Digital Neurotherapeutics

Neurotechnology for everybody, anytime by anyone

Javier Mínguez
Scientific Director of Bitbrain

Professor Universidad de Zaragoza

First steps in neurotechnology (2003-2012)

Bitbrain

Second demonstration of wheelchair control only with brain thoughts
One of the most cited papers on BCI for robot control
Best Science & Technology video of the month (April 2009, Global)

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- Pioneering brain-computer interfaces (BCI)
- 150+ scientific papers
- Large scientific impact in Robotics and BCI
- Very large traction in EU projects.

Research featured in:

nature WIRED BBC
Science NewScientist The Economist

[1] I Iturrate, et al. A noninvasive brain-actuated wheelchair based on a P300 neurophysiological protocol and automated navigation. IEEE transactions on robotics 25 (3), 614-627

First steps in neurotechnology (2003-2012)

First demonstration of a Robot that learns its operation from brain signals (2015)

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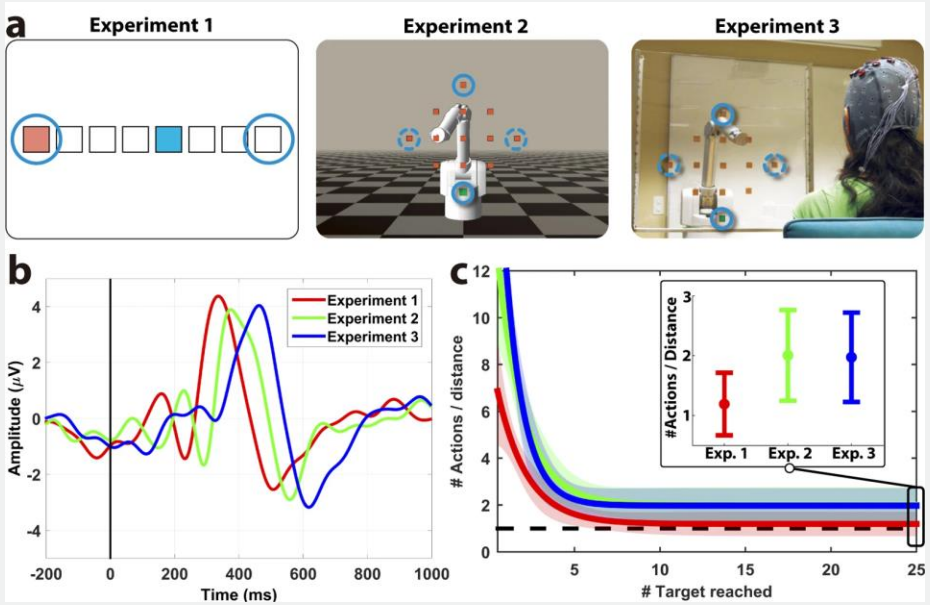
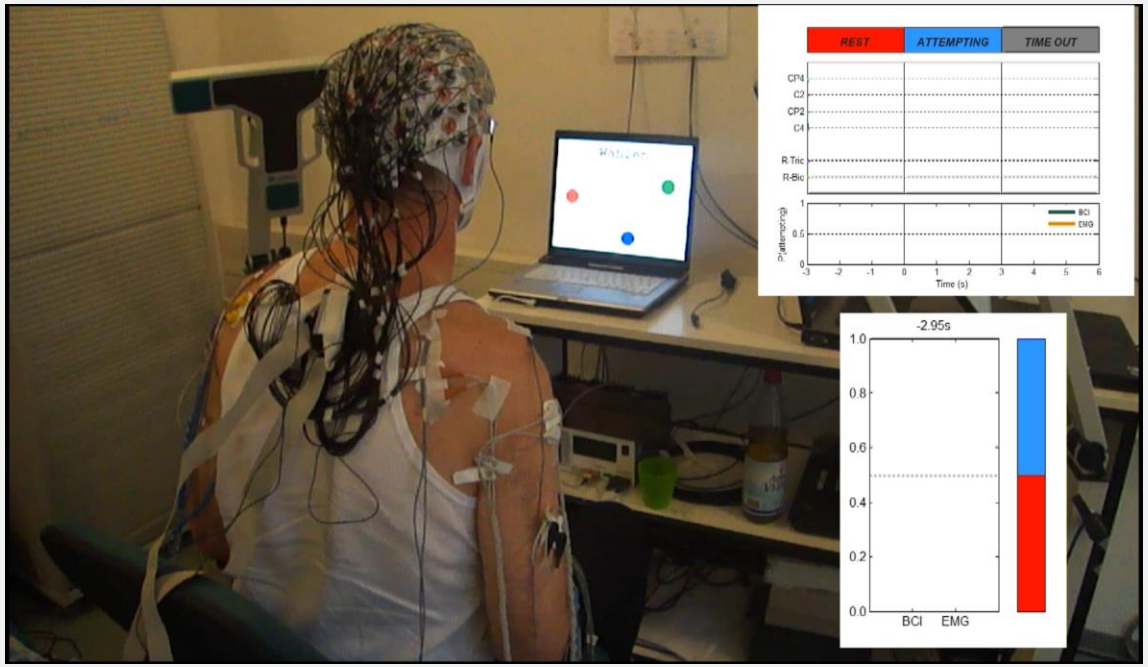


[2] Iturrate et. al, L. et al. Teaching brain-machine interfaces as an alternative paradigm to neuroprosthetics control. Scientific Reports - Nature 5, 13893 (2015).

First steps in neurotechnology (2003-2012)

Bitbrain



First demonstration that natural motor intention can be reliably captured in stroke patients from healthy motor cortex

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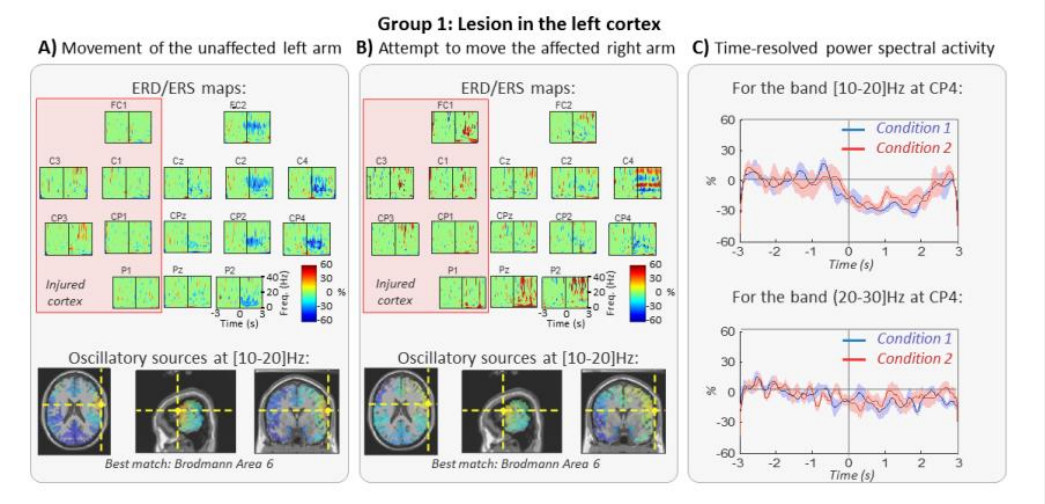


[3] J. Antelís Decoding upper limb movement attempt from EEG measurements of thecontralesional motor cortex in chronic stroke patients. IEEE Transactions on Biomedical Engineering 2016.

Mission

Bringing neurotechnology closer to society

I+D requerida
- EEG systems and Sw
- EEG SP and IA
- EEG biomarkers
- BCI treatments

Others
- Regulatoria
- Seguridad
- Etica
- Stakeholders

2003 — Universidad Zaragoza — 2012 — Bitbrain — 2023

Real world neurotech

Research company

- 60 people with organic growth.

R&D and Technology

- A team of more than 20 engineers and 15 R&D researchers (and growing!).
- Significant investment in R&D (+€6 million invested to date)

Commercialization

Distributors in BRICS countries (Brazil, Russia, India, China and South Africa).

Clients in more than 60 countries (Europe, US, Asia, Latam & Africa)

What is Digital Neurotherapeutics?

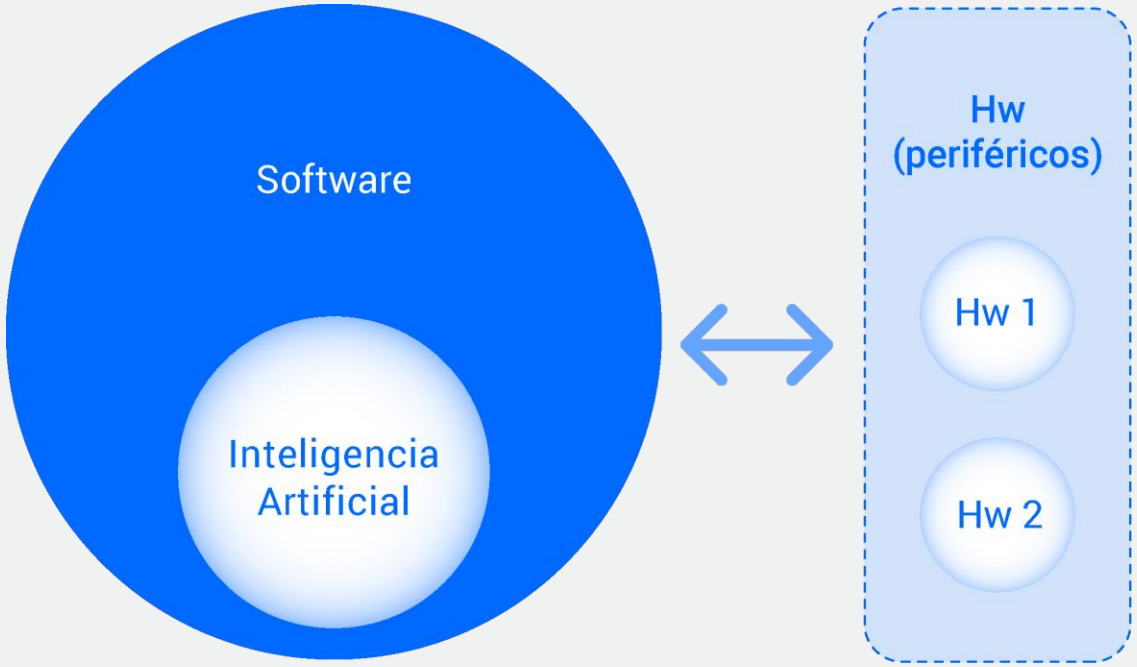
Bitbrain

Addressing the Continuum of Neurology and Mental Health

Digital neurotherapeutics

Prevent, treat, and manage with software-based solutions

Overcome the limitations of time, place, and a person's reach in delivering healthcare.



[1] Makin S. Nature 573, S106-S109 (2019) | [2] Abbadessa G. et al. Digital therapeutics in neurology Springer March 2022Journal of Neurology 269(13):1-16.

EEG recording in Digital Neurotherapeutics

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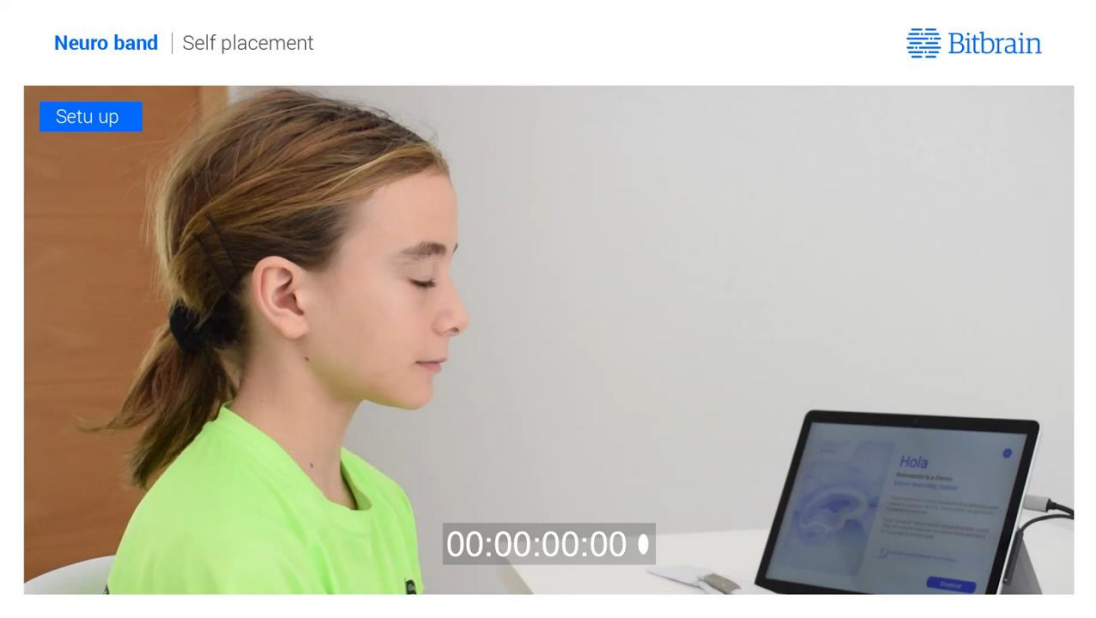
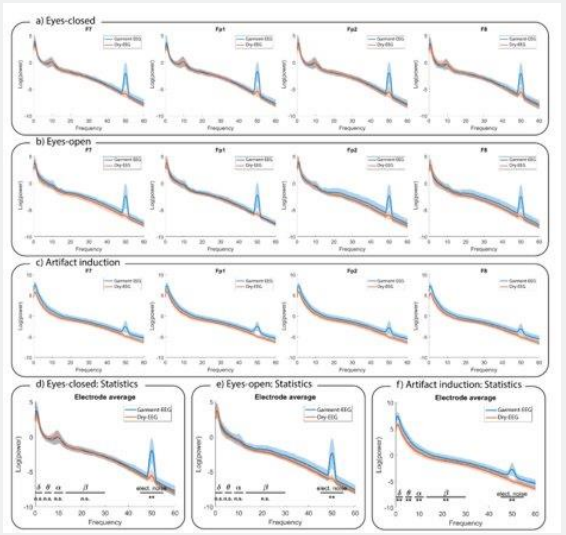
Wearable garments that measure brain activity (medical device)

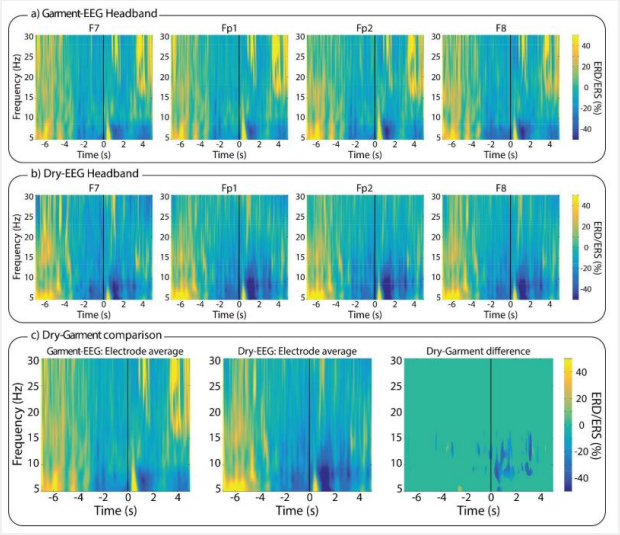
Equipment usability



A 12-year-old child using the equipment autonomously

Technical evaluation wrt medical-grade EEG





- Paper: Evaluation in Spontaneous and Evoked EEG Time-Frequency.
- Ongoing research for a medical device, such as self-administered partial EEG and PSG (with PPG) – for use by laypersons at home.

Participa: iis Instituto de Investigación Sanitaria Aragón · salud Servicio Aragonés de Salud · Bitbrain · Universidad Zaragoza

Financia: Gobierno de España · ai4 Healthy Aging · CDTI

Aprobado: CEICA (Ref: EC 22/12 | AEMPS (Ref: 1054/22/EC-R)

[2] Lopez et al. A garment to measure brain activity: proof of concept of an EEG sensor layer fully implemented with smart textiles. Frontiers in Human Neuroscience. May 2023

AI for sleep scoring

Automatic sleep labeling based on EEG (medical device)

Estado del arte

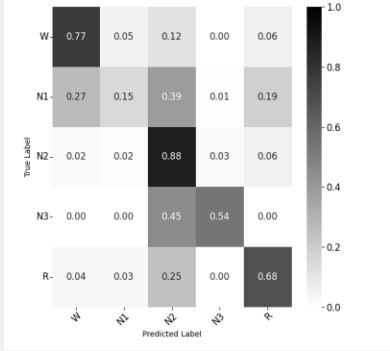
- Reliability is 80-85% among expert evaluators when manual scoring is performed [4].
- 83% with full PSG and deep learning AI [4].
- 82% with only two frontal sensors and deep learning AI [5].
- 83% (Bitbrain) replicated [5] with N=197 (Base SleepEDF) [6].

Objetivo y estado actual

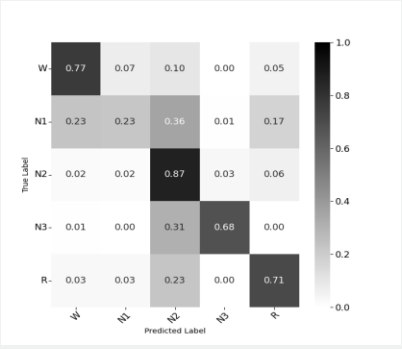
- Develop an AI that achieves >80% accuracy with data from the band (frontal sensors).
- Currently, with a sample size of N=100, it achieves 87% with PSG and 84% with the band.

PSG y Band recording

PSG-AI: 87%



Band-AI: 84%



[4] Inter-rater reliability when performing manual scoring is 80%, meaning that two well-trained scorers will, on average, agree on 80% of the labels they assign to each epoch.
[5] A. Koushik et al., Real-Time Sleep Staging using Deep Learning on a Smartphone for a Wearable EEG, Machine Learning for Health (ML4H) Workshop at NeurIPS 2018
[6] M. Esparza-Iaizzo et al.Automatic sleep scoring for real-time monitoring and stimulation in individuals with and without sleep apnea. BioRxiv. 2024

Cognitive deterioration in DTx

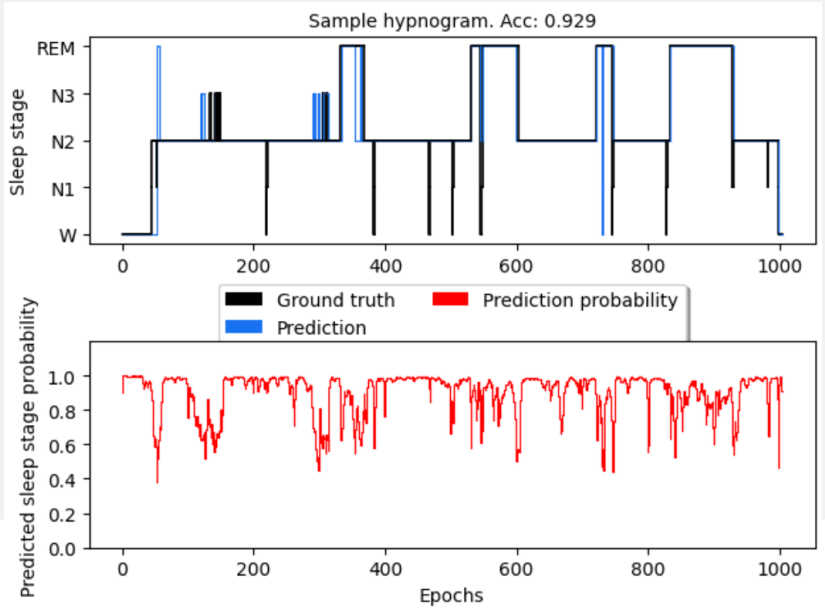
HOGAR: MCI/ALZ Monitorization

Estudio HOGAR -- 2024

- Objective: Monitoring the continuum of cognitive decline through self-administered EEG and PSG at the patient's home.
- Population: 500 participants across the Alzheimer's continuum Healthy, Subjective memory complaints, Mild Cognitive Impairment (MCI), Mild Alzheimer's Disease.

Status

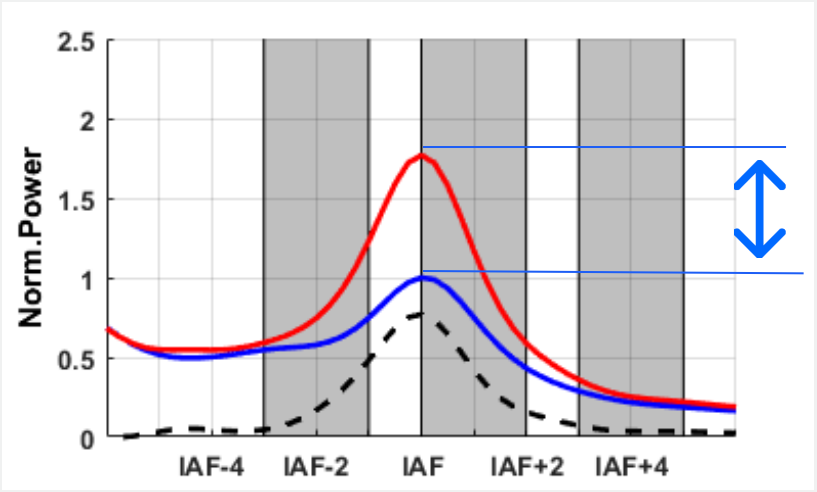
- Status: 103/200 (80% success rate)
- Home Instrument Results:
  - Self-administered EEG: 100% (2 recordings per subject ~15 minutes)
  - Self-administered PSG: 100% (2 recordings per subject: ~8 hours each)



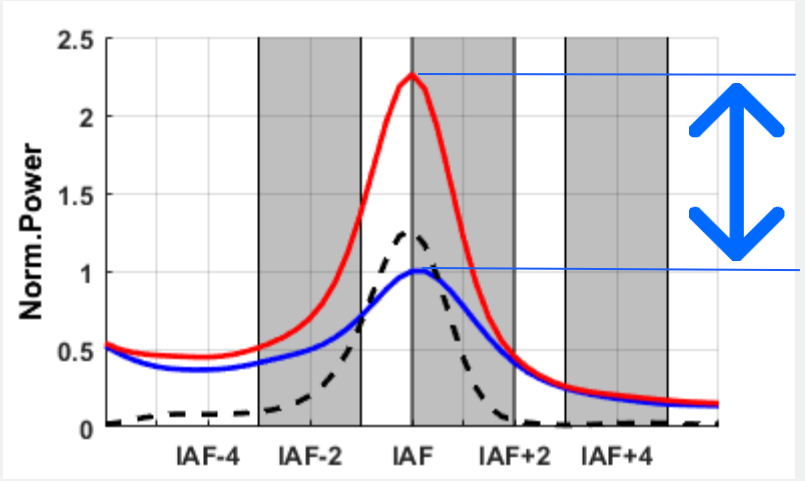
Treatment of Cognitive Deterioration in DTx (I)

Neurological basis

Greater desynchronization of individualized high-alpha rhythms in the parietal and parieto-occipital regions is associated with higher general cognitive ability, particularly in sustained attention and working memory.



Objective:
Use neurofeedback to induce a change in desynchronization during task-related EEG.



[7] Klimesch, W. (1999). EEG alpha and theta oscillations reflect cognitive and memory performance: a review and analysis. Brain Research Reviews,29(2-3):169

Treatment of Cognitive Deterioration in DTx (II)

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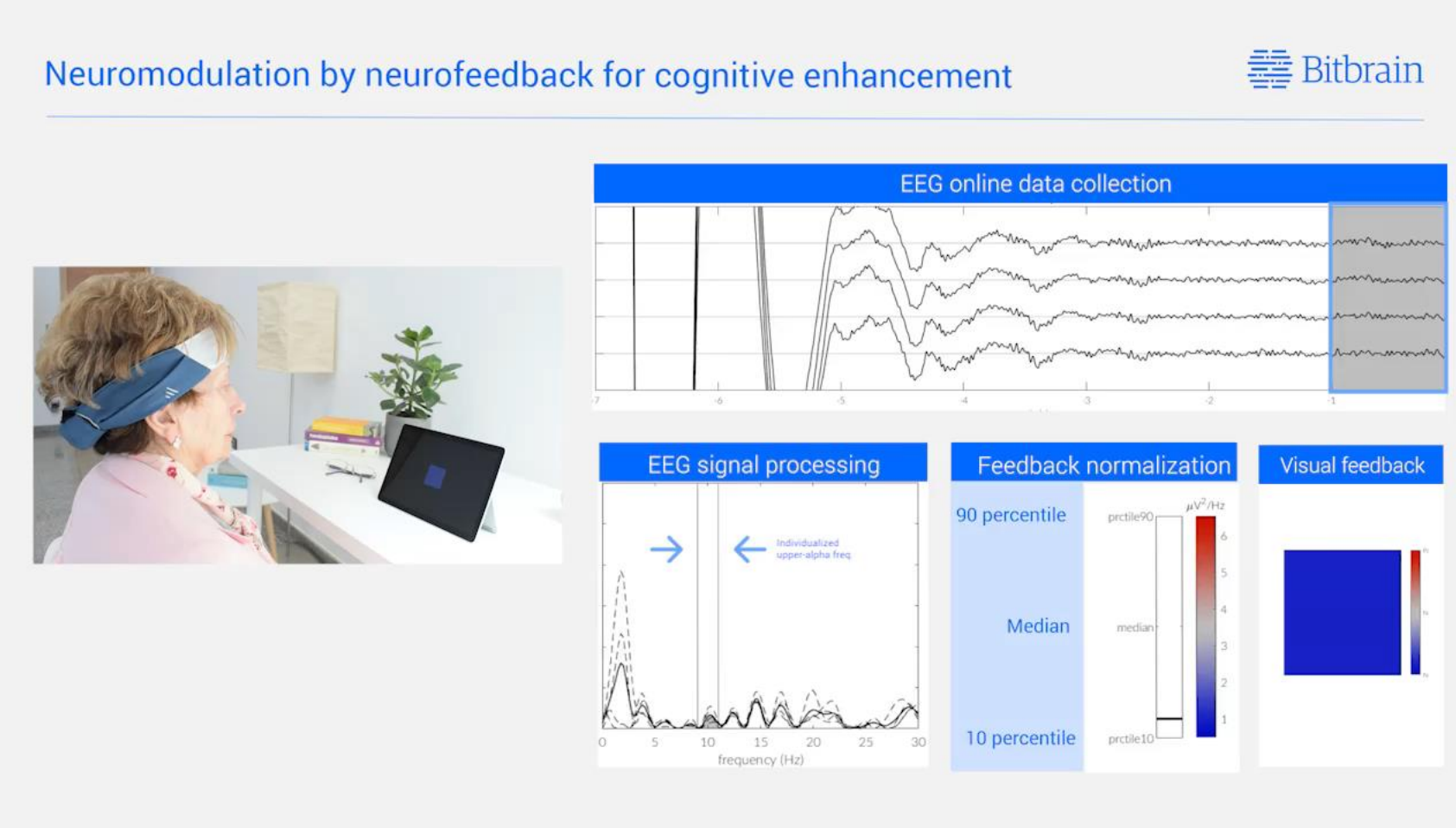
Neuromodulation through Neurofeedback (active treatment)



Treatment of Cognitive Deterioration in DTx (III)

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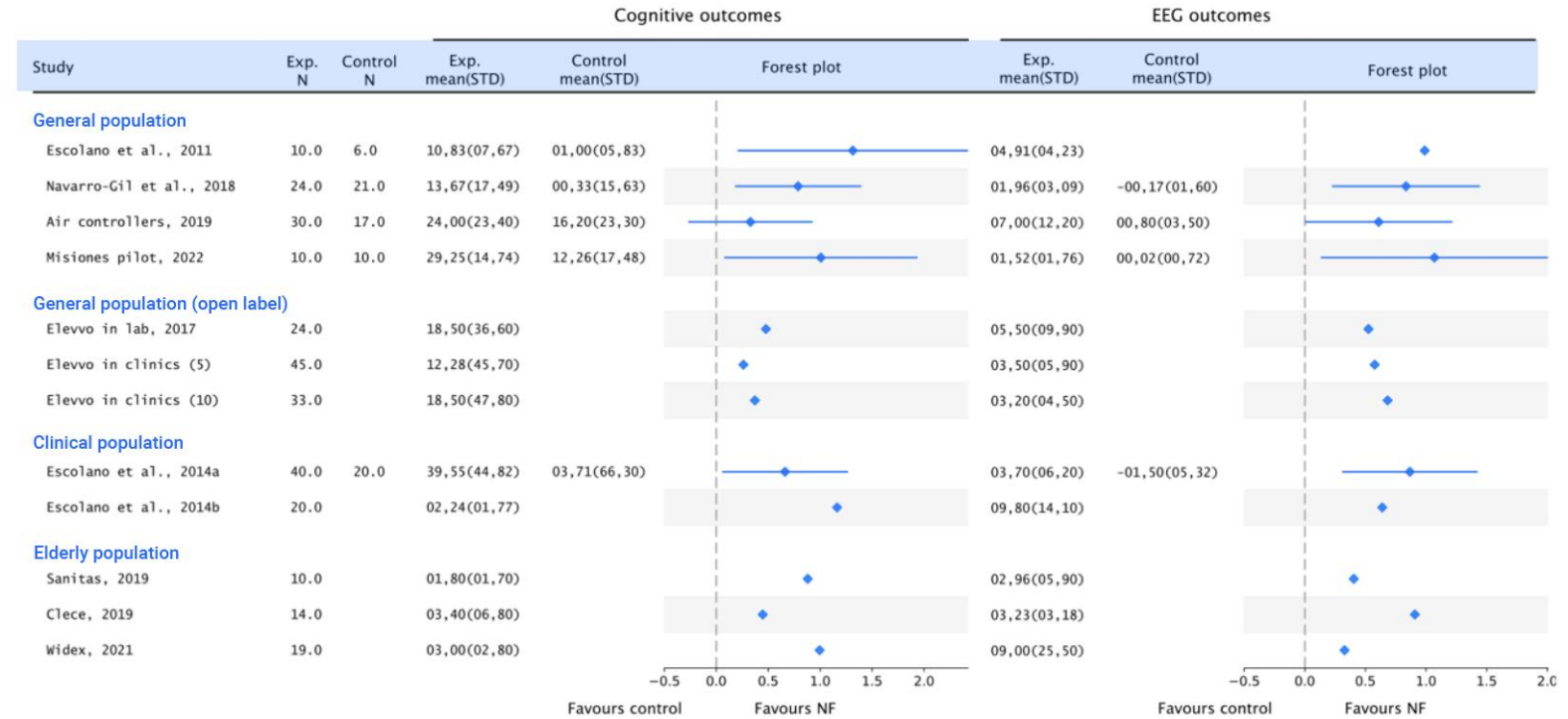
Evidence and currect studies



Study	Exp. N	Control N	Cognitive outcomes: Exp. mean(STD)	Cognitive outcomes: Control mean(STD)	Cognitive outcomes: Forest plot	EEG outcomes: Exp. mean(STD)	EEG outcomes: Control mean(STD)	EEG outcomes: Forest plot
General population								
Escolano et al., 2011	10.0	6.0	10,83(07,67)	01,00(05,83)		04,91(04,23)		
Navarro-Gil et al., 2018	24.0	21.0	13,67(17,49)	00,33(15,63)		01,96(03,09)	-00,17(01,60)	
Air controllers, 2019	30.0	17.0	24,00(23,40)	16,20(23,30)		07,00(12,20)	00,80(03,50)	
Misiones pilot, 2022	10.0	10.0	29,25(14,74)	12,26(17,48)		01,52(01,76)	00,02(00,72)	
General population (open label)								
Elevvo in lab, 2017	24.0		18,50(36,60)			05,50(09,90)		
Elevvo in clinics (5)	45.0		12,28(45,70)			03,50(05,90)		
Elevvo in clinics (10)	33.0		18,50(47,80)			03,20(04,50)		
Clinical population								
Escolano et al., 2014a	40.0	20.0	39,55(44,82)	03,71(66,30)		03,70(06,20)	-01,50(05,32)	
Escolano et al., 2014b	20.0		02,24(01,77)			09,80(14,10)		
Elderly population								
Sanitas, 2019	10.0		01,80(01,70)			02,96(05,90)		
Clece, 2019	14.0		03,40(06,80)			03,23(03,18)		
Widex, 2021	19.0		03,00(02,80)			09,00(25,50)		

References

- Escolano, C., Aguilar, M., & Minguez, J. (2011). EEG-based upper alpha neurofeedback training improves working memory performance. In International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC) (p. 2327-2330). Boston (USA).
- Escolano, C., Navarro-Gil, M., Garcia-Campayo, J., Congedo, M., De Ridder, D., & Minguez, J. (2014a). A controlled study on the cognitive effect of alpha neurofeedback training in patients with major depressive disorder. Frontiers in Behavioral Neuroscience, 8(296).
- Escolano, C., Navarro-Gil, M., Garcia-Campayo, J., Congedo, M., & Minguez, J. (2014b). The effects of individual upper alpha neurofeedback in ADHD: an open-label pilot study. Applied psychophysiology and biofeedback, 39, 193-202.
- Navarro-Gil, M., Escolano, C., Montero-Marín, J., Minguez, J., Shonin, E., & Garcia-Campayo, J. (2018). Efficacy of neurofeedback on the increase of mindfulness-related capacities in healthy individuals: a controlled trial. Mindfulness, 9, 303-311.

- Preclínica ESPERANZA (2023): doble ciego controlado randomizado N=20 de 40 a 60 años. 10 sesiones de 1h en 2 semanas.
- Feasability ESPERANZA (2023-2024): doble ciego controlado randomizado con N=30 DCLa de 30 sesiones de 1h en 1,5 meses.
- Pivotal ESPERANZA (2023-2024): doble ciego controlado randomizado con N=40 DCLa de 30 sesiones de 1h en 1,5 meses.

Participa: Instituto de Investigación Sanitaria Aragón · salud · Bitbrain · Universidad Zaragoza

Financia: · ai4 Healthy Aging · CDTI

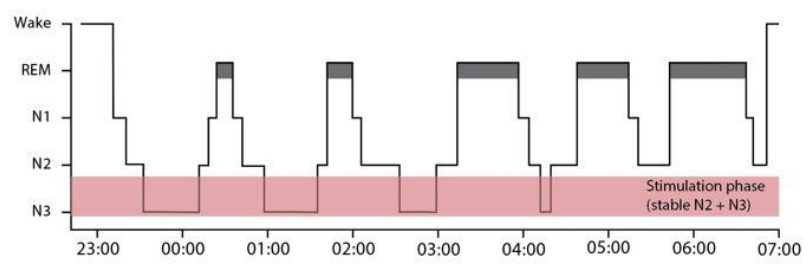
Aprobado: CEICA (Ref: EC 22/12 | AEMPS (Ref: 1054/22/EC-R)

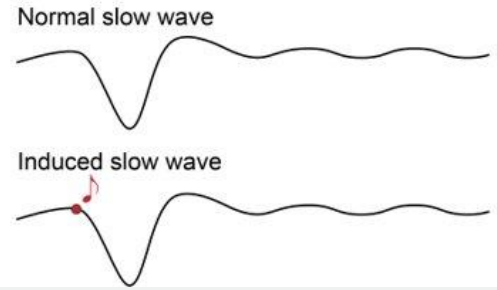
Treatment of Cognitive Deterioration in DTx (I)

Neurological basis

Increasing the number and magnitude of slow waves during deep sleep improves declarative memory.

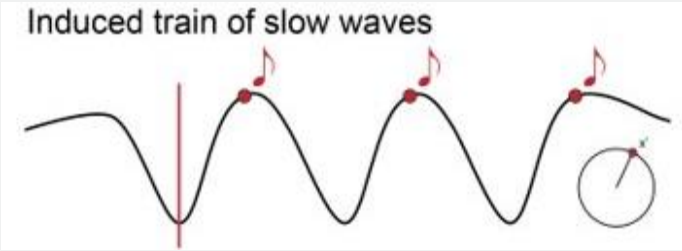
During the depolarized phase (positive surface) of slow waves in the EEG during Non-REM sleep, well-calibrated auditory stimulation can produce slow oscillations without causing awakening.





Objetivo :

Utilizar la estimulación auditiva durante el sueño para inducir trenes de ondas lentas adicionales



[8] Ngo et al. Ngo HV, Martinetz T, Born J, Mölle M. Auditory closed-loop stimulation of the sleep slow oscillation enhances memory. Neuron. 2013
[9] J. G Klinzing et al., Mechanisms of systems memory consolidation during sleep. Nature neuroscience. 2019

Treatment of Cognitive Deterioration in DTx (II)

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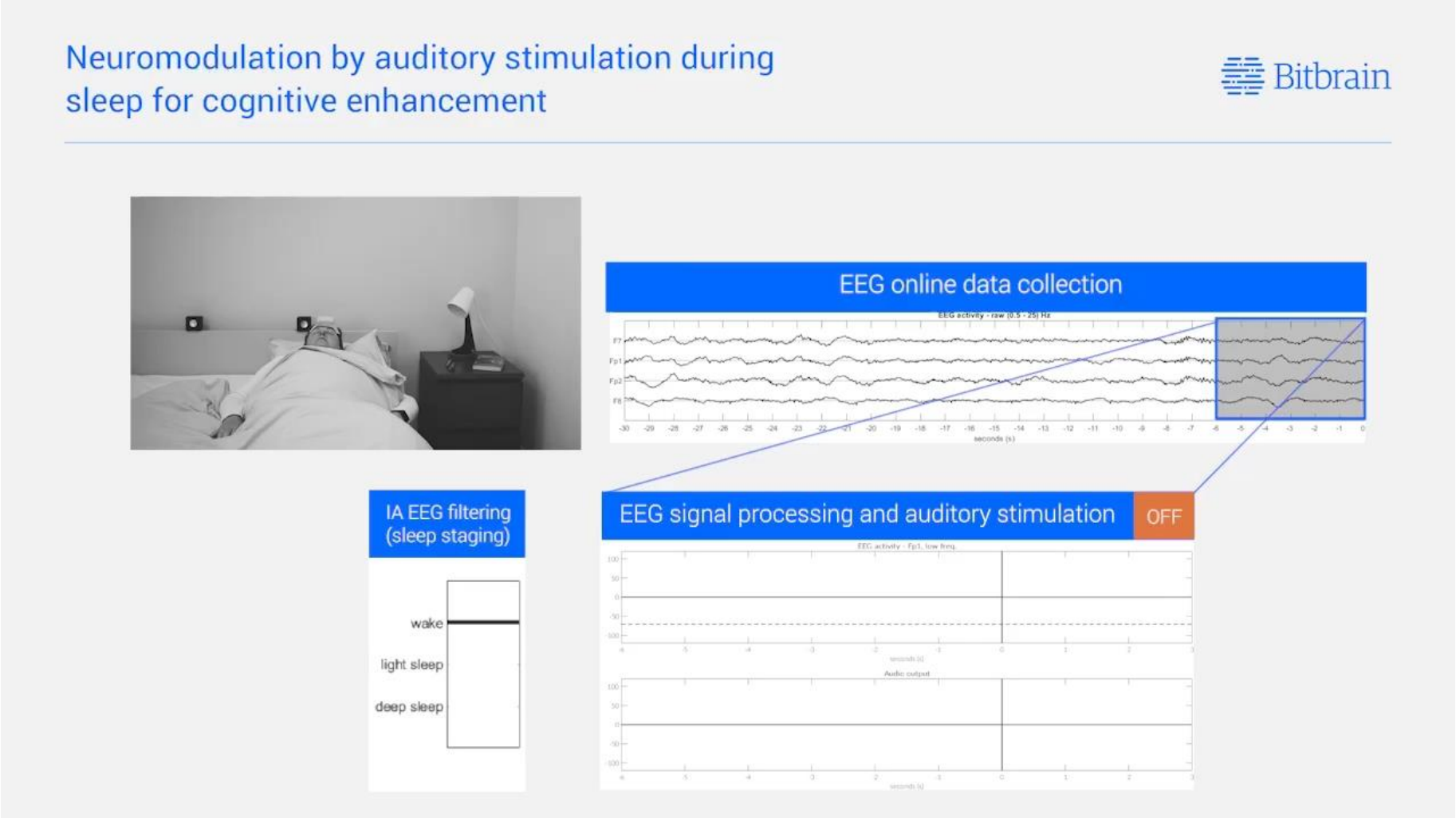
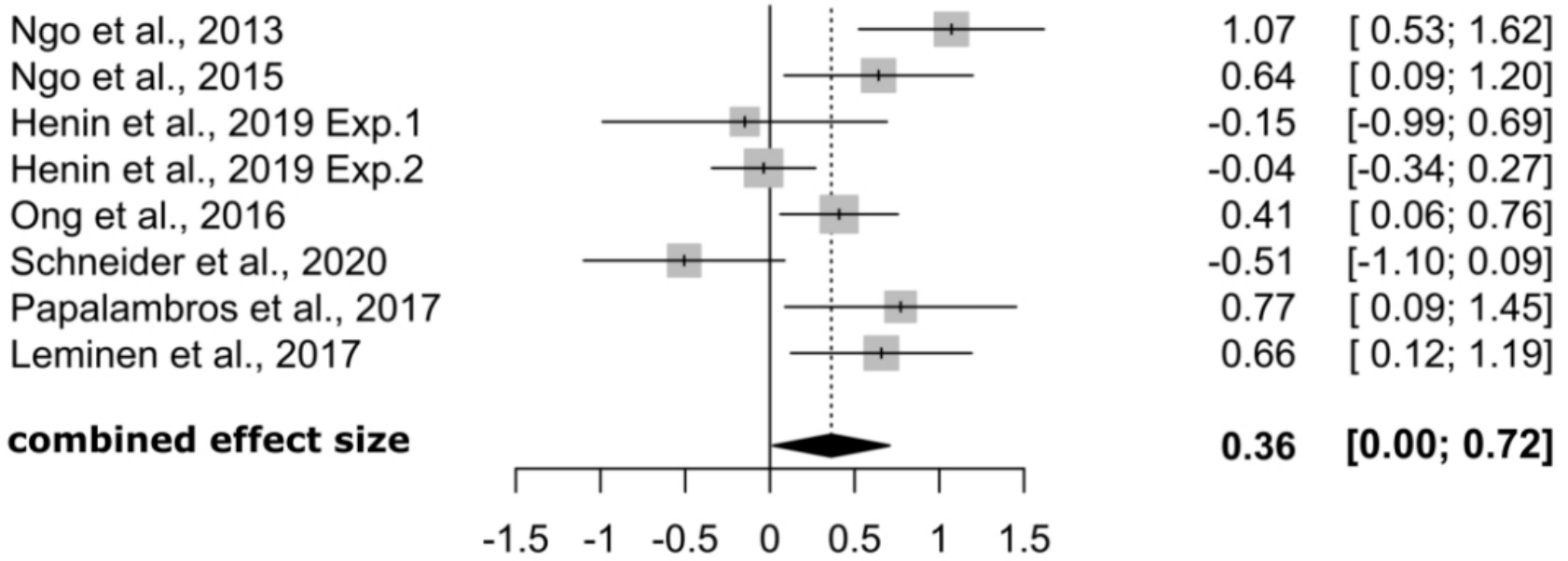
Neuromodulation through auditory stimulation during sleep



Treatment of Cognitive Deterioration in DTx (II)

Current Evidence and Project Status

Auditory stimulation (cognitive outcome)



[10] Wunderlin, M. et al. Modulating overnight memory consolidation by acoustic stimulation during slow-wave sleep: a systematic review and meta-analysis. Sleep, 44(7). 2021.

- Preclínica NANA (2023): estudio de investigación N=26 personas de 25 a 81 años. 1-3 noches a la semana.
- Feasability NANA (2023-2024): doble ciego controlado randomizado con N=10 DCLa de 30 sesiones de 1h en 1,5 meses.
- Pivotal NANA (2023-2024): doble ciego controlado randomizado con N=37 DCLa de 30 sesiones de 1h en 1,5 meses

Participa:
Financia:
Aprobado: CEICA (Ref: C.I. PI 23/186 y C.I. EC 22/011 | AEMPS (Ref: 1040/22/EC-R)

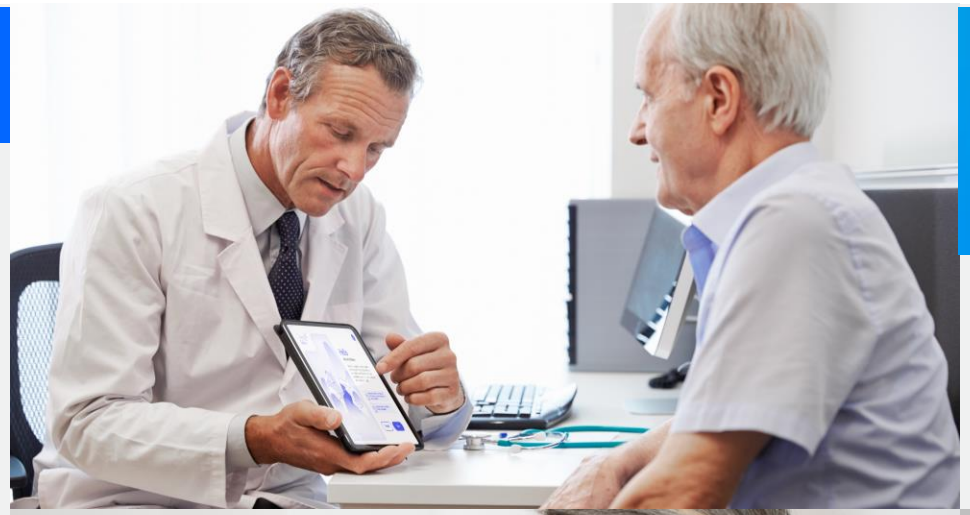
Conclusion

Bitbrain

Digital neurotherapeutics

Take home messages

- Prevent, manage, and treat with software-based solutions
- Overcome the limitations of time, location, and accessibility in delivering healthcare.
- Development of low-density EEG and PSG sensors for use by laypersons, allowing these records to be taken outside of healthcare facilities.
- Central role of artificial intelligence in automatically analyzing data and personalizing interventions.
- Approach enables very intensive treatments both during wakefulness and sleep, which are impractical to implement in healthcare centers.



The team!

Bitbrain

Participantes/Voluntarios

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Advanced neurotechnology

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