2017 European Neuro Convention Presentation

Perth, Australia & Malta – 8 *June 2017* – Please find enclosed the presentation accompanying a keynote speech delivered by Dr Adrian Attard Trevisan, at the European Neuro Convention in London yesterday.

Dr Attard Trevisan is the founder and Chief Scientific Adviser of Neurotech International Limited (ASX: NTI) ("Neurotech" or the "Company"), developer of quality medical solutions in the neuroscience space. Dr Attard Trevisan's presentation covered EEG-driven therapies used in the fields of autism and intellectual disabilities, highlighting the role that Mente Autism is seeking to play in helping children on the autism spectrum.

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About Neurotech

Neurotech International Limited is a medical device and solutions company incorporated in Australia and operating through its wholly-owned, Malta-based subsidiary AAT Research Limited. Neurotech's primary mission is to improve the lives of people with neurological conditions, with a vision of becoming the global leader in home-use and clinical neurotechnology solutions that are both accessible and affordable. Through flagship device Mente Autism and its associated platform, Neurotech is focused on the development and commercialisation of technological solutions for the diagnosis and treatment of such conditions, starting with autism.

Mente Autism is a clinical-quality EEG device that uses neurofeedback technology to help children with ASD. Designed for home use, Mente Autism helps relax the minds of children on the spectrum which in turns helps them to focus better and engage positively with their environment.

For more information about Neurotech and Mente Autism please visit:

http://www.neurotechinternational.com.
http://www.mentetech.com.

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EEG Driven Therapies: in the field of Autism and Intellectual Disabilities

Dr Adrian Attard Trevisan, Ph.D
Founder / Scientific Advisor - Neurotech International
Research Fellow – BMHR-CU
Date: 2017/06/07

BCMHR-CU.org
Bedfordshire Centre for Mental Health Research in association with the University of Cambridge

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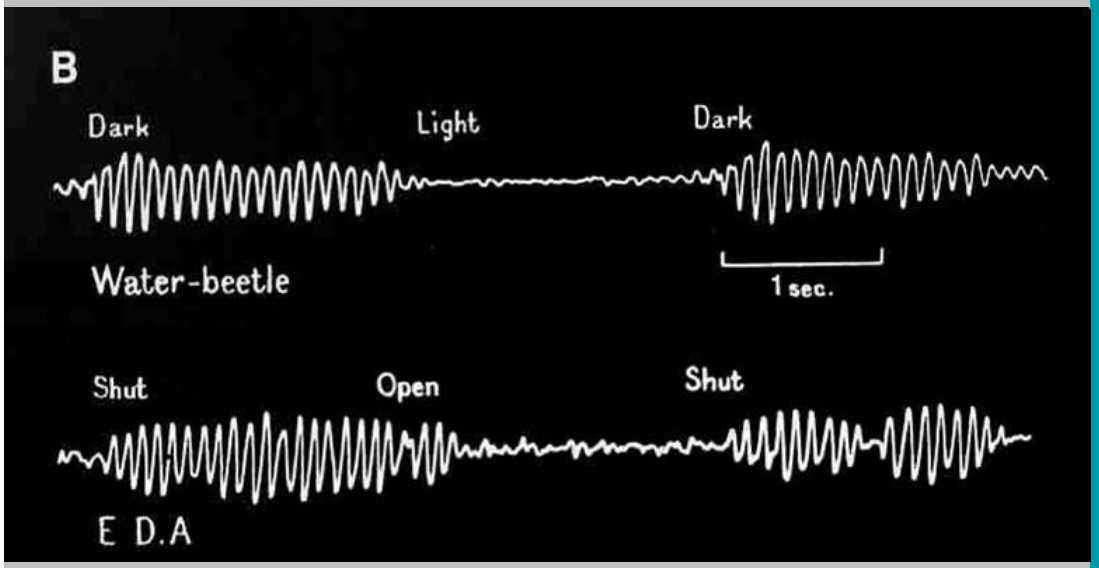
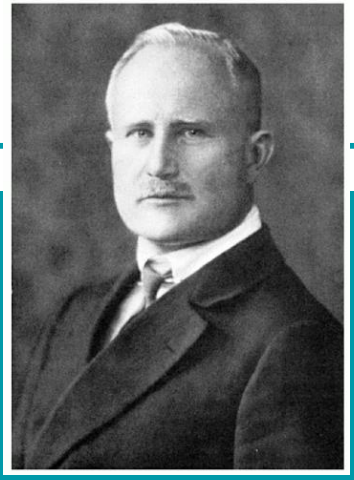
Contents:

- Introduction about Electroencephalography (EEG) and Entrainment
- EEG abnormalities in Autism
- Use of Neurofeedback to treat ASD
- Mente Autism – Neurofeedback for ASD

Introduction about Electroencephalography (EEG) and Entrainment

Introduction





Hans Berger (1929) already believed that abnormalities in EEG reflect clinical disorders.

In a large variety of psychiatric disorders or psychological diseases, indeed, several abnormalities in the brainwave activity can be observed, often related to alterations in the biochemistry of the brain

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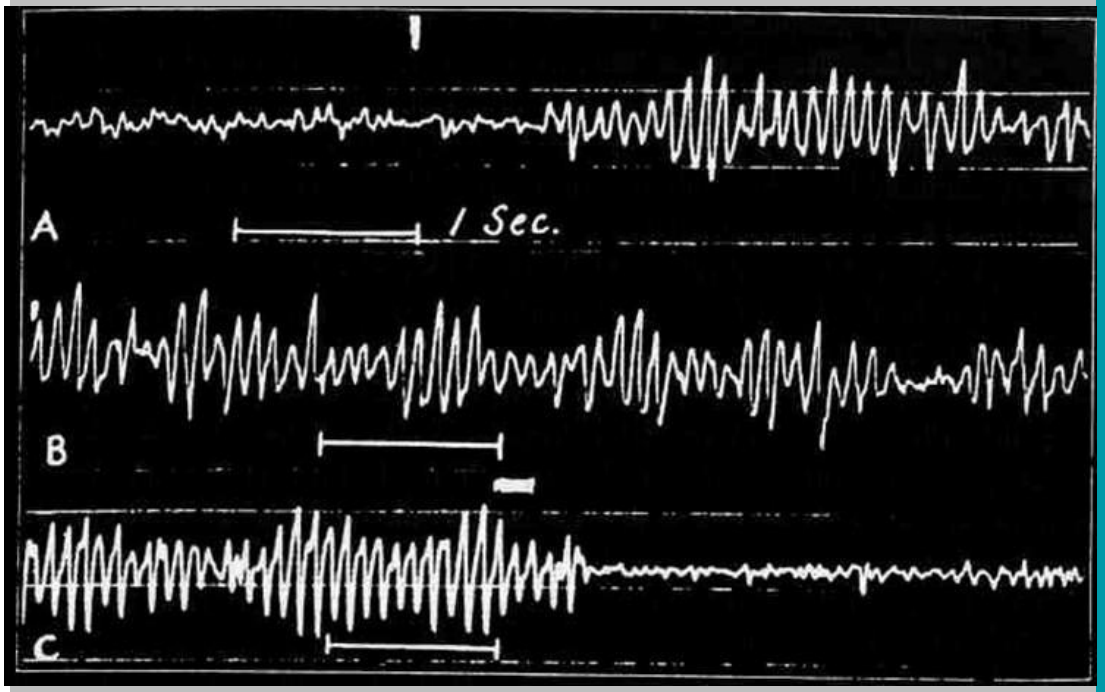
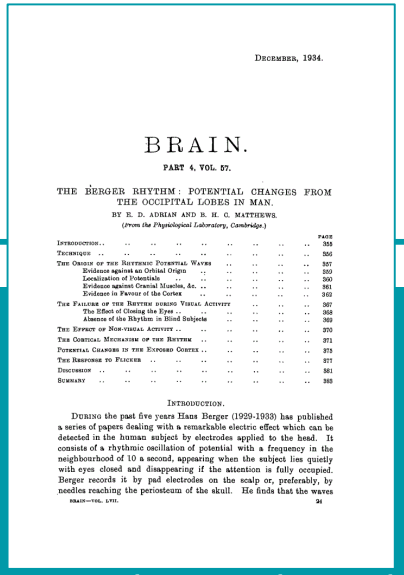
Introduction





DECEMBER, 1934.

BRAIN.

PART 4. VOL. 57.

THE BERGER RHYTHM: POTENTIAL CHANGES FROM THE OCCIPITAL LOBES IN MAN.

BY E. D. ADRIAN AND B. H. C. MATTHEWS.

(*From the Physiological Laboratory, Cambridge.*)

INTRODUCTION.

DURING the past five years Hans Berger (1929-1933) has published a series of papers dealing with a remarkable electric effect which can be detected in the human subject by electrodes applied to the head. It consists of a rhythmic oscillation of potential with a frequency in the neighbourhood of 10 a second, appearing when the subject lies quietly with eyes closed and disappearing if the attention is fully occupied. Berger records it by pad electrodes on the scalp or, preferably, by needles reaching the periosteum of the skull. He finds that the waves

In 1934, Adrian and Matthews showed, through their results, that the alpha rhythm could be "driven" above and below its natural frequency with photic stimulation (Adrian & Matthews, 1934).

EEG entrainment

Brain tends to follow and produce specific frequencies, within a range of 1-30 Hz, at the same frequency at which it is stimulated and is thought to rely on the principles of the classical conditioning learning paradigm.

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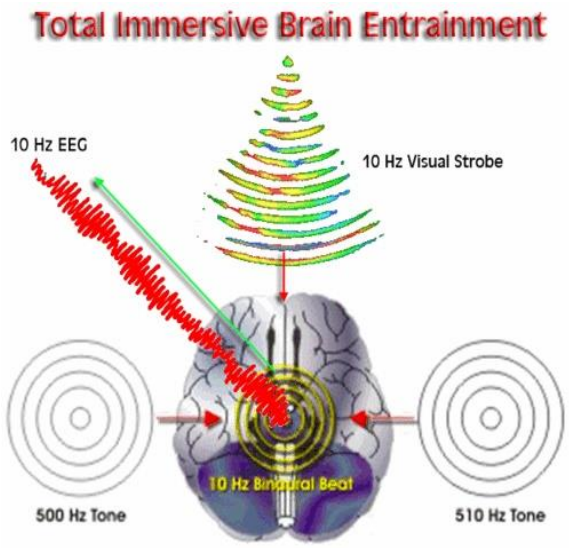
How can EEG entrainment be promoted ?

Visual or photic Stimulation

Auditory or binaural beats

Photic stimulation: flickering or flashing light where the more sophisticated is the stimulus the greater effect on endogenous rhythms.

AudioVisual Stimulation (AVE)



Binaural beats: two different signals are presented to each ear, and the perception of the frequency difference or " beat " is performed within the brain itself.

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What kind of Brain waves are the best to be entrained?

- **Delta: useful to relax and to promote sleep**
- Theta: relaxation
- Alpha: best entrainment
- Beta: best for ADHD

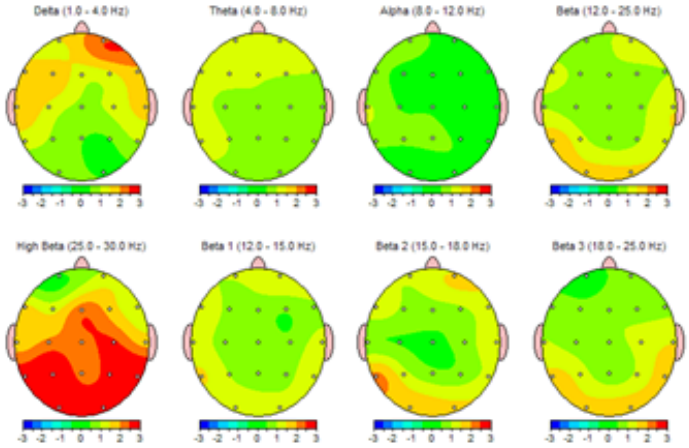
The collection of evidences from several studies pointed out a specific pattern named "EEG slowing" characterized by enhanced amplitudes of delta and theta waves over the other EEG frequencies and by a consistent alpha suppression.

These are general/standard even effective guidelines to choose a specific stimulation.

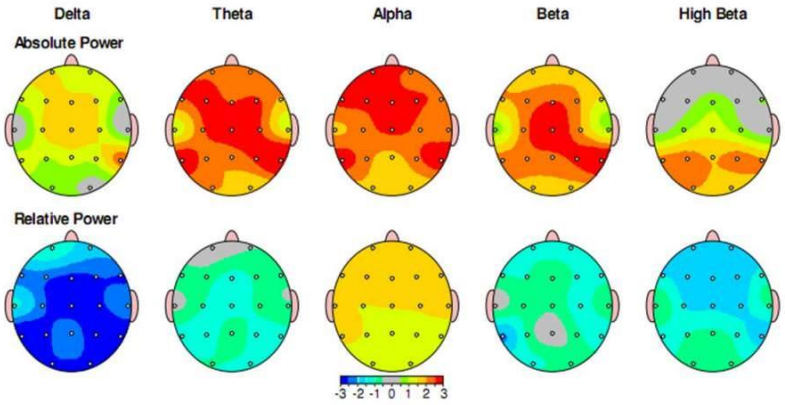
Every person, however, is unique and with the current understanding of qEEG and neural 'profile', we can easily confirm Berger's intuitions about the relationship between EEG brainwaves and neurological disorders

QEEG

- Quantitative EEG is a clinical diagnostic tool, which measures brain dysfunction and activity. It points to areas of dysfunction, quantifying specific abnormalities and assists in the differential diagnosis process. Unlike other testing, such as MRI, CAT Scan, FMRI, and SPECT Scans, QEEG analysis reflects problems in functioning of the brain; hence it is more useful for neurofeedback or EEG Biofeedback protocol development.



- QEEG utilizes a computerized spectral analysis, which breaks down the EEG into its component wave bands of differing frequencies or differing cycles per second [Hz} (Delta 1-4; Theta 4-8; Alpha 8-12; and Beta 12-25). Afterward the QEEG computerized analysis program measures, for each of 19 channels, the wave band frequencies, amplitudes, asymmetries between analogous points of measurement, and the phase relationship between different points of measurements (coherence). Each channel or local measurement is called a univariate measure.



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EEG abnormalities in Autism

ASD and EEG abnormalities

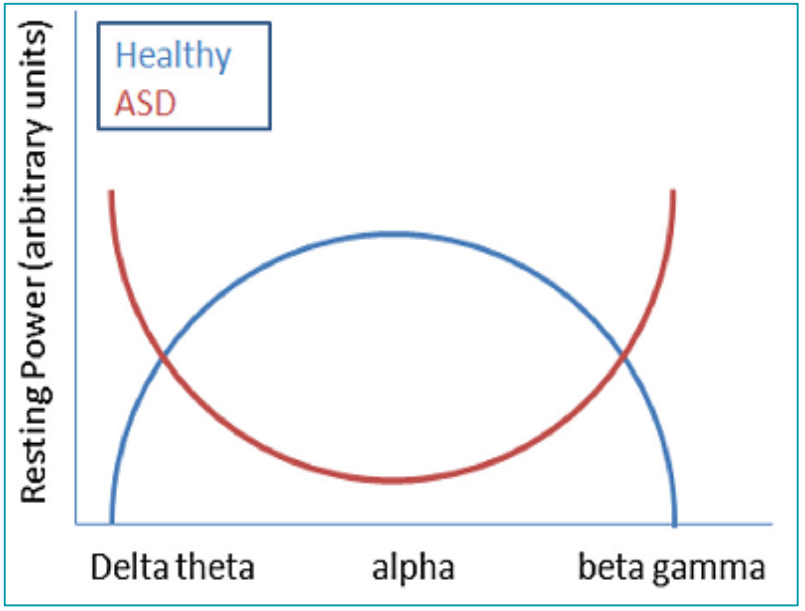
The aim of neurofeedback treatment in children and adolescents with ASD has been on normalizing abnormalities in:

- EEG power spectra (Jarusiewicz, 2002; Scolnick, 2005; Sichel et al., 1995),
- connectivity (Coben & Padolsky, 2007), and
- the mirror neuron system (Pineda et al., 2008),

because EEG studies in individuals with ASD have revealed abnormal patterns of EEG activity in each of these three domains.

EEG power bands in children with ASD

Resting-state EEG studies of ASD suggest a U-shaped profile of electrophysiological power alterations, with excessive power in low-frequency (delta and theta) and high-frequency bands (beta and gamma), but reduced power in the middle-range frequency band (alpha), abnormal functional connectivity, and enhanced power in the left hemisphere of the brain (Wang et al. 2013). These traits have been observed at all stages of development and in children with and children without comorbid ID (intellectual disability).



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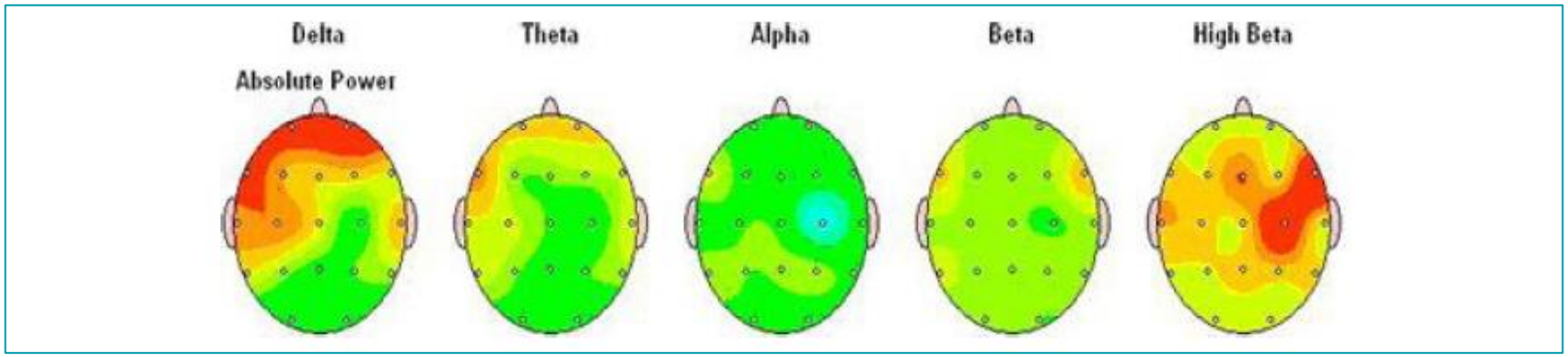
High Delta and Theta

A constant pattern in ASD has emerged showing excessive power at low-frequency delta and theta and high frequency (beta, gamma) bands; but reduced power in the middle-range frequency band alpha has been found in children at all stages of development (Cantor et al. 1986; Pop-Jordanova et al. 2010).



It is clear that absolute power for delta and theta are increased, but, due to high anxiety, the power of beta waves can also be increased in some cases. It is very important to know that generally, alpha brain waves are positively related to cortical information processing, i.e., cognitive abilities.

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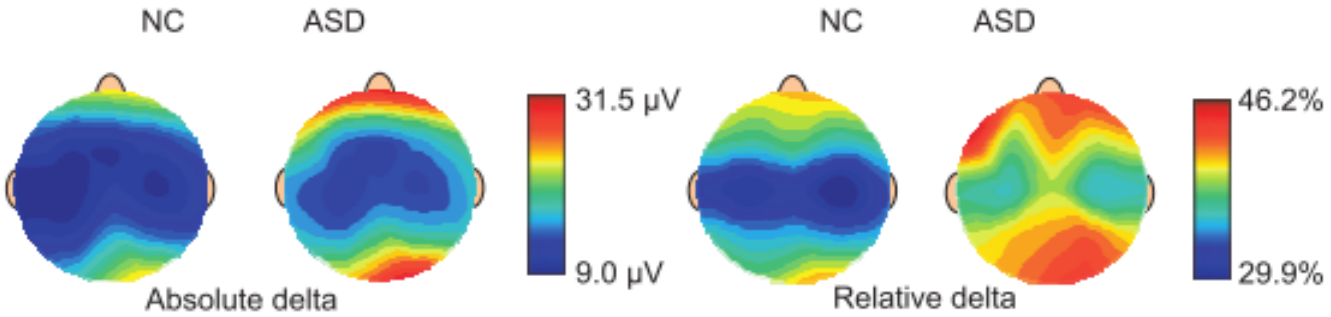
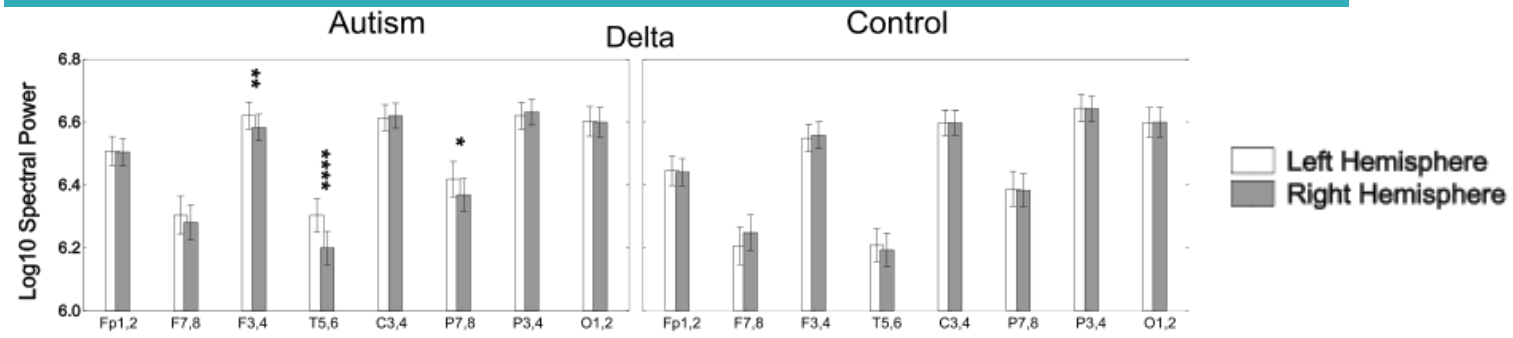
High Delta in ASD



Spectrum analyses revealed that children with ASD showed significantly less relative alpha and more relative delta than normal control subjects. (Chan et al., 2007)



The only between-group difference in absolute EEG Spectral Power was a higher amount of prefrontal delta in boys with autism. (Stroganova et al. 2007)

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High Theta in ASD

- Pop-Jordanova, N., Zorcec, T., Demerdzieva, A., & Gucev, Z. (2010).
  QEEG characteristics and spectrum weighted frequency for children diagnosed as autistic spectrum disorder.
  Nonlinear Biomedical Physics, *4*, 4.
- Daoust, A. M., Limoges, Elyse, Bolduc, C., Mottron, L., & Godbout, R. (2004).
  EEG spectral analysis of wakefulness and REM sleep in high functioning autistic spectrum disorders.
  Clinical Neurophysiology, *115*(6), 1368–1373.
- Murias, M., Webb, S. J., Greenson, J., & Dawson, G. (2007).
  Resting State Cortical Connectivity Reflected in EEG Coherence in Individuals With Autism.
  Biological Psychiatry, *62*(3), 270–273.
- Murias, M., Webb, S. J., Greenson, J., & Dawson, G. (2007).
  Resting State Cortical Connectivity Reflected in EEG Coherence in Individuals With Autism.
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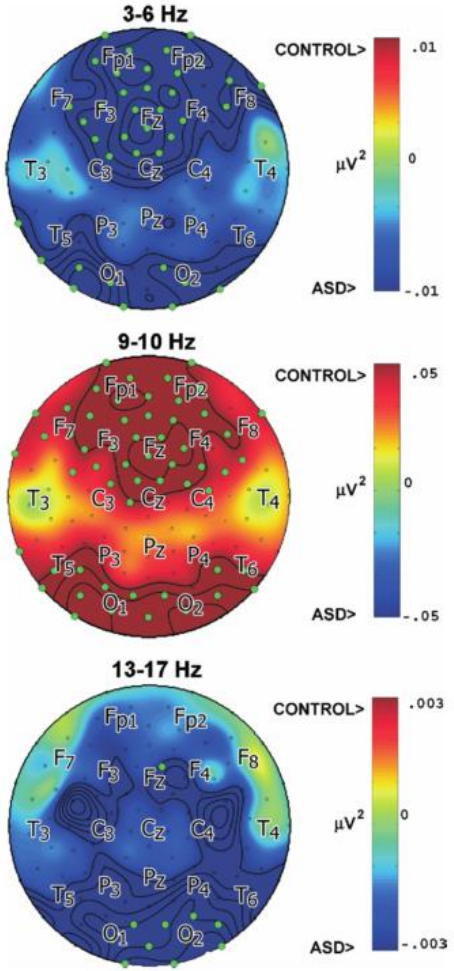

Figure 4. Topography of relative power differences (control − autism spectrum disorder [ASD]). Green dots indicate significant difference between groups at $p < .025$. The ASD relative power exceeded control at 3–6 Hz (top) and 13–17 Hz (bottom). Control potential relative power exceeded ASD at 9–10 Hz (middle).

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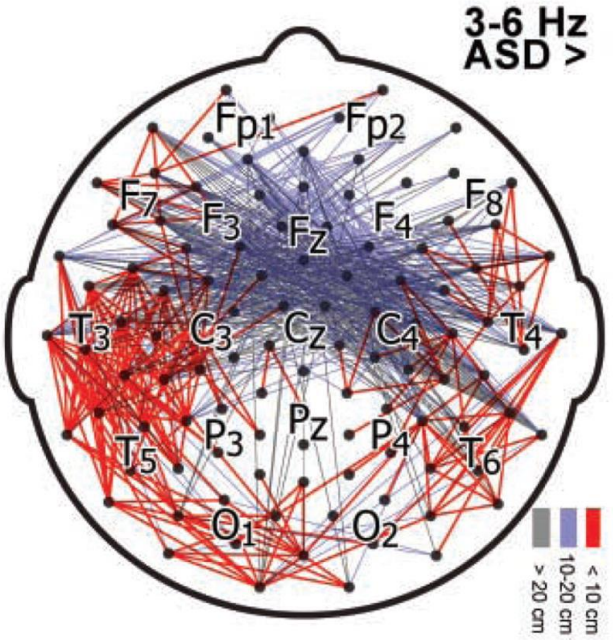
Abnormalities in connectivity & coherence

A study by Murias et al. (2007) explored the fact that theoretical conceptions of autism spectrum disorder (ASD) and experimental studies of cerebral blood flow suggest abnormalities in connections among distributed neural systems in ASD. Functional connectivity was assessed with electroencephalographic coherence between pairs of electrodes in a high-density electrode array in narrow frequency bands among 18 adults with ASD and 18 control adults in an eyes closed resting state.



In the theta (3-6 Hz) frequency range, locally elevated coherence was evident for the ASD group, especially within left hemisphere frontal and temporal regions.

Topography of significantly elevated ASD group coherences in the 3–6 Hz band. Lines are drawn between channel pairs at which ASD group coherence exceeded control with p-values below .025. Lines are coloured according to distance (cm) between electrode pairs, along the scalp surface.

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Abnormalities in connectivity & coherence

Robust patterns of over- and under-connectivity are apparent at distinct spatial and temporal scales in ASD subjects in the eyes closed resting state.
In the lower alpha range (8-10 Hz), globally reduced coherence was evident for the ASD group within frontal regions and between frontal and all other scalp regions. The ASD group exhibited significantly greater relative power between 3 and 6 Hz and 13-17 Hz and significantly less relative power between 9 and 10 Hz.
Robust patterns of over- and under-connectivity are apparent at distinct spatial and temporal scales in ASD subjects in the eyes closed resting state.
(Murias et al. 2007)

Abnormalities in connectivity & coherence

A study conducted by Coben et al. in 2008 explored the difference between a control group and a group with ASD in terms of connectivity and coherence. There were group differences in power, intrahemispheric and interhemispheric coherences. Findings included excessive theta, primarily in right posterior regions, in autistics. There was also a pattern of deficient delta over the frontal cortex and excessive midline beta. More significantly, there was a pattern of underconnectivity in autistics compared to controls. This included decreased intrahemispheric delta and theta coherences across short to medium and long inter-electrode distances. Interhemispherically, delta and theta coherences were low across the frontal region. Delta, theta and alpha hypocoherence was also evident over the temporal regions. Lastly, there were low delta, theta and beta coherence measurements across posterior regions.

These results suggest dysfunctional integration of frontal and posterior brain regions in autistics along with a pattern of neural underconnectivity. This is consistent with other EEG, MRI and fMRI research suggesting that neural connectivity anomalies are a major deficit leading to autistic symptomatology.

ASD and Delta and Theta Coherence

Table 3
Intrahemisperic and interhemispheric coherences for Autistic and Control groups

	Delta	Theta	Alpha	Beta
Intrahemispheric coherences				
Short-medium				
L vs. R	–	–	–	–
Autistic vs. Controls	****	***	–	$p = .071$
Autistic vs. Controls X L vs. R	–	–	–	–
Long				
L vs. R	–	–	–	–
Autistic vs. Controls	****	***	–	–
Autistic vs. Controls X L vs. R	–	–	–	–
Interhemispheric coherences				
Frontal				
Autistic vs. Controls	***	*	–	–
Temporal				
Autistic vs. Controls	*	***	**	–
Centralparietaloccipital				
Autistic vs. Controls	*	*	$p = .064$	*

* $p < .05$.
** $p < .01$.
*** $p < .005$.
**** $p < .001$.

- Coben, R., Clarke, A. R., Hudspeth, W., & Barry, R. J. (2008).

  EEG power and coherence in autistic spectrum disorder.

  Clinical Neurophysiology, *119*(5), 1002–1009.

- Barttfeld, P., Wicker, B., Cukier, S., Navarta, S., Lew, S., & Sigman, M. (2011).

  A big-world network in ASD: Dynamical connectivity analysis reflects a deficit in long-range connections and an excess of short-range connections.

  Neuropsychologia, *49*(2), 254–263.

- Duffy, F. H., & Als, H. (2012).

  A stable pattern of EEG spectral coherence distinguishes children with autism from neuro-typical controls - a large case control study.

  BMC Medicine, *10*(1), 64.

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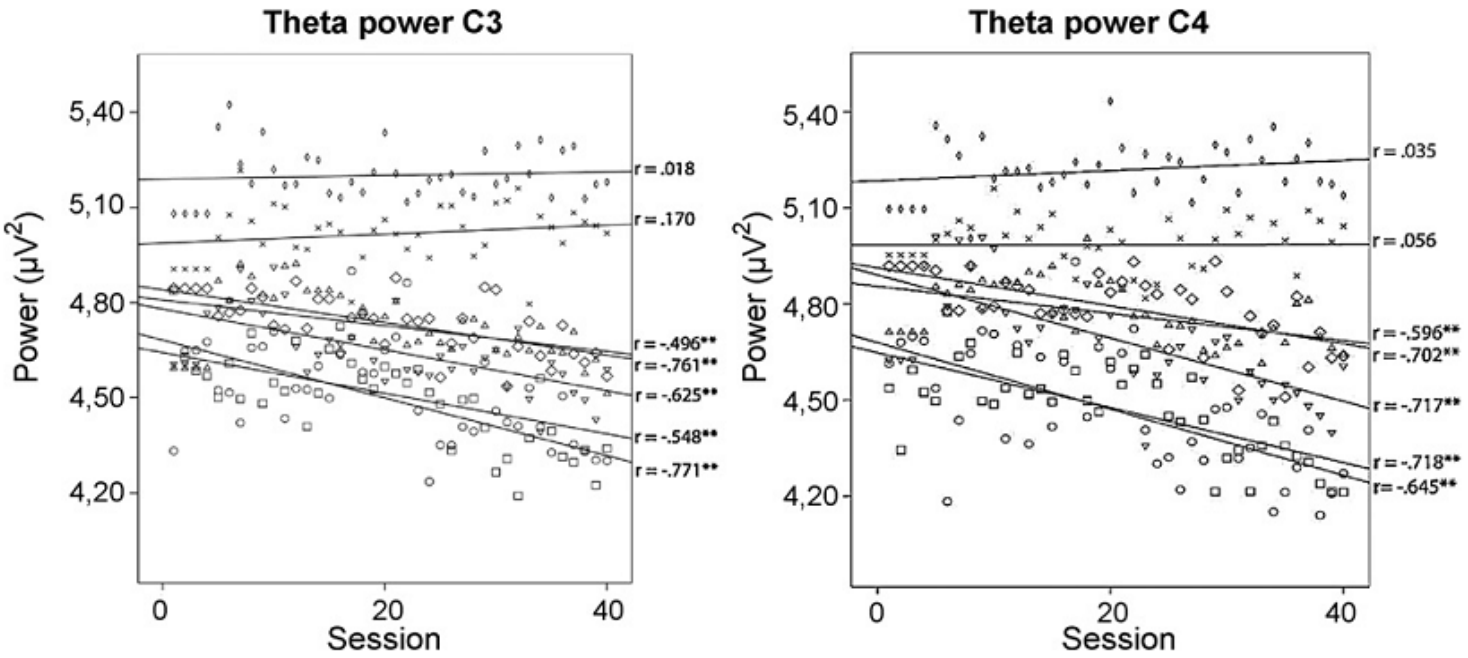
Use of Neurofeedback to treat ASD

Use of Neurofeedback to treat ASD

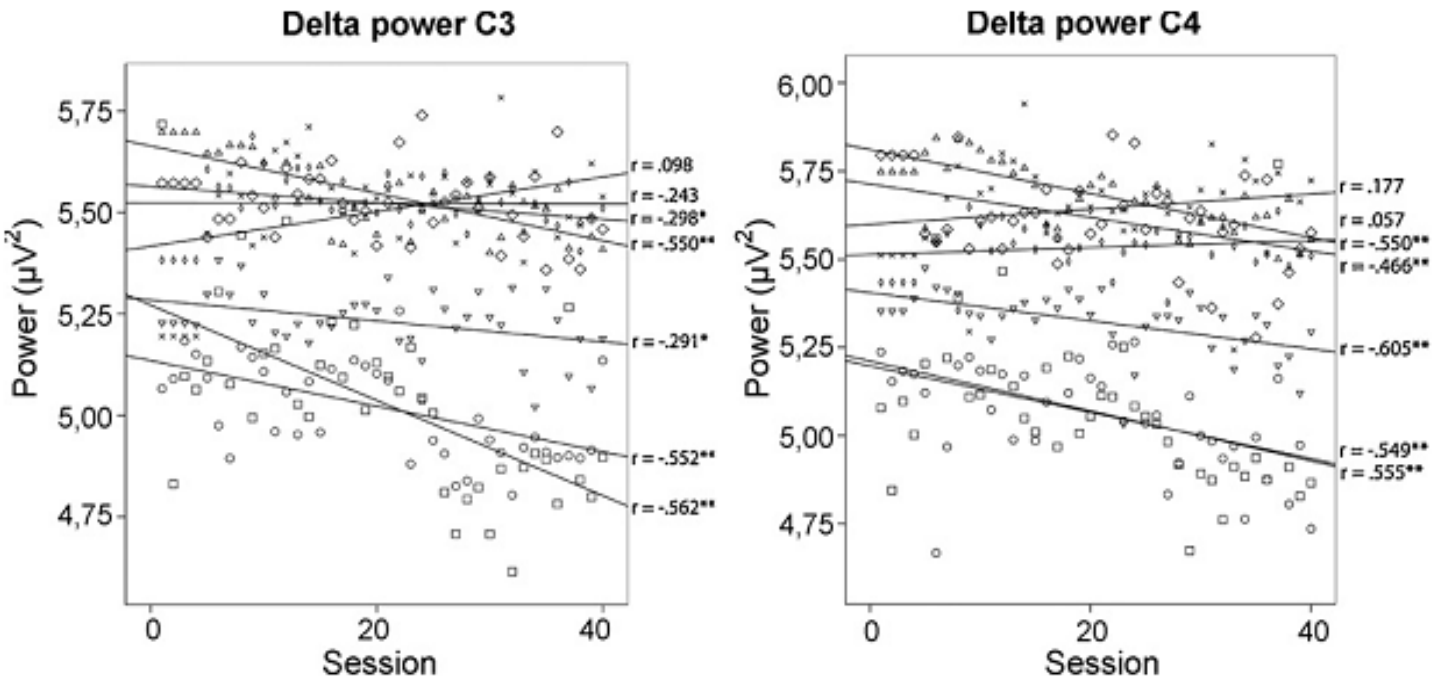
In a study published by Kouijzer (2009), subjects with ASD underwent Neurofeedback training aimed at reducing theta activity (4-7Hz) while increasing activity in the low beta band (12-15Hz). Results showed a significant reduction of theta power over 40 sessions of neurofeedback in five participants at C4 and C3. Low beta power increased significantly over time. Besides changes in theta and low beta power, changes in delta power (1.5-3.5Hz) were found as well.

Use of Neurofeedback to treat ASD



Average theta (4–7 Hz) power during neurofeedback sessions recorded over C3 (left graph) and C4 (right graph) indicating the reduction in theta power over consecutive sessions. Regression lines reflect the slope of theta reduction over time for each patient.

Use of Neurofeedback to treat ASD



Average delta (1.3–3.5 Hz) power during neurofeedback sessions recorded over C3 (left graph) and C4 (right graph) indicating the reduction in delta power over consecutive sessions. Regression lines reflect the slope of delta reduction over time for each individual patient

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Use of Neurofeedback to treat ASD

- Kouijzer conducted a trial in which seven out of 13 participants of the EEG-biofeedback group successfully reduced delta and theta power and were named as EEG-responders. EEG-responders furthermore showed a long term improvement in cognitive flexibility, whereas no such improvement was found in other participants (Kouijzer 2011).
- Thompson and Reid also conducted a trial in which neurofeedback sessions focused on decreasing slow wave activity, including delta and theta waves, decreasing beta spindling and increasing fast wave activity (SMR). Significant improvements were found on measures of attention, core symptoms of Asperger's Syndrome, achievement and intelligence (Thompson et al. 2010).

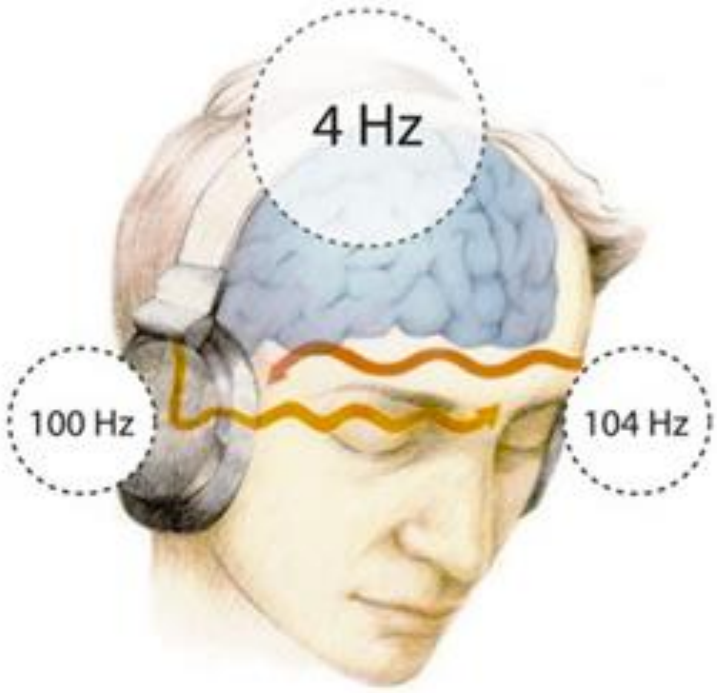
Mente Autism – Neurofeedback for ASD

Mente Autism – Neurofeedback for ASD

Mente Autism sessions aim to lower the theta/beta and delta/beta ratios. Wang et al. shows that by lowering the theta/beta ratios at the prefrontal site, there was a significant reduction in lethargy and social withdrawal in the patients. The theta/beta ratio is one of the classical indices for characterizing the ability to focus attention and to concentrate (Wang et al. 2016). By lowering both the theta/beta and delta/beta ratios through neurofeedback, Mente Autism aims at increasing children's concentration and interaction.

Our Idea to help children on the Autism Spectrum

Mente Autism - The science under the hood



Mente Autism presents the user with a mixture of warble tones and binaural beats that are tailor-made using a set of generative rules with the brain activity levels derived from the user.

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Our Idea to help children on the Autism Spectrum

Mente Autism - The science under the hood

With its sonified neurofeedback, Mente Autism affects the auditory cortex, which is very close to the thalamus, and stimulates it into reducing delta and theta activity while stabilizing alpha and beta. This is done in a closed loop feedback system.

A daily 40-minute session is enough to initiate the closed loop feedback system within the brain to give rise to better patterns.

When we sleep, our brain is refreshed and the neurofeedback effect fades.

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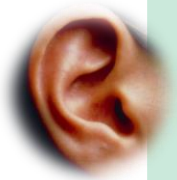
Our Idea to help children on the Autism Spectrum

Mente Autism - The science under the hood

Why choose sonified neurofeedback?



Auditory stimulation	Visual stimulation
• No registered side effects on auditory stimulation neuro-feedback • No risks of inducing seizures on patients with ASD • Access to brainstem stimulation • Auditory cortex can access and is linked to vital parts in the brain	• Can induce seizures on ASD patients • No access to brainstem stimulation • Has limited access to other parts in the brain – less than auditory cortex • Mostly used in clinical neurofeedback

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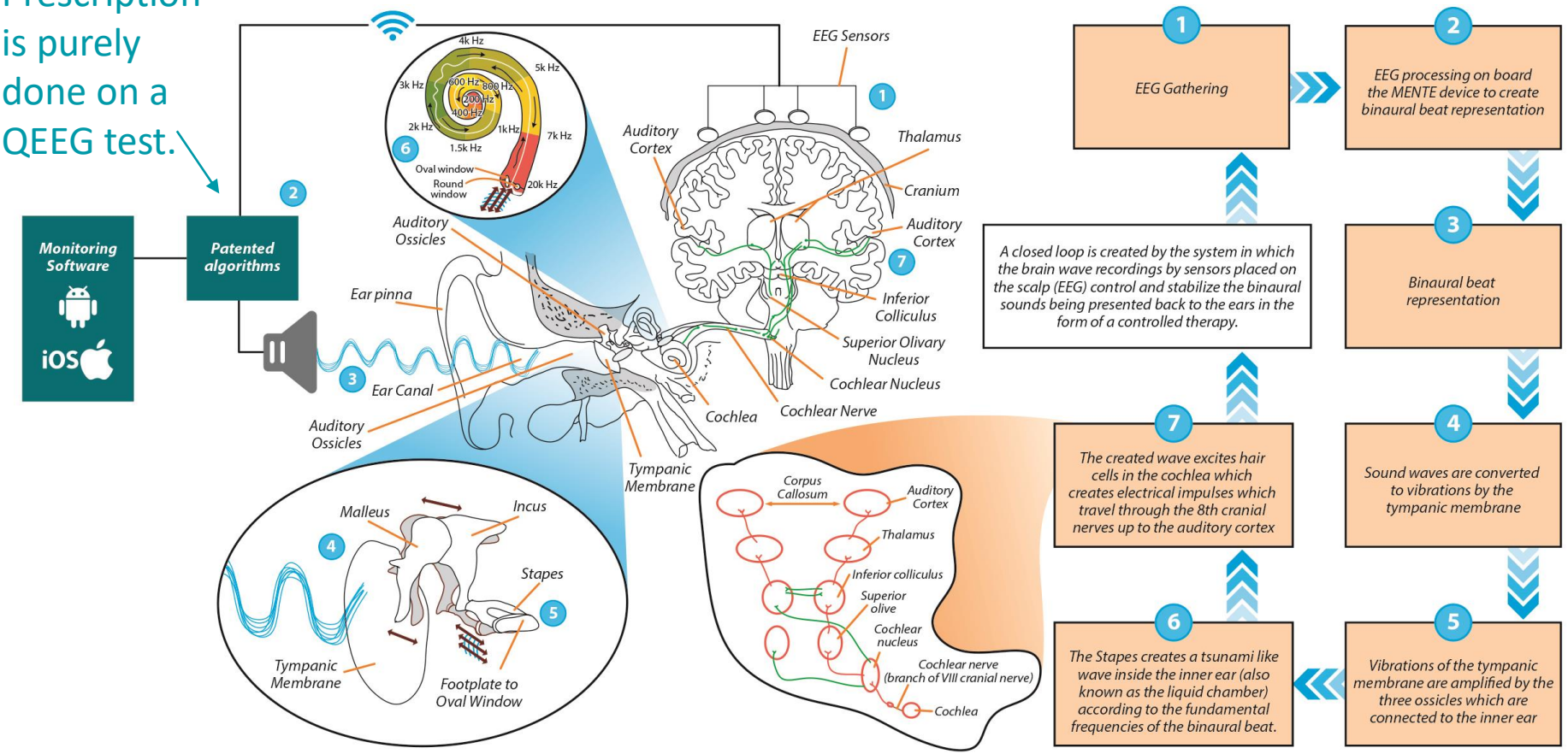
Our Idea to help children on the Autism Spectrum

Mente Autism - The science under the hood

Product Prescription is purely done on a QEEG test.



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Our Idea to help children on the Autism Spectrum

Mente Autism - The science under the hood

Validation:

CE Medical Certification for the product has been achieved

An Independent, double blinded , randomized clinical trial is currently underway in USA , more information on :
https://clinicaltrials.gov/ct2/show/NCT02773303?term=Mente+autism%23&rank=1

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Thank you.

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