause is that cortical thickness is very dependent of segmentation quality. These findings allow us a better understanding of the physio-pathological process and a follow-up process of treatment drugs even in the advanced diseases stages.

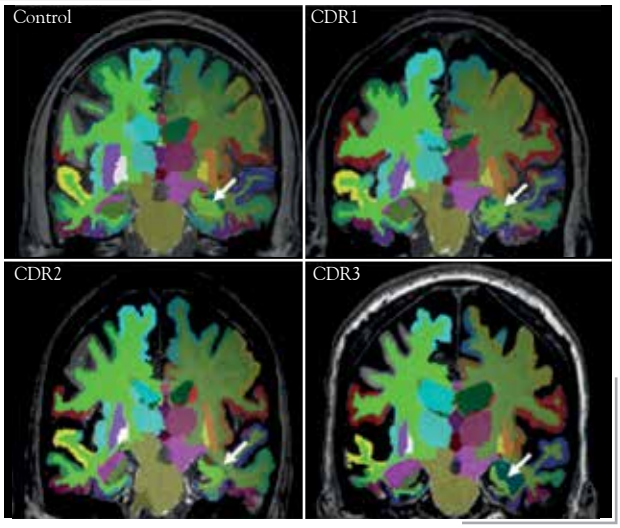

Figure 1. Brain segmentation for control (men, 79 years), CDR1 (men, 79 years), CDR2 (woman, 90 years) and CDR3 (woman, 79 years). Hippocampal atrophy is indicated by the white arrow.

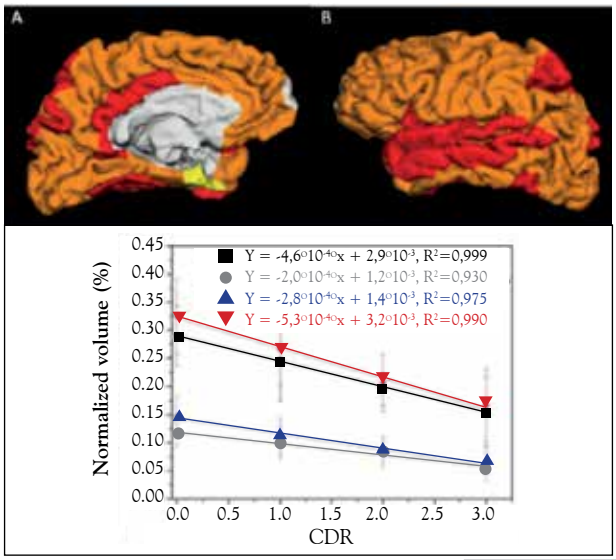

Figure 2. Atrophy brain areas along the progression of DAD. (A,B) colors represent regions with significant volumetric reduction (p 0.05) Between all groups (yellow), except controls and CDR1 (red), and controls, CDR1 and CDR2 (orange). (C) Linear correlation between normalized volume and CDR.

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CIRCULATING MICRORNAS IN MESIAL TEMPORAL LOBO EPILEPSY: HSA-MIR-134 IDENTIFIED AS A BIOMARKER OF MTLE

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Introduction: Drug resistant epilepsy (DRE) occurs in about 20-30% of all patients with. Major causes of DRE are focal cortical dysplasia (FCD) and mesial temporal epilepsy (MTLE). The identification of biomarkers for epilepsy could potentially improve diagnosis as well as treatment of these patients. Circulating microRNAs (miRNAs) are good candidates to be biomarkers; these are small noncoding RNAs present in extracellular human body fluids including plasma or serum. In this context, the objectives of this study are: i) to determine if changes in expression of three candidate miRNAs, hsa-miR-23a, hsa-miR-31 and hsa-miR-134 are present

in plasma of patients with FCD and MTLE both with refractory seizure and ii) to verify if plasma levels of these miRNAs are potentially associated with response to AEDs. **Materials and Methods:** We determined plasma levels of these miRNAs by RT-PCR. This study is divided into two phases. In phase I, we enrolled 13 patients with FCD, 14 patients with MTLE, both with refractory epilepsy and 16 controls. In phase II, we used MTLE who are responsive (n=27) and unresponsive (n=41) to AED and controls (n=83). We used ROC curve and t-tests, corrected by Bonferroni. Indeed, to improve discriminatory accuracy of circulating miRNAs, we combined the data of levels of miRNAs with clinical parameters, including epilepsy onset, history of febrile seizure (FS), familial history of epilepsy and the presence or not of MRI signs of hippocampal sclerosis (HS). **Results and Discussion:** We observed that hsa-miR-134 is significantly down-regulated in plasma of patients with MTLE (p= 0.018) when compared to controls. Furthermore, by using hsa-miR-134 data we were able to distinguish patients with and without epilepsy, with an area under the curve (AUC) of 0.71, with sensitivity of 45% and specificity of 100%. However, we were not able to discriminate satisfactorily between patients with drug-resistant and drug-responsive MTLE. In this case, the best scenario was achieved when adding expression levels of the three miRNAs, which resulted in an AUC=0.622 with sensitivity of 76% and specificity of 52%. Adding clinical data to the model did not increase power of discrimination. **Conclusion:** Our data indicate that hsa-miR-134 is a potential biomarker for MTLE and may have clinical applications in this context. **Supported by** CEPID-FAPESP.

INCIDENTAL FINDINGS OF GENOMIC TESTING: INVESTIGATING THE VIEW OF HEALTH PROFESSIONALS AND THE RESEARCH COMMUNITY

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Introduction/Objective: Due to the introduction and widespread of next generation sequencing technologies in recent years, genomic medicine became clinically available surpassing the research context, which was previously restricted. Nonetheless, the clinical use of genomic tests also involves a number of challenges, such as how to deal with incidental findings disclosed by the new genomic tests. Incidental or secondary findings are defined as results which are unrelated to the disorder for which testing was obtained [1]. Although there are consensus statements already published [2] on this matter, different cultures, have distinct opinions. In addition, with regard to genomic databases of public nature, there is a global call for researchers and professionals working with this type of data to share them in public databases, in order to accelerate genetics discoveries and help interpretation of variants of unknown significance. Despite this worldwide appeal and given the lack of regulatory context on genomic testing in Brazil, little is known about the views of health professionals and researchers on these matters. In this context, we propose this study which aims to know about the opinion of health professionals and scientists on reporting incidental findings both in the research context and in the clinical setting. **Methods/Results**: During the 3rd BRAINN Congress, a structured questionnaire will be applied to health professionals, researchers and students interested in participating in the survey. To assist participants answers, along with the questionnaire it will be available an informative flyer on genomic medicine, its diagnostic applicability and basic concepts of incidental findings in genomic context and public databases. Participation can be anonymous and the survey results will be timely published. **Conclusions:** Our results could provide input for discussions on incorporation and regulation of genomics tests in healthcare systems, involving health professionals, scientists, managers, support patients associations and other stakeholders. **Supported by:** CEPID-BRAINN, FAPESP, Brazil.

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CORTICAL THICKNESS CHANGES AND PSYCHIATRIC SYMPTOMS IN MTLE PATIENTS

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Introduction: Mood and anxiety disorders are highly prevalent in patients with mesial temporal lobe epilepsy (MTLE) carrying significant morbidity and decreasing the quality of life of these patients. Its neural basis is poorly understood and deserves to be deeply investigated. The number of studies examining the correlations among MTLE, depression, and anxiety symptoms in relation to neuroanatomical basis is a small and insufficient [1]. The aim of this study was to investigate the cortical changes associated with depression and anxiety symptoms in MTLE patients. **Materials and Methods:** We evaluated 145 patients with MTLE (with and without hippocampal atrophy, detected on high resolution MRI) and 74 healthy controls. MTLE patients were subdivided considering the presence or absence of hippocampal atrophy, yielding 4 groups: non-lesional (TLE-NEG,n=38), left (LTLE, n=48), right (RTLE, n=45) and bilateral (14). We excluded 14 patients with bilateral hippocampal atrophy given the small number of patients. Our final sample consisted of 131 MTLE patients (89 women) with a mean [± standard deviation] age of 44.37± 10.1 years and 74 controls (45 women) with a mean of age of 42.1±12.4 years. All participants underwent a high resolution MRI T1-weighted acquired in a 3T MRI scanner (Philips Medical Systems, Best, The Netherlands). We performed automated parcellation with FreeSurfer 5.3 (http://surfer.nmr.mgh.harvard.edu/) for volumetry and cortical thickness analyses. All participants completed both Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI) to measure depression and anxiety symptoms respectively. IBM® SPSS20 software was used for statistical analysis. We performed correlations using the Spearman's correlation coefficient. **Results:** In healthy controls we only observed a negative correlation between depression symptoms and thickness of right inferior parietal (r=-0.34, p<0.01). On TLE-NEG we detected a positive correlation between the BDI and cortical thickness of the left (r=0.32, p=0.04) and right (r=0.32, p=0.04) lateral occipital gyrus, and a negative correlation with the left pars triangularis (r=-0.4, p=0.01). BAI correlated negatively with the left caudal middle frontal (r=-0.35, p=0.03), left pars triangularis (r=-0.33, p=0.04), left superior frontal (r=-0.35, p=0.03), and right isthmus cingulate (r=-0.35, p=0.03). LTLE group presented negative correlation between BDI and right entorhinal cortex (r=-0.34, p=0.03). For RTLE group we observed positive correlations between BDI and cortical thickness of left caudal middle frontal (r=0.40, p<0.01), right frontal pole (r=0.37, p=0.01), right pars opercularis (r=0.41, p<0.01), right pars triangularis (r=0.33, p=0.04), right posterior cingulate (r=0.37, p=0.01), and right rostral anterior cingulate (r=0.34, p=0.02). In addition, there was a positive correlation between BAI and right isthmus cingulate (r=0.43, p<0.01), right posterior cingulate (r=0.6, p<0.01), and a negative correlation with right lateral occipital (r=-0.32, p=0.03). **Discussion and Conclusion:** These findings show multiple areas of altered cortical thickness associated with worsening depression and anxiety symptoms in patients with MTLE, indicating a large network of brain areas related to the co-occurrence of psychiatric symptoms and epilepsy, especially when compared with the healthy controls. Understanding these correlations in the future may help to develop a more specific treatment for MTLE patients with psychiatric disorders.

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ASSOCIATION BETWEEN DEPRESSION, QUALITY OF LIFE AND PHYSICAL ACTIVITY IN PEOPLE WITH TEMPORAL LOBE EPILEPSY

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Introduction: The prevalence of depression in patients with epilepsy with recurrent seizures ranges from 20% to 80%. Moreover, it is source of significant disruption in daily activities and social relations. In consequence, they have poor quality of life (QOL)[1]. Is known that regular physical activity (RPA) contributes to treatment of patients with depression [2]. Nevertheless, people with epilepsy (PWE) have presented lower level of daily physical activity (PA) than the general population [3]. Therefore, the purpose of the present study was evaluate the relationship between depression and QOL, and evaluate if PA is associated with depression and QOL in people with temporal lobe epilepsy (TLE). **Materials and Methods:** Ninety patients (Mean age = 44; SD = 8) answered the Beck Depression Inventory (BDI) which evaluate the level of depression, the Quality of Life in Epilepsy Inventory-31 (QOLIE-31) which evaluate the level of QOL and the International Physical Activity Questionnaire (IPAQ), in order to divide them in two groups (*Active* and *Inactive*). We used the SPSS software (SPSS Inc, Chicago, IL), and used the Mann-Whitney U test to compare differences of depression and QOL between groups; and Pearson's correlation Test to analyze the correlation between depression and QOL. **Results:** We observed significant correlation between the level of depression and QOL ($R=0.69$; $R^2=0.43$; p=0,001). There were differences between the level of depression (p=0.001) and QOL (p=0.001) between the groups *Active* and *Inactive*, with lower level of depression and better QOL for the *Active* group. **Discussion:** Our results showed that depression is a comorbidity that has a significant relation with QOL in PWE. On the other hand, patients that had high levels of daily PA, had low levels of depression and high levels of QOL. Previous interventional and longitudinal PA studies have shown that RPA can improve QOL and general health of PWE [4,5]. Thus, the present study suggests that RPA could improve level of depression, in addition to QOL, in PWE. **Conclusion:** Emotional comorbidities and worst QOL are common in PWE, therefore, mental health professionals must respond to the challenge of finding innovative ways to help these population, many of whom lack adequate resources to pay for extensive treatment programs. Interventions that initiate and maintain regular physical exercise activity might be particularly useful for achieving targeted psychosocial goals.

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WHITE MATTER ABNORMALITIES IN TEMPORAL LOBE PATIENTS WITH GOOD AND POOR SEIZURE CONTROL

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Introduction: Patients with mesial temporal lobe epilepsy (MTLE) have diffuse cerebral gray and white matter abnormalities. However, the mechanisms involved in this structural damage are not clear. **Objective:** The aim of this study was to evaluate the white matter architecture abnormalities of seizure-free or pharmaco-resistant MTLE patients with and without hippocampal sclerosis (HS). **Methods:** We performed diffusion tensor imaging (DTI) and fiber-tractography technique using a 3T MRI scanner in a group of 123 consecutive MTLE patients and 113 healthy controls. Patients were divided in four groups according to antiepileptic drug response and presence of HS on MRI: 68 MTLE-HS with pharmaco-resistant seizures (refractory) (rMTLE-HS); 14 TLE-HS seizure-free (benign) (bMTLE-HS); 28 MTLE-NL with drug-resistant seizures (rMTLE-NL); 13 MTLE-NL seizure-free (bMTLE-NL). We used an automatic deterministic method to measure fractional anisotropy (FA), mean (MD), axial (AD), and radial (RD) diffusivity in the cingulum, body of corpus callosum, fornix, inferior frontal occipital and uncinate fasciculi. The side of the epileptogenic zone was defined according to ictal and inter-ictal EEG and the side of the HS. **Results:** rMTLE-HS group had decreased FA and increased RD in all tracts ipsi and contralateral to the epileptogenic zone. bMTLE-HS showed decreased FA and incresead RD in the body of corpus callosum and fornix ipsi and contralateral and cingulum ipsilateral to the epileptogenic zone. rMTLE-NL and bMTLE-NL had decreased FA and increased RD only in the cingulum ipsi and contraleral to the epileptogenic zone. **Conclusion:** MTLE-HS patients with pharmaco-resistant seizures and seizure-freedom have diffuse white-matter abnormalities, although in the former group this abnormality is more pronounced. Conversely, MTLE-NL patients have restricted white matter abnormalities independently of the seizure control. These findings suggest that the presence of HS is possibly the main determinant of white matter abnormalities in patients with MTLE.

Keywords: diffusion tensor imaging, temporal lobe epilepsy, seizure free.

EVALUATION OF CEREBELLAR GRAY MATTER DAMAGE IN HUNTINGTON'S DISEASE: A VOXEL BASED MORPHOMETRY STUDY

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Introduction: In the last years, the cerebellar role in neurodegenerative diseases has been extensively studied[1]. However, few research related cerebellum and Huntington disease (HD)[2]. This is not only due to cerebellar contribution on motor refinement, but mainly by the discovery of its non-motor functions. The aim of our study is detail the cerebellar gray matter (GM) alterations in HD using the tool "spatially unbiased template atlas" (SUIT) for Voxel based morphometry (VBM) on magnetic resonance imaging (MRI). **Materials and Methods:** We compared 26 patients matched in gender and age with 26 healthy controls. They underwent neurological (Unified Huntington's disease rating scale – UHDRS) and cognitive (Montreal cognitive assessment - MOCA) evaluations. SUIT was used to analyze GM alterations. We created a two-sample test to analyze GM differences between both groups and another to correlate the cerebellar GM alterations with UHDRS (mood and motor) and MOCA scores, corrected for age, cytosine-adenine-guanine (CAG) repeats and disease duration. **Results:** While most previous studies found cerebellar atrophy in HD, we observed mostly increased GM density at the anterior cerebellum ($p<0.05$ FWE corrected and $k>100$ voxels), compared to controls. We only observed atrophy with a less restrictive analysis ($p<0.001$ uncorrected and $k>100$ voxels) at the postero-superior cerebellar lobes. Higher GM density in the postero-superior lobe was associated with mood disorders symptoms; worse motor function correlated with GM density alterations in the central portion of the postero-inferior lobe and lateral portion of the postero-superior lobe on the right; and better cognitive function with higher GM density in the left side of the postero-inferior lobe. **Discussion:** This study is the first to provide a detailed assessment of the cerebellum in HD. Even those that exclusively evaluated the cerebellum, only observed white matter changes, using a volumetric approach, rather than a voxel-by-voxel comparison. The SUIT tool isolates the cerebellum from other brain structures, providing a topographic detailing of each cerebellar lobe, and assessing both GM increases and reductions. We interpreted our GM excess results as a compensatory mechanism or as a structural anatomical breakdown caused by the disease, these findings may also have been influenced by reduced mean time of disease duration in our sample[3]. **Conclusion:** The listed areas are responsible for sensorimotor integration, motor planning, visuospatial function and emotional processing. We believe these findings may contribute to a better understanding of the neuropathological process of HD.

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VOLUMETRIC ANALYSIS OF HIPPOCAMPAL SUBFIELDS IN MESIAL TEMPORAL LOBE EPILEPSY: EVIDENCE OF BILATERAL DISEASE IN PATIENTS WITH LEFT HIPPOCAMPAL SCLEROSIS

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Introduction: Mesial temporal lobe epilepsy (MTLE) is the most common epileptic syndrome in adults, and in approximately 65% of cases is associated with hippocampal sclerosis (HS). Among hippocampal subfields, neuronal loss is usually greatest in CA1, intermediate in CA3 and CA4, and more subtle in CA2 areas. Previous studies had already shown more widespread pattern of atrophy in patients with left MTLE, associated with poor seizure control and longer duration of epilepsy. The aim of this study is to compare the different patterns of atrophy in hippocampal subfields between patients with right and left unilateral HS (RTLE and LTLE, respectively). **Materials and Methods:** The subjects were divided in three groups: 223 controls (78 males), 106 patients with LTLE (41 males) and 84 patients with RTLE (30 males). T1 high-resolution images from 3T scanner were submitted to automatic segmentation of hippocampal subfields (CA1, CA2, CA4/dentate gyrus, pre-subiculum, subiculum and fimbria), with Freesurfer 5.3. The statistic analysis was performed with SPSS 22, using Mixed Model Anova. We searched for interactions between side, volume and groups. Significance was considered at $p<0.05$, with Bonferroni adjustment for multiple comparisons. **Results:** Groups of patients (LTLE and RTLE) were balanced for age, gender, seizure frequency, age of onset and duration of epilepsy. Compared to controls, RTLE group presented atrophy within all ipsilateral subfields ($p<0.01$), and more subtle atrophy in the contralateral pre-subiculum and fimbria ($p<0.032$). On contrary, LTLE presented significant atrophy of all six subfields in both hemispheres (all $p<0.01$), most evident unilateral. **Conclusion:** The most evident bilateral involvement of the hippocampal subfields detected in LTLE may be likely related with the most severe cognitive impairment found in these patients. These findings may also have important implications in long term post-operative prognostic, as bilateral alterations may be associated with persistent seizures.

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DYSTONIA IN MACHADO-JOSEPH DISEASE: CLINICAL PROFILE, THERAPY AND ANATOMICAL BASIS

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Introduction: Machado-Joseph disease (MJD/SCA3) is the most frequent spinocerebellar ataxia and has remarkable clinical heterogeneity [1]. In this sense, dystonia is frequent in (MJD/SCA3), but several important aspects are not yet defined, such as the detailed clinical profile, response to treatment and anatomical substrate. **Materials and Methods:** We screened 75 consecutive patients and identified those with dystonia. The Burke-Marsden-Fahn Dystonia Rating Scale was employed to quantify dystonia severity. Patients with dystonia received levodopa 600 mg/day for 2 months and were videotaped before and after treatment. A blinded evaluator rated dystonia in the videos. Patients with disabling dystonia who failed to respond to levodopa treatment received botulinum toxin. Finally, volumetric T1 and diffusion tensor imaging sequences were obtained in the dystonic group using a 3T-MRI scanner (Philips Achieva) to identify areas of gray and white matter that were selectively damaged. **Results:** There were 21 patients with dystonia (28%): 9 classified as generalized and 12 as focal/segmental. Patients with dystonia had earlier onset and larger (CAG) expansions (28.9 ± 11.7 vs 40.6 ± 11.4; $p < 0.001$ and 75 vs 70; $p < 0.001$, respectively). Although group analyses failed to show benefit on levodopa ($p = 0.07$), some patients had objective improvement. In addition, ten patients received botulinum toxin resulting in a significant change in dystonia scores after 4 weeks ($p = 0.03$). Patients with dystonia had atrophy at pre- and paracentral cortices; whereas, non-dystonic patients had occipital atrophy. Basal ganglia volume was reduced in both groups, but atrophy at the thalami, cerebellar white matter and ventral diencephali was disproportionately higher in the dystonic group. We found similar white matter abnormalities in both groups. **Discussion:** We have shown that dystonia is frequent in MJD/SCA3, often disabling and clinically heterogeneous. However, it might respond to levodopa and to botulinum toxin injections. Dystonic patients showed a pattern of cerebral damage different than patients without dystonia. These results indicate that dystonia in MJD/SCA3 is associated with structural abnormalities in the basal ganglia and cerebral cortex. In addition, disproportionate thalamic atrophy in dystonic patients is in agreement

with a previous study from our group that employed manual volumetry [2]. This is a reasonable finding since the thalamus is involved both with motor output control and sensory-motor integration, which are two important aspects in the pathogenesis of dystonia. Furthermore, it is well established that focal thalamic lesions might lead to delayed contralateral dystonia in at least 30% of cases [3]. A novel finding in this study was the presence of cortical atrophy around the central sulcus in dystonic subjects. This is in line with recent neuroimaging studies that highlighted abnormal structure and function of sensory-motor cortices in different forms of primary dystonia [4]. **Conclusion:** Dystonia in Machado-Joseph disease is frequent and often disabling, but may respond to levodopa. It is associated predominantly with structural abnormalities around the motor cortices and in the thalami.

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ADAPTATION OF THE ALS-CBS COGNITIVE SECTION FOR BRAZILIAN POPULATION

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Introduction: Cognitive decline (CD) is frequent, but often underrecognized in ALS due to the scarcity of adequate cognitive screening methods, as formal neuropsychological assessment is not feasible in clinical ALS routine [1]. The Amyotrophic Lateral Sclerosis Cognitive Behavior Screen (ALS-CBS) is the most investigated instrument nowadays and presents high sensitivity to identify CD [2]. Currently, there are no validated screening tools for ALS patients in the Brazilian population and therefore, little is known about the frequency of ALS-related CD in the country. This study aims to assess the accuracy of the Brazilian Portuguese version of ALS-CBS Cognitive Section (ALS-CBS-Br) for classifying the cognitive status of Brazilian patients compared to a gold standard neuropsychological battery, and to estimate the prevalence rate of cognitive impairment in Brazilian ALS population. **Materials and Methods:** Forty consecutive ALS patients regularly followed at UNICAMP hospital and 10 healthy controls underwent a detailed neuropsychological assessment. The battery included visuospatial, memory, language and executive tests, and also the ALS-CBS-Br. ALS patients were classified as ALS cognitively impaired (ALSci) or ALS normal (not impaired) based on the battery results, according to current criteria [3]. Cognitive scores were compared using a General Linear Model (GLM), and post-hoc pair-wise comparisons were analyzed to identify group differences, corrected for multiple comparisons (Bonferroni, $\alpha = 0.01$). Correlations between ALS-CBS-Br scores, neuropsychological tests and clinical data were investigated in the ALS cohort using a linear regression model. Age, gender and education were used as covariates in these analyses. A receiver-operating characteristic (ROC) curve was created to assess the usefulness of ALS-CBS-Br as a cognitive classifying method. **Results:** Six ALS patients (15%) were classified as cognitively impaired (ALSci) based on the battery results. ALSci group performed significantly worse than ALS normal and control groups in executive, language and memory tests. ALS-CBS-Br scores did differ significantly between ALSci and ALS normal groups ($p=0.002$). ROC curve analysis demonstrated that an ALS-CBS-Br score of 10/20 or less differentiates ALSci and ALS normal groups with a specificity of 0.794 and a sensitivity of 1.000. The accuracy of the test (area under the curve) was 0.946. ALS-CBS-Br scores correlated with executive, visuospatial and language tests, but not with clinical data. All assumptions of linear regression were met, and errors were normally distributed for all parameters. **Discussion:** ALS-CBS-Br has excellent accuracy for identifying cognitive impairment in our Brazilian ALS population. Our results suggest that the ALS-CBS-Br is sensitive for detecting executive dysfunction and other neuropsychological deficits. The prevalence rate of CD in our cohort (15%) is lower than previously published data regarding ALS-related CD worldwide (30-50%) [1]. There are confounds related to the study of cognition in the Brazilian population, mostly due to the heterogeneity of educational status and the lack of adequate normative data for several cognitive tests. Because of these factors, and the fact that we excluded ALS patients with suspected dementia, our CD prevalence rate likely underestimates the true level of impairment in our population. **Conclusion**: In conclusion, the ALS-CBS-Br may facilitate the suspicion of ALSci in routine clinical care and complement future cognitive and phenotypic studies in our population.

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HOW FRAGILE IS THE LEFT HEMISPHERE? VBM ANALYSES COMPARING EPILEPSY, AMYOTROPHIC LATERAL SCLEROSIS AND PARKINSON'S DISEASE

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Introduction: Differences between left and right hemispheres regarding susceptibility to disease process is not entirely clear. In Temporal lobe epilepsy (TLE), left hippocampal sclerosis (HS; LTLE) is associated with bilateral structural damage, while in right HS (RTLE) there is more ipsilateral pattern of abnormalities. The reasons for such differences are unclear. Here we investigate the impact of neurodegenerative diseases [Amyotrophic Lateral Sclerosis (ALS) and Parkinson Disease (PD)] on patterns of structural grey matter alterations, comparing abnormalities on left and right hemispheres. **Materials and Methods:** We performed Voxel Based Morphometry analyses on T1 weighted images with MATLAB2014b/SPM12, comparing patients and paired controls (age and gender) for each separate disease. We included 99 patients with ALS, 113 patients with PD, 45 with RTLE and 50 with LTLE and 265 healthy controls. Basically, images were segmented into grey and white matter individual maps, modulated and smoothed. Posteriorly, we performed T-tests for ALS and PD, and a full factorial model for RTLE/LTLE. All statistical analyses were performed on SPM12. **Results:** As expected, we observed a more bilateral pattern of GM atrophy on LTLE, while RTLE present more ipsilateral GM atrophy. Interestingly, the analysis of other neurodegenerative diseases (which are not usually associated with specific MRI lesions such as hippocampal sclerosis) revealed a more left sided pattern of GM atrophy for both ALS and PD, as we can see in Figure1.

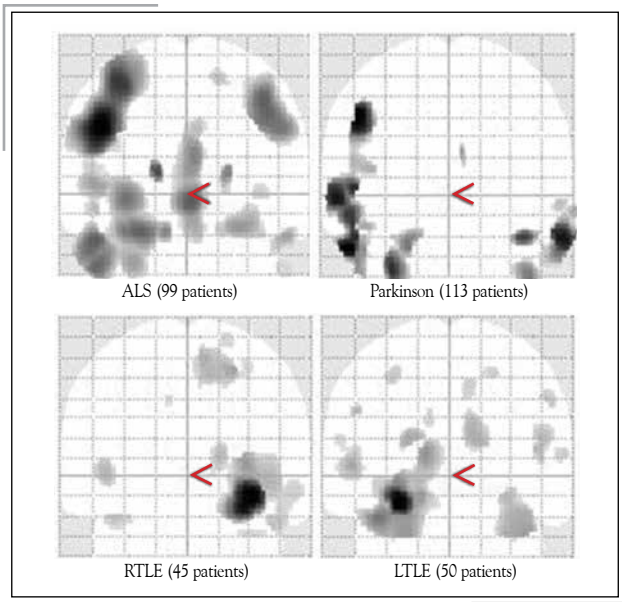

Figure 1. Patterns of GM reduction in different diseases. Both ALS and PD present more atrophy on left hemisphere.

Discussion: The results show an intriguing pattern of GM alterations on both ALS and PD, as visual analysis is usually unremarkable and mostly because neurological deficits are usually bilateral, especially at late stages. On TLE we speculate that left HS causes more widespread damage probably because left hemisphere is highly connected with right hemisphere, with more unidirectional pathways. **Conclusion:** The present work suggests that left hemisphere is somehow more susceptible to damage, regardless to the pathogenic process (i.e. seizures, neurodegeneration). Further analyses including hand dominance as covariate may help us to understand better these left/right side differences.

SENSORY LOSS MAY YIELD GRAY MATTER ABNORMALITIES IN SENSORY NEUROPATHY PATIENTS

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Introduction: Sensory Neuronopathy (SN) is a subgroup of diseases of the peripheral nervous system, that preserves muscle strength, although the sensory deficits normally lead to motor impairment. To the best of our knowledge, no study was able to identify any pattern of abnormality in gray (GM) and white matter (WM) of the brain, besides occasional cerebellar atrophy [1]. **Materials and Methods:** Thirty-three consecutive SN patients (51±10 years; 15 women) from the Hospital de Clínicas at Unicamp and 24 control subjects (48±10 years; 12 women) underwent a magnetic resonance T1-weighted image scan (TR/TE = 7/3.2 ms, FOV = 240 x 240 mm^2, slice thickness = 1 mm, flip angle = 8°, number of slices = 180) in a 3T MR scanner (Philips Achieva). Images were assessed for alterations in GM volume and in

cortical thickness using the FreeSurfer software (http://freesurfer.net/). Age, gender and intracranial volume were regressed out of the data before group-comparison analysis and no correction was used to control for false discoveries due to multiple comparisons. **Results:** Twenty-nine out of the 33 enrolled patients were clinically evaluated. Mean disease duration was 11±9 and despite extensive evaluation 18 patients were considered idiopathic. We found significant differences including cortical thickness reduction in: right occipital pole (p=0.020); transverse and superior right occipital sulci (p=0.021); and in the left anterior occipital sulcus (p=0.032). We also found thickness decrease in left calcarine sulcus (p=0.048). Moreover, we found reduction of GM volume in right ventral diencephalon (substancia nigra, the subthalamic nucleus, etc.; p = 0.035). **Discussion:** Due to the exploratory purpose of the study we did not use correction for multiple comparisons. Thus, the results we obtained must be viewed with caution. Nevertheless, they may suggest hypotheses regarding disease mechanisms and also indicate research lines to further explore and confirm the abnormalities found. The thickness reduction in the left calcarine sulcus, for instance, could point to a visual compensatory phenomenon to balance the loss of proprioception through the use of vision to guide movements. It is also noteworthy that SN patient cohort is very heterogeneous, what can mask other consistent alterations in a specific subgroup of patients. **Conclusion:** The present study indicates that sensory loss may lead to alterations in GM volume, specifically in visual areas. Further studies should target these regions to better understand their role in the reorganization of the central nervous system as a consequence of the disease.

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Experimental Basic Neuroscience

INTEGRATED ANALYSES OF ZEBRAFISH MIRNA AND MRNA EXPRESSION PROFILES AFTER PENTYLENETETRAZOLE-INDUCED SEIZURES

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Introduction: MicroRNAs (miRNAs) have been accepted as key molecules underlying seizures as well as associated with epilepsy development. This study aimed to integrated miRNA and mRNA transcript profile by applying ultra-high-throughput sequencing system and bioinformatics approach in order to identify molecular mechanisms underlying seizures in the zebrafish seizure model. **Materials and Methods:** Adult wild-type zebrafish and embryos were maintained according to standard procedures. Seven days post fertilization (7dpf) larvae were separated in three groups: controls (CTL, n=3), acute seizure (AS, n=2) and status epilepticus-*like* (SE-*like*, n=3). Larvae from groups AS and SE-*like* were exposed to PTZ 15mM for 20 minutes and 3 hours, respectively. MiRNA and mRNA libraries were achieved after RNA extraction using Illumina's Sample Prep Kit according instructions. Validated and pooled libraries were sequenced in the Illumina HiSeq 2500 System. MiRNA and mRNAs differentially expressed ($p<0.01$) were determined and the target genes for miRNA investigated by *in silico* analysis. **Results:** We identified three miRNAs (dre-miR-31, dre-miR-132-5p and dre-miR-459-3p) and 4622 mRNAs in the SE-*like* group compared to CTL group. In addition, we found two miRNAs (dre-miR-460-3p and dre-miR-725-3p) and 2897 mRNAs when comparisons were performed between AS and CTL groups. Comparisons between AS and SE-*like* groups showed that the time of exposition changed the expression pattern for the same miRNA. Our preliminary analysis for miRNA-mRNA integration data showed one putative miRNA-mRNA pair that was differential expressed in the AS group and seven for SE-*like* group. **Discussion:** Animals from AS group presented an inverse correlation between dre-miR-460-3p (down-regulated) and its target, *inhbaa* gene that is related to cell survival, growth and differentiation. This gene participates of TGF-β signaling pathway, which has been associated with neurotransmission regulation in other animal models and humans. Furthermore, seven putative miRNA-gene target pairs were differently expressed in the SE-*like* group, among them, dre-miR-459-3p and its target *adar* and *grm2a* genes, previously associated with seizures and neuroactive ligand-receptor interaction, respectively. Additionally, we demonstrated a relationship between dre-miR-459-3p and *pcdh19* gene, which plays a role in early stages of brain morphogenesis during the zebrafish development. **Conclusion:** To our knowledge, this is the first study investigating global integration between miRNA-mRNA transcript profile after seizures or SE-*like* states using the zebrafish as model. Besides, we have proposed a SE-*like* protocol for zebrafish. Our results showed that both, acute seizure and SE-*like* have distinct molecular profile. By integrating miRNA-mRNA data we hope to shed some light into the cellular pathways underlying seizure and SE. **Supported**: FAPESP (#2014/15640-8), CEPID-BRAINN (#2013/07559-3) and FAEPEX.

COX-1 EXPRESSION IS UP-REGULATED AFTER SEIZURE IN THE ZEBRAFISH SEIZURE MODEL

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Introduction: Experimental data have shown that microglia and astrocytes are activated in response to epileptic activity[1]. Microglia and astrocytes activation promotes the release of pro-inflammatory mediators such as prostaglandins, which are major players in the neuroinflammation process[1]. Cyclooxygenases (COX) -1 and 2 are enzymes responsible for the conversion of arachidonic acid into prostaglandins[1]. Traditionally, COX-1 and COX-2 isoforms have been considered constitutive and inducible expression, respectively. Therefore, most reports have focused on the role of COX-2 in the neuroinflammatory response in neurodegenerative diseases, and the contribution of COX-1 remains poorly investigated. Previous studies have demonstrated that COX-1 is inducible expressed in Alzheimer Disease, Multiple Sclerosis and following traumatic brain injury [2,3,4]. Moreover, it has been shown that *Cox-1* was increased with kindling progression, as well as in chronic upregulation of *Il-1*β expression in the hippocampus during brain aging in mouse hippocampus [1,5,6]. The main aim of this study was to evaluated the *cox-1* expression after PTZ-induced seizure in zebrafish brain. **Materials and Methods:** All experimental protocols used in this study were reviewed and approved by the Ethical Committee for Animal Research of the University of Campinas (protocol number 3098-1). Seven days post fertilization (dpf) larvae were placed in a 24-well plate (one larvae per well) containing 15 mM PTZ (seizure group; SG) or PTZ-free water (control group; CG) for 60 min. Following this time, animals were cryoanaesthetized and their heads were isolated, quickly frozen in liquid nitrogen, and stored at −80°C until further processing. A total of five samples (n=5) were used for each group, control (CG) or seizure (SG), and each sample was composed by pooling five larval heads. Total RNA was extracted by standard TRIzol® method and its concentration and quality were determined by EpochTM spectrophotometer and electrophoresis using agarose gels. cDNA was generated using the High Capacity first-strand synthesis system for RT-PCR. Relative mRNA quantification was performed using the ABI 7500 Real Time PCR system with LuminoCt® qPCR ReadyMix, and TaqMan® Gene Expression Assay. The housekeeping gene *eef1a1l1* was used to normalize the mRNA level of *ptgs1*. Data were analyzed using the SDS 7500 software to estimate qPCR efficiency and quantify the relative gene expression. **Results:** Our results showed an inducible *cox1* expression following 60 minutes of PTZ exposure. *Cox1* mRNA levels were up-regulated compared to control group ($p = 0.004$). The mean ± SEM of CG and SG were 1.1 ± 0.07 and 1.5 ± 0.07, respectively. **Discussion:** The present study showed that the expression of COX-1 significantly increased following PTZ-induced seizure in the zebrafish model. **Conclusion:** Our findings support evidence that COX-1 might play an important role in the neuroinflammatory response after seizure; thus, it may represent a possible therapeutic target to treat neuroinflammation in seizures. Because zebrafish seizure model is very willing to anti-epileptic drugs discovery and screening, this results can bring new opportunities to evaluate the effect of anti-inflammatory compounds on seizure suppression. **Supported by**: FAPESP #2014/15640-8, #2013/19151-9, CEPID-BRAIN #2013/07559-3.

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USING GENETIC INFORMATION TO PREDICTING RESPONSE TO TREATMENT IN PATIENTS WITH EPILEPSY

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Introduction: Mesial temporal lobe epilepsy (MTLE) is the most common form of adult epilepsy. Currently, the only characteristic, which seems to predict poor response to clinical treatment in these patients, is the presence of hippocampal sclerosis (HS). Studies showed that single nucleotide polymorphisms (SNPs) in genes encoding drug transporter and metabolism proteins could influence response to drug therapy. Therefore, we evaluated whether combining information from clinical variables and SNPs in candidate genes could improve the discriminatory accuracy of predicting response to drug therapy in patients with MTLE. **Materials and Methods:** We evaluated 78 patients with MTLE who were responsive to antiepileptic drug (AED) therapy and 163 patients refractory to drug therapy. We genotyped 119 SNPs within the *ABCB1, ABCC2, CYP1A1, CYP1A2, CYP1B1, CYP2C9, CYP2C19, CYP2D6, CYP2E1, CYP3A4,* and *CYP3A5* genes. We assessed a first scenario using only clinical variables and a second one including SNP information.

We used random forests combined with leave-one-out cross-validation to identify the best predictive model in each scenario and compared their discriminatory accuracies using the area under the curve statistic, by R software. Additionally, we built a variable importance plot to present the set of most relevant predictors on the best model. **Results:** The selected best model included the presence of HS and 56 SNPs among all genes evaluated. Additionally, including SNPs in the model improved the discriminatory accuracy from 0.4568 to 0.8177. **Discussion:** The present work showed that combining clinical information and SNPs located on candidate genes influencing drug transport and metabolism could improve the discriminatory accuracy of predicting response to drug therapy in patients with MTLE. **Conclusion:** To the best of our knowledge, this study demonstrated for the first time that genetic information improves the prediction of response to drug treatment in patients with MTLE. This may allow patients more likely to develop resistance to AED treatment to have a timely referral for epilepsy surgery, thus improving long-term prognosis. **Support**: CEPID-FAPESP.

COPY NUMBER VARIATIONS ANALYSIS IN BRAZILIAN AND ITALIAN PATIENTS WITH HEMORRHAGIC STROKE

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Introduction: Stroke is a heterogeneous and multifactorial condition, responsible for blockage in blood flow to the brain. Several studies have demonstrated evidence of genetic factors influencing stroke. However, due to its low population frequency and higher mortality rate, hemorrhagic stroke has been less studied. Copy number variations (CNVs) are common structural mutations, which have been identified as causing changes in gene expression, thus leading to disease. The main objective of this study is to study copy number variations in patients with hemorrhagic stroke, looking for possible functional correlates with genes affected. **Materials and Methods:** We used DNA samples from 45 patients with hemorrhagic stroke and 41 controls without stroke from the Stroke Biobank in Joinville/SC. In addition, we validated the results in a group of 18 Italian patients with hemorrhagic stroke. In order to evaluate if Brazilian and Italian sample have similar genetic structure, we performed a principal component analysis (PCA), using R software and the *mahalanobisDist-package*, developed in our laboratory. Only CNVs present exclusively in patients were recorded in our results. We used microarray chips based on SNPs (*Genome-Wide Human SNP Array* 6.0; Affymetrix Inc.) for CNV identification. The results were evaluated by Genotyping Console® Software (Affymetrix Inc.). We analyzed biological pathways containing genes with CNVs using the METACORE Software. The genes selected by this software were further analyzed at DGV and DECIPHER databases as well. **Results:** Our PCA showed that Brazilian and Italian patients present similar genetic structure (p-value = 0.1639). We identified 384 CNVs present only in Brazilian patients with hemorrhagic stroke. These CNVs were present in19 genes potentially related to stroke, with function related to angiogenesis, coagulation, immunology, tissue development and lipid metabolism process. According to DGV database, 4 of these genes (*CDH13*, *FNTA*, *MACROD2* e *NAALADL2*) had no common CNVs reported in the normal population. In addition, 8 of these genes (*CYP2E1*, *DEFB4B*, *MACROD2*, *NOMO1*, *NSF*, *PRODH*, *RAF1* e *RB1CC1*) have been described with relation to cardiovascular and neurological processes. The validation study identified two genes in Italian patients that were also present in Brazilian patients: *MACROD2* and *NSF*. **Discussion:** The genes identified in the present study are good candidates for further analysis, such as *NFS*, which is related to vascular repair and neurological process and*MACROD2*which is related to cardiac and neurological development as well as cardiomyopathy. **Conclusion:** We have demonstrated for the first time that CNVs in *NSF* and *MACROD2*genes may influence the risk for hemorrhagic stroke. In addition, our findings were confirmed in two independent samples of patients with hemorrhagic stroke. **Support:** CEPID-FAPESP.

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ADVANCED PROTEOMIC STUDY OF THE DENTATE GYRUS IN AN EPILEPSY MODEL PRESENTING HIPPOCAMPAL SCLEROSIS

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Introduction: Mesial Temporal Lobe Epilepsy (MTLE) is the most common type of severe epilepsy in adults and it is characterized by histopathological abnormalities in the mesial temporal lobe structures, such as hipocampal sclerosis (HS). The dentate gyrus (DG) is a cortical region that is an integral portion of the larger functional brain system called hippocampal formation. Thus, there are numerous features of the DG that makes it unique in a neuroanatomical and functional way. Therefore we propose to study the DG in its both layers, molecular (ML) and granule (GL), obtained from a rat epilepsy model induced by the perforant pathway stimulation and displaying the classical features of HS. **Materials and Methods:** Rats were induced as described by Norwood et al., 2010. Frozen sections were prepared and the DG was further divided into dorsal (dDG) and ventral portions (vDG) in the epilepsy model (n=3) as well as control animals (n=4). dDG (ML and GL) and vDG (ML and GL) were laser microdissected (Zeiss PALM). Total proteins were obtained using 8M urea extraction and analyzed by LC-MS/MS in an LQT-Orbitrap (Waters). Bioinformatics analysis was performed using MaxQuant and Perseus software and biological correlates were obtained using Metacore. **Results:** We identified a total of 1115 proteins in the dDG-GL of which 69 were differentially expressed in the epilepsy model. We found 465 proteins in the dDG-ML of which 22 were differentially expressed. For the vDG, we identified 1083 protein in the GL of which 55 were differentially expressed and 583 in the ML of which 33 were differentially expressed. Interestingly, we found that enriched biological pathways were different between the GL and the ML in both regions (dorsal and ventral) of the DG. Moreover the dDG and vDG showed distinct proteomic profiles (Figures 1 and 2).

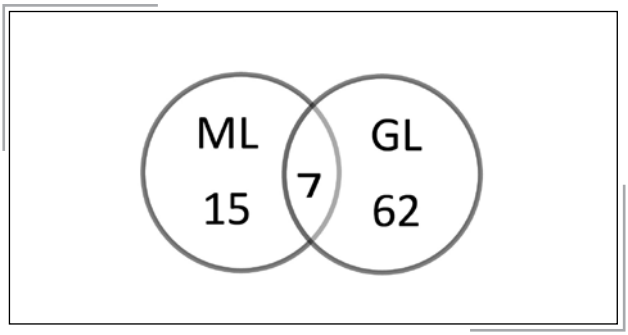

Figure 1. Venn diagram showing the number of proteins differentially expressed in the epilepsy model in the dDG-GL and in the dDG-ML.

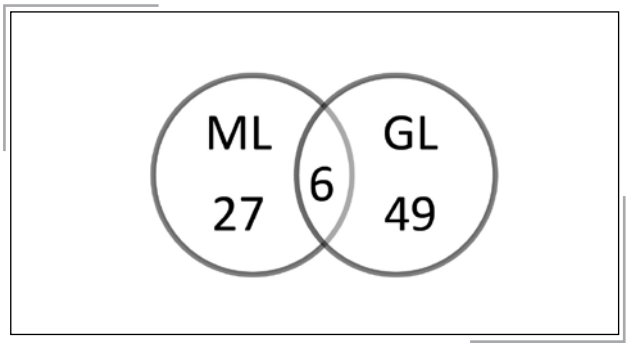

Figure 1. Venn diagram showing the number of proteins Differentially expressed in the epilepsy model in the vDG-GL and in the vDG-ML.

Discussion: GL is composed mainly by cell bodies; whereas, the ML presents predominantly dendrites. Therefore, it is expected that these two regions have differences in protein composition. In addition, there is evidence that the two regions of the DG, dDG and vDG, are functionally and molecularly distinct. Thus, our study was designed to analysis these regions separately. Our results show that the mainly enriched pathway found in the dDG-GL are involved with molecules transportation and neuronal development, while in the dDG-ML are involved with immune response and energy metabolism. In the vDG-GL the represented pathways found are GABA neurotransmission and pathways involving changes in *Cl*- homeostasis in neurons, while the vDG-ML showed alterations in AMPA receptors pathways and in vascular development. **Conclusion:** We have shown that there are remarkable differences in protein expression among different layers and sub-regions of the DG of an animal model of MTLE with HS. The identified proteins indicate new molecular mechanism potentially involved in epileptogenesis. These mechanisms can now be further explored and may eventually be target in development of new treatments to cure epilepsy. **Support:** CEPID-FAPESP.

BUILDING A PUBLIC AND REPRODUCIBLE WORKFLOW FOR WHOLE EXOME SEQUENCING DATA PROCESSING

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Introduction: Research and advancements in genome data processing are motivated by setting up and running *in silico* experiments, which complement the work done in the wet-laboratory. We call these sequential analytical steps workflows. As more workflows are built, scientists start sharing, reusing or repurposing services or workflow fragments, within and between research projects [1]. This propitiates the development of collaborative environments where researchers can publish, share and find workflows. As an example, "myExperiment" is the major public repository for scientific workflows. It makes it simple for scientists to contribute with their methods, by building communities and establishing relationships among researchers, reducing processing time, adding broader expertise and avoiding code reinvention [2]. Here, we present a workflow for whole exome sequencing, which is publically available in myExperiment. **Materials and Methods:** We developed the workflow using Taverna, an open source and domain-independent Workflow Management System consisting of a suite of tools used to design and execute scientific workflows and aid in silico experimentation [3]. The commands were adapted from those in GATK Best Practices Protocols for DNA sequence [4]. The inputs are the files containing the nucleotide sequences (FASTA files), resulting in an annotated variant file (VCF file). **Results:** Our workflow is available at http://goo.gl/KqhyJa and inherits the good practices of reproducibility and log tracking that Taverna offers natively. The possibility of an easy-to-use web interface to execute analytical workflows also represents an attractive alternative for non-trained professionals, who recently started using NGS technologies. **Discussion and Conclusion:** Taverna and myExperiment enable the creation and sharing of scientific workflows without performance loss when compared to traditional runs. They can be used together, enabling researchers to share workflows, input data, resulting analyses and execution log files. These features support the constant use of reproducibility techniques, unlike several other tools. As a result of this work, we deposited in myExperiment the first workflow for variant calling on WES data, designed for scientists interested in processing data using the current best practices set by the GATK team. **Support:** CEPID-FAPESP

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WHITE MATTER MICROSTRUCTURE IN IDIOPATHIC CRANIOCERVICAL DYSTONIA

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Introduction: This work consisted in evaluating the WM (white matter) microstructure in craniocervical dystonia (CCD) using DTI (diffusion tensor imaging). Dystonia consists in involuntary muscle contractions, causing twisting movements and abnormal postures. CCD involves contractions of head and neck's muscles. Recent neuroimaging studies have shown the involvement of sensorimotor areas and cerebellum in idiopathic dystonia[1-3]. **Materials and Methods:** We evaluated 40 patients (59.5±12.3 years-old) and compared than to 40 healthy controls (56.0±15.0 years-old). Secondarily, we divided the analysis in 4 groups according to dystonia localization: 5 patients with blepharospasm (BSP) (61.8±10.3 years-old), 9 with blepharospasm + oromandibular (BOM) (68.5±5.0 years-old), 8 with blepharospasm + oromandibular + cervical (BOM+ CD) (63.1±11.1 years-old) and 18 with cervical (CD) (52.8±12.2 years-old). MRI images were obtained on a 3T scanner 1-2 weeks after BoNT injections. We performed DTI with TBSS software and obtained fractional anisotropy (FA) and mean diffusivity (MD). We performed two confirmatory analyses: ROI (region of interest) based approach on obtaining the average FA values of all WM voxels, and tractography of the tracts: pyramidal, body of corpus callosum (CC), brainstem, uncinate fasciculus, inferior occipitofrontal fasciculus (IOF) cingulum and fornix [4-6]. **Results:** We did not find significant difference in the mean FA and MD between the groups in any analyses. ROI analyses: total group (p=0.18), CD group (p=0.41), BSP (p=0.62), BOM (p=0.90), BOM+CD (p=0.24). Tractography analyses: pyramidal: left (FA p=0.95; MD p=0.05) and right (FA p=0.22; MD p=0.92) inferior, left (FA p=0.24; MD p=0.60) and right (FA p=0.83; MD p=0.10) middle, left (FA p=0.27, MD p=0.77) and right (FA p=0.93; MD p=0.89) superior, body of CC (FA p=0.67; MD p=0.64), brainstem (FA p=0.29; MD p=0.35), uncinate fasciculus (FA p=0.11; MD p=0.95), IOF (FA p=0.46; MD p=0.27), cingulum (FA p=0.84; MD p=0.21) and fornix (FA p=0.17; MD p=0.06). **Discussion:** There are no studies using DTI to evaluate the whole WM in CCD. The lack of DTI changes in CCD suggests that the WM tracts are not primarily affected. WM tract involvement is probably functional and it does not translate into morphological changes [7-9]. **Conclusion:** These results suggest that WM tracts are not primarily affected in CCD. Further studies should evaluate the presence of functional and connectivity abnormalities. **Study Supported by:** Fapesp and CNPq.

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ASSOCIATION STUDY OF MICRORNA-BINDING SITE POLYMORPHISM OF *NEUROG2* GENE WITH FOCAL CORTICAL DYSPLASIA (FCD)

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Introduction: FCD is a malformation of the cerebral cortex usually associated with cell abnormalities, giant/dysmorphic neurons and balloon cells and severe drug-resistant epilepsy. The mechanisms involved in the pathogenesis of type II FCD are not completely understood. Our group previously identified the microRNA (miRNA) hsa-miR-34a and its target gene *NEUROG2* as possibly related to the mechanism of this type of cortical malformation, since both are found abnormally expressed in tissue from patients with FCD. This gene is a member of the family of transcription factors bHLH (basic helix loop-helix) which plays a central role in cell fate specification and neuronal differentiation in many regions of the central nervous system[1]. Computational predictions[2] indicate that there a single nucleotide polymorphism (SNP), rs57336627(G>A),within hsa-miR-34a binding site and also showed that hsa-miR-34a had a higher binding affinity for the G genotype than for the A genotype. Our hypothesis is that abnormal expression of *NEUROG2* could be caused by deregulation of hsa-miR-34a, which could be caused by the presence of this SNP in the 5'UTR region. This would lead to instability on miRNA binding sites or the miRNA inability to bind to *NEUROG2*, causing a less efficient suppression of gene expression. In this study, we evaluated whether SNP in miRNA-binding site is associated with the FCD. **Materials and Methods:** We performed a case-control study included 11 type II FCD patients and 315 control individuals. All donors provided written informed consent prior to enter the study. Genomic DNA was isolated from peripheral leukocytes by the phenol extraction method. Genotyping was employed by quantitative PCR (qPCR) with rs57336627, TaqMan™ (- Life Technologies). The results were analyzed using Thermo Fisher Cloud software. Hardy-Weinberg equilibrium was conducted to evaluate the genotype frequencies among groups. Fishers Exact Test (R statistical environment, α= 0.05) was used to evaluate the associations between FCD and SNP. **Results:** Our preliminary results indicate that Hardy-Weinberg equilibrium was not maintained between case and controls, p = 0.4801. We found that allelic distributions of the rs57336627 were different among cases and controls: G allele was found in 91.2% of control individuals and 86.3% of the patients and A allele was found in 8.8% of control individuals and 13.6% of the patients. Furthermore, we did not find any association between this SNP and FCD, p =0.4345. **Discussion:** We did not observe any statistically relevant association between SNP rs57336627 and FCD, most likely due to our relative smaller sample size. However, there is a difference between the two groups on the relative allelic frequencies. Allele A was more frequent in patients as compared to controls (1.5-fold difference).We expect to recruit additional patients as well as to perform functional studies in order to clarify the issue. **Conclusion:** Our preliminary results do not show significant association between SNP rs57336627 SNP and FCD. **Support:** CEPID-FAPESP

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SEARCHING FOR SOMATIC MUTATIONS IN FOCAL CORTICAL DYSPLASIA BY USING NEXT GENERATIONS SEQUENCING

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Introduction: Epilepsies are one of the most frequent neurological diseases, affecting 1.5-2% of the worldwide population [1]. Malformations of cortical development (MCD), including Focal Cortical Dysplasia (FCD), can cause epilepsy and are often associated with the occurrence of refractory seizures [2]. FCD is characterized by alterations in cytoarchitecture also observed in other MDCs, such as in Tuberous Sclerosis (ET) and Hemimegaencephaly (HME) [3,4]. Recently, an association among mosaic mutations, ET, HME and FCD has been reported [5]. The identification of mosaic mutations in FCD can contribute to the understanding of complex diseases. **Materials and Methods:** Deep-Whole-Exome sequencing was performed on genomic DNA extracted from brain tissue resected by surgery (BTRS) and blood of four patients with FCD. We performed capturing and enrichment with Nextera® Expanded Kit (Illumina®). Samples were sequenced following a 200bp paired-end protocol in a Hiseq2500 (Illumina®) to achieve at least 200x of average coverage. We aligned sequences using BWA MEM and performed realignment around SNPs and indels, quality recalibration and variant calling using the Genome Analysis Toolkit (GATK). We evaluated mosaicisms using SomaticSniper and finally we added annotation to the variants found using Variant Effect Predictor. Variants were classified as mosaic mutations when less than 50% of reads are not aligned to human genome reference and are present only in BTRS. Variants were filtered prioritizing frameshift, missense, nonsense and splicing site mutations that were localized in coding regions or exon-intron boundaries. In addition, we also focused in not described variants or variants whose minor allele frequency (MAF) is < 0.1. **Results:** We identified a total of eight mosaic mutations in BTRS, including four variants localized in genes belonging to mTOR pathway (*EIF4EBP1, IRS1, ULK1* and *STRADA*), three mutations localized in genes belonging to Tau pathway (*GAPDH, ADAM10* and *ERN1*) and one mutation in the *CLIC6* gene. **Discussion:** Somatic mutations were identified in genes with roles and expression in central nervous system (CNS). Since mosaic mutations in genes associated with Tau and mTor pathways have been reported in patients with FCD, we believe that the variants identified in our cohort of patients are strong candidates to be involved in FCD etiology. **Conclusion:** Further experiments will be necessary to validate our results**.** In addition**,** more patients should be sequenced in order to search for additional somatic mutations. We hope that this project will contribute to a better understanding of the genetic etiology of FCD as well as to identify molecular mechanisms involved in the developing of the cerebral cortex. **Supported by:** CEPID-FAPESP

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EPIGENETICS IN A MODEL OF TEMPORAL LOBE EPILEPSY: WHAT'S GOING ON IN *DENTATE GYRUS*?

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Introduction: In order to improve the pathophysiology knowledge of temporal lobe epilepsy (TLE) *in vivo* animal models that present features similar to those seen in TLE patients have been developed. One of these models is based on the systemic administration of chemoconvulsants, like pilocarpine, to induce an initial precipitating injury (*status epilepticus*). Epigenetics summarizes alterations to the chromatin template that collectively establish and propagate different patterns of gene expression without changes in DNA sequence. To better understanding the methylation pattern in animal models of TLE we performed whole genome bissulfite sequence (WGBS) in *dentate gyrus* samples of pilocarpine induced rats. **Material and Methods**: We used laser capture microdissection (LCM) to obtain the *dentate gyrus* structure from hippocampus region of control rats (*n*=2) and pilocarpine induced rats (*n*=2). DNA was exctrasted using proteinase K protocol with modifications and the DNA was converted by bissulfite with EZ DNA Methylation-Lightning™ Kit (Zymo Research). After the conversion library was generated using TruSeq DNA Methylation kit then this material was sequenced in Illumina HiSeq 2500. **Results**: Bioinformatics analysis found 18 different methylated regions (DMR) along the 20 chromosomes. In these regions we found several genes as Atp10d (ATPase, class V, type 10D) – involved with ATP binding, Puf60 (poly-U binding splicing factor 60) – involved with RNA/DNA binding. **Conclusion**: The regions are still under analysis in order to find others genes that may be involved with TLE. We are going to increase the number of sample to improve our data.

FUNCTIONAL CHARACTERIZATION OF SODIUM CHANNEL MUTATIONS ASSOCIATED WITH EPILEPSY

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Introduction: Many epilepsy syndromes are genetically inherited [1]. Mutations in *SCN1A*, a gene that encodes the α-subunit of the sodium channel voltage-dependent (Nav1.1), impair the flow control of sodium ions, resulting in abnormal sodium influx into neurons that causes a disruption in the channel activity, neuronal hyper excitability and epilepsy [2]. Previous studies carried out by our group found that 81% of patients with Dravet syndrome (DS) have de novo mutations in *SCN1A* [3]. Interpretation of the mutation impact in protein function is usually performed using pathogenicity prediction *softwares*. Therefore, functional studies are important both to confirm results from *in silico* analysis and to characterize mutations that are not suitable for analysis using bioinformatics tools. **Materials and Methods:** Mutations c.5434T> C, c.5329delG, c.5177G> A, and c.5864T> C were selected following two parameters: 1) mutations that are not described in literature and 2) high protein damage score obtained by bioinformatics tools as SIFT and Polypen2. Primers for site-directed mutagenesis were designed using the PrimerX program. The wild forms of *SCN1B*, *SCN2B* and *SCN1A* genes (wild-type genes) were cloned by recombinant DNA technology. Recombinant plasmids were isolated, purified and submitted to sequencing on a Miseq in order to evaluate if sequences were cloned properly. *SCN1A* recombinant plasmid will be submitted to site directed mutagenesis. **Results:** Bioinformatics studies show that c.5434T> C mutation causes an amino acid change resulting in a severe disruption of the protein. The c.5329delG and c.5177G> A mutations generate a truncated protein. The c.5864T> C mutation results in a change of amino acids, but sim effect on the protein, will be used as control. Recombinant plasmids were constructed for wild type sequences of *SCN1B*, *SCN2B* and *SCN1A* genes. At this moment, we are purifying recombinant plasmids in order to submit cloned genes for sequencing. **Discussion:** Mutations analyzed by bioinformatics showed deleterious effect in *SCN1A* function, but the real biological effect cannot be clearly demonstrated using these tools. I addition, *SCN1A* is subunit of a sodium channel; therefore pathogenicity is better evaluated when mutant forms of *SCN1A* are expressed together with *SCN1B* and *SCN2B.* **Conclusion:** We succeeded in obtaining recombinant plasmids containing wild type *SCN1A*, *SCN1B* and *SCN2B* genes. We are creating mutant forms of *SCN1A* to be co-expressed with *SCN1B* / *SCNB2* genes and to evaluate how sodium channel is impaired by these mutations using cell electrophysiology experiments.

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SYSTEMIC INFLAMMATION IS LINKED TO DEFAULT MODE NETWORK FUNCTIONAL CONNECTIVITY IN ALZHEIMER'S DEMENTIA AND AMNESTIC MILD COGNITIVE IMPAIRMENT

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Introduction: The default mode network (DMN) is early affected in Alzheimer's disease (AD). Inflammatory processes also play a role in pathological AD cascade, but its relationship with changes in the DMN is still unknown. We aimed to investigate the relationship between inflammatory cytokines and DMN functional connectivity (FC) in amnestic Mild Cognitive Impairment (aMCI) and AD patients. **Materials and Methods:** All images were acquired in a 3T scanner (Philips Achieva). 34 aMCI and 21 mild AD patients were included. DMN mask was used as a template to extract each patients FC value of the DMN subregions. We performed multiple regression tests, adding inflammatory cytokines (IL-1B, IL-6, IL-8, IL-10, IL-12, TNF-α) as independent variables and DMN regions FC values as dependent variables. **Results:** In the aMCI group, medial parietal region FC correlated with age ($p = 0.004$, $t = -3.38$) and IL 10 ($p = 0.03$; $t = -2.25$, model $R^2 = 0.50$). The frontal medial region FC correlated with age ($p = 0.03$; $t = -2.23$), IL 8 ($p = 0.001$; $t = -3.71$) and TNF-α ($p = 0.01$; $t = 2.71$, model $R^2 = 0.53$) and the temporal region FC correlated with TNF-α ($p = 0.001$; $t = 3.71$) and age ($p = 0.02$; $t = -2.47$, model $R^2 = 0.51$). Regarding the AD group, the medial temporal region FC correlated only with IL 6 ($p = 0.008$; $t = -3.04$, model $R^2 = 0.39$). **Discussion:** This study showed that the average serum concentrations of IL-6, IL-10, IL-12 and TNF-α was higher in aMCI group in comparison with AD and controls. As described above, both pro and anti-inflammatory interleukines predicted the FC of DMN subparts an AD and aMCI. These findings are interesting, since it suggests a systemic inflammatory condition in individuals with aMCI, which could contribute to the progression of cognitive impairment and development of dementia. In AD, only IL6 predicted the FC of the most commonly affected anatomical region, the medial temporal subpart. **Conclusion:** We showed that systemic inflammation predicts FC in the DMN of aMCI and mild AD patients. Peripheral inflammatory cytokines could be potential biomarkers and therapeutic targets in aMCI with physiopathological evidence of AD.

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INVESTIGATING A STOP-GAIN VARIANT ASSOCIATE WITH CELL DIFFERENTIATION AND SYNAPTIC MACHINERY IN FOCAL CORTICAL DYSPLASIA (FCD)

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Introduction: FCD is a malformation of the cerebral cortex usually associated with cell abnormalities, giant/dysmorphic neurons and balloon cells and severe drug-resistant epilepsy. The mechanisms involved in the pathogenesis of type II FCD are not completely understood. We have previously identified a rare stop-gain variant, rs76555439, located in in C-terminal binding protein 2 (*CTBP2)* gene in a few patients with FCD. This variant is absent in our in-house control database of 29 samples as well as in two independents control databases: Exome Variant Server and Exome Aggregation Consortium (ExAC). Furthermore, *CTBP2* gene has been related to: i) transcriptional corepressors that associate with DNA-binding transcription factors and have been linked to the regulation of the transition of neural precursor cells to a differentiated state[1]and ii) specialized synapses known as synaptic ribbons [2]. In this context, the goal of this work is to investigate the frequency of this *CTBP2* variant in an additional cohort of FCD patients and healthy control individuals in order to assess a possible genetic association. **Materials and Methods:** We are performing a validation study using Sanger sequencing in an additional cohort 17 type II FCD patients and 315 control individuals. All donors provided written informed consent prior to enter the study. Genomic DNA was isolated from peripheral leukocytes by the phenol extraction method. PCR primers targeting the variant region were designed using Primer3 on genomic DNA sequence. 50ng of genomic DNA for each sample was amplified and primer pair used for amplification was as follows: forward primer, 5'-GAAGACAGAAAAAGTTGCCATCCACACC-3', and reverse primer, 5'-TCATCATCAGCAGACATAAGCAAGGCAGA-3´. PCR touchdown was carried out using a thermocycler for 35 cycles with annealing temperature of 58.7°C. To confirm the specificity of amplification, the PCR products were subjected to electrophoresis in 1% agarose gel. Sanger sequenced will be done by capillary electrophoresis on ABI 3500XL (Applied Biosystems). **Results/Discussion and conclusion:** To date, we initiate the PCR standardization and our preliminary results indicate that this *CTBP2* variant could have a relevant role in molecular mechanisms involved in this cortical malformation.

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BDNF AND *KARLN* TRANSCRIPTS PROFILE IN IMMATURE ZEBRAFISH BRAIN AFTER PTZ-INDUCED SEIZURE

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Introduction: It is known that seizures are related to neuroplastic changes in the brain. Zebrafish has become an attractive *in vivo* model for epilepsy studies; however, the transcript profile of plasticity-related genes in immature zebrafish brain after seizures is unknown. In this study we aimed to investigate the transcript response of two genes associated to plastic changes in normal and pathological brain conditions, *karln* and *bdnf* [1,2] genes. **Materials and Methods:** This study was approved by Ethical Committee for Animal Research of the University of Campinas (#3247-1). Zebrafish were maintained according guidelines. Larvae at seven days post-fertilization (dpf) were separated in Seizure (SG) and Control (CG) groups. Seven dpf larvae from SG were placed individually in a 24 well-plate (one larvae per well) containing 15mM PTZ for 20 minutes. CG was handled in the same condition, but in normal bath water. According to their groups (0.05 or 24h after seizure), animals from SG were crioanesthetized and their heads were collected for RNA extraction. We did the same process for the CG at 0.05h and 24h. A total of five samples were used for each group. Each larvae sample was composed by pooling 10 heads. Reverse transcriptase quantitative-PCR amplifications were carried out in triplicates with ef1α as endogenous control using TaqManTM System (Applied Biosystems). The relative quantification (RQ) was calculated by the equation $RQ=2^{-\Delta\Delta CT}$. The results are presented as mean ± Standard Error of Mean (SEM). Statistical analyses were performed by One-way Analysis of Variance with $p \leq 0.05$. **Results:** Our results showed no statistical difference between SG and CG for both genes investigated at 0.05h or 24h after seizure. The mean ± SEM of *karln* mRNA levels and the p values obtained comparing each time-point between the CG and SG groups were the following: CG0.05h 1.014±0.04113 and SG0.05h 0.9112±0.07714 ($p \geq 0.5$); CG24h 0.4729±0.05264 and SG24h 0.4874±0.04331 ($p \geq 0.5$). The mean ± SEM of *bdnf* mRNA levels and the p values obtained comparing each time-point between the CG and SG groups were the following: CG0.05h 1.028±0.07193 and SG0.05h 1.017±0.1116 ($p \geq 0.5$); CG24h 0.3051±0.02934 and SG24h 0.3223±0.02866 ($p \geq 0.5$). **Discussion:** Although no differences were found between SG and CG for both genes in immature zebrafish brain, our previous data in adult zebrafish SG [3] showed an increase in *bdnf* transcript levels immediately (0.05h) after PTZ-induced seizure, which was significantly different from adult CG (data not shown). **Conclusion:** Our results showed that zebrafish appears to have different seizure-induced effects in the immature brain compared with the adult brain. Differences between immature and adult brain following seizures were reported in the literature in other animal models. Together with all other features that makes the zebrafish suitable for epilepsy studies, here, we demonstrate that zebrafish can be an alternative model to investigate the molecular mechanisms differences of seizure-induced damage between immature and mature brain. Further investigations are underway. **Supported** by Fapesp #2014/15640-8, CEPID-Brainn, Pibic-CNPq.

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ANALYSIS OF COPY NUMBER VARIATION IN PATIENTS WITH EPILEPTIC ENCEPHALOPATHIES AND GENERALIZED EPILEPSY WITH FEBRILE SEIZURES PLUS

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Introduction: Epileptic encephalopathy is a chronic disorder that consists of repeated disruptions in the electrical activity of the brain, which can culminate on psychomotor dysfunctions [1]. Associated issues of the Childhood Epileptic Encephalopathies (CEE) are neurological, intellectual, behavioral or psychiatric disorders [2]. Since CEEs are complex disorders, it is a challenge to confirm these conditions with molecular findings. As some patients with Dravet Syndrome were found to have copy number variations in the *SCN1A* gene [3], one of the most important genes in the molecular analysis of epileptic encephalopathies, testing patients with other encephalopathies and clinically related conditions such as Generalized (or Genetic) Epilepsy with Febrile Seizures Plus (GEFS+) is essential. GEFS+ is an inherited condition that consists of repeated febrile seizures, usually generalized, that either continue after the age of 6 or also present afebrile seizures [4]. Most people with GEFS+ do not have cognitive deficit; however, few patients with more severe presentation may have intellectual and physical disorders [5]. **Materials and Methods:** The technique used to assess copy number variations was Multiplex Ligation Probe Amplification (MLPA). The results of the MLPA were then evaluated in the computer program Coffalyzer. Samples of DNA from a total of 55 patients were analyzed though this technique, 48 of which were diagnosed with CEEs and 7 were diagnosed with GEFS+. **Results:** One patient with GEFS+ and borderline Dravet syndrome was found to have a deletion in exons 21 to 26 of the *SCN1A* gene. It is predicted that this mutation is deleterious to protein function, since significant domains would be disrupted. This is an ongoing study, therefore, additional patients are being analyzed.

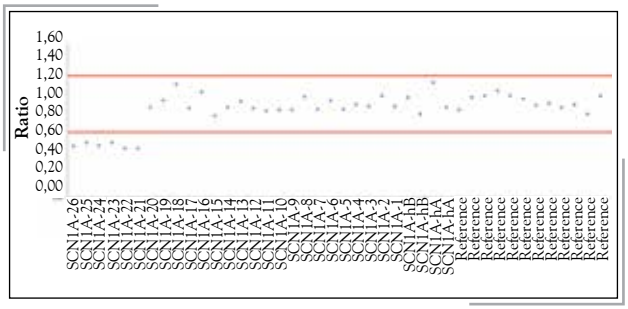

Figure 1. Illustration of probe ratios in the single patient with deletion in SCN1A. For reference, it was adopted as normal the interval from ratios 0.7-1.3, marked by the two red horizontal lines. Dots outside the normal interval depict the region where the deletion was found.

Discussion: The deletion found in this work is possibly associated with the phenotype of the patient, who was diagnosed with borderline Dravet Syndrome. The analysis of the patient family history shows additional family members with febrile seizures, indicating the most likely diagnosis of GEFS+. **Conclusion:** This work reinforced the importance of analyzing copy number variations, not only point mutations, in patients with CEEs other than Dravet Syndrome, including patients with GEFS+. Therefore, we can conclude that the clinical spectrum of microrearrangements in *SCN1A* is broader than previously described.

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FUNCTIONAL BRAIN NETWORKS IN RESTING STATE USING ARTERIAL SPIN LABELING TECHNIQUE

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Introduction: The presence of functional brain networks activated during resting state, i.e., no response to stimuli or tasks, is known and has been verified by different techniques (fMRI-BOLD, PET) [1]. The impairment of these networks has been associated with various mental illnesses, such as Alzheimer's Disease, sclerosis, and schizophrenia. The study of these networks using a noninvasive and quantitative technique, such as Arterial Spin Labeling (ASL), is of great importance and interest in Neuroscience field. Therefore, the present study aims to map brain functional networks activated during resting state using ASL, which also provides quantitative values of cerebral blood flow (CBF) in one image acquisition. **Materials and Methods:** Experiments were performed on a 3T Philips Achieva System (Philips Achieva, The Netherlands), using 32-channel head coil reception and body coil transmission. Axial pseudo-continuous ASL (pCASL) images were acquired using a 2D single-shot EPI sequence with the following parameters: TR/TE = 4000/14 ms, excitation angle = 90°, number of slices = 20, thickness slices = 5 mm, labeling time = 1650 ms, post-labeling delay = 1525 ms, number control/label images = 75 pairs. To validate ASL results, BOLD-fMRI images were also acquired using a 2D EPI sequence with the following parameters: TR/TE = 2000/30 ms, excitation angle = 90°, number of slices = 31, slice thickness = 4 mm, interval between slices (gap) = 0.5 mm, number of repetitions = 320. For anatomic reference, images were acquired using a T1-weighted GE sequence with the following parameters: TR/TE = 7/3.1 ms, excitation angle = 8°, FOV = 240 x 240 mm^2, number of slices = 160, slice thickness = 1 mm. **Results:** Resting state networks were obtained from pCASL data of one subject and using the proposed parameters. Figure 1 shows the Default Mode Network (DMN) obtained with (A') pCASL and (B') BOLD-FMRI. Both results agree with the literature [1]. However, some differences have been observed comparing the techniques, such as the size of activated areas. pCASL regions shown in the maps are more restrict [2]. **Discussion:** It was possible to obtain activation maps at resting state from a healthy volunteer using a 2D pCASL method available in our equipment. Differences between pCASL and BOLD-fMRI methods can be explained by the nature of MRI signal obtained from both techniques [2]. **Conclusion:** The present results allow future studies of Resting State Networks, functional connectivity between regions of interest and physiological relations with CBF values.

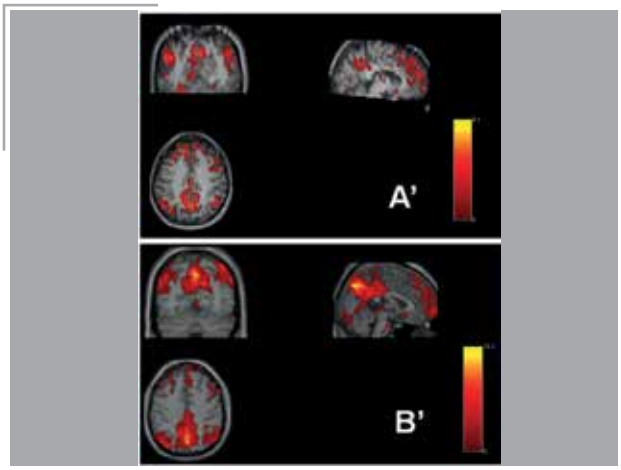

Figure 1.

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CEREBRAL BLOOD FLOW AND VASOREACTIVITY IN HEALTHY AGING: AN ASL STUDY

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Introduction: To comprehend neurovascular signs of age-related neurological diseases, it is essential to understand cerebral perfusion variations in healthy aging. Recent studies have shown decreased baseline cerebral blood flow (CBF) in healthy elderly [1, 2] and altered cerebrovascular reactivity (CVR) in mild cognitive impairment [3]. Therefore, the present study aimed to assess baseline CBF and CVR to CO_2 inhalation in young and elderly subjects using a pulsed arterial spin labeling (PASL) method. **Materials and Methods:** Sixteen asymptomatic volunteers (n = 10 young adults, age: 30 ± 7 years; n = 6 elderly, age: 64 ± 8 years) with no history of diabetes, hypertension and neurological diseases, participated in this study. All participants read and signed an informed consent approved by the Ethics in Research Committee of the Clinical Hospital of Ribeirao Preto (HCFMRP) before participating in the study. Experiments were performed on a 3T Philips Achieva System (Philips Achieva, The Netherlands), using 8-channel head coil reception and body coil transmission. PASL images were acquire using a 2D single-shot EPI sequence with the following parameters: TR/TE = 3000/15 ms, matrix = 64 x 64, FOV = 240 x 240 mm^2, 12 slices, slice thickness = 5 mm, gap = 0.5 mm, labeling plan thickness = 200 mm, number of control/label = 40 pairs, post-labeling delay (PLD) = 1500 ms (young group) and 2000 ms (elderly group). For CVR evaluation, PASL images were acquired under normocapnia and hypercapnia. A voxelwise analysis between groups was performed using a 2-sample *t*-test with FWE (p = 0.01) and a cluster size threshold of 50 voxels. **Results:** Under normocapnia, mean CBF value across the entire gray matter was significantly reduced for elderly (33 ± 9 mL/100g/min) compared to young adults (42 ± 4 mL/100g/min, p = 0.05). The same age-related difference was observed for different brain regions in both hemispheres: inferior, middle and superior frontal gyri; precentral and postcentral gyri; superior temporal gyrus; insula, putamen, thalamus, caudate, anterior cingulate gyrus, cuneus, inferior parietal lobule (supramarginal gyrus) and angular gyrus (Figure 1). No region showed significantly increased CBF in elderly. Moreover, CVR for the entire gray matter was significantly reduced for elderly compared to young adults (p = 0.05).

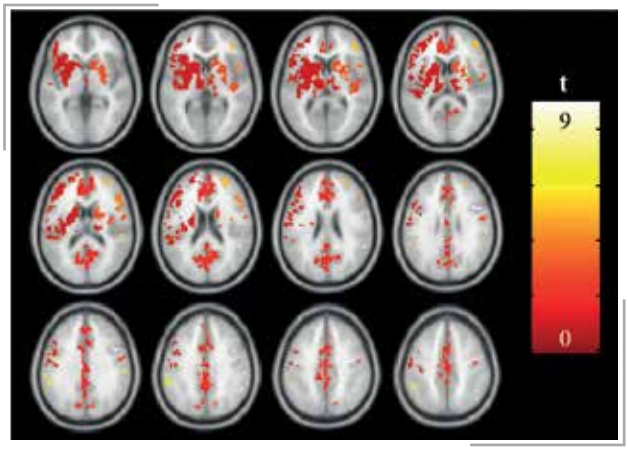

Figure 1. The Default Mode Network obtained using (A') pCASL and (B') BOLD-fMRI.

Discussion: The present study investigated the relationship between cerebral perfusion and normal aging, and the results are consistent with previous studies [1, 2]. Reduced baseline CBF and CVR in elderly is likely to be related to arteriosclerosis and small vessel disease. It has been shown that normal aging is associated with changes in cerebrovascular function, structure and cellular metabolism, and even in the absence of Alzheimer's disease and other degenerative illness, aging is accompanied by significant decline in functions related to memory, language, and motor functions [3]. Therefore, our results suggest that cerebral perfusion impairment observed, for example, in middle and inferior frontal gyri, and precentral gyrus may be associated with function decline in elderly. **Conclusion:** CBF and CVR were successfully investigated using a protocol that causes minimal or no discomfort for the subjects. Decreased CBF and CVR in healthy aging may be related to function decline in elderly.

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EPILEPSY: BEHIND THE WHITE MATTER INVOLVEMENT

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Introduction: Among the major neurological disorders, epilepsy is one of the main conditions. About 1% of people worldwide (around 65 million) have epilepsy. The pivotal pathophysiology is determined by changes in neurons behavior in specific regions of the brain, resulting in recurrent seizures [1]. However, recent neuroimaging studies indicate that white matter is altered in epilepsy as well, but its meaning remains unknown. It is known that after white matter injury, expression of Dishevelled Associated Activator of Morphogenesis 2 (Daam2) inhibits oligodendrocyte differentiation, precluding neuron remyelination [2]. In this context, the aim of this study is to evaluate Daam2 expression in epileptic and non-epileptic brain. **Materials**

and Methods: Formalin-fixed and paraffin-embedded (FFPE) sections of temporal lobe of autopsy specimen (control, n= 1) and surgical specimen of patient with mesial temporal lobe epilepsy (case, n= 1), who had undergone surgery for refractory seizures were evaluated using immunohistochemistry. Sections were deparaffinized, rehydrated and submitted to antigen retrieval (citrate pH 6.0). The primary antibody Daam2 (Sigma, MO, St. Louis, USA) was applied at 1:50 dilution. ADVANCE™ (Dako, CA, Santa Clara, USA) was used to detect primary antibody. The evaluation of immunohistochemical results was performed by an experienced neuropathologist (FR). **Results:** In the hematoxylin and eosin slices we did not observe any differences between case and control tissue. In Daam2 immunohistochemical analysis, both case and control tissue did not show Daam2 expression in gray matter. However, we observed that patient tissue had an unspecific higher expression of Daam2 in white matter when compared to control (Figure 1A and B). Interestingly, some neurons presented Daam2 expression in both case and control tissue (Figure 1C).

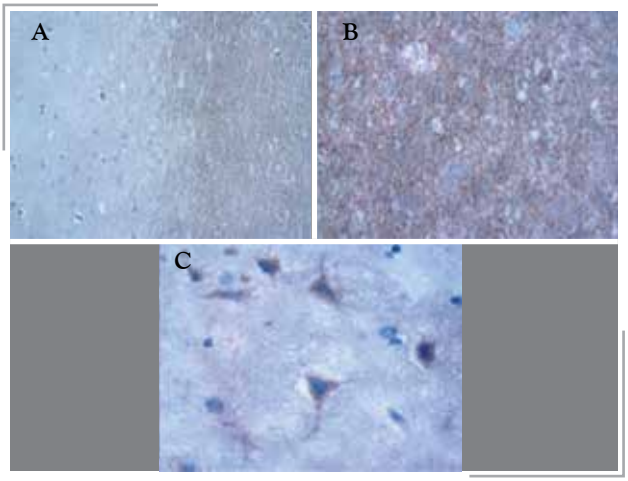

Figure 1. Surgical specimens of patients with mesial temporal lobe epilepsy: (A) represents the transition between gray matter (left), with no expression of Daam2, and white matter (right), with expression of Daam2 (100x); (B) represents a zoom in white matter with unspecific Daam2 reaction (400x); and (C) represents neurons with expression of Daam2 (400x).

Discussion: We are reporting on preliminary results; therefore, additional samples will be analyzed. Daam2 regulates Wnt pathway by direct PIP5K modulation. After injuries, increased expression of Daam2 determines inhibition of oligodendrocytes differentiation, and is responsible to reduced neuron remyalination. Thus, recurrent seizures could be a pivotal trigger to induce Daam2 expression causing further tissue damage by inhibiting remyelination of the affected region after seizure- induced damage. **Conclusion:** Daam2 signaling (Wnt pathway) could be involved in white matter damage in epilepsy.

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HIPPOCAMPAL ATROPHY SEVERELY DISRUPTS RECRUITMENT OF DEFAULT MODE NETWORK IN TLE

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Introduction: This work consisted on an investigation of the dysfunction of Default Mode Network (DMN) during resting-state functional Magnetic Resonance Imaging in mesial Temporal Lobe Epilepsy (mTLE) patients with Temporal Lobe Epilepsy-Hippocampal Sclerosis (TLE-HS) and without hippocampal atrophy (TLE-NEG). The DMN is a functional connectivity network known by being active during introspective thoughts, such as anticipating and planning the future. Studies have suggested that the DMN is less active or has an uncommon activation in patients with mTLE. However, little is known regarding the impact of hippocampal atrophy in disrupting DMN performance. **Materials and Methods:** We scanned 95 controls, 21TLE-NEG and 64TLE-HS on a 3T scanner. A seed based analysis was performed from the posterior cingulate cortex (PCC) to identify the DMN (coordinates: 0, -51, 21). Images were pre-processed and analyzed using the SPM12 (http://www.fil.ion.ucl.ac.uk/spm/software/spm12/) with an in-house built routine. After extracting individual activation maps at first-level of SPM, a full-factorial model at second level was applied to compare differences between groups. Significance was determined at $p<0.001$and clusters> 5 voxels. **Results:** Patients and controls were balanced for age and gender. We observed that controls presented normal activation of DMN regions, including temporal lobe, parahippocampal gyrus and cerebellum. TLE-NEG displayed a less activated pattern, but with similar spatial distribution. On the other hand, TLE-HS presented more severe disruption of activation with fewer areas recruited and no temporal activation of the DMN. **Discussion:** The results found are probably due to the important role that hippocampus and associated structures have on the DMN activation since the presence of atrophy is related with worse DMN activation. It is interesting to notice that we did not separate patients considering seizure frequency and thereby both groups mixed subjects with mild and refractory epilepsy. It suggests that the impact of hippocampal atrophy is greater than seizure frequency to generate disruptions on DMN. **Conclusion:** The present work suggests that the absence of hippocampal atrophy in mTLE allows activations of DMN similar to controls, whereas the presence of hippocampal atrophy in mTLE may impair the proper recruitment of DMN areas such as temporal lobe and hippocampus. In our next step, we plan to investigate associations between cognition, measured by neuropsychological tests and DMN alterations here detected.

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COMPARING RESTING STATE CONNECTIVITY PATTERNS BETWEEN NIRS AND FMRI

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Introduction: The resting state occurs when a subject is not performing any specific task and can reflect the brain spontaneous activity [1]. Over the last years, we have pioneered the measurement of resting state connectivity across different brain regions with near-infrared spectroscopy (NIRS) measurements [2]. For the most part, connectivity studies with NIRS resembles results from blood oxygenation level-dependent (BOLD) contrast in functional magnetic resonance imaging (fMRI) [1-3], but with the advantage of NIRS being a portable technique with a higher temporal resolution. Here we aimed to compare the NIRS and fMRI spontaneous networks during the resting state. **Materials and Methods:** We simultaneously collected data with NIRS and fMRI from 12 healthy adults (20 ± 2 years old). All subjects were initially instructed not to focus on any specific task. The optical geometry was designed to cover most of the head, including the parietal, temporal and frontal lobes. Up to six 5-minute runs were performed for each subject. For NIRS analysis, we band-pass filtered (0.009–0.08 Hz) the detected intensity and regressed out the global signal with Principal Components Analysis. Oxy-hemoglobin (HbO) and deoxy-hemoglobin (HbR) concentration changes were estimated with the modified Beer-Lambert law. Similarly, we preprocessed the fMRI data and applied the same cutoff frequencies and algorithms to get a BOLD time-course. For graph analysis, each measurement (i.e., source-detector separations in NIRS and a 90-region atlas parcelation in fMRI) was treated as a node. The links between nodes were computed based on the Pearson correlation coefficient, ρ, between their time series for each run. We varied the correlation coefficient threshold from 0.05 to 0.95 so that we could investigate the behavior of the networks as a function of ρ. For each threshold, we computed standard network parameters such as the average degree (K), the clustering coefficient (CC) and characteristic pathlength (P) [5]. **Results and Discussion:** Our preliminary results have shown a high reproducibility of the global network parameters among runs from the same subject in both techniques. Overall, we observed that K decays exponentially as a function of ρ (i.e., $K \alpha e^{-\lambda\rho}$). For a single representative subject, λ varied from 3.1 (0.2) to 4.7 (01) across all runs when the network was built using the HbR time-course. The variation from BOLD was very similar: λ varied from 3.7 (0.3) to 4.7 (0.2). The similar behavior between BOLD and HbR makes sense since the BOLD has been shown to be correlated with HbR previously [4]. In addition, P diverges and goes to infinity at similar thresholds for both techniques ($\rho = 0.30$ and 0.40 for NIRS and fMRI, respectively). Although further investigation is needed, these encouraging results suggest that NIRS and fMRI depict the same resting state components. Direct comparison between the resulting networks is currently ongoing. **Conclusion:** Simultaneous measurements of NIRS and fMRI can further elucidate the resting state networks derived from each of the techniques independently. Our preliminary results suggest that the network parameters are very stable for a narrow subject population (age and health). The quality of the NIRS signal is something that we have been improving over time due to a lower signal-to-noise ratio inside the MRI environment. In addition, we have been developing a novel NIRS head support to allow measurements of the occipital lobe with NIRS, which has not yet been done on a combined NIRS-fMRI whole head resting-state study.

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NEXT GENERATION SEQUENCING SUCCESSFULLY IDENTIFIES MUTATIONS IN PATIENTS WITH CHILDHOOD EPILEPTIC ENCEPHALOPATHIES

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Introduction: Childhood epileptic encephalopathies (CEE) are severe brain disorders in which abnormal electrical discharges may contribute to progressive psychomotor dysfunction. It is believed that the epileptic brain electrical activity during maturation is a major cause of regression or progressive deterioration in cognitive and neuropsychological development in children and may lead to early death [1]. Recently, genetic studies have identified genes related to the etiology of CEE [2,3]. However, there is still a great need to increase knowledge about the molecular and clinical characteristics of patients with mutations in specific genes. This knowledge can only be acquired if systematic studies are performed on large samples of clinically well characterized patients with CEE. Therefore, the main objectives of this study are i) to identify potentially deleterious changes in genes related to CEEs in a large group of patients and ii) to implement a panel of candidate genes constructed for the molecular diagnosis of these patients. **Materials and Methods:** We used two different strategies to investigate our cohort of patients with CEE. First, we used a gene panel, which was designed to investigate mutations in the most important gens related to Dravet/Doose syndrome: *CHD2, GABRG2, PCDH19, SCN1A, SCN1B* and *SCN2A*. We used this panel to study 14 patients with Dravet and Doose, as well as 34 additional patients with other types of CEE. For this strategy the SureSelect XT Target Enrichment System for Illumina Paired-End Sequencing Library (Agilent Technologies) kit was used and the sequencing was performed in MiSeq (Illumina®). In addition, whole exome sequencing (WES) was performed in two patients with Dravet syndrome with no mutations in *SCN1A*. For the WES experiment we used the Nextera Rapid Capture Expanded Exome (Illumina®) kit was used and the sequencing was performed on HiSeq (Illumina®). **Results:** This is an ongoing study and to date the analysis of the sequence data from the gene panel is still under way. As for WES we found six sequencing changes which have the potential to be pathogenic for patient 1 and seven changes for patient 2. All of these changes are predicted to have a deleterious effect on protein function as determined by *in silico* analysis. **Discussion and Conclusion:** We have successfully constructed and used a gene panel kit for the molecular investigation of patients with CEE. Furthermore, we found 13 putative deleterious changes in two patients with Dravet syndrome. Additional bioinformatics filters as well as validation studies and investigation in control individuals are under way in order to identify the deleterious changes which are most likely related to the phenotype in these two patients. Data from the gene panel is also under analysis. We believe that, when complete, our study will help to establish better clinical and molecular parameters for the diagnostic investigation of patients with CEE. **Supported by:** CEPID-BRAINN, FAPESP and CNPq.

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TRANSCRIPTOME PROFILE OF DORSAL AND VENTRAL DENTATE GYRUS OF THE PILOCARPINE MODEL OF TEMPORAL LOBE EPILEPSY

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Introduction: Mesial temporal lobe epilepsy (TLE) is the most frequent type, representing 40% of the patients and these are often refractory to medical treatment. One of the most used tools to study the mechanisms involved in TLE are animal models. Despite several animal models currently available and widely studied, the majority of these present lesions which are not commonly identified in patients such as: ischemia, trauma and status epilepticus (SE). The gene expression profile of specific tissue region provides relevant biological information on the molecular mechanisms potentially involved in complex biological phenomena. RNAseq-based transcriptome analyzes offers the possibility of accurate profiling global gene expression. The aim of this study was to analyze and correlate gene expression profile using next generation sequencing technology in different sub-regions of the dentate gyrus. **Materials and Methods:** Male Wistar rats were injected with methyl-scopolamine (1 mg/kg) thirty minutes before of the systemic injection of pilocarpine hydrochloride (320 mg/kg) to reduce peripheral cholinergic side effects. Four hours after the administration of pilocarpine diazepam was administrated (4 mg/kg) in order to stop seizures. Control rats were injected with saline after the methyl-scopolamine injection. Fifteen days following induction rats were euthanized (n=4) and the brains were processed for laser microdissection using Zeiss PALM LCM. Dorsal and ventral dentate gyrus (DG) were collected from each rat, total RNA was extracted, and libraries were prepared from total RNA and RNA sequencing was performed in an Illumina Hiseq platform. Sequences were aligned and quantified with the TopHat/DESeq2 pipeline for total RNA. Gene Onthologies, molecular networks and gene interactions were analyzed with the MetaCore® software. **Results and Discussion:** We found a total of 969 and 308 genes differentially expressed ($p<0.05$) when comparing control and pilocarpine rats dDG and vDG respectively. Gene ontology analysis indicates a predominance of inflammation related molecules in up-regulated genes and synaptic transmission in genes down-regulated in both dDG and vDG. Exclusively in the dDG there was a significant down-regulation of calcium transport network. We found various differentially regulated genes involved in neuropeptides signaling, potassium and sodium transport. The transcriptome data suggest an interaction among several molecular components leading to epileptogenesis in this animal model that displays hippocampal damage. **Conclusion:** The present data indicates that even though similar mechanisms may be found in different regions of the dentate gyrus, the molecular components involved in processes such as, ion transportation, seem to be region specific.

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RESTING-STATE NETWORKS AND BRAIN CONNECTIVITY IN ELDERLY PATIENTS WITH ASYMPTOMATIC UNILATERAL INTERNAL CAROTID ARTERY STENOSIS

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Introduction: Asymptomatic unilateral internal carotid stenosis has been associated with brain hemodynamic changes and cognitive impairment [1]. However, the effects on brain functional connectivity is not totally clear. Therefore, the present study aims to assess changes in functional connectivity and their relation to cognitive decline in a group of patients at presymptomatic stage. **Materials and Methods:** Two elderly patients with asymptomatic stenosis of the right internal carotid artery and three healthy elderly volunteers participated in this study. All participants read and signed an informed consent approved by the Ethics in Research Committee of the Clinical Hospital of Ribeirao Preto (HCFMRP) before participating in the study. Experiments were performed on a 3T Philips Achieva System (Philips Achieva, The Netherlands), using 32-channel head coil reception and body coil transmission. BOLD-fMRI images were acquired at resting state using a 2D EPI sequence with the following parameters: TR/TE = 2000/30 ms, excitation angle = 90°, number of slices = 31, slice thickness = 4 mm, interval between slices (gap) = 0.5 mm, number of repetitions = 320. For anatomic reference, images were acquired using a T1-weighted GE sequence with the following parameters: TR/TE = 7/3.1 ms, excitation angle = 8°, FOV = 240 x 240 mm^2, number of slices = 160, slice thickness = 1 mm. Resting state networks were assessed using Independent Component Analysis (ICA) with GIFT GROUP-ICA and functional connectivity were studied by graph analysis using CONN, Brain Connectivity Toolbox and Connectome Viewer toolboxes. **Results:** Compared with controls, patients showed marked changes in cluster size of some resting state networks in group and individual analysis. As an example, figure 1 shows the auditory network for both groups. Moreover, graph analysis showed "degree" and "global efficiency" impairment in the hemisphere ipsilateral to the stenosis. However, data from more patients has to be used in graph analysis to get results that are more robust.

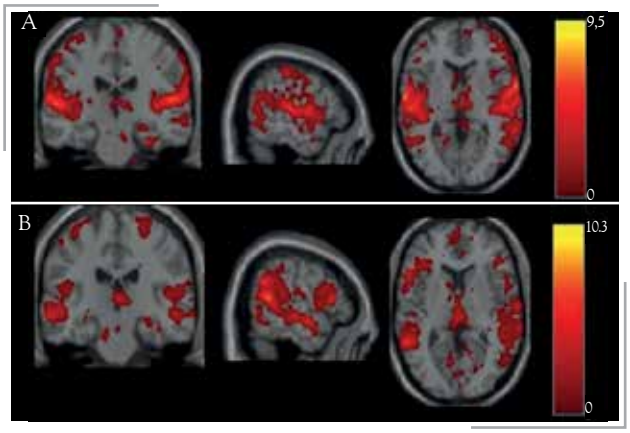

Figure 1. Auditory network of the (A) healthy control and (b) patient groups.

Discussion: Even at presymptomatic stage, compromised resting state networks are probably due to the presence of unilateral carotid stenosis [1, 2], which causes impairment in cerebral hemodynamics and, likely, disruption of ipsilateral hemisphere connectivity [3]. **Conclusion:** The present study confirmed abnormalities in resting state networks in patients with asymptomatic unilateral carotid stenosis, showing that brain connectivity may provide additional information to predict cases at risk of brain ischemia. The next steps of the study include the analysis of more patients' data and the assessment of the relationship between brain connectivity impairment and cognitive decline.

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WHOLE-EXOME SEQUENCING IDENTIFIES RARE CODING VARIANTS IN PATIENTS WITH FOCAL CORTICAL DYSPLASIA (FCD)

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Introduction: FCDs are a subtype of MCD which affects greater than 25% of all patients undergoing surgery for the treatment of refractory epilepsy[1]. Microscopically, FCD is usually associated with cell abnormalities, giant/dysmorphic neurons and balloon cells[2] and severe drug-resistant epilepsy. In this study, we examined type II FCD that consists of an isolated lesion characterized by cortical dyslamination and dysmorphic neurons without (Type IIA) or with balloon cells (Type IIB)[3]. The mechanisms involved in the pathogenesis of type II FCD are not completely understood[4] and it has been hypothesized that FCD is caused by brain somatic mutations in affected regions. In this context, the goal of this work is to identify potentially somatic and germline variants in FCD. **Materials and Methods:** We performed whole-exome sequencing (WES) in four blood-brain paired samples with FCD, including two individuals with FCD type IIA, two with type IIB. All donors provided written informed consent prior to enter the study. Genomic DNA derived from resected brain tissue and peripheral blood leukocytes were isolated by the phenol extraction method. Libraries underwent using the Agilent SureSelect Target Enrichment Kit for sequence capture and paired-end sequencing on an Illumina HiSeq2000 with an average read depth of 100–150×. Comparison of the brain vs blood sequencing results was performed using standardized bioinformatics methods followed by specific filter steps. **Results**: Histopathology of the resected tissue showed dyslamination, dysmorphic neurons and balloon cells consistent with focal cortical dysplasia type IIA and IIB. To date, our preliminary WES results detected 139 stop-gains variants included 24 novel variants, 227 frameshift variants wherein 66 variants were novel and 62 missense variants. Some of these findings were in homozygous state in at least one individual and we noticed a significant enrichment of rare and rare damaging variants based on our in-house control database of 29 samples as well as in two independents control databases: Exome Variant Server and Exome Aggregation Consortium (ExAC). In addition, we found that variants were present in genes belonging most frequently to specific biological pathways, which were associated with DNA/RNA and protein binding; cell adhesion; cell differentiation, growth and migration further ubiquitination. **Discussion and conclusion**: WES study has proven to be an efficient strategy to identify brain somatic and germline mutations in FCD, helping to better clarify the underlying mechanisms responsible for the disorder. **Supported by CEPID-FAPESP.**

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PROTON MAGNETIC RESONANCE SPECTROSCOPY IN THE PILOCARPINE MODEL OF TEMPORAL LOBE EPILEPSY

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Introduction: Proton Magnetic Resonance Spectroscopy (^{1}H-MRS) is a noninvasive technique which provides chemical metabolite report *in vivo*, allowing the detection of subtle changes, often not seen in structural magnetic resonance. This technique has contributed significantly in research in epilepsy. In animal models of epilepsy, ^{1}H-MRS is able to show metabolic changes during various stages of the disease and helps in lateralization and localization of epileptogenic regions. The aim of this study was to evaluate the chemical compounds Glycerophosphocholine (GPC) + Phosphocholine (PCh), N-Acetylaspartate (NAA) + N-Acetylaspartylglutamate (NAAG), Glutamate (Glu) + Glutamine (Gln) in the hippocampus of Wistar rats after induction of *status epilepticus* (SE) compared to sham-treated rats. **Materials and Methods:** This is a longitudinal and experimental study of 32 male Wistar rats with eight weeks of age. All spectroscopy data from hippocampus were acquired in a 3 Tesla Philips scanner using a volumetric coil with 8 integrated channels (Rapid Biomedical GmbH, Wurzburg, Germany). Spectra were obtained in the hippocampus using a single voxel with point-resolved spectroscopy (PRESS) at TE/TR: 135/2000ms and size of the VOI (Voxel of Interest): 5 x 8.5 x 9 mm^3. We acquired magnetic resonance imaging (MRI) prior to any intervention (MRI 1) and then 48 hours (MRI 2), 15 days (MRI 3) and 30 days (MRI 4) after pilocarpine induced SE. After MRI 1, we induced seizures with intraperitoneal injections of pilocarpine hydrochloride (380mg/kg). Thirty minutes prior to pilocarpine the animals received scopolamine methyl bromide (1mg/kg) to reduce systemic cholinergic side effects. After four hours of the onset of SE, we administrated diazepam (4mg/kg) to interrupt the seizures. The same procedures were performed to sham-treated rats except that they received saline injected instead of pilocarpine. The analysis of behavioral seizures followed the classical parameters according to the Racine scale. We observed SE between 1-2 hours after each injection. The SE-related mortality was 43,75% in this study. The metabolite biochemical quantification of these animals was performed by LCModel program – (Version 6.3-0D & LCM-gui-2012). Only values with standard deviation expressed as a percentage <15% were included, as recommended by LCModel. All metabolites were expressed in terms of their ratio to Creatine + Phosphocreatine. Statistical analysis was performed using SPSS (Statistical Package for the Social Science, SPSS, Inc., Chicago, IL) software (Version 21). **Results:** We found a significant difference between the means of the two groups in MRI 2 (GPC+PCh , t=-4.484, p<0.001; NAA+NAAG, t=-8.173, p<0.001; Glu+Gln, t=-6.583, p<0.001) , MRI 3 (GPC+PCh , t=-6.139, p<0.001; NAA+NAAG, t=-7.643, p<0.001; Glu+Gln, t=-7.438, p<0.001) and MRI 4 (GPC+PCh , t=-5.974,p<0.001; NAA+NAAG, t=-7.938, p<0.001; Glu+Gln, t=-8.163 p<0.001). The pilocarpine group showed lower values of chemical compounds when compared to the sham-treated. However, when these groups were individually evaluated between the times of acquisition of the spectra, there was no statistical difference between the means. **Discussion:** The results of this study showed changes in the chemical compounds in the hippocampus after induction of SE. These results may be indicative of neuronal or axonal loss, impairment in mitochondrial metabolism and excitotoxic neuronal death. **Conclusion:** The present work confirmed changes in the concentrations of chemical metabolites in the hippocampus, suggesting a decrease in metabolic levels after status epilepticus induced by pilocarpine.

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PREDICTION ANALYSIS OF RS2107595 AND RS2383207 POLYMORPHISMS IN LARGE ARTERY ATHEROSCLEROSIS STROKE PATIENTS

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Introduction: Large artery atherosclerosis stroke (LAAS) is a subtype of ischemic stroke. Several clinical factors are involved in LAAS, including sex, systemic artery hypertension, smoke, diabetes, and dyslipidemia. Meta-analysis and genome-wide association studies have identified the rs2107595 (*CDKN2B-AS-1* gene) and rs2383207 (*HDCA9* gene) single nucleotide polymorphisms (SNPs) in atherosclerosis stroke patients. However, there are no studies evaluating the level of accuracy of LAAS prediction including these polymorphism in the clinical practice. Therefore, we aimed to evaluate the accuracy to predict LAAS including clinical variables, rs2107595, and rs2383207 SNPs. **Materials and Methods:** This study involved samples collected during 2010-2015 in five hospitals in Joinville, Southern Brazil, pertaining the Univille Stroke Biobank. A total of 250 atherosclerotic patients and 250 non-affected individuals were genotyped by Taqman assay system (Life Technologies) in Real Time- PCR (ABI 7500). Allele and genotype frequencies were calculated by counting and Hardy-Weinberg equilibrium was estimated using Chi-square test. Hypertension, diabetes, hypercholesterolemia, and smoking habit were selected as clinical and environmental variables. We compared two models: one using the clinical variables only; and a second including the SNPs. For evaluating the predicition model we used an algorithm based in randon forests, with Leave-One-Out Cross-Validation (LOOCV) (2). The results were evaluated by area under the curve (AUC) from a receiver operating characteristic (ROC) curve to each scenarium. In addition, the importance of each variable were evaluated by mean decrease accuracy (MDA). **Results:** The rs2107595 SNP was not in Hardy-Weinberg equilibrium and was withdrawn of prediction analysis. We observed an increased risk for rs2383207*G allele (OR 3.05; 95% CI= 2.3- 4.1 p<0,0001). Prediction analysis showed that using the clinical variables only resulted in a prediction accuracy of 75.62% (sensitivity=39.5%; specificity=93.3%). However, the inclusion of rs2383207 SNP increased the prediction accuracy to 78,28% (sensitivity=42,99%; specificity= 92,49%). In addition, variant importance analysis demonstrated that hypertension, rs2383207*GG and dyslipidemia were the most important variables in the model. **Discussion:** The model included the rs2383207 SNP and the clinical variables. Despite the modest increase in the prediction accuracy, the rs2383207 presented as the second most important variable in the model. **Conclusion:** We showed that including rs2383207 could increase the accuracy of predicting LAAS, and this information may be useful in the type of LAAS treatment in the clinical practice.

EMPLOYING PROTEOMICS TO UNRAVEL THE MOLECULAR EFFECTS OF ANTIPSYCHOTICS ON OLIGODENDROCYTES AND THEIR RELATION WITH SCHIZOPHRENIA

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Introduction: Schizophrenia (SCZ) is a severe, debilitating and incurable mental

disorder, which affects about 1 % of world population. SCZ manifests between late adolescence and early adulthood and is one of the ten most costly illnesses worldwide. Despite its high prevalence and severity, it is not yet much known about the biochemical pathways that lead to disorder. Convergent data from our studies and other research fields have described the dysfunction of oligodendrocytes (OLDs) in SCZ brain tissue. This cell type is quite important in nerve transmission, due to its myelinating function, as well as an important role in energy supply to the neuron. This work seeks to understand, through proteomics, changes that occur in these cells when a patient is subjected to treatment with certain types of antipsychotics. **Materials and Methods:** Human oligodendroglia cell line (MO3.13 cells) (Cedarlane, CA) will be cultured and treated with antipsychotics as previously described (Iwata *et al*., 2013). Sample preparation and protein digestion will be done according to Melo-Braga *et al*., 2015. Finally, proteomic analyses will be performed in a bidimensional microUPLC coupled to nano ESI-Q-IM-TOF mass spectrometer by multiplexed data-independent acquisitions (DIA) experiments. The data will be processed using PLGS and Progenesis® QI softwares (Waters). **Expected Results:** With generated data and functional correlation bioinformatic analyses, we expect to unravel possible disturbances in biochemical pathways in drug-treated cells. It can help us better comprehend the neurological mechanisms of antipsychotics in SCZ pathophysiological process, and shed lights on potential biomarkers of disease and treated- patient by these medications. **Conclusion:** The present work is still in progress. We are conducting cell treatments using different antipsychotics, including some from 1st and 2nd generations. After proteomic analyses of treated-cells, conclusions regarding the biochemical pathways affected by treatments in oligodendrocyte cells are aimed. We also expect the data generated by this work might be used in clincal studies that seek the development of more effective drugs with fewer adverse effects.

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TWO-CLASS MOTOR IMAGERY BCI BASED ON THE COMBINED USE OF ICA AND FEATURE SELECTION: PRELIMINARY RESULTS

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Introduction: The sensorimotor areas of the brain respond in a similar way to an executed movement and to a motor imagery task [1]. Hence, it becomes possible to classify different brain states only with the electroencephalography (EEG) signal arising from the imagination e.g. of the movement of either the left or right hand. The use of oscillations found in the sensorimotor cortex, referred to as mu and central beta rhythms, its common, even with the complex spatiotemporal patterns present on these [1], a short simultaneous desynchronization exists in these rhythms. In this context, the use of spatial filters and of electrode and feature selection methods [2, 3, 4] has led to important results. The purpose of this paper is to use Independent Component Analysis (ICA) to discover features that allow the separation of two states of motor imagery in the potential presence of noise / interference in the EEG signal. An important fact is this is done with the aid of a feature selection strategy, which, according to the obtained results, significantly improves the performance of the classifiers. **Materials and Methods:** The procedure for data acquisition followed the conventional paradigm in motor imagery experiments [4], and was approved by the Ethics Committee of the University of Campinas (n. 791/2010). Six healthy volunteer subjects were part of these experiments that comprised 20 left hand and 20 right hand trials per subject. Sixteen electrodes were distributed on the subject scalp, most near to the sensorimotor region and a few in the occipital and frontal regions. The performed analysis included: (1) feature extraction using band power characteristics (FFT, Welch method and AR model); (2) comparison between common average reference (CAR) and ICA-based spatial filters; (3) feature selection using filters (Davies-Bouldin index and ROC) and a progressive wrapper, and, finally; (4) classification based on linear discrimination analysis (LDA), extreme learning machines (ELMs) and support vector machines (SVM). **Results:** Table 1 presents the results of mean accuracy between subjects for the cases tested. The use of SVM instead of LDA led to very good results too.

Table 1. Mean accuracy best results for the different case tested.

Mean accuracy Best case[%]	Without Filter	With CAR filter	With ICA Filter	Set of other signal processing used
Wrappers	82 ± 4	83 ± 8	85 ± 4	Welch, LDA
DB - Index	76 ± 4	76 ± 4	80 ± 4	FFT, SVM, LDA
ROC	71± 5	74± 4	78 ± 4	FFT, LDA, SVM

Discussion and Conclusion: The use of spatial filtering aiming at the separation of different brain activities that occur in motor imagination has been extensively studied, and many results have been presented in the literature combining techniques, such as Common Spatial Patterns (CSP) and feature selection techniques, with good results [3,4]. This study has a similar character, but, with a comparative analysis, revealed that a wrapper-based ICA strategy is very promising in the context of motor imagery BCI design. These results indicate the relevance of further investigation and also of potential application in an online system. **Acknowledgements:** The authors thank CAPES, CNPq and FAPESP for the financial support.

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IN SITU POSTMORTEM HUMAN BRAIN DIFFUSION TENSOR IMAGES OBTAINED IN LESS THAN 24H AFTER DEATH: WHITE MATTER HYPERINTENSITIES ANALYSIS FROM POSTMORTEM IN CRANIUM WHOLE BRAIN TISSUE IMAGES.

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Introduction: T2-weighted white matter hyperintensities (WMH) are frequent findings in clinical Magnetic Resonance Images (MRI) in adults and elders. At the moment, there is no evidence of histological specificity related to Diffusion Tensor Imaging (DTI) parameters – and so far no previous data was obtained without fixation artifacts in human brain *in situ* with short *postmortem* interval (PMI) (1,2,3). Here we show results of quantitative analysis of DTI images in normal appearing white matter regions (NAWM) and WMH obtained from a relatively large sample of brain specimens imaged without fixation compared to normal volunteers (4,5). **Materials and Methods:** Fractional Anisotropy (FA) and Apparent Diffusion Coefficient (ADC) were obtained from WMH and NAWM from groups: a) *Postmortem* (PM) - 24 subjects (12 males; age: 67.2±14.7 years; PMI: 14.4±2.3 hours, with no previous history of neurological impairment; and b) *in vivo* healthy volunteers (IV) - 10 subjects (5 males; age: 46.3 ±17.96 years). Both groups were imaged in the same 3.0T MR system - 8Ch head coil (Intera Achieva, Philips - Netherlands). All participants underwent the the same MRI acquisition protocol: a) FLAIR: AC-PC orientated oblique axial slices, TR/TI/TE = 9686.7/280/130 ms, 0.65mm x 0,87mm in-plane voxel size, 1 NEX, slice thickness/gap = 3/0.3 mm, FOV = 230 mm x 183 mm; b) DTI: axial oblique slices, TR = 23,650ms, TE = 65ms, 2/0, 0 mm slice thickness/gap; b value = 3000, FOV = 256mm x 256mm, 2.0mm x 2.0mm in-plane voxel size, 2 NEX; 32 directions, SENSE = 2. Image ROI data analysis was conducted using ImageJ, and co-registration between modalities using FSL analysis platform v. 5.0.2. **Results:** Average FA of postmortem subjects was 0.34±0.05 at WMH and 0.47±0.06 at NAWM, corresponding to a 26.8% reduction of FA at WMH ($p<0.001$). FA values measured at the IV group also showed a 18.6% difference between WMH vs NAWM (respectively, 0.35±0.04 vs 0.43±0.04; $p<0.05$). Average ADC from PM subjects was 0.130±0.03x10^{-3}mm^2/s at WMH regions and 0.121±0.03 x10^{-3}mm^2/s in NAWM areas – this 6.89% difference was not significant. Average ADC values from IV subjects were higher in WMH compared to NAWM areas (0.675±0.03x10^{-3}mm^2/s vs 0.593±0.03x10^{-3}mm^2/s), representing a 12.5% difference ($p<0.05$). Average NAWM FA in PM (0.47±0.06) was 6.16% above average values in IV (0.43±0.04). Similarly, the average WMH FA values were 5.40% lower in PM (0.34±0.04) than in IV (0.35±0.04). These differences did not reach statistical significance. PM and IV groups had different values in NAWM and WMH. ADC were decreased in PM (0.121±0.03 x10^{-3}mm^2/s) compared to IV (0.593±0.03 x10^{-3}mm^2/s; $p<0.001$) in NAWM and WMH (0.130±0.03 x10^{-3}mm^2/s vs 0.675±0.03 x10^{-3}mm^2/s, respectively; $p<0.001$). The average ADC difference between PM and IV reached 50,99% in NAWM and 51.84% at WMH. **Discussion:** Our results have demonstrated similar intra-group differences in quantitative DTI data between WMH and NAWM areas obtained from *in situ* PM and IV data. The average ADC was decreased in PM compared to IV, but the average FA was not significantly different. ADC values in NAWM from PM were also different to the values previously measured in NAWM IV described by literature. **Conclusion:** Our results indicates that studies correlating histological data with differences between WMH and NAWM in regard to ADC and FA values can be translated in to IV data. On the other hand, differences observed between PM in comparison with IV DTI data may be related to reduction of body temperature and molecular mobility change at image acquisition time.

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THE EFFECTS OF AUDITORY LANDMARKS AVAILABILITY IN GOAL-ORIENTED BEHAVIOR

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Introduction: The brain integrates a variety of sensory signals to build its representation of place [1]. In the hippocampus, place cells integrate excitatory signals arriving through entorhinal cortex (EC) projections [2]. Because EC encodes internal [3] and external [4] types of sensory information, one could expect that environmental sensory richness modulates the hippocampal spatial representation and affects performance during goal-oriented navigation. To access the relationship between the environmental density of sensory cues and performance during goal-oriented navigation, we conducted an experiment with humans performing a treasure hunt task within a sensory controlled environment. Auditory landmarks served for spatial navigation as a strategy to control localized sensorial stimuli. **Materials and Methods:** 23 subjects were recruited and requested to perform a 5 minutes navigation within a 3x3 meters arena where sounds were coupled to spatial locations. The subject's position was tracked via a Kinect sensor and sensory cues were delivered accordingly with the experimental protocol. Subjects were blindfolded and could not assess visual cues. Wireless headphones were provided so that subjects could assess auditory sensory cues. Eight conditions defined the amount of auditory cues scattered over the arena (1 to 14 sounds). Each sound was designated to a non-overlapping random location and was active when the subject was closer than 30cm from it. After the free-exploration, subjects were requested to reach a specific sound source location. **Results:** We accessed performance through the main spatial components of navigation, namely: absolute distance; angular offset; and distance offset. Results revealed a threshold for the efficacy in spatial encoding. Best performance in reaching a target-location occurred when either one or twelve sensory cues were scattered along the exploration arena, and more than twelve cues highly compromised performance. **Discussion:** Our results suggest that the density of environmental sensory cues, which might reflect the accuracy in representing ones surroundings through hippocampal activity, modulates spatial encoding. Within our experimental setup, we have found a bimodal state of performance optimality. A single target-cue environment might reinforce the unique grid-to-place-cells perforant pathway and avoid the accumulation path-integration error. Alternatively, we have identified a bifurcation point in the trade-off between hippocampal spatial representation optimality and density of sensory cues for the 12 cues condition, where more than 12 cues drastically affected navigational performance. **Conclusion:** How does the density of sensory cues affect the internal representation of space through the hippocampal circuitry? We found that humans display a threshold for environmental richness where little sensory information degrades navigational performance and above optimality ratio proper encoding is drastically abolished. Our results predict that sensorial configuration modulates the strength of internal and external inputs arriving to proper hippocampus.

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APPLICATION OF PATTERN RECOGNITION TECHNIQUES FOR QUANTITATIVE DATA FROM NEUROIMAGING MRI IN MULTIPLE SCLEROSIS PATIENTS

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Introduction: In the last decade, different neuroimaging modalities and quantitative techniques applied to the study of neurodegenerative diseases have been providing an increasing volume of data; making its use a complex task for the radiologists. At the same time, computational techniques of pattern recognition have been developed to increase the human performance in several classification problems. The purpose of this study is to apply techniques of pattern recognition to quantitative neuroimaging data acquired by magnetic resonance (MR) in patients with Multiple Sclerosis (MS). **Materials and Methods**: Retrospective data from a control group of 203 subjects without neurological diseases and a group of 144 patients with MS were evaluated. The data were obtained from the combination of image processing computational tools and neuroimages acquired in a 3T MR scanner. The brain was segmented in 126 anatomical regions not mutually excluding. Quantitative measurements of Fractional Anisotropy, Diffusivity, T2-Relaxometry, Magnetization Transfer Ratio (MTR), Volume and Cortical Thickness of the most of the regions were individually and collectively processed using the data mining software WEKA. The algorithms: *k*-nearest-neighbor (KNN) with different numbers of neighbors (k) and support vector machine (SVM) were assessed and used to classify these data. Different attribute selection procedures were also performed to identify the better attributes. Additionally, a restricted classification was executed considering data from few brain areas with a recognized involvement in the MS progression (SANTOS, 2007). Area under the receiver operating characteristic curve (AUROC) was the main parameter in the classification performance. **Results**: The white matter is the most affected by MS following a global pattern with higher involvement in the left hemisphere. The better attributes considering all data were related to corpus callosum, precuneus, cerebellum and left fusiform. MTR was the individual quantitative measurement with the highest power of differentiation between control and patients (AUROC=96,5%). The KNN5 (k=5) algorithm was considered the best classifier in the most of the classification tasks here performed. The restricted classification provided almost the same better attributes as the main classification, but the classification performance was slightly lower (AUROC=97,8% vs 97,3%). **Discussion**: Our results corroborated that the most affected regions in MS disease were contained in the white matter of the brain with a diffuse distribution pattern in total agreement with the literature (GOLDENBERG, 2012), (SANTOS, 2007). The MTR was confirmed as an important biomarker of the demyelization process. A fast strategy in this specific classification task would be the use of all quantitative measurements here discussed considering the regions of our restricted classification jointly with precuneus and fusiform, applying best feature selection procedure and KNN5 algorithm.

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Neuroeducation

THE CONTENT AND INTERACTIVITY OF A WEBDOCUMENTARY ABOUT EPILEPSY

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Introduction: In this poster we present some results of the BRAINN subproject that is aimed at the construction of a webdocumentary to provide information and raise awareness in the population about epilepsy. This webdocumentary is part of the work of the Education and Knowledge Dissemination Group. The focus of this poster is on two aspects of the development of this webdocumentary: the approaches that are being followed with regard to the development of the content of the webdocumentary (video animations) and with regard to its interactivity (website dynamics). In the banner, the presentation of the poster will be illustrated with pictures taken from the actual project (content and interactivity).**Webdocumentaries:** A webdocumentary is a system of audiovisual content that uses the interactivity and non-linearity of the web to provide new forms of learning experience. The creation of ways of structuring and organizing the audiovisual content on the webdocumentary allows new forms of interaction with the content facilitating its assimilation. **The Content of the Webdocumentary about Epilepsy:** Taking into account the specialized literature about epilepsy, the script of the webdocumentary was developed according to two perspectives. On one side, we have used social markers, like: age, gender, social class, level of education, as well as other factors that are fundamental for the inclusion of individuals into the society, like: productive activity (work), affective behavior (dating, marriage), and leisure. On the other side, we have created a main way of dividing the script in the four phases of life addressed by the webdocumentary (infancy, adolescence, adult life and old age) so that all other markers and factors are addressed in each of such divisions (situational videos). Finally, to avoid approaches that are too superficial in relation to each element addressed, in order not to stereotype or stigmatize the image of the people with epilepsy, we created explanations for the possible doubts and presentations with additional information (explanatory videos). **The Animations:** The content of the webdocumentary is based on animations that are being produced using softwares for drawing and for creating animations from draws. Each animation takes something between one and two weeks of work, being the first week for the development of the script and the first draws that will define the general aspect of the final product, and the second week for refining details, specially audio and timing issues. Most of the draws are hand made, but we also used some existent images, depending on what was the intention for a particular vídeo segment. Also, in most cases the visual identity was based on 8 bit vídeo games frames but it can vary from one to another. At this point we have ten episodes that follow the original flowchart designed at the begining of the project. The duration of each animation can vary, but it is aways something close to one minute. At the end of each episode there is a link to the following episodes, and the viewer can choose between two of them at each time in order to complete all the possible paths. **The Interactivity of the Webdocumentary about Epilepsy:** The site of the webdocumentary was programmed to provide the best navigation experience to the user. The inferior menu presents information about the video that the user is watching, as well as options to include subtitles and change the quality of the video (gear icon), or maximize the video (arrows icon). The superior menu allows the user to return to the initial menu (house icon), to access the informative contents that are accumulated over the video presentations, which present information in a more

direct form, turning away from the individual narratives, so that in case the users do not want to see this content in the moment it appears, they can access it later on (schoolbag icon), access the webdocumentary map, to know which paths were already covered (map icon), and also share information from the webdocumentary in social networks or e-mail (sharing icon). At the end of each video the users can choose paths for the character they are following, covering different narratives with the same character.

REQUIEM FILM: A HISTORICAL PORTRAIT OF EPILEPSY

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Introduction: This work presents a social study of epilepsy representation in cinema through the analysis of the movie Requiem[1], which is based on the real-life case of Anneliese Michel who had epilepsy. Since the work of Temkin, The Falling Sickness [2], there have been many analyzes of epilepsy representation in fiction literature, and these studies have found that in the early twentieth century characters with epilepsy were very bad and possessed, or occasionally were good people and blessed. It was only around the 60's that epilepsy has become recognized as a medical condition in the movies. **Materials and Methods:** To analyse the movie we used the film analysis theory based on studies of James Naremore[3] about the interpretation of the actor's body figure, and also the methods of analysis that Kerson [4] and Baxendale [5] used in their research on representation of epilepsy and seizures in film, using the classification of types of epilepsy and seizure of the International League Against Epilepsy (ILAE) [6]. The method consisted in the search for interpretation references and repeated analysis of each section of the film. **Results:** We found out that the main theme of the movie is about how religious fanaticism and conservatism can affect our lives as demonstrated by the movie through epilepsy presented by Michaela (main character), that afflicts and advances throughout the film, showing us the outdated religious belief that the attacks of seizures were caused by demons. Thus, the stigma of epilepsy is used as a tool to contextualize the discussion between religion and science, and also to bring drama to the plot. The actor's performance has an important role in that. The actor's body and all his gestures may have some meaning that represents not just the medical condition, but the psychological and social condition of people with epilepsy. **Discussion:** As demonstrated by Sallie Baxendale [4] despite the progression about the recognition of the medical condition and the depiction of the harsh reality of people with epilepsy in fiction films, the representation of possession stereotypes persist. In the documentary production, we can see the emergence of amateur videos made by people with epilepsy and their families, due to the low cost and popularization of audiovisual productions over the internet, which also contribute to the dissemination of the work of institutions dealing with epilepsy.
Conclusion: As pointed out by the researchers Kerson [3] and Baxendale [4], we conclude that the film helps us to analyze the context of social representation and the historical progression of epilepsy, reconstructing stereotypes and perceptions of society. With the advent of new technologies and the advancement of medical studies, the representation of epilepsy crises has become more loyal, and with the low cost of audiovisual equipment and a greater popularization of the Internet, people with epilepsy have gained more ways to express themselves and seek information.

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STORIES AND IMAGES ON EPILEPSY

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Introduction: The writer Eduardo Galeano said "We are not made of atoms, but stories." Storytelling is an interesting and enjoyable activity, and to some extent 'therapeutic', both for those who share their stories as well for those who listen it. This is a powerful way to convey new meaning to epilepsy, often perceived in negative and prejudicial manner by the society. People with epilepsy have over the century endured isolation, and the word Epilepsy has been cast away, and expression has not been always easy. A saying "A photo is worth a thousand words" portraits the perspective and the message in many ways. The possibility to start a dialogue by the patients and families to others appeared for us like an important way to dispel the myths and stigma of epilepsy.**Objective:** to promote discussion on epilepsy using written (narrative), and iconic (photographic) media to provoke reflections about epilepsy. **Material and Method:** We used social media as platform for interactions with people with epilepsy and to invite them to share their stories since 2014. In addition, we promote two photograph contest "How do I see Epilepsy", one in 2014 and other in 2015 using Facebook for upload of image with public voting, as well as a panel of judge. **Results:** We received 6 articles in 2014 and were compiled into

and e-book published on February 9, 2015, on the occasion of the first International Day for Epilepsy. These were stories of people with epilepsy and their families: "The story of Daniel" (by Joberto and Eric Yoshida de Freitas), "The Letter of Carolina "(by Carolina Correia)," My life with Epilepsy "(by Nívia Colin)," Love: the essence of healing "(by Clarinda Lima)," The history of Arlen "(by Ellen Aparecida da Silva), and" The story of Marcela and Milena "(by Rosemari Coradin). The 2014 Photograph Contest received 12 photos and 15 in 2015. These were presented in public exhibition during the National Epilepsy Awareness Week on September 9, and were printed in a booklet and a calendar. Purple day, purple way by Priscilla Carbone, winner 2014 | Love, unity, inclusion...a jump against prejudice by Tayna Leite, winner 2015 **Discussion:** The six narratives of people with epilepsy are indicative and representative of the personal coping processes with this disease. Also the photographs showed different views in distinct social and family contexts. Within this objective, the electronic-book "Olhares sobre a Epilepsia[1]" was originally designed. **Conclusion**: The voice of people with epilepsy and their families were heard through e-book, creating new perspectives about this illness experience. Other voices, represented by the images participants of the photographic competition summed up to the mosaic, breaking the single story culture. This showed alternative ways of conceiving, and to represent, the epilepsy, improving reflections about the impacts of this complex disease.

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ABCÉREBRO TV PRESENTS BRAINN REPORTER

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Introduction: ABCérebro TV [1] is an educational channel of scientific communication in Neurosciences and Health, inspired by the relevance of the researches conducted within the Cepid Brainn, Unicamp. **Objective:** To present a new TV programe, Brainn Reporter, aired by ABCérebro TV. **Materials and Methods:** This new TV program named Brainn Reporter uses a creative approach that allows a freedom of approach for dynamic interviews. The special episodes had limited edition and used a single camera. The production selects scientific research and the team goes to the laboratories and the academic spaces where research happens. The first series comprises of 5 special episodes with 15 minutes duration. These were made available on ABCérebro TV network [2, 3]. The visitations and views numbers

were evaluated on post-aired. The making of Brainn Reporter: Marcelo films Jéssica visiting a Lab (left) and is received by Nathália Volpato (interestingly, Nathalia later became a Brainn Reporter; b) Raphael interviews Alline about brain anatomy (middle); Brainn Reporter initial team comprises of Li Li Min as Diretor, Jéssica Vicentini, Brunno Campos, Raphael Casseb and Luciana Ramalho as the Brainn Reporters, and Sueli Adestro as Producer (not show as she was behind the lens). **Results:** The data of five special episodes of Brainn Reporter in the year 2015 are shown below, using the data collected from YouTube channel, Facebook [2], and the ABCérebro TV website [1].The brandmark of Brainn Reporter and the early assessment of number of visualizations of special episodes aired in the Internet for the year 2015.

Special Episodes - Brainn Reporter	Visualizations
Oficina Como o Cérebro Funciona	840
CAF – Ciência e Arte nas Férias - 2015	298
Brain Computer Interface - BCI	709
AVC Em(Cena)	256
Ações de Saúde no Combate ao AVC	208
Total	2311

Discussion: The number of views of the five episodes is good and it seems to awake the curiosity of public, signaling acceptance, even in its raw format, casual, not losing above all educational grip. After this initial positive result, we are finalizing 4 new episodes; Physical activity for Patients with epilepsy; What is magnetic resonance; The physical fatigue and their influence on brain; The sound resonance and cognition. **Conclusion:** The Brainn Reporter is a result of a work of creative expression for dissemination of neuroscience. The format by having interviews conducted by five graduated students, known as Brainn Reporters, has proven to be positive. They act as promoters and instigate young people the desire to learn and to know more about the science.

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Neurotechnology

ANALYSIS OF FEATURE EXTRACTION TECHNIQUES OF BRAIN SIGNALS FOR THE DEVELOPMENT OF SSVEP BCI SYSTEMS

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Introduction: A Brain-Computer Interface (BCI) is a communication system that establishes a direct communication between brain and machine [1]. The BCI based on steady state visually evoked potential (SSVEP) paradigm works with visual stimulation: when a subject focus his/her gaze in a pattern that flickers at a specific frequency, a SSVEP can be detected via EEG in his/her brain activity. The main objective of this study was to compare two different feature extraction approaches in this context: spectral analysis based on power spectral density by Welch's method and temporal analysis using Burg's method to estimate auto-regressive parameters. **Materials and Methods:** The database was collected in the scope of DESTINE/FINEP and BRAINN/FAPESP projects and has information of seven healthy volunteers, with average age of 26.3 years. Each volunteer was exposed to three screens, each one with two checkerboards blinking at different frequencies. The used pairs of frequencies are 6 Hz and 7.5 Hz, 12 Hz and 15 Hz, 20 Hz and 30 Hz. Each subject performed 8 trials of 12 s duration for each visual stimulus [2]. All the signal processing stage was implemented on MATLAB R2015a. The Common Average Reference (CAR) technique was used to pre-process the signal. The employed window length was four seconds, considering an overlap of 50% of the window length. The classification stage was carried out with a linear classifier (LC) based on the least squares method [3]. **Results:** Table 1 presents the accuracy rate of the classifier for each pair of frequencies considering the two feature extraction approaches. The accuracy rate was defined as the average performance of the seven subjects. The order of the auto-regressive model was determined by cross validation.

Table 1. Comparison between Burg and Welch's Methods.

Features Extraction Method	Pair of Frequencies	Accuracy [%]
Power Spectral Density – Welch	6 Hz e 7.5 Hz	82.5
Power Spectral Density – Welch	12 Hz e 15 Hz	92.5
Power Spectral Density – Welch	20 Hz e 30 Hz	85.0
Auto-regressive Coefficients - Burg	6 Hz e 7.5 Hz	75.0
Auto-regressive Coefficients - Burg	12 Hz e 15 Hz	72.5
Auto-regressive Coefficients - Burg	20 Hz e 30 Hz	67.5

Discussion: The results show that both feature extraction techniques, Burg and Welch, are appropriate in order to discriminate SSVEP signals with an accuracy rate higher than 65%. Furthermore, for both methods, the best-hit rate was for the pair 12 Hz and 15 Hz. On the other hand, in all scenarios, Welch's method demonstrated a better performance than Burg's method. The adopted window length – 4 s with 2 s of overlap – is a reasonable time for assistive applications, like controlling a wheelchair. **Conclusion:** We can conclude that both, spectral and temporal analyses are adequate tools to perform feature extraction in an SSVEP-BCI. However, Welch's method has an excellent performance, especially for the pair of frequencies 12 Hz and 15 Hz, for which achieves an accuracy rate higher than 90%.**Acknowledgments:** The authors thank CNPq and UFOP for the financial support.

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VALIDATION OF THE USE OF THREE-DIMENSIONAL PRINTING AND NEURONAVIGATION FOR SURGICAL PLANNING

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Introduction: In the case of refractory epilepsy, multimodal visual resources encompassing anatomical locations, functional variations, and structural relations provide evidence of the side and areas responsible for epileptogenic activity [1]. Therefore, three-dimensional (3D) printing and neuronavigation software for surgical planning may lead to a better performance of case study and surgery procedures [2]. However, the use of biomodels faces challenges in establishing protocols robust enough to avoid errors in image-processing pipeline. Our aim is to develop and validate a protocol for surgical planning with 3D printing and neuronavigation. **Materials and Methods:** A 3-year old boy suffering from refractory epilepsy on the right temporal lobe was elected as a benchmark for the processing pipeline. Volumetric T1-weighted images were acquired in a Siemens Achieva 3T scanner and submitted for segmentation. Surface was reconstructed with the InVesalius (CTI Renato Archer, Brazil) open-source software and printed using selective laser sintering. Four holes were made with a drill with depths of 54.0 ± 0.5, 43.0 ± 0.5, 43.0 ± 0.5 and 23.0 ± 0.5 mm. Linear distance measurements were performed independently using a

ruler and the function of marker creation during neuronavigation with a MicronTracker S40 (Claron Inc., Canada) device connected to the InVesalius Navigator software. **Results:** The object offered a strong and vivid visual impression and its quality allowed measurements of landmarks and navigation across brain hemispheres. Neuronavigation was satisfactory and provided real-time localization of brain structures based on the MRI of the subject. Neuronavigation measurements from surface to bottom of each hole were 55.09 ± 2.58, 42.93 ± 2.58, 40.42 ± 2.58 and 25.02 ± 2.58 mm. Mean difference from navigated measurement to ruler measurement was 1.44 ± 1.10 mm.

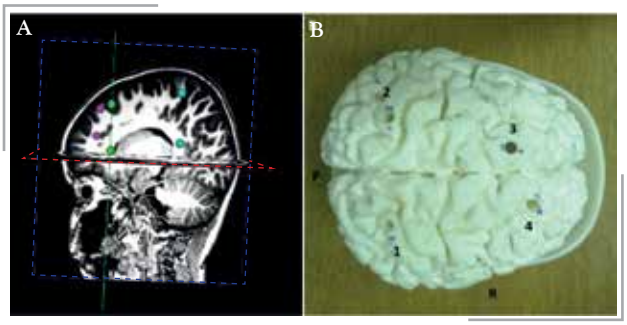

Figure 1. A) InVesalius Navigator screen with colored markers representing coordinates of superficial and hole measurements. B) Upper view of 3D printed biomodel with numbered holes.

Discussion: Our results validated the use of InVesalius Navigator and biomodeling for surgical planning and anatomical inspection with errors under the maximum acceptable for clinical applications, i.e. 3 mm. The potential to grasp and inspect details of the actual anatomy can enhance orientation during surgical procedures and can prove beneficial in patient outcome. **Conclusion:** In conclusion, the protocol proved to be robust and may open the possibility to define trajectories for surgical planning and improve physicists' decision-making and surgical outcome.

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DEVELOPMENT AND CHARACTERIZATION OF INVESALIUS NAVIGATOR WITH AN OPTICAL SPATIAL TRACKER

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Introduction: Neuronavigation systems are commonly used for instantaneous localization of brain structures with high accuracy during neurosurgeries [1]. Additionally, neuronavigators may aid transcranial magnetic stimulation (TMS) procedures and electroencephalography (EEG) electrode positioning. However, due to its high cost and reduced portability, this technology is not widely accessible. In order to overcome these difficulties, we developed the open-source, multiplatform and freeware InVesalius Navigator [https://github.com/biomaglab/invesalius3]. The aim of this study was to calculate the accuracy of InVesalius Navigator using a passive optical spatial tracker. **Materials and Methods:** The modules were written in Python 2.7. We used wxPython 2.8 for graphical user interface development, Numpy 1.6 for multidimensional array manipulation, GDCM for DICOM file type support, Visualization Toolkit 5.6 (VTK) for graphical rendering and visualization, MTCpy for device communication. The MicronTracker S40 (Claron Inc., Canada) device was used to register coordinates from two sensors. A cubic acrylic phantom with side length of 21.10 ± 0.05 cm and nylon wires crossed every 10.0 ± 0.5 mm forming a network of 484 points divided into four planes. Distances between planes 1 to 2, 2 to 3 and 3 to 4 are 1, 4 and 5 cm, respectively. Tomographic images of the cubic phantom were simulated as magnetic resonance images using the MATLAB (MathWorks, USA) software. Coordinates of all points created from the crossing nylon wires were measured using InVesalius Navigator (Biomag, Brazil) software. System accuracy was defined as mean distance between digitized and image coordinates, and precision defined as standard deviation of accuracy measurements. **Results:** A total of 1936 points were digitized. Neuronavigation system accuracy was 2,584 ± 0,465 mm and system precision was 1,284 ± 0,253 mm.
Discussion: The developed system with the optical spatial tracker have an error below the limit appropriate for clinical applications, defined as 3 mm [2]. Therefore, InVesalius Navigator may be used as a portable and low cost alternative for neuroscience experiments requiring neuronavigation. **Conclusion:** In conclusion, our study validates the use of InVesalius Navigator for clinical applications.

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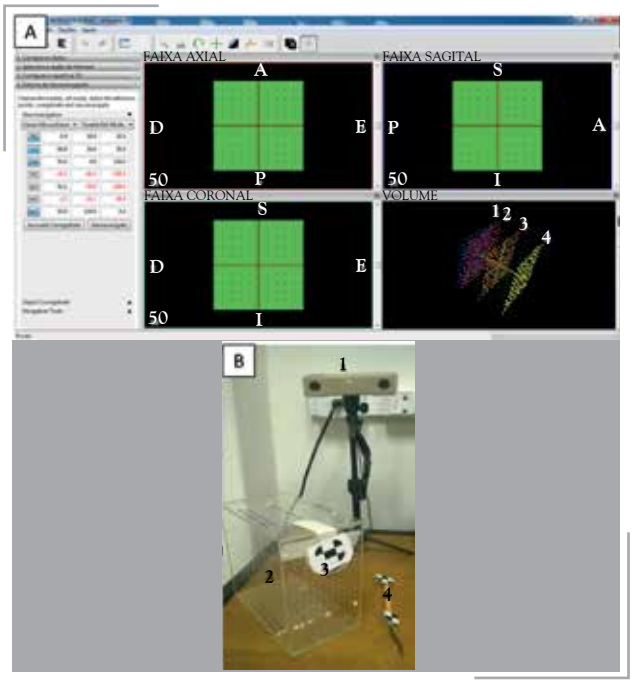

Figure 1. InVesalius Navigator screen with simulated images and digitized points (colored markers represent the planes 1, 2, 3 and 4. B) Cubic phantom and optical spatial tracker.

WHOLE-GENOME BISULFITE SEQUENCING DATA ANALYSIS REVEALS DIFFERENTIALLY METHYLATED REGIONS ON A DATASET OF EPILEPSY IN ANIMAL MODELS

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Introduction: Whole-genome bisulfite sequencing (WGBS) became the gold standard for mapping DNA methylation profile of vertebrate species. In this methodology, DNA molecules are treated with sodium bisulfite that chemically convert cytosine residues into uracil maintaining 5-methylcitosine unchanged. During polymerase chain reaction uracil residues are transcribed as thymine. Bisulfite-treated DNA are quantified by high-throughput sequencing technologies [1]. There are software tools available to process each analysis step, such as filtering and aligning bisulfite-treated reads [2]. However, there is a lack of bioinformatics protocols for WGBS data analysis. Differentially methylated regions (DMR) are sections of the genome where we observe significant differences in methylation levels when comparing treated to control individuals. We developed a data analysis protocol to process WGBS data and identify DMRs. We applied this protocol to study the genetic landscape of epilepsy on pilocarpine-induced animal model. **Materials and Methods:** The dataset consists of 2 samples of control animals and 2 samples of pilocarpine-treated animal model of epilepsy. We generated these data using Illumina TruSeq DNA Methylation kit and Illumina HiSeq 2500 sequencer. Our protocol for WGBS data analysis is comprised of several steps: A) quality assessment via Rqc Bioconductor package; B) trimming and adapter clipping through Tim Galore!; C) mapping to the *Rattus novergicus* reference genome (v5) using Bismark [3] (duplicate and multi-mapped reads were removed); D) determination of the DNA methylation frequency as the number of reads that aligned on dinucleotides CpG and; E) WGBS data smoothing and DMR identification performed with the bsseq software [4]. **Results:** Quality assessment of bisulfite sequencing dataset showed a potential bias on raw sequencing data: we expect a low percentage of cytosine calls due to bisulfite conversion; however, we observed an increase of cytosines towards the end of the reads. After trimming adapter sequences, we noticed that the proportion of cytosine calls was constant across all cycles. Comparison between control group and pilocarpine-treated groups showed differences on DNA methylation profiles. We identified eighteen DMRs on these WGBS data. **Discussion:** Due to the lack of alternatives, developing this protocol for bisulfite sequencing data analysis was essential to identify differences on DNA methylation profiles between control and pilocarpine-treated animal models. The identified DMRs are indicators for future studies, as they can be associated to gene expression regulation, playing a fundamental role on integrative genomic analyses.

Conclusion: We developed a WGBS data analysis protocol. We used this protocol to analyze dataset of control animals and pilocarpine-treated animals. We found differences on DNA methylation profiles. **Supported by**: CEPID-FAPESP

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CONSTRUCTION OF A BEDSIDE MONITOR WITH A HYBRID OPTICAL SYSTEM

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Introduction: The possibility to assess microvascular physiology of deep tissue over long periods of time at the bedside is a real clinical demand that should lead to more individualized – therefore more efficient – treatments. Diffuse optical techniques can greatly improve the current scenario and take an opportunity in this niche by offering direct, noninvasive and portable instrumentation to monitor tissue physiology at the patient's bedside. Recently, we have validated Diffuse Optical Spectroscopy (DOS, also known as Near Infrared Spectroscopy, NIRS) as a reliable tissue oxygenation marker. In particular, we have shown that Frequency-Domain (FD) DOS is capable of measuring absolute oxy and deoxy-hemoglobin concentrations, conveying information about tissue oxygenation with great accuracy if the correct model is employed [1,2]. We have also developed a homemade Diffuse Correlation Spectroscopy (DCS) system that was shown to assess microvascular tissue blood flow [3,4,5]. In this work, we developed a hybrid optical system by integrating both DOS and DCS. The developed system leverages the capability of DOS to measure tissue oxygenation and the DCS ability of measuring microvascular blood flow. In addition, the concurrent measurements of DOS and DCS allows for the unique bedside estimative of the metabolic rate of oxygen consumption (MRO_2). **Materials and Methods:** To develop the hybrid optical system we combined a DCS system previously developed in our lab and a commercial DOS system (Imagent, Iss Inc, Illinois). The homemade DCS instrument employs 16 detectors and one continuous-wave (CW) laser source at 785 nm (~100 mW). The commercial DOS system employs 4 detectors and 32 diode laser sources at 4 different wavelengths (690, 705, 750, 840 nm; ~10 mW each). To integrate both systems we built a homemade trigger capable of controlling the state of DOS/DCS, preventing them to interfere and damage each other. To control the trigger, we modified our DCS's control software, programming it to also control an Arduino board inside the trigger box, which allowed the communication of both systems. After making sure that the switching lasers were working, we moved the hybrid instrument to the hospital and proceeded with system characterization. **Results and Discussion:** The hybrid instrument is extremely stable, with laser power varying less than 2% over 21 hours. Despite the long period of monitoring, the system temperature was also kept constant at 29.0 ± 0.5 °C. Regarding temporal resolution, the whole cycle (DCS+DOS) takes approximately 3 s, which is excellent for long-term monitoring at the patient's bedside. Overall, the results of the system performance demonstrate the viability of the integration of a commercial DOS system with our homemade DCS system, allowing the monitoring of patients at the bedside during long periods of time. Our pilot results in the clinical phase are ongoing. **Conclusion:** On a series of previous studies our lab has shown the utility of DCS and DOS for measurements of microvascular blood flow and absolute tissue oxygenation, respectively. In this work we combined both techniques to develop a portable hybrid optical system capable of measuring deep tissue physiology. The main advantages of this system are that it allows the continuous monitoring of patients at the bedside for long periods, providing the clinician with noninvasive and direct measurements of tissue physiology, such as tissue oxygenation, blood flow and oxygen metabolism. We are currently on the first steps of implementing the system inside the clinic, with the main goal of monitoring stroke patients.

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BRAZILIAN INITIATIVE ON PRECISION MEDICINE (BIPMED): THE FIRST PUBLICALLY AVAILABLE GENOMIC DATABASE IN LATIN AMERICA

C.S. Rocha[1], B.S. Carvalho[2,3], I. Lopes-Cendes[1] * for the BIPMed Collaborative Group

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Introduction: BIPMed is an initiative of five Research Innovation and Dissemination Centers (RIDCs): The Brazilian Research Institute for Neuroscience and Neurotechnology (BRAINN), Center for Computational Science and Engineering (CCES); Center for Research in Cell Therapy (CTC); Obesity and Comorbidities Research Center (OCRC); and Center for Research on Inflammatory Diseases (CRID). Precision Medicine has emerged recently as a concept in which scientific knowledge and technology will come together to provide the basis for the 21st century medicine. It involves translational research, genomics and personalized medicine to propose a new data integration level to improve health care. The database was created from the need to have genetic information from the Brazilian population and make this information public available. **Materials and Methods:** BIPMed is based initially on a software platform, the Leiden Open Variation Database[1], it is a fully web-based gene sequence variation database, which is platform-independent and uses PHP and MySQL open source software. The design of the database follows the recommendations of the Human Genome Variation Society (HGVS) and focuses on the collection and display of DNA sequence variations. BIPMed fallows the guidelines and principles of the Global Alliance for Genomics and Health (http://genomicsandhealth.org/) observing the responsible sharing of genomic and clinical data. It has two levels of access, the open access that doesn't need registration nor identification, and the restrict access which allow access to individualized information of the deposited variants. **Results:** At the moment the database is filled with variants detected using Illumina Nextera Expanded Exome from 29 Brazilian Reference individuals, with 20842 genes and more than ten million variants. (Figure 1)

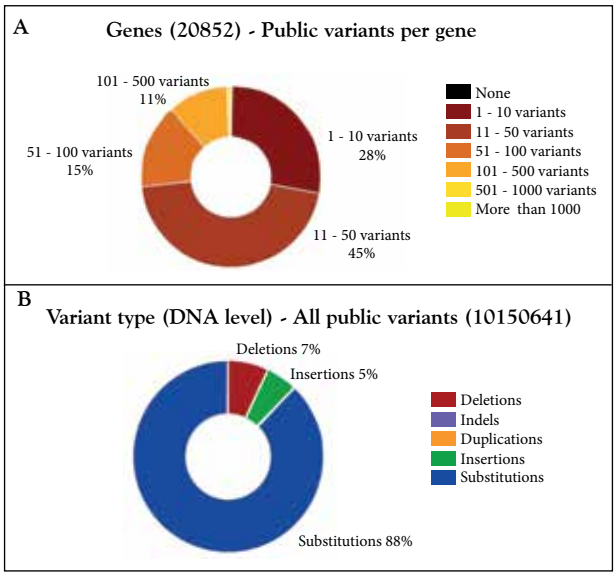

Figure 1. A - percentage of number of variants in genes; B - percentage of variation type.

Discussion and conclusion: The database is one of the first steps of the Brazilian Initiative on Precision Medicine, its objective is to provide an interface that allow responsible and safe sharing of genomic and clinical data. We expect the database to grow and include data-sets from specific diseases, as well as other types of data such as transcriptomes and proteomes. This platform is the first of its kind in Latin America and is intended to be used by clinicians and scientists all over the world, to share and obtain information about various aspects of genomic medicine and human health, as well as to support dissemination and training.

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A COMPLEX SYSTEM'S APPROACH TO STUDY HEMODYNAMICS WITH OPTICAL TECHNIQUES

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Introduction: Network science is an interdisciplinary approach used to characterize network structure and function. It has been widely explored in the last two decades mainly due to the increasing acceptance that macroscopic behavior of complex systems emerges from the interaction of their constituent particles [1]. In fact, different complex networks have similar properties in terms of global organization, information transference and connectivity despite their differences in microscopic structure. Therefore, it is often possible to characterize most of the system features with network parameters. In this work, we aimed to illustrate our novel applications of complex systems, and of network science in particular, to optical data acquired from biological tissue. **Materials and Methods:** We investigated the potential of complex systems approaches to 3 different experimental protocols: (1) the resting state properties measured with Near-Infrared Spectroscopy (NIRS) in both healthy adults and patients with carotid stenosis; (2) the connectivity of cerebral blood flow

measured by Laser Speckle Imaging in a rat model of ischemic stroke, and; (3) the tumor hemodynamics microenvironment in mice, both during the steady state and during Photodynamic Therapy (PDT). In all 3 cases, the spatial information from the light detector assumes the role of nodes of the network, while the links between two nodes were computed based on the Pearson correlation coefficient across the node's time series. In order to build undirected and binary graphs, we varied the threshold, *p*, so that we could analyze the network parameters as a function of the threshold. We estimated standard global networks parameters [2], such as the average degree, degree standard deviation, clustering coefficient, characteristic pathlength and diameter. The connectivity patterns among each cohort was established by projecting all networks in the same plane and then extracting the most frequent patterns. **Results and Discussion:** Our methodology suggests that the human brain seems to behave as a classical complex system at rest, in which there is only few allowed states that share similar network features. For the healthy volunteers, we observed a dominance of the left hemisphere in terms of connectivity and centrality. For the stenosis patients, we found that the resultant networks correlate with the level of occlusion in the carotid. The latter is similar to what we have found in the rat model of ischemia, in which the connections and clusters become denser and the average distance between two nodes tends to decrease as the level of ischemia increases. This result is coherent with the fact that ischemia can influence the system and force all its constituent particles to behave in such a way that it generates a more synchronized macroscopic behavior (lack of cerebral autoregulation). As a negative control, the tumor hemodynamics in mice does not appear to have complex system properties, and we could not find an indicator of the efficacy of the PDT treatment on cancer cells based on network parameters. **Conclusion:** In this work, we illustrate a procedure to combine complex networks and optical techniques, which appears to be promising and efficient to investigate a variety of physiological phenomena. In humans, our results contribute to the understanding of how the brain works and is organized, both in diseased and in healthy situations. Results from animal models strengthen the hypothesis that cerebral correlates with severity of ischemia. With further investigation, these results could be helpful to diagnose human stenosis patients. Finally, our results in tumor hemodynamics reinforce that the brain is unique as a complex system.

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MRI SCANNER ATTRIBUTION FROM ITS PATTERN NOISE

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Introduction: The usage of medical images has grown as well as the studies looking for methods that automatically detect diseases from them. Research centers collect images from different sites and specific data can be lost. When an image set presents undesirable characteristics which can jeopardize the study, like high noise, the original equipment attribution become necessary. This work aims to propose a method to identify the Magnetic Resonance (MR) equipment that generate the image, based on the image noise and the fact that normally sensors leave a mark in the image identified as source pattern noise. **Materials and Methods:** T2-weighted Fluid Attenuated Inversion Recovery (FLAIR) brain MR images were acquired in a 3T scanner using same protocol, with slice thickness of 3mm, as 2D type and axial. There are two MR sensors model Discovery MR750 from GE Medical Systems configured with TR = 9700, TE = 141, TI = 2200 and image size 256x256, and one model Triotim from Siemens configured with TR = 9000, TE = 119, TI = 2500 and image size 256x192. There were 25 exams per equipment with 48 slices each. Each sensor leaves marks at produced images related to its hardware characteristics. These marks, commonly called residual noise, are used to identify the MR scanner by calculating the correlation between noise of the image and the scanner pattern noise. The residual noise of the image is the difference of the original image and the same image filtered by a denoising filter based on wavelet domain. The sensor noise pattern is the mean of residual noise of images from the same scanner. Since our database has different image sizes, 9 regions of interest (ROIs) with fixed size were chosen focusing on the center of the image. The denoising filter was applied to each ROI. The dataset was split in 20% to calculate the scanner pattern noise, 60% to train a multiclass classifier, in which each class represents one scanner, and 20% to test the final classifier. The 3-class classifier training was performed in a 5*2-fold and no data normalization was necessary. **Results:** Experiments were performed training SVM classifier comparing multiclass algorithms *One versus One* and *One versus All*. Also two ROIs size were compared: 32 and 64. The *One versus All* SVM with ROI size of 32 achieved the best result, with average accuracy of 71.78% (Class1 with 68.38%, Class2 with 67.24% and Class3 with 79.81%). **Discussion:** The presented methodology were able to perform scanner attribution, given one unknown MR image from a controlled image dataset (obtained using the same protocol, but from differente scanners). But, when using the proposed approach in a practical problem, it is possible find one that the unknown image belongs to a scanner different from those used on the training, i.e, an unknown scanner. In this case, the desired outcome from the classifier is that the sensor is not recognized. This model attribution problem is called as Open Set scenario and was not tested, since it requires a larger dataset, containing images from a larger number of MR scanners. Also, adding ROIs from the peripheral image regions can enhance the sensor representation leading to better results. **Conclusion:** The present work confirmed that the modeling applied to camera attribution [1] [2] can be adapted to MR scanner attribution. The smaller ROI achieved better results.

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TEXTURE ANALYSIS OF NORMAL APPEARING WHITE MATTER IN ATHEROSCLEROSIS PATIENTS

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Introduction: White matter is a complex structure that connects the grey matter regions of the brain. This structure is not uniform and presents variation in the MR signal intensity [1]. Patients diagnosed with atherosclerosis present lesions in the white matter called white matter lesions (WML). The regions within the white matter that does not present WML are called normal appearing white matter (NAWM), and the analysis of their variability is relevant in the disease diagnosis and therapy monitoring [2]. This work aims to compare the degree of discrimination of texture descriptors extracted from NAWM regions with varying location and size to distinguish normal from pathological white matter. Materials and **Methods:** T2-weighted brain MR images from 61 atherosclerosis patients were acquired in three different sites. Two sites used the same MRI scanner (3T Discovery 750, GE Healthcare) and MRI acquisition parameters (TE 141.108ms, TR 9700ms, slice thickness 3mm); while images from the last site (3T Achieva, Philips Medical Systems) used similar acquisition parameters (except TE 125ms and TR 9000ms). WML regions were segmented by using a semi-automatic tool (Cerebra-WML [3]), while NAWM were automatically selected at three locations: in the contralateral hemisphere to the WML region, closest to the WML region and farthest away from the WML region. We also varied the NAWM size, ranging from 2x to 5x the size of the matching WML region (Figure 1). From each region, texture descriptors were computed using the histogram, gradient, co-occurrence matrix and run length matrix [4]. Finally, a linear discriminant analysis (LDA) classifier [6] was used to evaluate the discriminating ability of the texture descriptors. **Results and Discussion:** Similar accuracy rates were achieved when using the LDA classifier for regions of the same size, even when varying the NAWM region location. But lower accuracy rates were achieved when increasing NAWM region size (Table 1). The consistently lower accuracy for larger NAWM regions may be due to the increasing difference between regions containing WML and larger NAWM regions, making the classification task

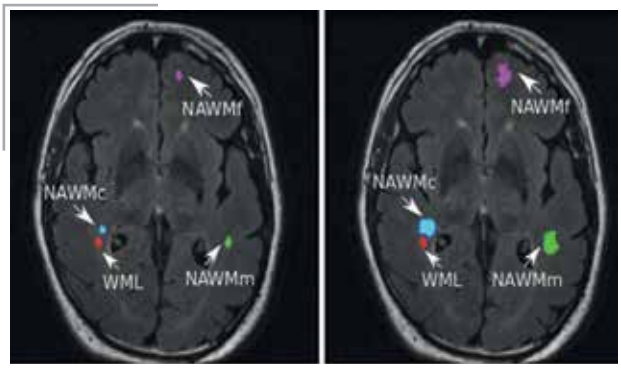

Figure 1. WML (red), NAWM in the contralateral region (green), NAWM in the closest region (blue), NAWM in the farthest region (pink).

Table 1. Achieved accuracy rates (percentage).

NAWM	1x	2x	3x	4x	5x
Contralateral	96.2	92.5	86.6	82.5	76.2
Closest	96.2	93.3	92.1	81.2	75.8
Farthest	96.2	90.0	87.5	80.0	75.8

easier, and thus less robust to new samples: a case of over-fitting. Besides, larger NAWM regions may contain different structures, generating samples with lower discrimination capability. **Conclusion:** Our main goal in this paper was to study the NAWM variability by evaluating the impact of location and size on the distinction of normal from pathological regions by using texture analysis and a LDA classifier. We found that increases in the size of the NAWM region decreased accuracy, while variation in NAWM location did not impact accuracy. Thus, the known variation in

the MR signal intensity within the white matter does not effect the texture analysis effectiveness. Besides, larger NAWM regions should be avoided on methods that aim to distinguish WML from NAWM.

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OBTAINING FUNCTIONAL DYNAMIC BRAIN NETWORKS WITH CONTIGUOUS CO-CLUSTERING

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Introduction: Contiguous co-clustering is a data mining technique useful for discovering co-occurring coherent patterns in simultaneous time series. For contiguous co-clustering, time-series are stacked to form a matrix, each series becoming a row, and each time point, a column. This matrix is then looked for co-clusters: groups of rows presenting simultaneous coherent patterns - occurring in the same columns. This method has been successfully applied to extract useful information from gene expression data, suggesting that application to other biological series is promising [1]. We applied this algorithm to brain fMRI time series. In this scenario, co-clustering allows the identification of co-functional regions, i.e., regions presenting coherent spatio-temporal activity patterns. This information can be exhibited in a dynamic functional brain network, for visualization purposes and also for helping to discriminate different groups of brain activity. **Methods:** fMRI data was collected on 19 controls and 19 patients suffering from a motor disorder. Subjects were asked to perform a motor task (finger tapping), following a rest/movement block protocol. Images were pre-processed and segmented in 90 regions. Averaging over the voxels of each region yields their corresponding time-series. Contiguous co-clustering was applied to the individual series and also to the average series of each group (controls and patients). The co-functionality information given by the co-clusters was used to define a functional network, with 90 nodes representing the brain regions, and edges between them indicating their co-activity, i.e. that they were present in the same co-cluster during that specific period of time. Edges were weighted by the correlation between the two regions. Two paths were followed: generation of a group network from the combination of individual networks, and also from the average series of the group. **Results:** Table 1 shows the quantity of co-clusters found in the individuals of each group (on average) and on the average series. Figure 1 shows snapshots of the networks generated from the average series for controls (top) and patients (bottom). Bigger nodes in red represent more connected regions. The snapshots correspond to the first 2 rest/movement blocks. Similar results were obtained from the combination approach, but networks with more edges are generated.

Table 1. Quantity of co-clusters.

Group	Group avg.	Avg. series
Control	107 ± 28	100
Patients	115 ± 32	162

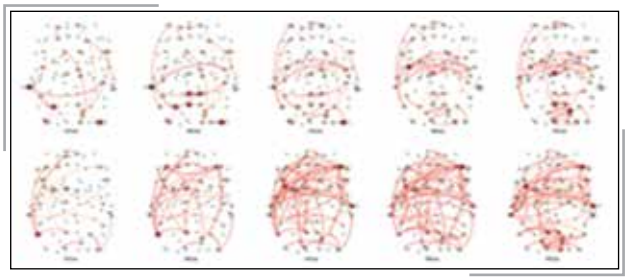

Figure 1. Network snapshots.

Discussion: A reasonable amount of patterns could be found, and the average quantity of patterns found for individual subjects is close to that found in the group average series. Networks derived from this method are clearly distinctive between controls and patients. However, the rest movement blocks do not appear to be clearly characterized, as the movement (and rest) periods are distinct. **Conclusion**: Contiguous co-clustering appears to be a promising method for generating dynamic brain networks. In our experiment, networks obtained are clearly distinct between controls and patients, although no clear pattern arose corresponding to the rest movement blocks. As future work, it might be interesting to calculate the temporal evolution of topological metrics in the network, in order to verify its capability to characterize both the blocks of experiments and the groups of subjects. **Supported by**: Fapesp, process 2014/11125-1.

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GRAPHS METRICS AS FEATURES FOR AN LDA BASED CLASSIFIER FOR MOTOR IMAGERY DATA

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Introduction: One of the strategies used to generate brain signals for brain-computer interfaces (BCIs) is motor imagery (MI). In this work, we explored the feasibility of using graph's metrics in a linear discriminant classifier to be used in a MI-BCI application. **Materials and Methods:** Electroencephalography (EEG) data from 8 healthy subjects were acquired at 5 kHz with 64 channels using a BrainAmp amplifier (BrainProducts). The experimental protocol consisted of interleaved task and rest blocks of 10 s each (total experiment time of 3 min), in which task blocks alternated between right or left hand MI. Two acquisitions were made for each volunteer. Pre-processing steps involved downsampling the data to 256 Hz, averaging the recorded signals within a 3 s window, CAR spatial filtering and frequency filtering in specific bands: 7–13 and 13–30 Hz. Data analysis was performed in MATLAB. The motifs method [1] was used to estimate similarities between the electrodes' time series, leading to building of two graphs, one for each scalp hemisphere. Central electrodes, except for Fz and Cz, were left out. A least-squares linear discriminant analysis (LDA) classifier was used to test classification of two simple graph's metrics: degree and clustering coefficient (CC). The classifier's input consisted of the difference between a specific graph metric of a node and its contralateral part, always in the way 'right minus left'. A single electrode, and combinations of two and three electrodes were used to evaluate accuracy results. Since the graphs were weighted, the degree of a node was calculated by the sum of each link value adjacent to this node, and the CC was evaluated by equation (7), discussed in [2]. **Results:** Various combinations of electrode sets for classification were explored. Results are shown below, as the maximum possible obtained classification accuracies with this method. They are averaged over all subjects, considering both acquisitions (mean value ± standard deviation). Classification was performed using the "leave-one-out" method.

Tabela1.

Band (Hz)	Feature	Mean maximum accuracy (%)		
		One electrode set	Two electrodes set	Three electrodes set
7-13	Degree	62 ± 4	73 ± 2	76 ± 2
	Clustering Coefficient	64 ± 5	70 ± 4	72 ± 6
13-30	Degree	64 ± 5	74 ± 5	78 ± 5
	Clustering Coefficient	61 ± 7	72 ± 6	77 ± 6

Discussion: Results obtained using degree or CC have similar mean values, with the degree presenting slightly larger accuracies for most cases. Using the CC provided larger standard deviations, which, under these circumstances, can make the use of the degree preferable. Also, results for the 13-30 Hz band are slightly better. In addition, it was found that the feature and the frequency band within which each subject performs better are not the same for all of them. Maximum possible classification accuracies obtained among all participants were 92.19% and 90.63%, using CC and degree, respectively. **Conclusion:** Our results suggest there are optimum sets of electrodes to be used specifically for a given subject. In general, the graphs metrics used seem promising for assessing which MI task has been performed. However, for a possible online application, further investigations are needed to improve the results, such as additional preprocessing techniques and how to find the optimum electrodes sets. Also, the combination of these metrics with the more traditional features used in MI-BCIs could be explored.

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DEVELOPING BIOINFORMATICS TOOLS TO USE IN HIGH PERFORMANCE COMPUTING

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Introduction: Parallelization of computer processes is one of the main methods of decreasing processing time. This task divides a process into several different threads that will be simultaneously run and then combined once they are complete. The Intel Xeon Phi processor not only offers great support for such tasks, given its large number of processing cores, but it also makes use of specific

optimization tools that speed up the application even further. SNP (Single-nucleotide polymorphism) genotyping through the use of finite mixture models can benefit from such infra-structure, allowing the determination of genotypes across thousands of genomic loci in a fraction of the time initially required by a serial process. **Materials and Methods:** We use a three components finite Gaussian mixture model to assess the *posterior* membership probability of every *loci* for each subject. Due to the lack of identifiability, we use an EM-algorithm to estimate *locus*-specific location and dispersion parameters. This approach allows a simple assessment of the *posterior* membership probability to determine individual genotypes. This approach has been successfully used in Affymetrix [3] and Illumina microarrays [4], but it has not scaled well to sequencing problems. We are implementing this optimized classifier using C and C++ programming languages combined with OpenMPI. This compromise allows the use of the hardware at its full potential. We will assess the quality of our calls by comparing our results to gold-standard outcomes generated by international teams [4]. **Results and Discussion:** Currently the serial version of the tool has been developed in the C programming language. Our optimized version of the software is under development and presents satisfactory performance on the determination of partial likelihoods, which will later be combined into the EM-algorithm for the final parameter estimation. **Supported by**: CEPID-FAPESP.

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NEURONAL OSCILLATIONS REVEALED: A DIDACTIC PROPOSAL FOR A FITZHUGH-NAGUMO ANALOG NEURONAL CIRCUIT

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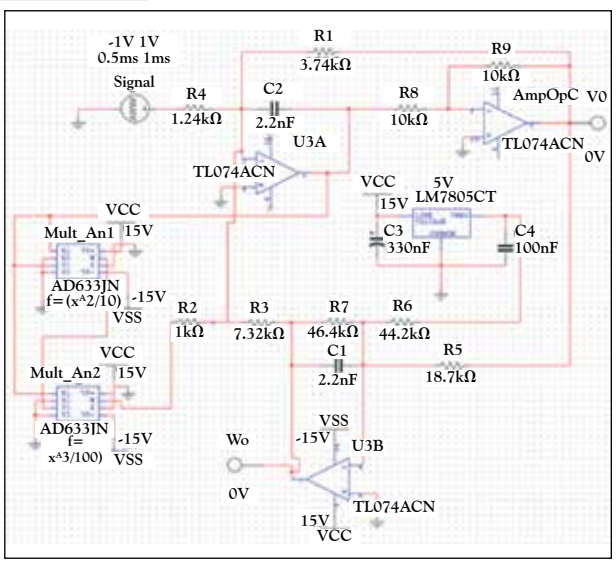
Introduction: Since its invention in 1983, the Chua's circuit has been extensively used as a paradigm for experimental chaos evaluation [1]. Its origin aimed to show that the chaos (i.e. the oscillatory behavior defined by aperiodic motion sensible to little changes in initial conditions) was a robust physical phenomenon, and not merely an artifact of computer round-off errors. Concerning that, this work aims to present an electronic implementation for the classical FitzHugh-Nagumo (FHN) neuronal model capable of capturing many aspects of real neurons (e.g. threshold for firing, all-or-none response, refractory period, etc), including periodic firing and chaotic bursting. Such approach provides a well-succeed approach for introducing students in the nonlinear world of spiking neurons, its processing capabilities and possible neuromorphic architectures. **Materials and Methods:** The proposed circuit was obtained from classical FHN equations by means of time and amplitude rescale as presented in [2], being adapted to use low cost analog multipliers, voltage controllers and high precision resistors, which reduced the cost and the number of laboratory devices required. It also increased modularity and integration capabilities. **Results:** Figure 1 shows the proposed circuit and typical periodic and chaotic oscillations of membrane potential obtained when sinus and square forcing are applied, respectively. Figure 1.



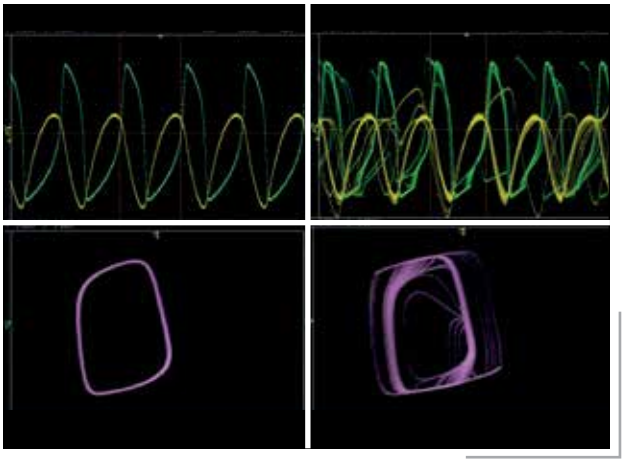


Figure 1. (left) FHN circuit schematic; (middle) periodic oscillations under sinus forcing and its phase plane (lower) – green: membrane potential (V_m); yellow: recovery variable; (right) chaotic V_m under square periodic forcing.

(left) FHN circuit schematic; (middle) periodic oscillations under sinus forcing and its phase plane (lower) – green: membrane potential (V_m); yellow: recovery variable; (right) chaotic V_m under square periodic forcing.
Discussion and Conclusion: The proposed FHN circuit can be used for illustrating, in practice, the strength-duration curve, the existence of the refractory period and the frequency coding curve associated to the strength of a sustained forcing. Noise can also be easily added to excitation, allowing a more accurate study of neural random dynamical systems, a task usually threatened by numerical errors in the digital environments. Finally, the existence of chaotic solutions under periodic forcing reveals the intrinsic complexity of neuronal oscillators, which widens and motivates the possible role of chaos for information processing in biological neuronal networks, which outlines a natural perspective of this work.

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CORPUS CALLOSUM SEGMENTATION ON DWI THROUGH VOXEL-BASED CLASSIFICATION

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Introduction: Defined as the region responsible for the connection between both brain hemispheres, the *Corpus Callosum* (CC) is where most of the brain white matter is located. Its structure is not only associated with diseases as Alzheimer and Multiple sclerosis, but also shows correlation with gender, handedness and aging [1], making its segmentation a necessary step to any further structural analysis, such as parcellation [2] and characterization. The accurate CC segmentation is challenging using magnetic resonance imaging (MRI), as shown in region-based [3], level-set [4] and statistical methods [5] approaches. Thus, our method proposes a 2D segmentation using voxel-based classification on diffusion-weighted imaging (DWI). **Materials and Methods:** Our image database was composed by Diffusion MRI from 15 subjects obtained in the axial plane (2.0 mm thickness, 1.0 x 1.0 mm, 32 directions) at Hospital de Clínicas of UNICAMP. To train our classification model we used only the midsagittal slice and its adjacent slices. Afterwards, the attribute matrix was built from these slices, with rows as samples (each voxel manually rotulated as CC or non-CC) and columns as features (voxels intensity values in 32 DWI, plus the morphological gradient computed over the B=0 image). Then, 40% of the non-CC samples were discarded in order to balance both classes. Hence, we trained a support vector machine (SVM) as a classifier using a radial basis function (RBF) kernel and used it for classifying each voxel on the midsagittal slice of five new subjects. In the end, after the classification, we chose the largest connected component to obtain the final CC segmentation. **Results:** The obtained segmentation was evaluated in comparison to the manual one (Figure 1), and the Dice and Jaccard index were computed (Table 1). **Discussion:** The final CC segmentation presented an average agreement with manual segmentation of: Jaccard=98% and Dice=84%. **Conclusion:** Although the CC segmentation using voxel classification has shown to be computationally expensive, it is a promising approach, having the advantage of high accuracy on the edges.

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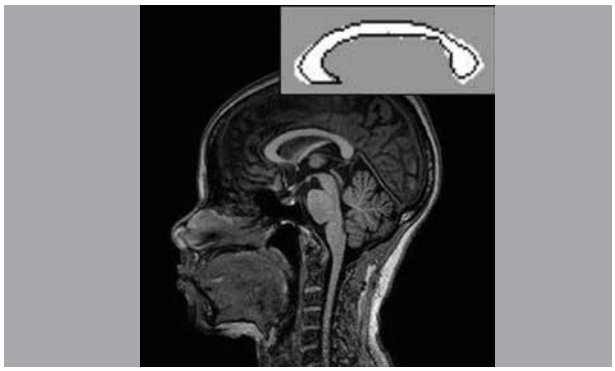

Figure 1. Midsagittal slice of one subject, depicting the obtained CC segmentation in white and the respective manual segmentation border in black (upper right).

Table 1. Segmentation agreement between the proposed method and the manual segmentation obtained from midsagittal slice of five subject.

Subjects	Jaccard	Dice
1	99%	88%
2	98%	79%
3	98%	84%
4	99%	86%
5	98%	85%

THE USE OF DYNEEMA FIBER PHANTOM FOR DTI QUALITY CONTROL: INFLUENCE OF IMAGING ACQUISITION PARAMETERS ON DTI INDEXES

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Introduction: Diffusion tensor images (DTI) have many applications in neurology. However, the measured signal is susceptible to the influence of noise and artifacts, being thus important to check if these factors do not compromise the parameters calculated from the images. Given that there are no standard routines for quality control (QC) of these images, the main goal of this study is to propose a fiber phantom for DTI QC. In this work we present a three bundles Dyneema fiber phantom for routine DTI QC and evaluate the stability of its DTI indexes when the acquisition parameters change at the 3T Philips Achieva MRI scanner of the Medical Sciences School of UNICAMP. **Materials and Methods:** The DTI phantom (see figure) consists of a rectangular insert containing3 parallel Dyneema [1] fiber bundles (130 fibers of 0.40 mm diameter, 150 fibers of 0.35 mm and 200 fibers of 0.25 mm). The insert is placed inside a cylinder filled by distilled water.DTI were acquired using a 8 channel head coil, with a standard (clinical) spin-echo pulse sequence. We acquired DTI using 7 different b-values, 6 echo times (TE) and 5 voxel dimensions, one one parameter changed at a time. The detection of imaging outliers and DTI processing were done using ExploreDTI (www.exploredti.com) and Matlab software. We evaluated the stability of the fiber phantom by estimation of coefficients of variation (CV) for fractional anisotropy (FA), apparent diffusion coefficient (ADC), relative anisotropy (RA) and volume ratio(VR) for each bundle, for each parameter changed. **Results:** We observed that from all DTI indexes calculated and pulse sequence parameters changed, the higher CV found was 0.23 for RA, obtained for the bundle of fibers of 0.35 mm, when the voxel size changed. For ADC and FA, the CV ranges were (0,02 - 0,18) and (0,02 - 0,21), respectively, considering all fiber bundles. The highest CV of these parameters were also found for the bundle of fibers of 0.35 mm, when TE or voxel size changed. For RA and VR the CV ranges were (0,02 - 0,23) and (0,002 - 0,07), respectively. For VR, the higher CV found was 0,07, also for the bundle of fibers of 0.35 mm when the voxel size changed. **Discussion:** The results obtained show that, for all bundles, there is no significant variation on DTI index values obtained when the pulse sequence parameters are changed one-at-a-time. These findings suggest that Dyneema fibers can be useful for building of stable and low-cost DTI phantoms. The highest CVs found were for the bundle of fibers of 0.35 mm. They might occur because of some compression differences between the bundles, which must be corrected for future essays. **Conclusion:** The findings suggest that the phantom developed could be useful for DTI QC. However, other pulse sequence parameters must be studied, as well as different MRI head coils. The compression of fiber bundles has to be improved to upgrade phantom stability and FA values, making the setup closer to the main axon tracts.

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Figure 1.

COMMUNICATION ORCHESTRATION WITH A COGNITIVE ARCHITECTURE

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Introduction: The field of Neurotechnology involves the integration of brain science and computational technologies. In one of its facets, computational techniques are used to help in the diagnose and treatment of brain diseases [1]. A completely different facet uses brain science findings in order to foster the development of computational algorithms to simulate cognitive functions, as e.g. language. These algorithms are particularly useful within the field of cognitive architectures and can be used to control virtual or physical robots to assist or replace humans in several activities [2]. In this work we present a neuroscience inspired cognitive architecture that orchestrates virtual robots communication in order to create a semantic infrastructure to nominate environment objects. This infrastructure evolves gradually, without relying on pre-established rules. **Materials and Methods:** We developed a cognitive architecture which was used to orchestrate and to simulate dialogs among robots from communities of different sizes (10, 50, and 100 virtual robots). In order to validate the system performance, the notion of language games was employed. A language game is a mechanism proposed by the philosopher Ludwig Wittgenstein to explain how words obtain meaning during established activities between a speaker and a listener [3]. This mechanism is a way of verifying if the robots are reaching linguistic consensus about the names of 4 objects. In the proposed language game, the players are virtual robots and a mediator who grants them the permission to dialog. Several dialogs may be established in parallel. Nevertheless, the mediator allows two robots to dialog only if none of them is already talking. In our experiment, the mediator maintains a list of playing robots and their current state. If a robot A (speaker) wants to talk to robot B (listener), the mediator checks if robot B is available. If not, robot A cannot talk to robot B at the moment, and it can try another one. In the case both robots are available to talk, the mediator sends a positive feedback and the dialog is started. During the dialog, the speaker robot picks up an object, creates a name for it and utters it to the listener robot. If the name is already known by the listener, it indicates the corresponding object according to its own dictionary of names. Otherwise, the listener answers that it does not know that name. The game is only successful if the listener indicates the object which the speaker has picked up. When the dialog is finished, the mediator updates the status of the robots. Then, the robots are once more available to start another dialog. The robots in the community have different names to reference the same object. Hence, each name receives a score, which increases when there is a communicative success and decreases when the opposite occurs. The names with highest score are always chosen to reference an object. On the hand, those with low scores are removed from the dictionary. The communicative convergence will always occur when the robot population has only one word to appoint each object and all robots use the same word for it. However, each population, according its size, will need a different number of played games (in total) to converge. **Discussion and Results:** The results indicate that the proposed cognitive architecture was especially interesting since many dialogs were established in parallel, apart from the size of the community. Moreover, the robots learned from their failing dialogs and their internal dictionaries converge towards a common language. Furthermore, the architecture does not depend on predefined linguistic terms and semantic rules, differently from traditional architectures in literature [4]. **Conclusion:** Our cognitive architecture is able to adequately simulate some aspects of language use among artificial agents. Since it does not depend on external synchronizing mechanisms and the linguistic consensus emerges evolutionarily, its performance is biologically plausible.

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ESTABLISHING A COST-EFFECTIVE METHOD TO RECORD ELECTROGRAPHIC ACTIVITY IN LARVAL ZEBRAFISH BRAIN

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Introduction: Over the last decades, the zebrafish (*Danio rerio*) has emerged as a promising animal model for studying neurological disorders such as epilepsies. Thus, being able to record zebrafish brain activity is essential to investigate and characterize the abnormal electrical discharges during seizure-like responses in this animal model. A recent work has described a method to record extracellular field potentials in the larval zebrafish forebrain [1]. However, the procedure implemented was an adaptation of conventional extracellular recording techniques, using a patch clamp amplifier that was already available for the authors. In the present work, we aim to establish a protocol to obtain electrographic recordings of zebrafish with a simpler and more cost-effective setup for laboratories intending to implement this technique in their routine. **Materials and Methods:** Each zebrafish larvae (7 days post fertilization) was positioned in a clear Petri dish, with the addition of a droplet containing anesthetic (400μM tricaine) and the paralyzing agent (10μM d-tubocurarine). After complete loss of movement, the animal was placed in a lid removed from a 1.0 ml eppendorf tube filled with 1% low-melting agarose prepared with aquarium water. The larval zebrafish was positioned horizontally, with the dorsal side exposed to the surface. Quartz/platinum-tungsten microelectrodes were attached to a pair of connectors and fitted onto a MN-153 Narishige micromanipulator. One electrode was placed slightly in front of the forebrain of the animal, and another in the agarose. Electrical activity was recorded using the RHD2000 Evaluation System (Intan Technologies®). We used a setup that includes an interface board connected to a host computer via standard USB cable, and a small amplifier board connected to the interface board via a 0.9m serial peripheral interface cable. The amplifier board contains an amplifier chip with 16 bipolar inputs. To prevent external electromagnetic interferences during the electrographic recordings, the immobilized animal with the microelectrode and the amplifier board were placed inside a Faraday cage built using a cardboard box wrapped in aluminum foil. To validate the system, we performed preliminary recordings of larvae with and without addition of 30 mM pentylenetetrazol (PTZ). **Results:** To date, we have built a setup to record extracellular field potentials in zebrafish brain using a system that transform weak electrode signals directly into a digital data stream. Background noises were successfully eliminated by the Faraday cage, as recordings acquired by placing the electrodes only in saline (NaCl 0.9%) showed no signals. Our pilot study showed high amplitude electrographic discharges in the animal exposed to PTZ compared to the control, starting approximately after 30 minutes of exposition to PTZ, with intervals of 5-10 minutes. **Discussion:** The method presented here appear to be advantageous for recording electrographic activity in zebrafish brain. The components used are considerably less expensive than those of the system previously described, since it does not require a patch clamp amplifier. We have accomplished stable long-term monitoring of brain activity in immobilized zebrafish larvae and we are currently working towards a characterization of the epileptiform discharges in order to study the seizure-like responses evoked by the convulsant agent PTZ. **Conclusion:** In the present work, we described a cost-effective protocol for electrographic recordings on immobilized zebrafish larvae. Since studies using zebrafish to elucidate the basis of seizure generation are still scarce, this study provides new tools to study the mechanisms underlying seizures in this model. Supported by Fapesp #2014/15640-8, CEPID-BRAINN, FAPESP.

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AIC-TOOLBOX: AUTOMATED INDIVIDUAL CLASSIFIER THROUGH PROBABILISTIC GREY MATTER ABNORMALITIES

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Introduction: Grey matter abnormalities (GMA) is associated with several conditions and may guide clinical management, such as indication for epilepsy surgery [1]. Individual GMA investigation is usually based on visual evaluations, which is a tricky and time-consuming task, since abnormalities can be very subtle. We created a toolbox (AIC) that can aid in this process by: (i) comparing the tested image with an age-paired control database (DB) and (ii) automatically classifying and ranking it into "a surgery candidate scale", also pointing the significant GMA. **Materials and Methods:** For the toolbox development, we created a DB of grey matter probabilistic maps (GMPM) derived from T1WI from 168 control subjects (four per age; 19-60 years), acquired on a 3T MR. All DB images were segmented (yielding the GMPMs), normalized (Dartel tools) and smoothed (FWHM 8cm^3). AIC works applying the same preprocessing on the tested image and subtracts its GMPM from GMPMs of a subsample of the DB (automatically matched by age; ±4 years=36 subjects) resulting in 36 difference maps. A one-sample t-test (Bonferroni corrected) is used to obtain the consistently altered areas. Then, it estimates parameters to characterize the resultant alterations: number of clusters, clusters volumes, distance between clusters, clusters mean t-score, hippocampus alterations laterality index and a final laterality index. To define our standard classification thresholds, we first ran the AIC-toolbox with a reference group (20 controls and 40 patients, evaluated and classified by experts: Yasuda, Coan, and Cendes). The six parameters obtained were included in a logistic regression followed by a ROC curve analysis. For this ideal sample, the area under the curve was 0.92, with a cut-off value of 0.665. The logistic regression cut-off and beta values were defined as AIC standard parameters. To evaluate the AIC with a different group of subjects, we selected 80 subjects previously classified by the experts: 20 controls and three patient's groups (non-lesionals and temporal lobe epilepsy patients with left (LTLE) or right (RTLE) hippocampal sclerosis (20 in each group)). **Results:** Despite the high false positive rate for controls (30%), AIC effectively separated lesional patients with only 12% of false negatives. The classification of the non-lesional resulted in 13 concordant with visual analysis and 7 (35%) classified as lesional.

Table 1. Results.

AIC Classification	Controls	LTLE	RTLE	Non-lesionals
Lesional	6	19	16	7
Non-lesional	14	1	4	13

Discussion: Most imaging analyses of GMA enable only group analyses, however, AIC can be employed to detect atrophy individually, which have potential clinical applications. Limitations are related to image resolution and infrequent normal anatomical variants. Larger number of matched controls and better criteria should be studied in order to reduce the false positive rates. Advantages refer to the unbiased analysis and the sensitivity to subtle abnormalities. Hence, our preliminary results show that this toolbox has potential to be a useful and reliable complementary tool to the clinical and pre-surgical evaluations. **Conclusion:** Our large DB and the proposed methodology enabled the effectiveness of the AIC-toolbox in classifying and separating automatically lesional from non-lesional subjects.

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SSVEP-BASED BCIS: THE BRAIN AS A DIGITAL COMMUNICATION CHANNEL

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Introduction: Brain-computer Interfaces (BCIs) allow the translation of intentions of a subject using brain signals processed by computing machines. This reveals something that may seem obvious, but has most profound consequences – in the operation of a BCI with a limited and discrete repertoire of commands, the brain works, in essence, as a digital communication channel. The signal associated with each command plays the role of an element of a modulation scheme and the stages of signal processing/feature extraction/classification perform the required demodulation and decision tasks. This connection establishes a very rich research program, which is, in our opinion, in its beginnings, but that holds a key to promoting a more consistent synergy between neurotechnology and communication/information theory, thereby leading to more customized and efficient BCIs. In the following, we will discuss some consequences of this interpretation. **Discussion:** We will concentrate our attention on SSVEP-BCIs (steady-state visually evoked potentials), which our group has been working on for a longer span of time. The paradigm is based on some form of stimulation associated with specific visual frequencies capable of inducing electrical signal frequencies in EEG recordings. The information brought by the analysis of these frequencies is then processed to decode the user's intention. The canonical setup is basically an FSK (frequency-shift keying) scheme in which each command is related to a specific frequency, such as in [1]. However, notice that this scheme can be expanded in several directions, such as: (1) Using phase information to increase the number of possible commands without necessarily increasing the number of employed frequencies. In particular, [2] has presented a strategy combining frequency and phase for a BCI-SSVEP capable of dealing with 15 different targets and possibly attaining information transfer rates (ITR) up to 60 bits/min. (2) Introducing elements of amplitude modulation using, for instance, the intensity of the luminous stimulation and developing in a systematic way color and shape modulations [3]. (3) Using error-correcting codes ranging from simple repetition strategies to more complex approaches. This calls for a sound investigation of BCIs from an information-theoretical standpoint. In [4], for instance, different code words associated with determined cyclic phase changes define a specific target. Given the phase cycle structure, a Hamming code corrector is successfully used to improve system efficiency. (4) Performing channel identification for each user, in order to choose the most efficient modulation on a case-by-case basis.

As indicated, some research groups have already taken important steps in some of these directions [1-4], and our group is starting to perform experiments related to the first three of the aforementioned fronts. Our intention is that the community consider these remarks as an outline of a research program that is vigorous and, in a certain sense, inevitable. **Conclusion:** This work has brought elements of an interpretation of SSVEP-Based BCIs in the context of the theory of digital communications. This interpretation gives rise to a vast research program, some elements of which have been given here. It is our firm belief that high-performance BCIs will have to be increasingly conceived according to this perspective. **Acknowledgments:** The authors thank CAPES, CNPq, FAPESP and FEEC for financial support.

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SPECTRAL VS. CANONICAL CORRELATION ANALYSIS FOR FEATURE EXTRACTION IN BCI-SSVEP SYSTEMS

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Introduction: Brain-Computer Interface (BCI) systems outline alternative communication channels that map brain signals directly onto an external application [1], which can be extremely useful to improve the quality of life for severely disable people. One of the most employed paradigms for designing BCI systems is based on steady-state visually evoked potentials (SSVEP), in which multiple periodic visual stimulation signals are associated with different commands through the synchronization of the electrical activity in the visual cortex with the stimulus that retains the user attention. In this work, classical spectral estimation technique based on Welch method [1] is compared to the coefficients obtained by canonical correlation analysis (CCA), a strategy that seeks to the best linear combination of EEG channels in order to maximize the correlation with reference signals [2]. **Materials and Methods:** The database was collected in the scope of DESTINE/FINEP and BRAINN/FAPESP projects and has information of nine healthy volunteers. Each volunteer was exposed to screens with two checkerboards blinking at different frequencies: 6, 7.5, 12, 15, 20 Hz with different windowing lengths. Two different feature extraction approaches in this 5-command BCI system were used: (1) Welch method for estimating spectral coefficients just in the stimulation frequencies; (2) the CCA coefficients of the reference signals (sinusoids and cossenoides at the stimulus frequencies) that maximizes the correlation with a linear combination of the electrodes. A leave M out approach was adopted using 70% of the trials for training and 30 % for testing, in 100 rounds. A least square classifier was used in both approaches. **Results:** Table 1 shows the mean accuracy rate of (1) and (2) under different trials length concerning all volunteers and the mean processing time for feature extraction.

Table 1. Comparison between the feature extraction methods.

Feature Extraction Method	Trial length [s]	Mean accuracy [%]	Mean Proc. Time [s]
Welch Method	1	46	1.05
	2	52	0.94
	3	55	0.91
	4	56	0.90
CCA	1	30	0.24
	2	40	0.16
	3	44	0.14
	4	47	0.12

Discussion and Conclusions: Despite the claim of CCA as a powerful feature extraction technique [2], Table 1 reveals that the classical Welch approach was (around 10%) more accurate for our data, although CCA was, in general, 5 times faster. In fact, given the processing time required and the possibility of suitably combine the electrodes for achieving maximum correlation with the stimulus, we speculate that CCA could be a promising technique for spatial filtering when combined with suitable feature extraction methods, which outlines a future investigation of this work.

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EMBEDDED SYSTEM FOR REAL TIME DETERMINATION OF BRAIN CONNECTIVITY

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Introduction: Since the 90s considerable effort has gone into approaches to study the dynamical interrelations between brain regions [1]. Through EEG (electroencephalogram) one may identify immediate relations between multivariate signal structures via a technique termed 'partial directed coherence' (PDC) [2] which portrays brain connectivity in the frequency domain and is intimately related to Granger "causality" [3] whereby the mutual influence between observed time series can be quantified. Most current PDC applications (as for other techniques) are mainly carried out off-line, bringing little experience about their practical feasibility in real time processing. The main goal of this work was to develop a system that computes PDC continuously and in real time on an embedded device (henceforth referred as RTMcarns). **Materials and Methods:** RTMcarns was developed as a multithreading application in C that facilitates its portability to other platforms. The development board used for this work was the Wand Board Quad, which has an ARM cortex-A59 processor and whose accuracy was checked against an existing program written in MATLAB. **Results:** RTMcarns allows PDC calculation for signals ranging from 2 to 32 channels, with calculation times varying from a few milliseconds to a few seconds, depending on the number of channels. The signals are received through a TCP/IP interface and the computed results are stored in local disk and later sent via TCP/IP to LAN/WAN connected devices. A maximum error of 10^{-15} was attained when compared to offline MATLAB algorithm implementation. **Discussion:** Most connectivity inference implementations, including PDC's are carried out off-line. Data are first collected and stored for later processing. Hence RTMcarns is a first step towards a real time computational infrastructure for connectivity which should facilitate pathophysiological evaluation by the clinical staffs that usually perform data interpretation and diagnostic decisions in parallel with patient observation. **Conclusion:** The current project has met the expectations related to creating an implementation of a real time application, respecting certain time limits that depend on the signal characteristics. The desired numerical accuracy was reached. More importantly, its development has opened a new research venue for a practical diagnostic tool.

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TOPIRAMATE DISRUPTS GRAPH THEORY PROPERTIES IN MIGRAINE PATIENTS AND TLE

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Introduction: Despite the efficacy for epilepsy and migraine, cognitive dysfunction (mainly language) is a relatively common side effect of topiramate (TPM), for subjects with and without epilepsy. Here we applied Graph theory (GT) to evaluate the impact of TPM on functional connectivity (on both global and local properties), comparing parameters between controls and subjects taking TPM (patients with epilepsy and others with migraine). **Materials and Methods:** Resting-state fMRI (RS) was acquired from 95 healthy controls [without topiramate, 15 TLE patients (TLE-TOP) and 16 migraine patients (MIG-TOP), both groups taking TPM]. All subjects underwent neuropsychological evaluation, with verbal fluency (FAS tests) and category fluency tests (naming animals). Each RS-fMRI was preprocessed with an in-house routine for SPM12/MATLAB and then parcellated into 90 regions of interest (based on AAL); by computing Pearson correlation values between all pairs, we finally constructed 90x90 matrices. Global parameters of GT (clustering coefficient, path length, local and global efficiency) were calculated for a range of sparsity values. Finally, the significant between-group differences were examined at each sparsity by non-parametric Wilcoxon rank-sum test. Cognitive tests were examined with MANOVA. **Results:** Both groups of patients presented lower performance for verbal fluency and category, compared to controls ($p<0.05$). TOP-MIG performed similarly to TLE-TPM. For GT we only investigated a range of sparsities defined by gamma ($>>1$) and delta (≈ 1), according to the criteria established by Watts and Strogatz [1]. Considering these parameters (for a sparsity range between 0.21 – 0.25), statistical analyses revealed that MIG-TPM presented significant reduction of local efficiency related to controls ($p<0.05$); in addition there were no differences between MIG-TPM and TLE-TPM groups ($p>0.05$), as follows: **Discussion:** These results suggest that MIG-TPM behave similarly to TLE-TPM regarding cognition and brain connectivity. The lowest performance of GT parameters for MIG-TPM suggest a negative impact of TPM on brain connectivity which may be associated with cognitive dysfunction commonly observed in subjects taking this drug.

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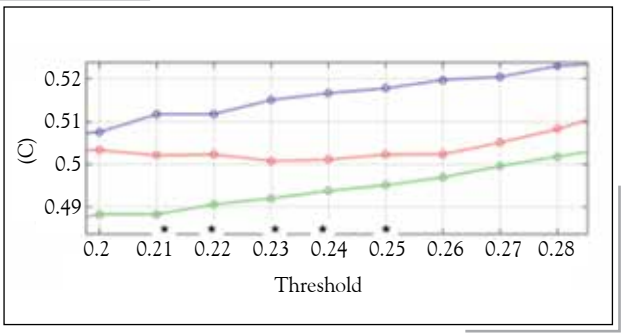

Figure 1. Clustering coefficient for sparsities. Blue – Controls; Red – TOP-TPM; Green – TOP-MIG. Stars indicate significant between-group (CTRL and TLE-MIG) differences at the given sparsity ($p<0.05$).

METHOD FOR OPTIMIZING QUANTITATIVE TEMPORAL LOBE EPILEPSY MR IMAGING

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Introduction: Epilepsy is one of the major neurobiological diseases in Canada and worldwide. Approximately 1% of Canadians suffer from epilepsy and in less than 50% of these patients seizure cure is achieved mostly by surgical removal of the seizure focus[1]. Standard clinical magnetic resonance images (MRI) exams are able to detect large abnormalities but small foci are often not seen. Transverse relaxometry, a quantitative MRI technique that measures the signal decay time (T2), has shown promise in detection of subtle abnormalities including but not limited to hippocampal sclerosis in temporal lobe epilepsy (TLE)[2]. Historically, this technique has produced inconsistent results, due primarily to sub-optimal data fitting. A recently proposed fitting method, called stimulated echo correction (SEC)[3], estimates major confounds associated with fitting errors in the transmit field and returns less biased results. SEC is a one-step least square method in which 3 parameters are estimated. Our aim is to develop and employ an improved SEC (iSEC) technique to reduce inconsistencies associated with T2 estimation, leading to better identification of the seizure focus in TLE patients. Materials and Methods: iSEC is a two-step method in which Gaussian smoothed transmit field (B1) maps (obtained in the first step) are used in a 2 parameters fitting algorithm involving amplitude and T2 values (second step). We compared and investigated validity and reliability between our iSEC and the standard SEC fitting methods by using simulated and *in-vivo* data. Simulated data was generated assuming nominal acquisition and tissue parameters: 16 echoes, 10 ms echo spacing, T1/T2 of 3000/100 ms, and B1 reduced to 0.75 of its ideal value. Gaussian noise ($10<SNR<100$) was added to mimic real MRI data. T2 values were estimated using the original SEC and our proposed iSEC algorithm. Furthermore, to investigate our iSEC success rate in real MRIs, we examined 10 sequentially axial repeated scans with 2.5 mm for slice thickness in one volunteer on a 3.0T GE scanner. T2 maps generated with both methods were evaluated based on variance across trials. **Results:** Using simulated data, T2 values estimated with the proposed iSEC method had ~25% less variance than with the original SEC method, Fig. 1. iSEC was found to be particularly beneficial when the SNR is below 35. Overall, according to both simulated results and repeated real MRIs, the iSEC method is ~25% more precise than the standard SEC method.

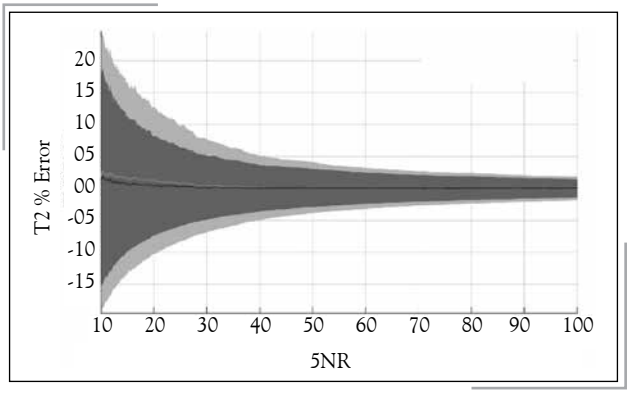

Figure 1. T2 percent errors using SEC (grey) and iSEC (dark) over SNR range of 10-100.

Discussion: iSEC utilizes 2 parameters; therefore reducing one degree of freedom and increasing precision compared with SEC. However, effectiveness of iSEC is directly correlated to accurate estimation of B1 values. It may be possible to increase our precision improvement even further by implementing a polynomial-smoothing factor instead of a Gaussian one. **Conclusion:** Simulations and repeated MRIs indicate that precision in T2 estimations has been considerably improved by using iSEC method. This is expected to translate into more reliable T2 maps than can currently be generated, which may provide reliable detection of pathology in epilepsy and other neurological disorders. We anticipate achieving similar results when employing our proposed iSEC method to TLE patients.

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CURVILINEAR REFORMATTING FOR FOCAL CORTICAL DYSPLASIA DIAGNOSIS

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Introduction: Focal Cortical Dysplasia (FCD) is a malformation of cortical development, which is the most common cause of medically refractory epilepsy. Bastos *et al.* have showed the advantages of a non-invasive curvilinear reformatting (CR) in providing visual analysis of the brain to identify FCD [1]. It improves the anatomical display of the gyral structure of the hemispheric convexities. In this work we develop a GPU-based algorithm for performing CR in native space without resorting to skull stripping. Instead of applying 3D image processing techniques, we propose to deal the problem with geometric and rendering methods. The addressed issued are: selection of the region of interest, generation of curvilinear cerebral layers, and rendering of curvilinear reformatted volume. **Materials and Methods:** An interactive method, proposed in [2], has been devised for assisting a user to select with the mouse the region of interest on the scalp of the patient's rendered MR image. This region is sampled and a triangular mesh is built from the samples. When more than one region is selected, the corresponding meshes are zippered as presented in [3]. The final mesh is displaced towards the brain and a stack of offset meshes is constructed. Depending on the depth selected by a user, an specific offset mesh is used for discarding the voxels on the visible side of the mesh while the MR volume is raycast. In this way we can show different curvilinear cerebral layers. Besides interactive rendering, GPU-based computation has been extensively explored in mesh sampling, mesh zippering and voxel discarding. We have assessed our algorithm with MRI volumes acquired by a MR 3T Philips Intera-Achieva Scanner at our university hospital. **Results:** The following images illustrate how our proposed algorithm works: (a) regions selection; (b) mesh built; (c) generation of mesh stack; and (d) rendering of curvilinear reformatted volume.

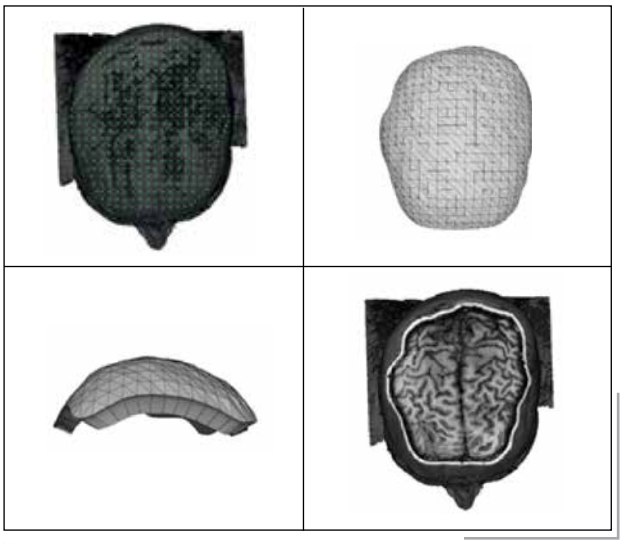

Figure 1.

Discussion: The procedure is integrated into the in-house developed interactive multimodal exploration system VMTK and it has shown effective in revealing the children's cerebral convolutions. However, for adults who have thicker skull and/or deformed brain the scalp-based clipping geometry cannot uncover the brain at the same depth, compromising visual assessment of gyral structure. **Conclusion:** The GPU-based CR algorithm presents an interactive performance. This makes possible

exploring visually at interactive rate the gyral structure at different depth. Reformatting parallel to meningeal layer for accurately displaying cortical convolutions is under investigation.

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MULTIMODAL VISUALIZATION OF DIFFUSION TENSOR IMAGING

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Introduction: Multimodal imaging techniques, such as computer tomography (CT), magnetic resonance (MR), positron emission tomography (PET) and single-photon emission computed tomography, may either improve the diagnostics of focal cortical dysplasia (FCD) or reduce the occurrence of deficits after surgical resection of detected lesions. The diffusion tensor imaging (DTI) is an imaging technique that may be helpful to assess the extent of cortical dysplasia with disrupted white matter structure, abnormal myelination, gliosis and increased number of cells. The lesion in DTI often appears larger than lesion revealed by conventional MRI and in patients with normal MRI [1]. The goal of this work is to integrate into the in-house developed interactive multimodal exploration environment VMTK the DTI modality. Three problems have been addressed: estimation of DTIs from diffusion-weighted images (DWIs) which contain measures of the motion of free water molecules within a voxel of tissue under different gradient-directions, visualization of DTI and co-location of DTI and other imaging modalities. **Materials and Methods:** Comparative studies, including implementation, of a homogeneous polynomial parameterized symmetric tensor estimator [2], the well-known modified Cholesky parameterized least squares methods (linear, weighted linear and nonlinear) [3] and the robust estimator with outliers rejection (RESTORE) [4] have been conducted. Comparative visual assessment and recommendations from the previous works led us to opt for RESTORE as our diffusivity estimator. A new color map has been proposed for displaying unambiguously the diffusivity direction. And to co-locate the brain's diffusivity with other multimodal signals, maximum mutual information (MMI) based rigid co-registration algorithm is employed [5]. We evaluate our proposal with the MR images from the Philips Intra-Achieva at our university hospital. **Results:** Co-registered coronal DTI (a) and FLAIR (b) images illustrate the extension of a suspect lesion indicated by a red arrow. The axial view of the lesion in the FLAIR image is presented in (c).

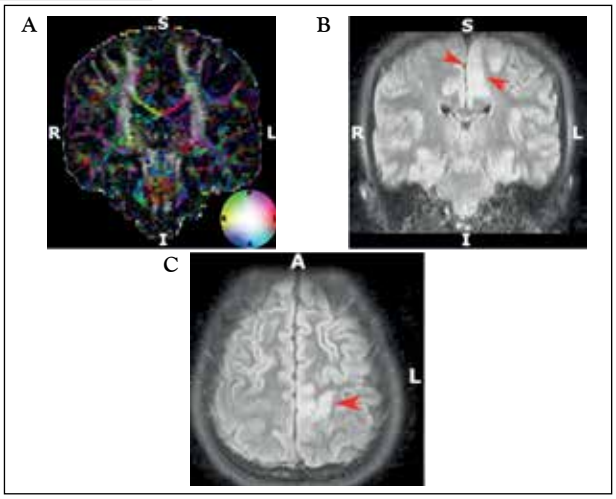

Figure 1.

Discussion: Due to some distortions caused by the diffusion EPI sequence used, the co-registration has failed in some slices. One way to correct these distortions is through the use of field maps obtained during the acquisition of the diffusion images. However, it increases the patient's discomfort once the acquisition time becomes much longer. **Conclusion:** Despite of distortions, the implemented algorithm has shown effective in conveying unambiguously the diffusivity direction and the lesion extension when co-located with other modalities. Non-rigid co-registration algorithms may ameliorate the multimodal alignment.

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HUMAN COMPUTER CONTROL BY GESTURAL INTERACTION: APPLICATION TO NEUROSCIENCE

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Introduction: Human Computer Control (HCC) considers that interaction with a virtual environment is natural and instinctive, such as limbs movements. It can be used for simulating real situations that require motor and/or cognitive stimuli, such as in neurorehabilitation therapies. The main objective of this work was to develop an interface to allow the user to precisely control the computer mouse through hand gestures. **Materials and Methods:** Gesture recognition was achieved by means of the Kinect [1] sensor. Kinect has an infrared camera that can scan the environment and find a human silhouette, using an Application Programming Interface (API) called OpenNI [2], which allows the sensor to be recognized by the computer. The NITE middleware [3] was then used to transform the hand gestures in inputs, and the output was to control the mouse cursor. **Results:** A software tool that allows the user to control the computer from motor gestures was developed. The user can be either in the sitting or in the standing position. The hand movement to start the application is a push in depth (larger than 5 cm movements required), and from there spatial coordinates are created for the mouse cursor location. These coordinates are increased according to the hand movements. Thus, patients with limited movement of the upper limbs can control their computers and benefit from the motivation provided by virtual environments. **Discussion:** In the field of neurorehabilitation, the use of software systems can provide greater motivation, cognitive and motor stimuli simultaneously and also enable other forms of interaction accessible by the patient. Cameirão et al. [4] highlight that virtual environments can be used with other therapeutic interventions in order to increase the complexity of the tasks; their findings demonstrate a consistent transfer of movement kinematics between the physical and virtual tasks. Shin et al. [5] highlight that rehabilitation programs based on virtual environments are an alternative therapy for motor recovery; they found that the use of this type of technology can enhance motor function, but did not improve functional independence. In order to do so, we propose that our system should be used together with software or applications that can simulate situations of daily life. **Conclusion:** A software system to control the computer (mouse) by gestures was developed. During user interaction with a virtual environment using this system, movements of the upper limbs can be explored to stimulate motor tasks commonly required in neurorehabilitation therapies. Choosing, in the computer or in the internet, software tools controlled by the mouse cursor, this system can provide cognitive stimulation through human-computer interaction.

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AUGMENTED REALITY FOR MOTOR STIMULATION: A PILOT STUDY

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Introduction: This work presents a case study of the feasibility of using the NeuroR computer system in rehabilitation programs. We propose a task protocol using NeuroR, an augmented reality system, and aim to verify whether this protocol is able to provide upper limb motor stimulation of stroke patients. We used resting state (RS) fMRI to evaluate possible connectivity changes after rehabilitation. **Materials and Methods:** A male patient, 47 years old, right-handed, who suffered an ischemic stroke 10 months previously, was enrolled in this study. He presented aphasia with right hemiparesis. The patient took part in four physiotherapy sessions (Center of Reference for Rehabilitation of Sousas, Campinas), and was evaluated using a RS-fMRI protocol followed by acquisition of a high-resolution structural MRI (performed at a 3T Philips Achieva scanner at Unicamp), before and after training. During RS (6 min long), the patient was instructed to open his eyes and not to think of anything in particular. In the training sessions, standard and NeuroR-based physiotherapy were performed. Standard physiotherapy was performed using the right (injured) upper limb: shoulder lifting without assistance, weight discharge without assistance, shoulder abduction with assistance, shoulder flexion with assistance and internal and external shoulder rotation with assistance. All exercises were repeated 10 times. After standard physiotherapy, NeuroR was run to provide visual stimuli to shoulder abduction and shoulder flexion. The patient was instructed to perform the exercises with the injured arm while looking at the virtual arm moving in the projection screen (10 repetitions each). RS-fMRI data were analyzed using UF2C (www.lni.hc.unicamp.br/app/uf2c). **Results:** Structural MRI data showed that the patient had a large lesion on the left hemisphere, as expected. Functional connectivity analyses of the RS data were performed using a seed placed at the motor cortex. Setting the correlation threshold to 0.2 and using the AAL atlas, we found positive correlations with the motor area for cerebelum_6_R, cerebelum_6_L and cerebelum_8_L in the pre-test. Neither of

these regions were correlated with the motor area in the post-test. **Discussion:** Some requirements must be fulfilled to allow using NeuroR to provide visual stimuli to physical rehabilitation in parallel with standard physiotherapy sessions. These include a minimum of 2.30 m distance between the tripod with the attached camera and the patient, and for an electromyography device to be available to provide the electrical stimulus to trigger the animation of the virtual arm. If the distance is below the threshold of 2.30 m, the patients do not see the whole virtual arm on the projection screen in front of them. If the animation of the virtual arm is triggered by hand, timing issues may occur. Although data analysis is still ongoing, the functional connectivity analyses showed cerebellum areas correlating with motor areas at the pre-test and no more at the post-test, that is,after the rehabilitation sessions. This may be related to the fact that the supervised learning of motor control is related to the functions of the cerebellum [1]. Also, the topological configuration of task state motor execution networks seems to undergo significant shift during stroke recovery. **Conclusion:** The proposed protocol is feasible to use, provided that the minimum requirements are fulfilled. The connectivity results found in this pilot study seem promising. For long-term prospects, we will investigate whether NeuroR is able to improve stroke patients' recovery.

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A STUDY ON HOW INTERACTIVE MUSICAL TECHNOLOGY COULD BE APPLIED IN EDUCATIONAL AND THERAPEUTIC PURPOSES

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Introduction: Recent studies have shown the effectiveness of interactive technology in education and therapeutic frameworks [1, 2]. Here a Case Study, anchored on interactive musical technology, investigates how Creative Empowerment (CE) and Sensorimotor Maps (SM) demonstrate how interactive musical system could be an alternative tool on therapeutic and rehabilitation processes. Our study is based on user's proprioceptive interaction, integration of diverse perceptual modalities and we created an interactive system E-MOCOMU (for e-motion, colors and music) to procedure our experiments [3]. **Materials and Methods:** In order to verify the potential of interactive music systems, an experiment was set at the Interdisciplinary Nucleus for Sound Studies (NICS), University of Campinas (UNICAMP). It was implemented in four stages: 1) Emotional Evaluation using SAM Test (Self-Assessment Manikin) by Lang [4], 2) Guided Instructions on the system behavior, 3) Free Improvisation, and 4) Final Emotional Evaluation. We had 17 participants and every experiment section was videotaped and we gathered acceleration of movements during stage 3. Finally, we compared participant's Arousal and Valence levels and we also evaluated their movements based on video annotations. **Results:** As every section of the experiment was videotaped, we compared participant's Arousal and Valence, on stages 1 and 4, with the duration and acceleration curves assessed on stage 3. The results outline a positive change both in Arousal and in Valence. The positive correlation between Valence and the duration of stage 3 might show that the motor response of the participant was related to the positive outcome of the interaction. Also, this kind of interaction verify the potential of interactive music system in the development of CE and SM. **Discussion and Conclusion:** The Case Study highlights that the capacity of interactive technology into arouse the creative empowerment, gained through a proprioceptive awareness, would bound to benefit the motor rehabilitation of patients through an effective game systems.

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AUTOMATIC GENERATION OF INTERNATIONAL 10-20 SYSTEM FOR ELECTRODE PLACEMENT

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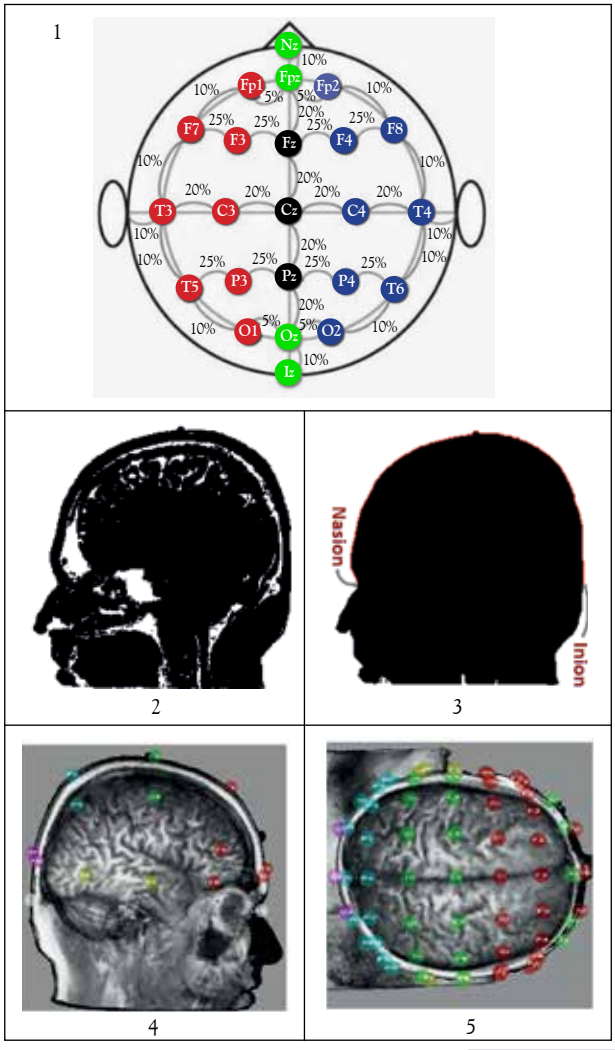
Introduction: Focal cortical dysplasia (FCD) is a malformation of cortical development. It's closely related to pharmacoresistant epilepsy. Its diagnosis is based on medical history, histological, imaging and electrophysiological evidences. The presence of spikes and sharp waves on a routine electroencephalogram (EEG) is a strong evidence of seizure focus. Because of the variability of cortical landmarks underlying electrode positions [1], correlating scalp electrodes with cerebral structures may improve the identification of cortical generators of epileptiform potentials. Our main goal is to co-localize electrophysiological signals with other functional and anatomical data for better supporting dicision-making on a diagnosis of FCD. In this work we present a novel GPU-based algorithm for generating the electrode positions from the external anatomical landmarks according to the international 10-20 and 10-10 systems (Figure 1)[2] and for visualizing them with respect to the underlying gyral and sulcal convolutions. **Materials and Methods:** Five anatomical landmarks, nasion (N), inion (I), a midline point (M), left (A1) and right pre-auricular (A2), are input by an expert through a pointing device. From N, I and M a mid-plane is defined and the voxels above a specified threshold in this plane are segmented with a GPU-based threshold technique (Figure 2). After filling the white holes, a piecewise linear curve from inion and nasion is segmented by a gradient-based method (Figure 3). If it's a 10-20 system, the curve is partitioned in 10%, 20%, 20% 20%, 20%, 10% from N to I at the Fpz, Fz, Cz Pz and Oz, respectively. The process is repeated with the plane A1CzA2 for getting T3, C3, C4 and T4. Then the planes IT3N, IT4N are constructed and the segmentation steps repeated for getting positions F7, F8, T5 and T6; and again with the planes F7FzF8 and T5PzT6 for computing F3, F4, P3 and P4. The positions labeled with the corresponding identifications are opaquely rendered, whereas the tissue surrounding the brain is rendered at lower opacity, as shown in Figure 4. Following the same reasoning, we implemented the 10-10 system. We have evaluated our algorithm with MRI volumes acquired by a MR 3T Philips Intera-Achieva Scanner. **Result**: Figure 5 presents the visualization of the 10-10 system. Note that the transparent skull and the electrode location rendering allow us to easily assess the spatial relationship between the electrode position on the scalp and the underlying cortical structure even when the number of electrodes increases from 10-20 to the 10-10 system.



Discussion and Conclusion: By reducing a 3D placement to a 2D placement problem, simple well-known image processing algorithms are directly applicable. In addition, we explore GPU processing capabilities to make the procedure interactive. Nevertheless, despite visually convincing results, it is necessary to validate numerically the generated positions.

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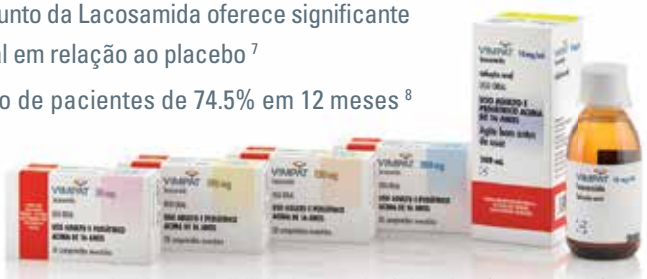

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VIMPAT™ lacosamida (lista C1 Port 344/98)
Vimpat™ (lacosamida) comprimidos revestidos de 50 mg em embalagem com 14 comprimidos ou de 100, 150 e 200 mg em embalagens com 28 comprimidos. **Indicações:** terapia adjuvante no tratamento de crises parciais com ou sem generalização secundária em pacientes a partir de 16 anos de idade com epilepsia. **Contraindicações:** em casos de hipersensibilidade ao princípio ativo (lacosamida) ou a qualquer um dos excipientes. **Cuidados e Advertências:** Advertências (vide bula completa do produto): **Vimpat** pode causar tonturas, que podem aumentar o risco de acidente ou queda. Um pequeno número de pessoas que iniciaram tratamento com antiepilépticos, como a lacosamida, apresentou pensamentos de autoagressão ou suicídio. Não é recomendável tomar **Vimpat** com álcool, pois **Vimpat** pode provocar tonturas ou sensação de cansaço. **Vimpat** é um medicamento. Durante seu uso, não dirija veículos ou opere máquinas, pois sua agilidade e atenção podem estar prejudicadas. Nos estudos clínicos foram observados prolongamentos no intervalo PR com o uso de lacosamida. Bloqueio AV de segundo grau ou maior foi reportado na experiência pós-comercialização. *Gravidez:* categoria C de risco de gravidez. Interações medicamentosas (vide bula completa do produto): A lacosamida deve ser usada com cautela em pacientes tratados com medicamentos conhecidos por prolongar o intervalo PR e em pacientes tratados com medicamentos antiarrítmicos classe I. Dados in vitro sugerem que a lacosamida possui potencial para inibir CYP2C19 em concentrações terapêuticas. A análise farmacocinética populacional estimou que o tratamento concomitante com outros medicamentos antiepilépticos indutores enzimáticos (carbamazepina, fenitoína, fenobarbital, em várias doses) reduz a exposição sistêmica geral da lacosamida em 25%. Reações adversas (vide bula completa do produto): Muito comuns: tontura, dor de cabeça, náusea e diplopia. Comuns: distúrbio cognitivo, nistagmo, distúrbio de equilíbrio, coordenação anormal, falha de memória, tremor, sonolência, disartria, distúrbio de atenção, hipoestesia, parestesia, visão embaçada, vertigem, zumbido, vômitos, constipação, flatulência, dispepsia, boca seca, diarreia, prurido, espasmos musculares, distúrbio ao andar, astenia, fadiga, irritabilidade, sensação de embriaguez, quedas, laceração da pele, contusão. **Posologia:** A dose inicial recomendada é de 50 mg duas vezes por dia, a qual deverá ser aumentada para uma dose terapêutica inicial de 100 mg duas vezes por dia após uma semana. O tratamento com lacosamida também pode ser iniciado com uma dose de ataque única de 200 mg, seguida por uma dose de regime de manutenção, após aproximadamente 12 horas, de 100 mg duas vezes ao dia (200 mg/dia). A dose de ataque deve ser administrada sob supervisão médica considerando sua farmacocinética e o potencial para o aumento de incidência de reações adversas relacionadas ao SNC. A administração da dose de ataque não foi estudada em condições agudas em estados epilépticos. Dependendo da resposta clínica e tolerabilidade, a dose de manutenção pode ser aumentada 50 mg, duas vezes por dia, a cada semana, até uma dose diária máxima de 400 mg (200 mg duas vezes por dia). **USO ADULTO E PEDIÁTRICO ACIMA DE 16 ANOS DE IDADE. USO ORAL. VENDA SOB PRESCRIÇÃO MÉDICA – SO PODE SER VENDIDO COM RETENÇAO DA RECEITA. SE PERSISTIREM OS SINTOMAS, O MEDICO DEVERA SER CONSULTADO.** Para maiores informações, consulte a bula completa do produto. (0302040001R5 Rev. Dezembro 2014). www.ucb-biopharma.com.br **Reg. MS – 1.2361.0081**

Vimpat™ (lacosamida) solução oral 10mg/mL em embalagem contendo 1 frasco de 200mL e um copo-medida. **Indicações:** terapia adjuvante no tratamento de crises parciais com ou sem generalização secundária em pacientes a partir de 16 anos de idade com epilepsia. **Contraindicações:** em casos de hipersensibilidade ao princípio ativo (lacosamida) ou a qualquer um dos excipientes. **Cuidados e Advertências:** Advertências (vide bula completa do produto): **Vimpat** pode causar tonturas, que podem aumentar o risco de acidente ou queda. Um pequeno número de pessoas que iniciaram tratamento com antiepilépticos, como a lacosamida, apresentou pensamentos de autoagressão ou suicídio. Não é recomendável tomar **Vimpat** com álcool, pois **Vimpat** pode provocar tonturas ou sensação de cansaço. **Vimpat** é um medicamento. Durante seu uso, não dirija veículos ou opere máquinas, pois sua agilidade e atenção podem estar prejudicadas. Nos estudos clínicos foram observados prolongamentos no intervalo PR com o uso de lacosamida. Bloqueio AV de segundo grau ou maior foi reportado na experiência pós-comercialização. *Gravidez:* categoria C de risco de gravidez. Interações medicamentosas (vide bula completa do produto): A lacosamida deve ser usada com cautela em pacientes tratados com medicamentos conhecidos por prolongar o intervalo PR e em pacientes tratados com medicamentos antiarrítmicos classe I. Dados in vitro sugerem que a lacosamida possui potencial para inibir CYP2C19 em concentrações terapêuticas. A análise farmacocinética populacional estimou que o tratamento concomitante com outros medicamentos antiepilépticos indutores enzimáticos (carbamazepina, fenitoína, fenobarbital, em várias doses) reduz a exposição sistêmica geral da lacosamida em 25%. Reações adversas (vide bula completa do produto): Muito comuns: tontura, dor de cabeça, náusea e diplopia. Comuns: distúrbio cognitivo, nistagmo, distúrbio de equilíbrio, coordenação anormal, falha de memória, tremor, sonolência, disartria, distúrbio de atenção, hipoestesia, parestesia, visão embaçada, vertigem, zumbido, vômitos, constipação, flatulência, dispepsia, boca seca, diarreia, prurido, espasmos musculares, distúrbio ao andar, astenia, fadiga, irritabilidade, sensação de embriaguez, quedas, laceração da pele, contusão. **Posologia:** A dose inicial recomendada é de 50 mg duas vezes por dia, a qual deverá ser aumentada para uma dose terapêutica inicial de 100 mg duas vezes por dia após uma semana. O tratamento com lacosamida também pode ser iniciado com uma dose de ataque única de 200 mg, seguida por uma dose de regime de manutenção, após aproximadamente 12 horas, de 100 mg duas vezes ao dia (200 mg/dia). A dose de ataque deve ser administrada sob supervisão médica considerando sua farmacocinética e o potencial para o aumento de incidência de reações adversas relacionadas ao SNC. A administração da dose de ataque não foi estudada em condições agudas em estados epilépticos. Dependendo da resposta clínica e tolerabilidade, a dose de manutenção pode ser aumentada 50 mg, duas vezes por dia, a cada semana, até uma dose diária máxima de 400 mg (200 mg duas vezes por dia). **USO ADULTO E PEDIÁTRICO ACIMA DE 16 ANOS DE IDADE. USO ORAL. VENDA SOB PRESCRIÇÃO MÉDICA – SO PODE SER VENDIDO COM RETENÇAO DA RECEITA. SE PERSISTIREM OS SINTOMAS, O MEDICO DEVERA SER CONSULTADO.** Para maiores informações, consulte a bula completa do produto. (0302040011R5 Rev. Dezembro 2014). www.ucb-biopharma.com.br **Reg. MS – 1.2361.0081**

O 1° PASSO para uma vida com NOVAS POSSIBILIDADES

AGORA no BRASIL

- ***Keppra®** é o **único FAE** considerado **nível A** de evidência para o **tratamento de crises focais**, em terapia adjuvante, pelos guidelines da **ILAE***, em pediatria[1]*
- ***Keppra®** tem **bom perfil de tolerabilidade**, **baixa incidência de eventos adversos significativos**, **sem interação medicamentosa** clinicamente significativa[2]*
- ***Keppra®** é um fármaco **antiepiléptico** de **amplo espectro de ação**[2]*

**International League Against Epilepsy*

CONTRAINDICAÇÃO: Hipersensibilidade ao princípio ativo ou a outros derivados da pirrolidona ou a qualquer um dos excipientes. **INTERAÇÃO MEDICAMENTOSA:** Foram observados relatos isolados de diminuição de eficácia quando o laxante osmótico macrogol foi administrado concomitantemente a levetiracetam oral. Assim, a administração oral de macrogol não deve ser realizada dentro de 1 hora (antes ou após) da administração de levetiracetam.

Referência Bibliográfica: 1. Wilmshurst JM, Summary of recommendations for the management of infantile seizures: Task Force Report for the ILAE Commission of Pediatrics. - Epilepsia. 56(8):1185-97. Aug. 2015. **2.** Panayiotopoulos CP, A Clinical Guide to Epileptic Syndromes and their Treatment - Revised Second Edition - Chapter 18, Symptomatic and Cryptogenic (Probably Symptomatic) Focal Epilepsies, -ed. London UK - Springer-Verlag; page 485, 2007.

Keppra® (levetiracetam). **Apresentação**: comprimidos revestidos de 250 mg em embalagens com 30 ou 60 comprimidos ou comprimidos de 750 mg também em embalagens com 30 ou 60 comprimidos. **Indicações**: é indicado como monoterapia para o tratamento de crises parciais, com ou sem generalização secundária em pacientes a partir dos 16 anos com diagnóstico recente de epilepsia. Keppra® também é indicado como terapia adjuvante no tratamento de: - crises convulsivas parciais com ou sem generalização secundária em adultos, adolescentes e crianças com idade superior a 6 anos, com epilepsia; - crises convulsivas mioclônicas em adultos, adolescentes e crianças com idade superior a 12 anos, com epilepsia mioclônica juvenil; - crises convulsivas tônico-clônicas primárias generalizadas em adultos, adolescentes e crianças com mais de 6 anos de idade, com epilepsia idiopática generalizada. **Contraindicações**: Hipersensibilidade ao princípio ativo ou a outros derivados da pirrolidona ou a qualquer um dos excipientes. **Cuidados e Advertências**: para informações completas de advertências, vide bula do produto. A administração de Keppra® em pacientes com comprometimento renal poderá necessitar de um ajuste da dose. Foram notificados suicídio, tentativa de suicídio e ideias e comportamento suicida em pacientes tratados com levetiracetam. *Gravidez*: categoria C de risco de gravidez. Este medicamento não deve ser utilizado por mulheres grávidas sem orientação médica ou do cirurgião-dentista. Levetiracetam é excretado no leite humano materno. **Keppra®** é um medicamento. Durante seu uso, não dirija veículos ou opere máquinas, pois sua agilidade e atenção podem estar prejudicadas. *Interações medicamentosas* (*vide bula completa do produto*): Dados indicam que levetiracetam não influencia as concentrações séricas de medicamentos antiepilépticos existentes (fenitoína, carbamazepina, ácido valproico, fenobarbital, lamotrigina, gabapentina e primidona) e que estes medicamentos antiepilépticos não influenciam a farmacocinética de levetiracetam. A probenecida (500 mg quatro vezes ao dia), um agente bloqueador da secreção tubular renal, mostrou inibir a depuração renal do metabólito primário, mas não a do levetiracetam. Contudo, a concentração deste metabólito permanece baixa. Levetiracetam 1000 mg por dia não influenciou a farmacocinética dos contraceptivos orais (etinilestradiol e levonorgestrel). Foram observados relatos isolados de diminuição de eficácia quando o laxante osmótico macrogol foi administrado concomitantemente a levetiracetam oral. Assim, a administração oral de macrogol não deve ser realizada dentro de 1 hora (antes ou após) da administração de levetiracetam. A extensão de absorção do levetiracetam não sofreu qualquer alteração com a ingestão de alimentos, mas a taxa de absorção diminuiu ligeiramente. Não estão disponíveis dados sobre a interação do levetiracetam com o álcool. *Reações Adversas*: para informações completas de reações adversas, vide bula do produto. Os eventos adversos mais comumente reportados nos estudos clínicos foram astenia, fadiga, dor de cabeça e sonolência. Adicionalmente às reações adversas relatadas durante os estudos clínicos, as seguintes reações adversas foram reportadas na experiência pós-comercialização, além de outras mencionadas na bula completa do produto: comportamento anormal, raiva, ataque de pânico, ansiedade, estado de confusão, alucinação, distúrbios psicóticos, suicídio, tentativa de suicídio e ideação suicida, parestesia, coreoatetose, discinesia, letargia. **Posologia**: A dose inicial recomendada para monoterapia no tratamento de crises parciais, com ou sem generalização secundária em pacientes a partir dos 16 anos com diagnóstico recente de epilepsia, é de 250 mg duas vezes ao dia, a qual poderá ser aumentada para uma dose terapêutica inicial de 500 mg duas vezes ao dia, após duas semanas. A dose máxima é de 1500 mg duas vezes ao dia. Nos casos de terapia adjuvante, para adultos e crianças acima de 12 anos e com mais de 50 kg, a dose terapêutica inicial é de 500 mg/duas vezes ao dia. Esta dose poderá ser iniciada no primeiro dia de tratamento, a dose diária poderá ser aumentada até o máximo de 1500 mg/duas vezes ao dia. Ainda nos casos de terapia adjuvante, para crianças (dos 6 aos 11 anos) e adolescentes com peso inferior a 50 kg a dose terapêutica inicial é de 10 mg/kg duas vezes ao dia, a dose pode ser aumentada até 30 mg/kg duas vezes ao dia. A alteração das doses não deve exceder aumentos ou reduções de 10 mg/kg duas vezes ao dia, a cada duas semanas. Deve ser utilizada a dose eficaz mais baixa. A posologia em crianças com peso igual ou superior a 50 kg é igual à dos adultos. A forma farmacêutica comprimido revestido não é adaptada para bebês e crianças com menos de 6 anos. Keppra® solução oral é a forma farmacêutica ideal para uso nesta população. **USO ADULTO E PEDIÁTRICO ACIMA DE 06 ANOS DE IDADE. USO ORAL. VENDA SOB PRESCRIÇÃO MÉDICA – SÓ PODE SER VENDIDO COM RETENÇÃO DA RECEITA. SE PERSISTIREM OS SINTOMAS, O MÉDICO DEVERÁ SER CONSULTADO.** Para maiores informações, consulte a bula completa do produto. (0302040013 R9 Rev. Agosto 2015). www.ucb-biopharma.com.br **Reg. MS – 1.2361.0083**

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