PLoS One. 2014 Feb 10;9(2):e88672. doi: 10.1371/journal.pone.0088672. eCollection 2014.

Endocannabinoid modulation of cortical up-states and NREM sleep.

Pava MJ[1], den Hartog CR[1], Blanco-Centurion C[2], Shiromani PJ[2], Woodward JJ[3].

Author information

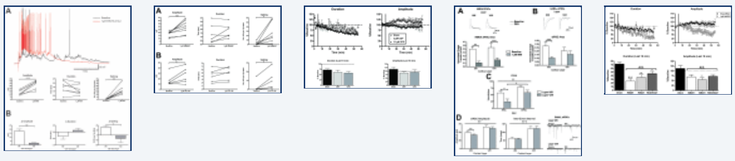
Abstract

Up-/down-state transitions are a form of network activity observed when sensory input into the cortex is diminished such as during non-REM sleep. Up-states emerge from coordinated signaling between glutamatergic and GABAergic synapses and are modulated by systems that affect the balance between inhibition and excitation. We hypothesized that the endocannabinoid (EC) system, a neuromodulatory system intrinsic to the cortical microcircuitry, is an important regulator of up-states and sleep. To test this hypothesis, up-states were recorded from layer V/VI pyramidal neurons in organotypic cultures of wild-type or CB1R knockout (KO) mouse prefrontal cortex. Activation of the cannabinoid 1 receptor (CB1) with exogenous agonists or by blocking metabolism of endocannabinoids, anandamide or 2-arachidonoyl glycerol, increased up-state amplitude and facilitated action potential discharge during up-states. The CB1 agonist also produced a layer II/III-selective reduction in synaptic GABAergic signaling that may underlie its effects on up-state amplitude and spiking. Application of CB1 antagonists revealed that an endogenous EC tone regulates up-state duration. Paradoxically, the duration of up-states in CB1 KO cultures was increased suggesting that chronic absence of EC signaling alters cortical activity. Consistent with increased cortical excitability, CB1 KO mice exhibited increased wakefulness as a result of reduced NREM sleep and NREM bout duration. Under baseline conditions, NREM delta (0.5-4 Hz) power was not different in CB1 KO mice, but during recovery from forced sleep deprivation, KO mice had reduced NREM delta power and increased sleep fragmentation. Overall, these findings demonstrate that the EC system actively regulates cortical up-states and important features of NREM sleep such as its duration and low frequency cortical oscillations.

PMID: 24520411 PMCID: PMC3919802 DOI: 10.1371/journal.pone.0088672

[Indexed for MEDLINE] Free PMC Article

Images from this publication. See all images (11) Free text



Publication types, MeSH terms, Substances, Grant support

LinkOut - more resources

Full text links

Save items

Add to Favorites

Similar articles

Multiple Forms of Endocannabinoid and Endovanilloid Signalin [J Neurosci. 2015]

Increased Contextual Fear Conditioning in iN [Int J Neuropsychopharmacol. 2015]

Endocannabinoid Signaling Regulates Sleep Stability. [PLoS One. 2016]

Review Endocannabinoid-mediated retrograde m [Curr Opin Neurobiol. 2014]

Review Why do cannabinoid receptors have [Philos Trans R Soc Lond B Biol...]

See reviews...

See all...

Cited by 6 PubMed Central articles

Effects of Cannabinoid Agonists and Antagonists on Sleep and I [Sleep. 2017]

Review Integrating Endocannabinoid Signa [Neuropsychopharmacology. 2018]

Role of N-Arachidonoyl-Serotonin (AA-5-HT) in [Front Mol Neurosci. 2017]

See all...

Related information

Articles frequently viewed together

Gene

Nucleotide (RefSeq)

Nucleotide (Weighted)

Protein (RefSeq)

Protein (Weighted)

PubChem Compound (MeSH Keyword)

References for this PMC Article

Taxonomy via GenBank

UniGene

GEO Profiles

Free in PMC

Cited in PMC

Cited in Books

Recent Activity

Turn Off Clear

Endocannabinoid modulation of cortical up-states and NREM PubMed

Cannabidiol, a constituent of Cannabis sativa, modulates s PubMed

Effect of Delta-9-tetrahydrocannabinol and PubMed

Effects of acute systemic administration of cannabidiol PubMed

Cannabis, pain, and sleep: lessons from therapeutic clinical trials PubMed

See more...

You are here: NCBI > Literature > PubMed Support Center

GETTING STARTED
NCBI Education
NCBI Help Manual
NCBI Handbook
Training & Tutorials
Submit Data

RESOURCES
Chemicals & Bioassays
Data & Software
DNA & RNA
Domains & Structures
Genes & Expression
Genetics & Medicine
Genomes & Maps
Homology
Literature
Proteins
Sequence Analysis
Taxonomy
Variation

POPULAR
PubMed
Bookshelf
PubMed Central
BLAST
Nucleotide
Genome
SNP
Gene
Protein
PubChem

FEATURED
Genetic Testing Registry
GenBank
Reference Sequences
Gene Expression Omnibus
Genome Data Viewer
Human Genome
Mouse Genome
Influenza Virus
Primer-BLAST
Sequence Read Archive

NCBI INFORMATION
About NCBI
Research at NCBI
NCBI News & Blog
NCBI FTP Site
NCBI on Facebook
NCBI on Twitter
NCBI on YouTube
Privacy Policy