Athira PHARMA

Virtual KOL Event: Educational Webinar on the Clinical Applications of ERP P300 with Drs. John Olichney, Hans Moebius and Kevin Church

NOVEMBER 5, 2021

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This presentation and the accompanying oral commentary contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements are based on our management's beliefs and assumptions and on information currently available to our management. Forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified. In some cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "could," "expect," "plan," anticipate," "believe," "estimate," "predict," "intend," "potential," "would," "continue," "ongoing" or the negative of these terms or other comparable terminology. Forward-looking statements include all statements other than statements of historical fact contained in this presentation, including, but not limited to, information concerning timing and success of our planned development activities and the potential therapeutic benefits of our product candidates,.

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This presentation contains estimates, projections and other information concerning market, industry and other data. We obtained this data from our own internal estimates and research and from academic and industry research, publications, surveys, and studies conducted by third parties, including governmental agencies. These data involve a number of assumptions and limitations, are subject to risks and uncertainties, and are subject to change based on various factors, including those discussed in our filings with the SEC. These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us. While we believe such information is generally reliable, we have not independently verified any third-party information.

This presentation concerns drug candidates that are under clinical investigation and which have not yet been approved for marketing by the U.S. Food and Drug Administration. The drug candidates are currently limited by federal law to investigational use, and no representation is made as to their safety or effectiveness for the purposes for which they are being investigated.

We announce material information to the public through a variety of means, including filings with the SEC, press releases, public conference calls, our website (www.athira.com), our investor relations website (investors.athira.com), and our news site (investors.athira.com/news-and-events/press-releases). We use these channels, as well as social media, including our Twitter account (@athirapharma) and Facebook page (https://www.facebook.com/athirapharmainc), to communicate with investors and the public about Athira, our products, and other matters. Therefore, we encourage investors, the media, and others interested in Athira to review the information we make public in these locations, as such information could be deemed to be material information.

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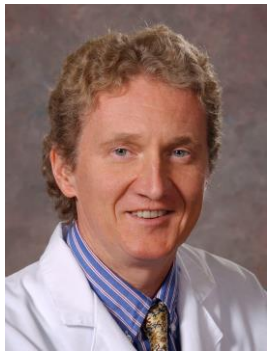
Presenter Introductions



John M. Olichney, M.D. is a board-certified Behavioral Neurologist and Dementia specialist whose research interests include: Alzheimer's disease (AD) and other neurodegenerative disorders; electrophysiological and neuroimaging studies of memory and language processes; and the treatment and early diagnosis of Alzheimer's disease (MCI, pre-clinical AD). He serves as the Leader of the UC Davis Alzheimer's Disease Center's Clinical Core and Clinical Trials Unit. He also directs a 2 year UCNS-accredited Fellowship on "Behavioral Neurology and Neuropsychiatry in Neurodegeneration and Aging" which trains neurologists and psychiatrists to become experts in dementia research and care.

Hans Moebius, M.D., Ph.D. has served as our Chief Medical Officer since April 2019. Prior to joining Athira, Dr. Moebius co-founded Exciva GmbH, a company focusing on targeted drug rescue, and served as its Chief Executive Officer and Chief Medical Officer from 2016 to 2019, and again as acting Chief Medical Officer since April 2020. For the past 30+ years, his focus was on drug development, starting at Novartis, and later EU and US companies as Chief Medical Officer, working in neuropsychiatric indications and with diverse approaches in neurodegenerative disorders. Six CNS drugs made it to market with his leadership, e.g. memantine and incobotulinumtoxin A. He is co/inventor of Namzaric®, Deraphan®, and several more patents. Dr. Moebius earned his M.D. from University of Heidelberg followed by a Ph.D. in experimental pharmacology.

Kevin Church, Ph.D. has served in various roles at Athira since 2016, including Research Scientist, Director of Discovery, now as Vice President of Discovery. Dr. Church has research experience in diverse fields of study including neurodegenerative diseases, wound healing, and cancer. Dr. Church earned his Ph.D. in molecular biosciences from Washington State University in 2016, and prior to that earned his B.S. in microbiology from the University of Idaho in 2006. Dr. Church leads the drug discovery teams at Athira which have developed a series of novel small-molecules that are designed to activate a key neurotrophic system and may have substantial therapeutic potential in a variety of neurological disorders.

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Agenda

Mark Litton, Ph.D., M.B.A.	Opening and Athira Overview
Kevin Church, Ph.D.	ATH-1017 mechanism of action and rationale for translational measures, qEEG and ERP P300
John Olichney, M.D.	Introduction to Event-Related Potentials (ERPs) and Quantitative EEG (qEEG) in Alzheimer's Disease (AD)
Hans Moebius, M.D., Ph.D.	Athira's strategy and rationale for clinical trial design and summary of ERP P300 latency data in Alzheimer's subjects
Moderated by Mark Litton, Ph.D., M.B.A.	Questions

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Athira Overview

Novel approach to rapidly improve cognition

Leveraging a critical repair pathway, HGF/MET, and naturally occurring repair mechanisms that are agnostic to underlying disease pathology

Lead Asset
ATH-1017

Lead indication is in potentially pivotal trial

Encouraging Phase 1 clinical data in Alzheimer's disease

- **LIFT-AD trial actively recruiting, topline data by late 2022**
- **ACT-AD trial topline data by first half 2022**

Efficient clinical development strategy

Clinical development strategy to investigate fast onset, tangible cognitive improvement

Potential follow-on indications with established regulatory pathway and faster timelines

Pipeline of novel, small molecule compounds

Opportunity to explore several neurological indications

- **CNS degenerative, PNS disorders, neuropsychiatric indications**

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ATH-1017 mechanism of action and rationale for translational measures, qEEG and ERP P300

Kevin Church, Ph.D.
Vice President of Discovery, Athira

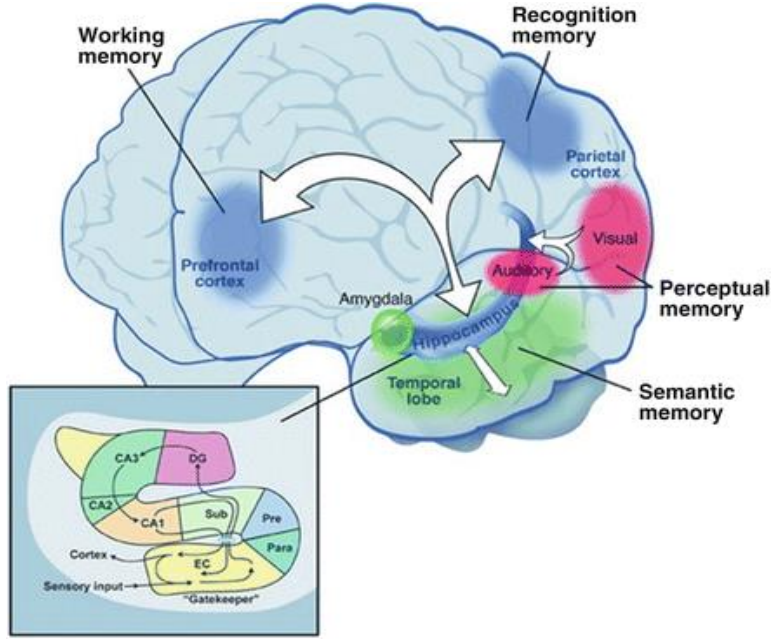
HGF/MET System is Critical to Normal Brain Function

MET is one of the most stably expressed genes in the adult human brain

- Stable MET expression is a signature of the healthy adult brain[1]

Suggests that dysregulation of HGF/MET could be implicated in brain pathologies

MET expression is reduced in the brains of AD patients[2]



Adapted from *Hokama et al, Cerebral Cortex 2014*

Neuronal MET expression in AD:

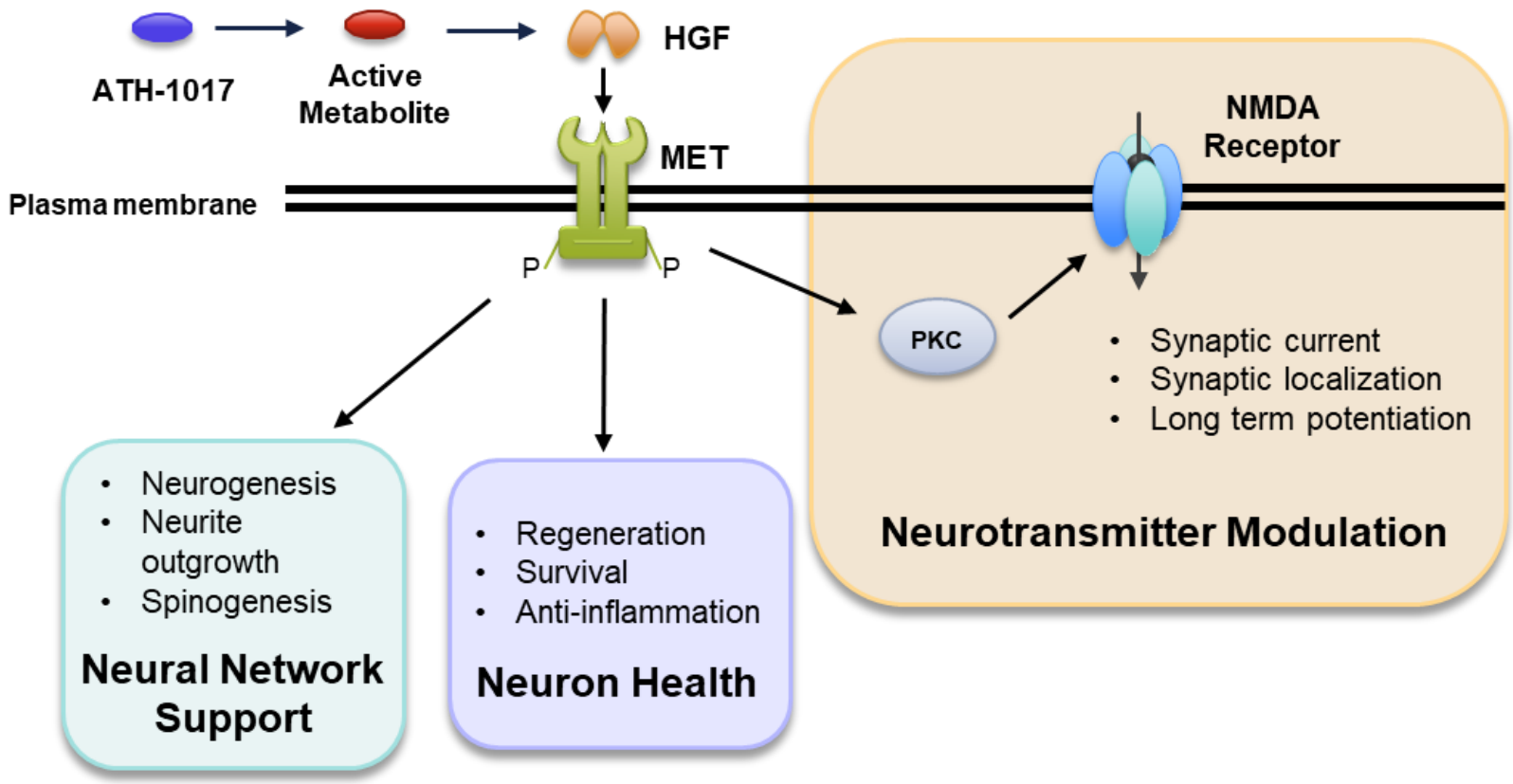
- **75%** reduction in the hippocampus
- **25%** reduction in the frontal cortex

[1]*Hawrylycz et al, Nature Neuroscience 2015*
[2]*Hamasaki et al, Neuropathology 2014*

ATH-1017 is a Positive Modulator of the HGF/MET Neurotrophic System

ATH-1017:

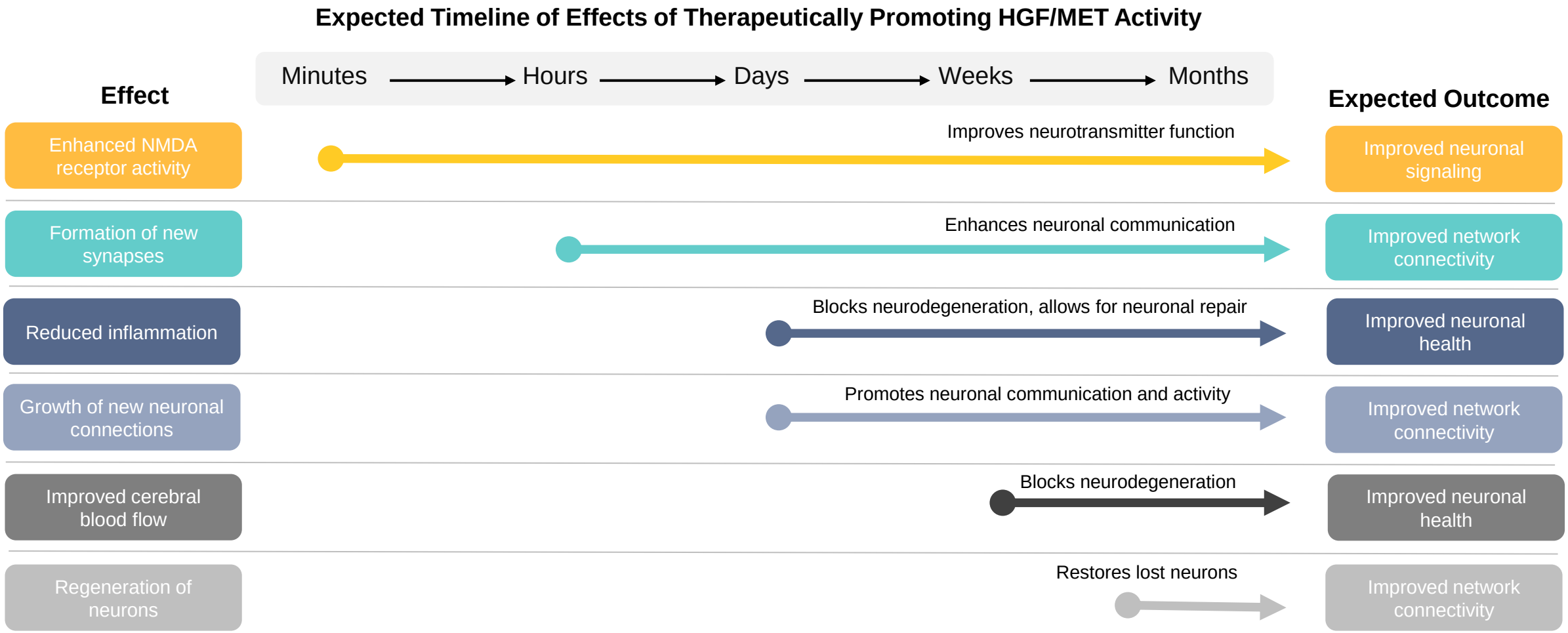
- Administered via subcutaneous injection
- Is a small molecule prodrug that is immediately converted to an active metabolite in plasma
- Crosses the blood-brain barrier
- Positively modulates HGF/MET



Multimodal, protective, and regenerative

HGF/MET signaling and downstream effects described in:
Desole et al, Frontiers in Cell and Developmental Biology 2021
Funakoshi and Nakamura, Current Signal Transduction Therapy 2011

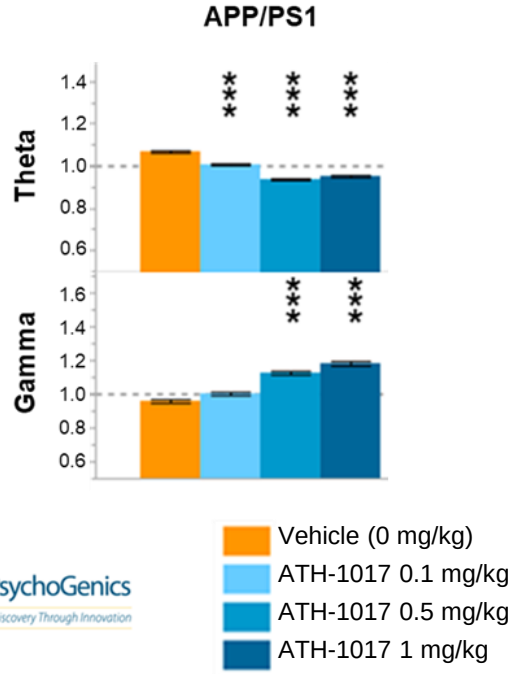
Promoting HGF/MET Activity May Lead to Both Short and Long-Term Beneficial Effects



ATH-1017 Induces Immediate and Sustained EEG Effects in APP/PS1 Mice

Induction of <u>acute EEG effects</u>

- ↑ Gamma power
- ↓ Theta
- Dose-dependency

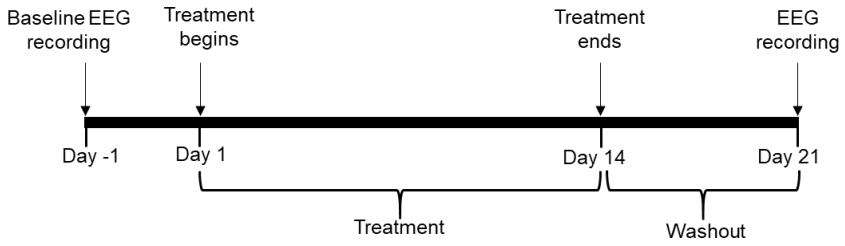


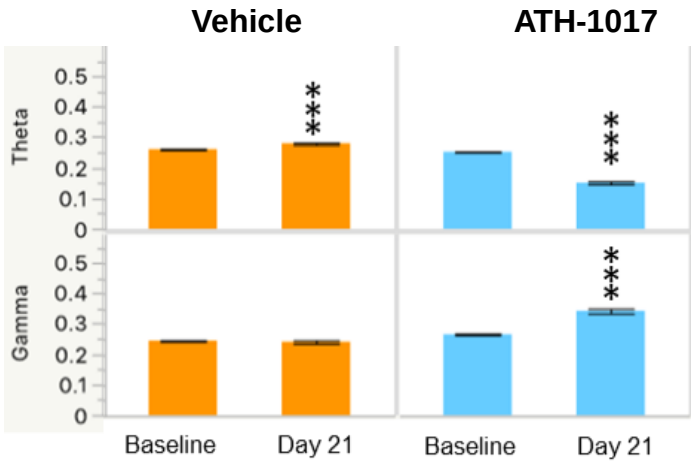
PsychoGenics
Redefining Drug Discovery Through Innovation

ATH treatment induced significant dose-dependent effects on EEG within 1 hr post treatment. N=5, ***p<0.001

Induction of <u>sustained EEG effects</u>

After 7 days of washout, persistent EEG effects are observed (↑ Gamma; ↓ Theta)





ATH-1017 treatment induced significant and persistent EEG effects after 2 weeks of treatment. N=5, ***p<0.001

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ATH-1017 Therapeutic Rationale

- HGF/MET is a well-established neurotrophic factor system that is critical for normative brain function in the healthy brain
- ATH-1017 is a highly specific, brain-penetrant small molecule therapeutic designed to positively modulate HGF/MET
- Multi-pronged downstream effects potentially addresses several pathologies in neurodegenerative diseases, including Alzheimer's disease
- Steady state PK is not necessary, pulsatile activation of the target is sufficient
- Modulates EEG signals at exposures that overlap with procognitive effects – suggests EEG as a translatable biomarker to inform clinical dosing
- Improvement in neuronal health and synaptic connectivity may positively impact ERP signals

CENTER FOR MIND AND BRAIN

UNIVERSITY OF CALIFORNIA, DAVIS

Introduction to Event-Related Potentials (ERPs) and Quantitative EEG (qEEG) in Alzheimer's Disease (AD)

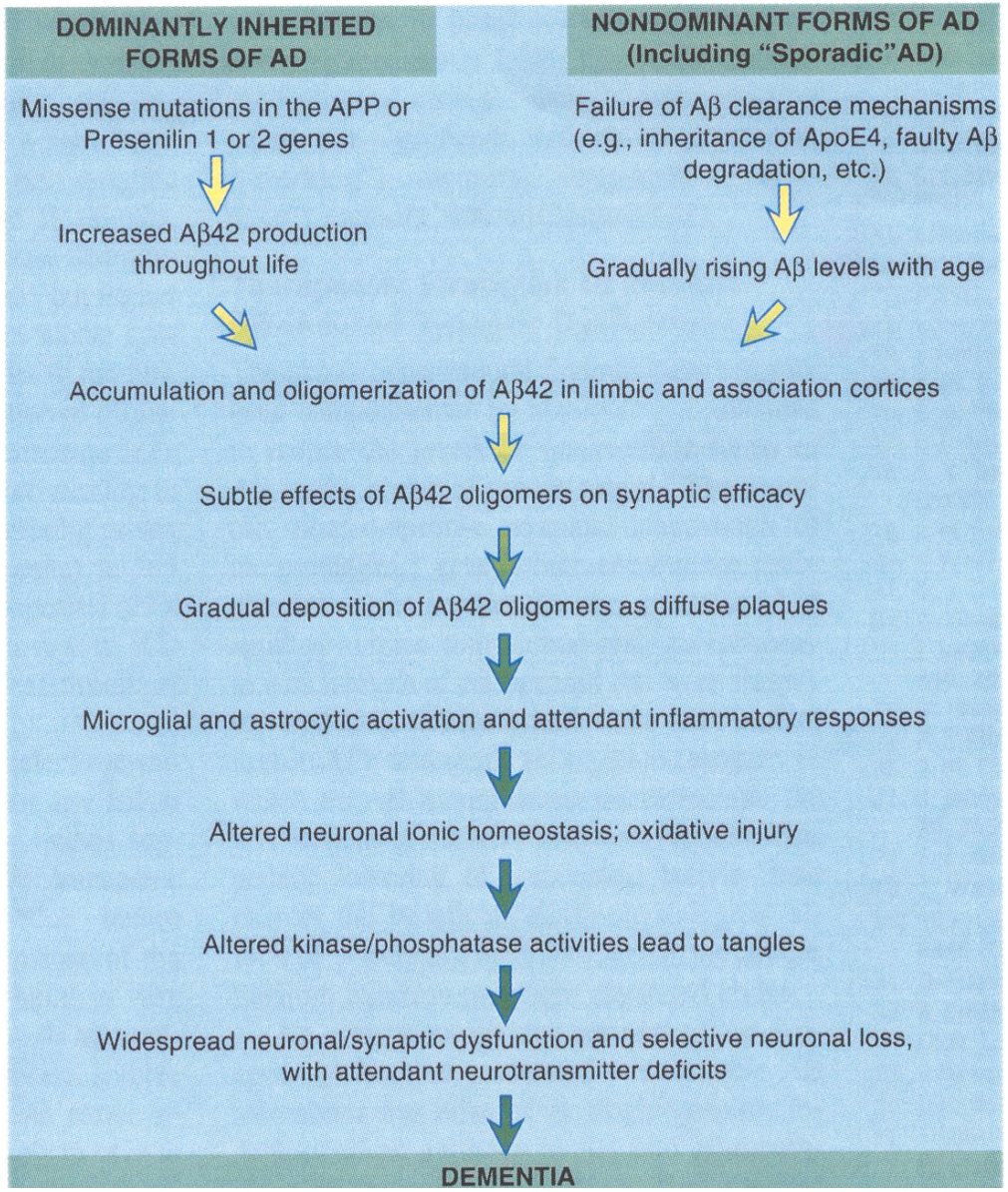
John M. Olichney, MD

Professor of Neurology

UC Davis School of Medicine

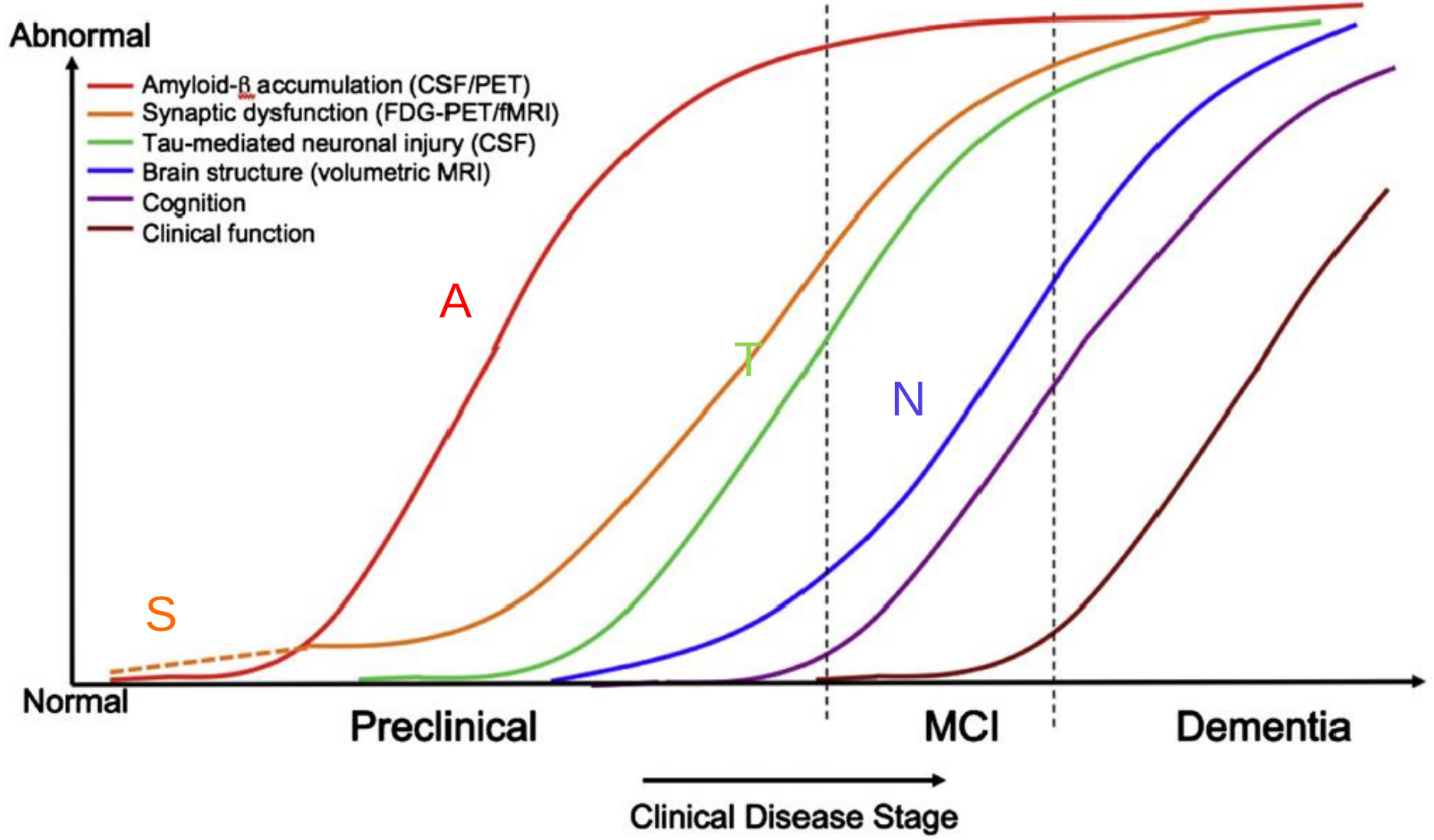
Alzheimer's Disease Is a Synaptic Failure

Dennis J. Selkoe



www.sciencemag.org SCIENCE VOL 298 25 OCTOBER 2002

- In its earliest clinical phase, Alzheimer's disease characteristically produces a remarkably pure impairment of memory.
- The amnesia of early AD has been interpreted as evidence for a primary disorder of synaptic plasticity (Selkoe, 2002; Mesulam, 1999).
- Mounting evidence suggests that this syndrome begins with subtle alterations of hippocampal synaptic efficacy prior to frank neuronal degeneration, and that the synaptic dysfunction is caused by diffusible oligomeric assemblies of the amyloid β protein.
- Aβ oligomers and β-amyloid derived diffusible ligands (ADDLs) can inhibit LTP (e.g., Walsh et al., 2002), decrease NMDA receptors (Lacor et al., 2007) and **disrupt synaptic transmission**.

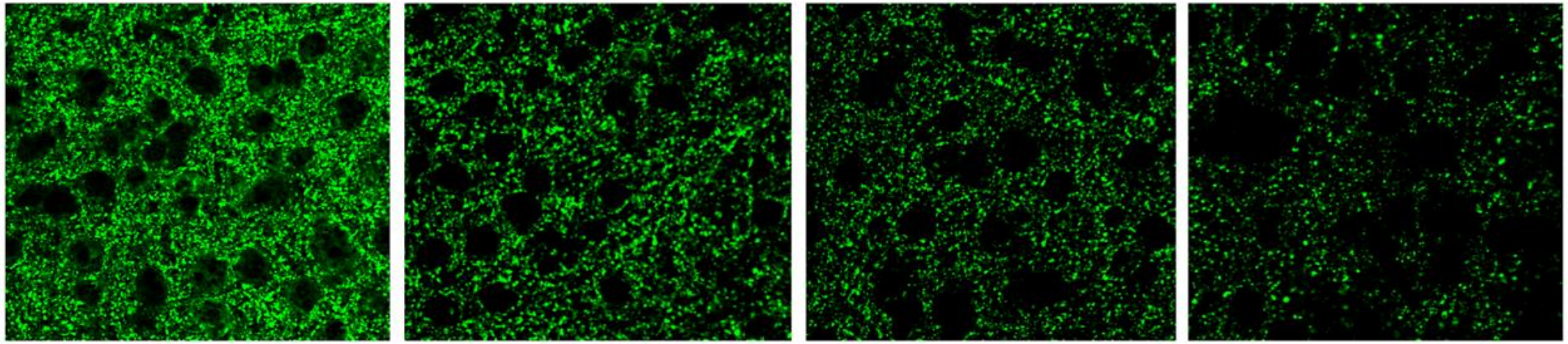


Sperling R, et al., Alzheimer's & Dementia 2011; 7: 280–292.

Jack CR, et al., The Lancet Neurology 2010;1:119-128

Synapse loss in Alzheimer's Disease:

- *Immunochemical and ultrastructural studies indicate that in AD there is 20-42% loss of presynaptic terminals.*
- *Synapse loss is an EARLY event that begins in the hippocampus, followed by the frontal cortex, temporal, cingulate and parietal.*
- *Early loss of synapses following the known anatomical patterns of dennervation is also observed in experimental animal models*



Non-demented Early Intermediate Advanced

EEG measures of neural synchronization and connectivity in AD

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journal homepage: www.elsevier.com/locate/neuaging

Review

What electrophysiology tells us about Alzheimer's disease: a window into the synchronization and connectivity of brain neurons

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REVIEW ARTICLE

Alzheimer's & Dementia®
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Measures of resting state EEG rhythms for clinical trials in Alzheimer's disease: Recommendations of an expert panel

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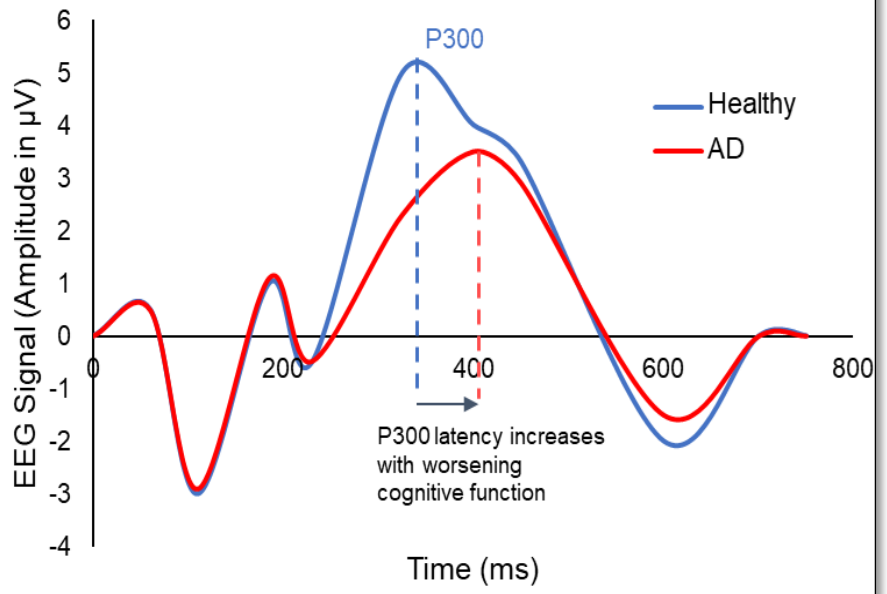
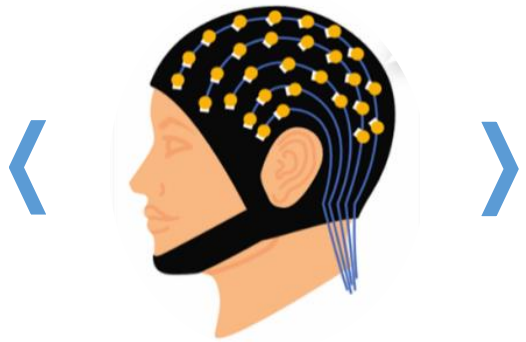
EEG/ERP Measure Electrical Activity from Firing Neurons & Synapses

EVENT RELATED POTENTIALS (ERP): P300 Latency

- Functional measurement for working memory access and executive function
- Strongly suggestive of memory improvement

Pathological changes in P300 latency correlate with cognitive impairment



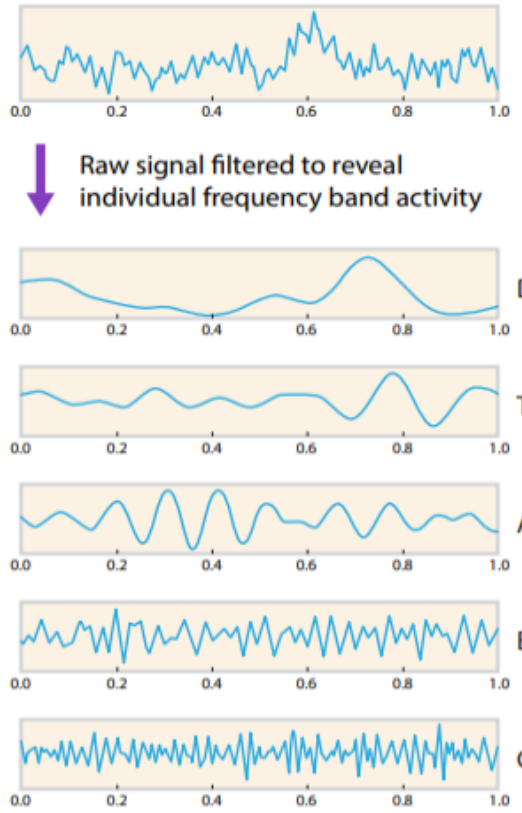


EEG records brain electrical activity from electrodes placed on the scalp

QUANTITATIVE EEG (qEEG)

- Translational tool from rodents to humans
- PK/PD modeling for dose selection

Noninvasive EEG recordings reflect brain activity and function



Event-Related Potentials and Cognition

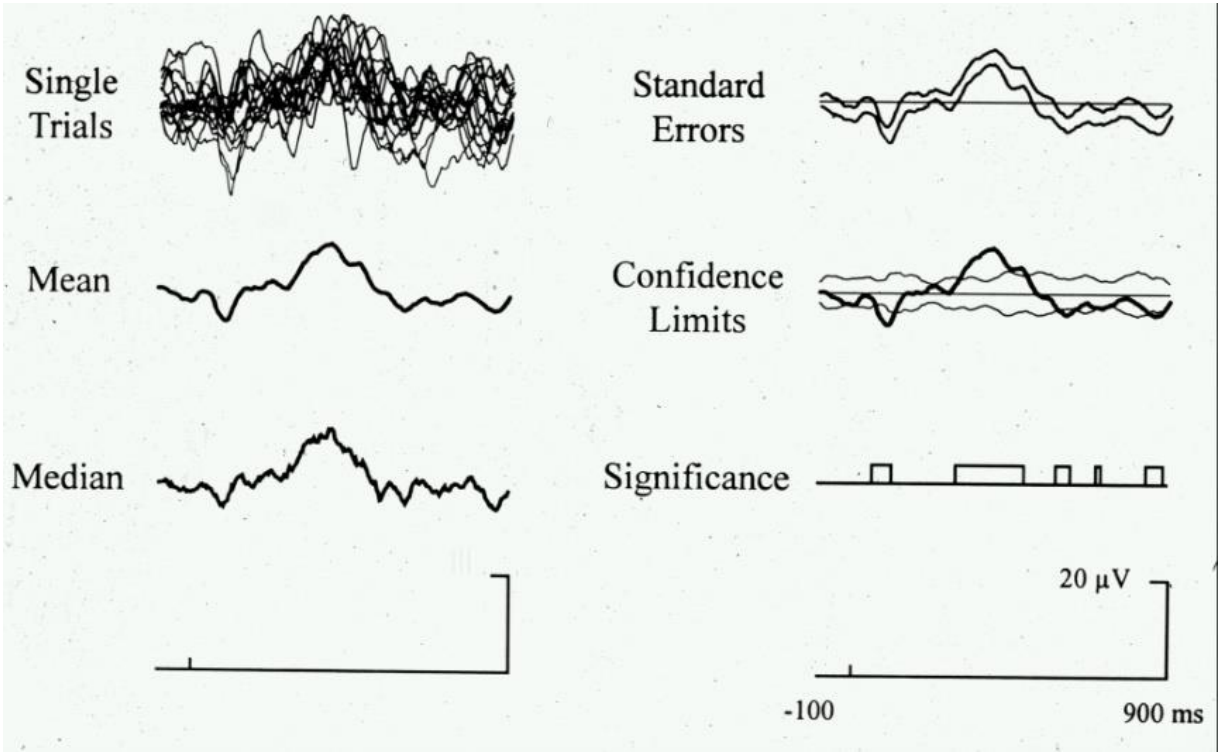
PROS

1. Temporal Resolution (milliseconds)

2. Summation of EPSPs & IPSPs

3. Sensitive to Task Manipulations

4. Sensitive to Temporal pattern of neural responses (stages of cognitive processing, frequency domain



CONS

1. Spatial Resolution

2. Difficult to Isolate and Locate “Neural Generators”(dependent on neuronal & dipole orientation)

What electrophysiology tells us about Alzheimer's disease: a window into the synchronization and connectivity of brain neurons

Cognitive ERPs offer several advantages for studying cognition, such as:

- Millisecond temporal resolution, and the ability to separate the various stages of cognitive processes.
- Event-related potentials (ERPs) directly measure the speed and strength of cognitive processing.
- Since they are mainly composed of summated EPSPs & IPSPs, they should be particularly **sensitive to detecting Synaptic disorders.**

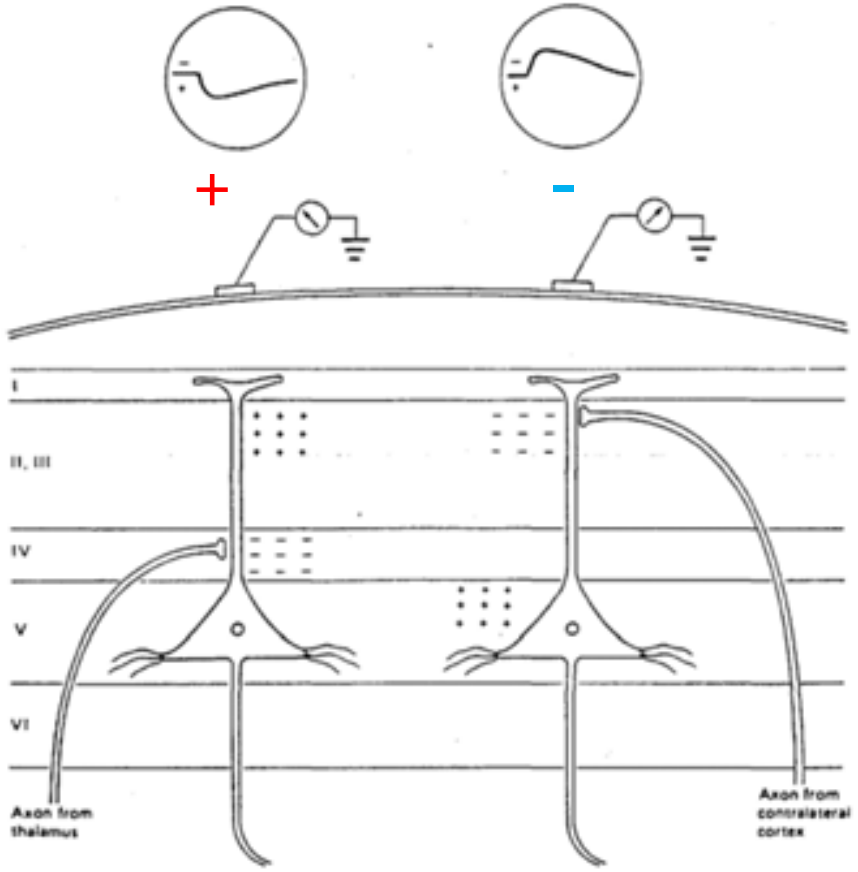
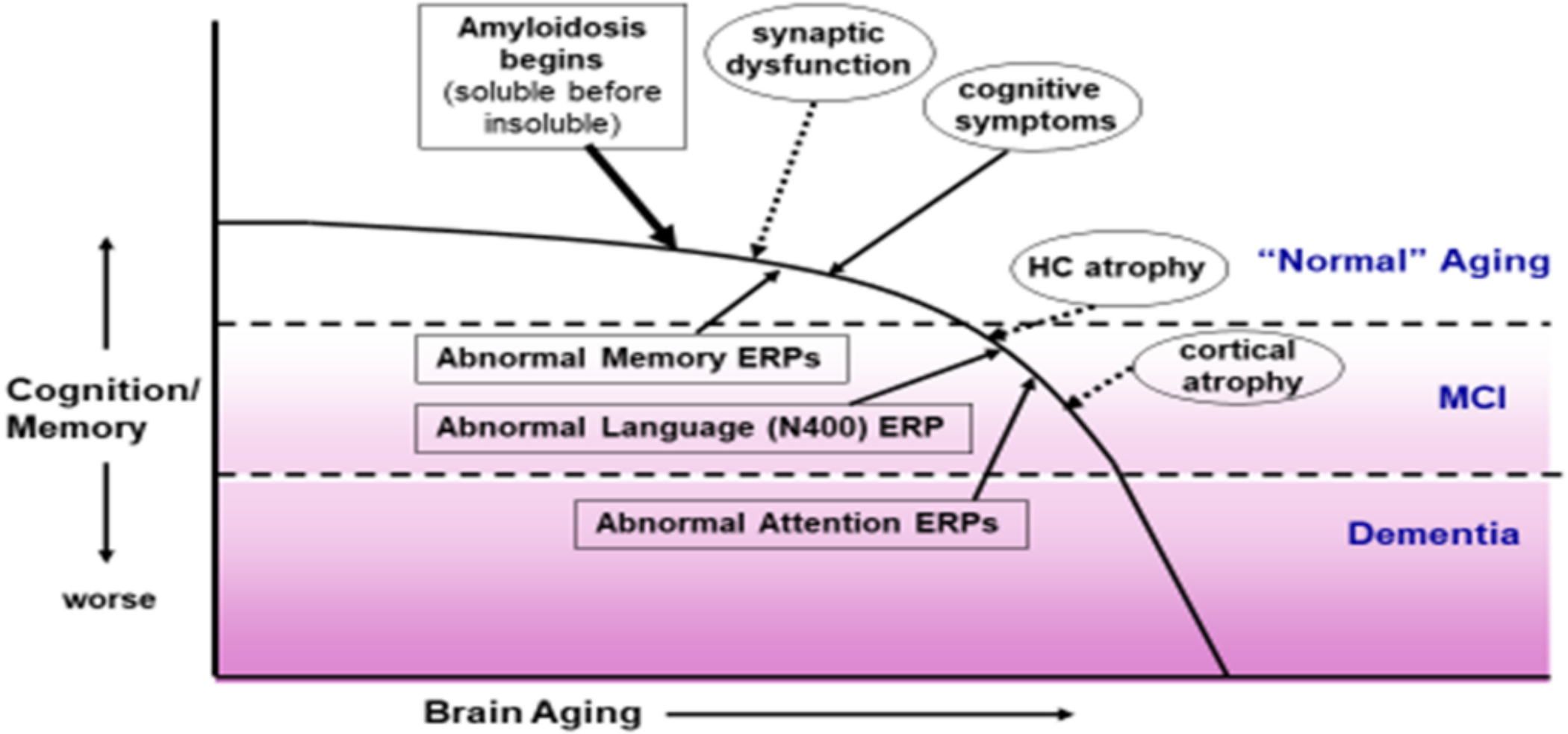


FIGURE 2. Generation of extracellular voltage fields from graded synaptic activity (from Martin, 1991). Relationship between polarity of surface potentials and site of dendritic postsynaptic potentials.

Babiloni C, et al., Neurobiology of Aging 2020; 85:58-73

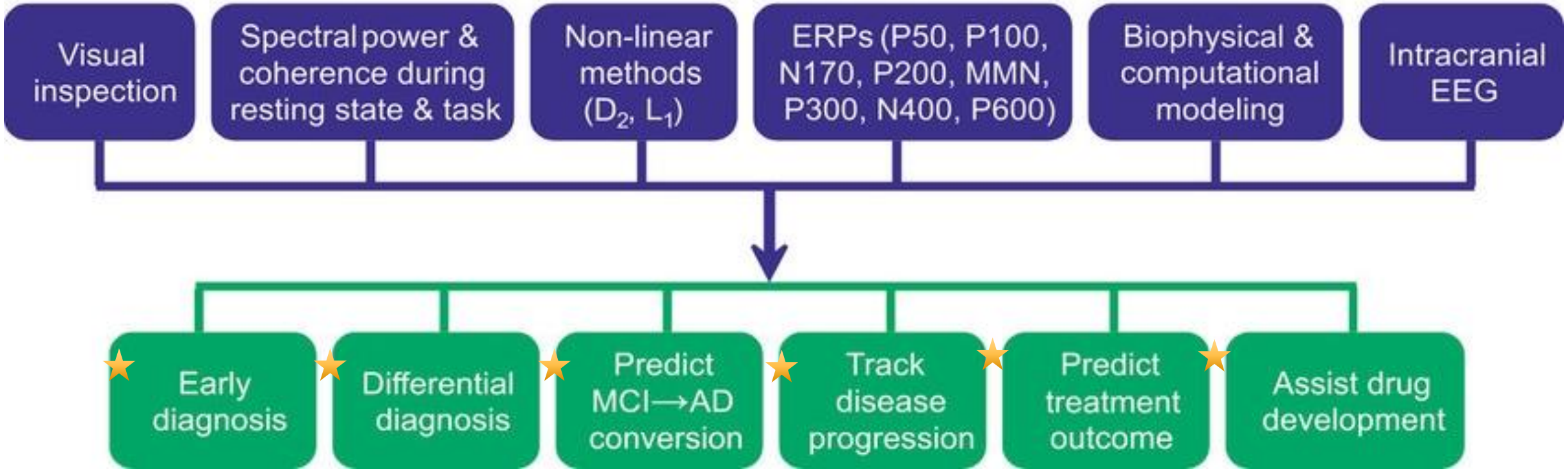
Longitudinal Cognitive ERPs: Applications for AD treatment trials

Fig 1. Provisional Model: Temporal sequence of events in the evolution of AD



Applications of ERP/EEG for AD treatment trials

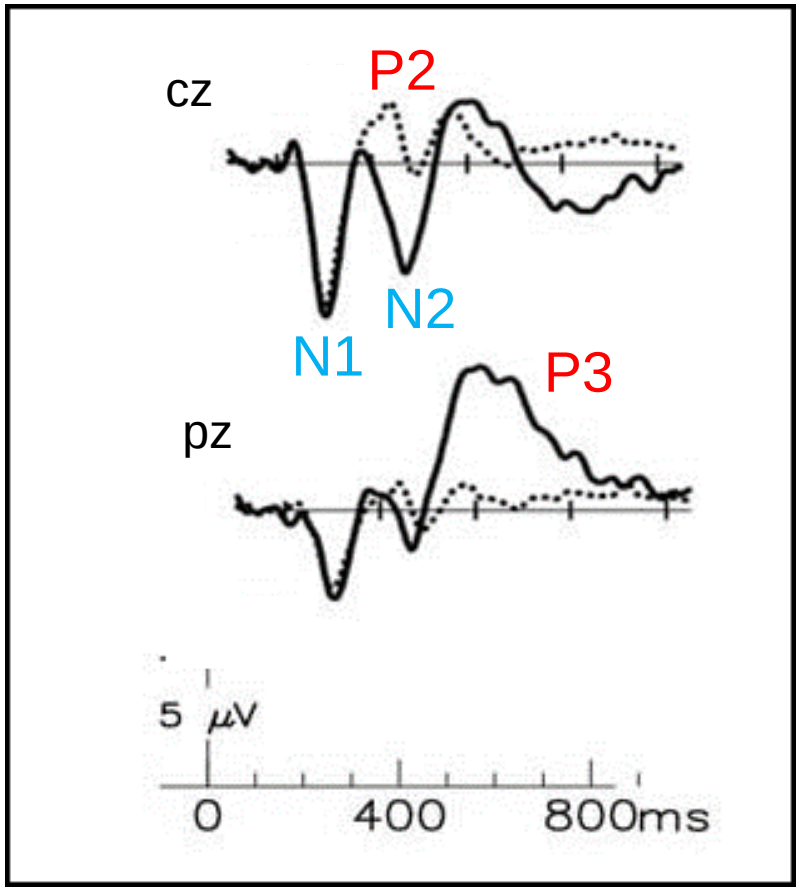
- **Sensitive to medication treatment effects (e.g. Reeves et al 1999, Kubova et al 2010). *Aid clinical trial development*.**
- **Tracking of disease progression: Physiological biomarker of real time brain function.**
- **Subject selection/enrichment.**
- **Understand *how therapies work*, which neural systems and cognitive stages of processing are affected.**



Horvath A, Szucs A, Csukly G, et al., Frontiers in Bioscience 2018; 23:183-220.

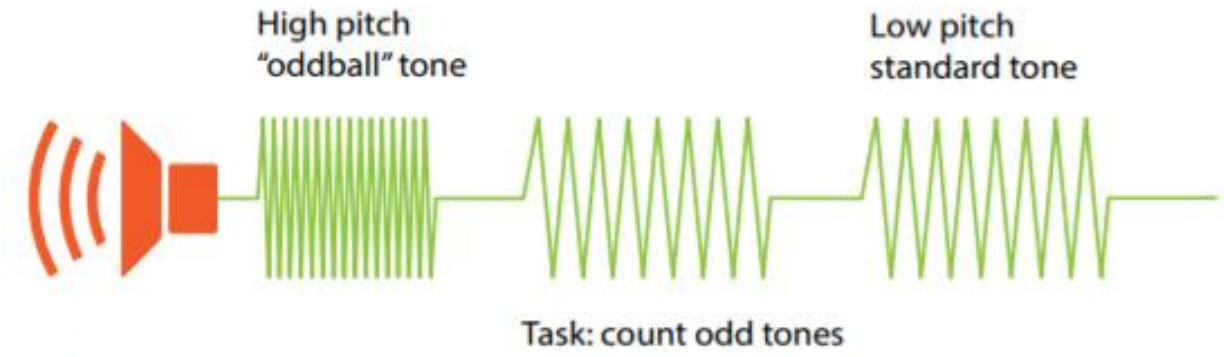
Auditory ERP components

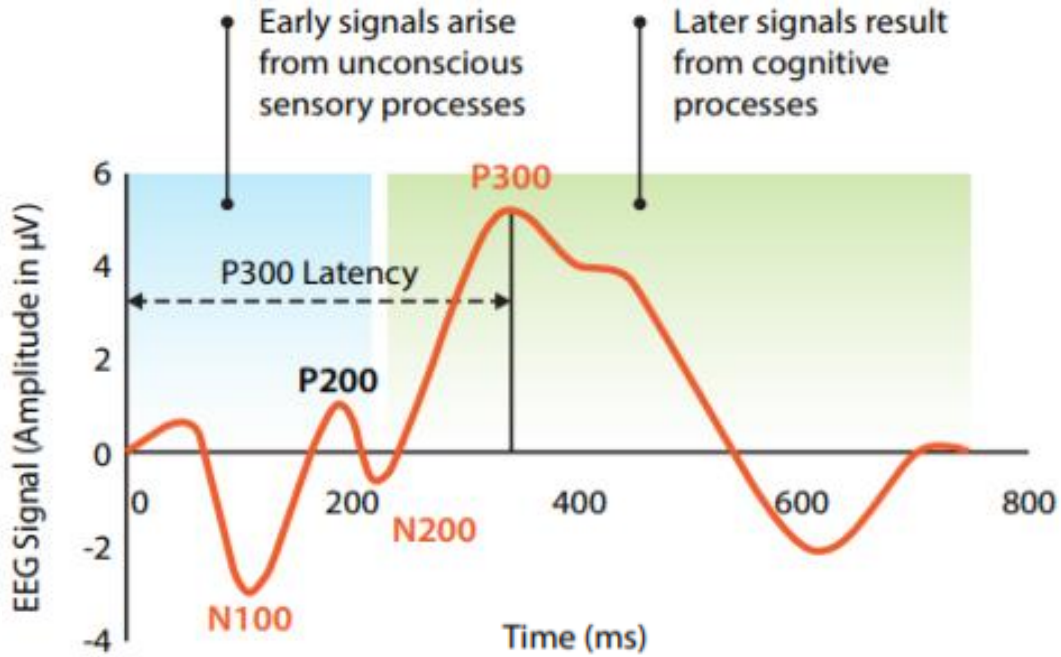
- N1:
  - ***Early attention*** (mostly automatic)
  - Sensitive to sensory characteristics of stimuli
  - Generated in the primary auditory cortex
- N2:
  - ***Later attention*** (MMN: automatic attention; N2b controlled/selective attention)
  - Generated in the superior temporal gyrus
- P3:
  - Context/***working memory updating***
  - Larger response to targets with lower probability, higher saliency, or more attentional resources
  - Distributed generators: temporoparietal junction, hippocampus, parahippocampal gyrus, pos. cingulate and frontal lobe.



Auditory P300 ERP Paradigm

- Task is to count the “oddball” tones (more WM than simple button press) or simple button press.
- A P300 wave is generated in response to the “oddball” tone
- Repetition is key, the more trials the better the data quality
- Phase-locked responses to a target “oddball” tone are averaged to produce an ERP waveform

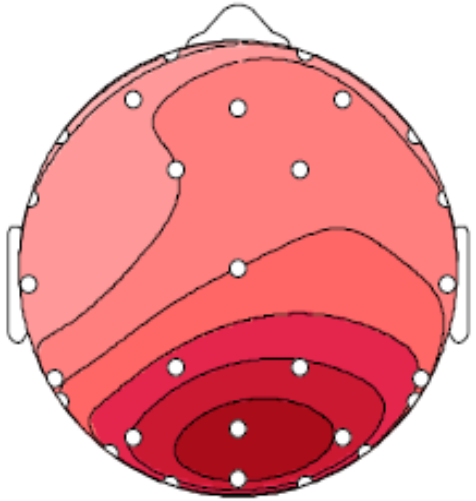




“Controlled” Attention & Working Memory Access

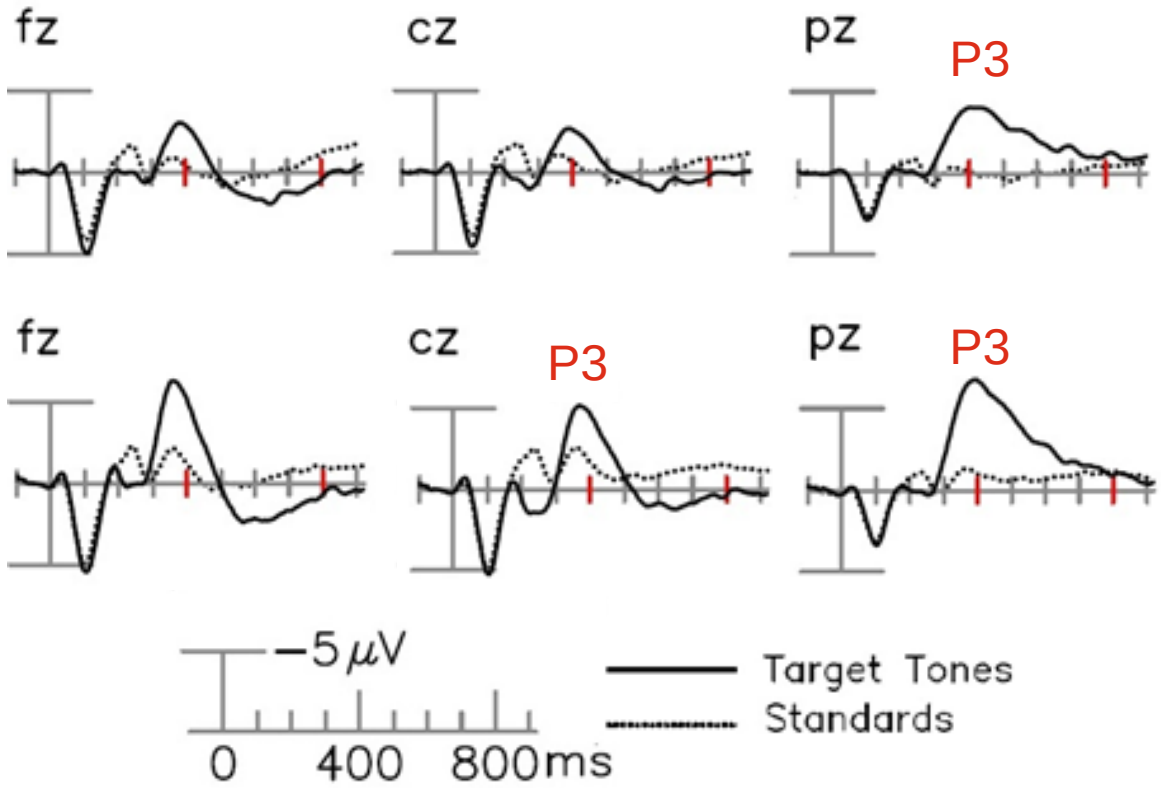
Pre-attentional & “Automatic” Attention

“Binding” of Events, Emotional Processing

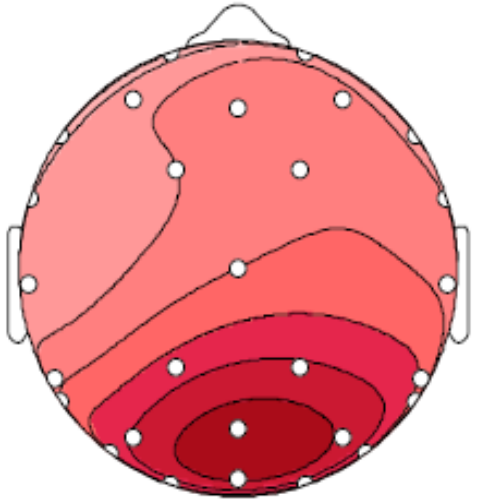


P300 amplitude: Is bigger better?

- **P3 Amplitude related to Stimulus Probability, Attentional resources, Saliency (R. Johnson Triarchic Model)**



P300 & Aging



Scalp positivity, parietal peak 300 ms
"Updating of Working Memory & Memory storage"

P300 amplitude (Pz) decreases with age = 0.14 uV/year
P300 latency (Pz) increases with age by 1-2 ms/yr (Fjell & Walhovd, 2001; Polich 2012)

Modulated by cholinergic agents (Meador et al 1989; Pineda et al 1996; Potter et al 2000, Thomas et al 2001, Polich 2012)

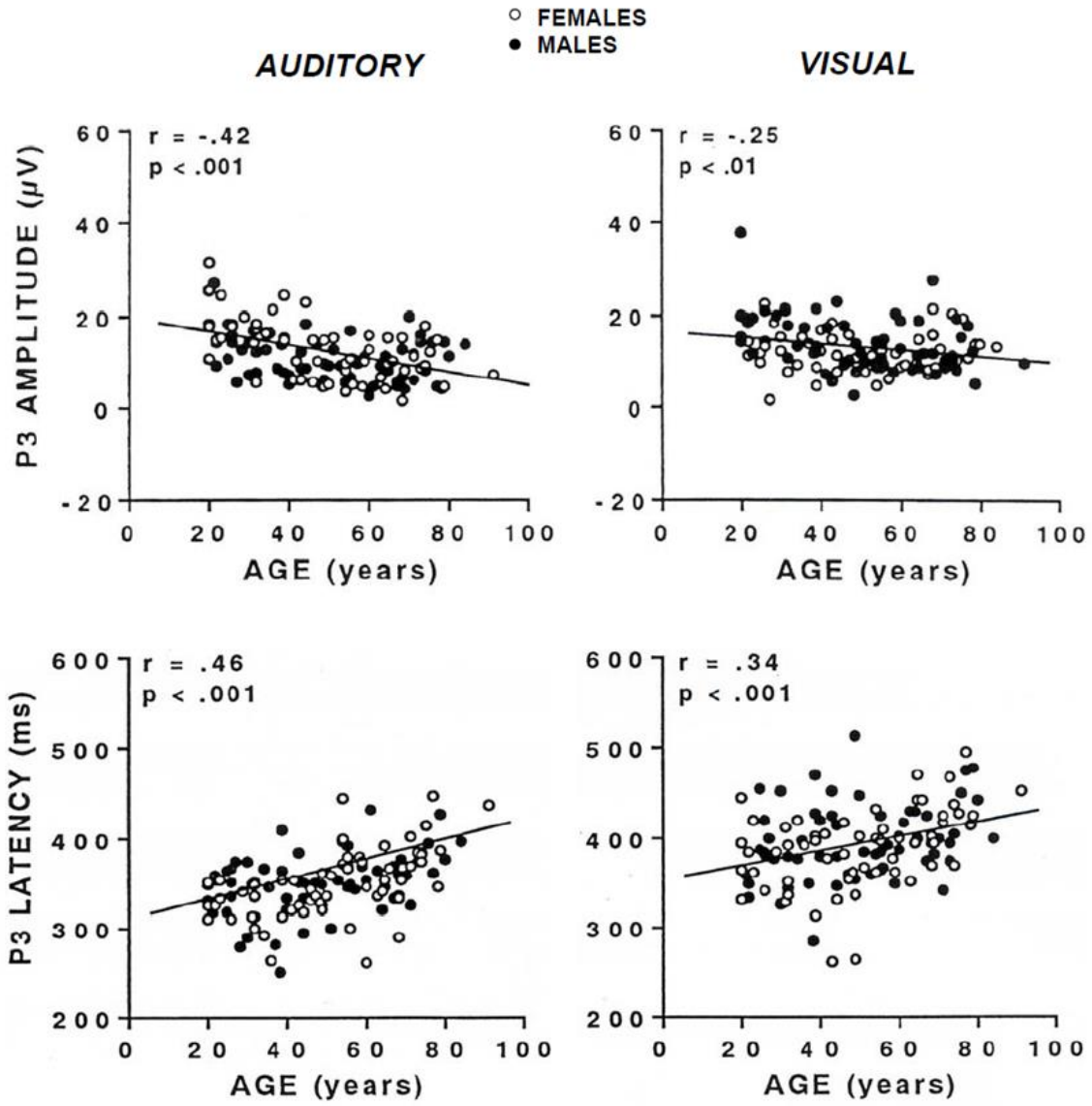
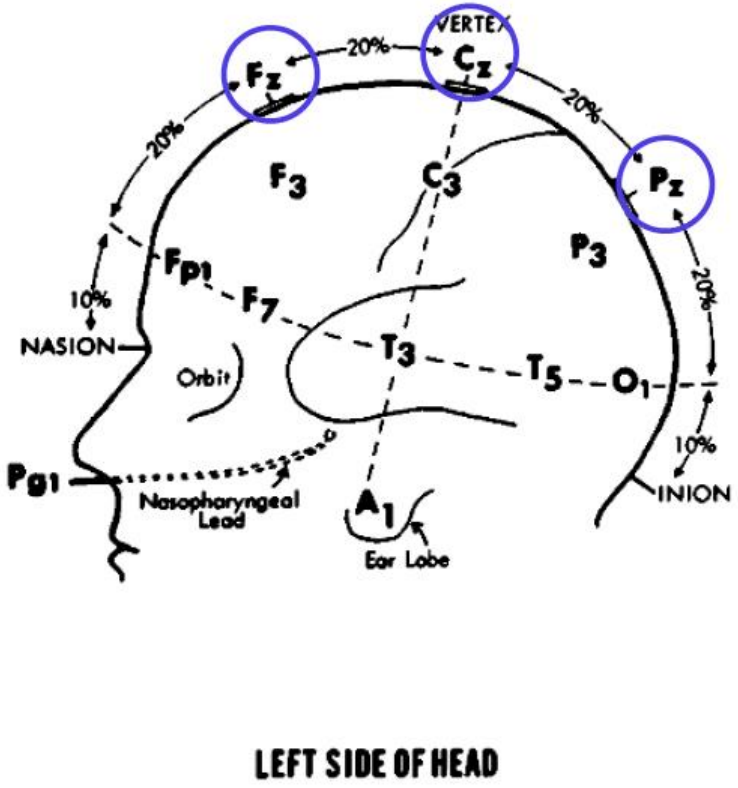
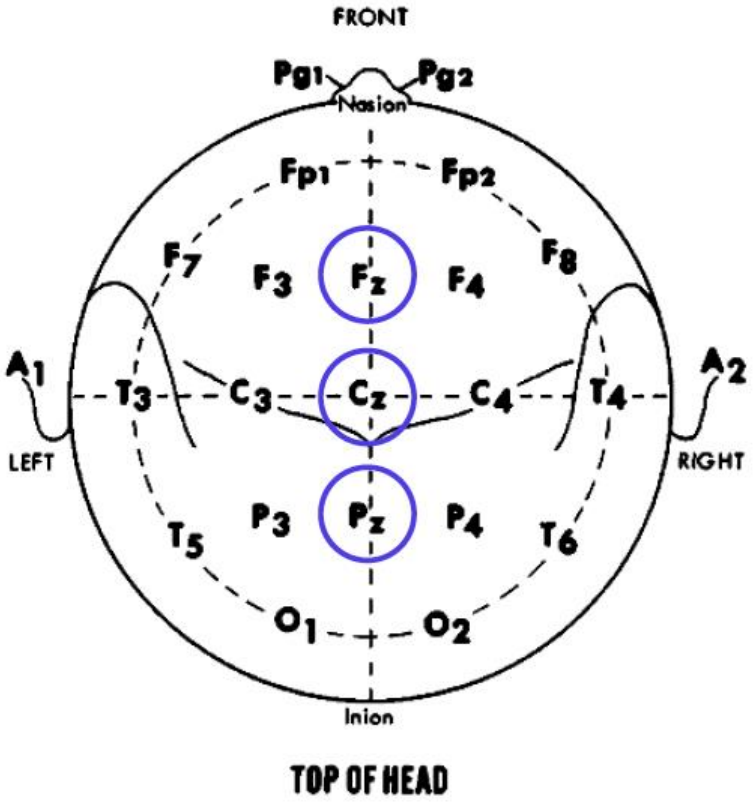
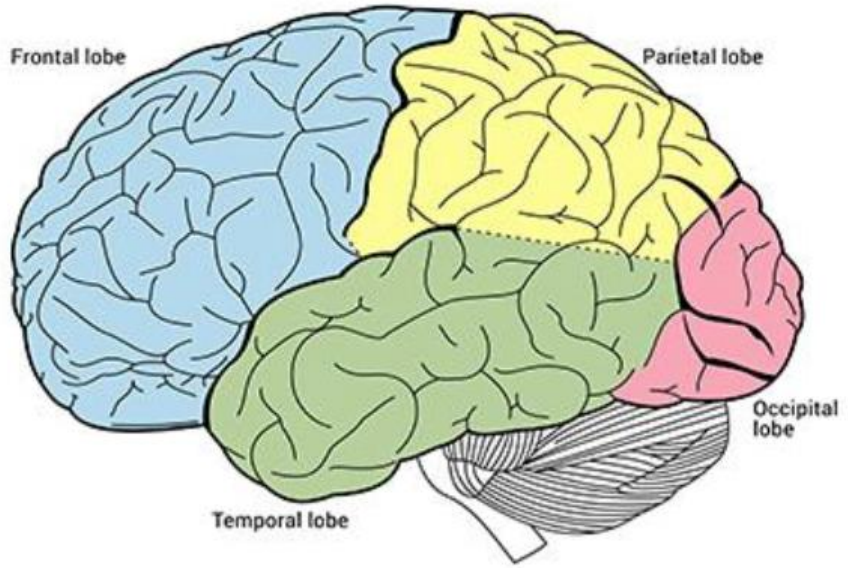


Diagram of Standard 10-20 Montage: Electrode Placement on Scalp

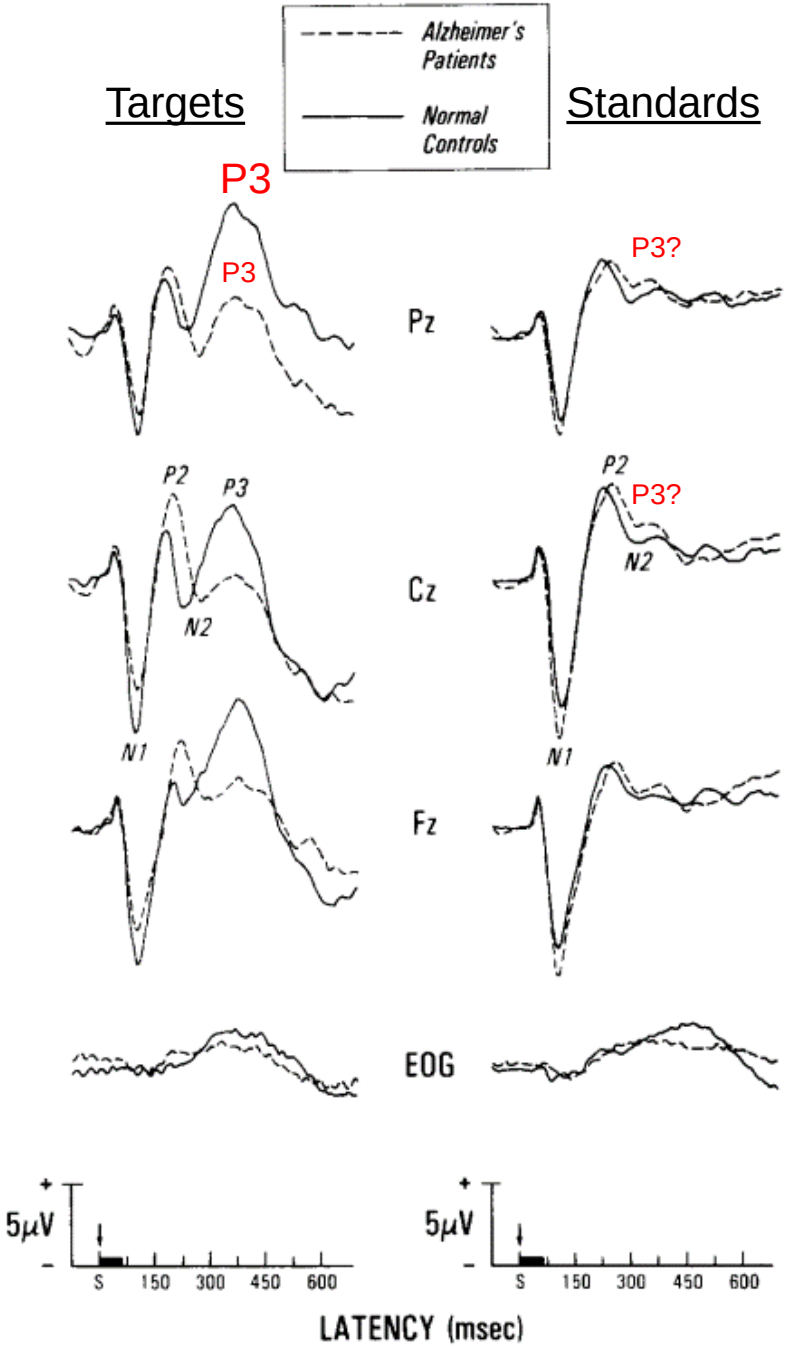






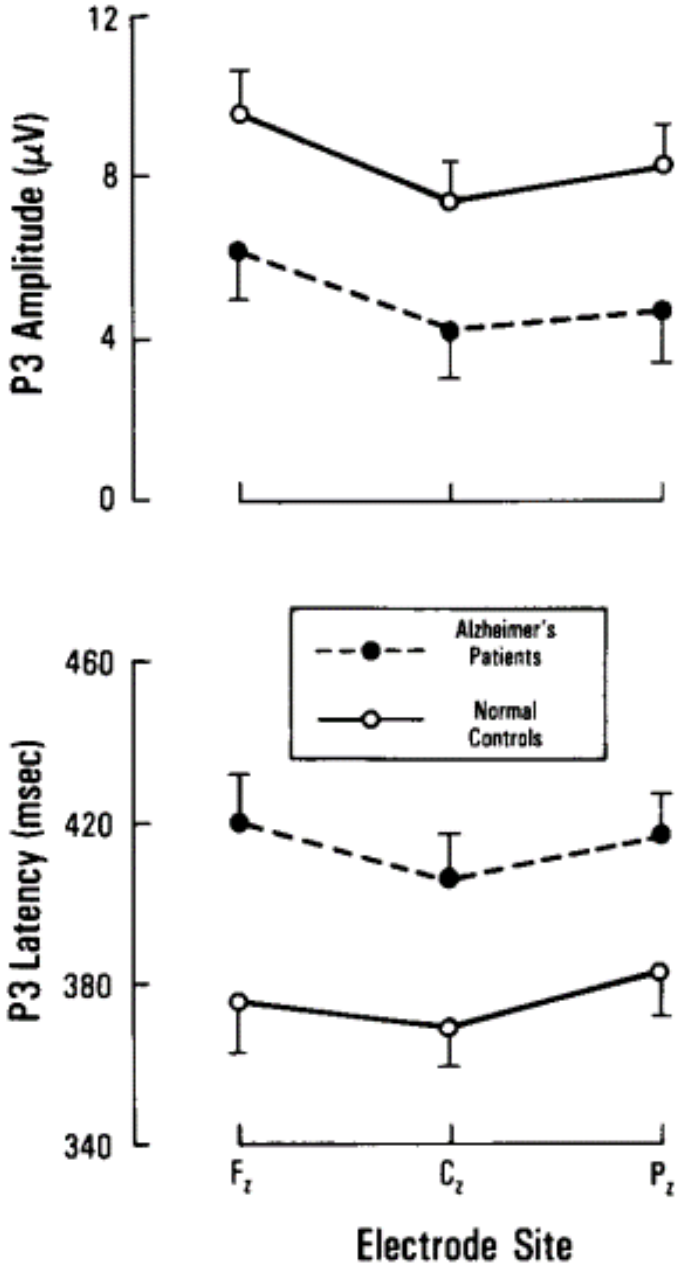
Midline structures (circled) considered most relevant for ERP

- Frontal Fz
- Frontal Parietal= “Central’ Cz
- Parietal Regions Pz



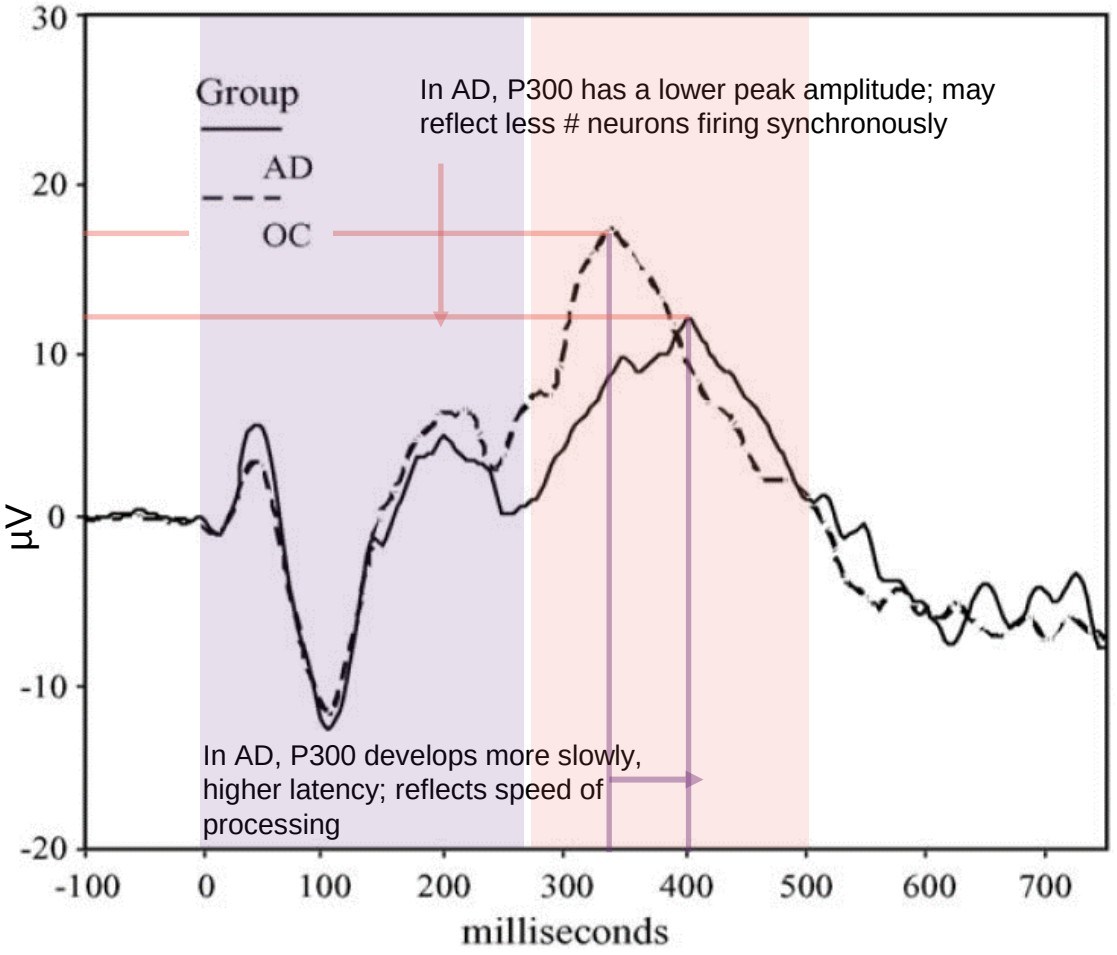
1. Alzheimer's patients compared to matched controls, showed longer latencies for the P300 component.

2. Alzheimer's patients had less amplitude difference between the target and standard tones in the auditory oddball task: reflects poor discriminability.



Polich J, Ladish C, & Bloom F, Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section, 1990; 77(3), 179-189.

P300 ERP in Alzheimer's Disease (and MCI)



Study	Population (n)	Electrode placement	P300 Latency	P300 Amplitude
Caravaglios et al., 2008	HC (16) AD (21)	Fz, Cz and Pz	AD > HC	--
O'Mahony et al., 1996	HC (20) AD (18)	Fz, Cz and Pz	AD > HC	--
Lai et al., 2010	HC (16) AD (16)	Fz, Cz and Pz	AD > HC	--
Yamaguchi et al., 2000	HC (16) AD (16)	Cz and Pz	AD > HC	HC > AD
Golob and Starr, 2000	HC (12) AD (10)	Fz, Cz and Pz	AD > HC	HC > AD
Bennys et al., 2007	HC (10) MCI (20) AD (30)	Fz, Cz and Pz	AD > MCI > HC	HC > MCI = AD
Juckel et al., 2008	HC (16) AD (18)	32 channels	AD > HC	HC > AD
Frodl et al., 2002	HC (26) MCI (26) AD (30)	29 channels	AD > MCI > HC	HC > MCI = AD
Ally et al., 2006	HC (80) AD (80)	10-20	AD > HC	HC > AD
Cecchi et al., 2015	HC (101) Mild AD (103)	Fz, Cz, Pz, F3, P3, F4, and P4	AD > HC	HC > AD

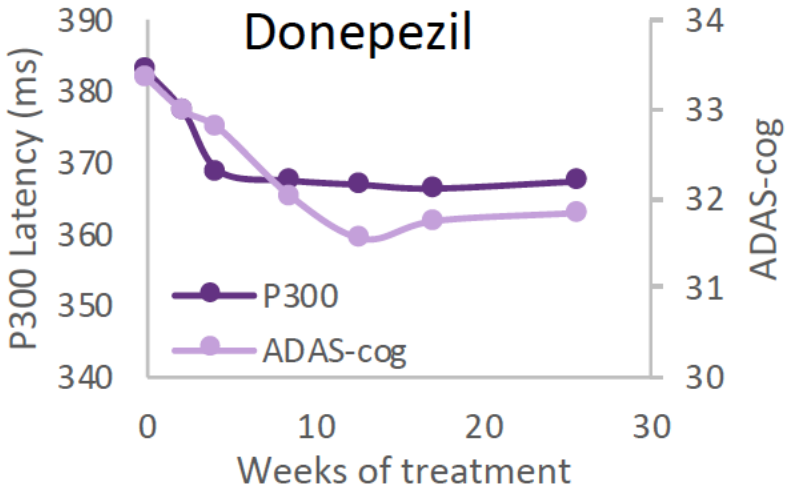
- Many studies have identified differences in P300 in AD and MCI
- P300 latency more consistent than amplitude reduction
- Fewer subjects yield significant and reproducible amplitude reduction

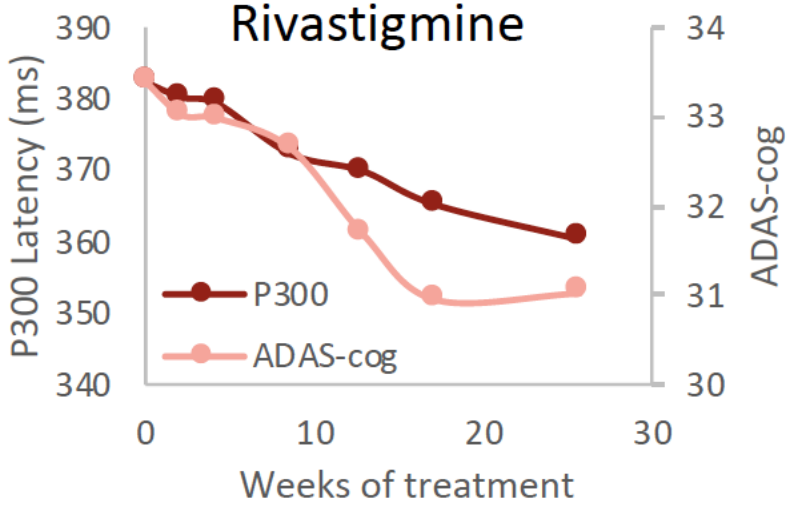
Figure adapted from Ally et al, 2006

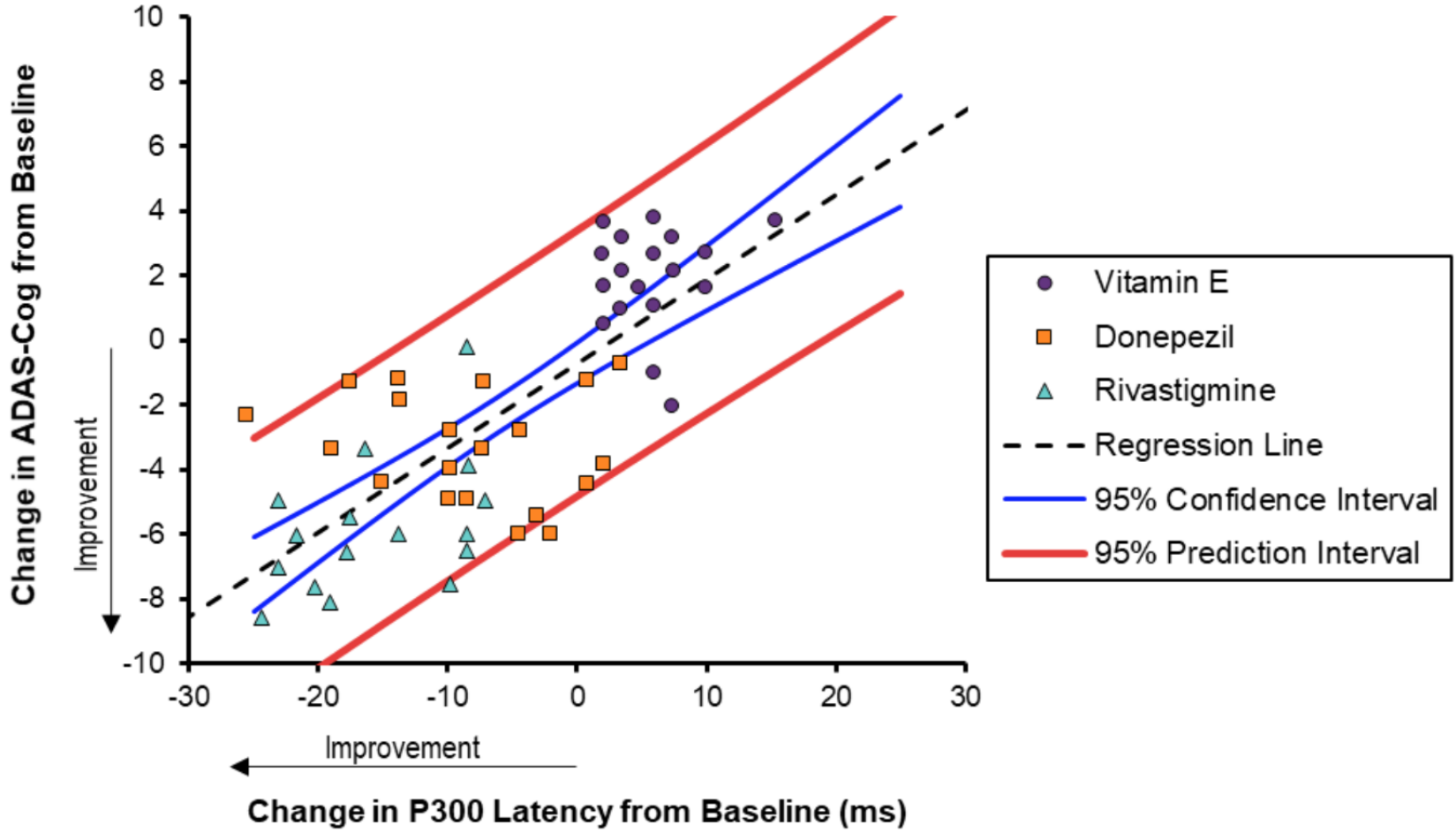
ERP Studies of Treatment in AD Dementia

	Paradigm	Sample	Results
Saletu et al. 1995	P300- Auditory	N= 67 (35 AD, 32 MID) Txd. w/ 30 mg Nicergoline BID x 8 wks	↓ P300 latency (-30 ms vs. + 10 ms w/ placebo in AD)
Reeves et al. 1999	P300- Auditory & Visual	N= 12 mild AD, txd. x 1 month w/ 5mg donepezil	↓ P300 latency (Vis: -25 ms, Aud: -9 ms) n.s. Δ MMSE (0.5 pts)
Werber et al. 2003	P300- Auditory	N= 32 dementia Pts (14 AD) Txd. x 26 wks w/ AChEI: 19 THA	↓ P300 latency (-24 ms, p= .0001), n.s. Δ ADAS-Cog (2 pts, p= .08)
Katada et al. 2003	P300-Auditory	N=13 probable AD txd. w/ donepezil.	↓ P300 latency (-23 ms at 1 mon.), P300 latency correlated w/ ADAS-J.
Thomas et al. 2001	P300-Auditory	N=60 mild-moderate AD txd. 5-10 mg of donepezil or rivastigmine.	↓ P300 latency (-15 ms DPZ, -22 ms RIV) correlated w/ cognitive improvement (ADAS-Cog, WAIS, MMSE).
Kubova et al. 2010	Visual P300, VEPs (pattern + motion)	N= 17 mild-mod AD txd. w/ Memantine x 6 mos.	No sig. P300, but 42% w/ $\geq$ 20 ms Δ vs. 29% w/ ADAS- Cog Δ $\geq$ 4pts

ERP P300 Data with Suggestive Correlation to Cognitive Changes







Modified from Thomas et al 2001

Auditory ERP Components in Clinical Trial Design

Purpose	Methods	Design	Patient samples	EEG biomarkers	Main Findings	References
Assessment of treatment effects	ERP	Longitudinal	AD	P300, N200	▪ *Assessment over time - AChEIs* ○ Reduced P300 latency* (studies varying between 1 to 6 months of treatment). ○ Reduced P300 jitter* ○ Suggestions of reduced N200 latency* (that when unreliable at baseline, became more pronounced).	Selected articles: Katada et al. 2003; Reeves et al., 1999; Onofrj et al., (2003); Thomas et al., 2001*

* Randomized, double-blind, placebo-controlled clinical trial design

Babiloni C, Blinowska K, Bonanni L, et al., Neurobiology of Aging 2020; 85:58-73

Resting state EEG alterations in the power spectrum in AD and MCI

Purpose	Methods	Design	Patient samples	EEG biomarkers	Main findings	References
Detection and monitoring	rsEEG	Cross-sectional	AD, aMCI, AD at different stages of severity,	Delta, theta, alpha, beta power density, sources and connectivity. Alpha and beta coherence	▪ **AD vs aMCI**: Widespread higher theta power; posterior lower alpha and beta power; higher delta and theta coherence in the default-mode and sensoriomotor networks; lower alpha coherence in the default-mode network; lower fronto-parietal connectivity in theta, alpha and beta. ▪ **AD disease stage:** Higher delta and theta power and no alpha peak in more severe stages of AD. ▪ **rsEEG synchronization:** Widespread power density decrease of alpha, especially in low alpha at posterior regions, and/or beta rhythms. Widespread power density increase of delta and theta rhythms. ▪ **rsEEG connectivity:** ○ Decreased intra and inter-regional connectivity in delta and theta bands in frontal, temporal and parietal areas in aMCI. ○ *Alpha connectivity*: Decrease of connectivity in the alpha band, mainly in posterior regions. Decrease of parietal to frontal information flux at alpha band, especially at parietal electrodes. ○ Weaker small-world network, more random brain networks. ▪ Loss of complexity of brain dynamics in AD.	Selected reviews: Babiloni et al., 2016a Selected articles: Babiloni et al., 2008b, 2009a; Hsiao et al., 2013, 2014; Jelic et al., 2000; Rodríguez et al., 1999 Selected reviews: Babiloni et al., 2016a; Hamm et al., 2015 and Tsolaki et al., 2014 Selected articles: Babiloni et al., 2010d; Canuet et al., 2012 Reviews: Babiloni et al., 2016a; D'Amelio and Rossini, 2013; Dauwels et al., 2010a; Tijms et al., 2013 Selected articles: Babiloni et al., 2008b, 2009a, 2016c; Canuet et al., 2012; Dauwels et al., 2009, 2010b; Miraglia et al., 2016; Vecchio et al., 2014b Selected reviews: Dauwels et al., 2010a Selected articles: Zhang et al., 2013

Bablioni C et al. Alzheimers Dement 2021 17:1528-53

Resting state EEG alterations in the power spectrum in AD and MCI; Longitudinal Studies

Purpose	Methods	Design	Patient samples	EEG biomarkers	Main findings	References
Detection and monitoring	rsEEG	Longitudinal	AD, aMCI	Delta, theta, alpha, beta power density and sources EEG mean frequency	▪ **Baseline-follow ups in AD:** increase of theta and delta power, decrease of alpha and beta power, decrease of mean frequency at the temporo-occipital electrodes; reduced connectivity	Selected reviews: Drago et al., 2011 Selected articles: Huang et al., 2000; Rossini et al., 2006; Luckhaus et al., 2008; Moretti et al., 2011; Babiloni et al., 2011; Bonanni et al., 2015

Bablioni C et al. Alzheimers Dement 2021 17:1528-53

Frequency-specific changes find alterations in the power spectrum and provide phase information for a given frequency band as it relates to the given stimuli/task

Table 1
Summary of the time-frequency dynamics of AD and MCI patients in the literature.

Frequency	Delta response	Theta response	Alpha response	Beta response	Gamma response
AD	↓ Decreased delta ERS	↓ Decreased theta power/ ERS, decreased theta phase locking	↓ Decreased ERD ↑ Increased ERD	↓ Decreased, beta power/ERS ↓ Decreased beta ERD	↓ Decrease early gamma ERS, ↑ Increased Gamma power ↓ Decreased gamma ERD
MCI	↓ Decreased delta ERS	↓ Decreased theta power/ ERS, decreased theta phase locking	↓ Decreased alpha phase locking	↓ Decreased, beta power/ERS ↓ Decreased, beta phase locking ↓ Decreased beta ERD	
References	Caravaglios et al. (2008) Kurt et al. (2014) Yener et al. (2008, 2012, 2013) Yener and Başar (2013)	Caravaglios et al. (2008) Cummins et al. (2008) Deiber et al. (2009, 2015) Yener et al. (2007)	Babiloni et al. (2000, 2005) Deiber et al. (2015) Fraga et al. (2017) Karrasch et al. (2006)	Deiber et al. (2015), Fraga et al. (2017) Güntekin et al. (2013), Kurimoto et al. (2012) Missonnier et al. (2007)	Başar et al. (2016), Osipova et al. (2006) van Deursen et al. (2011) Kurimoto et al. (2012)

AD: Alzheimer's Disease. MCI: mild cognitive impairment. ERS: event-related synchronization. ERD: event-related desynchronization. MCI: mild cognitive impairment.

Rossini P, Di Iorio F, Vecchio M, et al., Clinical Neurophysiology 2020; 131(6):1287-1310

Electrophysiology as a Measure for Brain Function in Alzheimer's Disease

Sources of disruptions include:

- Neurotransmitter dysregulation
- Neuronal loss
- Synaptic loss/dysfunction
- Insufficient glucose and oxygen delivery
- Sleep deprivation

- Normal brain connectivity
- Normal cognition

Disrupted Network Communication

Disease onset

- Impaired brain connectivity
- Impaired cognition

ERP
P300 Latency

300 ms → **350 ms** → **400+ ms**

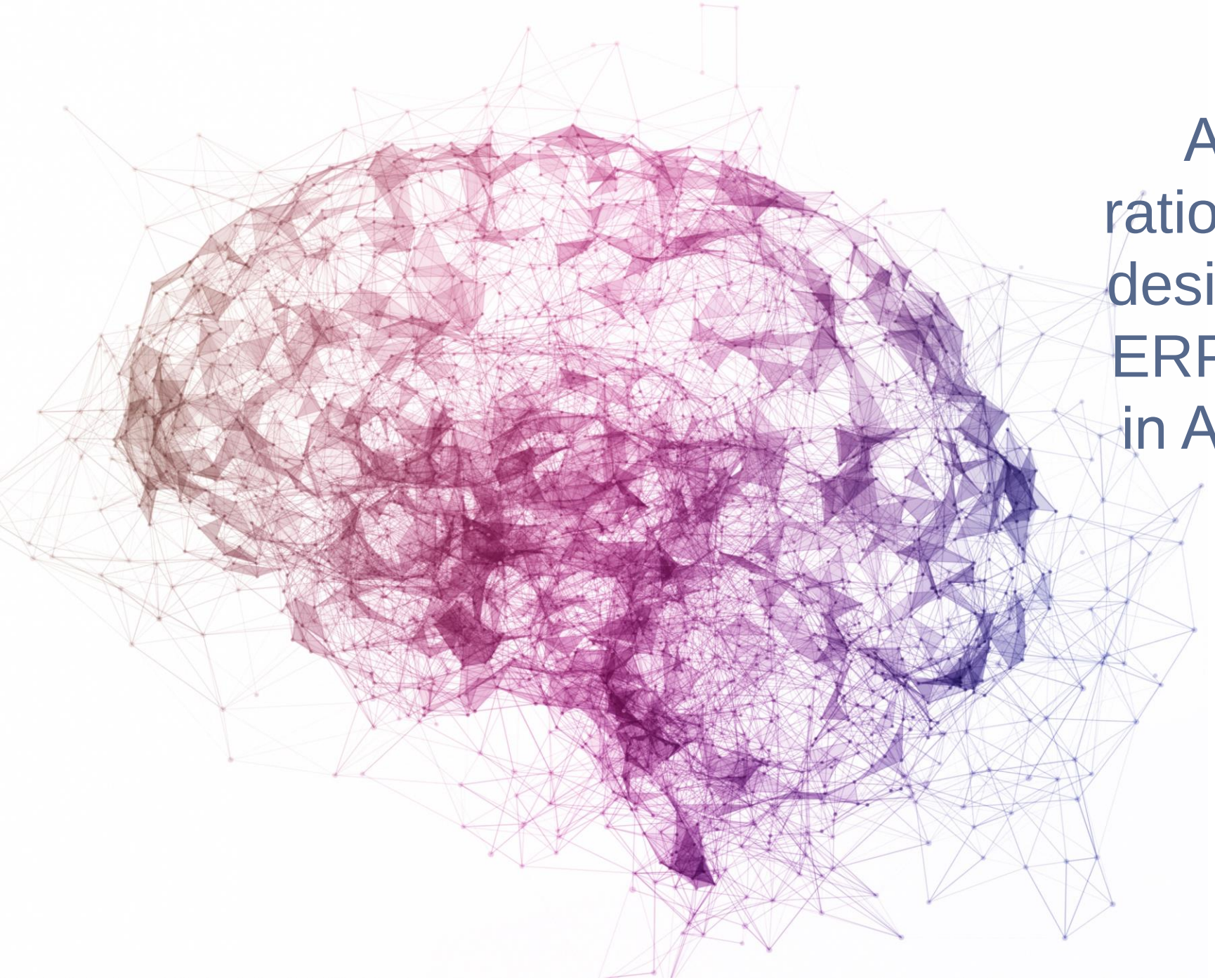
SUMMARY/CONCLUSIONS

1. P300 is sensitive to Aging, AD dementia & MCI.

2. EEG/ERP provide important digital biomarkers of AD; Direct measure of synaptic function and brain dynamics.

3. P300 is proven responsive to cholinergic therapies. ERP components, if selected well, can provide excellent markers of a biological response to cognitive therapies.

4. Faster P300 latencies indicate faster cognitive processing and correlates with attentional and executive abilities.



Athira's strategy and rationale for clinical trial design and summary of ERP P300 latency data in Alzheimer's subjects

Hans Moebius, M.D., Ph.D.
Chief Medical Officer, Athira

Independent Partners for Athira's Phase 1a/b Trial of ATH-1017

Athira's trial conduct and analysis plus audit of Phase 1a/b data

Biotrial is an independent, specialized full-service CRO with large qEEG and ERP database

Biotrial is a member of the PRISM consortium

Services:

- IRT Randomization and Trial Supply Management
- Central Lab
- Statistical Analysis and CSRs
- Bioanalysis / Pharmacokinetics
- Drug Safety & Pharmacovigilance (DSMB Management)
- Data Management
- Electronic Data Capture
- Phase 1 study participants were in-house

Statistics consulting services

Services:

- Consulting
- Statistical analysis of ERP P300 latency results

Quality assurance, compliance, and computer validation consulting services

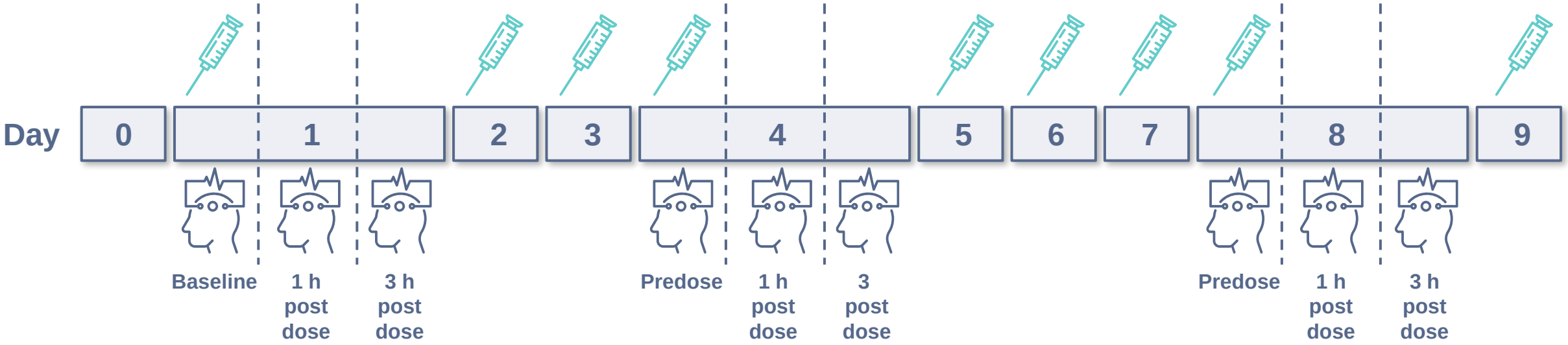
Services:

- Confirmation of GCP compliance
- Confirmation of data management quality for Phase 1a/b trial

Repeat P300 Latency Monitoring in a Phase 1b Trial of ATH-1017

Trial population: Alzheimer's Disease (n=11, mean MMSE 19)

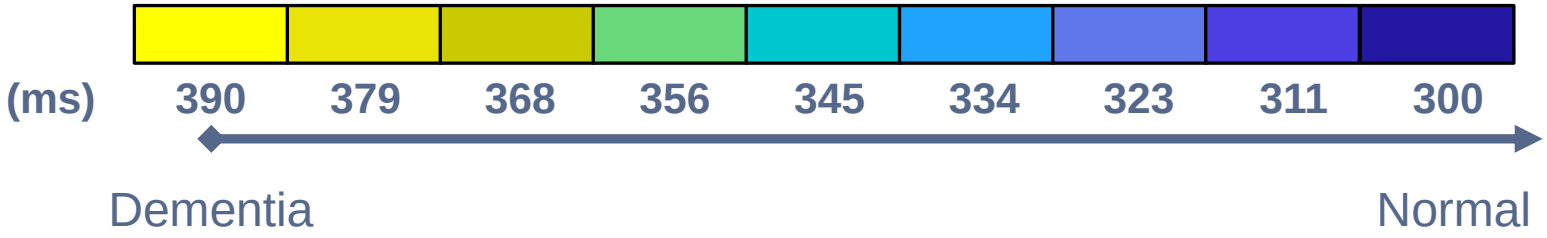
ATH-1017; Subcutaneously; once daily 40 mg or Placebo

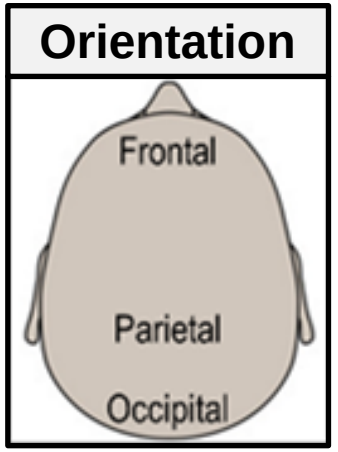


Assessments of qEEG and ERP P300 Latency

ATH-1017 Improved ERP P300 Latency in AD Subjects

Decrease (blue) = improvement

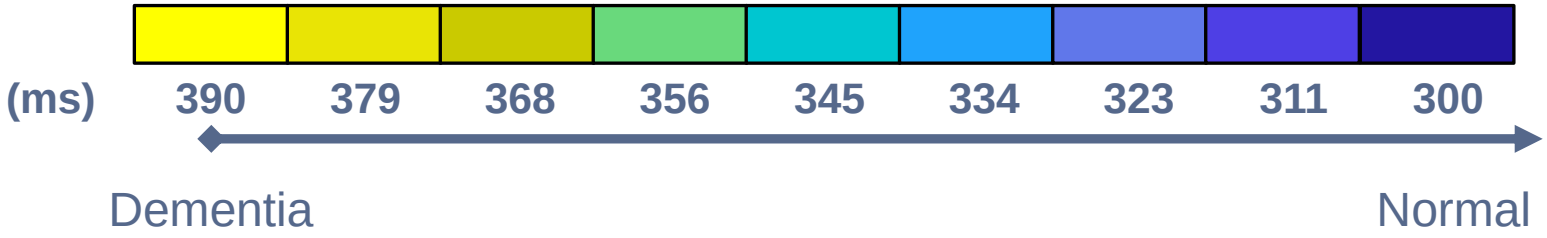


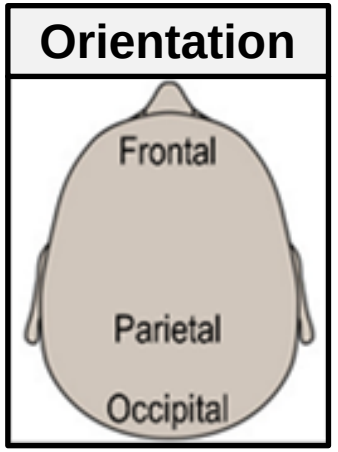


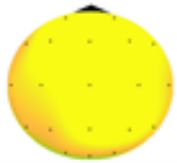
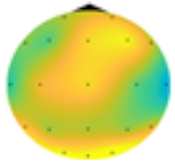
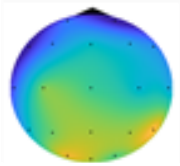
P300 Latency (ms)									
Treatment	**Day 1**			**Day 4**			**Day 8**		
	Baseline	Hour 1	Hour 3	Pre-dose	Hour 1	Hour 3	Pre-dose	Hour 1	Hour 3
40 mg ATH-1017 (n=7)									

ATH-1017 Improved ERP P300 Latency in AD Subjects

Decrease (blue) = improvement

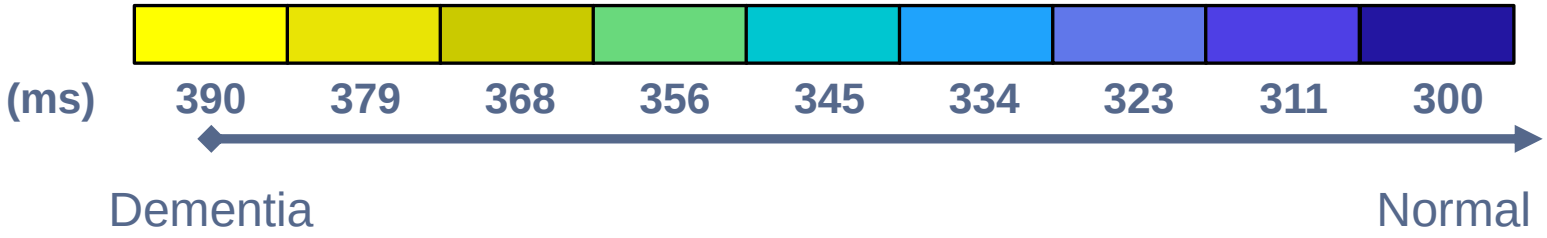


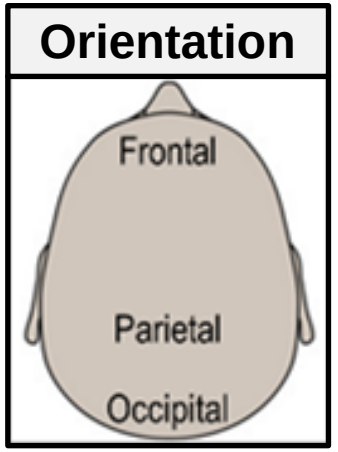


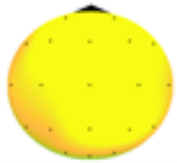
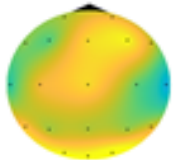
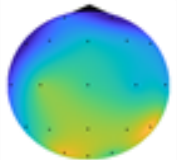
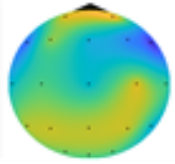
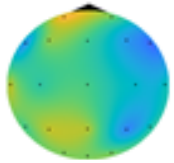
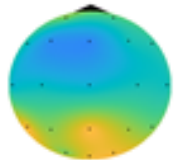
P300 Latency (ms)									
Treatment	**Day 1**			**Day 4**			**Day 8**		
	Baseline	Hour 1	Hour 3	Pre-dose	Hour 1	Hour 3	Pre-dose	Hour 1	Hour 3
40 mg ATH-1017 (n=7)									

ATH-1017 Improved ERP P300 Latency in AD Subjects

Decrease (blue) = improvement

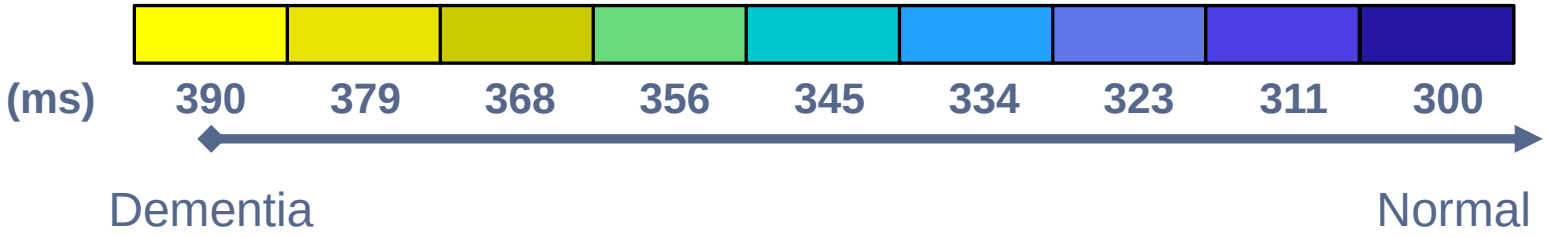


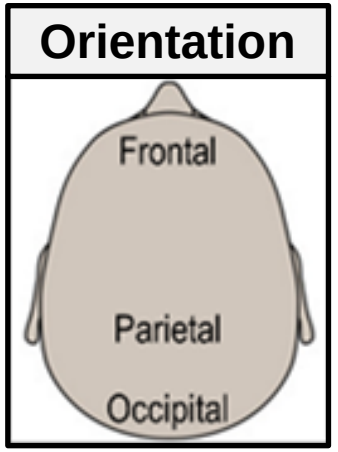


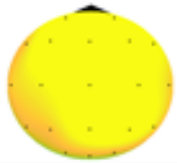
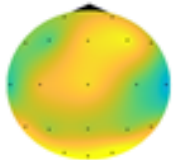
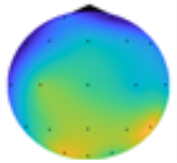
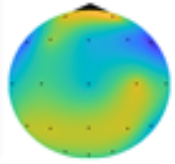
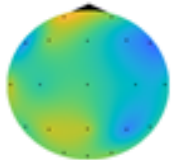
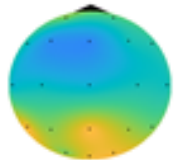
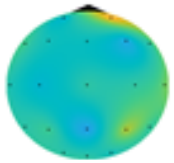
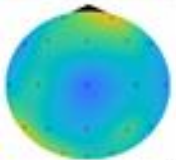
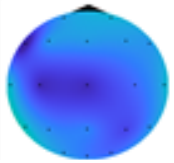
P300 Latency (ms)									
Treatment	**Day 1**			**Day 4**			**Day 8**		
	Baseline	Hour 1	Hour 3	Pre-dose	Hour 1	Hour 3	Pre-dose	Hour 1	Hour 3
40 mg ATH-1017 (n=7)									

ATH-1017 Improved ERP P300 Latency in AD Subjects

Decrease (blue) = improvement

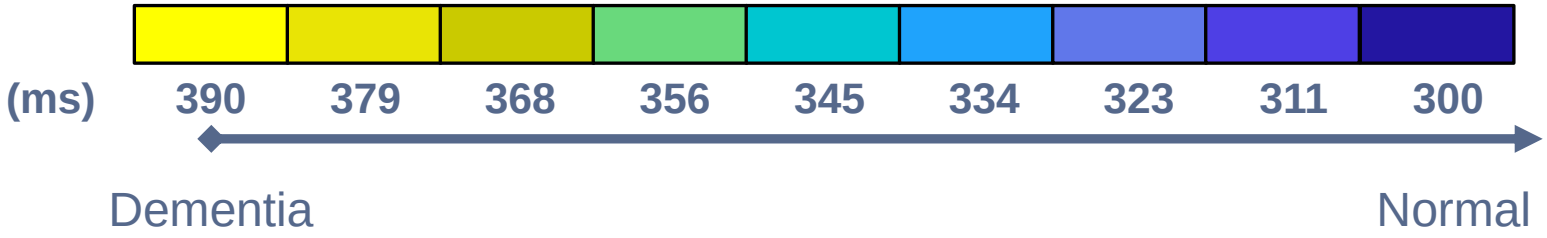


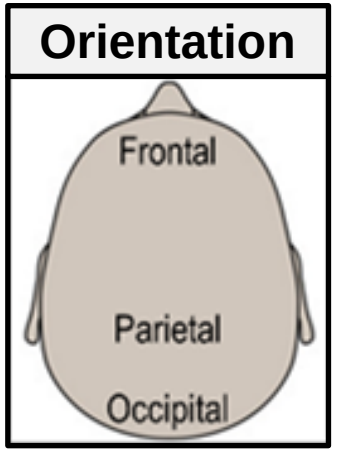


P300 Latency (ms)									
Treatment	**Day 1**			**Day 4**			**Day 8**		
	Baseline	Hour 1	Hour 3	Pre-dose	Hour 1	Hour 3	Pre-dose	Hour 1	Hour 3
40 mg ATH-1017 (n=7)									

ATH-1017 Improved ERP P300 Latency in AD Subjects

Decrease (blue) = improvement





P300 Latency (ms)									
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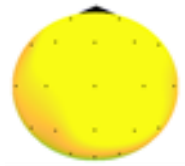
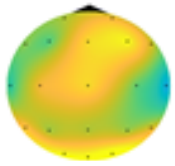
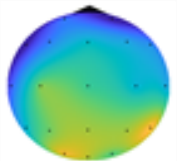
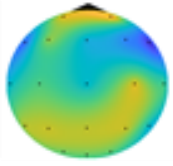
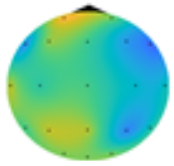
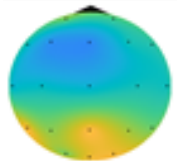
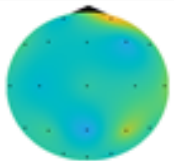
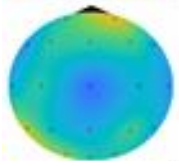
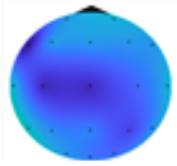
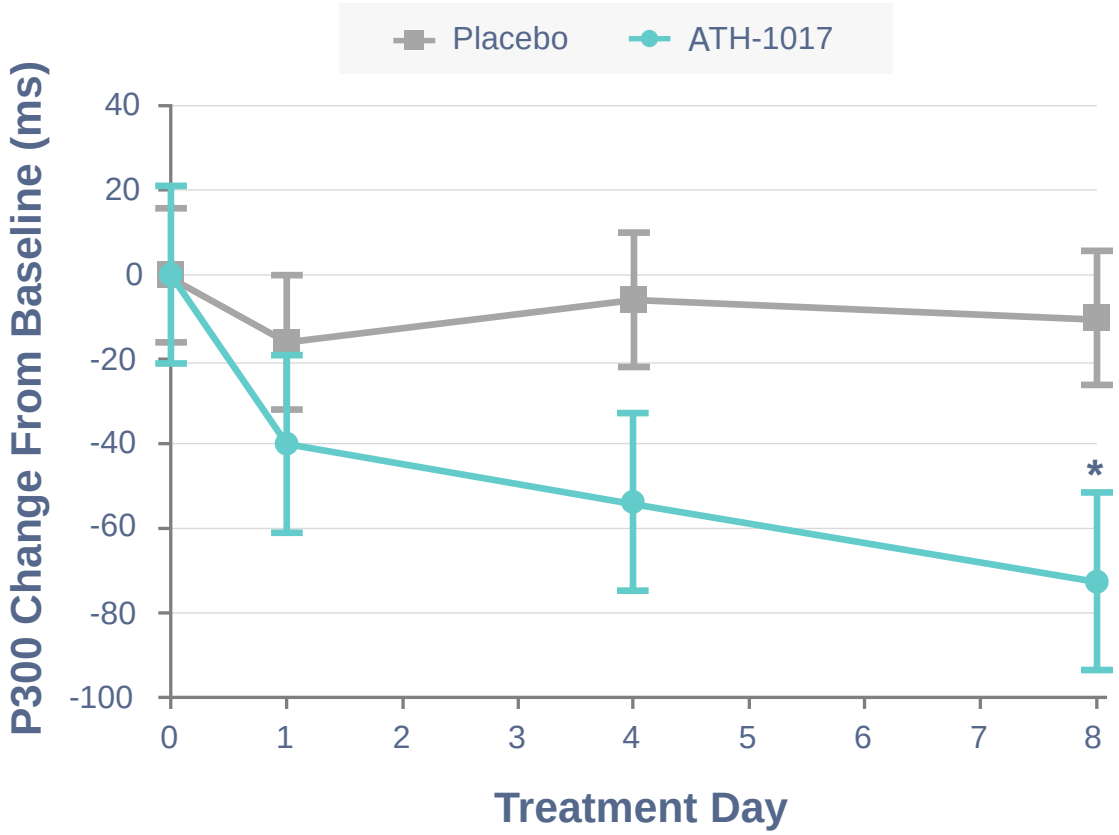
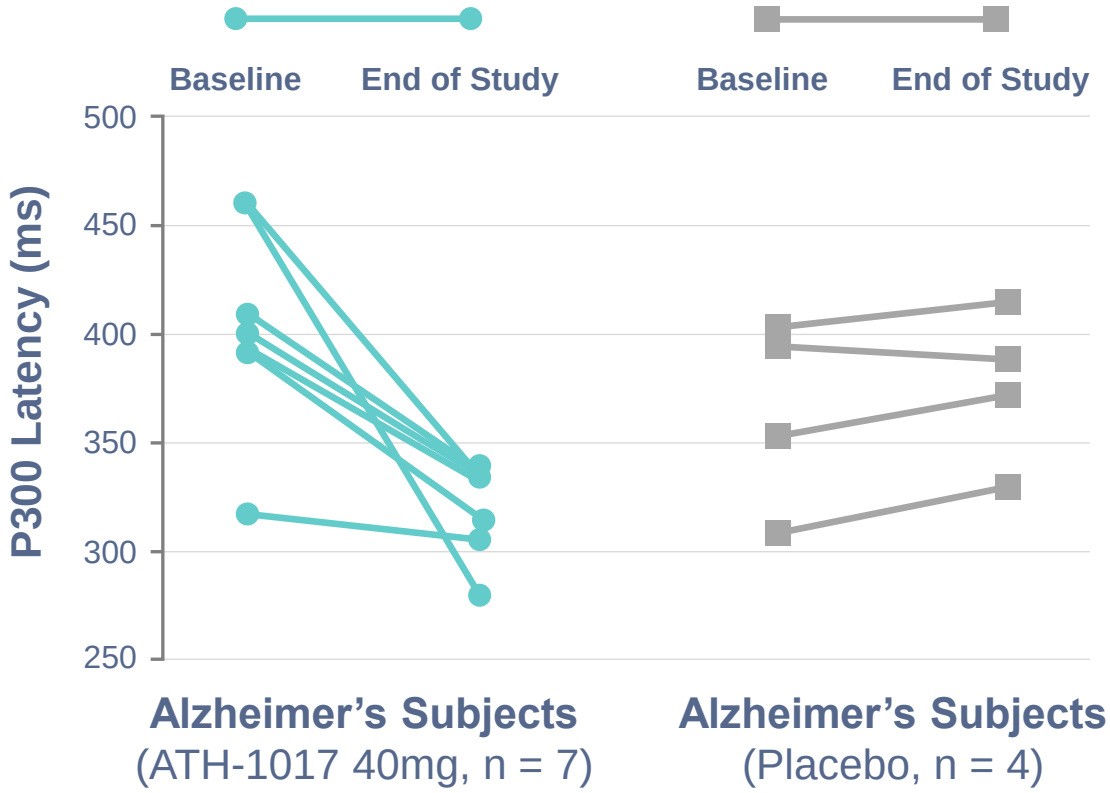
40 mg ATH-1017 (n=7)									

Decreased latency on pre-dose recordings (arrows) taken 24 hours after the last dose on the previous day is suggestive of sustained improvement

ATH-1017 Treatment Improved P300 Latency in AD Subjects





Note: P300 data from FZ, CZ, and PZ electrodes, Data plotted as mean +/- SE *p < 0.05 at Day 8 (MMRM)

ATH-1017 Phase 2/3 Trial (LIFT-AD)

Trial may provide pivotal evidence to support product registration

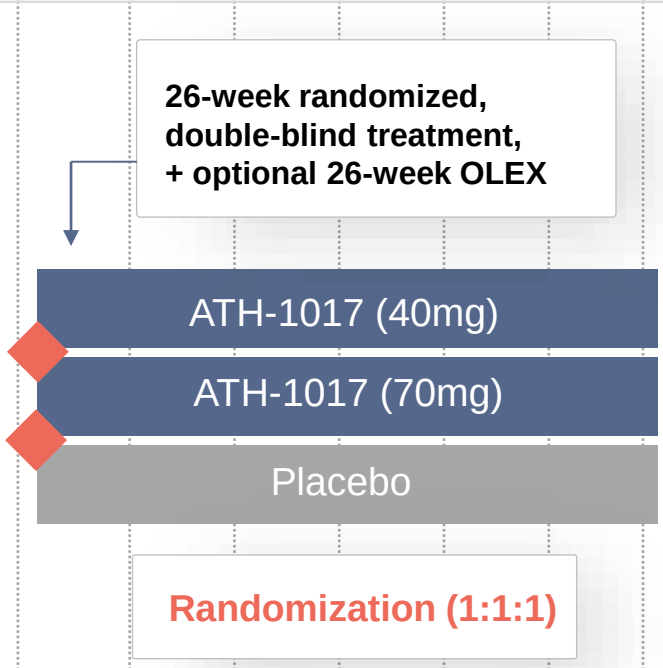
POPULATION

LIFT-AD: N=300 tbc
mild-to-moderate
AD dementia subjects
(55-85 years; CDR 1 and 2;
MMSE 14-24 incl.)

Potential pivotal study design

- If both key secondaries are positive
- If key secondaries are positive GST will also be positive

TREATMENT DURATION



ENDPOINTS

PRIMARY ENDPOINT

- Global Statistical Test (GST, O'Brien 1984)
- Safety

SECONDARY ENDPOINTS WITH HIERARCHY

1. Cognition (key secondary): ADAS-Cog11
2. Global (key secondary): ADCS CGIC - Clinician
3. Function (key secondary for ex-US): Alzheimer's Disease Cooperative Study - Activities of Daily Living (ADCS-ADL23)

INTEGRAL GST PROVIDES PRIMARY READ OUT

GST - unbiased composite, fed by data from two key secondaries

ATH-1017 Phase 2 Trial (ACT-AD)

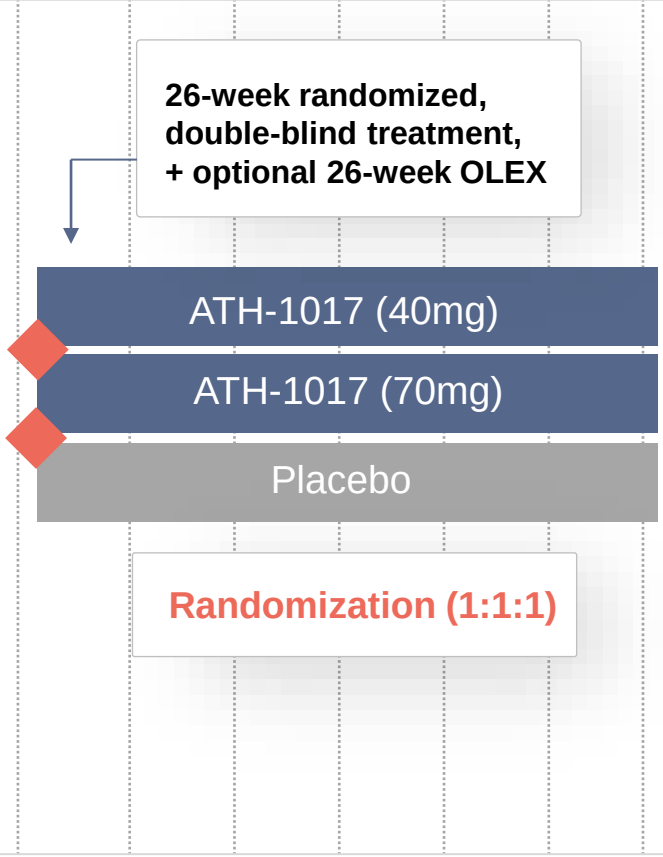
POC Trial to help better understand nature of novel intervention and refine LIFT-AD

POPULATION

ACT-AD: N=77 (rec. completed) mild-to-moderate AD dementia subjects
(55-85 years; CDR 1 and 2; MMSE 14-24 incl.)

- Enables readout 1H2022, ahead of LIFT-AD
- Informs LIFT SAP and enables earlier strategic decisions

TREATMENT DURATION



ENDPOINTS

PRIMARY ENDPOINT

- Change of P300 latency
- Safety

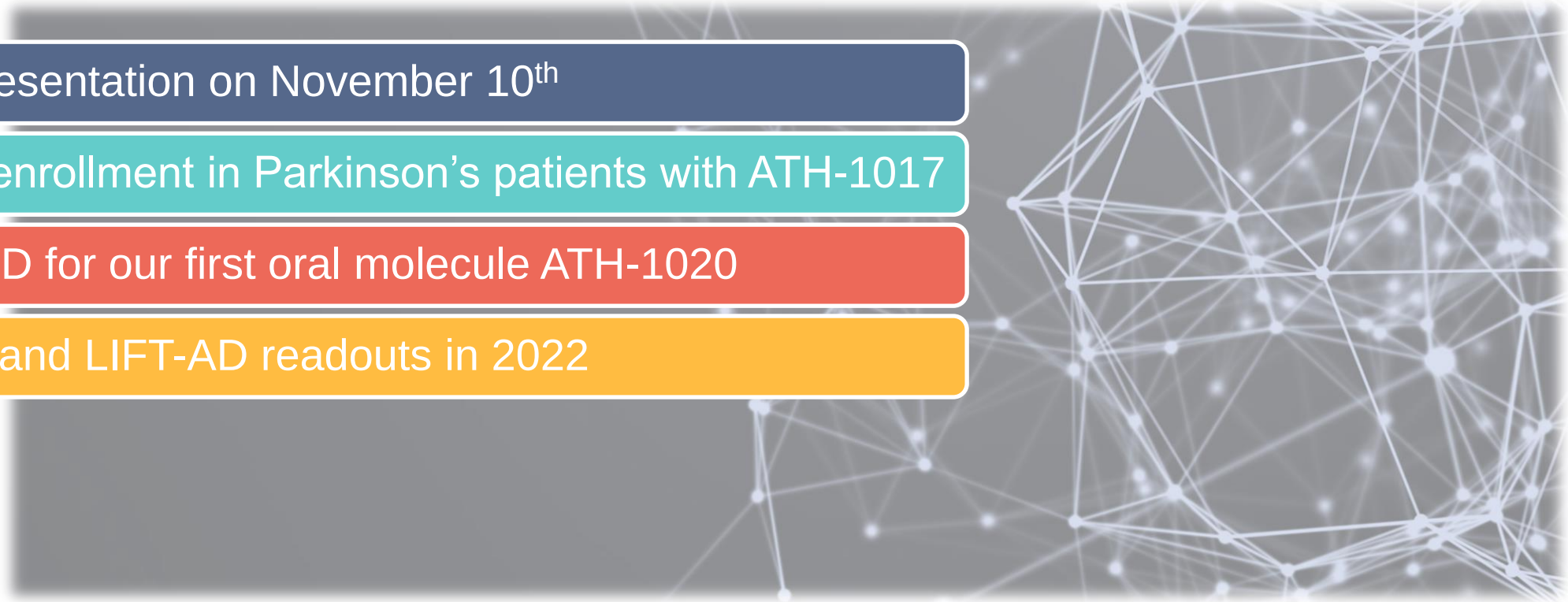
SECONDARY ENDPOINTS WITH HIERARCHY

1. Global Statistical Test (GST, O'Brien 1984)
2. Cognition: ADAS-Cog11
3. Global clinical change: ADCS CGIC - Clinician
4. Function: ADCS-ADL23

Looking to the Future

Upcoming milestones and potential value-inflection points

- CTAD presentation on November 10th
- Starting enrollment in Parkinson's patients with ATH-1017
- A new IND for our first oral molecule ATH-1020
- ACT-AD and LIFT-AD readouts in 2022



Athira PHARMA

Thank You