

SIMPOSIO XIII: NEUROMODULATION OF GAMMA OSCILLATIONS: FROM BASIC RESEARCH TO CLINICAL APPLICATIONS

Effects of gamma neuromodulation on memory and Alzheimer's Disease

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Gamma Oscillations and Memory

INMED/TINS special issue

Human gamma-frequency oscillations associated with attention and memory

Ole Jensen^{1*}, Jochen Kaiser^{2*} and Jean-Philippe Lachaux^{3*}

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³INSERM, Unite 821, 95 Boulevard Pinel, 69675 BRON CEDEX, France

Review

Gamma oscillations and episodic memory

Benjamin J. Griffiths^{1,*} and Ole Jensen¹

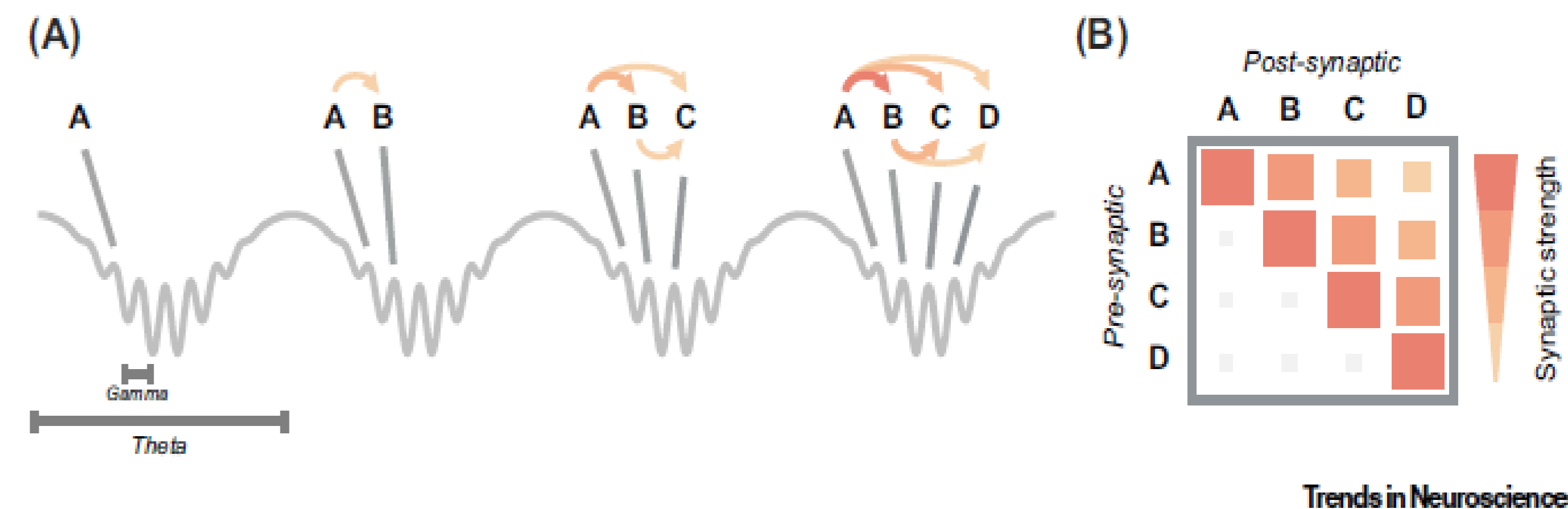
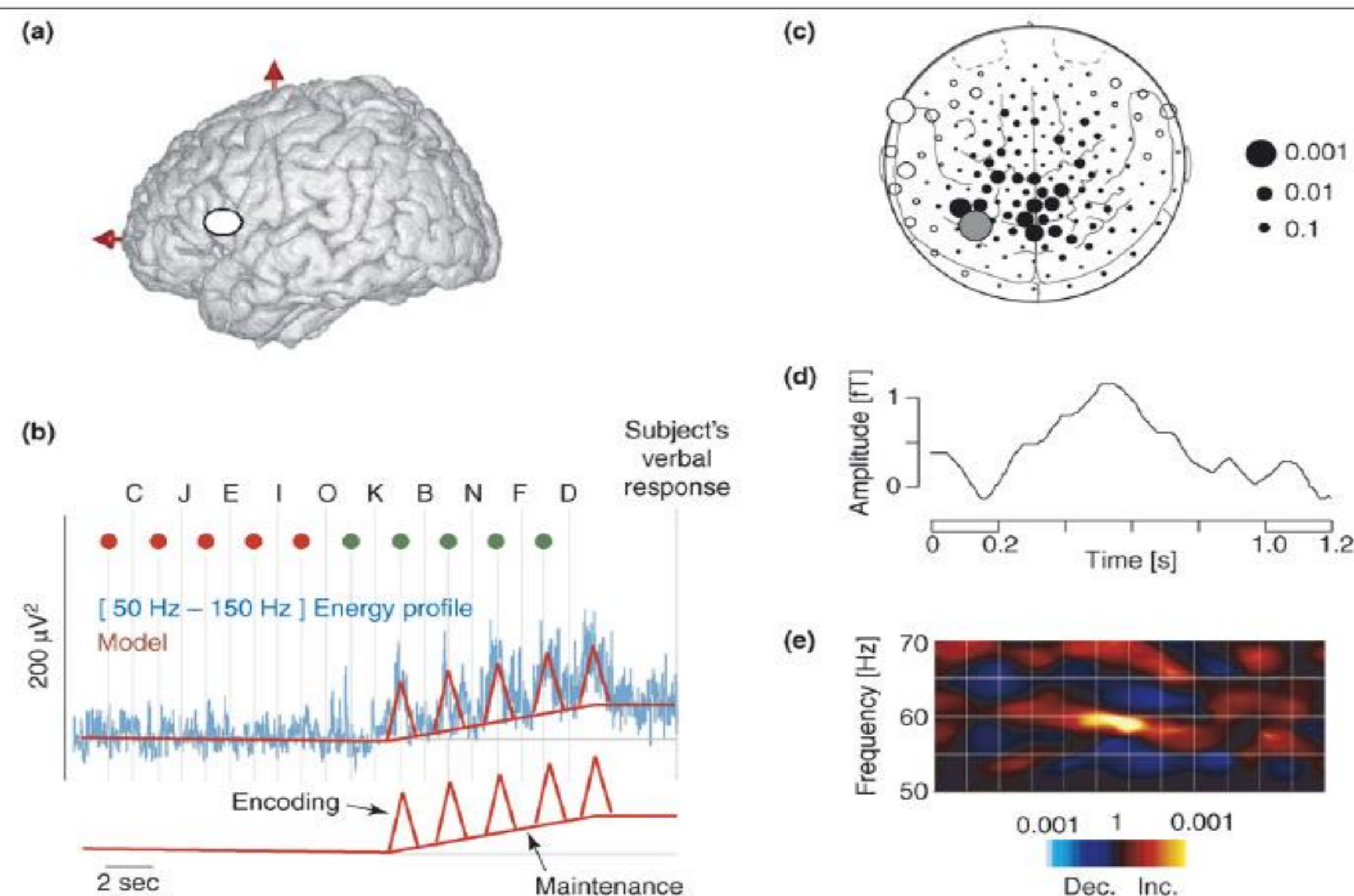


Figure 2. Depiction of the contribution of theta-gamma coupling to episodic memory. (A) Individual elements of an event are represented on individual gamma cycles, which are nested within an ongoing theta oscillation. Given the inhibitory nature of theta, individual elements of an event occur at the trough of the theta cycle. Given that early elements always precede later elements, unidirectional synaptic links can form between elements via asymmetric long-term potentiation (LTP). (B) Sequential learning establishes synaptic links between elements, such that early elements can induce firing in later elements, but not vice versa. Adapted from [88].

Trends in Neurosciences

Gamma Oscillations and AD

updates

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Open Access

ALZHEIMER'S DISEASE AND RELATED DISORDERS - ORIGINAL ARTICLE

Increased EEG gamma band activity in Alzheimer's disease and mild cognitive impairment

J. A. van Deursen · E. F. P. M. Vuurman ·
F. R. J. Verhey · V. H. J. M. van Kranen-Mastenbroek ·
W. J. Riedel

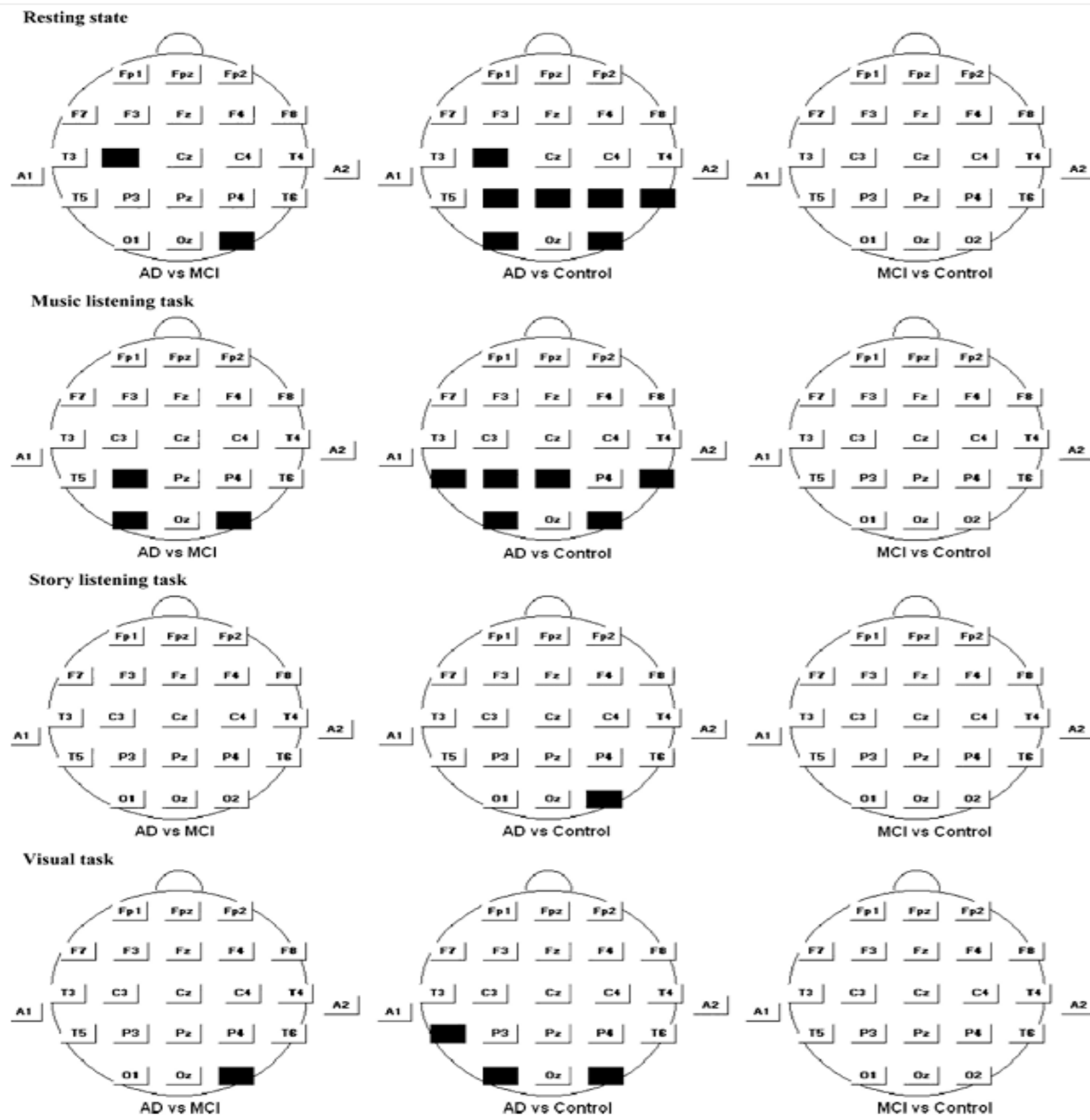
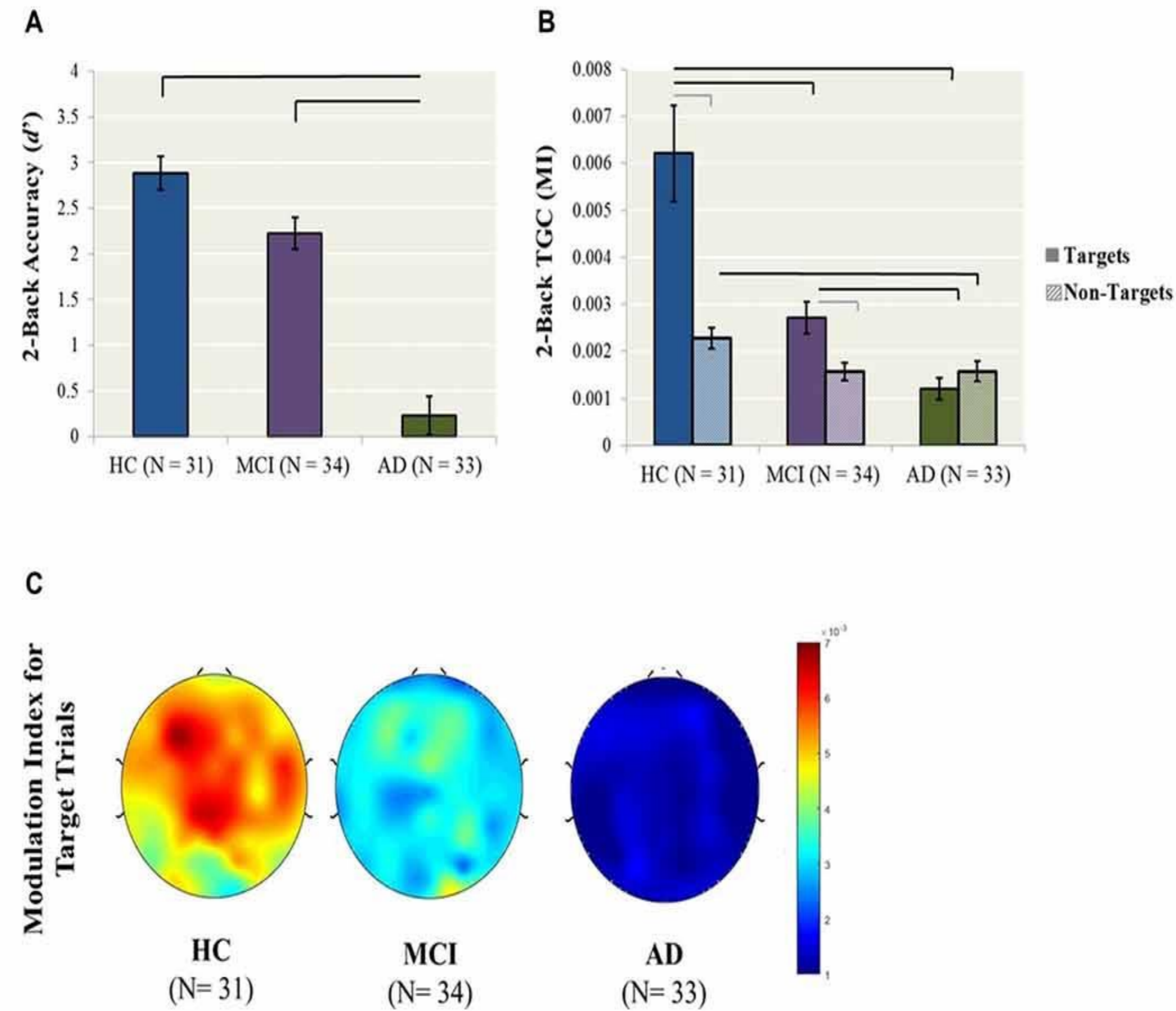


Fig. 1 Group comparison of GBP in different paradigms. *Solid electrodes* represent significantly increased GBP in AD compared to MCI, AD compared to control and MCI compared to control. All solid electrodes ($P < 0.05$)

Theta-Gamma Coupling and Working Memory in Alzheimer's Dementia and Mild Cognitive Impairment

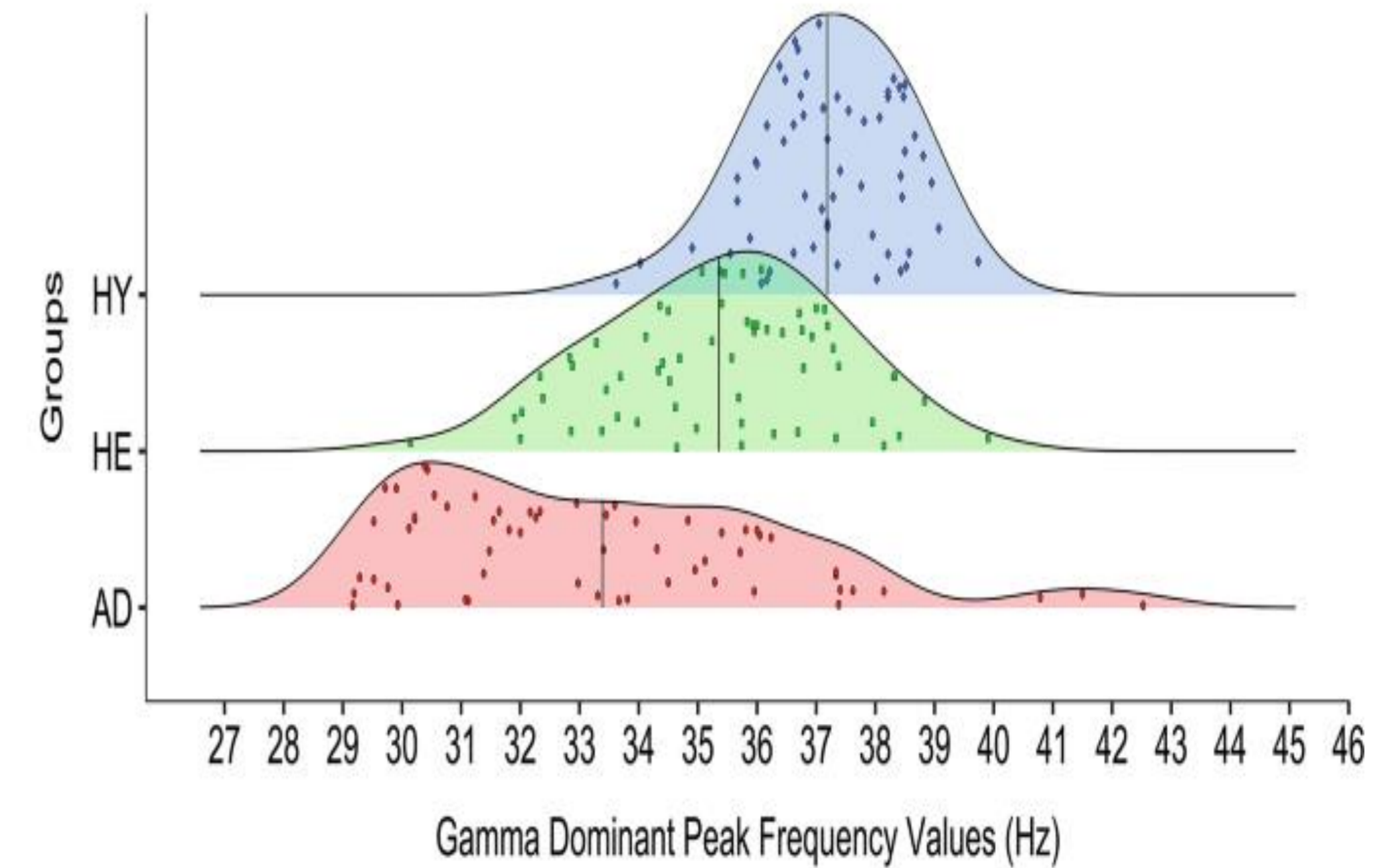
Michelle S. Goodman^{1,2}, Sanjeev Kumar^{1,2,3}, Reza Zomorodji^{1,2}, Zaid Ghazala^{1,2,3,4},
Amay S. M. Cheam^{1,2}, Mera S. Barr^{1,2,4}, Zafiris J. Daskalakis^{1,2,4},
Daniel M. Blumberg^{1,2,3,4}, Corinne Fischer^{4,5}, Alastair Flint^{4,6}, Linda Mah^{4,7},
Nathan Herrmann^{4,8}, Christopher R. Bowie^{1,3}, Benoit H. Mulsant^{1,2,3,4}
and Tarek K. Rajji^{1,2,3,4*} on behalf of PACT-MD Study Group



Alterations of resting-state Gamma frequency characteristics in aging and Alzheimer's disease

Bahar Güntekin^{1,2} · Furkan Erdal^{2,3,8} · Burcu Bölükbaş^{2,3} · Lütfü Hanoğlu^{2,4} · Görsev Yener^{5,6,7} · Rümeyza Duygun^{2,3}

Gamma Dominant Peak Frequency Value Differences of Groups in Eyes-Opened Condition



Groups ■ Alzheimer's Disease (AD) ■ Healthy Elderly (HE) ■ Healthy Young (HY)

Gamma Entrainment

Review article

Theta and gamma oscillatory dynamics in mouse models of Alzheimer's disease: A path to prospective therapeutic intervention

Sonam Fathima Mehak, Apoorva Bettagere Shivakumar, Sparsha Kumari, Bhadra Muralidharan, Gireesh Gangadharan*

Department of Cell and Molecular Biology, Manipal School of Life Sciences, Manipal Academy of Higher Education, Manipal, Karnataka 576104, India

Gamma frequency entrainment attenuates amyloid load and modifies microglia

Hannah F. Iaccarino^{1,3*}, Annabelle C. Singer^{2,3,4*}, Anthony J. Martorell^{1,3}, Andrii Rudenko^{1,3}, Fan Gao^{1,3}, Tyler Z. Gillingham^{1,3}, Hansruedi Mathys^{1,3}, Jinsoo Seo^{1,3}, Oleg Kritskiy^{1,3}, Fatema Abdurrob^{1,3}, Chinnakkaruppan Adaikkan^{1,3}, Rebecca G. Canter^{1,3}, Richard Rueda^{1,3}, Emery N. Brown^{1,3,5,6}, Edward S. Boyden^{2,3,4} & Li-Huei Tsai^{1,3,7}

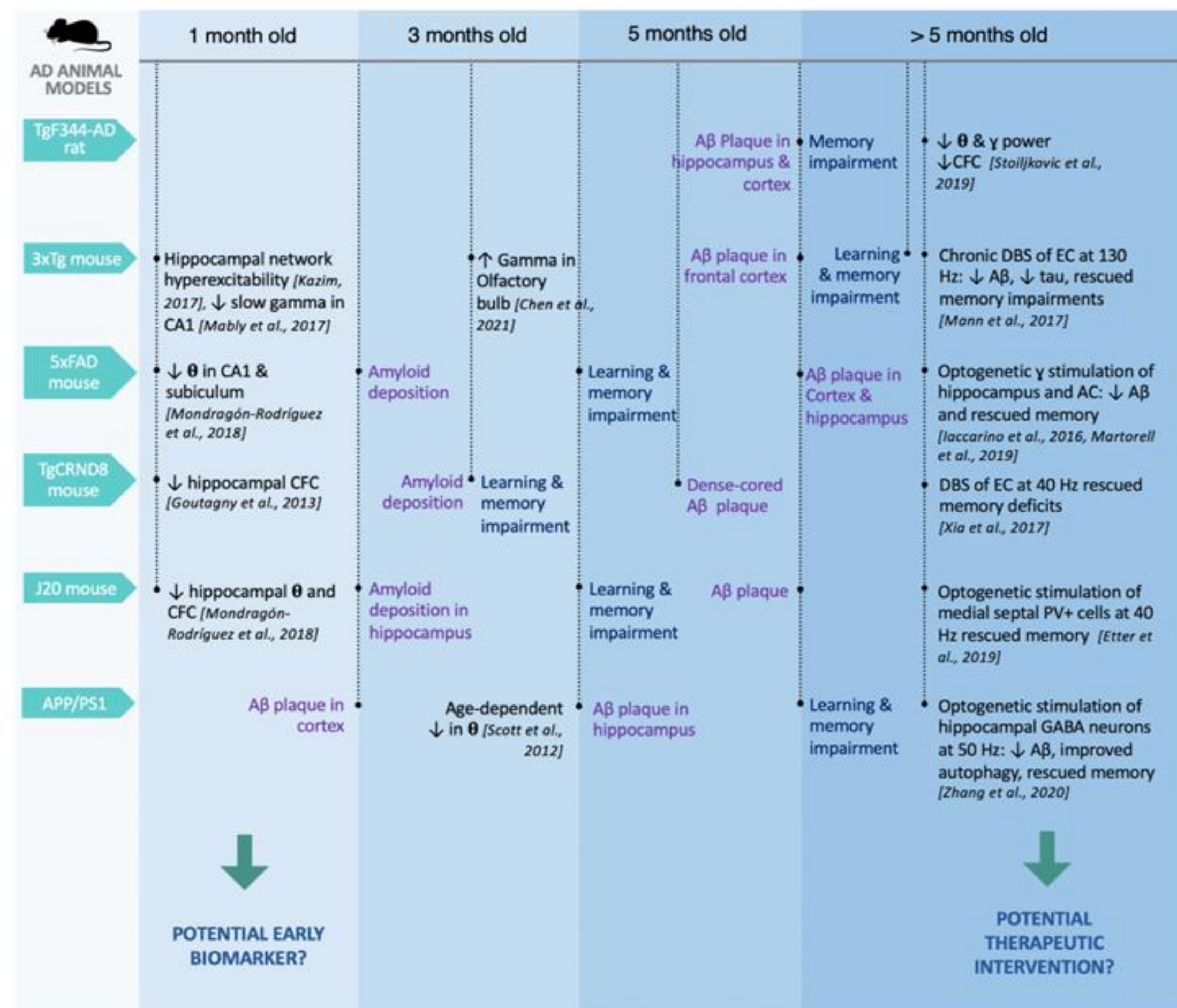
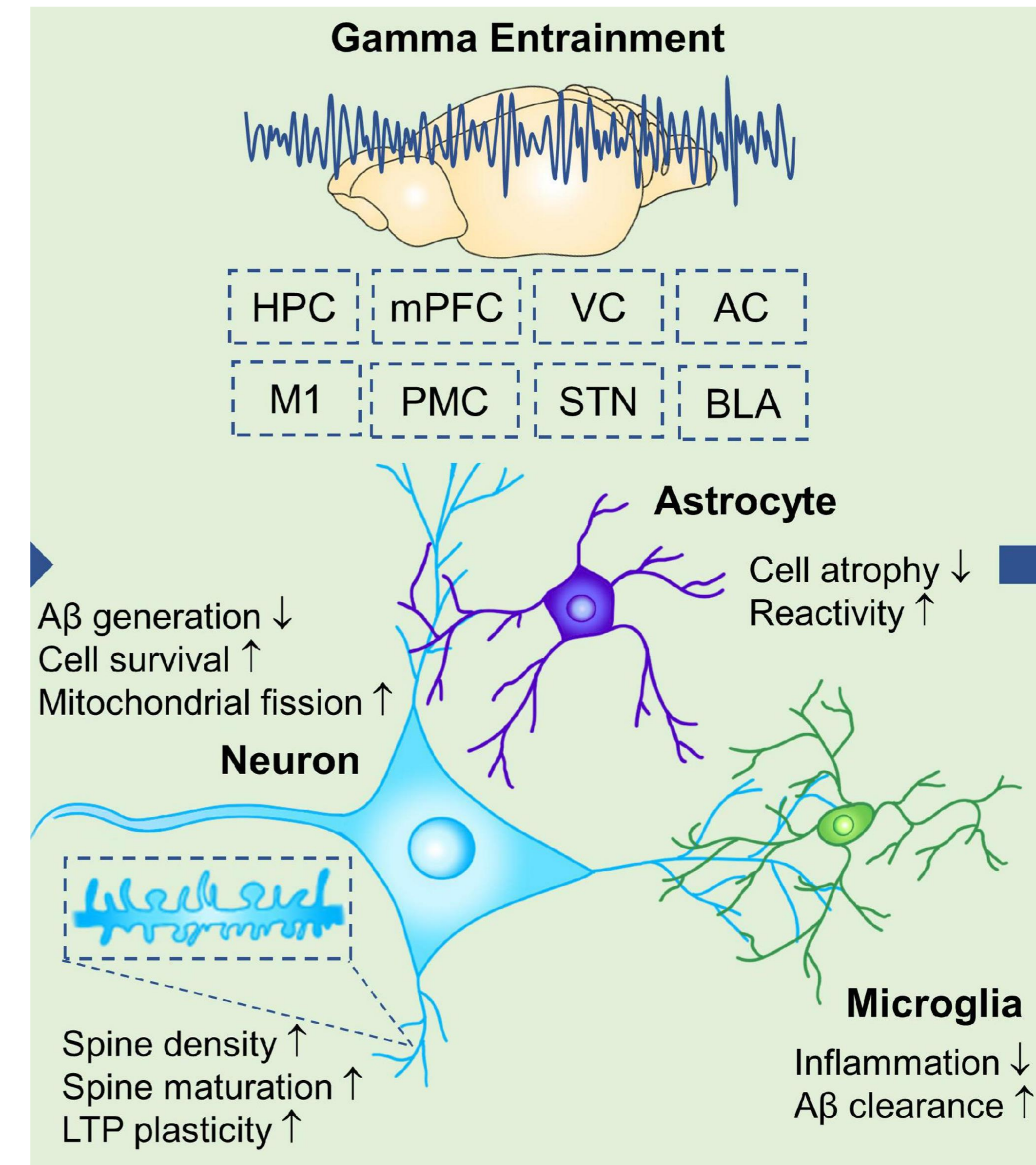


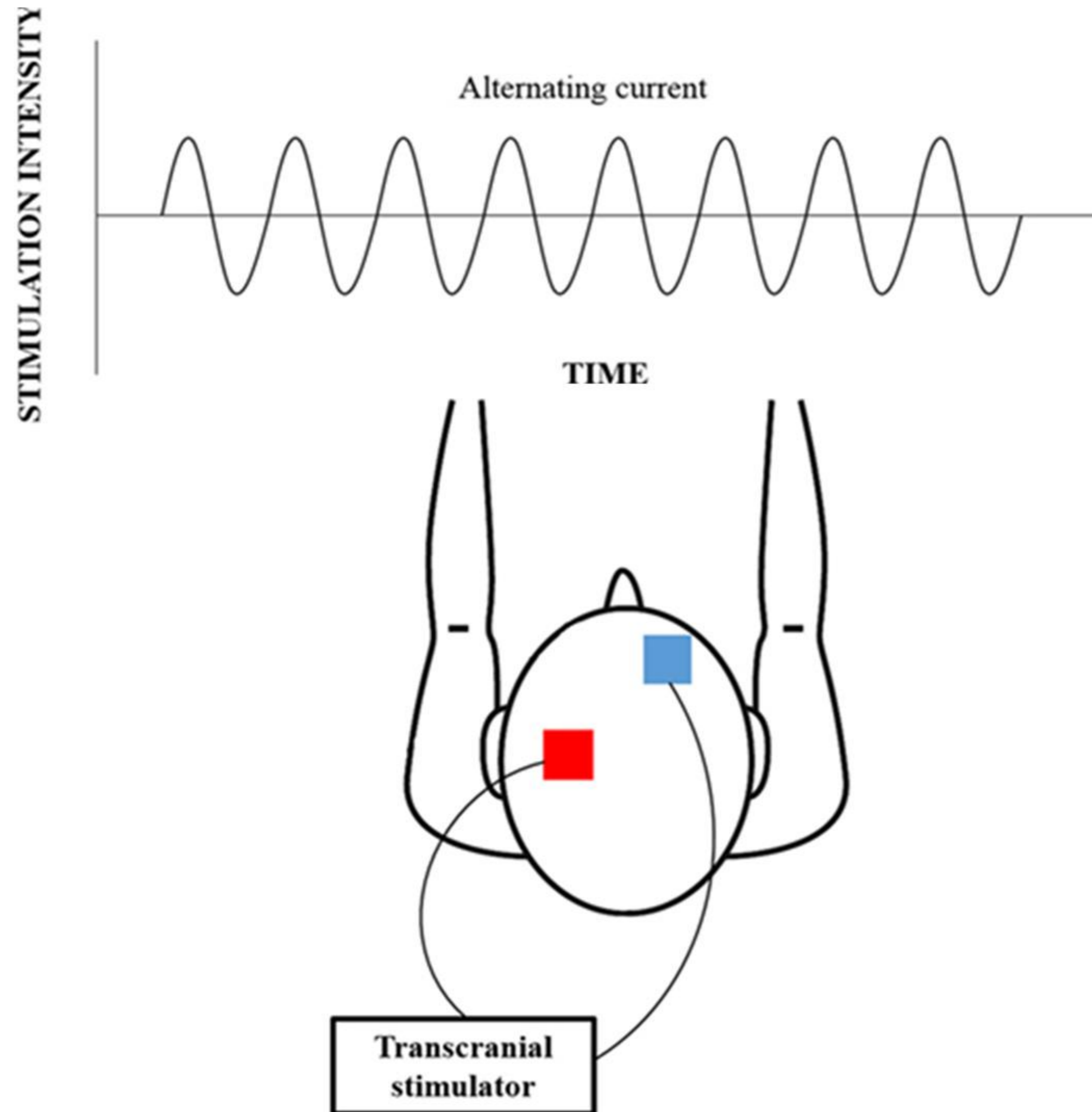
Fig. 1. An overview of the altered theta and gamma oscillatory activity in rodent models of AD. Several rodent models of AD that recapitulate the disease show aberrant theta and gamma oscillations, even before the detection of any amyloid load. These observations posit the use of disrupted oscillatory activities as an early biomarker of AD. It could prove to be more useful than CSF markers that use invasive techniques and is less discriminatory between AD and non-AD dementia. The entrainment of these oscillations using sensory stimuli, optogenetics, and deep brain stimulations (DBS) have been shown to reduce amyloid load and rescue memory impairments, suggesting their potential use in AD therapy.



Gamma Entrainment

tACS

Rythmic (multi-)sensory stimulation



Gamma-tACS and Memory

Review

The effects of transcranial alternating current stimulation on memory performance in healthy adults: A systematic review

Samantha J. Booth ^a, Jason R. Taylor ^{a,1}, Laura ^a, Gorana Pobric ^{a,*,1}

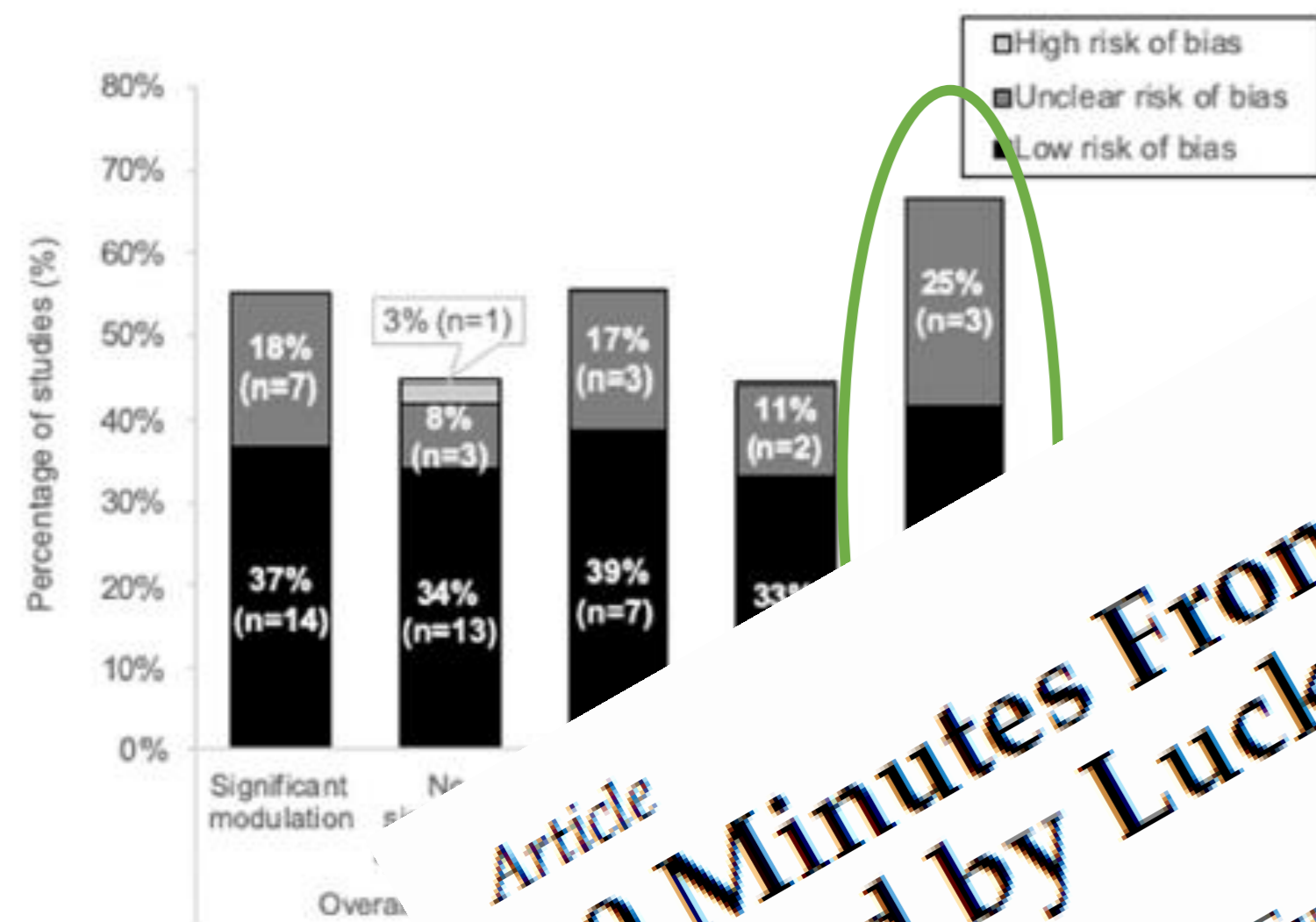


Fig. 5 – Effect of theta-tACS on W.

Article
10 Minutes Frontal 40 Hz tACS—Effects on Working Memory Tested by Luck-Vogel Task
 Eugen Kvašňák ¹, Eva Magyarová ², Miroslav Domankuš ¹, Michael Tesar ³, Jaroslava Kyplová ⁴, Vitaly Fetissov ⁵, Mohammed Abubaker ¹ and Wiam Al Qasem ^{1,*}

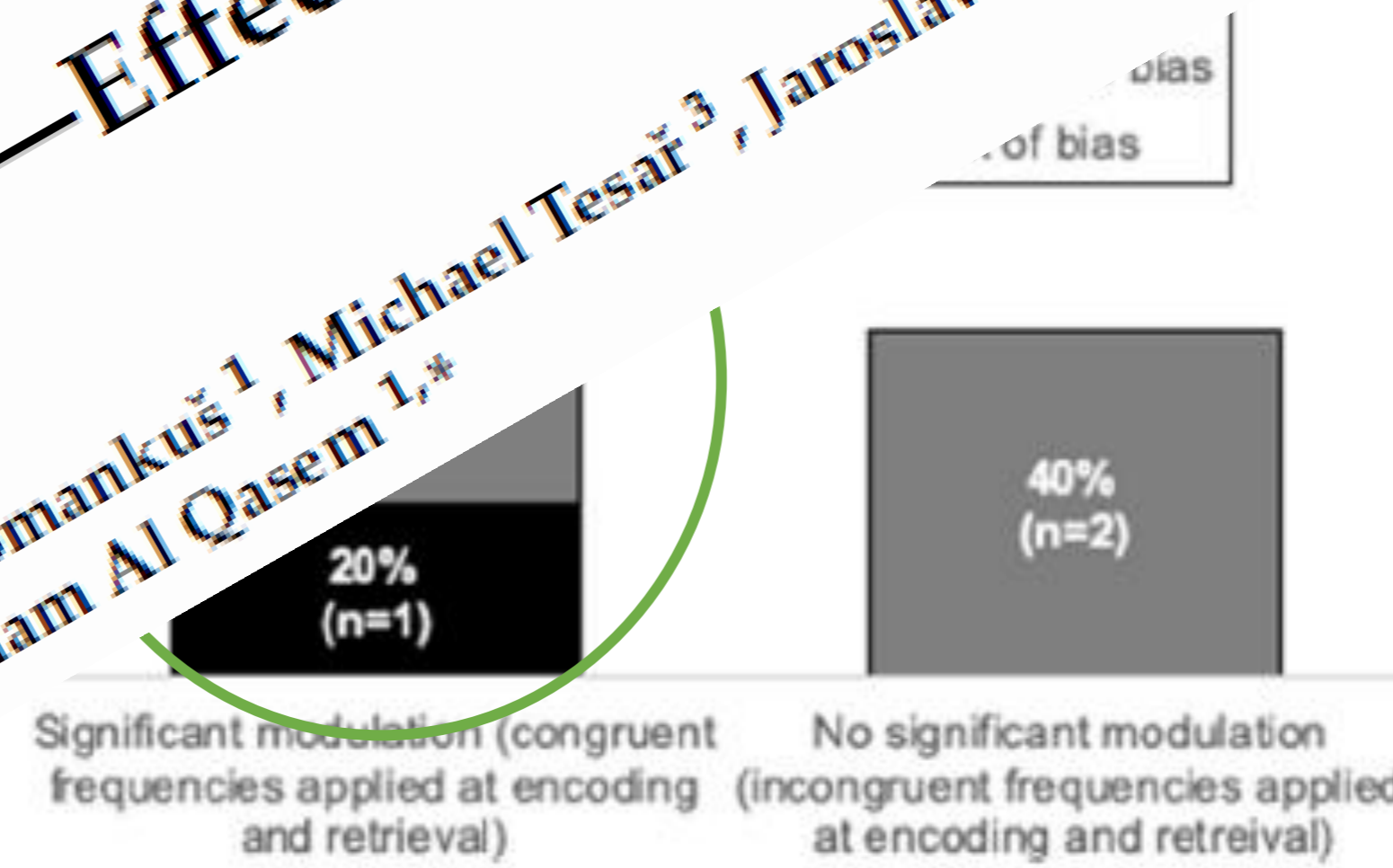
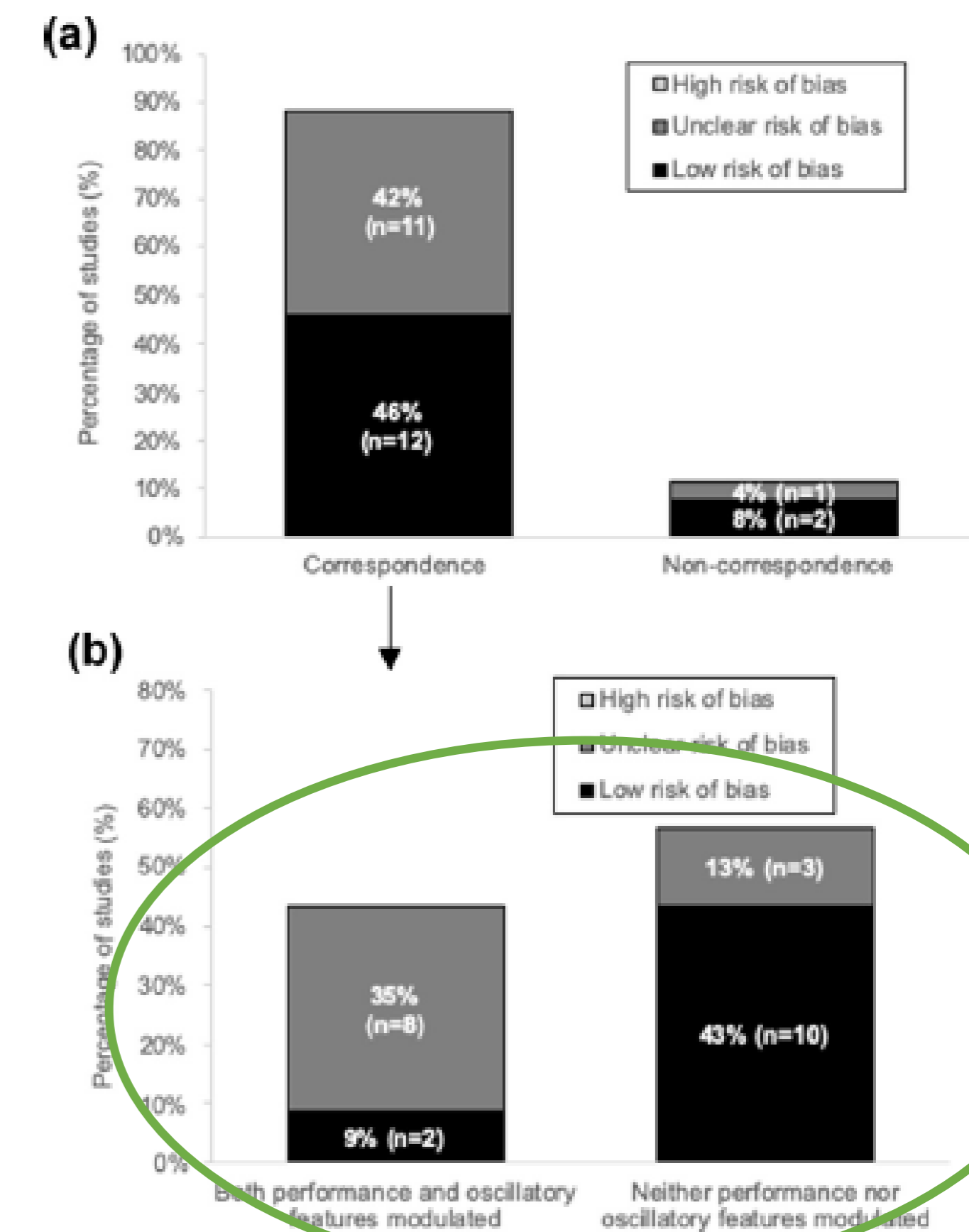


Fig. 6 – Effect of congruent gamma frequencies and incongruent gamma frequencies applied at encoding and retrieval on LTM. Abbreviation(s): n, number of studies.



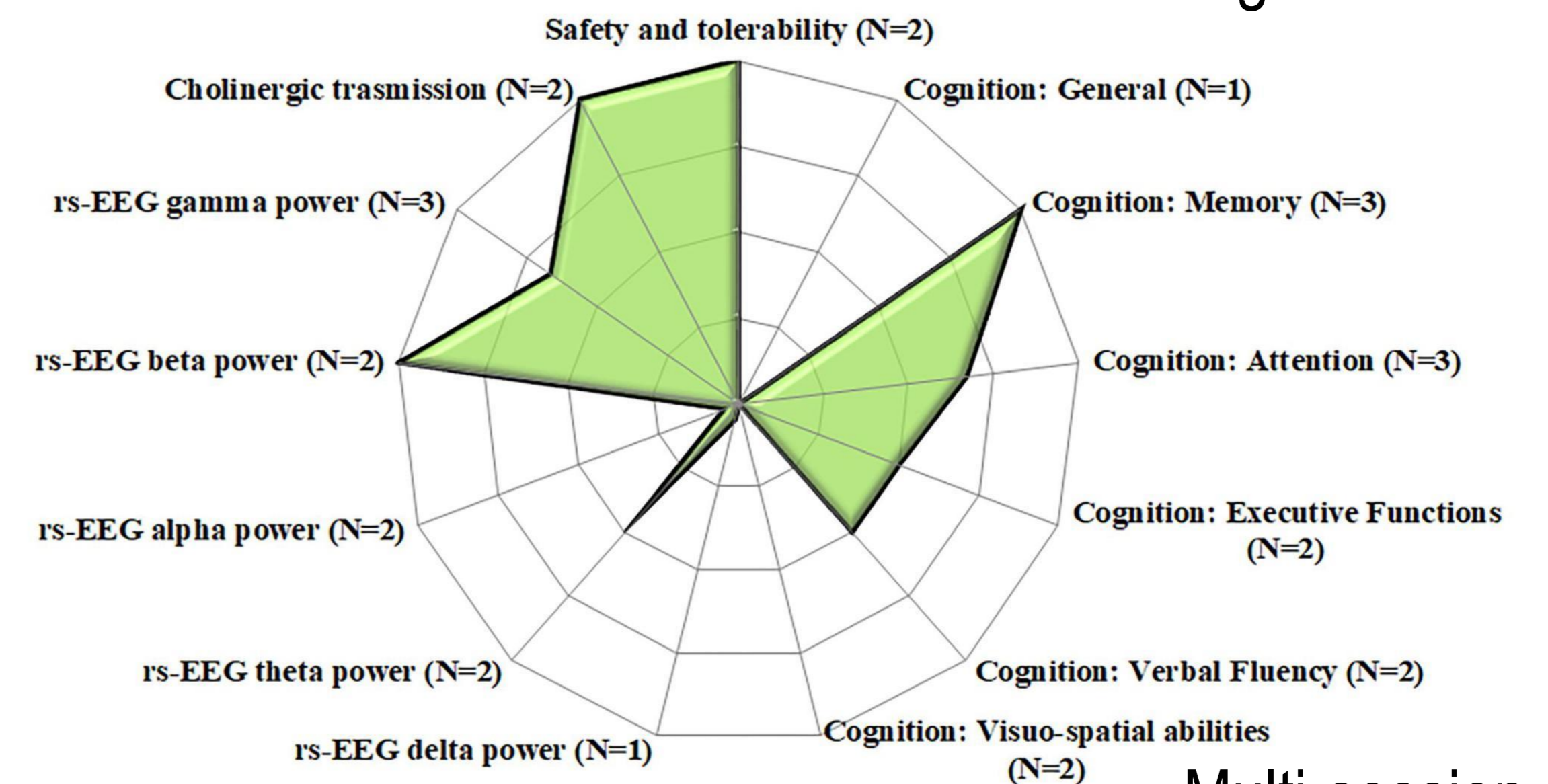
- Parietal theta (40 Hz) => WM enhancement
- Frontal gamma (60 Hz)-tACS => LTM enhancement

Gamma-tACS in AD

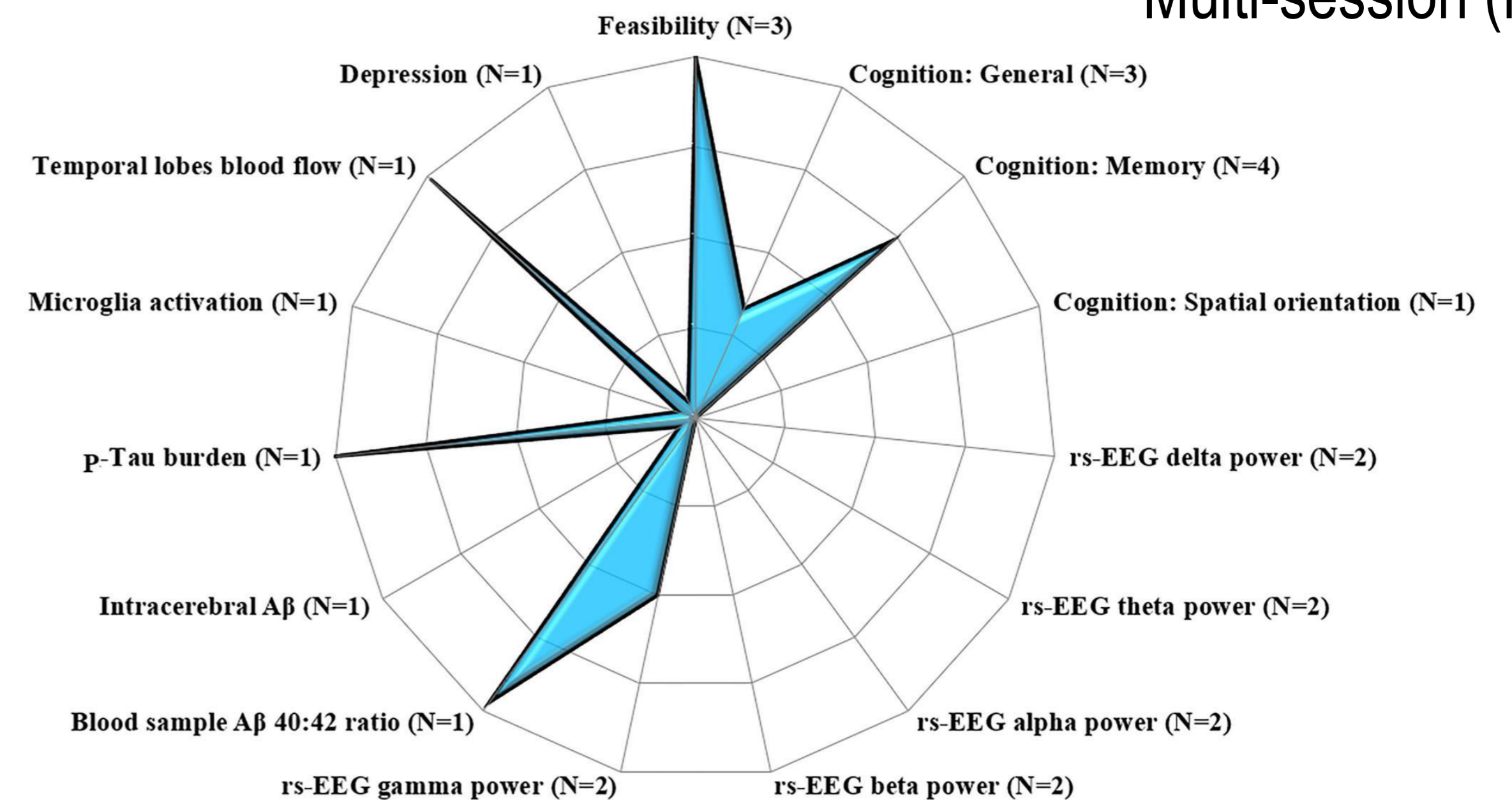
Cognitive and Neuropathophysiological Outcomes of Gamma-tACS in Dementia: A Systematic Review

Valerio Manippa¹ · Annalisa Palmisano¹ · Michael A. Nitsche^{2,3} · Marco Filardi^{4,5} · Davide Vilella⁴ · Giancarlo Logroscino^{4,5} · Davide Rivolta¹

Single-session (N=4)



Multi-session (N=6)

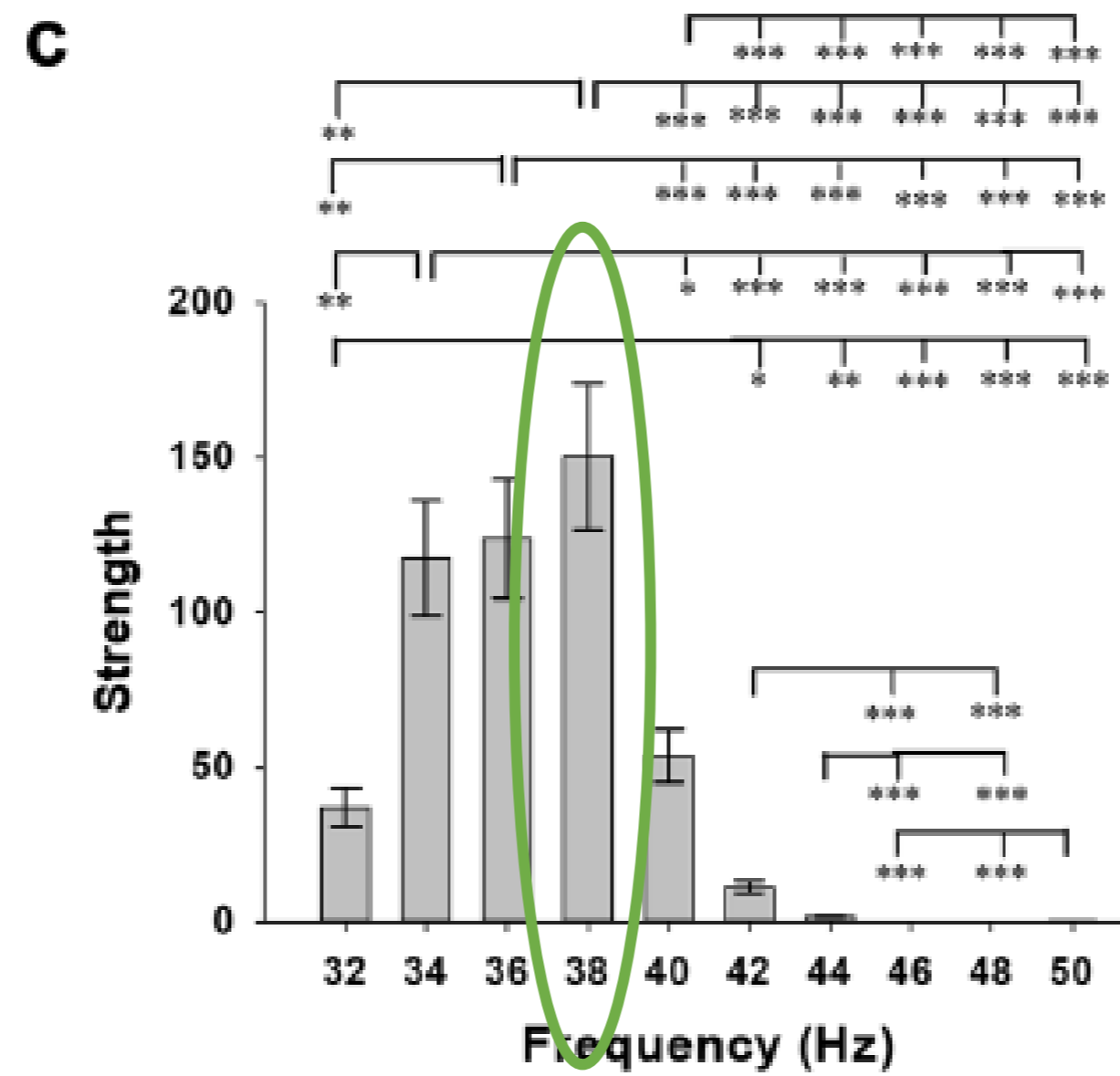


- Site of stimulation
- Intensity/Frequency of stimulation
- Session numbers
- Sample selection
- Outcomes


GENUS in HC

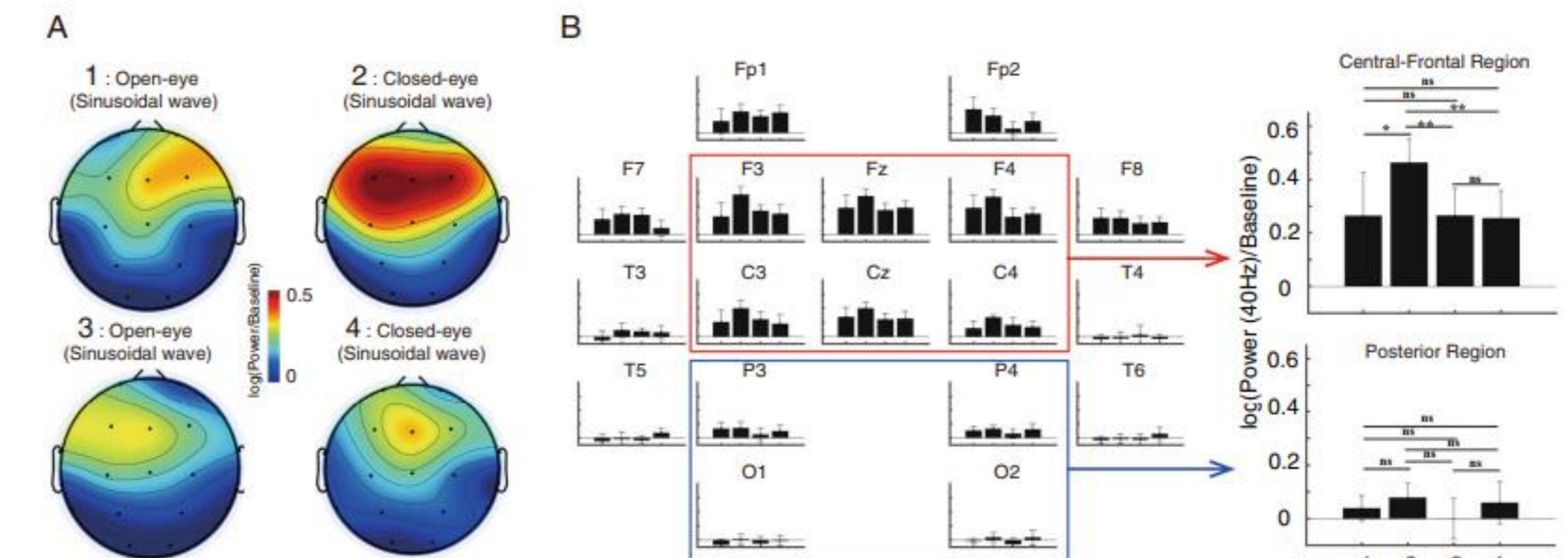
Optimal flickering light stimulation for entraining gamma waves in the human brain

Kanghee Lee^{1,7}, Yeseung Park^{1,2,7}, Seung Wan Suh³, Sang-Su Kim⁴, Do-Won Kim⁴, Jaeho Lee⁵, Jaehyeok Park⁵, Seunghyup Yoo⁵ & Ki Woong Kim^{1,2,6}✉



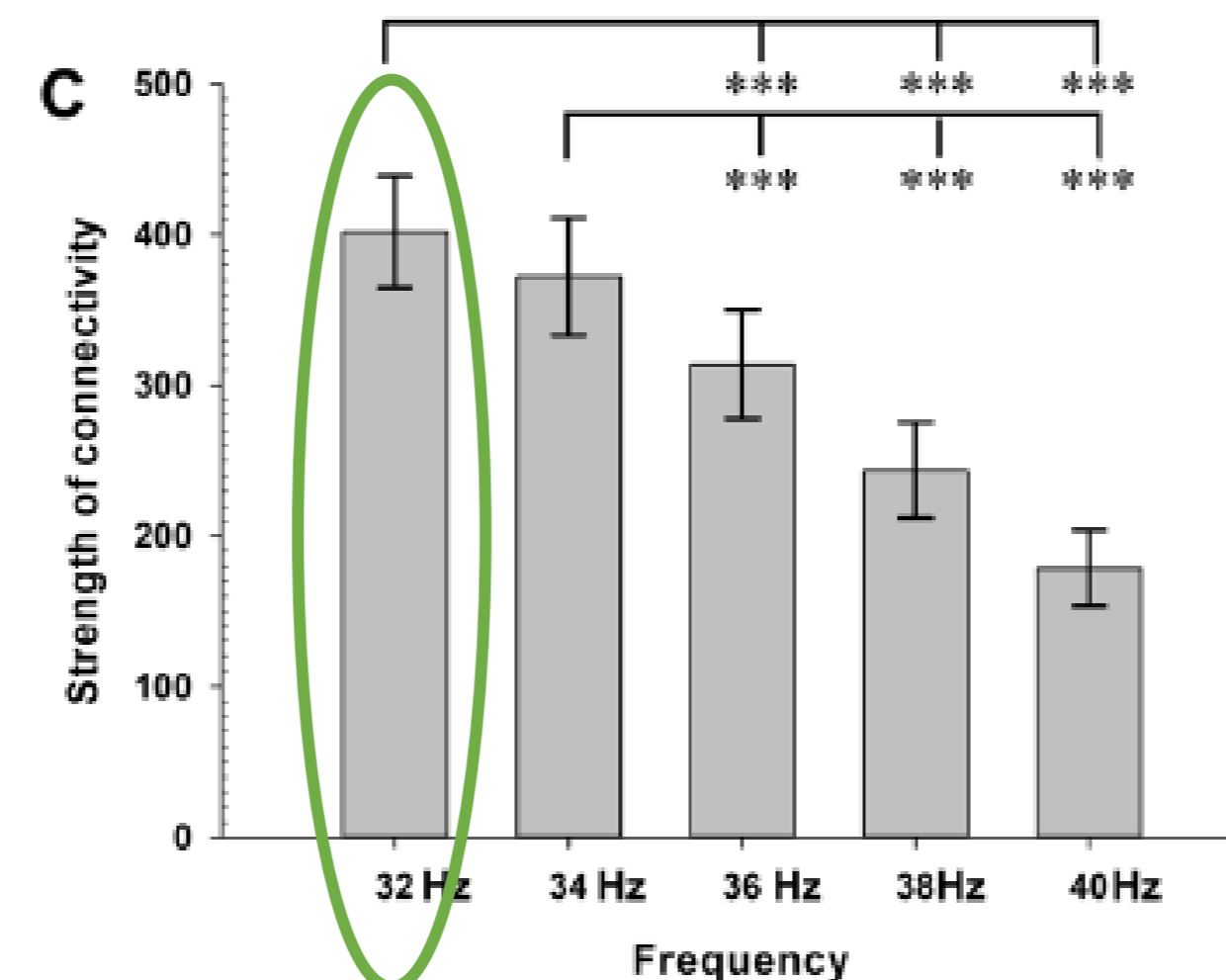
Enhancement of the neural response during 40 Hz auditory entrainment in closed-eye state in human prefrontal region

Chuanliang Han¹  · Xixi Zhao^{2,3} · Meijia Li⁴ · Naem Haihambo⁴ · Jiayi Teng^{5,6} · Sixiao Li^{5,7} · Jinyi Qiu⁸ · Xiaoyang Feng⁹ · Michel Gao⁵



Optimal flickering light stimulation for entraining gamma rhythms in older adults

Yeseung Park^{1,2,8}, Kanghee Lee^{1,8}, Jaehyeok Park³, Jong Bin Bae^{1,7}, Sang-Su Kim⁴, Do-Won Kim⁴, Se Joon Woo^{5,6}, Seunghyup Yoo³ & Ki Woong Kim^{1,2,7}✉



GENUS in AD

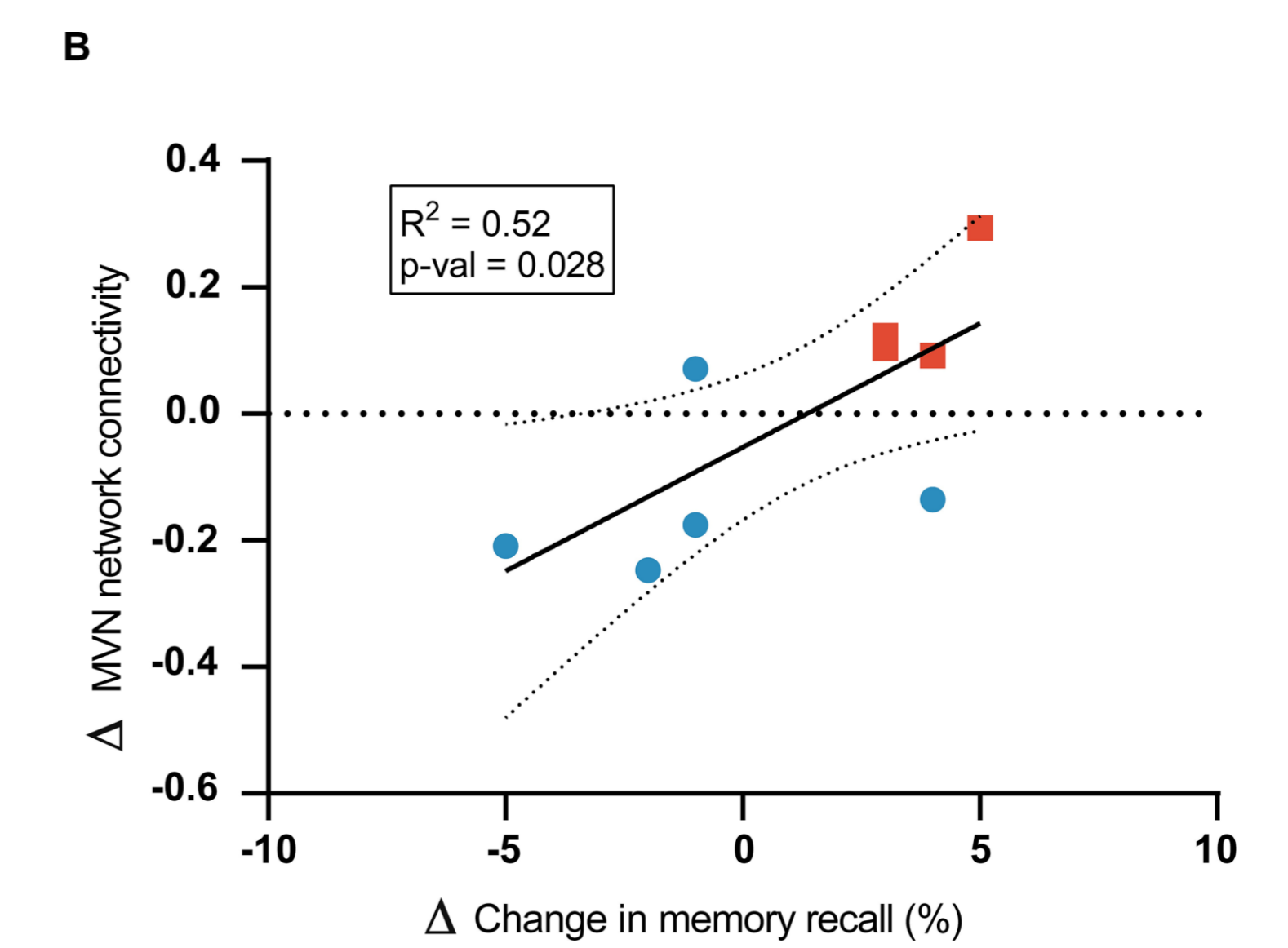
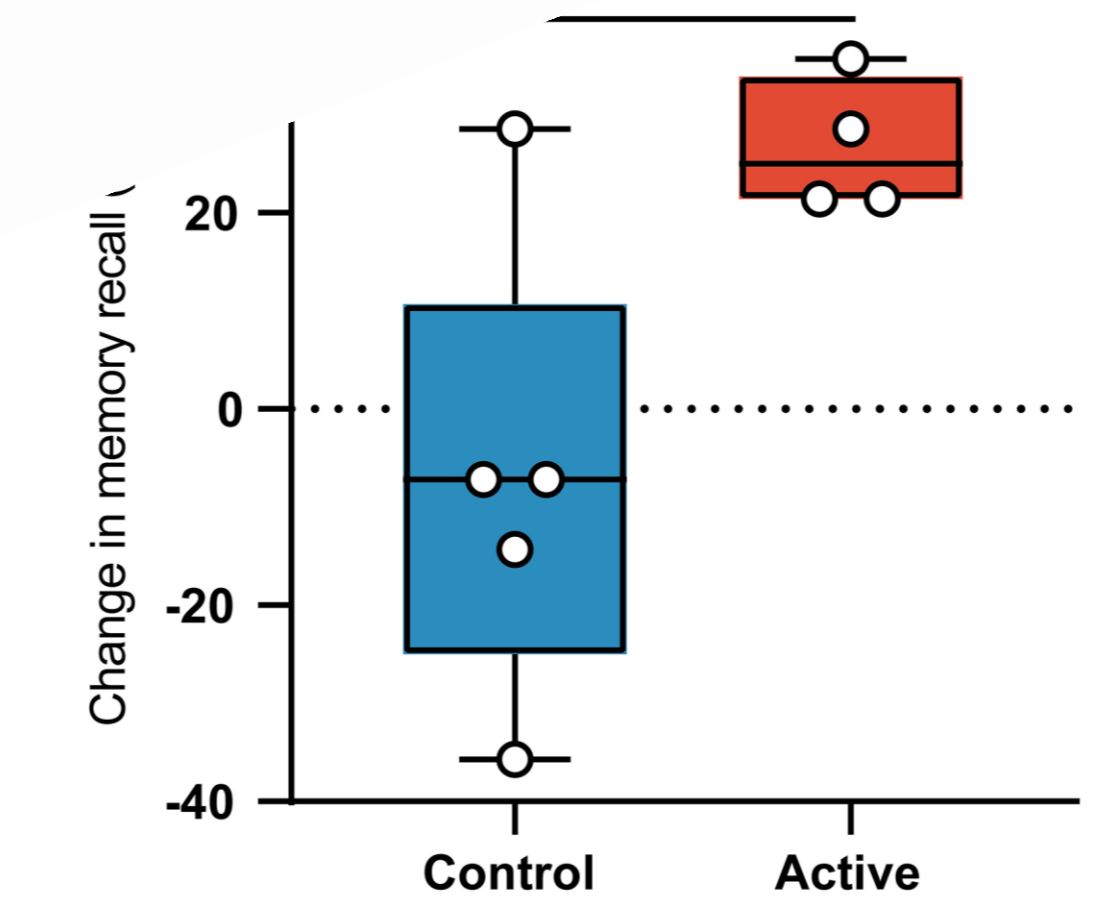
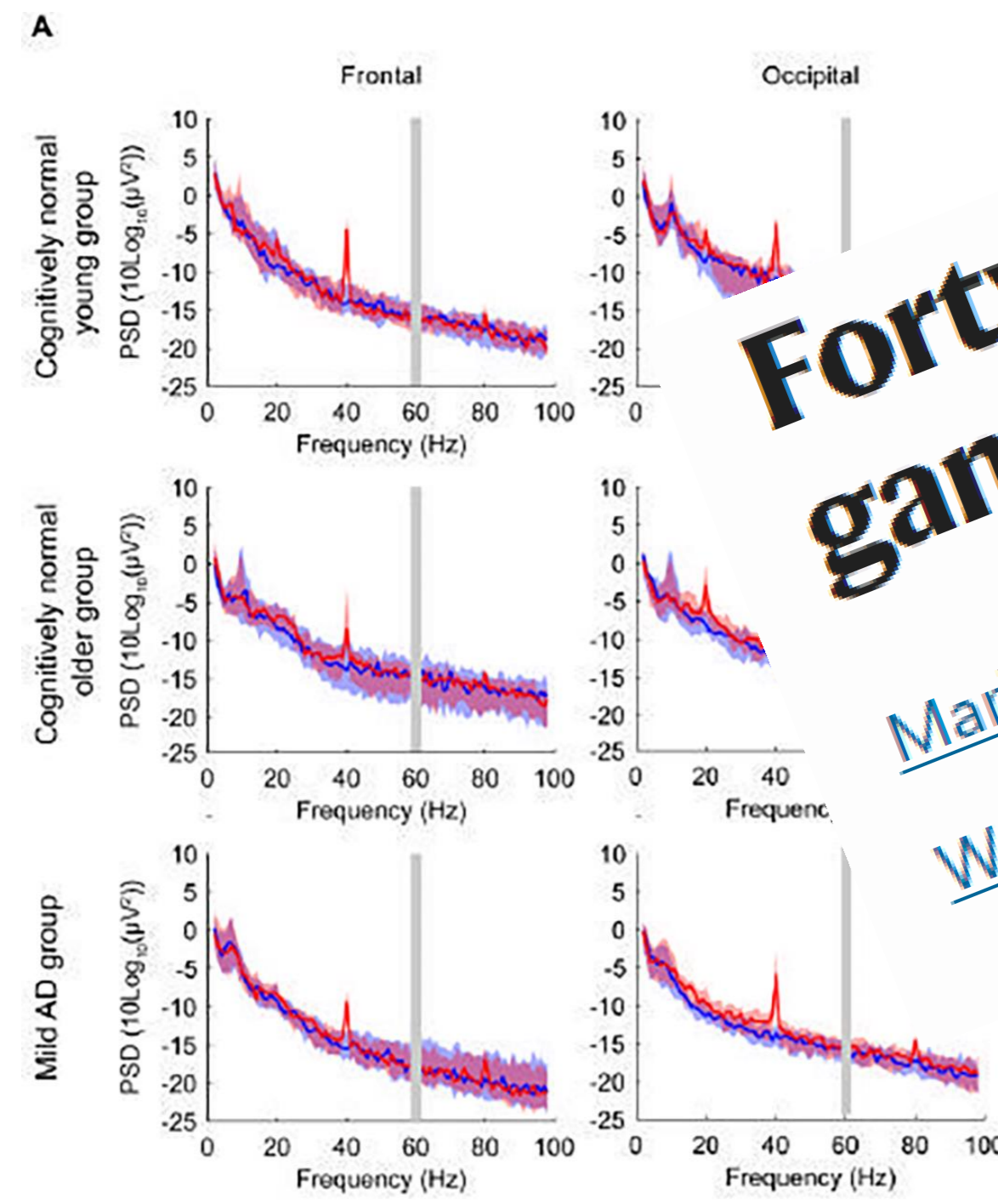
RESEARCH ARTICLE

Gamma frequency sensory stimulation in mild probable Alzheimer's dementia patients: Results of feasibility and pilot studies

Diane Chan^{1,2,3,4}, Ho-Jun Suk^{1,2}, Brennan L. Jackson^{1,2,5,6}, Noam Nitzan^{1,2}, Danielle Stark^{1,2}, Elizabeth B. Klerman^{3,8}, Erin Kitchener^{1,2}, Sara Avalos^{1,2}, Gabrielle de Weck^{1,2}, Arit Banerjee^{1,2}, Sara Colton Stearns⁹, Aaron D. Boes¹⁰, Brandt Uitermark III^{11,12}, Eliezer J. Sternberg^{13,14}, Alfonso Nieto-Castanon¹⁵, Susan Whitfield-Gabrieli⁷, Emery N. Browne¹⁶, Bradford C. Dickerson^{3,4}, Li-Huei Tsai^{1,2}

Forty-hertz light stimulation does not entrain native gamma oscillations in Alzheimer's disease model mice

Marisol Soula, Alejandro Martín-Ávila, Yiyao Zhang, Annika Dhingra, Noam Nitzan, Martin J. Sadowski, Wen-Biao Gan & György Buzsáki



C

Open questions

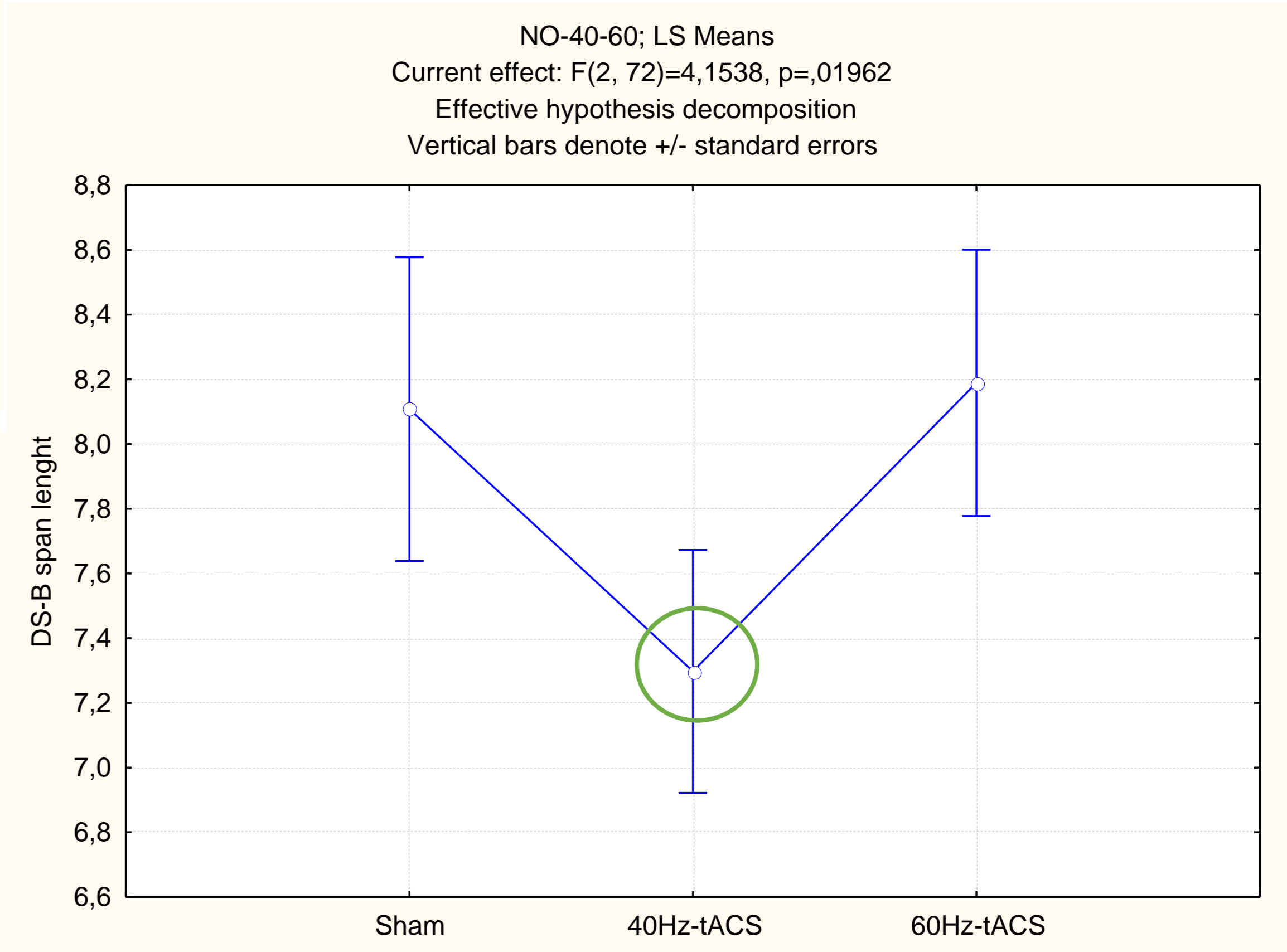
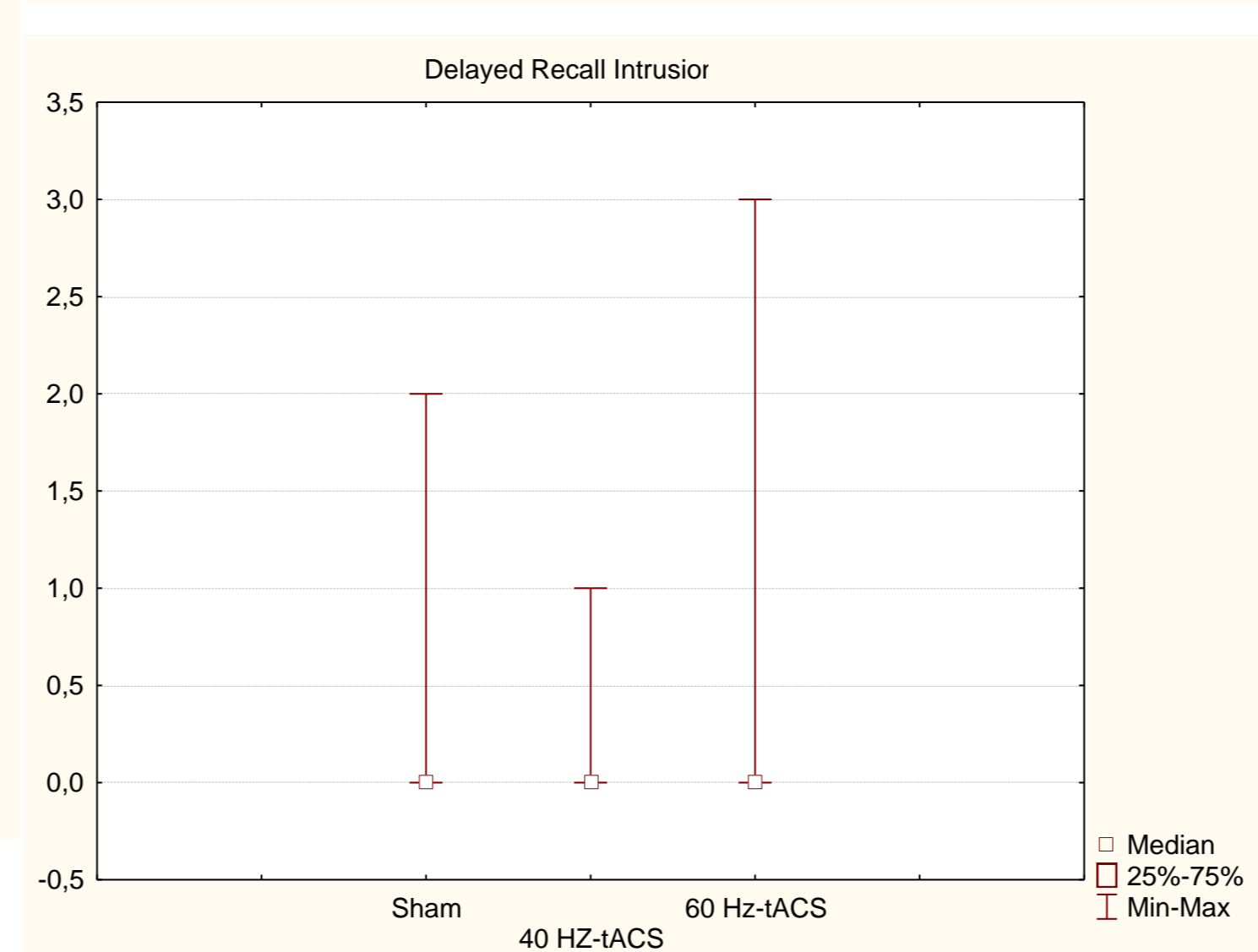
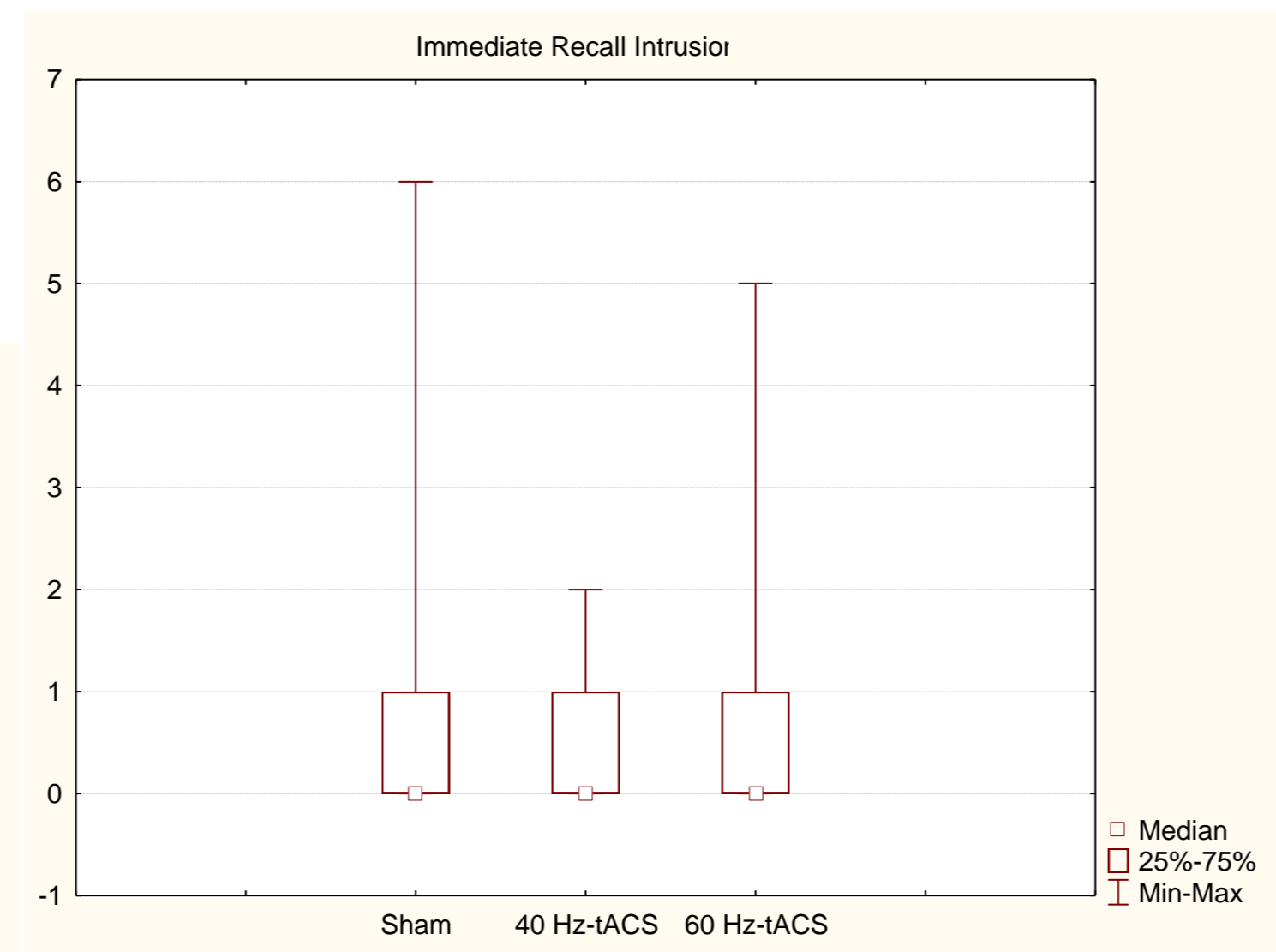
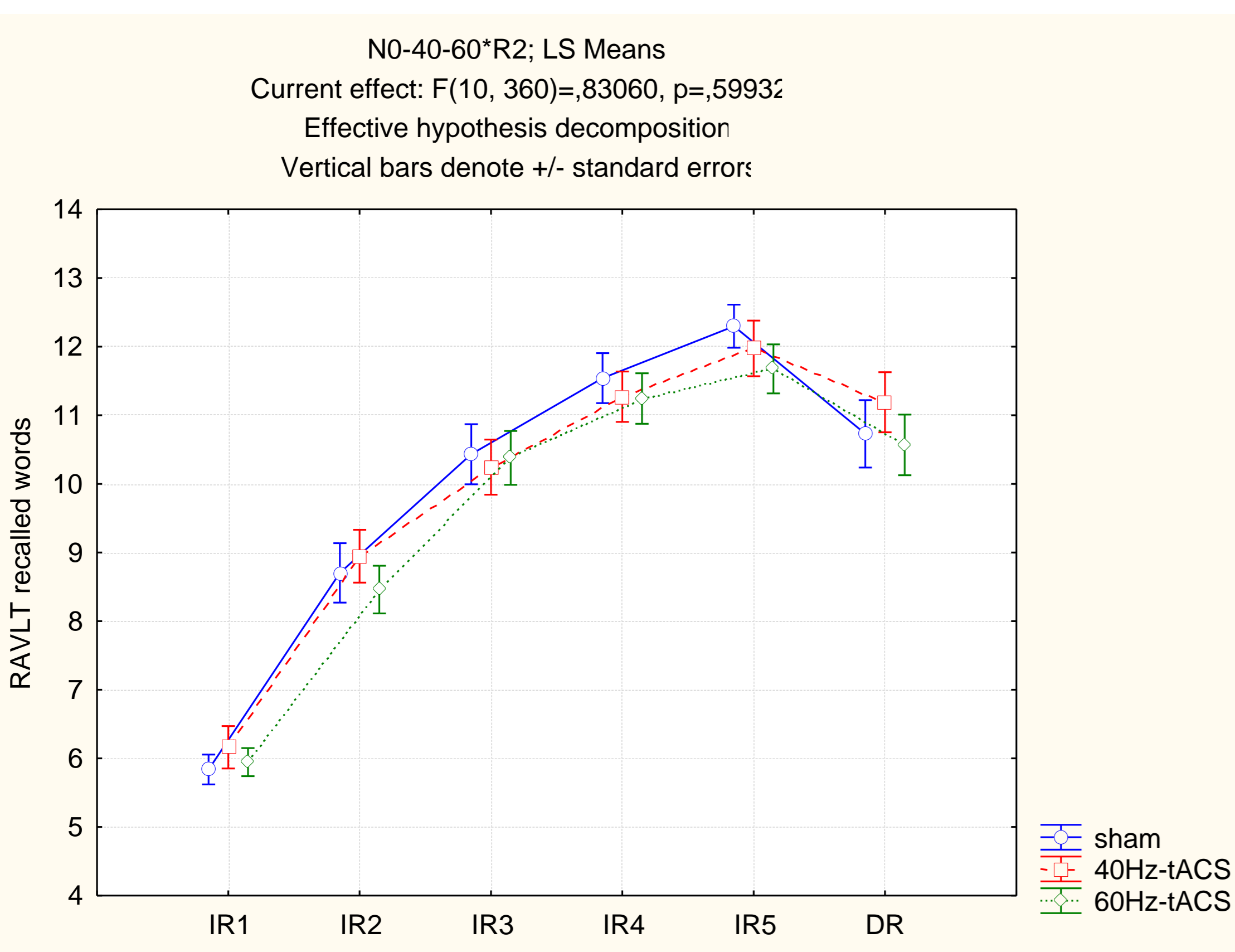
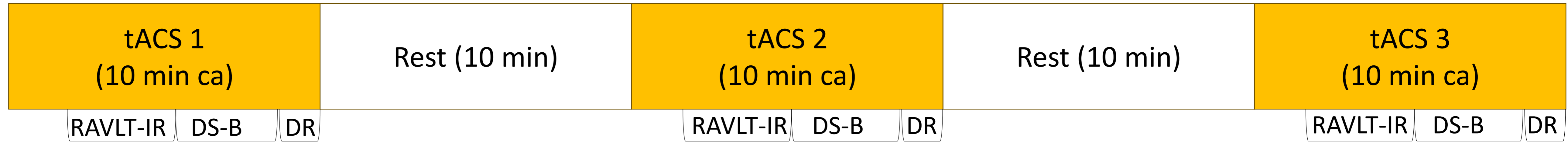
1. Is the effect of gamma stimulation specific to memory?
2. What happens if we stimulate healthy individuals at 40 Hz?
3. Do GENUS and Gamma-tACS have the same effects on memory processes?

Gamma-tACS and Memory

Manippa et al., in prep

T7/T8, 2mA

- Sham
- 40Hz
- 60Hz



GENUS in HC

Gamma (60 Hz) auditory stimulation improves intrusions but not recall and working memory in healthy adults

Valerio Manippa ^{a,*,1}, Marco Filardi ^{b,c}, Davide Vilella ^b, Giancarlo Logroscino ^{b,c}, Davide Rivolta ^a

- rAS, 40db
- NO_AS
 - 40Hz
 - 60Hz

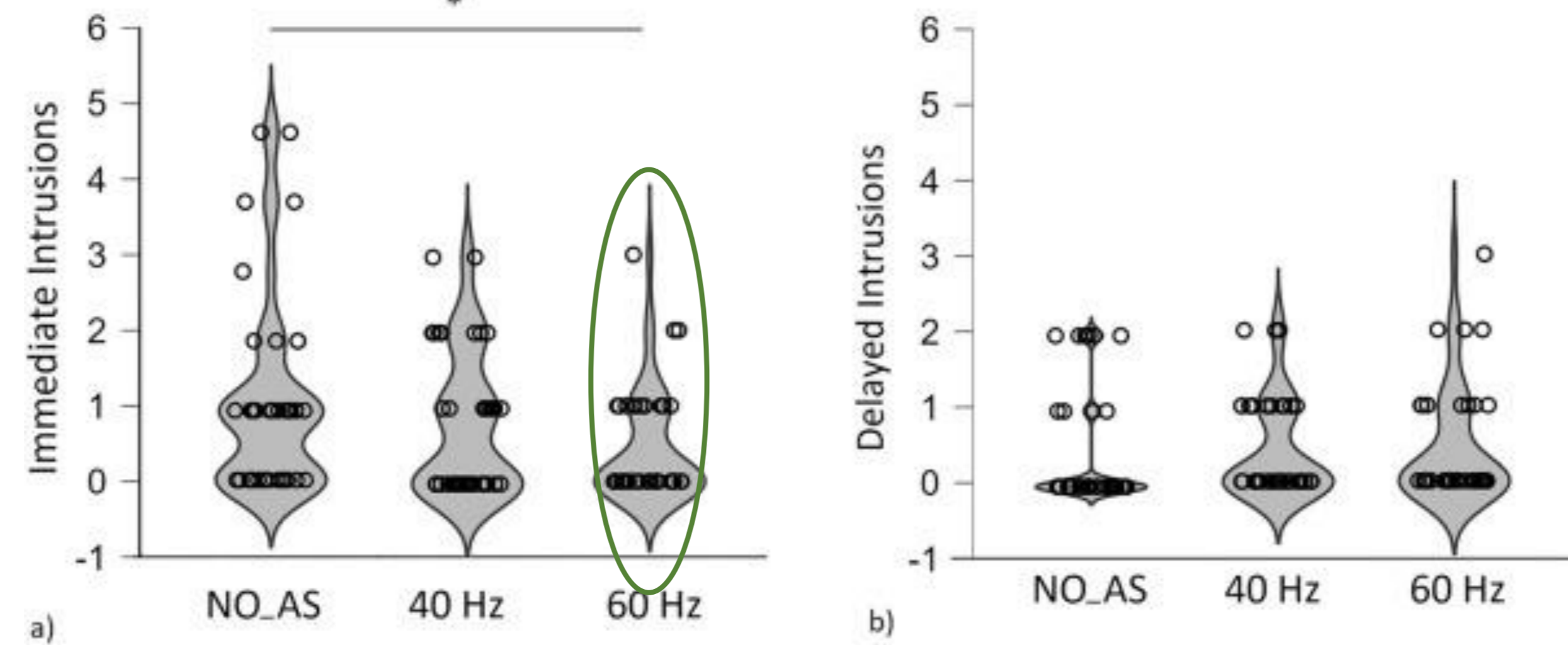
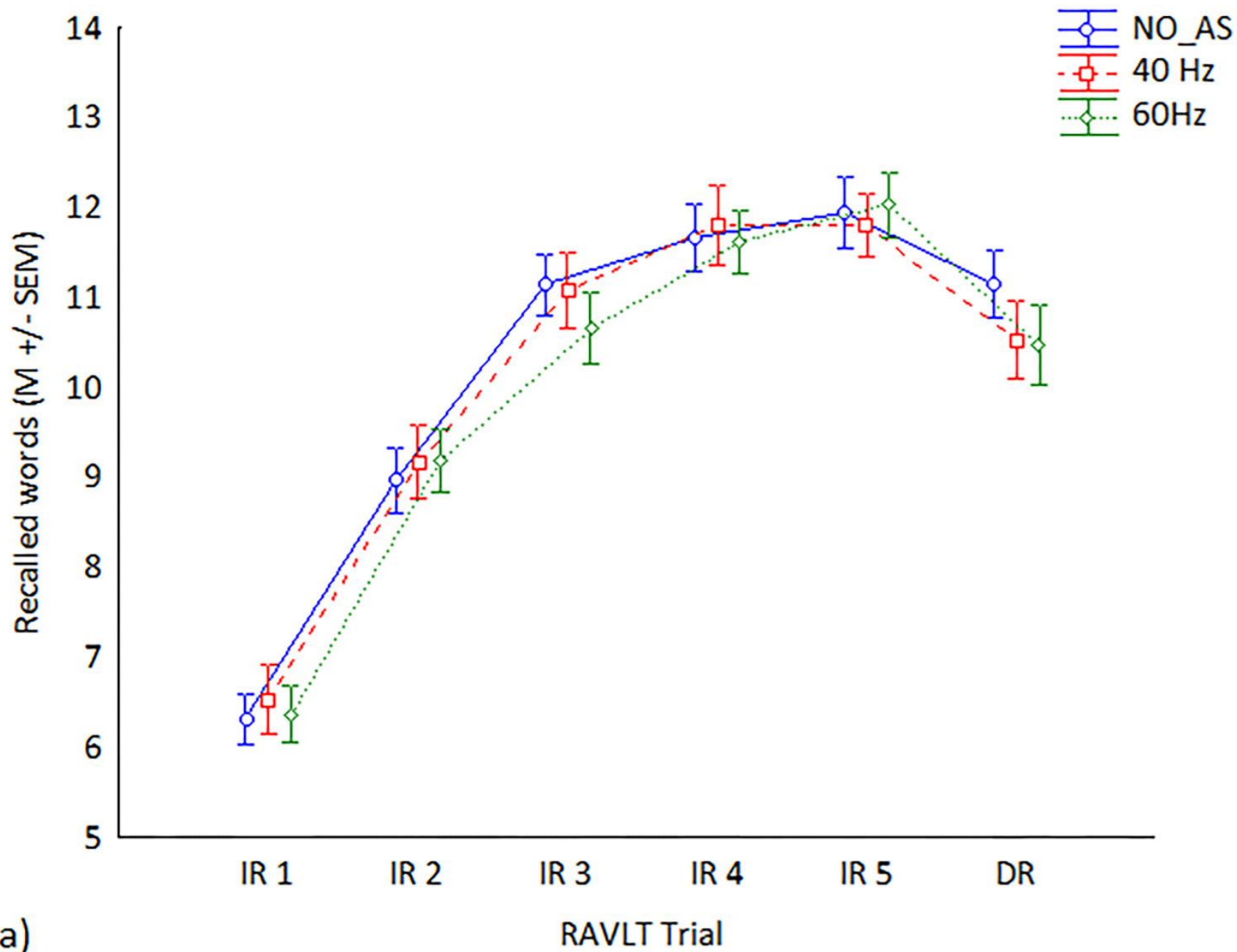
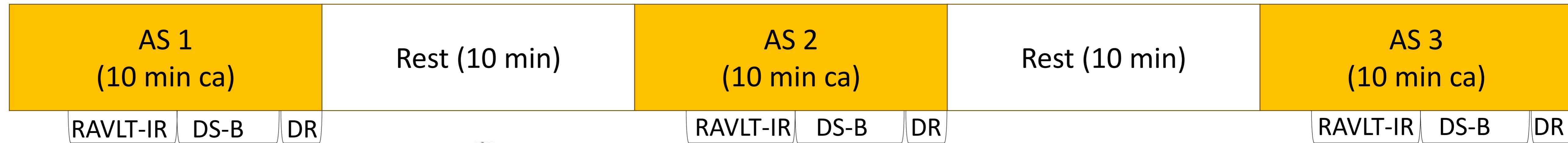
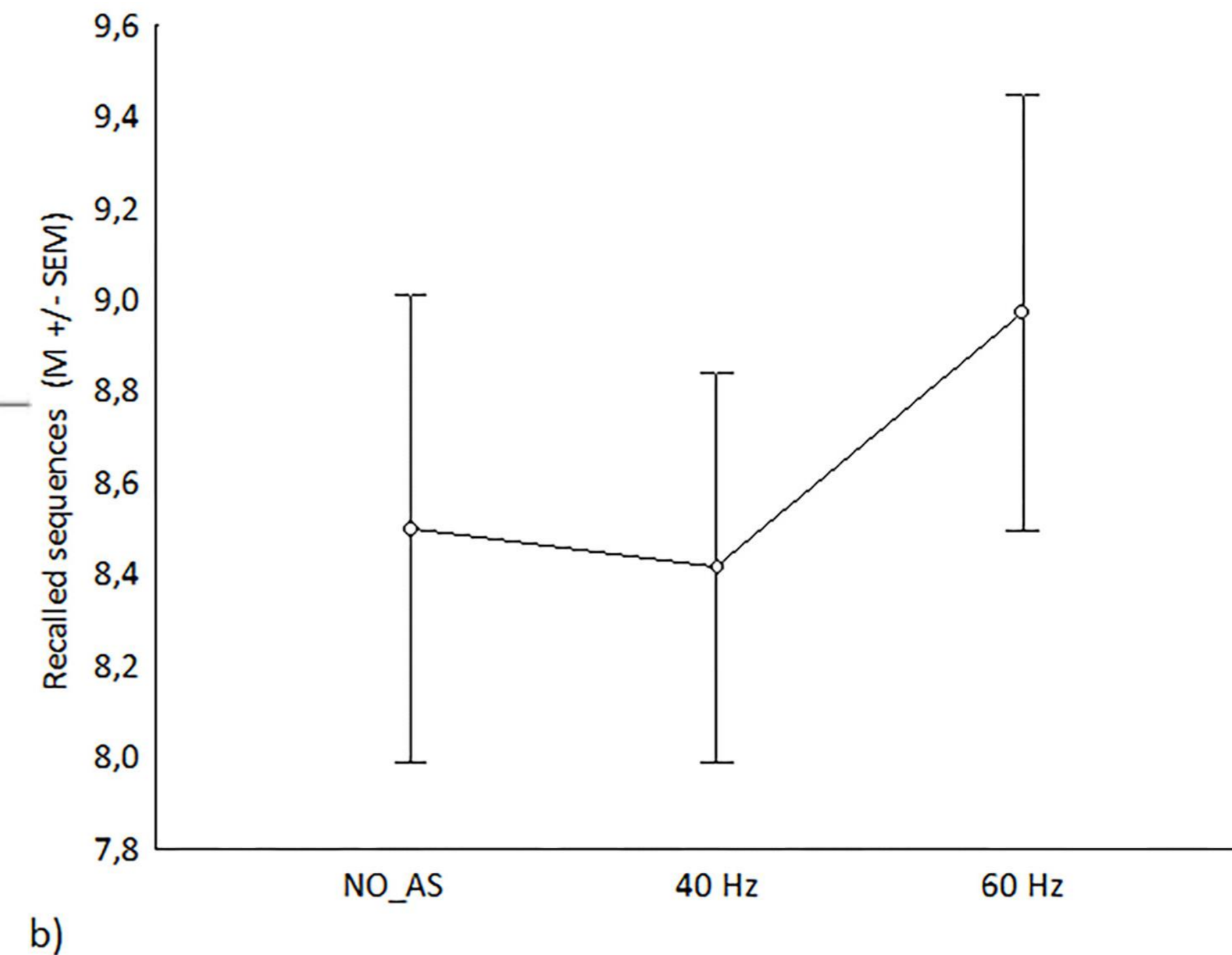


Table 2
Correlation between the DS-B score and the RAVLT scores for each stimulation condition. * ($p < 0.05$).

	Digit Span Backward		
	NO_AS	40 Hz	60 Hz
Pearson's correlation	<i>r</i>	<i>r</i>	<i>r</i>
RAVLT-IR	.460*	.308	.535*
RAVLT-DR	.253	.156	.353*
Spearman's correlation	<i>r</i>	<i>r</i>	<i>r</i>
RAVLT-II	-.109	-.077	-.381*
RAVLT-DI	.245	.037	-.093



Take home message

- Gamma stimulation holds promising potential in the field of neuroenhancement and therapies for neurodegenerative diseases
- There is a need to further investigate how gamma oscillations/stimulations influence cognitive processes in both healthy and clinical samples
- The optimization of stimulation parameters is essential for the development of effective clinical protocols