Eliciting the Neural Basis of Music Medicine in Epilepsy

Barbara C. Jobst, MD, Dr. med



Geisel School of Medicine at Dartmouth The Louis and Ruth Professor of Neuroscience Chair, Department of Neurology, Dartmouth Health





ISEL SCHOOL OF MEDICINE Dartmouth



Disclosures

- Research:
 - Federal
 - •CDC
 - •NIH
 - •Department of Defense
 - Commercial:
 - •Neuropace, Inc.
 - •Harvard Pilgrim Inc.

Associate Editor of
 Neurology

• Endowed Professorship: The Louis and Ruth Frank Professor of Neuroscience (established in honor of Dr. James Bernat)



Richard Quon, PhD



Department of Neurology, Dartmouth-Hitchcock Epilepsy Center, Geisel School of Medicine at Dartmouth

Overview

What is epilepsy?
Memory loss in epilepsy
The effects of music therapy in epilepsy



Department of Neurology, Dartmouth-Hitchcock Epilepsy Center, Geisel School of Medicine at Dartmouth

What is epilepsy?

• Seizures





• 3.4 Mio people in the US have epilepsy



•1% of the population will have a seizure in their lifetime



EEG

Department of Neurology, Dartmouth-Hitchcock Epilepsy Center, Geisel School of Medicine at Dartmouth

[EKG1-EKG2]







~~Fp1,F3~~~	m	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	hanne	munn	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	~~~~~
~~~ <del>~~~~~</del> ~~~~~~~~~~~~~~~~~~~~~~~~~~~~	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	www.	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	www.www	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	~~~~~
~~ <del>63•P3</del> ~~	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		~~~~~
MP3-01	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	L. Martin	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	~~~~~
~~ <del>Fp2~F4</del> ~~~	www.	hunner		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	mm	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~ <del>F</del> & <del>64</del> ~~~	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	mmm	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	m	m	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	~~~~~
~~ <mark>C4-P4</mark> ~~~	······································	mmm	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~			~~~~
\/~ <mark>R4-02</mark> /~~	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	······	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		y		
~~Fp1~Fo7~~~	- man - m	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	mm	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	~~~~~~	~~~~~
~~~ <del>K7~T3</del> ~^	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	~~~ \	····	·····		~~~~ ·
~~~ <del>73</del> ~75~	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	m	m mm	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	m w		nm r
~~ <del>75-01</del> ~	man n	·	~ ~~~~		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		~~~ ~
~Æp2-F8~~~	man	www.uni	n turn	ment and and	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	
<b>∕∕F8₇I4</b> ~~√	Munn	month	mywww	mmmy	mm	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	m
JVT#=76~~~)	Winn	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	man	mmW	hanne	m
~~. <del></del>	mun	m	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		h	· · · · · · · · · · · · · · · · · · ·	mm



## Treatment for epilepsy



70 % have no more seizures













If frequent seizures persist there are other problems

 Memory loss, that is variable but disabling for many



- Problems with mood, anxiety and depression







### 40 Hz tones and visual stimuli in mice

#### Multi-sensory Gamma Stimulation Ameliorates Alzheimer's-Associated Pathology and Improves Cognition

#### **Graphical Abstract**



#### Authors

Anthony J. Martorell, Abigail L. Paulson, Ho-Jun Suk, ..., Edward S. Boyden, Annabelle C. Singer, Li-Huei Tsai

Correspondence Ihtsai@mit.edu

#### In Brief

Auditory stimulation combined with lightinduced gamma oscillations in the hippocampus CA1 and auditory cortex regions of the brain reduces amyloid levels and improves memory in animal models of Alzheimer's disease.



Janůary 26, 2023



### "The K448 Effect"



- Mozart's Sonata for Two Pianos in D Major (K448)
   reduces seizures and epileptic spikes
  - Rauscher et al. (1993)
    - "Mozart K448 effect" first described
  - Lin et al. (2011)
    - Randomized Controlled trial with children listening before bedtime correlated with a reduction in seizures

Sonata KV 448 (375a) - 1st movement
Durand Vienne, Normaline (1981) For two planets Wok blower (1986-1981)
¦\$¶```u`r@rorororori  ₩```ror@rorororori  ₩``ror@rorororo
- اندری بی بی این برد را به این - اندری بی راز بیرزا به این
Sammer man on
194- 5551 · · · · · · · · · · · · · · · · ·
، ولغله طلقه من ، . ولغنه معنه من ولائم المشارق المسلمات المسلمات (مارار) المع
351 1
light i region of the second s





### 40 Hz and KV448



 Received: 13 January 2021
 Revised: 8 March 2021
 Accepted: 11 April 2021

 DOI: 10.1111/ane.13437

#### ORIGINAL ARTICLE

110

Neurologica Scandinavica WILEY

#### 40-Hz auditory stimulation for intracranial interictal activity: A pilot study

Robert J. Quon¹ | Grace A. Leslie² | Edward J. Camp³ | Stephen Meisenhelter³ | Sarah A. Steimel¹ | Yinchen Song^{1,3} | Alan B. Ettinger⁴ | Krzysztof A. Bujarski^{1,3} | Michael A. Casey^{5,6} | Barbara C. Jobst^{1,3}  $\circ$ 

- 40 Hz and KV448 did reduce epileptic spikes
- White noise and modulated KV448 and a 440 Hz tone did not



### **Musical Stimuli**



- Original version of **K448**
- Altered version of K448
- Negative controls: Wagner and Violet Noise



altered

b

Frequency (Hz)

2048 -512 -128 -0 10 20 30 40 50 60 70 80 90 Time (s)

Tonic Key - D Major)

- Other stimuli:
  - Frederic Chopin's Bolero in C Op. 19 for piano, performed by Nikita Magaloff ("Classical T")
  - Franz Liszt's Piano Sonata in B Minor, 1st movement: Lento assai Allegro energico, performed by Leslie Howard ("Classical N")
  - Three songs from a preferred musical genre ("Preferred N") ("Preferred T")
- **"T" or "N"** indicates if the gamma-range auditory modulation spectrum of that song matched ("T") or did not match ("N") that of K448
- "Altered" indicates signals with secondary gamma modulations





### Music and Spikes



#### scientific reports



OPEN Musical components important for the Mozart K448 effect in epilepsy

> Robert J. Quon^{©1,4}[∞], Michael A. Casey^{2,3}, Edward J. Camp⁴, Stephen Meisenhelter⁴, Sarah A. Steimel¹, Yinchen Song^{1,4}, Markus E. Testorf^{4,5}, Grace A. Leslie⁶, Krzysztof A. Bujarski^{1,4}, Alan B. Ettinger⁷ & Barbara C. Jobst^{®1,4}



Wagner Liszt Chopin Preferred music

**No effect** 





## Where in the brain do we see most of this effect?







### Main Conclusions

- Mozart's K448 may reduce epileptiform activity and seizures, possibly memory
- Evidence for the preferential reduction of epileptiform activity in bilateral frontal regions
  - Implications for the activation of emotion networks regulated by the frontal cortex
- Maybe we can engineer some music that is antiepileptic and helps memory