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Ciencias Médicas y de la Salud / Medicina Básica  
Categorización actual: Nivel I (Activo)

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## Datos Generales

### INSTITUCIÓN PRINCIPAL

Universidad de la República/ Facultad de Medicina / Fisiología- laboratorio de neurobiología del sueño / Uruguay

### DIRECCIÓN INSTITUCIONAL

Institución: Universidad de la República / Facultad de Medicina / Sector Educación Superior/Público  
Dirección: General Flores, 2125. / 11800  
País: Uruguay / Montevideo / Montevideo  
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## Formación

### Formación académica

#### CONCLUIDA

#### DOCTORADO

##### Doctorado en Ciencias Biológicas (UDELAR-PEDECIBA) (2014 - 2018)

Universidad de la República - Facultad de Ciencias , Uruguay  
Título de la disertación/tesis/defensa: Estudio de las oscilaciones gamma del EEG durante la vigilia, el sueño y en un modelo farmacológico de psicosis  
Tutor/es: Pablo Torterolo  
Obtención del título: 2018  
Financiación:  
Agencia Nacional de Investigación e Innovación / Agencia Nacional de Investigación e Innovación , Uruguay  
Palabras Clave: gamma EEG  
Áreas de conocimiento:  
Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias / neurociencias cognitiva y sueño

#### MAESTRÍA

##### Maestría en ciencias medicas PRO.IN.BIO (2009 - 2012)

Universidad de la República - Facultad de Medicina , Uruguay  
Título de la disertación/tesis/defensa: Estudio de la coherencia de la banda gamma de frecuencias (35-45 Hz) del EEG durante la vigilia y el sueño  
Tutor/es: Pablo Torterolo  
Obtención del título: 2013  
Sitio web de la disertación/tesis/defensa: [no](#)  
Palabras Clave: sueño coherencia vigilia gamma alerta  
Áreas de conocimiento:  
Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias / Neurobiología cognitiva y sueño

#### GRADO

##### Medicina (2000 - 2012)

Universidad de la República - Facultad de Medicina , Uruguay  
Título de la disertación/tesis/defensa:  
Obtención del título: 2012  
Palabras Clave: medicina  
Áreas de conocimiento:

## Formación complementaria

### CONCLUIDA

#### CURSOS DE CORTA DURACIÓN

##### **Miledi Neuroscience Training Program. (01/2011 - 01/2011)**

Sector Educación Superior/Público / Universidad de la República / Facultad de Medicina , Uruguay  
200 horas

Palabras Clave: neuroscience

Areas de conocimiento:

Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias / FISIOLÓGÍA

##### **VII Escuela de Neurociencias (como estudiante de pregrado). (2002)Montevideo-Uruguay. (01/2002 - 01/2002)**

Sector Educación Superior/Público / Universidad de la República / Facultad de Medicina , Uruguay  
150 horas

Palabras Clave: neurobiología

Areas de conocimiento:

Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias / FISIOLÓGÍA

#### PARTICIPACIÓN EN EVENTOS

##### **World Sleep 2023 (2023)**

Tipo: Congreso

Institución organizadora: World Sleep Society, Brasil

Alcance geográfico: Internacional

Palabras Clave: Sleep Neuroscience

##### **15th International Workshop on NEURAL CODING 2023 (2023)**

Tipo: Congreso

Institución organizadora: IBRO, Uruguay

Alcance geográfico: Internacional

Palabras Clave: Codes

Areas de conocimiento:

Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias /

##### **XV Latin American Symposium on Chronobiology 2019 (2019)**

Tipo: Congreso

Institución organizadora: IBRO, Uruguay

Alcance geográfico: Internacional

Palabras Clave: Sueño Cronobiología

Areas de conocimiento:

Ciencias Médicas y de la Salud / Medicina Básica / Fisiología /

##### **X Jornada de la SUB (2014)**

Tipo: Congreso

Institución organizadora: Sociedad Uruguaya de Biociencias, Uruguay

Areas de conocimiento:

Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias / Neurobiología cognitiva y sueño

##### **XXXIV Congreso Argentino de Neurología Infantil y II Congreso Uruguayo de Neuropediatría. (2014)**

Tipo: Congreso

Institución organizadora: SOCIEDAD ARGENTINA DE NEUROLOGÍA INFANTIL y SOCIEDAD URUGUAYA DE NEUROPEDIATRÍA, Uruguay

Areas de conocimiento:

Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias / Neurobiología cognitiva y sueño

##### **Primer congreso FALAN Cancún Quintana Roo (2012) (2012)**

Tipo: Congreso

Institución organizadora: International Brain Research Organization, México  
Palabras Clave: neurobiología  
Áreas de conocimiento:  
Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias / neurociencias

#### **IX Jornada de la SUB Piriápolis-Maldonado-Uruguay (2012)**

Tipo: Congreso  
Institución organizadora: sociedad uruguaya de biociencias, Uruguay  
Áreas de conocimiento:  
Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias /

#### **Society for Neuroscience 2011 Annual Meeting (2011)**

Tipo: Congreso  
Institución organizadora: Society for Neuroscience, Estados Unidos  
Palabras Clave: neuroscience  
Áreas de conocimiento:  
Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias / neurociencias

#### **Terceras Jornadas Uruguayas de Comportamiento Animal (2011)**

Tipo: Congreso  
Institución organizadora: facultad de ciencias, Uruguay

#### **Cambridge Electronic Design Training Days (2011)**

Tipo: Taller  
Institución organizadora: Cambridge Electronic Design, Estados Unidos

#### **Jornada Científica Internacional sobre Medicina del Sueño (2011)**

Tipo: Taller  
Institución organizadora: SUIDES, Uruguay

#### **XIII Jornada de la SUB Piriápolis-Maldonado-Uruguay (2010)**

Tipo: Congreso  
Institución organizadora: sociedad uruguaya de biociencias, Uruguay

#### **3rd International Congress on Sleep Medicine (2009)**

Tipo: Congreso  
Institución organizadora: World Association of Sleep Medicine, Brasil  
Palabras Clave: sueño  
Áreas de conocimiento:  
Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias / SUEÑO

#### **Segundas Jornadas Uruguayas de Comportamiento Animal (2009)**

Tipo: Congreso  
Institución organizadora: facultad de ciencias, Uruguay

#### **Primer simposio internacional sobre yerba mate y salud (2008)**

Tipo: Simposio

## **Idiomas**

### **Inglés**

Entiende muy bien / Habla bien / Lee muy bien / Escribe bien

## **Áreas de actuación**

### **CIENCIAS MÉDICAS Y DE LA SALUD**

Medicina Básica / Neurociencias / fisiología

## **Actuación profesional**

## Facultad de Medicina

### VÍNCULOS CON LA INSTITUCIÓN

#### **Funcionario/Empleado (09/2021 - a la fecha)** Trabajo relevante

Profesor Adjunto 40 horas semanales / Dedicación total  
Gane el concurso de profesor adjunto (G3) titular del departamento de fisiología el 7 de julio de 2021. La CDC de facultad de medicina homologó el fallo del tribunal del concurso y me declaró ganador el 28 de julio de 2021 y tome posesión del cargo el 9 de octubre de 2021  
Escalafón: Docente  
Grado: Grado 3  
Cargo: Efectivo

#### **Funcionario/Empleado (12/2014 - 09/2021)** Trabajo relevante

40 horas semanales / Dedicación total  
Concurso G2 en fisiología fecha del 21/11/14 al 10/12/14 al ganar el concurso mi cargo se hace titular El 30/08/2017 obtuve la dedicación total en este cargo  
Escalafón: Docente  
Grado: Grado 2  
Cargo: Efectivo

#### **Funcionario/Empleado (06/2013 - 08/2017)**

Profesor adjunto de fisiología general 15 horas semanales  
Prof. adj. de fisiología general y aplicada a la nutrición en la cátedra de nutrición básica de la escuela de nutrición  
Escalafón: Docente  
Grado: Grado 3  
Cargo: Interino

#### **Funcionario/Empleado (06/2011 - 12/2014)** Trabajo relevante

30 horas semanales  
Escalafón: Docente  
Grado: Grado 2  
Cargo: Interino

#### **Funcionario/Empleado (08/2008 - 08/2011)**

20 horas semanales  
Escalafón: Docente  
Grado: Grado 1  
Cargo: Efectivo

### ACTIVIDADES

#### LÍNEAS DE INVESTIGACIÓN

##### **Estudio de las oscilaciones gamma del EEG durante la vigilia, el sueño y en un modelo farmacológico de psicosis (06/2009 - a la fecha )**

Comencé a trabajar en el Laboratorio de Neurobiología del Sueño en el año 2008. En el año 2009 comencé una línea de investigación propia, bajo la guía del Dr. Pablo Torterolo quien dirige el laboratorio, sobre las interacciones funcionales en la actividad eléctrica de la corteza cerebral durante la vigilia y el sueño y luego bajo el efecto de fármacos que alteran las funciones cognitivas. Esa línea de investigación surgió de una idea mía y fue la base de mi doctorado, y de 4 trabajos que publiqué como primer autor (el 1ero en 2013) y masa de 10 en los que fui coautor. Mi Doctorado recibió la mención del premio "ELIO GARCÍA-AUSTT". Para generar los procesos cognitivos, distintas áreas corticales interactúan intensamente entre sí y con regiones subcorticales como el tálamo. Se ha postulado que las oscilaciones en la banda gamma de frecuencia (30 a 45 Hz) del electroencefalograma (EEG), son producto de estas interacciones y por lo tanto están involucradas en las funciones cognitivas. En el marco de esta línea de investigación, utilizando el gato como modelo animal, estudiamos las oscilaciones gamma del EEG de distintas regiones corticales. Para ello utilizamos distintas funciones matemáticas, pero principalmente la "coherencia cruzada

cuadrada". La actividad gamma fue estudiada durante la vigilia y el sueño, así como en un modelo farmacológico de psicosis (dosis subanestésica de ketamina). También, utilizando antagonistas de receptores muscarínicos (atropina y escopolamina), estudiamos el rol del sistema colinérgico (componente de los sistemas activadores) en la modulación de la actividad gamma. Demostramos que durante la vigilia alerta (AW) hay un gran aumento de la coherencia (acoplamiento entre áreas alejadas) en la banda gamma entre áreas corticales alejadas con respecto a los demás estados. La coherencia alcanza valores mínimos durante el sueño REM, aunque su potencia (sincronización local), es similar a la de la vigilia. Se ha propuesto que las ondas lentas y los husos de sueño, característicos del sueño, son incapaces de sostener el fenómeno de la consciencia. Sin embargo, recientemente hemos demostrado que bajo el efecto de antagonistas colinérgicos muscarínicos (atropina o escopolamina), los animales mantienen la vigilia a pesar de presentar ondas lentas y husos de sueño similares al sueño NREM. En contrapartida, la presencia de oscilaciones gamma (40 Hz coherentes bajo este tratamiento), que son características de la vigilia, podrían explicar el mantenimiento de la V a pesar del enlentecimiento del EEG. Por otra parte, hemos observado en gatos que durante el estado psicótico desarrollado por la administración de dosis subanestésicas de ketamina, la actividad gamma de frecuencias (principalmente a 40 Hz) se comporta como en el sueño REM. Es decir, en los dos estados existe un aumento de la potencia gamma, pero una disminución de la coherencia a esa frecuencia (acoplamiento entre áreas alejadas). A su vez en el marco de esa línea de investigación gané un proyecto I+D de CSIC (como responsable científico) titulado "Abordaje fisiológico y farmacológico al estudio del correlato electroencefalográfico de la consciencia".

30 horas semanales , Otros

Equipo: CASTRO, S , TORTEROLO P , Joaquín González , Diego Gallo Alfonso , Juan Pedro Castro , Serantes D , PASCOVICH C , COSTA A

Areas de conocimiento:

Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias / FISIOLÓGIA

#### **Regulación hipotalámica de la frecuencia cardíaca y su variabilidad: Rol de los sistemas hipocretinérgico y MCHérgico (12/2011 - a la fecha )**

Las enfermedades cardiovasculares son la primera causa de muerte en Uruguay y en el mundo. Muchas de estas patologías están relacionadas con cambios en el ritmo cardíaco como los que se observan en la transición entre vigilia-sueño o dentro de las diferentes fases del sueño. Una herramienta de análisis del ritmo cardíaco es la llamada variabilidad de la frecuencia cardiaca (VFC), que evalúa la regulación cardiovascular, es especial las modificaciones autonómicas. Dado el rol jerárquico del hipotálamo en el control de la homeostasis y el ciclo sueño-vigilia, y su control sobre las neuronas preganglionares autonómicas, esta estructura es crítica en la regulación de la VFC. En el hipotálamo postero-lateral y regiones adyacentes se encuentran dos grupos neuronales que podrían participar en el control central de la VFC. Estas neuronas utilizan como neuromoduladores hipocretinas o la hormona concentradora de melanina (MCH). Nos proponemos estudiar la regulación central de la VFC del gato durante la vigilia y el sueño. La FC y su variabilidad serán analizados en condiciones basales y luego de distintas manipulaciones experimentales de los sistemas hipocretinérgico y MCHérgico. Los resultados obtenidos ayudarán a comprender un capítulo muy importante de la regulación cardiovascular como lo es, el papel del hipotálamo en dicha regulación y en particular el rol de las neuronas hipocretinérgicas y MCHérgicas. En virtud de las conexiones de estas neuronas con otras funciones orgánicas (respiración apetito, temperatura) y psíquicas (depresión) estos conocimientos ayudarán a la comprensión de complejos mecanismos fisiológicos y su proyección a la patología

Fundamental

5 horas semanales , Integrante del equipo

Equipo: FALCONI, A , BRANDO, V , MIGLIARO, E , CAVELLI, M , CASTRO, S , RICCA, R

#### **SECTOR EDUCACIÓN SUPERIOR/PÚBLICO - UNIVERSIDAD DE LA REPÚBLICA - URUGUAY**

Escuela de Nutrición

#### **VÍNCULOS CON LA INSTITUCIÓN**

##### **Funcionario/Empleado (06/2013 - 10/2017)**

10 horas semanales

Escalafón: Docente

Grado: Grado 3

Cargo: Interino

#### **CARGA HORARIA**

Carga horaria de docencia: 10 horas  
Carga horaria de investigación: 29 horas  
Carga horaria de formación RRHH: Sin horas  
Carga horaria de extensión: 1 hora  
Carga horaria de gestión: Sin horas

## Producción científica/tecnológica

Comencé a trabajar en el Laboratorio de Neurobiología del Sueño en el año 2008. En el año 2009 comencé una línea de investigación propia, bajo la guía del Dr. Pablo Torterolo quien dirige el laboratorio, sobre las interacciones funcionales en la actividad eléctrica de la corteza cerebral durante la vigilia y el sueño y luego bajo el efecto de fármacos que alteran las funciones cognitivas. Esa línea de investigación surgió de una idea mía y fue la base de mi doctorado, y de 4 trabajos que publiqué como primer autor (el 1ero en 2013) y más de 10 en los que fui coautor. Mi Doctorado recibió la mención del premio "ELIO GARCÍA-AUSTT".

Para generar los procesos cognitivos, distintas áreas corticales interactúan intensamente entre sí y con regiones subcorticales como el tálamo. Se ha postulado que las oscilaciones en la banda gamma de frecuencia (30 a 45 Hz) del electroencefalograma (EEG), son producto de estas interacciones y por lo tanto están involucradas en las funciones cognitivas.

En el marco de esta línea de investigación, utilizando el gato como modelo animal, estudiamos las oscilaciones gamma del EEG de distintas regiones corticales. Para ello utilizamos distintas funciones matemáticas, pero principalmente la "coherencia cruzada cuadrada". La actividad gamma fue estudiada durante la vigilia y el sueño, así como en un modelo farmacológico de psicosis (dosis subanestésica de ketamina). También, utilizando antagonistas de receptores muscarínicos (atropina y escopolamina), estudiamos el rol del sistema colinérgico (componente de los sistemas activadores) en la modulación de la actividad gamma.

Demostramos que durante la vigilia alerta (AW) hay un gran aumento de la coherencia (acoplamiento entre áreas alejadas) en la banda gamma entre áreas corticales alejadas con respecto a los demás estados. La coherencia alcanza valores mínimos durante el sueño REM, aunque su potencia (sincronización local), es similar a la de la vigilia.

Se ha propuesto que las ondas lentas y los husos de sueño, característicos del sueño, son incapaces de sostener el fenómeno de la consciencia. Sin embargo, recientemente hemos demostrado que bajo el efecto de antagonistas colinérgicos muscarínicos (atropina o escopolamina), los animales mantienen la vigilia a pesar de presentar ondas lentas y husos de sueño similares al sueño NREM. En contrapartida, la presencia de oscilaciones gamma (40 Hz coherentes bajo este tratamiento), que son características de la vigilia, podrían explicar el mantenimiento de la V a pesar del entrecimiento del EEG.

Por otra parte, hemos observado en gatos que durante el estado psicótico desarrollado por la administración de dosis subanestésicas de ketamina, la actividad gamma de frecuencias (principalmente a 40 Hz) se comporta como en el sueño REM. Es decir, en los dos estados existe un aumento de la potencia gamma, pero una disminución de la coherencia a esa frecuencia (acoplamiento entre áreas alejadas).

A su vez en el marco de esa línea de investigación gané un proyecto I+D de CSIC (como responsable científico) titulado "Abordaje fisiológico y farmacológico al estudio del correlato electroencefalográfico de la consciencia".

## Producción bibliográfica

### ARTÍCULOS PUBLICADOS

#### ARBITRADOS

#### **Cortical high-frequency oscillations (? 110 Hz) in cats are state-dependent and enhanced by a subanesthetic dose of ketamine (Completo, 2024)** Trabajo relevante

CASTRO, S , Gonzalez J , Cavelli M , Diego Mateos , claudia pascovich , Adriano Tort , Mark Jeremy Hunt , TORTEROLO P

Behavioural Brain Research, v.: 476 11523, 2024

Palabras clave: HFO gamma REM cognition psychedelic anesthesia

Áreas de conocimiento:

Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias /

Medio de divulgación: Otros

ISSN: 01664328

DOI: <https://doi.org/10.1016/j.bbr.2024.115231>

journal homepage: [www.elsevier.com/locate/bbr](http://www.elsevier.com/locate/bbr)

Ketamine is an NMDA receptor antagonist that has antidepressant and anesthetic properties. At subanesthetic doses, ketamine induces transient psychosis in humans, and is used to model psychosis in experimental animals. In rodents, subanesthetic doses of ketamine increase the power of high-frequency oscillations (HFO, > 100 Hz) in the electroencephalogram (EEG), a frequency band linked to cognitive functions. However, to date, the effects of ketamine in carnivores and primates have been poorly investigated. Here, we examined in the cat, cortical HFO during wakefulness, sleep, and after administering a sub-anesthetic dose of ketamine. Four cats were prepared with cortical electrodes for chronic polysomnographic recordings in head-restrained conditions. The cortical HFO power, connectivity, direction of the information flow using Granger Causality (GC) analysis, their relationships with respiratory activity, and the effect of auditory stimulation were analyzed. During wakefulness, but not during sleep, we found that HFO were coupled with the inspiratory phase of the respiration. After ketamine administration, HFO power was enhanced and remained associated with the inspiratory phase. GC analysis suggests that ketamine-enhanced HFO originate from the olfactory bulb (OB) and stream towards the prefrontal cortex (Pf). Accordingly, occluding the nostrils significantly reduced the power of the ketamine-enhanced HFO in both the OB and Pf. Finally, auditory stimulation did not affect HFO. In conclusion, the HFO are associated with respiration during wakefulness, but not during sleep. The enhancement of this rhythm by ketamine may disrupt cortical information processing, which could contribute to some of the neuropsychiatric effects associated with ketamine.

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### **Differential effects of haloperidol on neural oscillations during wakefulness and sleep (Completo, 2024)**

Gallo D., CASTRO, S., Cavelli M., Juan Pedro Castro Nin, Claudia Pascovich, Joaquin Gonzalez, claudia pas

Neuroscience, v.: 560 p.:67 - 76, 2024

Palabras clave: Haloperidol aperiodic periodic

Areas de conocimiento:

Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias /

Medio de divulgación: Internet

ISSN: 03064522

DOI: <https://doi.org/10.1016/j.neuroscience.2024.09.020>

journal homepage: [www.elsevier.com/locate/nsc](http://www.elsevier.com/locate/nsc)

Abstract The electrical activity of the brain, characterized by its frequency components, reflects a complex interplay between periodic (oscillatory) and aperiodic components. These components are associated with various neurophysiological processes, such as the excitation-inhibition balance (aperiodic activity) or interregional communication (oscillatory activity). However, we do not fully understand whether these components are truly independent or if different neuromodulators affect them in different ways. The dopaminergic system has a critical role for cognition and motivation, being a potential modulator of these power spectrum components. To improve our understanding of these questions, we investigated the differential effects of this system on these components using electrocorticogram recordings in cats, which show clear oscillations and aperiodic 1/f activity. Specifically, we focused on the effects of haloperidol (a D2 receptor antagonist) on oscillatory and aperiodic dynamics during wakefulness and sleep. By parameterizing the power spectrum into these two components, our findings reveal a robust modulation of oscillatory activity by the D2 receptor across the brain. Surprisingly, aperiodic activity was not significantly affected and exhibited inconsistent changes across the brain. This suggests a nuanced interplay between neuromodulation and the distinct components of brain oscillations, providing insights into the selective regulation of oscillatory dynamics in awake states.

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### **Breathing modulates gamma synchronization across species (Completo, 2023)**

Gonzalez, J., Cavelli, M., Mondino, A., CASTRO, S., Branka?k, J., Draguhn, A., TORTEROLO P., Tort, A B. L.

European Journal of Neuroscience, v.: 475 1 1, p.:49 - 63, 2023

Palabras clave: respiration gamma coupling modulation

Areas de conocimiento:

Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias /

Medio de divulgación: Internet

ISSN: 0953816X

E-ISSN: 14609568

DOI: [DOI: 10.1007/s00424-022-02753-0](https://doi.org/10.1007/s00424-022-02753-0)

DOI: 10.1007/s00424-022-02753-0

Nasal respiration influences brain dynamics by phase-entraining neural oscillations at the same frequency as the breathing rate and by phase-modulating the activity of faster gamma rhythms. Despite being widely reported, we still do not understand the functional roles of respiration-entrained oscillations. A common hypothesis is that these rhythms aid long-range communication and provide a privileged window for synchronization. Here we tested this hypothesis by analyzing electrocorticographic (ECoG) recordings in mice, rats, and cats during the different sleep-wake states. We found that the respiration phase modulates the amplitude of cortical gamma oscillations in the three species, although the modulated gamma frequency bands differed with faster oscillations (90-130 Hz) in mice, intermediate frequencies (60-100 Hz) in rats, and slower activity (30-60 Hz) in cats. In addition, our results also show that respiration modulates olfactory bulb-frontal cortex synchronization in the gamma range, in which each breathing cycle evokes (following a delay) a transient time window of increased gamma synchrony. Long-range gamma synchrony modulation occurs during quiet and active wake states but decreases during sleep. Thus, our results suggest that respiration-entrained brain rhythms orchestrate communication in awake mammals.

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### **Ibogaína: un psicodélico atípico con potencial antiadictivo (Completo, 2023)**

Gallo, D., Gonzalez, J., Rodriguez, P., CASTRO, S., Scorza, S., TORTEROLO P., Carrera, I.

Revista de psiquiatría del Uruguay, 2023

Medio de divulgación: Internet

E-ISSN: 16881257

El trastorno por uso de sustancias es una enfermedad crónica de graves consecuencias. Actualmente, los tratamientos farmacológicos no apuntan a corregir los cambios neurobiológicos generados en el cerebro por el uso crónico de sustancias de abuso, sino que se enfocan principalmente en la atenuación de algunos de los síntomas que padece el consumidor. La ibogaína es un psicodélico atípico que, tanto en estudios observacionales como en ensayos clínicos abiertos, ha mostrado una propiedad antiadictiva que perdura en el tiempo. Sin embargo, su delicado perfil de toxicidad cardíaca, así como su uso en entornos sin adecuadas medidas de seguridad, han limitado su progresión en las investigaciones clínicas. Los efectos antiadictivos de ibogaína han disparado diversas líneas de investigación básica, preclínica y clínica, que buscan confirmar su efectividad, entender sus mecanismos de acción y delimitar su perfil de seguridad. Dada la poca información disponible para los profesionales de salud sobre esta sustancia, esta revisión busca aportar información acerca de su potencial terapéutico, posibles mecanismos de acción y riesgos asociados a su administración. Palabras clave adicción depresión antidepresivos sueño REM Summary Substance use disorder is a chronic disease with severe consequences. Currently, pharmacological treatments do not aim to correct the neurobiological changes generated in the brain by the chronic use of substances of abuse, but rather focus mainly on attenuating some of the user's symptoms. Ibogaine is an atypical psychedelic that has shown long-lasting and interesting antiaddictive properties in both observational studies and open-label clinical trials. However, its delicate profile of cardiac toxicity, as well as its use in settings without adequate safety measures, have limited its progression in clinical research. The anti-addictive effects of ibogaine have triggered diverse scientific research in basic, preclinical, and clinical areas, which seek efficacy confirmation and to fully understand ibogaine's underlying mechanisms of action and its safety profile. Given that there is little information available to health professionals about ibogaine and its antiaddictive properties, this review aims to provide published data about its therapeutic potential in drug addiction, its mechanisms of action, and risks associated with its administration. Keywords addiction depression antidepressants sleep REM

latindex

### **Ketamine and sleep modulate neural complexity dynamics in cats (Completo, 2022)**

Pascovich, C., CASTRO, S., Pedro A. M. Mediano, Daniel Bor, Andrés Canales-Johnson,

TORTEROLO P., Tristan A. Bekinschtein

European Journal of Neuroscience, v.: 1 17 17, p.:1 - 16, 2022

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<https://doi.org/10.1111/ejn.15646>

There is increasing evidence that level of consciousness can be captured by neural informational complexity: for instance, complexity, as measured by the Lempel Ziv (LZ) compression algorithm, decreases during anesthesia and non-rapid eye movement (NREM) sleep in humans and rats, when

compared to LZ in awake and REM sleep. In contrast, LZ is higher in humans under the effect of psychedelics, including subanesthetic doses of ketamine. However, it is both unclear how this result would be modulated by varying ketamine doses, and whether it would extend to other species. Here we studied LZ with and without auditory stimulation during wakefulness and different sleep stages in 5 cats implanted with intracranial electrodes, as well as under subanesthetic doses of ketamine (5, 10, and 15 mg/kg i.m.). In line with previous results, LZ was lowest in NREM sleep, but similar in REM and wakefulness. Furthermore, we found an inverted U-shaped curve following different levels of ketamine doses in a subset of electrodes, primarily in prefrontal cortex. However, it is worth noting that the variability in the ketamine dose-response curve across cats and cortices was larger than that in the sleep-stage data, highlighting the differential local dynamics created by two different ways of modulating conscious state. These results replicate previous findings, both in humans and other species, demonstrating that neural complexity is highly sensitive to capture state changes between wake and sleep stages while adding a local cortical description. Finally, this study describes the differential effects of ketamine doses, replicating a rise in complexity for low doses, and further fall as doses approach anesthetic levels in a differential manner depending on the cortex.

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### **EEG Gamma Band Alterations and REM-like Traits Underpin the Acute Effect of the Atypical Psychedelic Ibogaine in the Rat (Completo, 2021)**

Joaquín González, CAVELLI M., CASTRO, S., MONDINO, A., Tort, A., NICOLÁS RUBIDO, CARRERA, I., TORTEROLO P

ACS Pharmacology & Translational Science, v.: 4 2, p.:517 - 525, 2021

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DOI: [DOI: 10.1021/acsptsci.0c00164](https://doi.org/10.1021/acsptsci.0c00164)

DOI: 10.1021/acsptsci.0c00164

Ibogaine is a psychedelic alkaloid that has attracted large scientific interest because of its antiaddictive properties in observational studies in humans as well as in animal models. Its subjective effect has been described as intense, vivid dream-like experiences occurring while awake; hence, ibogaine is often referred to as an oneirogenic psychedelic. While this unique dream-like profile has been hypothesized to aid the antiaddictive effects, the electrophysiological signatures of this psychedelic state remain unknown. We previously showed in rats that ibogaine promotes a waking state with abnormal motor behavior along with a decrease in NREM and REM sleep. Here, we performed an in-depth analysis of the intracranial electroencephalogram during ibogaine wakefulness. We found that ibogaine induces gamma oscillations that, despite having larger power than control levels, are less coherent and less complex. Further analysis revealed that this profile of gamma activity compares to that of natural REM sleep. Thus, our results provide novel biological evidence for the association between the psychedelic state and REM sleep, contributing to the understanding of the brain mechanisms associated with the oneirogenic psychedelic effect of ibogaine.

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### **Power and Coherence in the EEG of the Rat: Impact of Behavioral States, Cortical Area, Lateralization and Light/Dark Phases (Completo, 2021)**

MONDINO, A., CAVELLI M., Joaquín González, CASTRO, S., Lucia osorio, COSTA A, GIANCARLO VANINI, TORTEROLO P

Clocks & Sleep, v.: 2 4, p.:536 - 556, 2021

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DOI: [DOI: 10.3390/clockssleep2040039](https://doi.org/10.3390/clockssleep2040039)

DOI: 10.3390/clockssleep2040039

The sleep-wake cycle is constituted by three behavioral states: wakefulness (W), non-REM (NREM) and REM sleep. These states are associated with drastic changes in cognitive capacities, mostly determined by the function of the thalamo-cortical system, whose activity can be examined by means of intra-cranial electroencephalogram (iEEG). With the purpose to study in depth the basal activity of the iEEG in adult rats, we analyzed the spectral power and coherence of the iEEG during W and sleep in the paleocortex (olfactory bulb), and in neocortical areas. We also analyzed the laterality of the signals, as well as the influence of the light and dark phases. We found that the iEEG power and coherence of the whole spectrum were largely affected by behavioral states and highly dependent on the cortical areas recorded. We also determined that there are night/day differences in power and coherence during sleep, but not in W. Finally, we observed that, during REM sleep, intra-hemispheric coherence differs between right and left hemispheres. We conclude that the iEEG dynamics are highly dependent on the cortical area and behavioral states. Moreover, there are

light/dark phases disparities in the iEEG during sleep, and intra-hemispheric connectivity differs between both hemispheres during REM sleep.

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**Electrocortical temporal complexity during wakefulness and sleep: an updated account. (Completo, 2020)**

González, J , Cavelli, M , MONDINO, A. , PASCOVICH C , CASTRO, S , TORTEROLO P , NICOLÁS RUBIDO

Scientific Reports, v.: 9 18457 , 2020

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DOI: [doi.org/10.1038/s41598-019-54788-6](https://doi.org/10.1038/s41598-019-54788-6)

<https://www.nature.com/articles/s41598-019-54788-6>

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**Acute effect of vaporized Cannabis on sleep and electrocortical activity (Completo, 2019)**

MONDINO, A. , CAVELLI, M , Gonzalez, J , Santana, N , CASTRO, S , TORTEROLO P , A. FALCONI

Pharmacology Biochemistry and Behavior, v.: 179 p.:113 - 123, 2019

Medio de divulgación: Internet

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DOI: [DOI: 10.1016/j.pbb.2019.02.012](https://doi.org/10.1016/j.pbb.2019.02.012)

DOI: 10.1016/j.pbb.2019.02.012.

WEB OF SCIENCE™ Scopus®

**Nasal respiration entrains neocortical long-range gamma coherence during wakefulness. (Completo, 2019)**

Cavelli, M , CASTRO, S , TORTEROLO P , Líbano. DR , Rubido N , Velásquez N

European Journal of Neuroscience, v.: 51 6 , p.:1463 - 1477, 2019

Medio de divulgación: Internet

ISSN: 0953816X

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DOI: <https://doi.org/10.1111/ejn.14560>

<https://doi.org/10.1111/ejn.14560>.

Recent studies have shown that slow cortical potentials in archi?, paleo? and neocortex can phase-lock with nasal respiration. In some of these areas? gamma activity (? 30?100 Hz) is also coupled to the animal's respiration. It has been hypothesized that these functional relationships play a role in coordinating distributed neural activity. In a similar way, inter?cortical interactions at ? frequency have also been associated as a binding mechanism by which the brain generates temporary opportunities necessary for implementing cognitive functions. The aim of the present study is to explore if nasal respiration entrains inter?cortical functional interactions at ? frequency both during wakefulness and sleep. Six adult cats chronically prepared for electrographic recordings were employed in this study. Our results show that during wakefulness, slow cortical respiratory potentials are present in the olfactory bulb and several areas of the neocortex. We also found that these areas exhibit cross?frequency coupling between respiratory phase and ? oscillations amplitude. We demonstrate that respiratory phase modulates the inter?cortical gamma coherence between neocortical electrode pairs. On the contrary, slow respiratory oscillation and ? cortical oscillatory entrainments disappear during NREM and REM sleep. These results suggest that a single unified phenomenon involves cross?frequency coupling and long?range ? coherence across the neocortex. This fact could be related to the temporal binding process necessary for cognitive functions during wakefulness. This article is protected by copyright. All rights reserved.

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**Electrocortical high frequency activity and respiratory entrainment in 6-hydroxydopamine model of Parkinson's disease (Completo, 2019)**

Cavelli, M , PRUNELL GF, PRUNELL G , Costa G , Velazqjez N , González J , CASTRO, S , M S Lima M , TORTEROLO P

Brain Research, 2019

Medio de divulgación: Internet

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Brain Research 1724:146439 DOI: 10.1016/j.brainres.2019.146439.

Parkinson's disease is characterized by motor symptoms (akinesia, rigidity, etc.), which are associated with the degeneration of the dopaminergic neurons of the midbrain. In addition, olfactory impairment that usually develops before the detection of motor deficits, is detected in

90% of Parkinsonian patients. Recent studies in mammals, have shown that slow cortical potentials phase-lock with nasal respiration. In several cortical areas, gamma synchronization of the electrographic activity is also coupled to respiration, suggesting that nasal respiratory entrainment could have a role in the processing of olfactory information. In the present study, we evaluate the role of midbrain dopaminergic neurons, in the modulation of the electrocorticogram activity and its respiratory entrainment during wakefulness and sleep. For this purpose, we performed a unilateral lesion of dopaminergic neurons of the substantia nigra pars compacta of the rat, with 6-hydroxydopamine. An increase in beta (20-35 Hz) together with a decrease in gamma power (60-95 Hz) in the motor cortex ipsilateral to the lesion was observed during wakefulness. These results correlated with the degree of motor alterations and dopamine measured at the striatum. Moreover, we found a decline in gamma coherence between the ipsilateral olfactory bulb and motor cortex. Also, at the olfactory bulb we noticed an increase in respiratory-gamma cross-frequency coupling after the lesion, while at the motor cortex, a decrease in respiratory potential entrainment of gamma activity was observed. Interestingly, we did not observe any significant modification either during Non-REM or REM sleep. These waking dysrhythmias may play a role both in the anosmia and motor deficits present in Parkinson disease.

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### **Decreased electrocortical temporal complexity distinguishes sleep from wakefulness. (Completo, 2019)**

Gonzalez, J., MONDINO, A., CAVELLI M., PASCOVICH C., CASTRO, S., TORTEROLO P  
Scientific Reports, v.: 7817, 2019

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E-ISSN: 20452322

DOI: [doi.org/10.1038/s41598-019-54788-6](https://doi.org/10.1038/s41598-019-54788-6)

DOI: 10.1016/j.pbb.2019.02.012.

In most mammals, the sleep-wake cycle is constituted by three behavioral states: wakefulness (W), non-REM (NREM) sleep, and REM sleep. These states are associated with drastic changes in cognitive capacities, mostly determined by the function of the thalamo-cortical system. The intracranial electroencephalogram or electrocorticogram (ECoG), is an important tool for measuring the changes in the thalamo-cortical activity during W and sleep. In the present study we analyzed broad-band ECoG recordings of the rat by means of a time-series complexity measure that is easy to implement and robust to noise: the Permutation Entropy (PeEn). We found that PeEn is maximal during W and decreases during sleep. These results bring to light the different thalamo-cortical dynamics emerging during sleep-wake states, which are associated with the well-known spectral changes that occur when passing from W to sleep. Moreover, the PeEn analysis allows us to determine behavioral states independently of the electrodes' cortical location, which points to an underlying global pattern in the signal that differs among the cycle states that is missed by classical methods. Consequently, our data suggest that PeEn analysis of a single EEG channel could allow for cheap, easy, and efficient sleep monitoring.

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### **Distribution of MCH-containing fibers in the feline brainstem: Relevance for REM sleep regulation (Completo, 2018)**

COSTA A, CASTRO, S., Lagos, P., Chase, M.H., TORTEROLO P

Peptides, v.: 104 p.:50 - 61, 2018

Palabras clave: Energy homeostasis Hypothalamus Melanin-concentrating hormone Mood peptide

Áreas de conocimiento:

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<https://www.ncbi.nlm.nih.gov/pubmed/29680268>

Neurons that utilize melanin-concentrating hormone (MCH) as a neuromodulator are localized in the postero-lateral hypothalamus and incerto-hypothalamic area. These neurons project diffusely throughout the central nervous system and have been implicated in critical physiological processes, such as sleep. Unlike rodents, in the order carnivora as well as in humans, MCH exerts its biological functions through two receptors: MCHR-1 and MCHR-2. Hence, the cat is an optimal animal to model MCHergic functions in humans. In the present study, we examined the distribution of MCH-positive fibers in the brainstem of the cat. MCHergic axons with distinctive varicosities and boutons were heterogeneously distributed, exhibiting different densities in distinct regions of the brainstem. High density of MCHergic fibers was found in the dorsal raphe nucleus, the laterodorsal tegmental nucleus, the periaqueductal gray, the pedunculo-pontine tegmental nucleus, the locus coeruleus and the prepositus hypoglossi. Because these areas are involved in the control of REM

sleep, the present anatomical data support the role of this neuropeptidergic system in the control of this behavioral state.

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**EEG 40 Hz coherence decreases in REM sleep and ketamine model of psychosis (Completo, 2018)** Trabajo relevante

CASTRO, S., CAVELLI M., Gonzales, J., Nardi, AE., Machado, S., SCORZA C., TORTEROLO P  
Frontiers in Psychiatry, 2018

Palabras clave: Gamma schizophrenia electroencephalogram NMDA cognition dreams

Areas de conocimiento:

Ciencias Médicas y de la Salud / Ciencias de la Salud / Ciencias de la Salud / Neurociencia Cognitiva  
Ciencias Médicas y de la Salud / Ciencias de la Salud / Ciencias de la Salud / Neurociencia Cognitiva  
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Cognitive processes are carried out during wakefulness by means of extensive interactions between cortical and subcortical areas. In psychiatric conditions, such as psychosis, these processes are altered. Interestingly, REM sleep where most dreams occurs, shares electrophysiological, pharmacological and neurochemical features with psychosis. Because of this fact, REM sleep is considered a natural model of psychosis. Ketamine is a non-competitive N-methyl-D-aspartate (NMDA) receptor antagonist that at sub-anesthetic dose induces psychotomimetic-like effects in humans and animals, and is employed as a pharmacological model of psychosis. Oscillations in the gamma frequency band of the electroencephalogram (EEG), mainly at about 40 Hz, have been involved in cognitive functions. Hence, the present study was conducted to analyze the EEG low gamma (30-45 Hz) band power and coherence of the cat, in natural (REM sleep) and pharmacological (sub-anesthetic doses of ketamine) models of psychosis. These results were compared with the gamma activity during alert (AW) and quiet wakefulness (QW), as well as during non-REM (NREM) sleep. Five cats were chronically prepared for polysomnographic recordings, with electrodes in different cortical areas. Basal recordings were obtained and ketamine (5, 10 and 15 mg/kg, i.m.) was administered. Gamma activity (power and coherence) was analyzed in the abovementioned conditions. Compared to wakefulness and NREM sleep, following ketamine administration gamma coherence decreased among all cortical regions studied; the same coherence profile was observed during REM sleep. On the contrary, gamma power was relatively high under ketamine, and similar to QW and REM sleep. We conclude that functional interactions between cortical areas in the gamma frequency band decrease in both models of psychosis. This uncoupling of gamma frequency activity may be involved in the cognitive features shared by dreaming and psychosis.

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**EEG dissociation induced by muscarinic receptor antagonists: Coherent 40?Hz oscillations in a background of slow waves and spindles (Completo, 2018)** Trabajo relevante

CASTRO, S., matias cavelli, Gonzales, J., Jaime Monti, A. FALCONI, TORTEROLO P  
Behavioural Brain Research, v.: 359 p.:28 - 37, 2018

Palabras clave: EEG Gamma Scopolamine Atropine

Areas de conocimiento:

Ciencias Médicas y de la Salud / Ciencias de la Salud / Ciencias de la Salud / Neurociencias

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<https://www.sciencedirect.com/science/article/pii/S0166432818310258?via%3Dihub>

Mesopontine and basal forebrain cholinergic neurons are involved in the control of behavioral states and cognitive functions. Animals treated with cholinergic muscarinic receptor antagonists display a dissociated state characterized by behavioral wakefulness (W) associated with high amplitude slow oscillations and spindles in the electroencephalogram (EEG), similar to those that occur during non-REM (NREM) sleep. Oscillations in the gamma frequency band (? 40?Hz) of the EEG also play a critical role during W and cognition. Hence, the present study was conducted to determine the effect of muscarinic antagonists on the EEG gamma band power and coherence. Five cats were implanted with electrodes in different cortices to monitor the EEG. The effects of atropine and scopolamine on power and coherence within the low gamma frequency band (30?45? Hz) from pairs of EEG recordings were analyzed and compared to gamma activity during sleep and W. Muscarinic antagonists induced a NREM sleep-like EEG profile that was accompanied by a large increase in gamma power and coherence. The values of gamma coherence were similar to that occurring during alert W (AW), and greater than in quiet W, NREM and REM sleep. We conclude that under atropine or scopolamine, functional interactions between cortical areas in the gamma frequency band remain high, as they are during AW. This significant functional connectivity at high

frequency may explain why the animals remain awake in spite of the presence of slow waves and spindles.

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**Absence of EEG gamma coherence in a local activated neocortical state: a conserved trait of REM sleep. (Completo, 2017)**

CAVELLI, M , CASTRO, S., FALCONI, A., CHASE, M., TORTEROLO, P

Translational Brain Rhythmicity , v.: 2 2 1, p.:1 - 13, 2017

Palabras clave: wakefulness

Areas de conocimiento:

Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias / Neurobiología cognitiva y sueño

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During cognitive processes, there are extensive interactions between various regions of the cerebral cortex. Oscillations in the gamma frequency band (30-100 Hz) of the electroencephalogram are involved in the binding of spatially separated but temporally correlated neural events, which results in a unified perceptual experience. Like wakefulness, REM sleep is characterized by gamma oscillations in the EEG. Dreams, that are considered a special type of cognitive activity or proto-consciousness, mostly occur during this state. The power of the gamma band, assessed by the fast Fourier transform, reflects the local degree of synchronization at that frequency. On the other hand, the extent of interactions between different cortical areas at the gamma frequency band can be explored by means of a mathematical function called coherence, which reflects the strength of functional interactions between cortical areas. The objective of the present report was to study in the rat the dynamic relationship between gamma power and coherence in the low (30-48 Hz) and high (52-98 Hz) gamma bands during waking and sleep, in occipital, parietal, and frontal neocortical areas, as well as in the olfactory bulb, that is a critical site of gamma rhythm-generation. In addition, we re-analyzed previous recordings in cats, in order to evaluate the same dynamic relationship as in rats. In both species, the main result was that during REM sleep, gamma power increased, while gamma coherence between distant neocortical areas decreased. The fact that this profile is present in rodentia as well as in carnivora suggests that this is a trait that characterizes REM sleep in mammals.



**Power and coherence of cortical high-frequency oscillations during wakefulness and sleep (Completo, 2017)**

CAVELLI, M , CASTRO, S., SCHWARZKOPF N , FALCONI, A., ROJAS-LÍBANO D , TORTEROLO, P

European Journal of Neuroscience, v.: Sep 18 2017

Palabras clave: HFO

Areas de conocimiento:

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Medio de divulgación: Internet

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DOI: [10.1111/ejn.13718](https://doi.org/10.1111/ejn.13718)

Recently, a novel type of fast cortical oscillatory activity that occurs between 110 and 160 Hz (high-frequency oscillations (HFO)) was described. HFO are modulated by the theta rhythm in hippocampus and neocortex during active wakefulness and REM sleep. As theta-HFO coupling increases during REM, a role for HFO in memory consolidation has been proposed. However, global properties such as the cortex-wide topographic distribution and the cortico-cortical coherence remain unknown. In this study, we recorded the electroencephalogram during sleep and wakefulness in the rat and analyzed the spatial extent of the HFO band power and coherence. We confirmed that the HFO amplitude is phase-locked to theta oscillations and is modified by behavioral states. During active wakefulness, HFO power was relatively higher in the neocortex and olfactory bulb compared to sleep. HFO power decreased during non-REM and had an intermediate level during REM sleep. Furthermore, coherence was larger during active wakefulness than non-REM, while REM showed a complex pattern in which coherence increased only in intra and decreased in inter-hemispheric combination of electrodes. This coherence pattern is different from gamma (30-100 Hz) coherence, which is reduced during REM sleep. This data show an important HFO cortico-cortical dialog during active wakefulness even when the level of theta comodulation is lower than in REM. In contrast, during REM, this dialog is highly modulated by theta and restricted to intra-hemispheric medial-posterior cortical regions. Further studies combining behavior, electrophysiology and new analytical tools are needed to plunge deeper into the

functional significance of the HFO.

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### **Neocortical 40 Hz oscillations during carbachol-induced rapid eye movement sleep and cataplexy.**

**(Completo, 2016)** Trabajo relevante

TORTEROLO, P, CASTRO, S, CAVELLI, M, CHASE, M, FALCONI, A

European Journal of Neuroscience, v.: 43 4 4, p.:580 - 589, 2016

Palabras clave: coherence EEG REM sleep

Areas de conocimiento:

Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias / Neurobiología cognitiva y sueño

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DOI: [10.1111/ejn.13151](https://doi.org/10.1111/ejn.13151)

Higher cognitive functions require the integration and coordination of large populations of neurons in cortical and subcortical regions. Oscillations in the gamma band (30-45 Hz) of the electroencephalogram (EEG) have been involved in these cognitive functions. In previous studies, we analysed the extent of functional connectivity between cortical areas employing the mean squared coherence analysis of the EEG gamma band. We demonstrated that gamma coherence is maximal during alert wakefulness and is almost absent during rapid eye movement (REM) sleep. The nucleus pontis oralis (NPO) is critical for REM sleep generation. The NPO is considered to exert executive control over the initiation and maintenance of REM sleep. In the cat, depending on the previous state of the animal, a single microinjection of carbachol (a cholinergic agonist) into the NPO can produce either REM sleep [REM sleep induced by carbachol (REMc)] or a waking state with muscle atonia, i.e. cataplexy [cataplexy induced by carbachol (CA)]. In the present study, in cats that were implanted with electrodes in different cortical areas to record polysomnographic activity, we compared the degree of gamma (30-45 Hz) coherence during REMc, CA and naturally-occurring behavioural states. Gamma coherence was maximal during CA and alert wakefulness. In contrast, gamma coherence was almost absent during REMc as in naturally-occurring REM sleep. We conclude that, in spite of the presence of somatic muscle paralysis, there are remarkable differences in cortical activity between REMc and CA, which confirm that EEG gamma (40 Hz) coherence is a trait that differentiates wakefulness from REM sleep.

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### **Coherent neocortical gamma oscillations decrease during REM sleep in the rat (Completo, 2015)**

CAVELLI, M, CASTRO, S, SCHWARZKOPF N, CHASE, M, FALCONI, A, TORTEROLO, P

Behavioural Brain Research, v.: 281 p.:318 - 325, 2015

Palabras clave: coherencia gamma

Areas de conocimiento:

Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias / Neurobiología cognitiva y sueño

ISSN: 01664328

Higher cognitive functions require the integration and coordination of large populations of neurons in cortical and subcortical regions. Oscillations in the high frequency band (30-100 Hz) of the electroencephalogram (EEG), that have been postulated to be a product of this interaction, are involved in the binding of spatially separated but temporally correlated neural events, which results in a unified perceptual experience. The extent of this functional connectivity can be examined by means of the mathematical algorithm called coherence, which is correlated with the strength of functional interactions between cortical areas. As a continuation of previous studies in the cat [6,7], the present study was conducted to analyze EEG coherence in the gamma band of the rat during wakefulness (W), non-REM (NREM) sleep and REM sleep. Rats were implanted with electrodes in different cortical areas to record EEG activity, and the magnitude squared coherence values within the gamma frequency band of EEG (30-48 and 52-100 Hz) were determined. Coherence between all cortical regions in the low and high gamma frequency bands was greater during W compared with sleep. Remarkably, EEG coherence in the low and high gamma bands was smallest during REM sleep. We conclude that high frequency interactions between cortical areas are radically different during sleep and wakefulness in the rat. Since this feature is conserved in other mammals, including humans, we suggest that the uncoupling of gamma frequency activity during REM sleep is a defining trait of REM sleep in mammals.

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### **Heart rate variability during carbachol-induced REM sleep and cataplexy (Completo, 2015)**

TORTEROLO, P, CASTRO, S, CAVELLI, M, VELAZQUES N, BRANDO, V, FALCONI, A, CHASE, M, MIGLIARO, E

Behavioural Brain Research, 2015

Palabras clave: HVR

Areas de conocimiento:

Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias / Neurobiología cognitiva y sueño

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DOI: [10.1016/j.bbr.2015.05.015](https://doi.org/10.1016/j.bbr.2015.05.015)

The nucleus pontis oralis (NPO) exerts an executive control over REM sleep. Cholinergic input to the NPO is critical for REM sleep generation. In the cat, a single microinjection of carbachol (a cholinergic agonist) into the NPO produces either REM sleep (REMc) or wakefulness with muscle atonia (cataplexy, CA). In order to study the central control of the heart rate variability (HRV) during sleep, we conducted polysomnographic and electrocardiogram recordings from chronically prepared cats during REMc, CA as well as during sleep and wakefulness. Subsequently, we performed statistical and spectral analyses of the HRV. The heart rate was greater during CA compared to REMc, NREM or REM sleep. Spectral analysis revealed that the low frequency band (LF) power was significantly higher during REM sleep in comparison to REMc and CA. Furthermore, we found that during CA there was a decrease in coupling between the RR intervals plot (tachogram) and respiratory activity. In contrast, compared to natural behavioral states, during REMc and CA there were no significant differences in the HRV based upon the standard deviation of normal RR intervals (SDNN) and the mean squared difference of successive intervals (rMSSD). In conclusion, there were differences in the HRV during naturally-occurring REM sleep compared to REMc. In addition, in spite of the same muscle atonia, the HRV was different during REMc and CA. Therefore, the neuronal network that controls the HRV during REM sleep can be dissociated from the one that generates the muscle atonia during this state.

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#### **Inter-hemispheric coherence of neocortical gamma oscillations during sleep and wakefulness (Completo, 2014)**

CASTRO, S., CAVELLI, M., TORTEROLO, P., FALCONI, A., CHASE, M., VOLLONO, P.  
Neuroscience Letters, v.: 578 p.:197 - 202, 2014

Areas de conocimiento:

Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias / Neurobiología cognitiva y sueño

Medio de divulgación: Papel

ISSN: 03043940

DOI: [j.neulet.2014.06.044](https://doi.org/10.1016/j.neulet.2014.06.044)

Oscillations in the gamma frequency band (mainly  $\approx 40$  Hz) of the electroencephalogram (EEG), have been involved in the binding of spatially separated but temporally correlated neural events that results in a unified perceptual experience. The extent of these interactions can be examined by means of a mathematical algorithm called coherence, which reflects the strength of functional interactions between cortical areas. As a continuation a previous study of our group [10], the present study was conducted to analyze the inter-hemispheric coherence of the EEG gamma frequency band in the cat during alert wakefulness (AW), quiet wakefulness (QW), non-REM (NREM) sleep and REM sleep. Cats were implanted with electrodes in the frontal, parietal and occipital cortices to monitor EEG activity. The degree of coherence in the low (30-45 Hz) and high (60-100 Hz) gamma frequency bands from pairs of EEG recordings was analyzed. A large increase in coherence between all inter-hemispheric cortical regions in the low gamma bands during AW was present compared to the other behavioral states. Furthermore, both low and high gamma coherence between inter-hemispheric heterotopic cortices (different cortical areas of both hemispheres) decreased during REM sleep; this is a pattern that we previously reported between the cortical areas of the same hemisphere (intra-hemispheric coherence). In the high gamma band, coherence during REM sleep also decreased compared to the others behavioral states. In contrast, between most of the inter-hemispheric homotopic cortical areas (equivalent or mirror areas of both hemispheres), low gamma coherence was similar during NREM compared to REM sleep. We conclude that in spite of subtle differences between homotopic and heterotopic inter-hemispheric cortices, functional interactions at high frequency decrease during REM sleep.

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#### **Statistical, spectral and non-linear analysis of the heart rate variability during sleep (Completo, 2014)**

BRANDO, V., CASTRO, S., FALCONI, A., TORTEROLO, P., MIGLIARO, E.  
Behavioural Brain Research, 2014

Areas de conocimiento:

Ciencias Médicas y de la Salud / Medicina Básica / Fisiología / fisiología cardiovascular

Medio de divulgación: Internet

ISSN: 01664328

As a first step in a program designed to study the central control of the heart rate variability (HRV)

during sleep, we conducted polysomnographic and electrocardiogram recordings on chronically-prepared cats during semi-restricted conditions. We found that the tachogram, i.e. the pattern of heart beat intervals (R-R intervals) was deeply modified on passing from alert wakefulness through quiet wakefulness (QW) to sleep. While the tachogram showed a rhythmical pattern coupled with respiratory activity during non-REM sleep (NREM), it turned chaotic during REM sleep. Statistical analyses of the R-R intervals showed that the mean duration of R-R interval increased during sleep. HRV measured by the standard deviation of normal R-R intervals (SDNN) and by the square root of the mean squared difference of successive intervals (rMSSD) were larger during REM and NREM sleep than during QW. SD-1 (a marker of short-term variability) and SD-2 (a marker of long-term variability) measured by means of Poincaré plots increased during both REM and NREM sleep compared to QW. Furthermore, in the spectral analysis of R-R intervals, the band of high frequency (HF) was larger in NREM and REM sleep in comparison to QW, whereas the band of low frequency (LF) was larger only during REM sleep in comparison to QW. The LF/HF ratio was larger during QW compared either with REM or NREM sleep. In conclusion, in comparison to quiet wakefulness sleep increases HRV parameters in the cat.

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### **Coherent neocortical 40-Hz oscillations are not present during REM sleep (Completo, 2013)** Trabajo relevante

CASTRO, S., TORTEROLO, P., FALCONI, A., CHASE M.H

European Journal of Neuroscience, p.:1 - 10, 2013

Palabras clave: coherence gamma sleep

Areas de conocimiento:

Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias / FISIOLÓGIA

Medio de divulgación: Internet

ISSN: 0953816X

E-ISSN: 14609568

DOI: [10.1111/ejn.12143](https://doi.org/10.1111/ejn.12143)

Abstract During cognitive processes there are extensive interactions between various regions of the cerebral cortex. Oscillations in the gamma frequency band (40 Hz) of the electroencephalogram (EEG) are involved in the binding of spatially separated but temporally correlated neural events, which results in a unified perceptual experience. The extent of these interactions can be examined by means of a mathematical algorithm called coherence, which reflects the strength of functional interactions between cortical areas. The present study was conducted to analyse EEG coherence in the gamma frequency band of the cat during alert wakefulness (AW), quiet wakefulness (QW), non-rapid eye movement (NREM) sleep and rapid eye movement (REM) sleep. Cats were implanted with electrodes in the frontal, parietal and occipital cortices to monitor EEG activity. Coherence values within the gamma frequency (30-100 Hz) from pairs of EEG recordings were analysed. A large increase in coherence occurred between all cortical regions in the 30-45 Hz frequency band during AW compared with the other behavioral states. As the animal transitioned from AW to QW and from QW to NREM sleep, coherence decreased to a moderate level. Remarkably, there was practically no EEG coherence in the entire gamma band spectrum (30-100 Hz) during REM sleep. We conclude that functional interactions between cortical areas are radically different during sleep compared with wakefulness. The virtual absence of gamma frequency coherence during REM sleep may underlie the unique cognitive processing that occurs during dreams, which is principally a REM sleep-related phenomenon.

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### **Hormona Concentradora de Melanina (MCH): neuropéptido hipotalámico que facilita la generación del sueño (Completo, 2010)** Trabajo relevante

TORTEROLO, P., CASTRO, S., FALCONI, A., LAGOS, P

DELETED, v.: 11 1, p.:46 - 51, 2010

Palabras clave: MCH

Areas de conocimiento:

Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias / FISIOLÓGIA

Medio de divulgación: Papel

E-ISSN: 16655044

El sistema MCHérgico está compuesto por neuronas hipotalámicas que utilizan al neuropéptido denominado hormona concentradora de melanina (MCH) como neuromodulador, y que proyectan hacia diversas regiones del sistema nervioso central, entre las cuales se destacan las áreas vinculadas con la regulación de la vigilia y el sueño. Numerosos estudios han involucrado al sistema MCHérgico con el control de la homeostasis energética. Sin embargo, estudios recientes han comenzado a mostrar un rol de este sistema en la regulación de la vigilia y el sueño. Principalmente se le ha atribuído un rol preponderante en la generación del sueño REM. En este trabajo realizamos

una breve revisión de la fisiología general del sistema MCHérgico, y de las evidencias que relacionan a este sistema con el control del sueño.

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## LIBROS

### **Methodological Approaches for Sleep and Vigilance Research ( Participación , 2021)**

TORTEROLO P , Joaquín González , CASTRO, S , Cavelli M , MONDINO, A. , PASCOVICH C , NICOLÁS RUBIDO , Eric Murillo-Rodriguez , Vanini G Publicado

Editor/Compilador: Eric Murillo-Rodriguez

Editorial: Eric Murillo-Rodriguez , normal

Tipo de publicación: Material didáctico

Escrito por invitación

Medio de divulgación: Internet

ISSN/ISBN: 9780323852357, 97803

Abstract Sleep is one of the great mysteries of life. We spend a third of our life sleeping without awareness of the outside world. Part of this time, during dreams, we have a bizarre cognitive activity disconnected from reality and guided by internal stimuli. In the last 70 years, as a result of basic research, there has been a remarkable increase in the knowledge of the physiology of sleep. Some of this knowledge has been transferred to the medical practice, where about 80 different sleep disturbances have been described. In most mammals (including humans) and birds, two sleep states can be readily distinguished: rapid eye movement sleep and nonrapid eye movement sleep. Polysomnography (PSG) is the basic tool used to recognize and characterize these behavioral states, and to explore brain activity during sleep. In the present work, we present a brief review of the main PSG procedures and data analysis in clinical and humans research settings, as well as in animal models.

Capítulos:

Chapter 2 - Polysomnography in humans and animal models: basic procedures and analysis

Página inicial 17, Página final 32

### **Arousal in Neurological and Psychiatric Diseases ( Participación , 2019)**

TORTEROLO P , CASTRO, S , Cavelli M , Joaquín González Publicado

Editor/Compilador: Edgar Garcia-Rill

Editorial: Academic Press , normal

Tipo de publicación: Material didáctico

DOI: [DOI: 10.1016/B978-0-12-817992-5.00001-5](https://doi.org/10.1016/B978-0-12-817992-5.00001-5)

Escrito por invitación

Palabras clave: Wakefulness Sleep NREM REM Anesthesia Slow waves Gamma EEG

Medio de divulgación: Internet

ISSN/ISBN: 9780128179932

Abstract In the last decades, there has been a substantial increase in the knowledge of the anatomy, electrophysiology, and neurochemistry of the neuronal networks that generate normal conscious state during wakefulness. Consciousness is suppressed during deep nonrapid eye movement sleep, while a different type of consciousness arises during rapid eye movement sleep, where most dreams occur. Consciousness can be also suppressed or altered by different pathologies and drugs. In this chapter, focusing on the information provided by the electroencephalogram, we reviewed the most significant concepts of the electrocortical correlates of normal conscious cognition. Furthermore, we analyzed the electrocortical adjustments during physiological lost or alteration of consciousness and the effects produced by paradigmatic drugs.

Capítulos:

Arousal and normal conscious cognition

Página inicial 1, Página final 24

## PUBLICACIÓN DE TRABAJOS PRESENTADOS EN EVENTOS

### **Role of information flow dynamics (top-down or bottom-up) in the gamma frequency band (?40 Hz) of the EEG in cognitive functions and consciousness (2024)**

CASTRO, S , Joaquín González , TORTEROLO P

Resumen

Descripción: 33rd Annual Computational Neuroscience Meeting (CNS 2024)

Ciudad: Natal

Año del evento: 2024

Anales/Proceedings:no

Publicación arbitrada

Palabras clave: gamma Top-down Bottom-up

Areas de conocimiento:

Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias / Neurociencias cognitivas

Financiación/Cooperación:

Comisión Sectorial de Investigación Científica / Apoyo financiero, Uruguay

Cognitive processes and consciousness rely on extensive thalamocortical and corticocortical recurrent interactions at a large scale. It has been hypothesized that oscillations within the gamma frequency band (30 to 45 Hz) of the electroencephalogram (EEG) are generated as a result of these interactions and play a role in cognitive functions. These oscillations have been implicated in the integration of spatially separated yet temporally correlated neural events, leading to a cohesive perceptual experience. It is widely recognized that top-down processing refers to the brain's ability to utilize our expectations, attentional focus, and other cognitive factors to dynamically influence bottom-up sensory processing. However, the precise directionality of the information flow encoded by gamma band oscillations remains unknown. Therefore, the primary objective of our study is to investigate the specific information flow patterns within the gamma band during both wakefulness and sleep. To achieve this, five cats were chronically prepared for polysomnographic recordings, with electrodes placed in various cortical regions. To investigate the directionality of information flow of the gamma band during wakefulness and sleep, we quantified the phase shifts of amplitude envelopes of filtered gamma oscillations and employed the "Granger causality" analysis. This statistical test allowed us to determine if one time series could predict or forecast the other. In the baseline condition when analyzing 500-second windows, the results revealed that during wakefulness, the primary direction of information flow in the gamma band was from the dorsolateral prefrontal cortex (Pfdl) to the posterior parietal cortex (Pp), as well as from Pfdl to the primary somatosensory cortex (S1), primary visual cortex (V1), and primary auditory cortex (A1). Additionally, there was a predominance of directionality from Pp to the primary cortices (S1, A1, V1). This indicates a significant influence of top-down information processing. However, this top-down flow of information was not observed during both NREM and REM sleep. Furthermore, when investigating late gamma oscillations induced by click stimuli (analyzed within 1 second windows starting 0.5 seconds after the stimulus), we found a predominant bottom-up directionality from the Pp to the Pfdl, as well as from A1 to Pfdl. In contrast, late gamma oscillations induced by more complex stimuli, such as 0.2 seconds variable sounds, demonstrated a predominant top-down directionality from Pfdl to Pp, A1, and V1 cortex. Notably, these specific directionalities were not observed during sleep. The data indicate that during wakefulness, different patterns of information flow emerge depending on the nature of the stimuli. Specifically, bottom-up processing was found to predominate in the case of simple repetitive sound stimuli, while top-down processing prevailed for complex and variable sounds, as well as in the baseline condition (without stimuli). In addition, no specific directionality of information flow was observed during NREM and REM sleep, suggesting a different mode of cognitive processing during sleep. This research was supported by CSIC-I+D grupos 2022 and CSIC-I+D-2020-393.

### **Top-down directionality of gamma band (?40 Hz) functional interactions in cognitive functions and consciousness (2023)**

CASTRO, S., Gonzalez, J., TORTEROLO P

Publicado

Resumen

Evento: Internacional

Descripción: 15th International Workshop on NEURAL CODING 2023

Ciudad: Piriapolis

Año del evento: 2023

Anales/Proceedings:15th International Workshop on NEURAL CODING 2023 Piriápolis, Uruguay

27 February ? 4 March 2023 Book of Abstracts

Palabras clave: Top-Down Bottom-Up Gamma Directionality

Areas de conocimiento:

Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias /

Medio de divulgación: Otros

Cognitive processes and consciousness depends on large-scale thalamocortical and corticocortical recurrent interactions (1?3). It has been postulated that the oscillations in the gamma frequency band (30 to 45 Hz) of the electroencephalogram (EEG) are the product of these interactions and therefore are involved in cognitive functions (4,5). Oscillations in the gamma frequency band of the

electroencephalogram are involved in the binding of spatially separated but temporally correlated neural events, which results in a unified perceptual experience (2,6,7). Top-down processing is how the mind uses our expectations, attentional focus, and other cognitive variables to adaptively influence bottom-up sensory processing (3,8). In our previous work, we demonstrated that during alert wakefulness (AW) there is a large increase in coherence in the gamma band between intrahemispheric cortical areas with respect to the other states, it decreases to moderate values during NREM sleep and reaches minimum values during REM sleep (7,9). In the ketamine-induced psychosis model, we found the a decrease in gamma coherence between all cortical regions, an effect similar to what is observed during REM sleep (10). Finally, administration of atropine or scopolamine causes a slowing of the EEG, with increased delta waves and sleep spindles (as in NREM sleep); however, the animals remain active. This dissociated state was accompanied by power and gamma coherence values, similar to W. This great functional connectivity in the gamma band of frequencies could explain why the animals remain awake despite the presence of slow waves and spindles in the EEG (11). Nevertheless, coherence do not show the directionality of gamma functional interactions. The aim of our study is, using the cat as an animal model, to address the directionality of gamma band functional interactions during wakefulness and sleep and under the ketamine-induced psychosis model and under scopolamine induced dissociated state. For this, five cats were chronically prepared for polysomnographic recordings, with electrodes in different cortical areas. Gamma activity was studied during wakefulness and sleep, as well as in a pharmacological model of psychosis (subanesthetic dose of ketamine). Also, using muscarinic receptor antagonists (atropine and scopolamine). We used two different methods to access directionality. The first and simplest was quantifying the direction of the phase shifts of the amplitude envelopes of filtered gamma oscillations, the second was the algorithm ?granger causality? (12). We found that during wakefulness there is a predominant Top-down directionality of gamma band functional interactions. Directionality from dorsolateral Prefrontal cortex (Pfdl) to posterior parietal cortex (Pp), from Pfdl to projection areas like somato-sensory cortex(S1), primary visual cortex (V1) and primary auditory cortex (A1) Predominant directionality was also from Pp to projection areas (S1, A1, V1). This predominant directionality disappeared during sleep, in the ketamine-induced psychosis model. It also disappeared during scopolamine induced dissociated state in spite of the high gamma power and coherence, similar to W. Our finding highlight the role of top-down processing in gamma frequencies in cognitive functions and consciousness. Only during W when cognitive functions and consciousness are in their max expression, directionality from dorsolateral Prefrontal cortex (Pfdl) to posterior parietal cortex (Pp) and from Pfdl and Pp to projection areas predominated. This predominant directionality disappeared in the lack of and, or altered consciousness induced by sleep and ketamine-induced psychosis model. Scopolamine induce a conscious state with altered cognitive functions and it correlates with an EEG with high gamma power and coherence but lacking a predominant directionality. Our results strongly suggest that gamma coupling between distant cortical areas is sufficient to be in a conscious state but top-down processing is necessary for complete cognitive functions. This research was supported by CSIC-I+D grupos 2022 and CSIC-I+D-2020-393. References 1. Redinbaugh MJ, Phillips JM, Kambi NA, Mohanta S, Andryk S, Dooley GL, et al. Thalamus Modulates Consciousness via Layer-Specific Control of Cortex. *Neuron*. abril de 2020;106(1):66-75.e12. 2. Schneider M, Dann B, Sheshadri S, Scherberger H, Vinck M. A general theory of coherence between brain areas [Internet]. *Neuroscience*; 2020 jun [citado 27 de diciembre de 2020]. Disponible en: <http://biorxiv.org/lookup/doi/10.1101/2020.06.17.156190> 3. Vinck M, Uran C, Canales-Johnson A. The neural dynamics of feedforward and feedback interactions in predictive processing [Internet]. *PsyArXiv*; 2022 oct [citado 16 de diciembre de 2022]. Disponible en: <https://osf.io/n3aff> 4. Llinás R, Ribary U. Coherent 40-Hz oscillation characterizes dream state in humans. *Proc Natl Acad Sci USA*. marzo de 1993;90(5):2078-81. 5. Mashour GA. 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EEG 40 Hz Coherence Decreases in REM Sleep and Ketamine Model of Psychosis. *Front Psychiatry*. 17 de enero de 2019;9:766. 11. Castro-Zaballa S, Cavelli M, González J, Monti J, Falconi A, Torterolo P. EEG dissociation induced by muscarinic receptor antagonists: Coherent 40 Hz oscillations in a background of slow waves and spindles. *Behavioural Brain Research*. febrero de 2019;359:28-37. 12. Barnett L, Seth AK. The MVGC multivariate Granger causality toolbox: A new approach to Granger-causal inference. *Journal of Neuroscience Methods*. 15 de febrero de 2014;223:50-68.

### **Examining the information flow dynamics (top-down or bottom-up) in the gamma frequency band (40 Hz) of the EEG during wakefulness and sleep (2023)**

CASTRO, S., Gonzalez, J., TORTEROLO P

Publicado

Resumen

Evento: Internacional

Descripción: World Sleep 2023

Ciudad: Rio de Janeiro

Año del evento: 2023

Areas de conocimiento:

Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias /

Cognitive processes and consciousness rely on extensive thalamocortical and corticocortical recurrent interactions at a large scale. It has been hypothesized that oscillations within the gamma frequency band (30 to 45 Hz) of the electroencephalogram (EEG) are generated as a result of these interactions, and play a role in cognitive functions. These oscillations have been implicated in the integration of spatially separated yet temporally correlated neural events, leading to a cohesive perceptual experience. It is widely recognized that top-down processing refers to the brain's ability to utilize our expectations, attentional focus, and other cognitive factors to dynamically influence bottom-up sensory processing. However, the precise directionality of the information flow encoded by gamma band oscillations remains unknown. Therefore, the primary objective of our study is to investigate the specific information flow patterns within the gamma band during both wakefulness and sleep. To achieve this, we utilized the cat as an animal model. To achieve this, five cats were chronically prepared for polysomnographic recordings, with electrodes placed in various cortical regions. To investigate the directionality of information flow of the gamma band during wakefulness and sleep, we quantified the phase shifts of amplitude envelopes of filtered gamma oscillations, and employed the "Granger causality" analysis. This statistical test allowed us to determine if one time series could predict or forecast the other. In the baseline condition, when analyzing 500-second windows, the results revealed that during wakefulness, the primary direction of information flow in the gamma band was from the dorsolateral prefrontal cortex (Pfdl) to the posterior parietal cortex (Pp), as well as from Pfdl to the primary somatosensory cortex (S1), primary visual cortex (V1), and primary auditory cortex (A1). Additionally, there was a predominance of directionality from Pp to the primary cortices (S1, A1, V1). This indicates a significant influence of top-down information processing. However, this top-down flow of information was not observed during both NREM and REM sleep. Furthermore, when investigating late gamma oscillations induced by click stimuli (analyzed within 1 second windows starting 0.4 seconds after the stimulus), we found a predominant bottom-up directionality from the Pp to the Pfdl, as well as from A1 to Pfdl. In contrast, late gamma oscillations induced by more complex stimuli, such as 0.2 second variable sounds, demonstrated a predominant top-down directionality from Pfdl to Pp, A1, and V1 cortex, as well as from Pp to V1 cortex. Notably, these specific directionalities were not observed during sleep. The data indicate that during wakefulness, different patterns of information flow emerge depending on the nature of the stimuli. Specifically, bottom-up processing was found to predominate in the case of simple repetitive sound stimuli, while top-down processing prevailed for complex and variable sounds, as well as in the baseline condition (without stimuli). In addition, no specific directionality of information flow was observed during NREM and REM sleep, suggesting a different mode of cognitive processing during sleep.

### **EEG 40 Hz oscillations in the prefrontal cortex anticipate the appearance of sound stimuli presented at regular intervals (2019)**

-, CASTRO, S., Cavelli, M., González, J., PASCOVICH C., Juan Pedro Castro-Nin, Diego Gallo Alfonso, A. FALCONI

Publicado

Resumen

Descripción: XV Latin American Symposium on Chronobiology 2019

Ciudad: Colonia del Sacramento

Año del evento: 2019

Medio de divulgación: Otros

Oscillations in the gamma frequency band (30-45 Hz) of the electroencephalogram (EEG) have been involved in cognitive functions. In previous reports of our lab, we explored the role of spontaneous gamma oscillations both during wakefulness (W) and sleep. In contrast, in the present study we have focused in the gamma oscillations induced by auditory stimulation. Four cats were chronically prepared for polysomnographic recordings, with electrodes in prefrontal, parietal-posterior, primary auditory cortices, as well as in the medial geniculate nucleus (auditory thalamus). The cats were stimulated with complex sounds of 200 ms, either with regular (interval of 5 seconds) or irregular presentation of the stimuli. The auditory stimulation was also performed

during sleep. The EEG gamma envelopes and gamma power was analyzed using the stimulus as trigger. We found that when cats received the sound stimuli at regular or irregular intervals, an induced gamma burst of activity was detected with a latency of 800-1200 ms. In addition, following a bunch of regular stimuli (but not following irregular-presented stimuli) a burst of gamma activity appeared in anticipation of the stimuli (300 to 800 ms before the stimuli). This signal was larger in the prefrontal cortex. Both the anticipative and induced gamma oscillations disappeared when the animal was habituated to the stimuli, as well as during sleep (NREM and REM sleep). We conclude that gamma oscillations in the prefrontal cortex of the cat can anticipate auditory stimuli presented at regular intervals. Supported by CSIC, ANII and PEDECIBA

### **EEG gamma (40 Hz) activity in animal models of psychosis (2019)**

CASTRO, S

Publicado

Completo

Evento: Nacional

Descripción: XV Latin American Symposium on Chronobiology 2019

Ciudad: Colonia del Sacramento

Año del evento: 2019

Cognitive processes are carried out during wakefulness by means of extensive interactions between cortical and subcortical areas. In psychiatric conditions, such as psychosis, these processes are altered. Interestingly, REM sleep where most dreams occurs, shares electrophysiological, pharmacological, and neurochemical features with psychosis. Because of this fact, REM sleep is considered a natural model of psychosis. Ketamine is a non-competitive N-methyl-D-aspartate (NMDA) receptor antagonist that at sub-anesthetic dose induces psychotomimetic-like effects in humans and animals, and is employed as a pharmacological model of psychosis. Oscillations in the gamma frequency band of the electroencephalogram (EEG), mainly at about 40Hz, have been involved in cognitive functions. Hence, the present study was conducted to analyze the EEG low gamma (30-45Hz) band power and coherence of the cat, in natural (REM sleep) and pharmacological (sub-anesthetic doses of ketamine) models of psychosis. These results were compared with the gamma activity during alert (AW) and quiet wakefulness (QW), as well as during non-REM (NREM) sleep. Five cats were chronically prepared for polysomnographic recordings, with electrodes in different cortical areas. Basal recordings were obtained and ketamine (5, 10, and 15 mg/kg, i.m.) was administered. Gamma activity (power and coherence) was analyzed in the abovementioned conditions. Compared to wakefulness and NREM sleep, following ketamine administration gamma coherence decreased among all cortical regions studied; the same coherence profile was observed during REM sleep. On the contrary, gamma power was relatively high under ketamine, and similar to QW and REM sleep. We conclude that functional interactions between cortical areas in the gamma frequency band decrease in both experimental models of psychosis. This uncoupling of gamma frequency activity may be involved in the cognitive features shared by dreaming and psychosis.

### **EEG dissociation induced by muscarinic receptor antagonists: slow waves and sleep spindles together with coherent 40 Hz oscillations (2016)**

CASTRO, S, CAVELLI, M, FALCONI, A, TORTEROLO, P

Publicado

Resumen

Evento: Internacional

Descripción: 23rd Congress of the European Sleep Research Society

Ciudad: Bolonia

Año del evento: 2016

Palabras clave: EEG

Areas de conocimiento:

Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias / Neurobiología cognitiva y sueño

Medio de divulgación: Papel

Mesopontine and basal forebrain cholinergic neurons are critically involved in the control of behavioral states and cognitive functions. Animals treated with muscarinic receptor antagonist display a dissociate state characterized by high amplitude slow oscillations and sleep spindles in the electroencephalogram (EEG) that are characteristics of non-REM (NREM) sleep. However they remain awake and are responsive to exteroceptive stimuli. Oscillations in the gamma frequency band ( $\approx$  40 Hz) of the EEG play a critical role in cognition. These oscillations have been involved in the binding of spatially separated, but temporally correlated, neural events, which results in a unified perceptual experience. Studies in cats have shown that, while EEG gamma power is higher in AW and REM sleep, EEG intra-hemispheric coherence in the 35-40 Hz band is greater during alert (AW) than quiet (QW) wakefulness; decreases to a lower level during NREM sleep, and

reaches its nadir during rapid eye movement (REM) sleep (Castro et al., 2013). Nowadays is still not clear if the cholinergic system is involved in the EEG gamma activity.

#### **Análisis cuantitativo de la actividad eléctrica cortical en recién nacidos: estudio de la coherencia para la banda gamma de frecuencias (2014)**

CASTRO, S., CAVELLI, M., TORTEROLO, P., FALCONI, A., RAVA M., CRIADO A., CHIAPPELLA L., SCAVONE C., ARDANAZ J., GONZALEZ G

Publicado

Resumen

Evento: Internacional

Descripción: XXXIV Congreso Argentino de Neurología Infantil y II Congreso Uruguayo de Neuropediatría.

Ciudad: Colonia del Sacramento

Año del evento: 2014

Palabras clave: sueño gamma neonatos

Áreas de conocimiento:

Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias / Neurobiología cognitiva y sueño  
Medio de divulgación: Papel

La actividad gamma del electroencefalograma (EEG) es uno de los parámetros cuantificables para mantener el proceso de integración de las funciones ejecutivas. Se postula que las oscilaciones en la banda gamma de frecuencias (30 a 45 Hz) evidenciadas en el (EEG), son críticas para la integración en el procesamiento de la información y el desempeño de estas funciones. La coherencia entre dos ondas es una medida de su similitud en contenido de frecuencias y se expresa en función de la frecuencia y varía de 0 (totalmente incoherentes) a 1 (ondas totalmente coherentes). Esto implica que dos áreas corticales que coordinan su actividad eléctrica, presentarán un aumento de coherencia entre sus actividades eléctricas. El grado de coherencia entre el EEG de distintas cortezas registradas simultáneamente reflejaría la fuerza de las interconexiones funcionales, que ocurren entre ellas. **Objetivo:** Describir en recién nacidos (RN) las características dinámicas básicas de las oscilaciones en la banda gamma (30-45 Hz) de los EEG y su coherencia durante la vigilia, sueño lento y REM. **Métodos:** Se emplearon registros poligráficos de RN realizados con fines diagnósticos. Equipo NicoletOne, Sistema Internacional 10-20. Se utilizaron ventanas del registro para cada estado comportamental. Para analizar la coherencia se examinaron periodos de 100 segundos, para cada estado comportamental utilizando el algoritmo matemático Magnitude Squared Coherence. **Resultados y Conclusiones:** Se observa que la coherencia gamma disminuye durante el sueño REM en los recién nacidos. Resultados similares se encuentran en modelos animales. ESTE TRABAJO HA SIDO PREMIADO POR SER SELECCIONADO COMO MEJOR TRABAJO DE PÓSTER EN RECORRIDA.

#### **Efecto de la atropina sobre el EEG: ondas lentas y oscilaciones gamma (30-45 Hz) coherentes (2014)**

CASTRO, S., CAVELLI, M., VELASQUEZ, N., TORTEROLO, P., MIGLIARO, E

Publicado

Resumen

Evento: Nacional

Descripción: X Jornada de la SUB

Ciudad: Piriapolis

Año del evento: 2014

Áreas de conocimiento:

Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias / Neurobiología cognitiva y sueño  
Medio de divulgación: Papel

Las oscilaciones en la banda gamma de frecuencia (30-45 Hz) generadas por interacciones entre áreas corticales y subcorticales juegan un rol preponderante en las funciones cognitivas. Recientemente analizamos estas interacciones por medio del análisis cuantitativo del electroencefalograma (EEG), utilizando el algoritmo matemático llamado "coherencia" (Castro et al., European J Neuroscience, 37:1330). Observamos que la coherencia gamma es muy alta durante la vigilia alerta (AW), disminuye en vigilia tranquila (QW) y en sueño no-REM (NREM), desapareciendo durante el sueño REM. Dado que para la generación y mantenimiento de la vigilia es crítica la actividad de neuronas colinérgicas que forman parte de los sistemas activadores, estudiamos la coherencia gamma bajo el efecto de la atropina, antagonista colinérgico muscarínico. Cuatro gatos fueron implantados con macroelectrodos en varias regiones corticales para registros polisomnográficos en condiciones semirestringidas. Se administró atropina (0.4 mg/kg i.m.) durante la vigilia y registró durante 4 horas y se analizó la coherencia del EEG entre pares de regiones corticales. Dosis de atropina que aumentan la frecuencia cardíaca y eliminan su variabilidad, generaron un comportamiento de vigilia en presencia de un EEG con ondas lentas similares al sueño NREM. Sin embargo, la atropina generó oscilaciones gamma coherentes, similares a AW. La

coherencia gamma fue significativamente mayor a la observada durante QW, NREM y REM ( $P < 0.0001$ ). El aumento de la coherencia gamma producida por atropina explicaría la disociación en que un comportamiento de vigilia coexiste con la presencia de ondas lentas características de sueño NREM.

**Estudio de la coherencia de la banda gamma de frecuencias (35-45 Hz) del EEG durante la vigilia y el sueño (2012)**

CASTRO, S., TORTEROLO, P., FALCONI, A., CHASE, M

Publicado

Resumen

Evento: Nacional

Descripción: IX Jornada de la SUB

Ciudad: Piriápolis-Maldonado-Uruguay

Año del evento: 2012

Palabras clave: coherence

Areas de conocimiento:

Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias /

Medio de divulgación: Papel

**Coherent neocortical 60-200 Hz high gamma band oscillations are not present during REM sleep (2012)** Trabajo relevante

CASTRO, S., TORTEROLO, P., FALCONI, A

Publicado

Resumen

Evento: Internacional

Descripción: I congreso FALAN 2012

Ciudad: Cancun Mexico

Año del evento: 2012

Palabras clave: coherence

Areas de conocimiento:

Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias / FISIOLÓGIA

Medio de divulgación: Papel

During cognitive processes there is a profuse interaction amongst different regions of the cerebral cortex. The extent of these interactions can be examined by quantitative electroencephalographic activity (EEG) analysis using a mathematical algorithm called coherence, which reflects the strength of functional interactions between cortical areas. Since the states of sleep and wakefulness may have a deep impact in these interactions, the present study was conducted to analyze the EEG coherence during alert wakefulness (AW), quiet wakefulness (QW), non-REM (NREM) sleep and REM sleep. Current evidence from electro- and magnetoencephalography (EEG/MEG) has consistently shown oscillations  $> 60$  Hz (high gamma band) are correlated to a wide range of cognitive processes. So, in this report we focused in the high gamma EEG frequency band (60-200 Hz). Four adult cats were implanted with electrodes in the frontal, parietal and occipital cortices to monitor EEG activity. The z-coherence and power spectrum values of the high gamma frequency band, separated in 3 bands, 60-100 Hz, 100-150 Hz, and 150-200 Hz, from pairs of EEG recordings from these areas were determined. An increase in z-coherence values occurred between almost all cortical regions in the 3 separated high gamma frequency bands during AW compared with the other behavioral states ( $p < 0.05$ ). As the animal transitioned from AW to QW and NREM sleep, coherence decreased to a moderate level. Remarkably, the EEG coherence of the high gamma band was almost absent during REM sleep ( $p < 0.05$ ). Gamma power was also greatest during alert wakefulness, minimal during NREM sleep and of an intermediate value during REM sleep and quiet wakefulness ( $p < 0.05$ ). The virtual absence of high gamma frequency coherence during REM sleep may underlie the uniqueness of the cognitive processes that occur during dreams, which is mostly a REM sleep phenomenon.

**Absence of EEG gamma (35-40Hz) coherence characterizes REM sleep and differentiates it from wakefulness. (2011)**

CASTRO, S

Publicado

Resumen

Evento: Internacional

Descripción: Terceras Jornadas Uruguayas de Comportamiento Animal

Ciudad: Montevideo

Año del evento: 2011

Palabras clave: coherence

Areas de conocimiento:  
Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias /  
Medio de divulgación: Papel

**ABSENCE OF EEG GAMMA (35-40Hz) COHERENCE CHARACTERIZES REM SLEEP AND DIFFERENTIATES IT FROM WAKEFULNESS (2011)** Trabajo relevante

CASTRO, S

Publicado

Resumen

Evento: Internacional

Descripción: 41st annual meeting of the Society for Neuroscience.

Ciudad: Washington, 2011

Año del evento: 2011

Palabras clave: coherence

Areas de conocimiento:

Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias / FISILOGÍA

Medio de divulgación: Papel

Absence of EEG gamma (35-40Hz) coherence characterizes REM sleep and differentiates it from wakefulness \*S. CASTRO<sup>1</sup>, M. GUTIERREZ<sup>1</sup>, A. FALCONI<sup>1</sup>, M. CHASE<sup>2</sup>, P. TORTEROLO<sup>1</sup>; <sup>1</sup>Facultad de Med., Univ. De La Republica, Montevideo, Uruguay; <sup>2</sup>Web Sci. Intl. and UCLA Sch. of Med., Los Angeles, CA Abstract: Areas of the cerebral cortex interact in the promotion of cognitive processes, the evaluation of sensory information, the generation of motor activity, etc. The extent of these interactions can be examined by analyzing electroencephalographic activity (EEG) using a mathematical algorithm called coherence, which reflects the strength of interactions between cortical areas. Since these interactions are impacted by the states of sleep and wakefulness, the present study was conducted to analyze the degree of coherence between cortical areas during alert wakefulness, quiet wakefulness, NREM sleep and REM sleep. Four adult cats were implanted with electrodes in the frontal, parietal and occipital cortices to monitor EEG activity. The degree of coherence between one-hundred second epochs of EEG recordings from these areas was determined. A large increase in coherence occurred between all cortical regions in the gamma frequency band (30-45 Hz) during alert wakefulness compared with the other behavioral states ( $p < 0.001$ ). As the animal transitioned from alert wakefulness to quiet wakefulness and NREM sleep, coherence decreased to a moderate level during both states. Coherence was minimal during REM sleep ( $p > 0.05$ ). Gamma power was also greatest during alert wakefulness, minimal during NREM sleep and of an intermediate value during REM sleep and quiet wakefulness. We conclude that the interactions between cortical areas are reflected by the EEG coherence in the gamma frequency band, which differ between wakefulness and REM sleep. These changes in gamma band coherence underlie different cortical patterns of information processing during the states of sleep and wakefulness.

**ACTIVIDAD COHERENTE DEL ELECTROENCEFALOGRAMA DURANTE LA VIGILIA Y EL SUEÑO (2010)**

CASTRO, S, GUTIÉRREZ, FERNÁNDEZ, BENEDETTO, FALCONI, TORTEROLO

Publicado

Completo

Evento: Nacional

Descripción: XIII Jornadas de la Sociedad Uruguaya de Biociencias

Ciudad: Piriápolis

Año del evento: 2010

Palabras clave: coherencia

Areas de conocimiento:

Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias / FISILOGÍA

Medio de divulgación: Papel

Introducción Durante el sueño existen dos estados completamente diferentes; el sueño lento y el sueño REM. Mientras que el sueño lento se caracteriza por actividad sincrónica de las neuronas de diversas regiones corticales y escasa actividad cognitiva, en el sueño REM la actividad eléctrica cerebral se asemeja a la vigilia y existe una importante actividad cognitiva: los ensueños. Durante la vigilia, el procesamiento de estímulos sensoriales, la generación de actos motores, así como las funciones cognitivas, están sustentados por la actividad de regiones corticales y subcorticales que se activan en forma secuencial y/o sincrónica. Actualmente se considera que las interconexiones funcionales mutuas entre distintas cortezas (reentradas), cumplen un rol fundamental para las funciones cognitivas. Se considera que el resultado del algoritmo matemático llamado "coherencia", aplicado a pares de registros electroencefalograficos (EEG), reflejaría la magnitud de las reentradas entre las cortezas registradas. Es así que cuando se está realizando cierta función cognitiva,

aumenta la coherencia entre las regiones corticales involucradas en dicha función. Dado que son escasos los trabajos enfocados al estudio de la coherencia durante el sueño, nuestro objetivo fue estudiar la coherencia entre distintas regiones corticales durante la vigilia, sueño lento y sueño REM. Métodos. Este trabajo fue realizado en dos gatos adultos. Estos animales presentan un sueño consolidado y cortezas de asociación relativamente desarrolladas, que lo hacen óptimo para este estudio. Los animales fueron implantados bajo anestesia general, con electrodos en las cortezas somestésica primaria, parietal de asociación, visual de asociación, y con electrodos subcorticales y musculares para el diagnóstico de sueño o vigilia mediante polisomnografía. Una vez recuperados de la cirugía y adaptados al lugar de registro, los animales se registraron diariamente durante 4 horas en condiciones semirestringidas. Secciones de 100 segundos del EEG de distintas cortezas fueron seleccionadas durante distintos estados comportamentales (12 pares de registros por cada estado). La coherencia entre pares de registros corticales fue analizada utilizando el programa Spike 2, mediante el algoritmo matemático conocido como coherencia cruzada al cuadrado (Bullock et. al. 1995). Los resultados fueron convertidos mediante la transformada z de Fisher. La significancia entre los distintos estados comportamentales fue analizada utilizando la prueba de ANOVA y el posthoc de Tukey. Resultados y Conclusiones Encontramos una coherencia significativamente mayor entre las actividades de las pares de cortezas registradas durante el sueño REM que durante los demás estados comportamentales en las bandas de frecuencia theta (4,5-8,5 Hz) y delta (0,5-4,5 Hz), tanto entre pares corticales del mismo hemisferio (intrahemisfericos) como de ambos hemisferios (interhemisfericos). Consideramos este aumento de coherencia en el sueño REM se debe a un aumento de las interacciones funcionales entre los pares de cortezas registradas durante este estado. En estudios posteriores se intentará conocer si este es un fenómeno global o específico para la interrelación entre determinadas cortezas.

#### **Actividad sincrónica cortical durante los comportamientos de vigilia y de sueño. (2009)**

CASTRO, S., BENEDETTO, L., FALCONI, A., TORTEROLO, P

Publicado

Completo

Evento: Nacional

Descripción: Segundas Jornadas Uruguayas de Comportamiento Animal.

Ciudad: Montevideo

Año del evento: 2009

Palabras clave: coherencia

Areas de conocimiento:

Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias / FISILOGÍA

Medio de divulgación: Papel

#### **Coherence in the cortical electrical activity during sleep and wakefulness (2009)**

CASTRO, S., TORTEROLO, P., FALCONI, A., GUTIERREZ, M

Publicado

Completo

Evento: Internacional

Descripción: 3rd International Congress on Sleep Medicine

Ciudad: San Pablo-Brasil

Año del evento: 2009

Palabras clave: coherencia

Areas de conocimiento:

Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias / FISILOGÍA

Medio de divulgación: Papel

## **Producción técnica**

### **OTRAS PRODUCCIONES**

### **OTRA PRODUCCIÓN TÉCNICA**

#### **Abordaje fisiológico y farmacológico al estudio del correlato electroencefalográfico de la consciencia (2020)**

CASTRO, S

País: Uruguay

Idioma: Español

Proyecto I+D CSIC 2020

# Formación de RRHH

## TUTORÍAS CONCLUIDAS

### GRADO

#### **Efectos del Haloperidol en las oscilaciones gamma del EEG (2019 - 2023)**

Tesis/Monografía de grado

Sector Educación Superior/Público / Universidad de la República / Facultad de Medicina /

Departamento de Fisiología, Uruguay

Programa: Licenciatura en Biología Humana

Tipo de orientación: Asesor

Nombre del orientado: Diego Gallo

País: Uruguay

Areas de conocimiento:

Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias

Para este propósito, en este proyecto estudiaremos cómo el haloperidol (un antagonista del receptor dopaminérgico D2) afecta la potencia y la coherencia de la banda gamma de frecuencias del EEG. Se utilizarán cinco gatos preparados con implantes crónicos para registros polisomnográficos en condiciones semi-restringidas durante la vigilia, el sueño y después de la administración de haloperidol (2 y 4 mg / kg, i / m). Se analizará la potencia y la coherencia dentro de la banda de frecuencia gamma de pares de registros de EEG. Registros preliminares mostraron que el haloperidol indujo dos estados diferentes, que llamamos estado activo (AH) y tranquilo (QH). En ambos estados, la potencia gamma y la coherencia se alteraron. Además, hubo una disminución en la frecuencia del pico de amplitud gamma (de aproximadamente 37-39 Hz a 32-34 Hz). Finalmente, observamos que la actividad gamma inducida por la estimulación auditiva está ausente después de la administración de haloperidol. Estos resultados preliminares sugieren que el sistema dopaminérgico regula las oscilaciones gamma. Además, el efecto observado puede estar relacionado con el efecto conductual producido por haloperidol (inactividad conductual en un estado QH). Estos resultados preliminares también fueron presentados en XV Latin American Symposium of Chronobiology 2019. Este proyecto será realizado por el estudiante Diego Gallo como tesis de grado de la licenciatura en biología humana y yo seré su orientador.

## Otros datos relevantes

### PREMIOS, HONORES Y TÍTULOS

#### **Abordaje fisiológico y farmacológico al estudio del correlato electroencefalográfico de la consciencia (2020)**

(Nacional)

CSIC

Gané un proyecto I+D de CSIC (como responsable científico) titulado: Abordaje fisiológico y farmacológico al estudio del correlato electroencefalográfico de la consciencia (que incluye la financiación de un cargo remunerado para un estudiante)

#### **Mención "Elio Garcia-Austt" (2018)**

(Nacional)

PEDECIBA

Mención "Elio Garcia-Austt" por tesis de doctorado "Estudio de las oscilaciones gamma del EEG durante la vigilia, el sueño y en un modelo farmacológico de psicosis"

### PRESENTACIONES EN EVENTOS

#### **World Sleep 2023 (2023)**

Congreso

Cognitive processes and consciousness rely on extensive thalamocortical and corticocortical recurrent interactions at a large scale. It has been hypothesized that oscillations within the gamma frequency band (30 to 45 Hz) of the electroencephalogram (EEG) are generated as a result of these interactions, and play a role in cognitive functions. These oscillations have been implicated in the integration of spatially separated yet temporally correlated neural events, leading to a cohesive perceptual experience. It is widely recognized that top-down processing refers to the brain's ability to utilize our expectations, attentional focus, and other cognitive factors to dynamically influence bottom-up sensory processing. However, the precise directionality of the information flow encoded

by gamma band oscillations remains unknown. Therefore, the primary objective of our study is to investigate the specific information flow patterns within the gamma band during both wakefulness and sleep. To achieve this, we utilized the cat as an animal model. To achieve this, five cats were chronically prepared for polysomnographic recordings, with electrodes placed in various cortical regions. To investigate the directionality of information flow of the gamma band during wakefulness and sleep, we quantified the phase shifts of amplitude envelopes of filtered gamma oscillations, and employed the "Granger causality" analysis. This statistical test allowed us to determine if one time series could p

Brasil

Tipo de participación: Expositor oral

Nombre de la institución promotora: world sleep society

Alcance geográfico: Internacional Palabras Clave: Top-Down Bottom-Up Direccionalidad Gamma

Areas de conocimiento:

Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias

Cognitive processes and consciousness rely on extensive thalamocortical and corticocortical recurrent interactions at a large scale. It has been hypothesized that oscillations within the gamma frequency band (30 to 45 Hz) of the electroencephalogram (EEG) are generated as a result of these interactions and play a role in cognitive functions. These oscillations have been implicated in the integration of spatially separated yet temporally correlated neural events, leading to a cohesive perceptual experience. It is widely recognized that top-down processing refers to the brain's ability to utilize our expectations, attentional focus, and other cognitive factors to dynamically influence bottom-up sensory processing. However, the precise directionality of the information flow encoded by gamma band oscillations remains unknown. Therefore, the primary objective of our study is to investigate the specific information flow patterns within the gamma band during both wakefulness and sleep. To achieve this, five cats were chronically prepared for polysomnographic recordings, with electrodes placed in various cortical regions. To investigate the directionality of information flow of the gamma band during wakefulness and sleep, we quantified the phase shifts of amplitude envelopes of filtered gamma oscillations and employed the "Granger causality" analysis. This statistical test allowed us to determine if one time series could predict or forecast the other. In the baseline condition when analyzing 500-second windows, the results revealed that during wakefulness, the primary direction of information flow in the gamma band was from the dorsolateral prefrontal cortex (Pfdl) to the posterior parietal cortex (Pp), as well as from Pfdl to the primary somatosensory cortex (S1), primary visual cortex (V1), and primary auditory cortex (A1). Additionally, there was a predominance of directionality from Pp to the primary cortices (S1, A1, V1). This indicates a significant influence of top-down information processing. However, this top-down flow of information was not observed during both NREM and REM sleep. Furthermore, when investigating late gamma oscillations induced by click stimuli (analyzed within 1 second windows starting 0.4 seconds after the stimulus), we found a predominant bottom-up directionality from the Pp to the Pfdl, as well as from A1 to Pfdl. In contrast, late gamma oscillations induced by more complex stimuli, such as 0.2 seconds variable sounds, demonstrated a predominant top-down directionality from Pfdl to Pp, A1, and V1 cortex, as well as from Pp to V1 cortex. Notably, these specific directionalities were not observed during sleep. The data indicate that during wakefulness, different patterns of information flow emerge depending on the nature of the stimuli. Specifically, bottom-up processing was found to predominate in the case of simple repetitive sound stimuli, while top-down processing prevailed for complex and variable sounds, as well as in the baseline condition (without stimuli). In addition, no specific directionality of information flow was observed during NREM and REM sleep, suggesting a different mode of cognitive processing during sleep. This research was supported by CSIC-I+D grupos 2022 and CSIC-I+D-2020-393.

### **15th International Workshop on NEURAL CODING 2023 (2023)**

Congreso

Cognitive processes and consciousness depends on large-scale thalamocortical and corticocortical recurrent interactions (1,2). It has been postulated that the oscillations in the gamma frequency band (30 to 45 Hz) of the electroencephalogram (EEG) are the product of these interactions and therefore are involved in cognitive functions (4,5). Oscillations in the gamma frequency band of the electroencephalogram are involved in the binding of spatially separated but temporally correlated neural events, which results in a unified perceptual experience (2,6,7). Top-down processing is how the mind uses our expectations, attentional focus, and other cognitive variables to adaptively influence bottom-up sensory processing (3,8). In our previous work, we demonstrated that during alert wakefulness (AW) there is a large increase in coherence in the gamma band between intrahemispheric cortical areas with respect to the other states, it decreases to moderate values during NREM sleep and reaches minimum values during REM sleep (7,9). In the ketamine-induced psychosis model, we found a decrease in gamma coherence between all cortical regions, an effect similar to what is observed during REM sleep (10). Finally, administration of atropine or scopolamine causes a slowing of the EEG, with increased delta waves and sleep spindles (as in

NREM sleep); however, the animals remain active. This dissociated state was accompanied by power and gamma coherence values, similar to W. This great functional connectivity in the gamma band of frequencies could explain why the animals remain awake despite the presence of slow waves and spindles in the EEG (11). Nevertheless, coherence do not show the directionality of gamma functional interactions. The aim of our study is, using the cat as an animal model, to address the directionality of gamma band functional interactions during wakefulness and sleep and under the ketamine-induced psychosis model and under scopolamine induced dissociated state. For this, five cats were chronically prepared for polysomnographic recordings, with electrodes in different cortical areas. Gamma activity was studied during wakefulness and sleep, as well as in a pharmacological model of psychosis (subanesthetic dose of ketamine). Also, using muscarinic receptor antagonists (atropine and scopolamine). We used two different methods to access directionality. The first and simplest was quantifying the direction of the phase shifts of the amplitude envelopes of filtered gamma oscillations, the second was the algorithm "granger causality" (12). We found that during wakefulness there is a predominant Top-down directionality of gamma band functional interactions. Directionality from dorsolateral Prefrontal cortex (Pfdl) to posterior parietal cortex (Pp), from Pfdl to projection areas like somato-sensory cortex(S1), primary visual cortex (V1) and primary auditory cortex (A1) Predominant directionality was also from Pp to projection areas (S1, A1, V1). This predominant directionality disappeared during sleep, in the ketamine-induced psychosis model. It also disappeared during scopolamine induced dissociated state in spite of the high gamma power and coherence, similar to W. Our finding highlight the role of top-down processing in gamma frequencies in cognitive functions and consciousness. Only during W when cognitive functions and consciousness are in their max expression, directionality from dorsolateral Prefrontal cortex (Pfdl) to posterior parietal cortex (Pp) and from Pfdl and Pp to projection areas predominated. This predominant directionality disappeared in the lack of and, or altered consciousness induced by sleep and ketamine-induced psychosis model. Scopolamine induce a conscious state with altered cognitive functions and it correlates with an EEG with high gamma power and coherence but lacking a predominant directionality. Our results strongly suggest that gamma coupling between distant cortical areas is sufficient to be in a conscious state but top-down processing is necessary for complete cognitive functions. This research was supported by CSIC-I+D grupos 2022 and CSIC-I+D-2020-393. References 1. Redinbaugh MJ, Phillips JM, Kambi NA, Mohanta S, Andryk S, Dooley GL, et al. Thalamus Modulates Consciousness via Layer-Specific Control of Cortex. *Neuron*. abril de 2020;106(1):66-75.e12. 2. Schneider M, Dann B, Sheshadri S, Scherberger H, Vinck M. A general theory of coherence between brain areas [Internet]. *Neuroscience*; 2020 jun [citado 27 de diciembre de 2020]. Disponible en: <http://biorxiv.org/lookup/doi/10.1101/2020.06.17.156190> 3. Vinck M, Uran C, Canales-Johnson A. The neural dynamics of feedforward and feedback interactions in predictive processing [Internet]. *PsyArXiv*; 2022 oct [citado 16 de diciembre de 2022]. Disponible en: <https://osf.io/n3afb> 4. Llinás R, Ribary U. Coherent 40-Hz oscillation characterizes dream state in humans. *Proc Natl Acad Sci USA*. marzo de 1993;90(5):2078-81. 5. Mashour GA. Consciousness Unbound. *Anesthesiology*. 1 de febrero de 2004;100(2):428-33. 6. Cantero JL, Atienza M, Madsen JR, Stickgold R. Gamma EEG dynamics in neocortex and hippocampus during human wakefulness and sleep. *NeuroImage*. julio de 2004;22(3):1271-80. 7. Castro S, Falconi A, Chase MH, Torterolo P.

Uruguay

Tipo de participación: Expositor oral

Nombre de la institución promotora: International Brain Research Organization

Alcance geográfico: Internacional Palabras Clave: Top-Down Bottom-Up Gamma Directionality  
Conectivity

Areas de conocimiento:

Ciencias Médicas y de la Salud / Medicina Básica / Neurociencias

Cognitive processes and consciousness depends on large-scale thalamocortical and corticocortical recurrent interactions (1,3). It has been postulated that the oscillations in the gamma frequency band (30 to 45 Hz) of the electroencephalogram (EEG) are the product of these interactions and therefore are involved in cognitive functions (4,5). Oscillations in the gamma frequency band of the electroencephalogram are involved in the binding of spatially separated but temporally correlated neural events, which results in a unified perceptual experience (2,6,7). Top-down processing is how the mind uses our expectations, attentional focus, and other cognitive variables to adaptively influence bottom-up sensory processing (3,8). In our previous work, we demonstrated that during alert wakefulness (AW) there is a large increase in coherence in the gamma band between intrahemispheric cortical areas with respect to the other states, it decreases to moderate values during NREM sleep and reaches minimum values during REM sleep (7,9). In the ketamine-induced psychosis model, we found the a decrease in gamma coherence between all cortical regions, an effect similar to what is observed during REM sleep (10). Finally, administration of atropine or scopolamine causes a slowing of the EEG, with increased delta waves and sleep spindles (as in NREM sleep); however, the animals remain active. This dissociated state was accompanied by power and gamma coherence values, similar to W. This great functional connectivity in the gamma band of frequencies could explain why the animals remain awake despite the presence of slow waves and spindles in the EEG (11). Nevertheless, coherence do not show the directionality of gamma functional interactions. The aim of our study is, using the cat as an animal model, to address the directionality of gamma band functional interactions during wakefulness and sleep and under the ketamine-induced psychosis model and under scopolamine induced dissociated state. For this, five cats were chronically prepared for polysomnographic recordings, with electrodes in different cortical areas. Gamma activity was studied during wakefulness and sleep, as well as in a pharmacological model of psychosis (subanesthetic dose of ketamine). Also, using muscarinic receptor antagonists (atropine and scopolamine). We used two different methods to access directionality. The first and simplest was quantifying the direction of the phase shifts of the amplitude envelopes of filtered gamma oscillations, the second was the algorithm "granger causality" (12). We found that during wakefulness there is a predominant Top-down directionality of gamma band functional interactions. Directionality from dorsolateral Prefrontal cortex (Pfdl) to posterior parietal cortex (Pp), from Pfdl to projection areas like somato-sensory cortex(S1), primary visual cortex (V1) and primary auditory cortex (A1) Predominant directionality was also from Pp to projection areas (S1, A1, V1). This predominant directionality disappeared during sleep, in the ketamine-induced psychosis model. It also disappeared during scopolamine induced dissociated state in spite of the high gamma power and coherence, similar to W. Our finding highlight the role of top-down processing in gamma frequencies in cognitive functions and consciousness. Only during W when cognitive functions and consciousness are in their max expression, directionality from dorsolateral Prefrontal cortex (Pfdl) to posterior parietal cortex (Pp) and from Pfdl and Pp to projection areas predominated. This predominant directionality disappeared in the lack of and, or altered consciousness induced by sleep and ketamine-induced psychosis model. Scopolamine induce a conscious state with altered cognitive functions and it correlates with an EEG with high gamma power and coherence but lacking a predominant directionality. Our results strongly suggest that gamma coupling between distant cortical areas is sufficient to be in a conscious state but top-down processing is necessary for complete cognitive functions. This research was supported by CSIC-I+D grupos 2022 and CSIC-I+D-2020-393. References 1. Redinbaugh MJ, Phillips JM, Kambi NA, Mohanta S, Andryk S, Dooley GL, et al. Thalamus Modulates Consciousness via Layer-Specific Control of Cortex. *Neuron*. abril de 2020;106(1):66-75.e12. 2. Schneider M, Dann B, Sheshadri S, Scherberger H, Vinck M. A general theory of coherence between brain areas [Internet]. *Neuroscience*; 2020 jun [citado 27 de diciembre de 2020]. 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### **XV Latin American Symposium on Chronobiology 2019 (2019)**

Congreso

Cognitive processes are carried out during wakefulness by means of extensive interactions between cortical and subcortical areas. In psychiatric conditions, such as psychosis, these processes are altered. Interestingly, REM sleep where most dreams occurs, shares electrophysiological, pharmacological, and neurochemical features with psychosis. Because of this fact, REM sleep is considered a natural model of psychosis. Ketamine is a non-competitive N-methyl-D-aspartate (NMDA) receptor antagonist that at sub-anesthetic dose induces psychotomimetic-like effects in humans and animals, and is employed as a pharmacological model of psychosis. Oscillations in the gamma frequency band of the electroencephalogram (EEG), mainly at about 40Hz, have been involved in cognitive functions. Hence, the present study was conducted to analyze the EEG low gamma (30-45Hz) band power and coherence of the cat, in natural (REMsleep) and pharmacological (sub-anesthetic doses of ketamine) models of psychosis. These results were compared with the gamma activity during alert (AW) and quiet wakefulness (QW), as well as during non-REM (NREM) sleep. Five cats were chronically prepared for polysomnographic recordings, with electrodes in different cortical areas. Basal recordings were obtained and ketamine (5, 10, and 15 mg/kg, i.m.) was administrated. Gamma activity (power and coherence) was analyzed in the abovementioned conditions. Compared to wakefulness and NREM sleep, following ketamine administration g

Uruguay

Tipo de participación: Expositor oral

Nombre de la institución promotora: XV Latin American Symposium on Chronobiology 2019

### **Información adicional**

I+D CSIC 2020 ?Abordaje fisiológico y farmacológico al estudio del correlato electroencefalográfico de la consciencia?. CSIC. Responsable científico: Santiago Castro. Abril 2021- noviembre 2023. Monto \$U 1250000. CSIC-I+D-2020-393

Concursé y gane el cargo de profesor adjunto del departamento de fisiología del cual tome posesión el 08/09/2021

CSIC-I+D grupos 2022 ?Estudio de la actividad eléctrica cortical durante la vigilia, sueño y estados alterados de consciencia? CSIC. Participante. Abril 2023- abril 2027. Monto \$U 3.400.000 ID-22620220100148

También recientemente fui nombrado G3 del programa PEDECIBA

Voy a participar del proyecto de doctorado titulado "Interacciones funcionales entre la actividad bioeléctrica de las cortezas sensoriomotoras cerebrales, actividad bioeléctrica cerebelar y la actividad muscular ocasionada por la mioclonía en caninos infectados naturalmente con el virus del Distemper Canino" de la licenciada Mary Gutiérrez en el rol de coorientador.

FCE 2024 Dirección del flujo de información (top-down o bottom-up) de la banda gamma(40 Hz) del EEG en las funciones cognitivas y la consciencia. Responsable científico: Santiago Castro.

FCE\_3\_2024\_1\_180456. Abril 2025-2027. Monto \$U 1300000

### **Indicadores de producción**

<b>ACTIVIDADES</b>	<b>2</b>
<b>Líneas de investigación</b>	<b>2</b>
	<b>41</b>

<b>PRODUCCIÓN BIBLIOGRÁFICA</b>	
<b>Artículos publicados en revistas científicas</b>	24
Completo	24
<b>Trabajos en eventos</b>	15
<b>Libros y Capítulos</b>	2
Capítulos de libro publicado	2
<b>Otros tipos</b>	1
<b>PRODUCCIÓN TÉCNICA</b>	<b>1</b>
<b>FORMACIÓN RRHH</b>	<b>1</b>
<b>Tutorías/Orientaciones/Supervisiones concluidas</b>	1
Tesis/Monografía de grado	1