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THE personalized medicine resource

# EEG Phenotypes predict treatment outcome to stimulants in children with ADHD.

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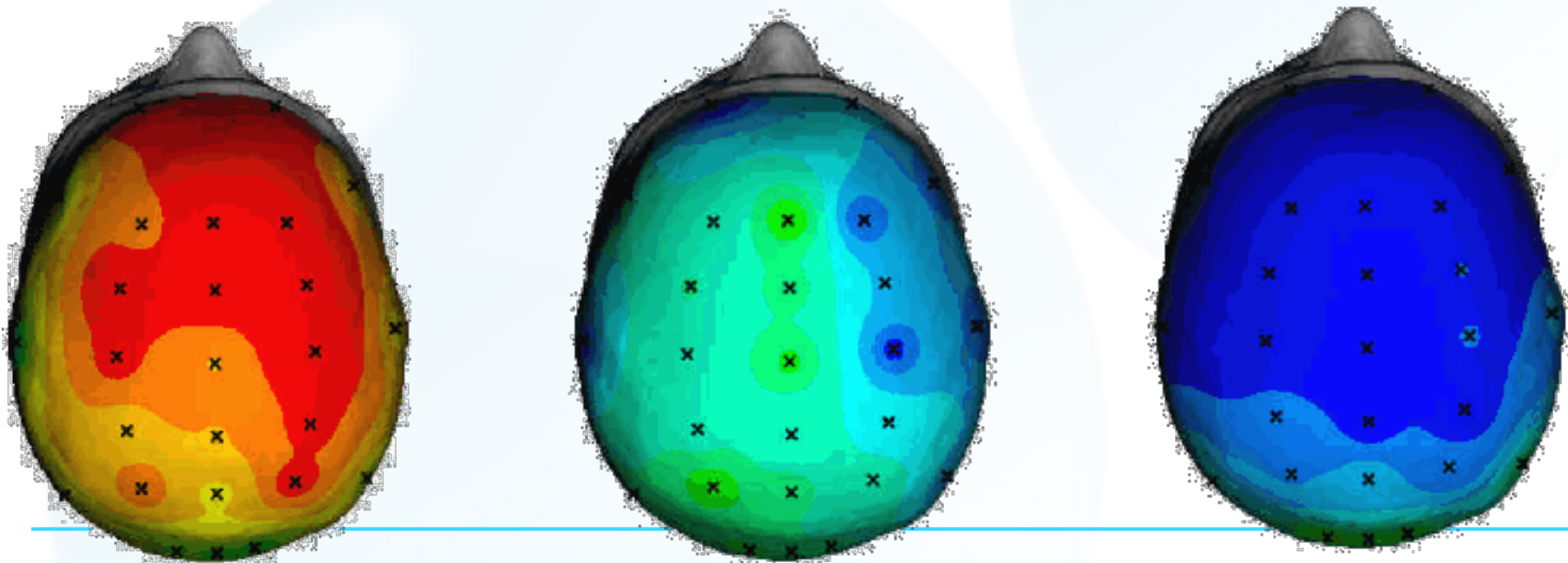
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*Brainclinics is part of the Brain Resource Network*



# EEG findings in ADHD

- Increased slow (Theta)
- Decreased fast (Beta)
- Data from 250 unmedicated children with ADHD: Brain Resource International Database



# Individual data

**50% have increased theta**

**25% have increased Beta**

**Only 2 decreased Beta!!!**

	theta	alpha	beta		theta	alpha	beta
2014	↑	↑		3824			
2193	↑		↑	3857	↑	↑	
2306		↑		4061			
2395		→		4151	↑		↑
2418		↑		4162	↑	↑	↑
2520		↑		4409	↑		
2553	↑	←		4397		→	↓
2575				4465			
2744	↑	←↓	↑	4476		↑	
2777	↑			4487	↑	→↑	↑
3149		↑		4926		↑	
3251	↑	↑		5163		→	↑
3330	↑	↑		5118	↑	↑	
3521				5208		↑	
3532				5400	↑	↑	
3576	↑	←↑		5411		↑	↑
3813		↑		5422	↑	←	↓
3846	↑	↑	↑	5332		←	

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# Average data vs. Individual data

- Discrepancy between average data vs. Individual data.
  - Example: averaging eye color: black eyes?
  - Could this explain heterogeneity in medication responses?
  - EEG Phenotype model.
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# EEG Phenotypes (Johnstone, Gunkelman et al., 2005)

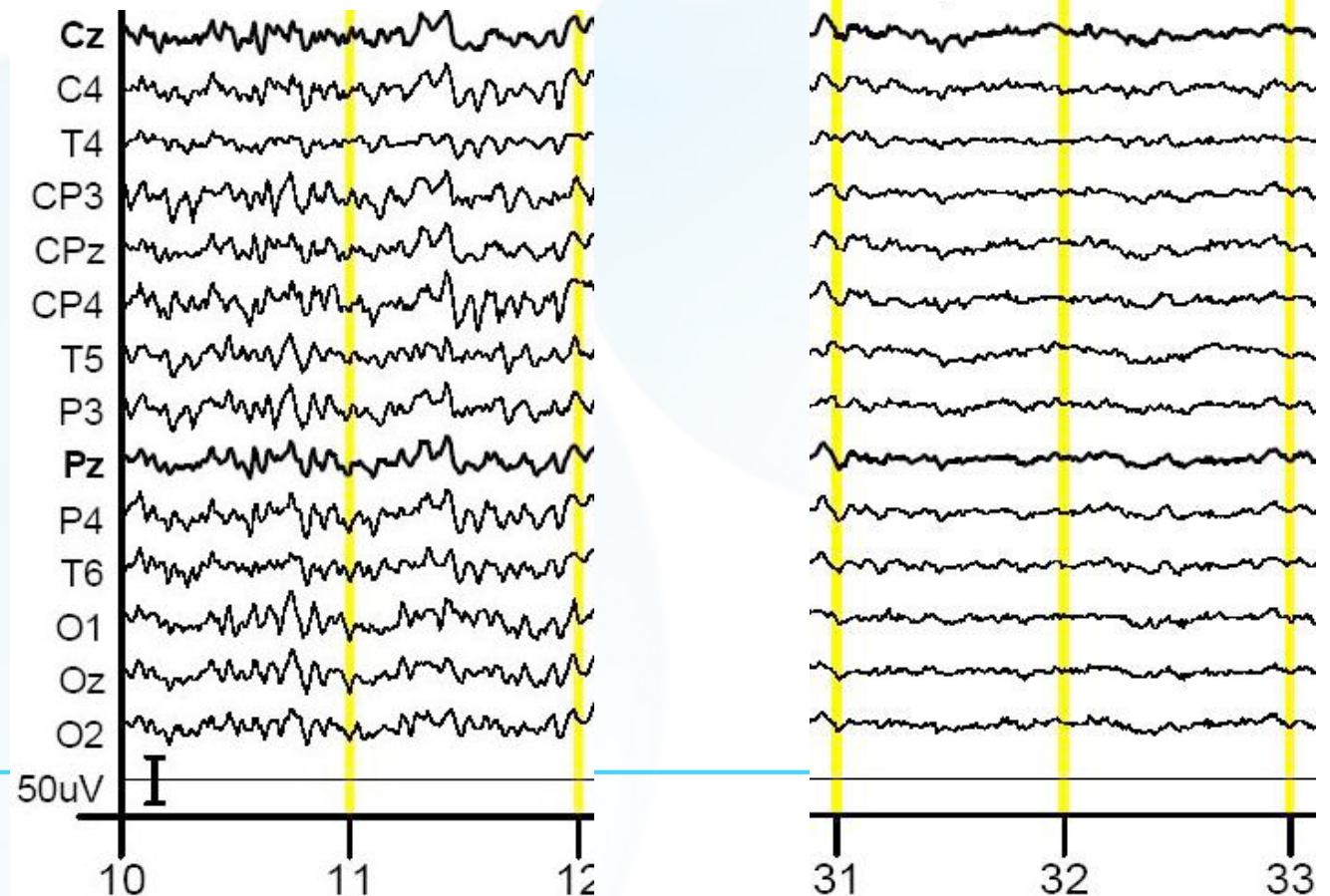
- Diffuse slow activity, with or without low frequency alpha
- Focal abnormalities, not epileptiform
- Mixed fast and slow
- Frontal lobe disturbances
- Frontal Asymmetries
- Excess temporal lobe alpha
- Epileptiform
- Faster alpha variants, not low voltage
- Spindling excessive beta
- Generally low magnitudes (fast or slow)
- Persistent alpha with eyes open

**Arns, Gunkelman, Breteler & Spronk 2008**

	N- ADHD	N-Controls	Inter-rater reliability
'Normal EEG'	5	11	Kappa: .90; p<.000
Frontal Slow	13	9	Kappa: .94; p<.000
Slow APF	13	5	Kappa: .90; p<.000
High APF	3	5	Kappa: .94; p<.000
Frontal Beta Spindles	8	10	Kappa: .97; p<.000
Mu	22	19	Kappa: .94; p<.000
Frontal Alpha	8	4	Kappa: .47; p<.000
Temporal Alpha	5	6	Kappa: .89; p<.000
Persistent Alpha	7	5	Kappa: .64; p<.000
Low Voltage	6	1	Kappa: .93; p<.000

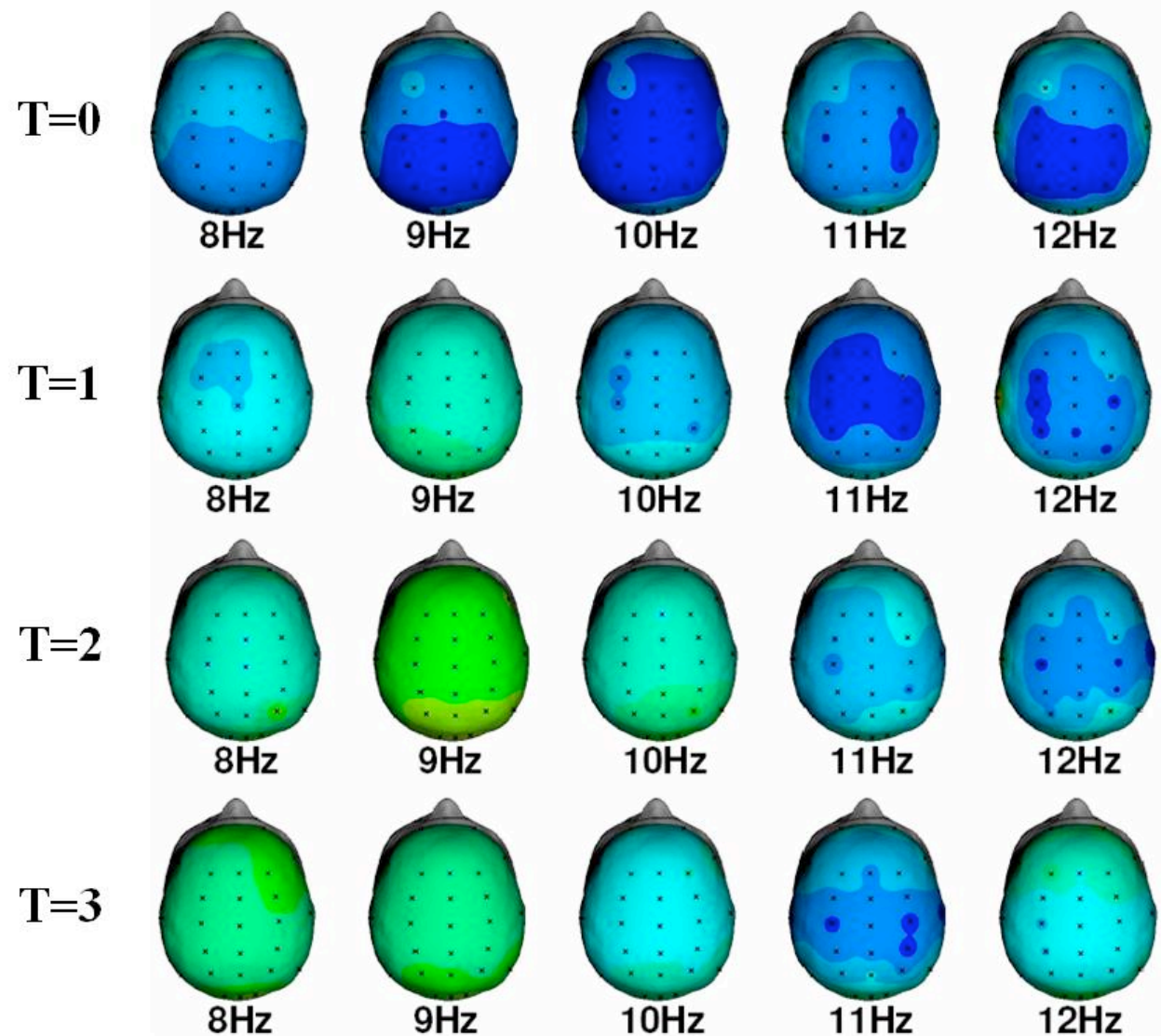
# Low Voltage EEG

- Low Voltage fast pattern has been linked to alcoholism and GABA-A receptor genes (Porjesz et al., 2002)
- Gene number 4's regulation over GABA receptor (Bierut et al., 2002)



# The effect of alcohol intake on low-voltage EEG

## Case Example



# Beta spindles

## Beta is not beta spindles

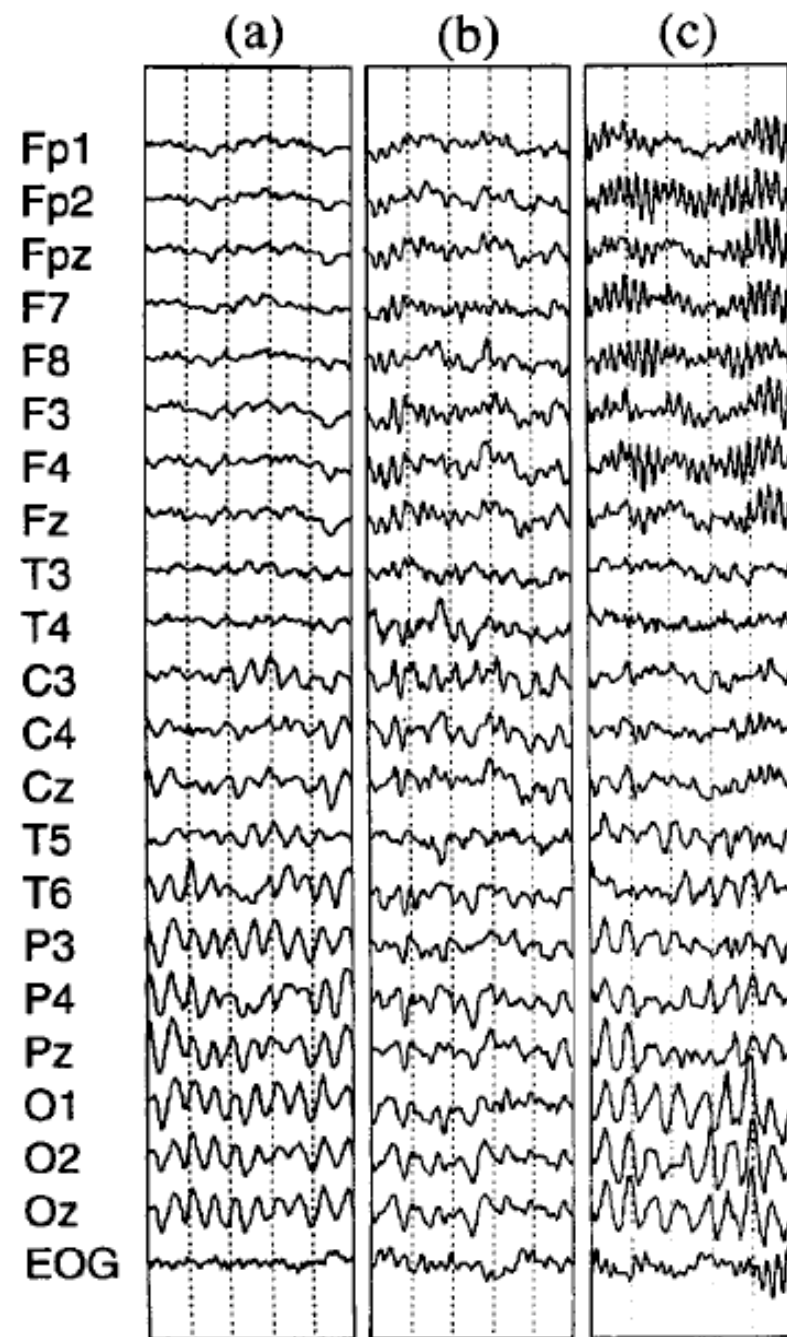
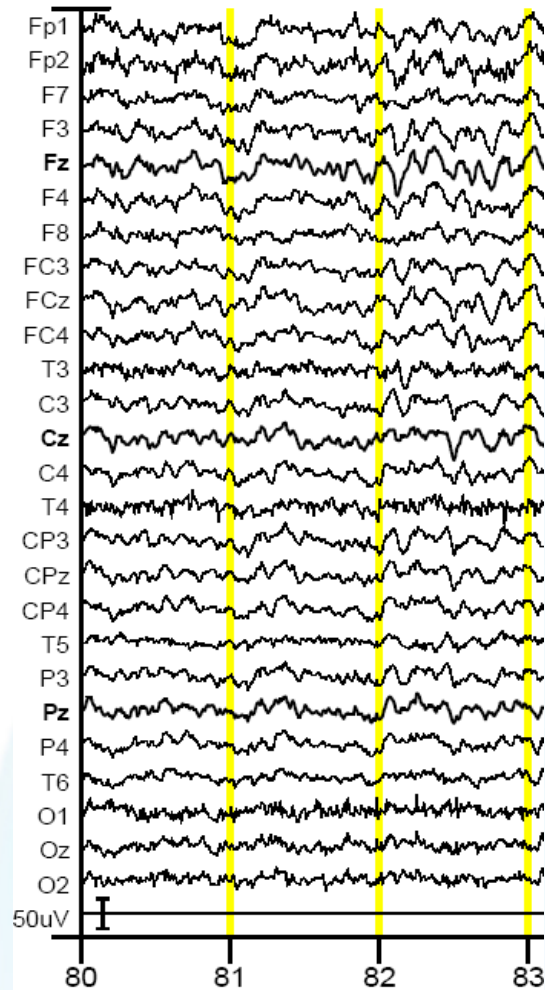
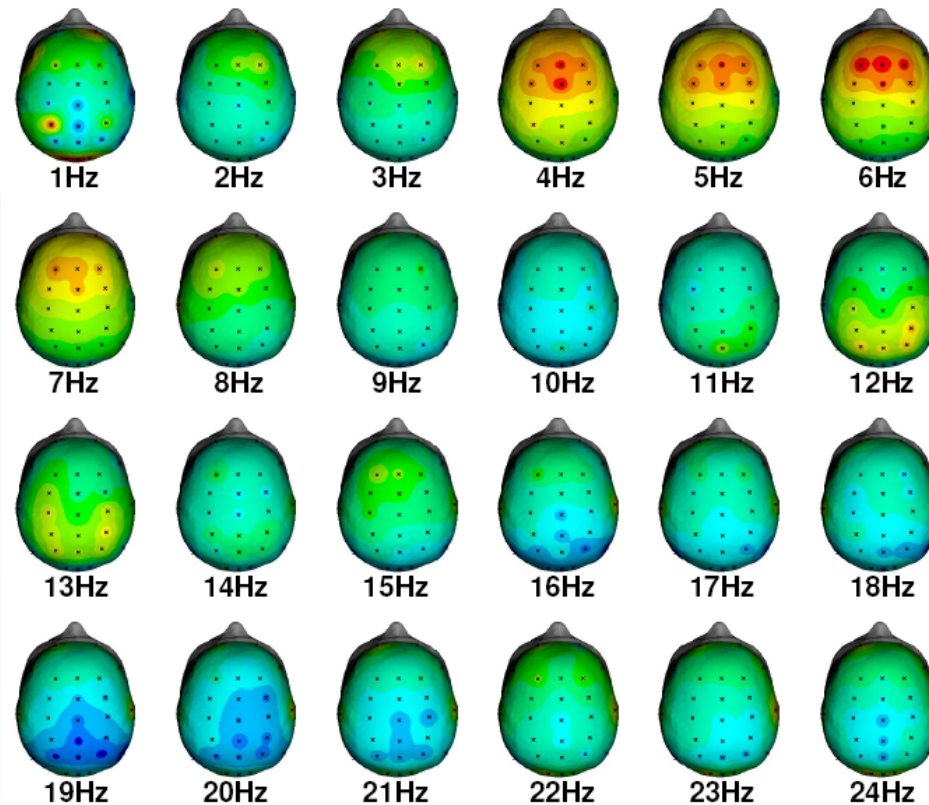


Fig. 1. Representative 1-s epochs from: (a) normal amplitude excess beta subjects; (b) high amplitude excess beta subjects; (c) excess beta subjects with frontal beta spindles.

# Frontal Disturbances: Theta



12008214: EO; 13 yrs.

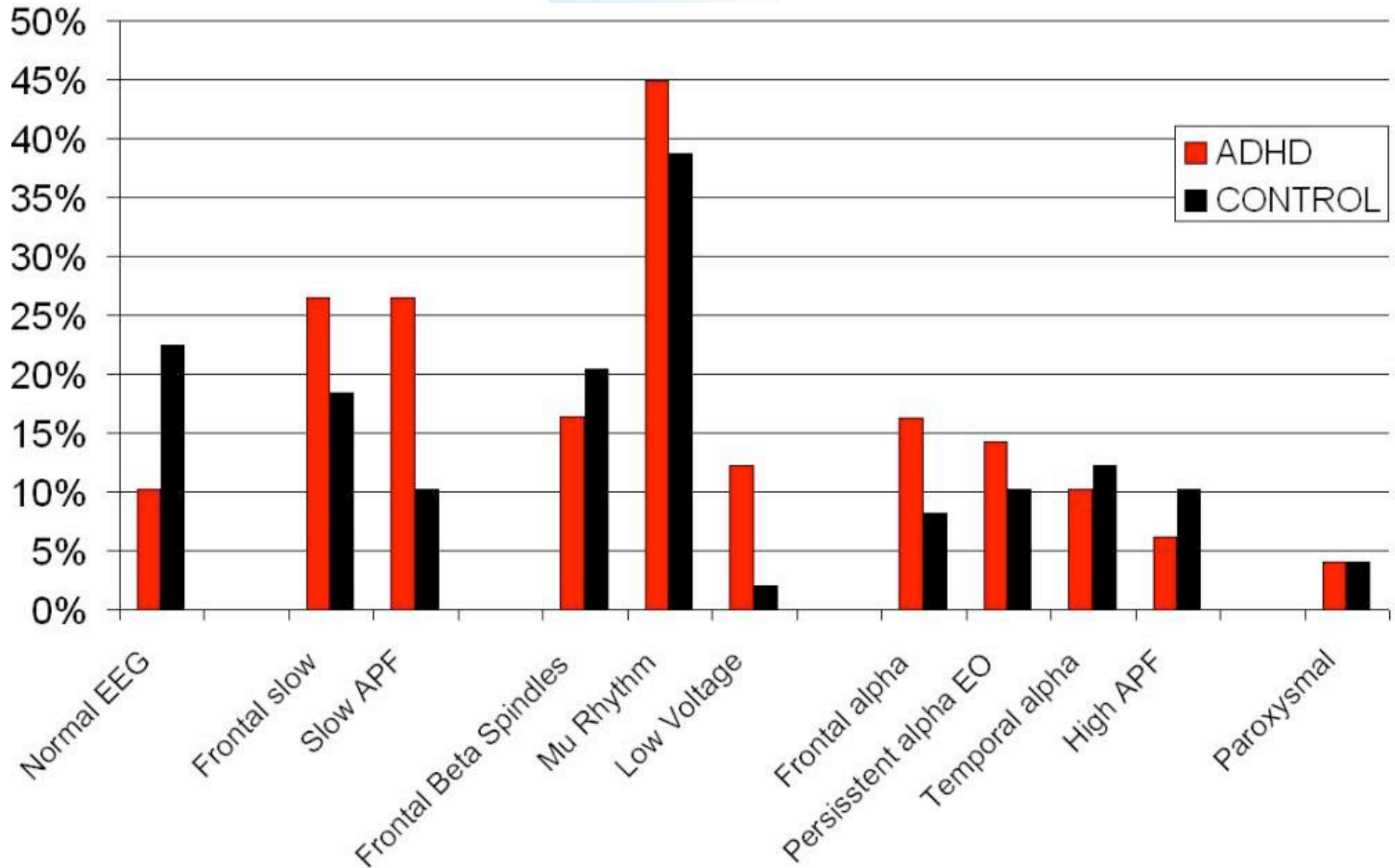


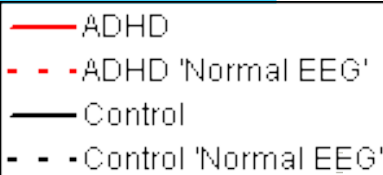
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# EEG Phenotype study in ADHD

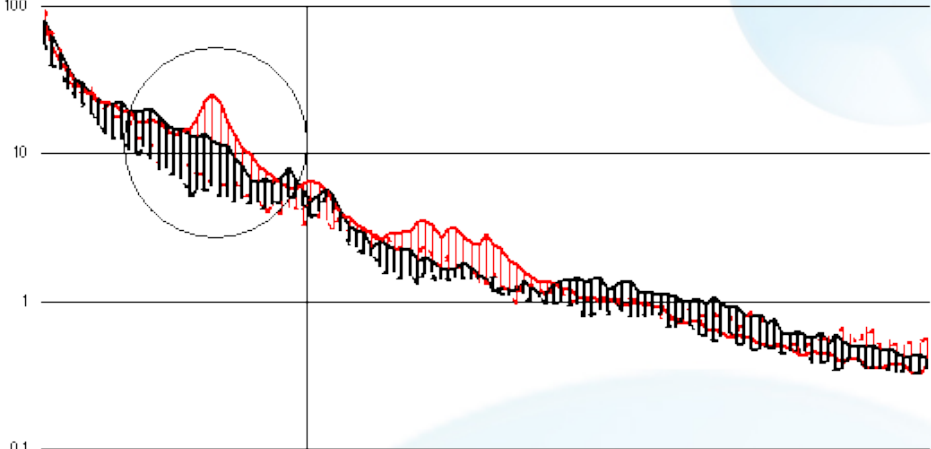
- 50 ADHD children from the Brain Resource International Brain Database and 50 matched controls. All unmedicated.
  - Individually EEG Phenotyped by 2 raters (IRR Kappa >.90)
  - All ADHD children treated with stimulant medication.
  - Treatment response assessed using CPT.
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# Prevalence of different EEG Phenotypes in 50 children with ADHD vs. 50 matched healthy controls

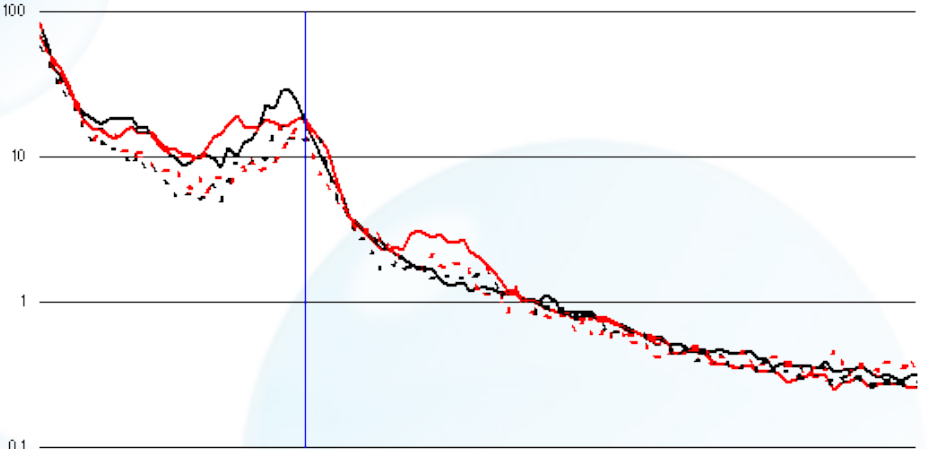




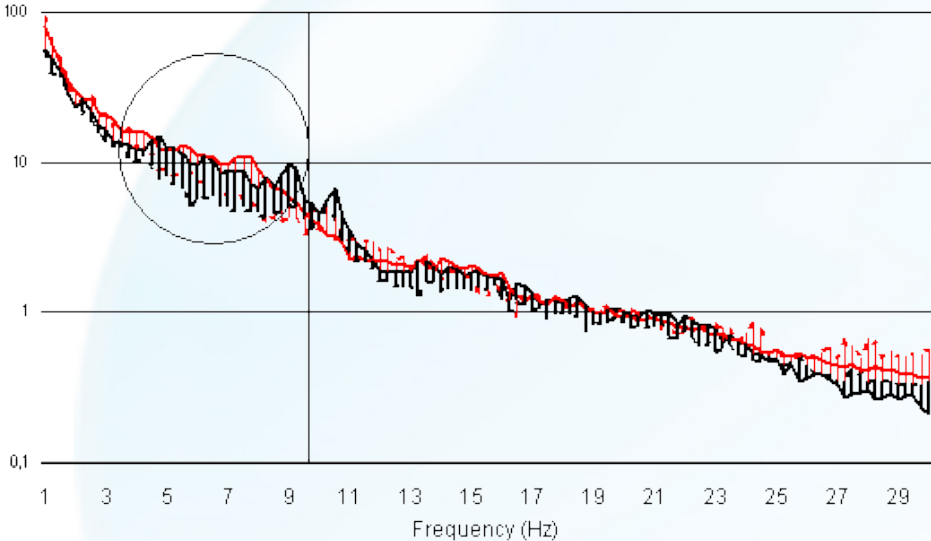
Frontal Slow: Fz



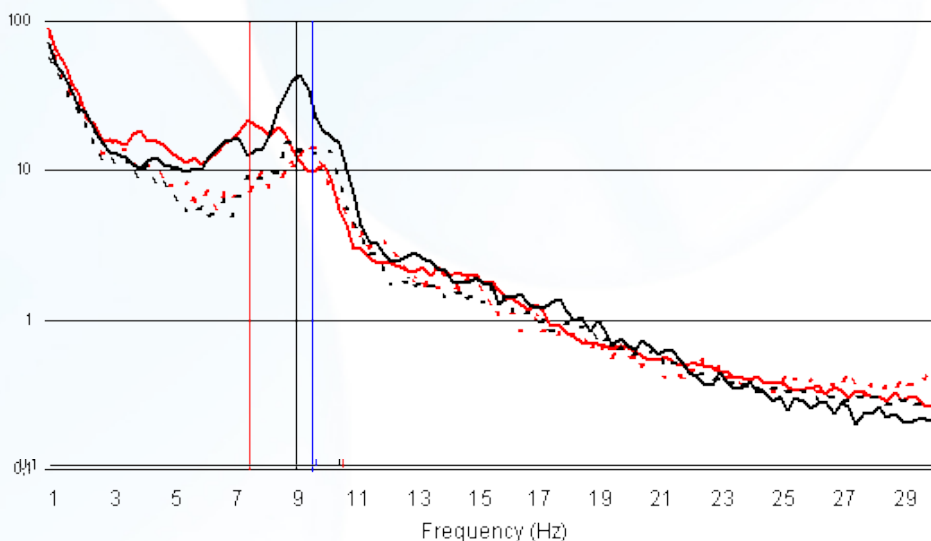
Frontal Slow: Pz



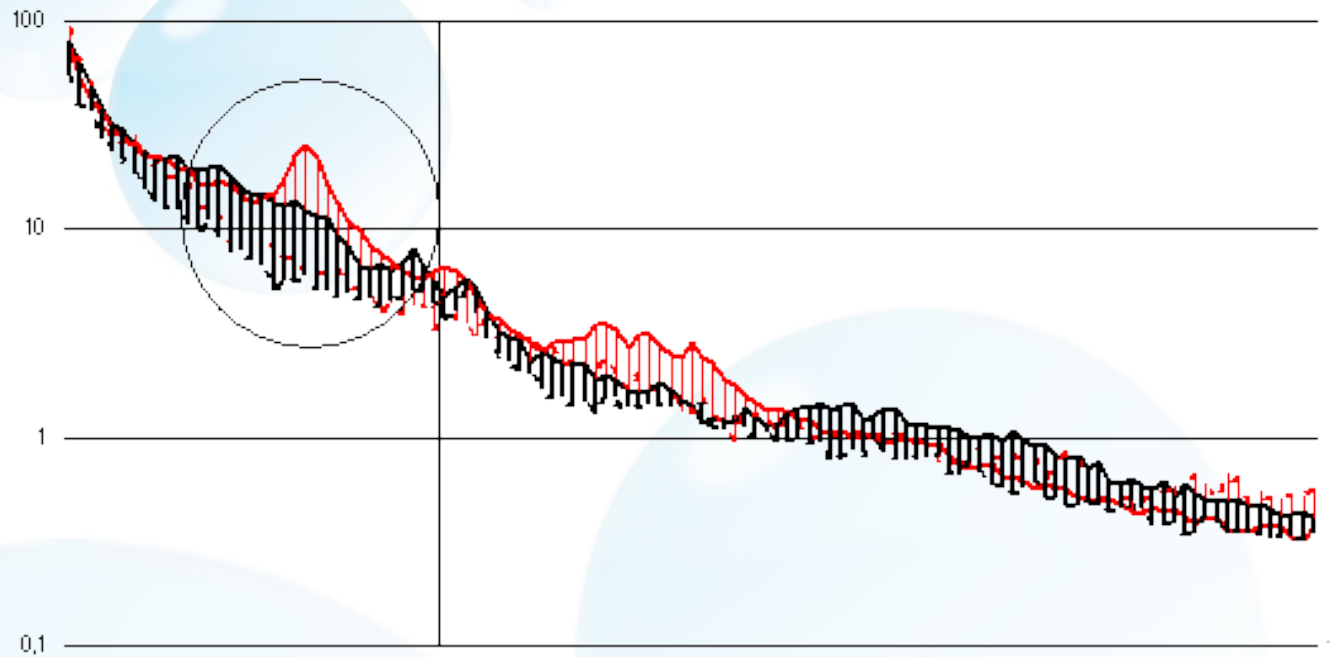
Slow Alpha Peak Frequency: Fz



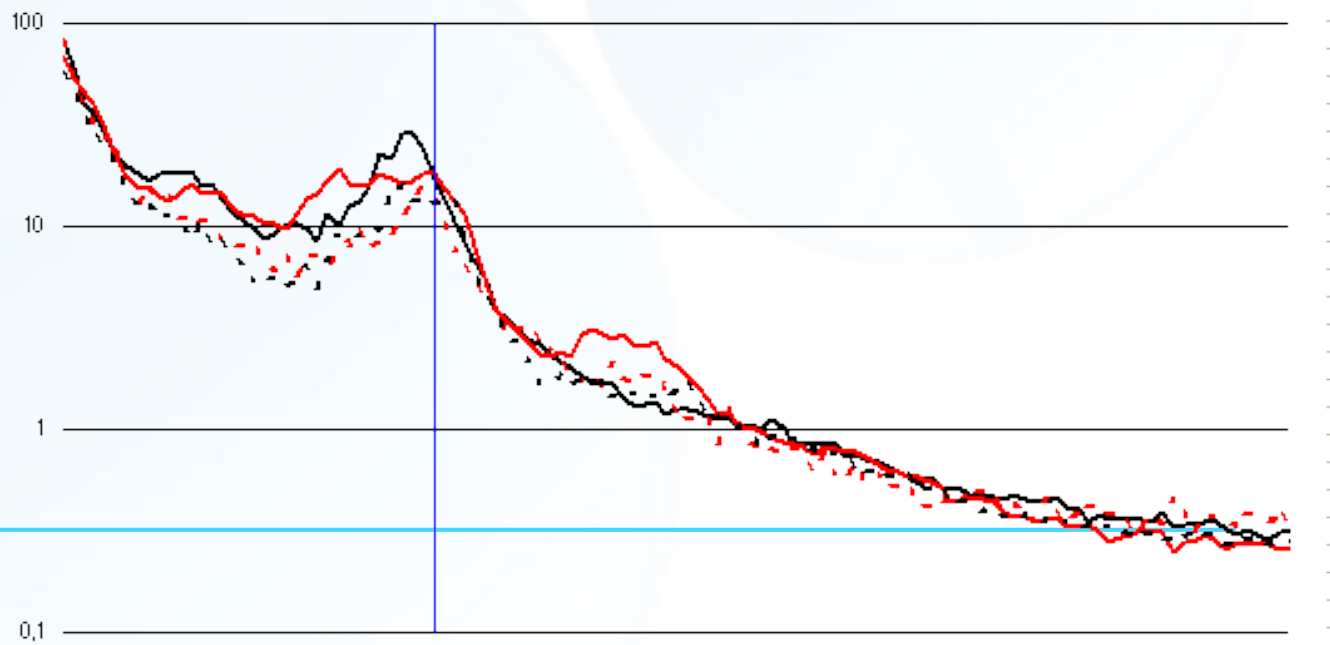
Slow Alpha Peak Frequency: Pz



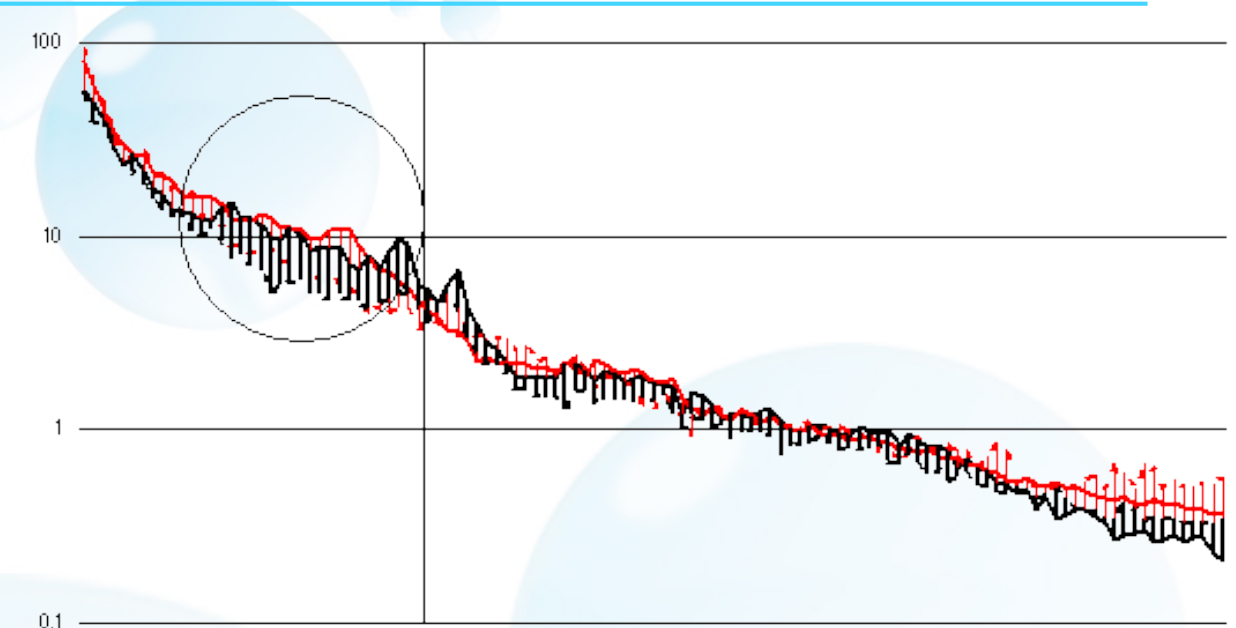
### Frontal Slow: Fz



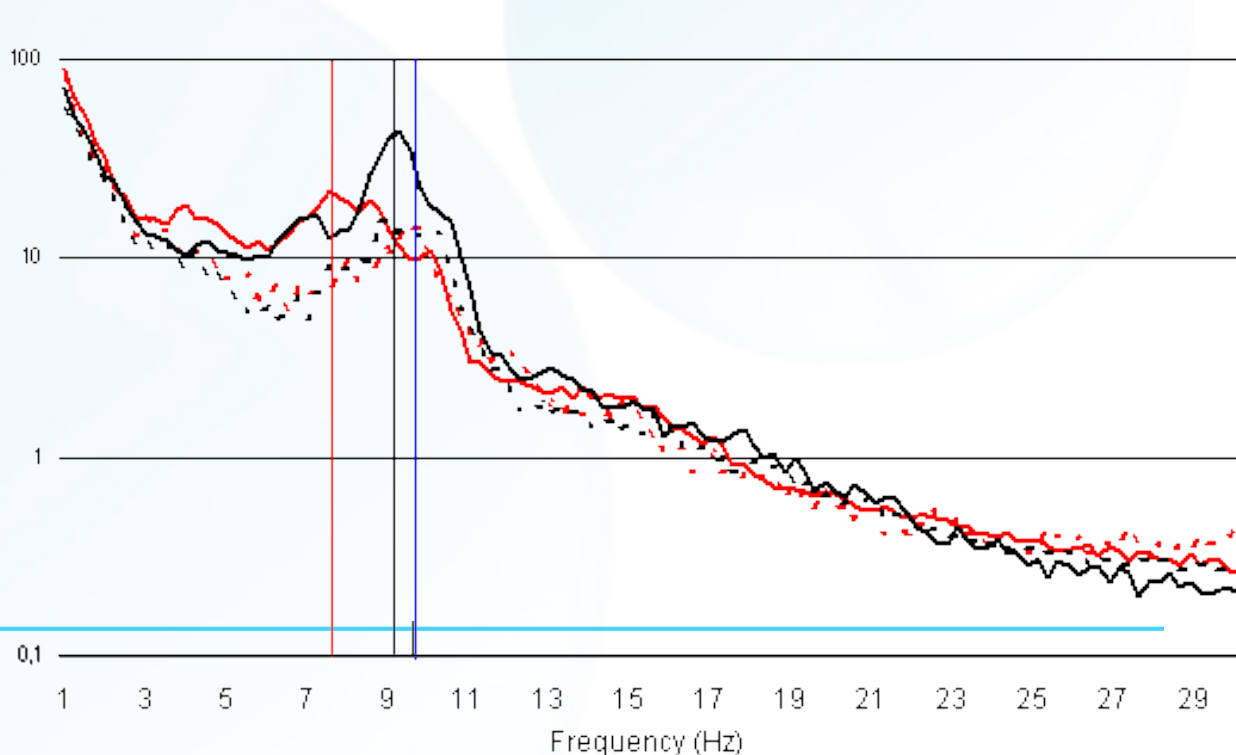
### Frontal Slow: Pz



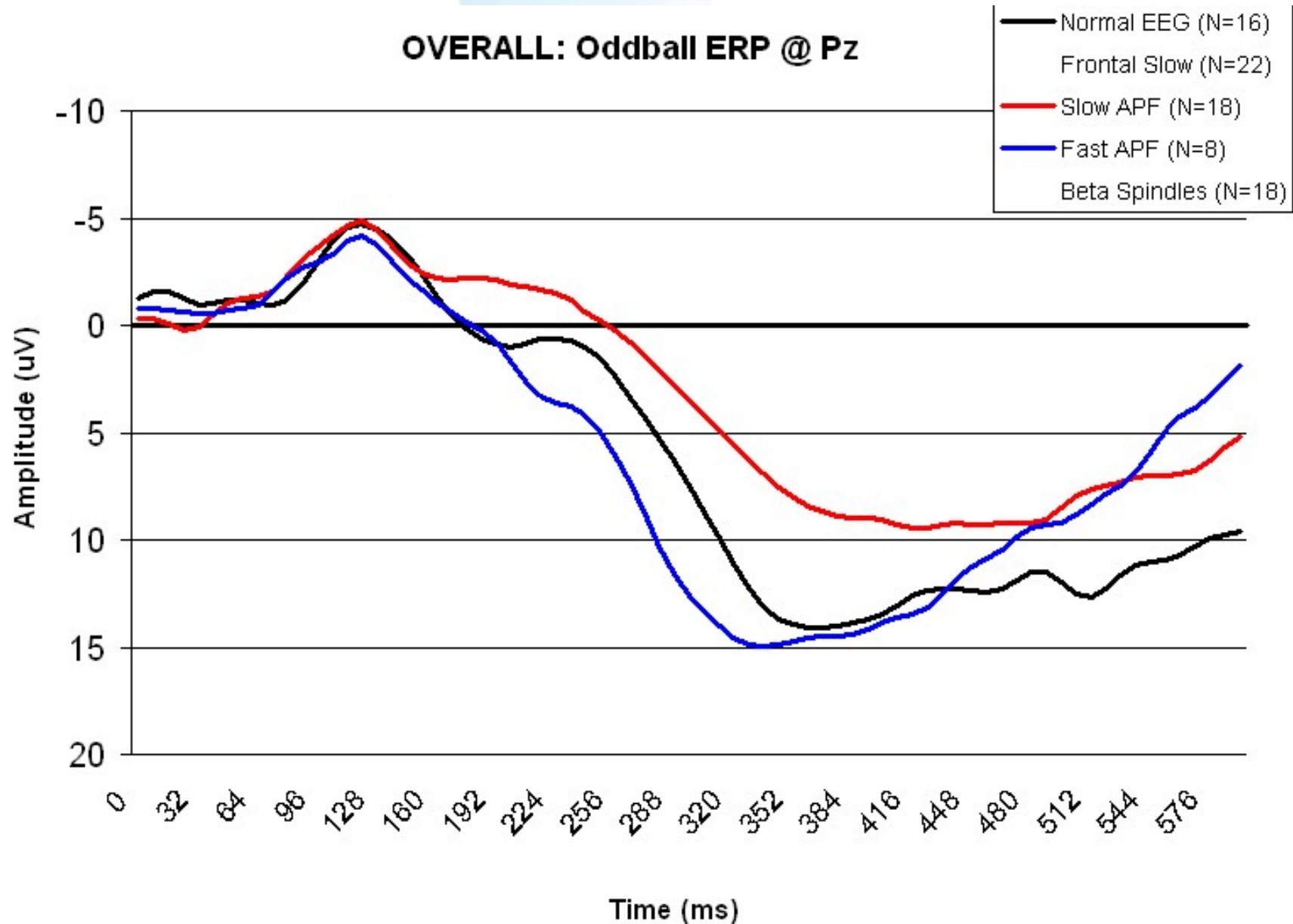
Slow Alpha Peak Frequency: Fz



Slow Alpha Peak Frequency: Pz



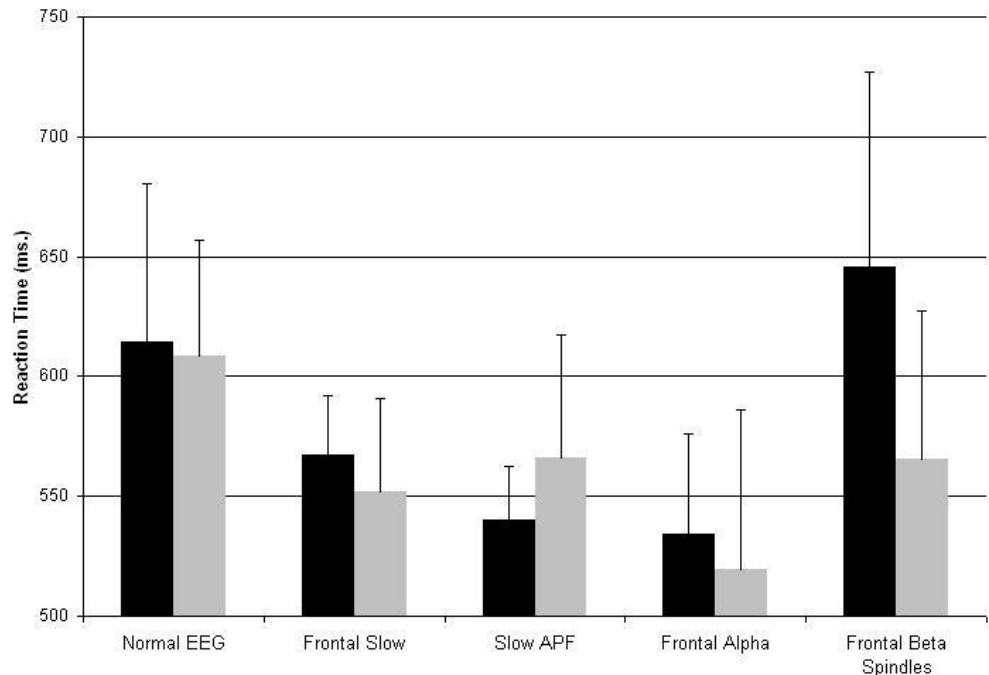
# EEG Phenotype relation to ERP's



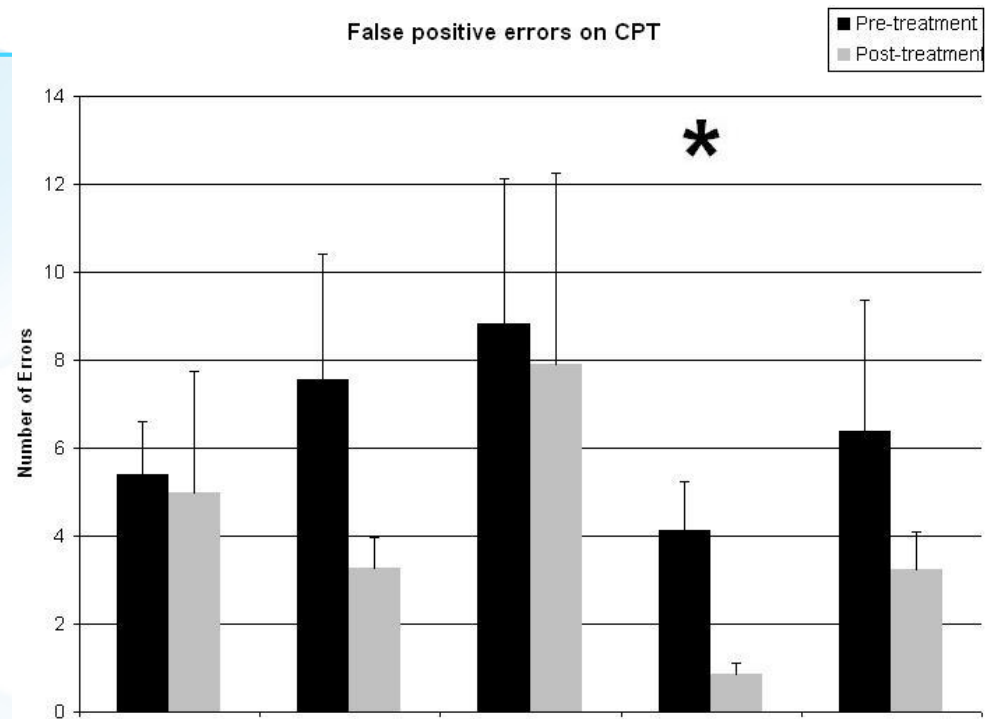
# Does EEG predict treatment outcome?

- Frontal theta EEG phenotype only predicted treatment outcome (decreased false negative errors: inattention)
- Frontal alpha: decreased false positive Errors: impulsivity. Clinically relevant?

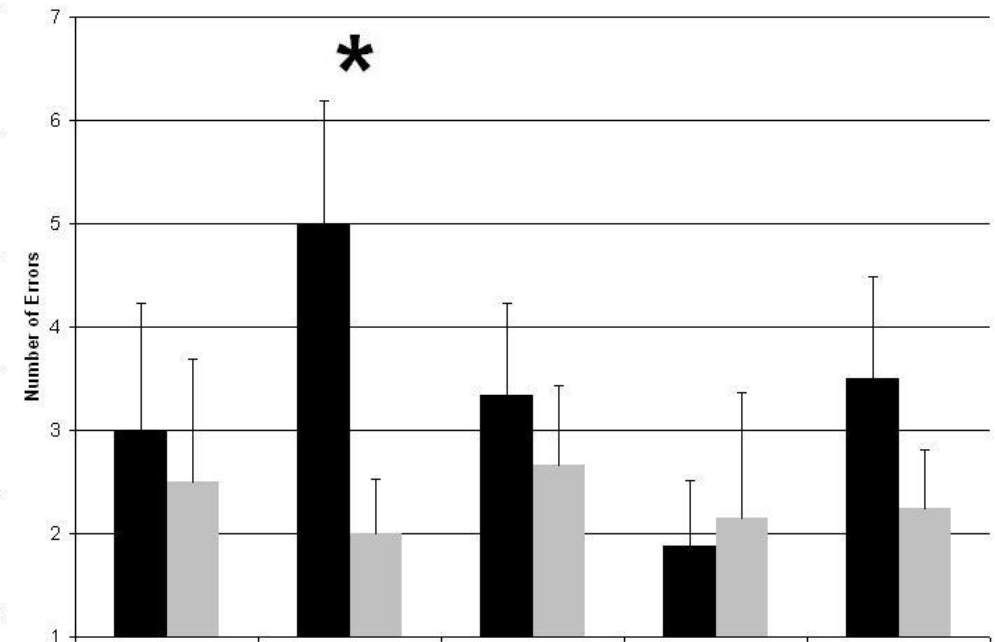
Reaction time during CPT



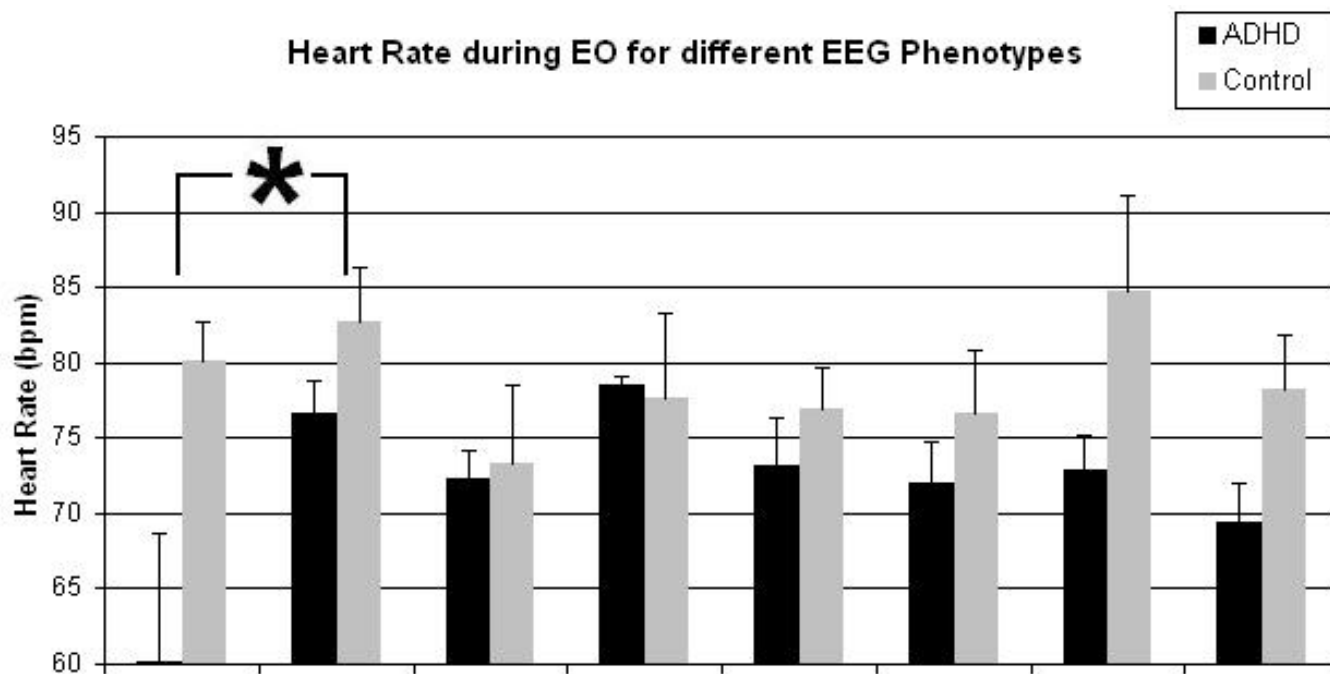
False positive errors on CPT



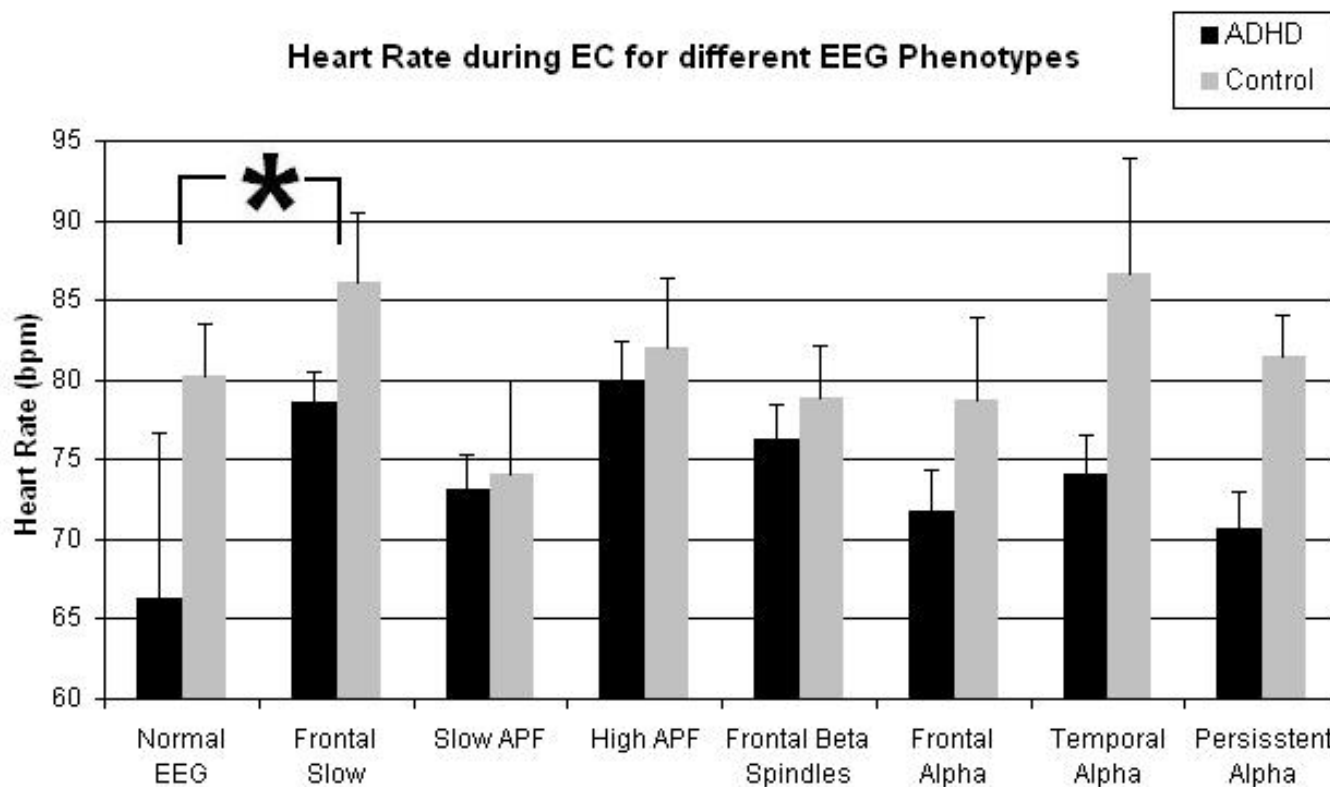
False negative errors on CPT



Heart Rate during EO for different EEG Phenotypes



Heart Rate during EC for different EEG Phenotypes



# Summary

- EEG Phenotypes have good inter-rater reliability.
- No relation to ADHD subtypes (inattentive, combined, hyperactive/impulsive).
- Prevalence similar in ADHD as compared to control group, trend for more frontal slow and more slowed APF: More severe expression in clinical group.
- Previous studies have averaged frontal slow and slowed APF into 1 group.
- Only frontal slow predicted treatment outcome (clinically relevant).
- Frontal slow also associated with increased HR – stimulants also increase HR!?

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# Considerations

- EEG Phenotypes real Phenotypes? Further research into genetic linkages.
  - Small sample size, due to sub-grouping
  - Further replication of EEG Phenotypes concept.
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- Thanks for your attention!

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