John S Butler

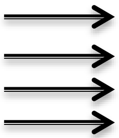
An Examination of the Neural Unreliability Thesis of Autism for Visual and Somatosensory Evoked Responses.

John S Butler

How I learned to Stop Worrying and Love the Null Result

My background

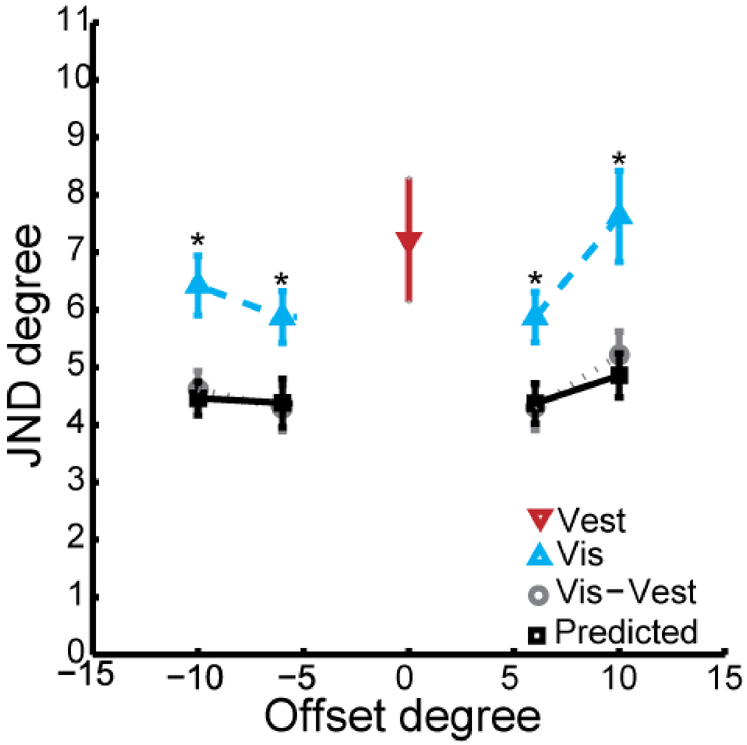
- Numerical Analysis (Trinity College Dublin, PhD work)
  - Robust Numerical methods of Prandtl Boundary Layer Problems

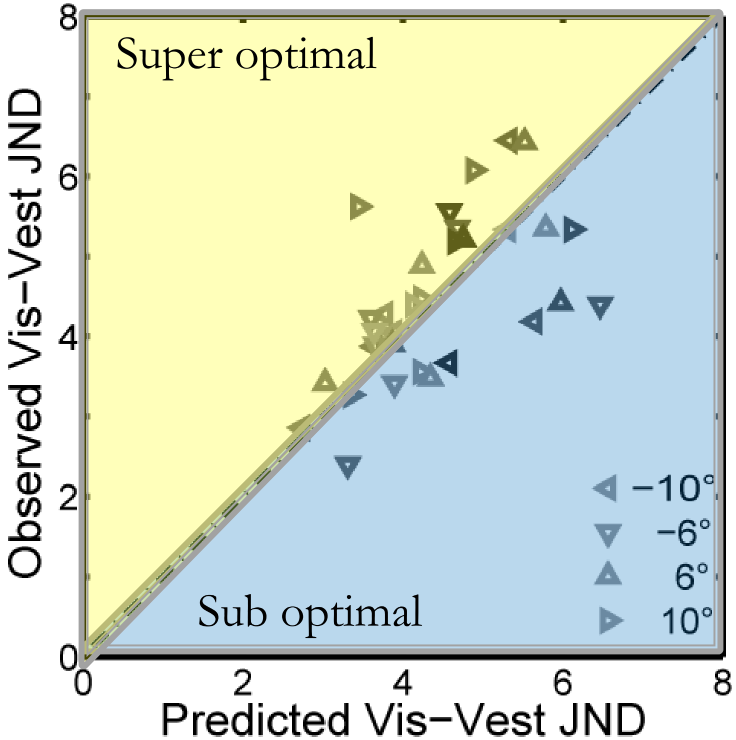


- Self-motion Perception (Max Planck Institute for Biological Cybernetics)
  - Walking
  - Driving

- Unisensory and Multisensory processing
  - Developmental Disorders (Albert Einstein College of Medicine)
    - Autism Spectrum Disorder, Niemann Pick Type C
  - Movement Disorders (Trinity Centre for Bioengineering)
    - Parkinson's Disease
    - Dystonia

Optimal reduction in variance

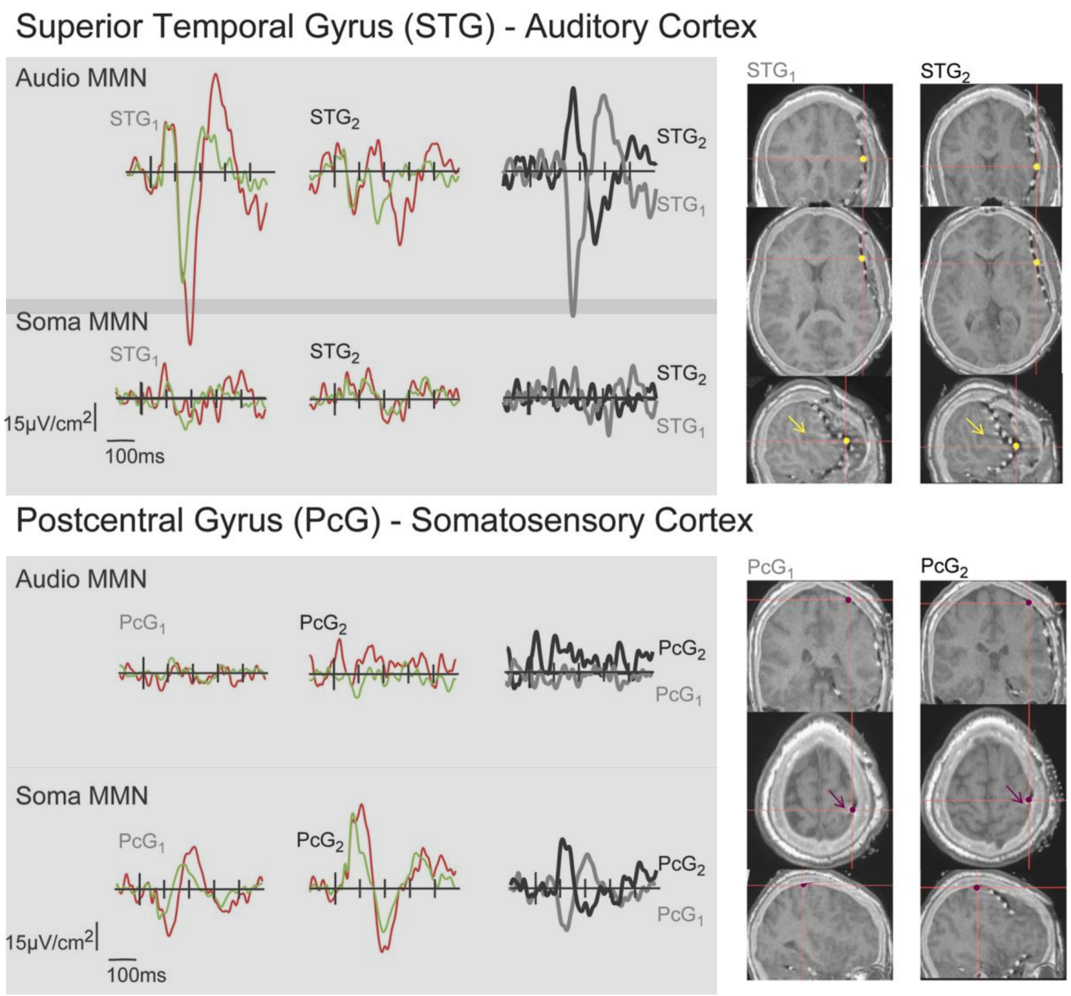




The combination of visual and vestibular cues observe an optimal rule of integration

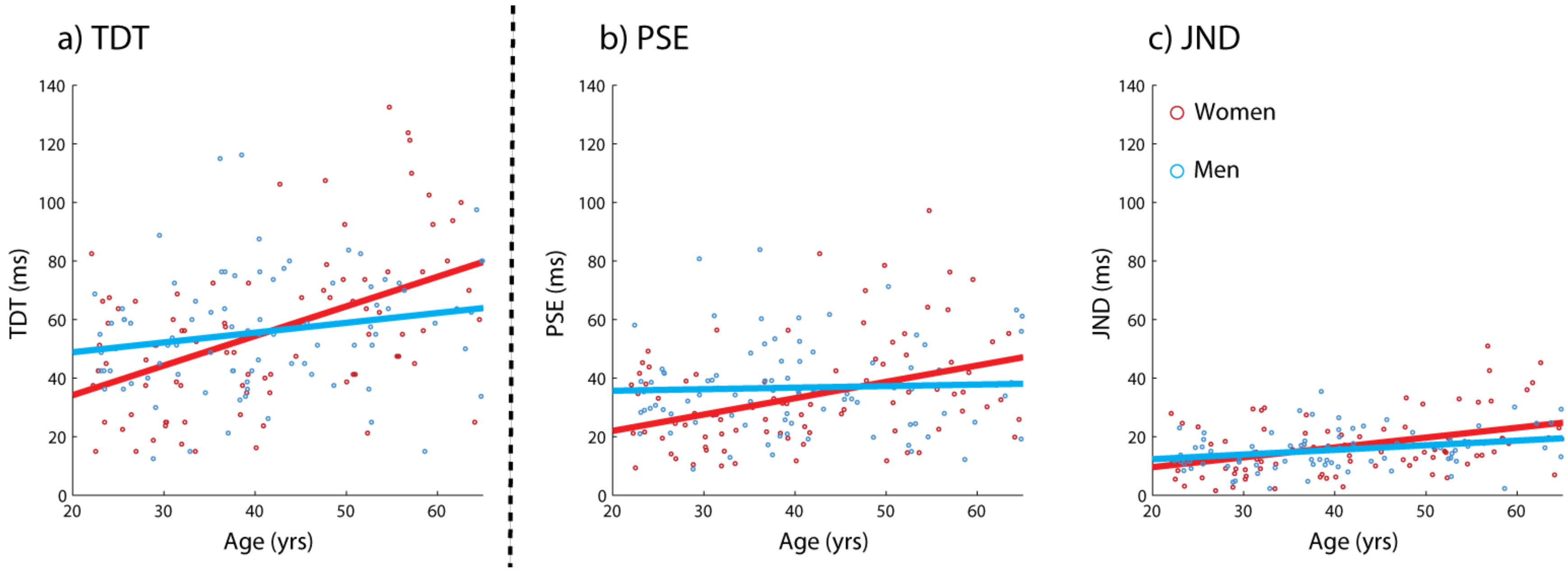
Butler et al. Journal of Vision 2010

Common or Redundant Sensory Processing



Butler et al. Journal of Neuroscience 2011

Sexual Dimorphism of Sensory Processing



Williams, Butler et al. Frontiers 2015

Autism

Autism Spectrum Disorder

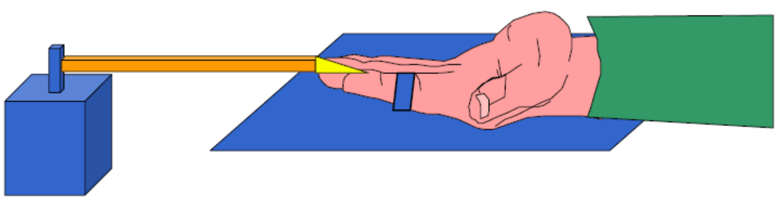
- Social interactions and relationships
- Verbal and nonverbal communication
- Limited interests in activates or play
- Sensory processing DSM V
  - Hypo activity
  - Hyperactivity

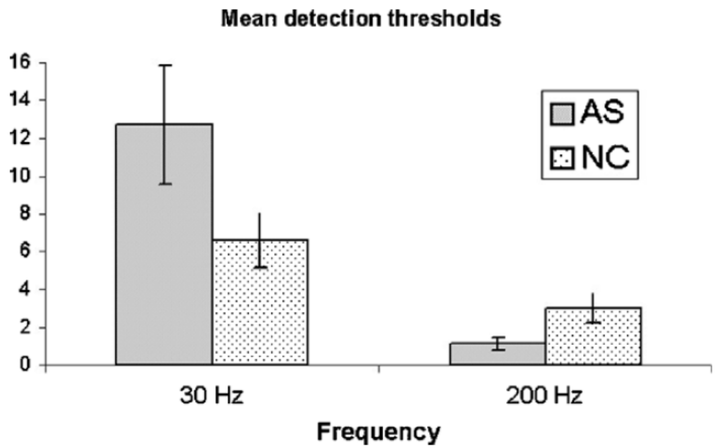
Tactile sensitivity in Asperger syndrome

Sarah-Jayne Blakemore *, Teresa Tavassoli, Susana Calò, Richard M. Thomas, Caroline Catmur, Uta Frith, Patrick Haggard

Institute of Cognitive Neuroscience, Department of Psychology, University College London, 17 Queen Square, London WC1N 3AR, UK

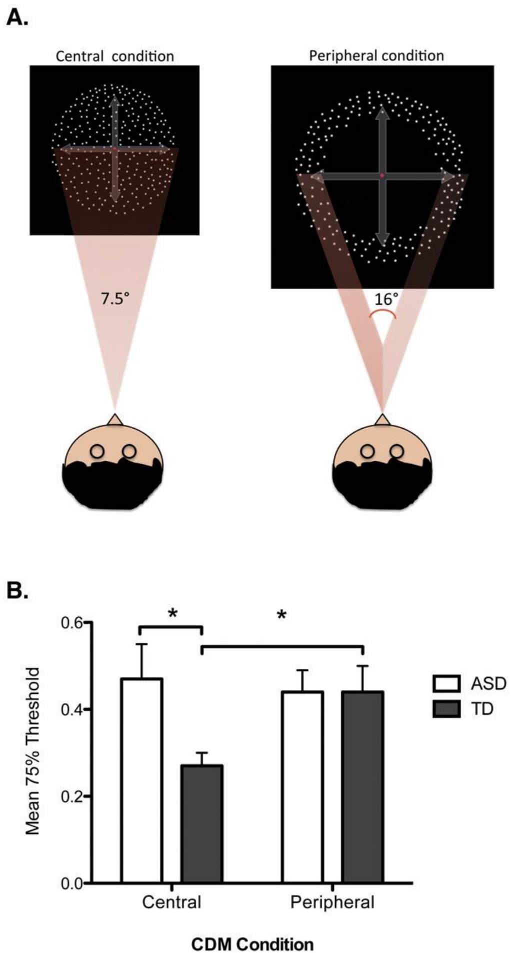
Accepted 9 December 2005
Available online 24 February 2006





N=9(TD), 10(AS)

Decreased Coherent Motion Discrimination in Autism Spectrum Disorder: The Role of Attentional Zoom-Out Deficit

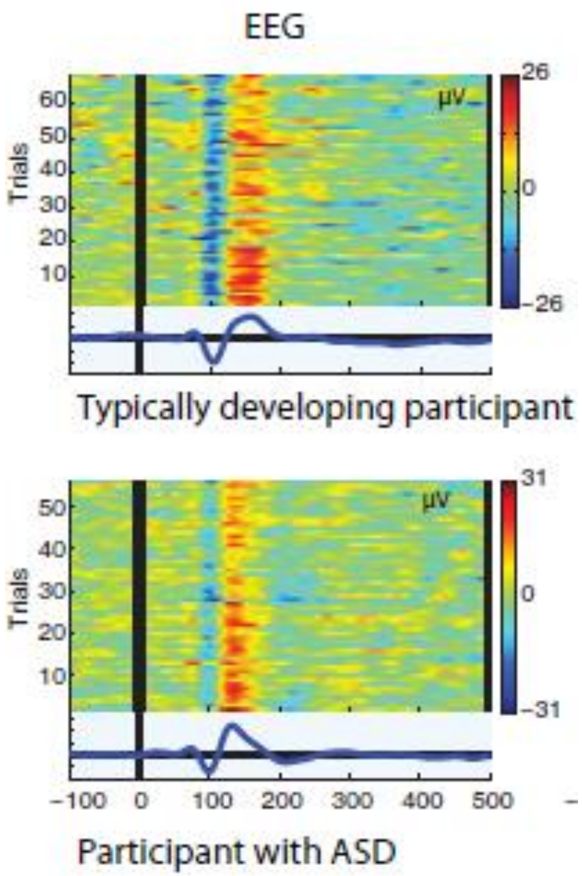


- 11 ASD, 11 TD
- Coherent motion task

Ronconi et al. 2012, PloS One

Increased intra-participant variability in children with autistic spectrum disorders: evidence from single-trial analysis of evoked EEG

Elizabeth Milne*



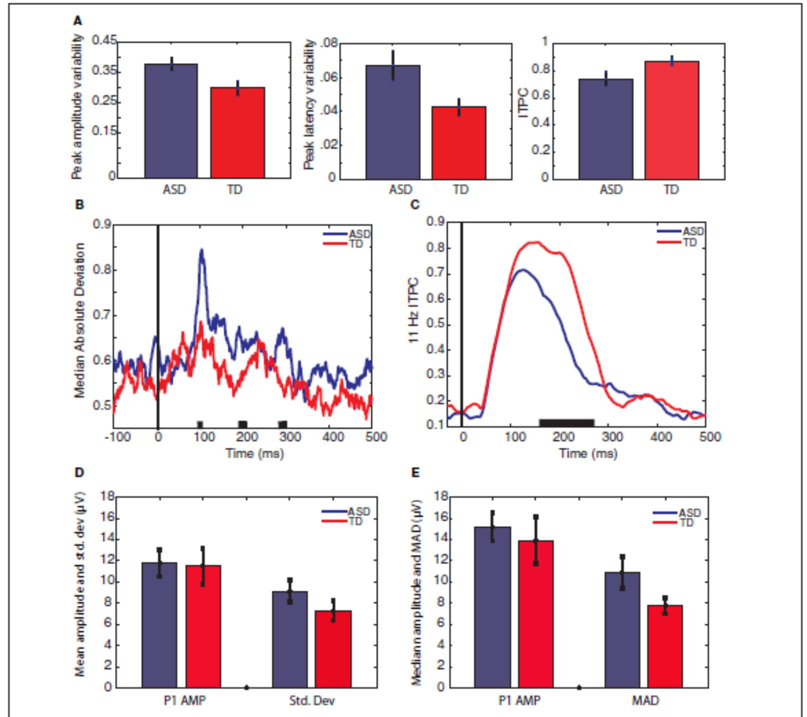


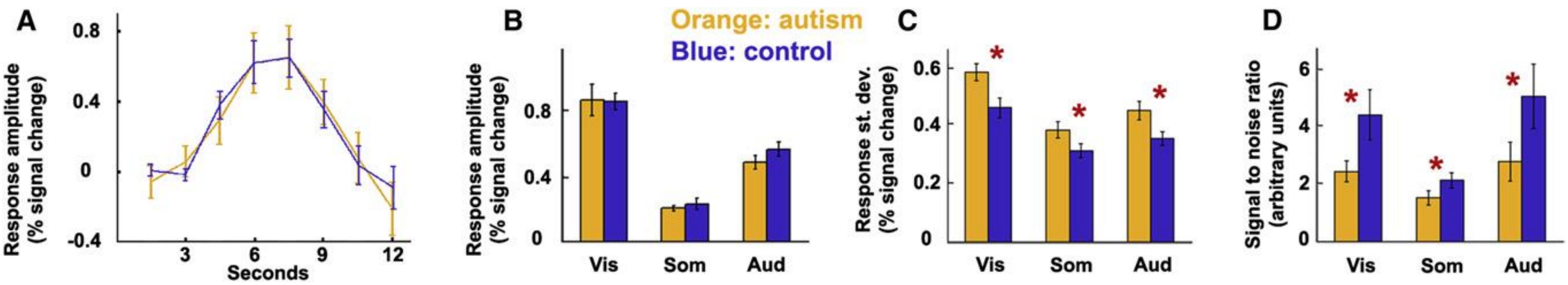
FIGURE 3 | Estimates of variability averaged across group. |(A) (normalized)| measures of peak variability. The left graph shows mean variation in the amplitude of the P1 peak, the middle graph shows mean variation in the latency of the P1 peak, and the right graph shows the mean maximum ITPC between 100 and 170 ms. |(B) (normalized)| median absolute deviation in amplitude across trials at each time-point, averaged across participant groups. **(C)** ITPC at each time-point, averaged across participant groups. The black lines on the *x*-axis of plots **(B)** and **(C)** indicate time-points of group difference ($p < 0.05$). P1 amplitude is shown in plots **(D)** and **(E)**. **(D)** P1 amplitude calculated from the ERP peak, and the SD of the single-trial P1 peaks. **(E)** P1 amplitude calculated as the median of the single-trial P1 peaks, and the median absolute deviation of the single-trial P1 peaks. Bars represent ±1 SE.

N=12(TD), 13(ASD)

Neuron
Case Study

Unreliable Evoked Responses in Autism

Ilan Dinstein,[1,*] David J. Heeger,[2] Lauren Lorenzi,[1] Nancy J. Minshew,[3] Rafael Malach,[4] and Marlene Behrmann[1]



N=14

Predictions

Behavioural Predictions

1) ASDs should have more variable responses
2) ASDs should have worse detection thresholds

Neuronal Predictions

1) the averaged evoked response should be broader and have a delayed peak for all components
2) ASD individuals should have a greater variability of phase dispersion across single trials.

3) More variability in the single trial amplitude

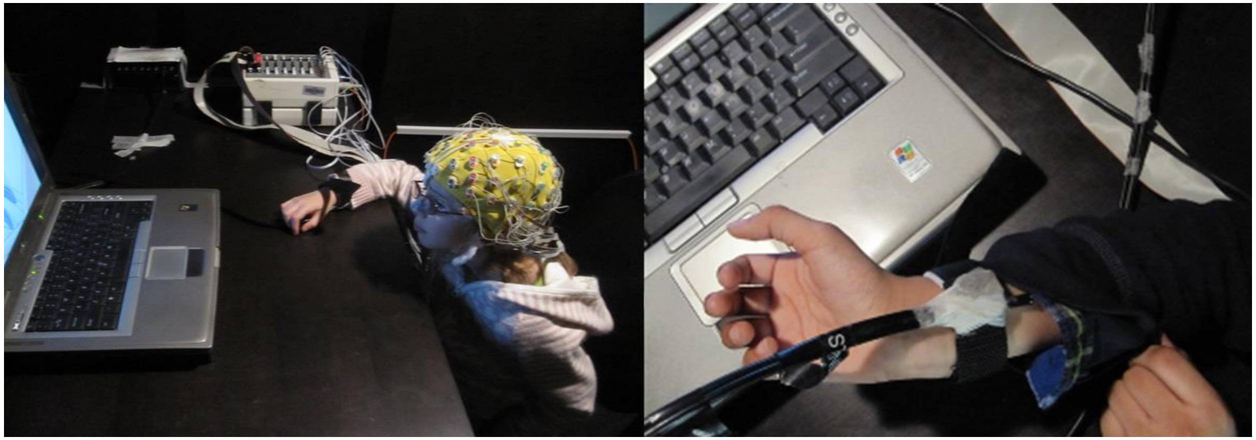
Overview

1) The reliability of the ASD and TD groups average evoked response
2) to investigate the reliability of the phase dispersion and amplitude across trials
3) Link the group average data with single trial
4) Unreliable evoked response was simulated by introducing a temporal jitter (and amplitude variability) at a single trial level in the TD data.

Soma Condition

Inter-Stimulus Interval

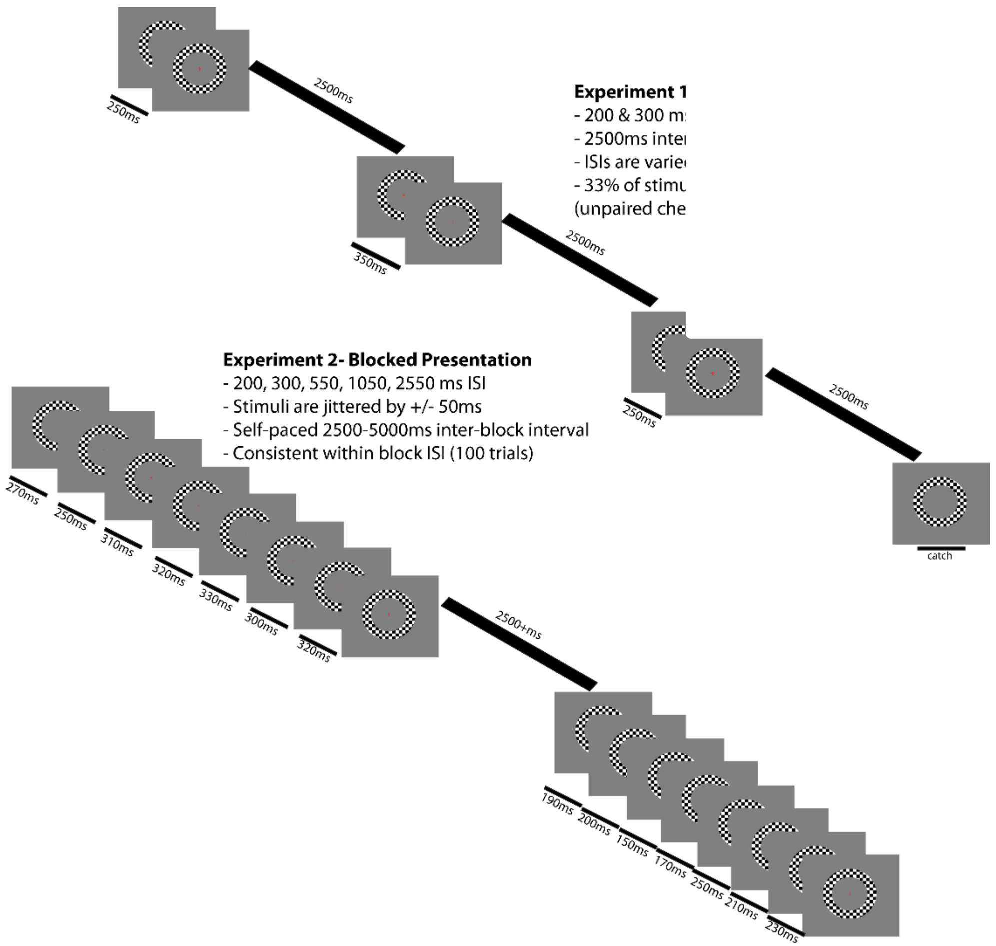
- 150ms
- 250ms
- 350ms
- 550ms
- **1050ms**



Visual Condition

Inter-Stimulus Interval

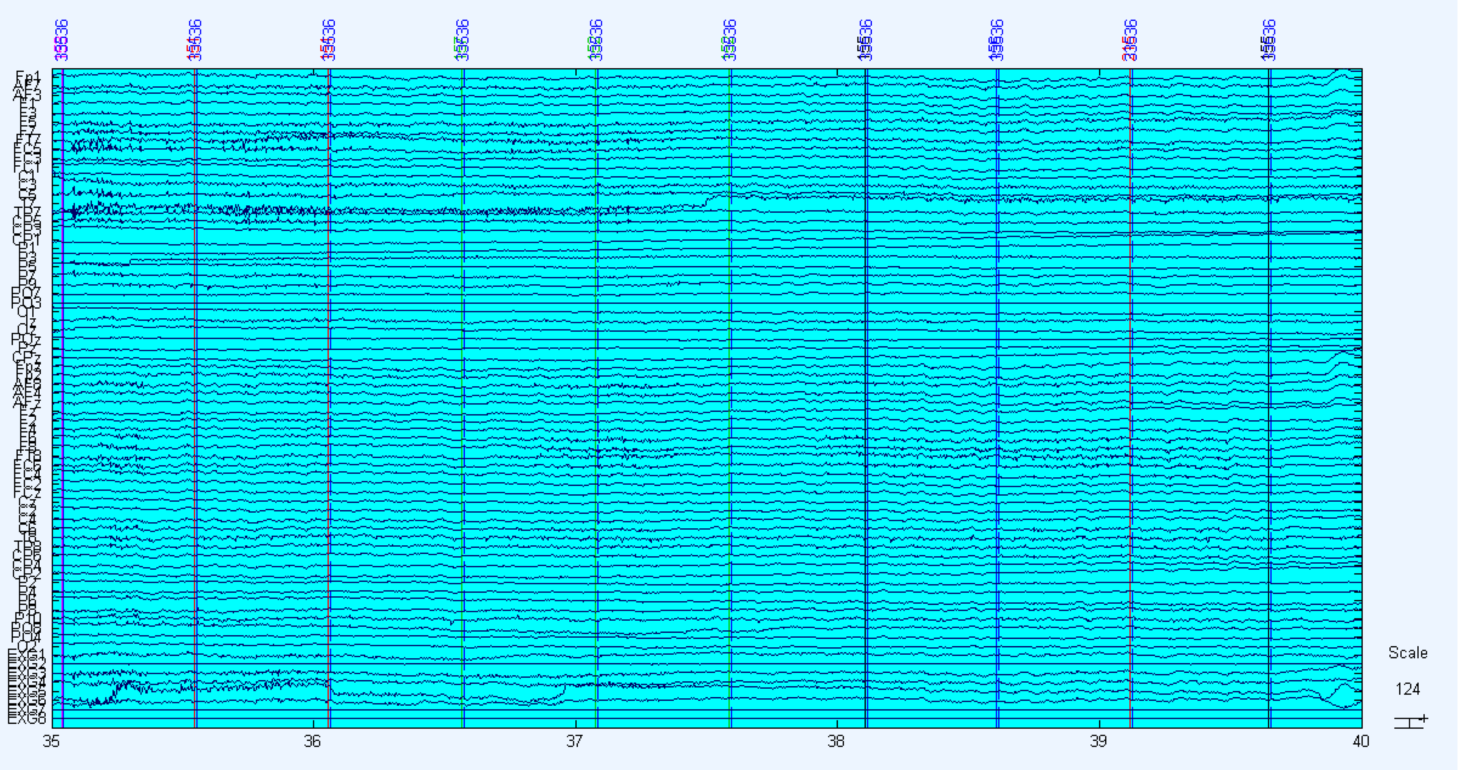
- 200ms
- 300ms
- 550ms
- **1050ms**
- 2050ms



Matched Groups

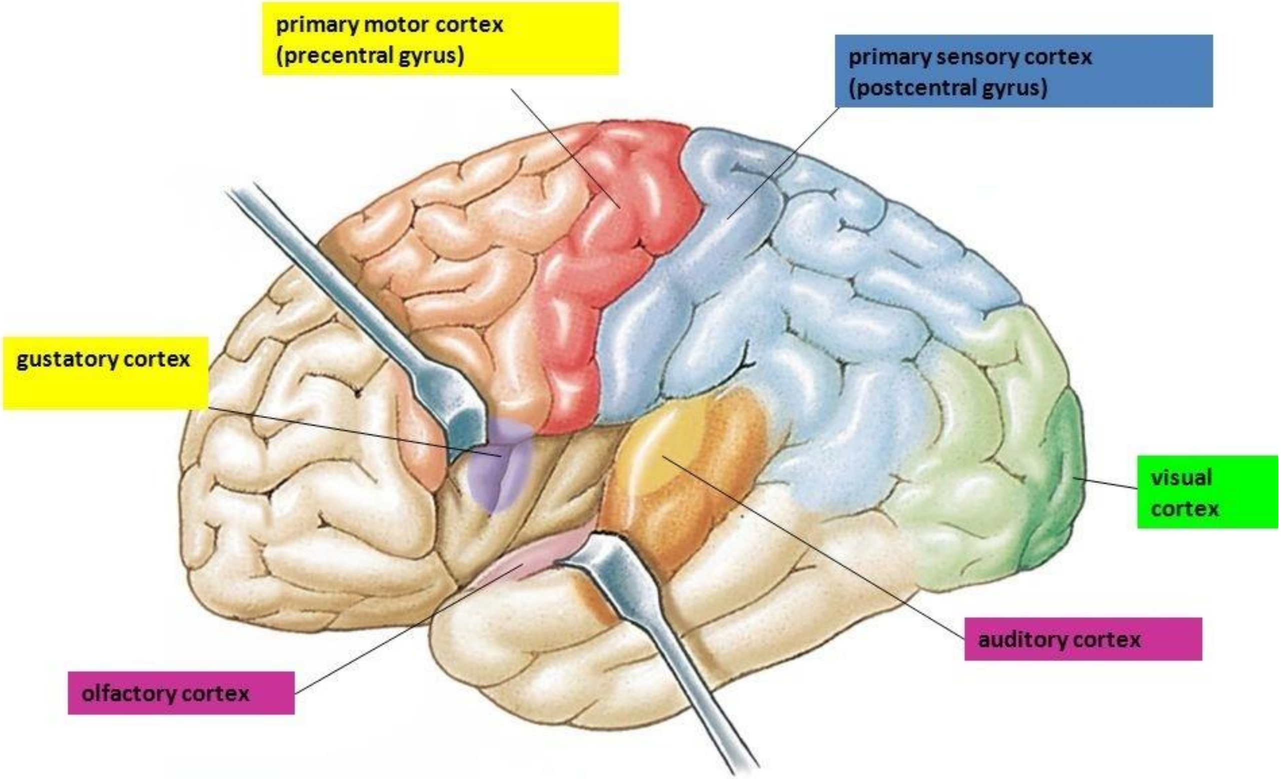
	VISUAL				SOMATOSENSORY		
	TD	ASD	P		TD	ASD	P
Age (Mean±SD)	11.2±2.3	10.9±2.3	0.7		11.0±2.3	10.7±2.3	0.7
VIQ (Mean±SD)	111.8±15.7	101.±17.5	0.04		111.8±12.0	108.4±18.0	0.1
FSIQ (Mean±SD)	109.1±12.4	108.4±17.1	0.9		113.5±13.3	105.7±17.5	0.6
N	20	20			20	20	
No of males	19	19			18	18	

Electroencephalography (EEG)

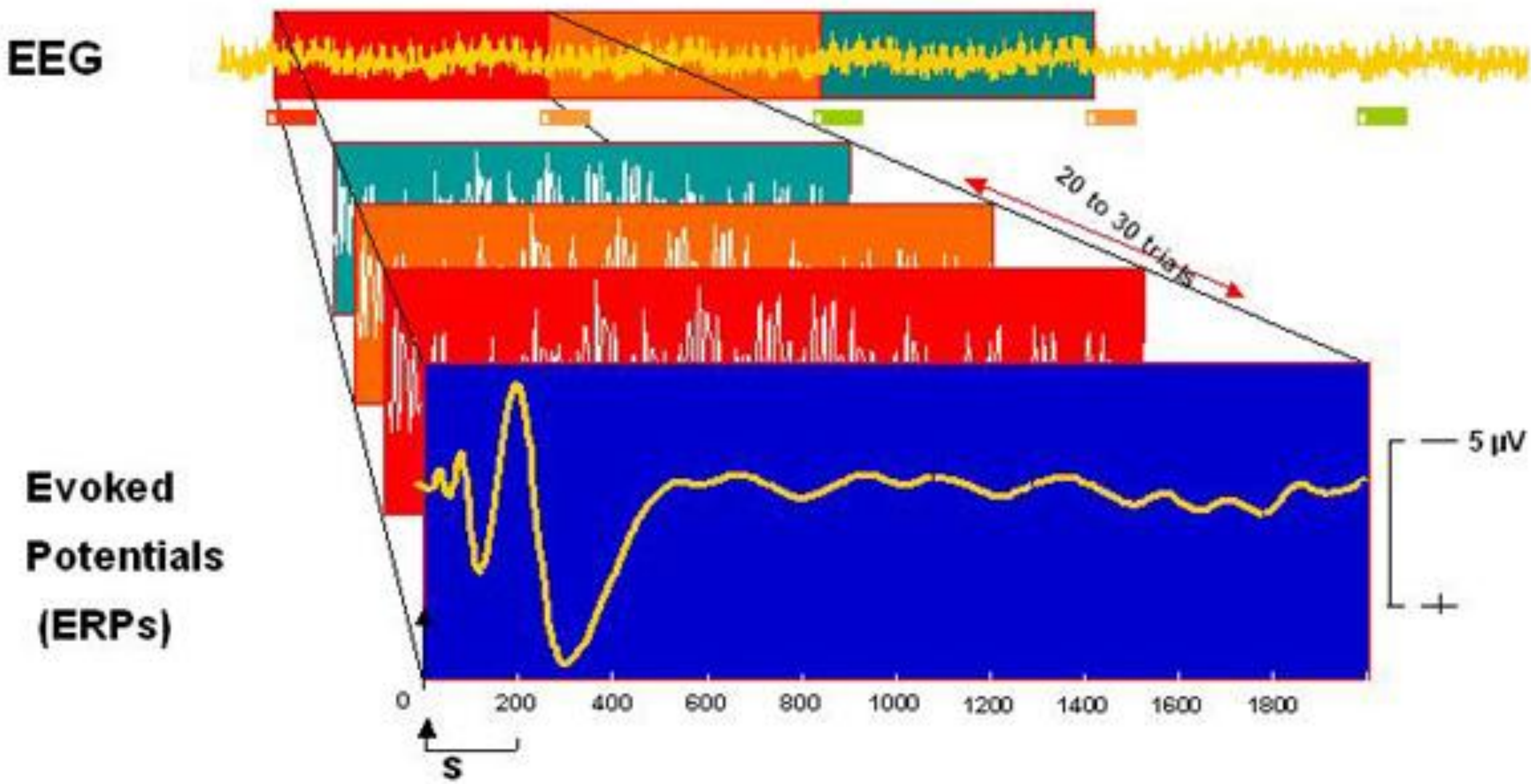


Sensory Cortex

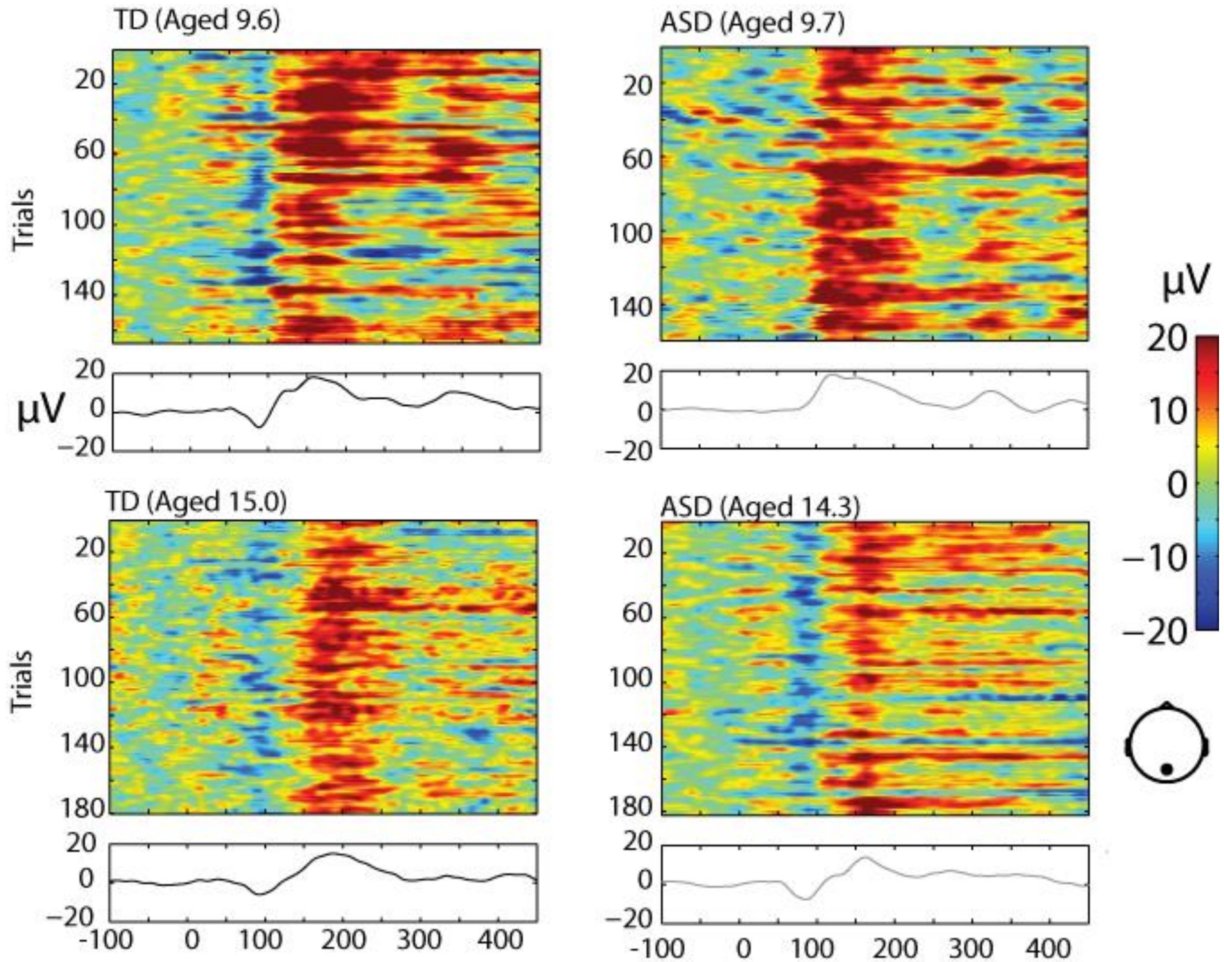
Motor & Sensory



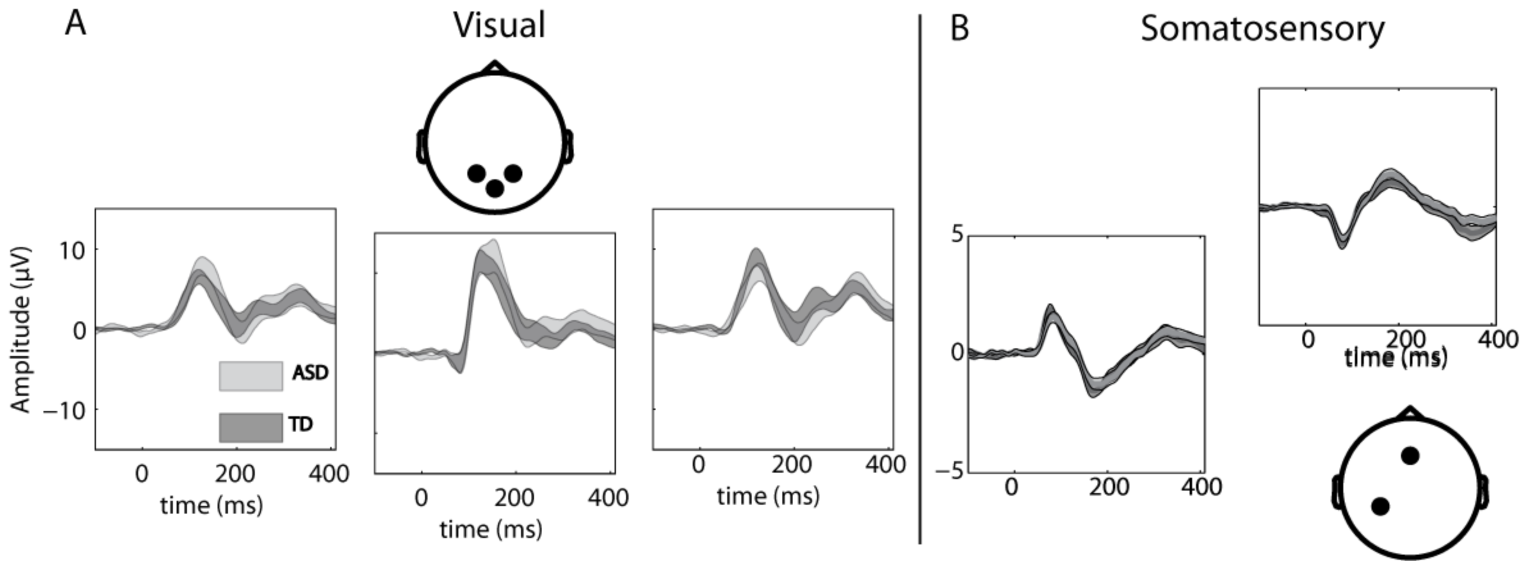
Event-Related Potential (ERPs)



Event-Related Potential (ERPs)

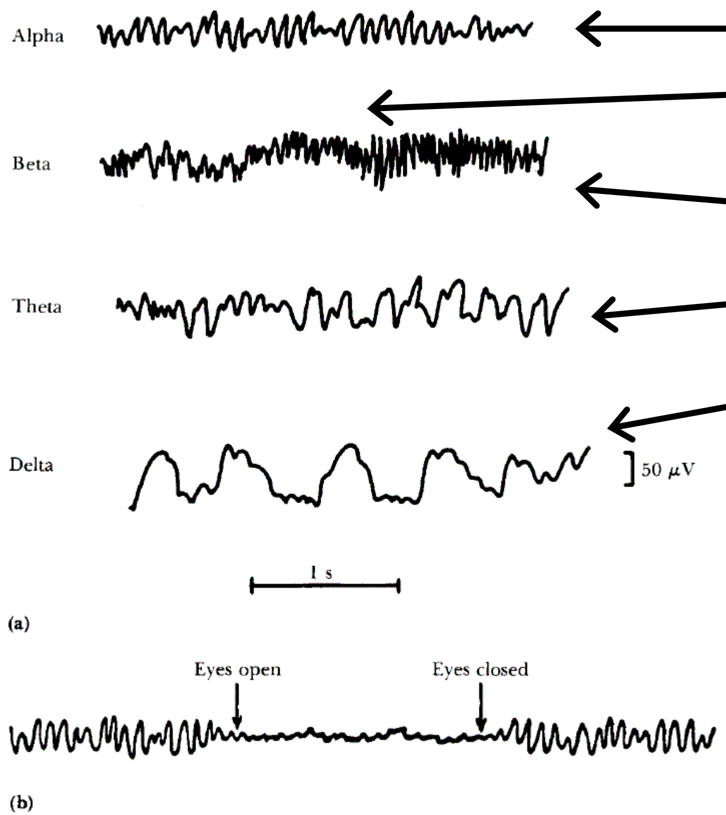


Results



	VISUAL		SOMATOSENSORY	
	TD	ASD	TD	ASD
SNR	34.2±9.2	29.3±9.1	19.0±6.2	16.4±8.0
Acc. Trials	256.6±82.5	237.4±91.3	366.2±58.2	377.6±50.5

Frequency decomposition



Alpha 7 - 14 Hz (“~10 Hz”)

Beta 14 - 20 Hz

Gamma > 20 Hz (“~40 Hz”)

Theta 3 - 7 Hz

Delta 0.5 – 3 Hz

Hans Berger:

First Human EEG recording in 1929

- Alpha waves discovered

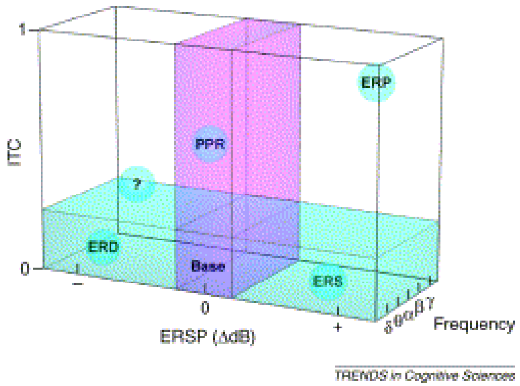
Frequency decomposition

POWER

- Event Related Spectral Perturbation (ERSP)
- Baseline power versus post stimulus

PHASE

- Inter-trial Coherence (ITC)
- Alignment of response



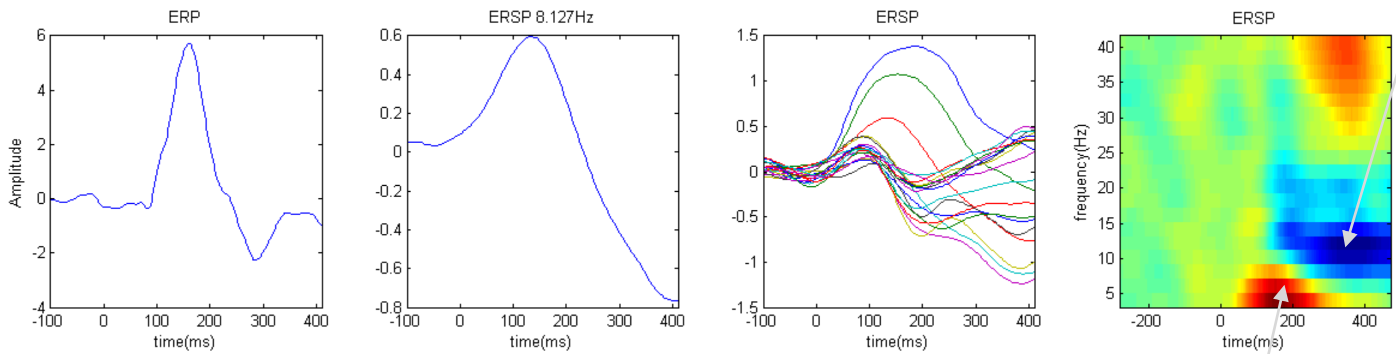
Scott Makeig , Stefan Debener , Julie Onton , Arnaud Delorme

Mining event-related brain dynamics

Trends in Cognitive Sciences, Volume 8, Issue 5, 2004, 204 - 210

Power

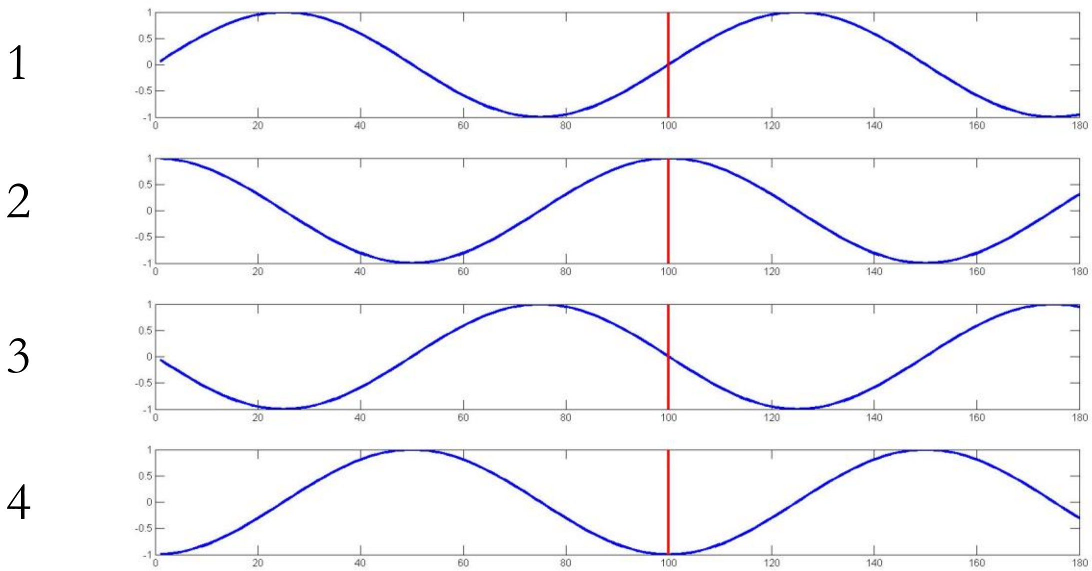
event-related
desynchronization

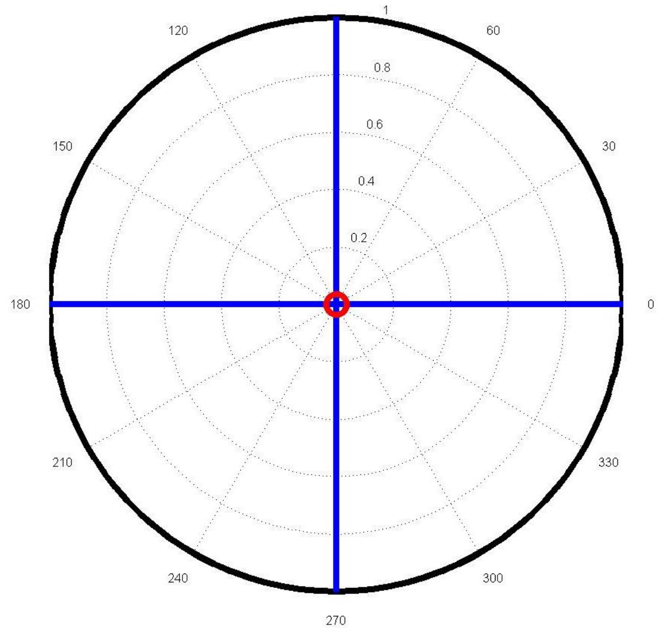


event-related
synchronization

Inter-trial Coherence (ITC) -Phase

Trial





ITC=0, unreliable response

Inter-trial Coherence (ITC) -Phase

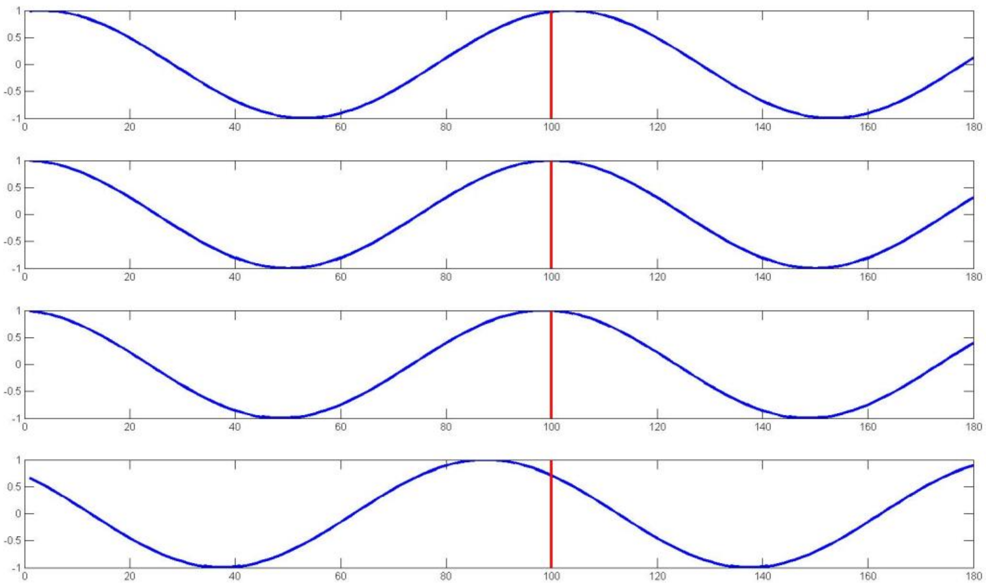
Trial

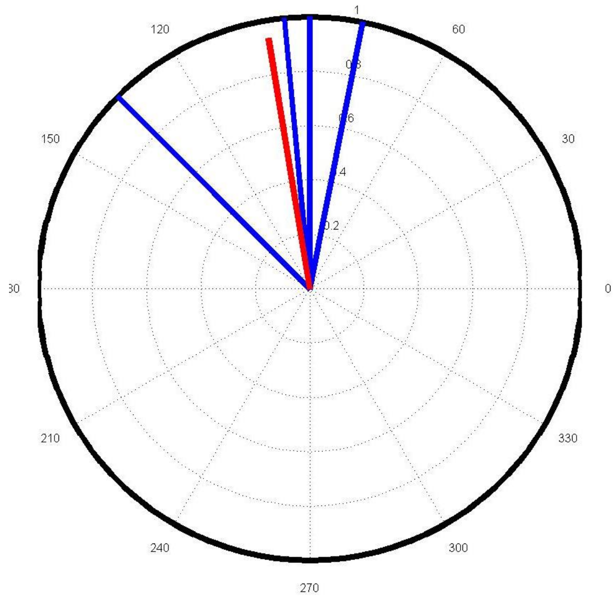
1

2

3

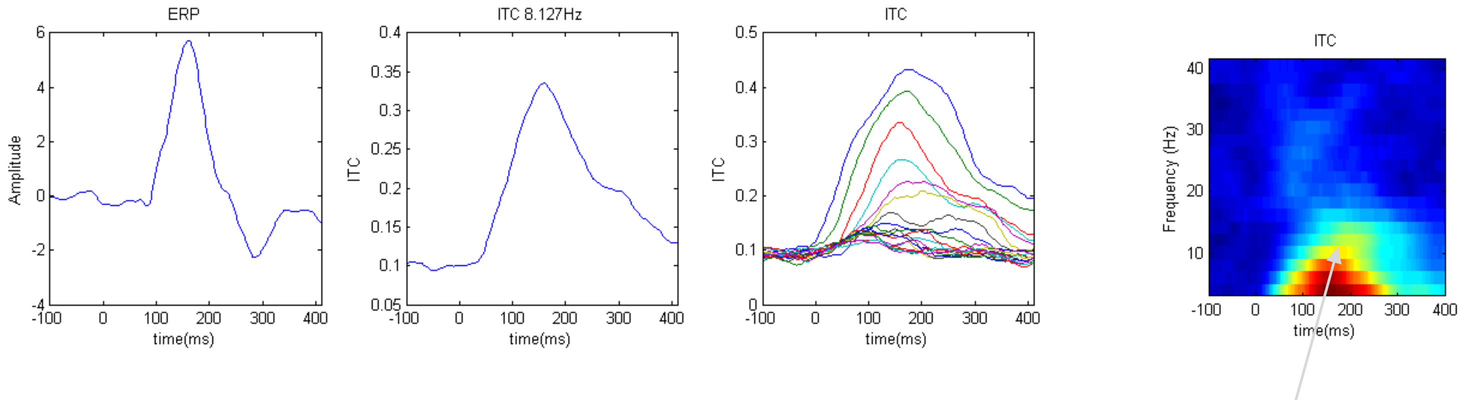
4





ITC=0.9, reliable response

Inter-trial Coherence (ITC) -Phase

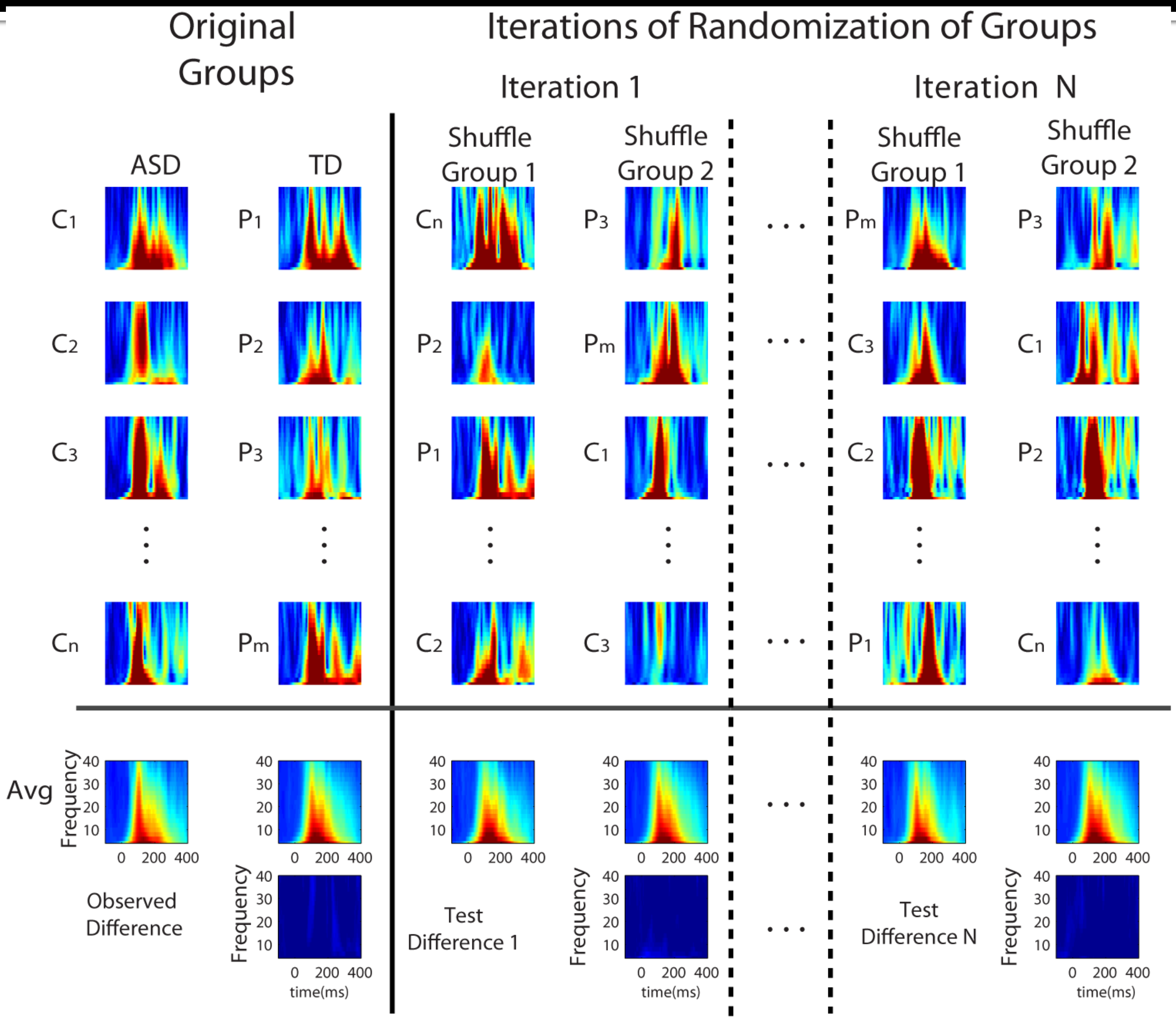


Alignment of similar response

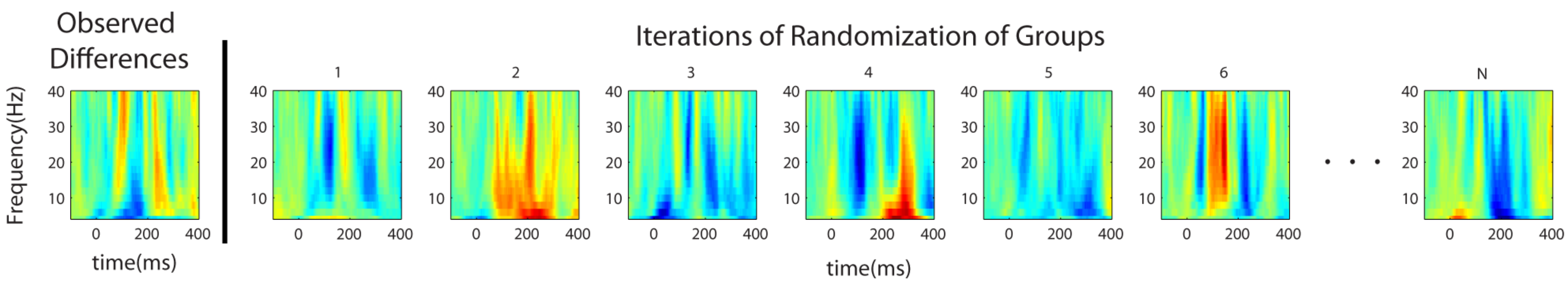
Statistics

- Comparison between groups at each time and frequency point
- All stats presented are uncorrected

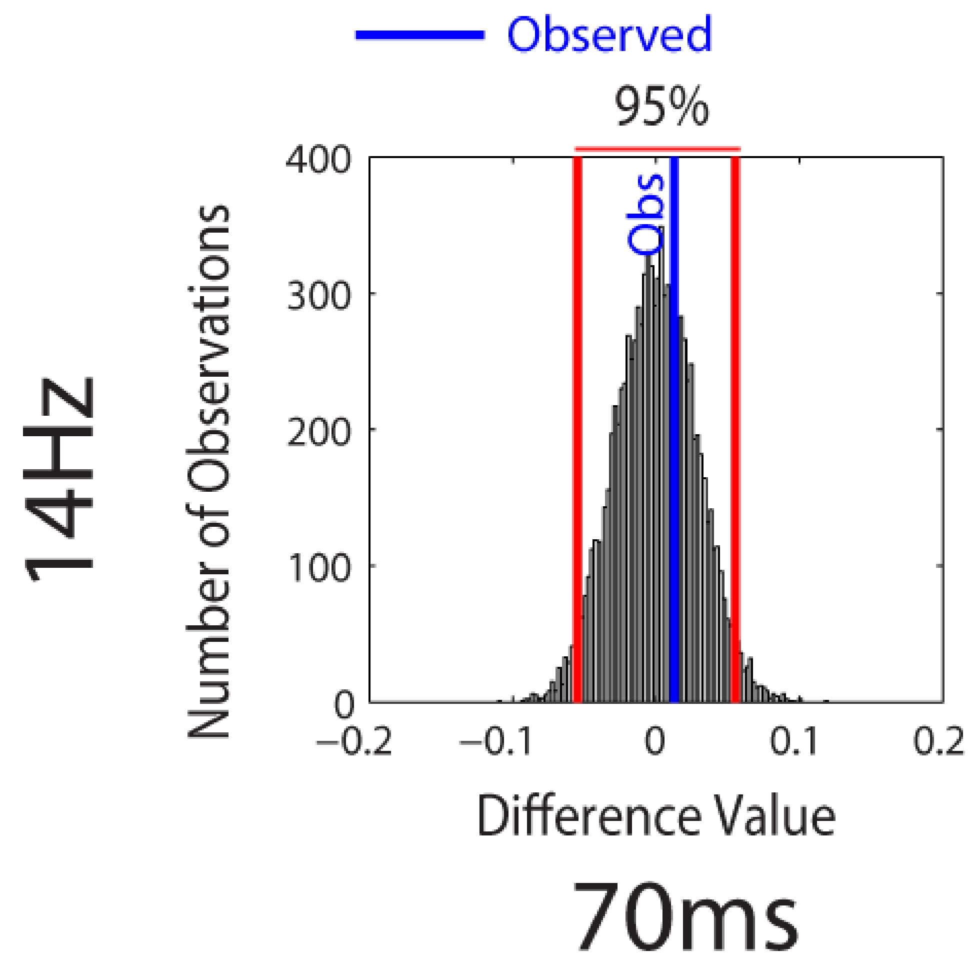
Bootstrapped Analysis



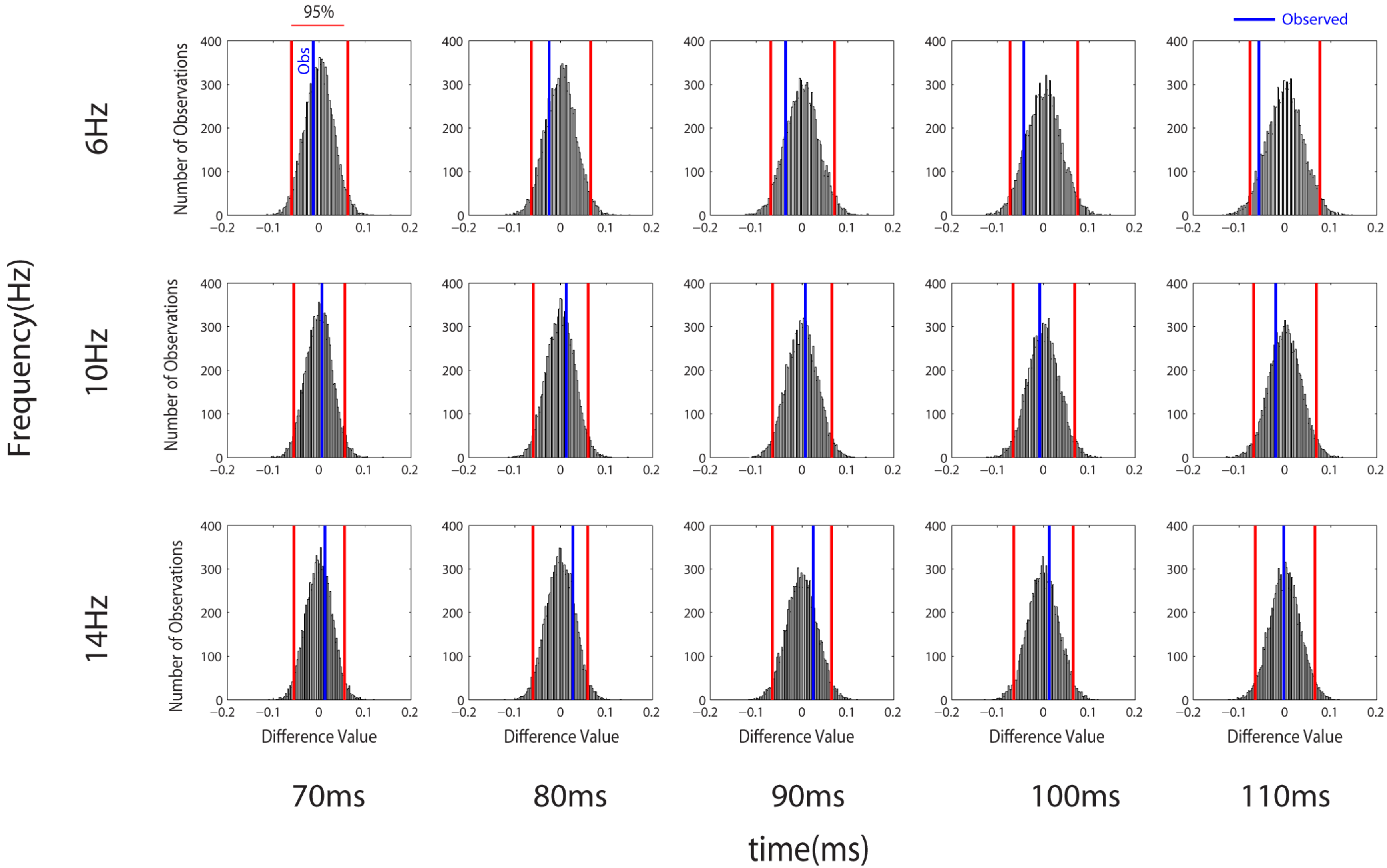
Bootstrapped Statistics



Bootstrapped Statistics

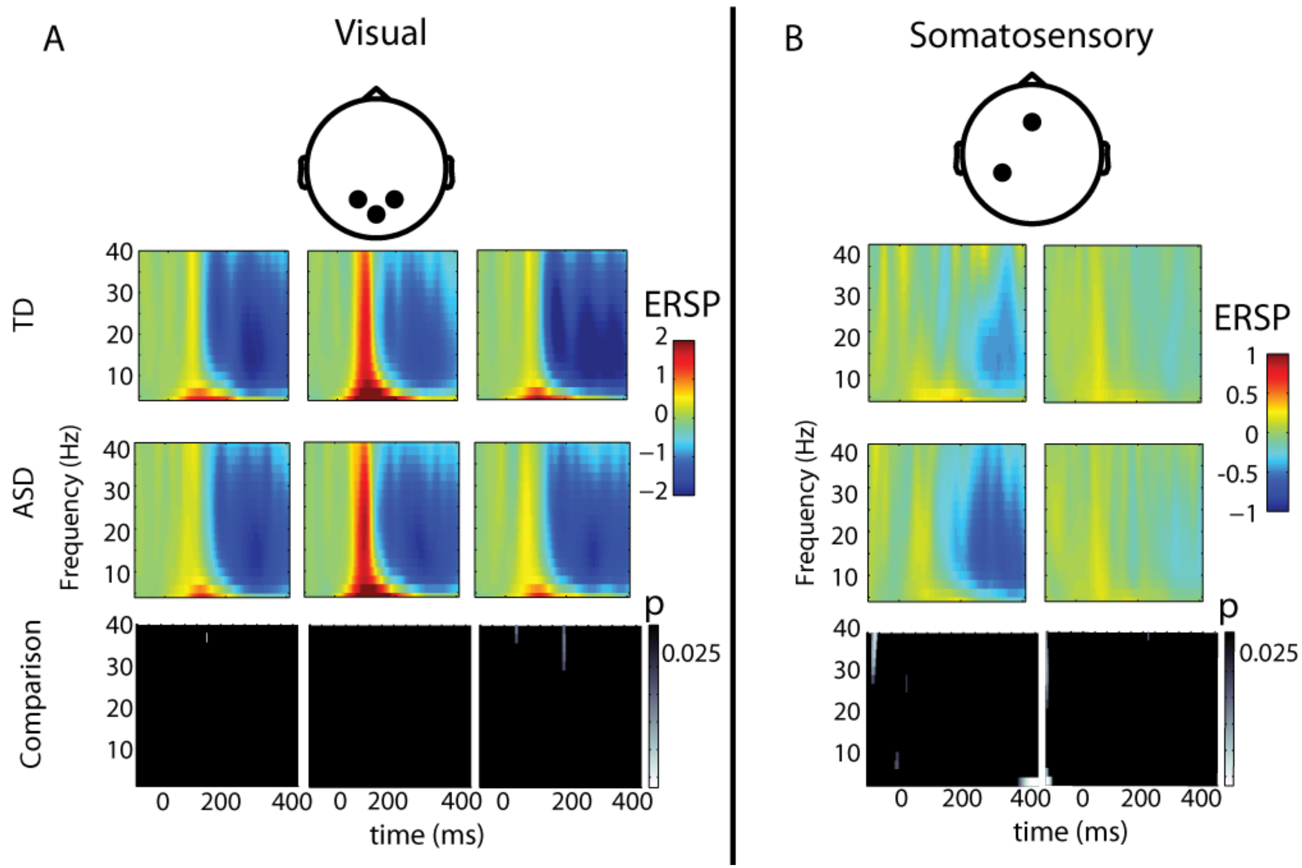


Bootstrapped Statistics

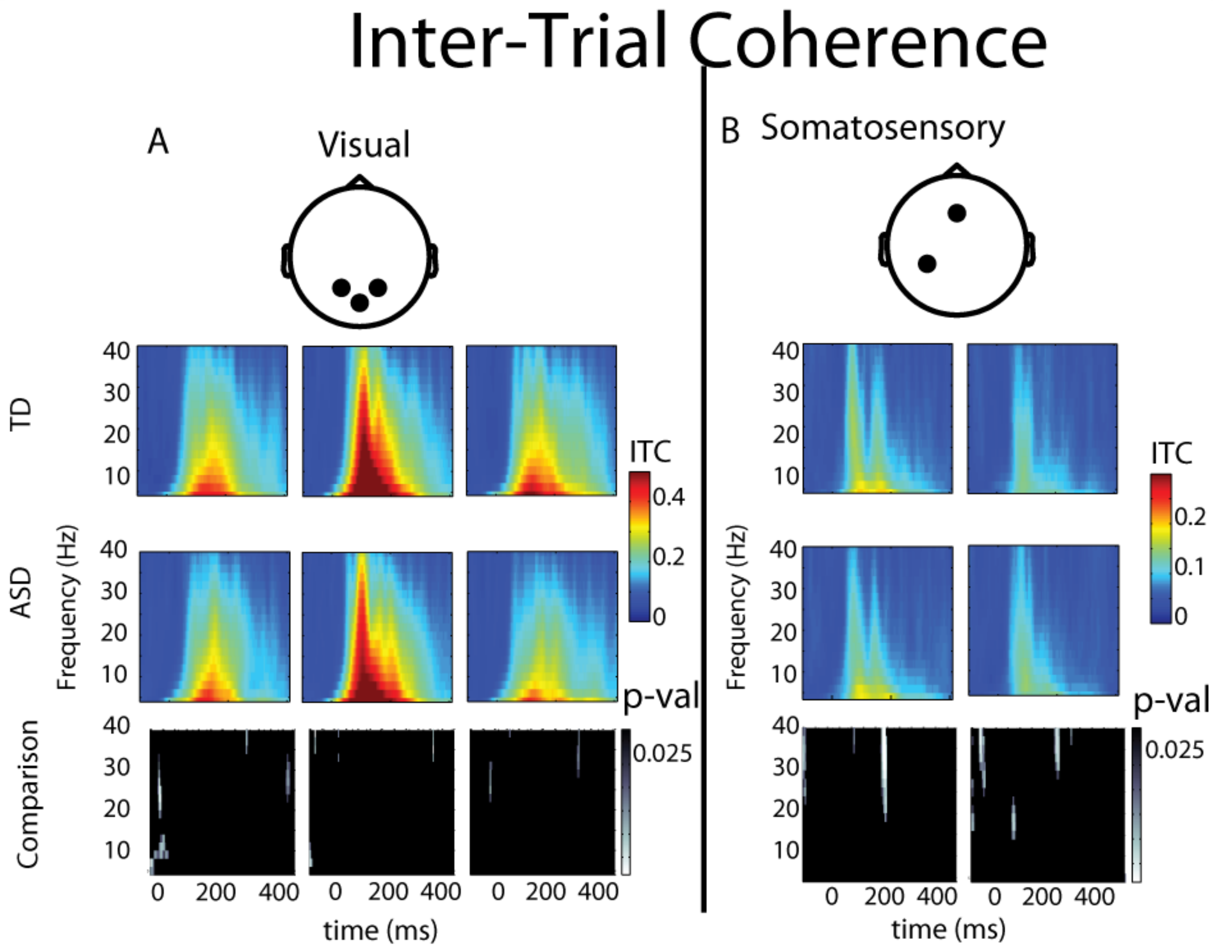


Power (Amplitude)

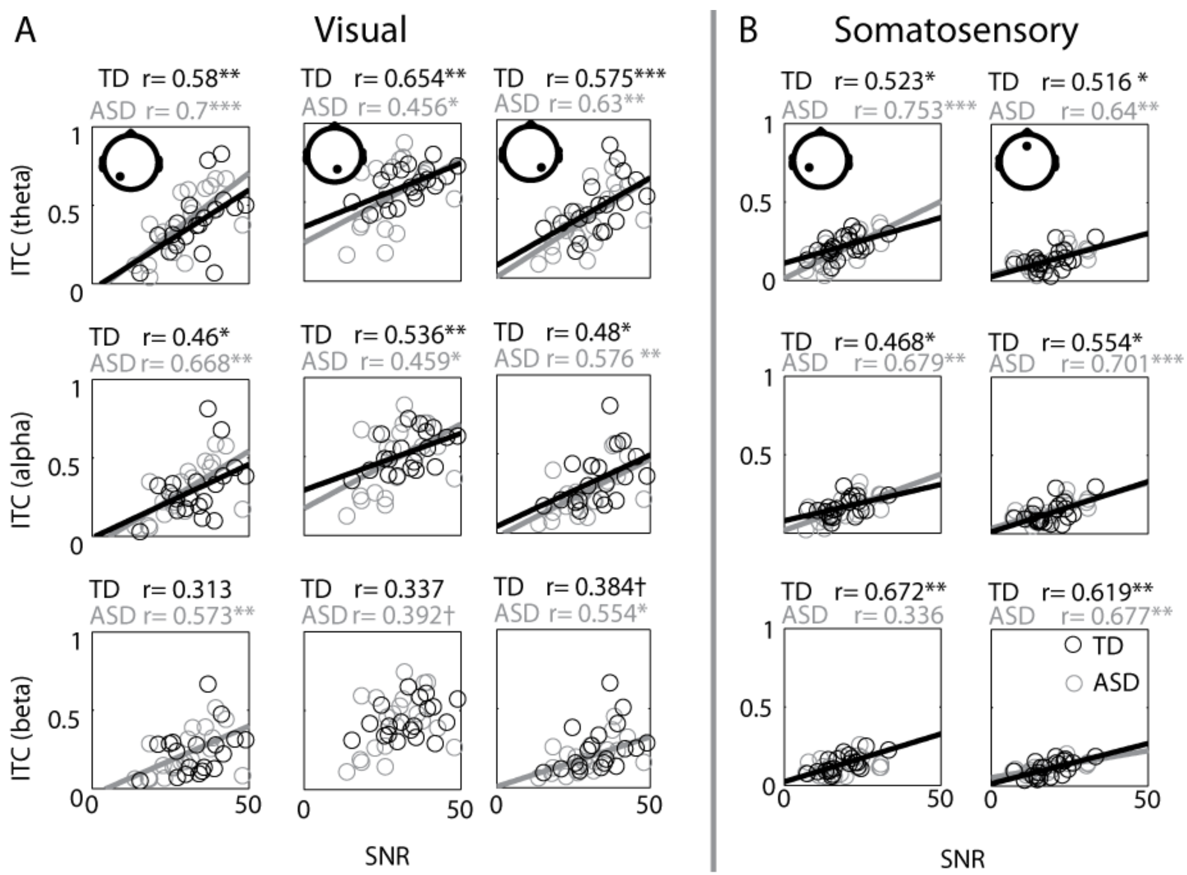
Event-related spectral perturbations



Alignment (Phase)



Single trial vs Averages



Bayesian Statistics

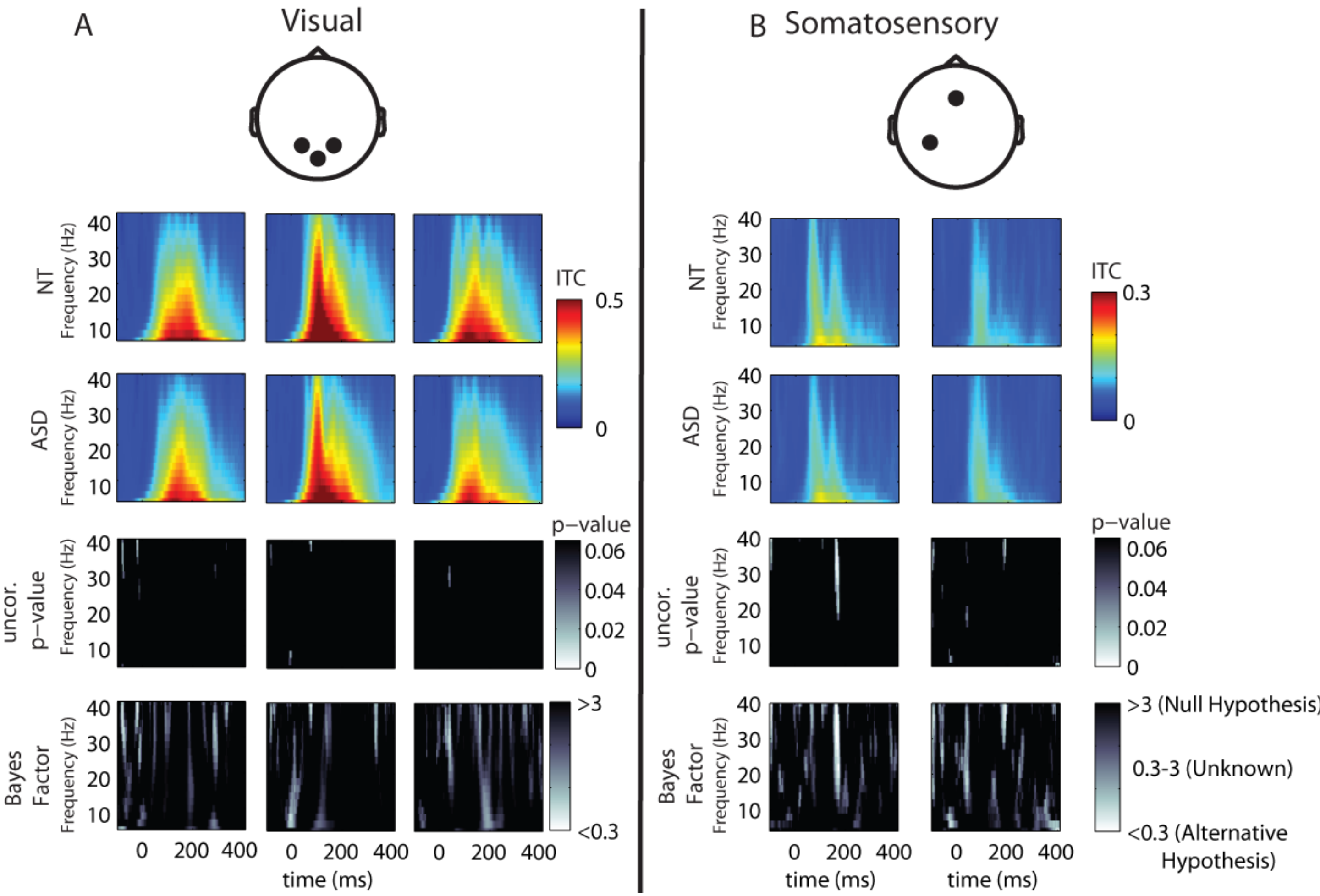
- Classical statistical test give evidence of an alternative hypothesis
- Bayesian Factor Analysis allows for the continuum of hypotheses, from the alternative to the null
- Jefferys, Zellner and Siow (JZS) Bayes Factor which uses the classical t-statistic to calculate a ratio of the null versus the alternative.

Table 1
Critical *t* Values

	JZS Bayes Factor Value			
	Favors Null		Favors Alternative	
N	10	3	1/3	1/10
5	–	0.40	3.15	4.97
10	–	0.89	2.73	3.60
20	–	1.20	2.64	3.26
50	–	1.51	2.68	3.17
100	0.69	1.72	2.76	3.20
200	1.08	1.90	2.86	3.27
500	1.44	2.12	2.99	3.38

Rouder, Speckman, Sun, Morey, and Iverson (2009)

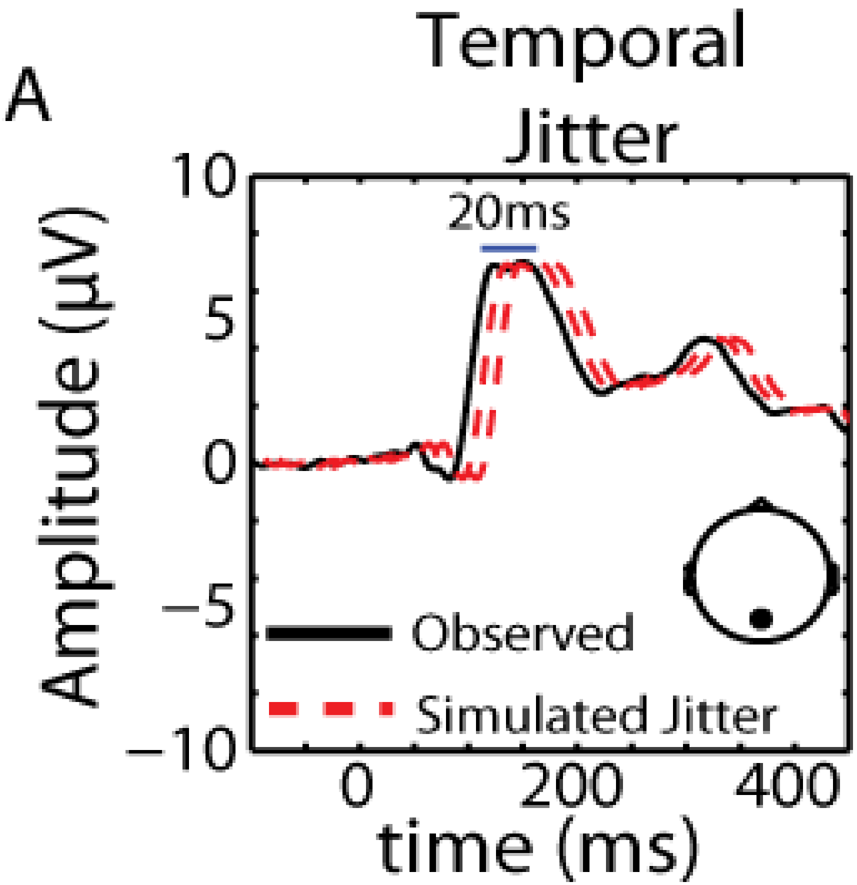
Bayes Factor



Overview Results

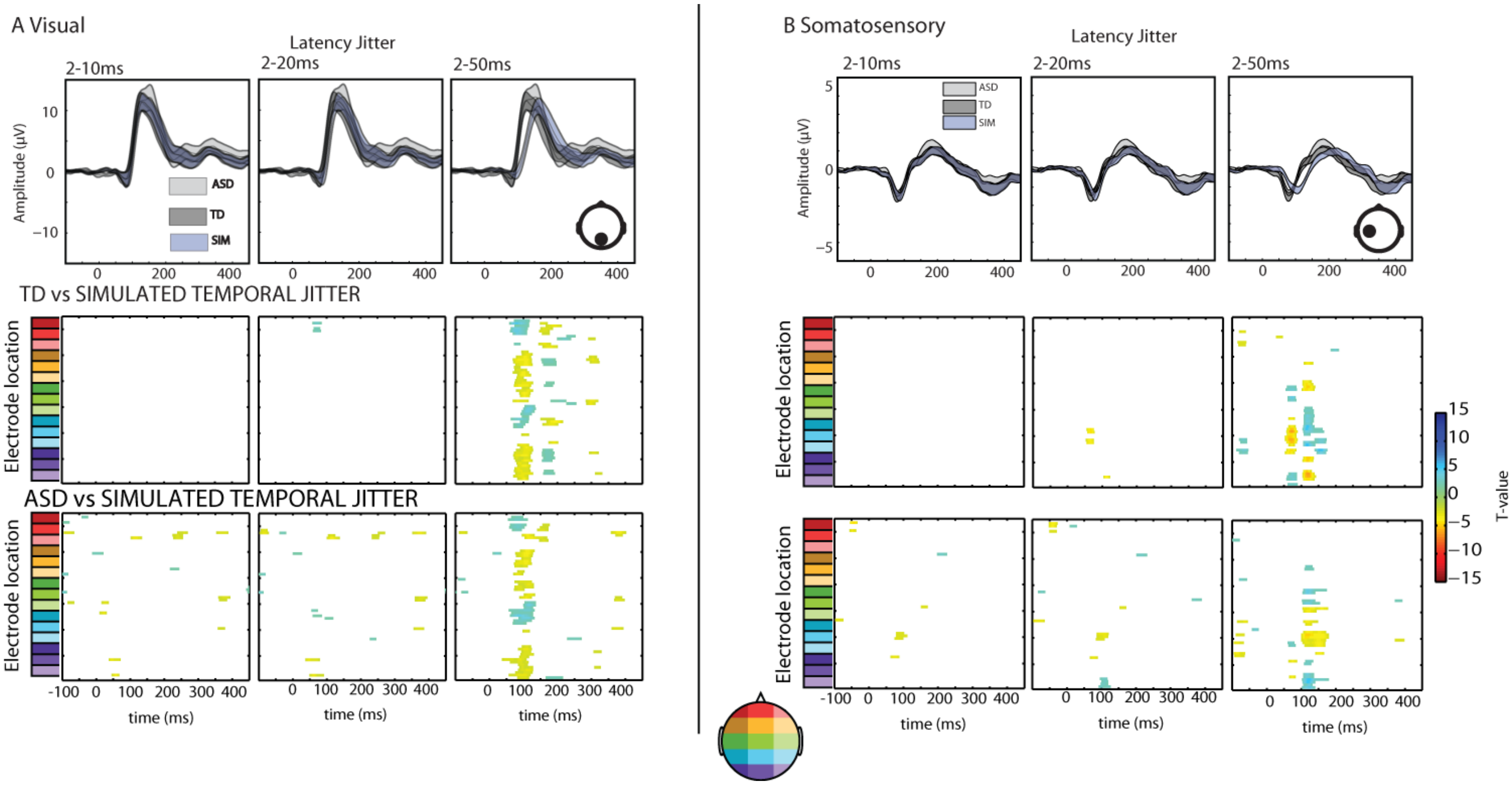
- Not statistically different average evoked response
- Not statistically different single trial data
- Highly similar correlation of average evoked response
- Are our metrics sensitive enough; what would an unreliable evoked response look like

Simulation



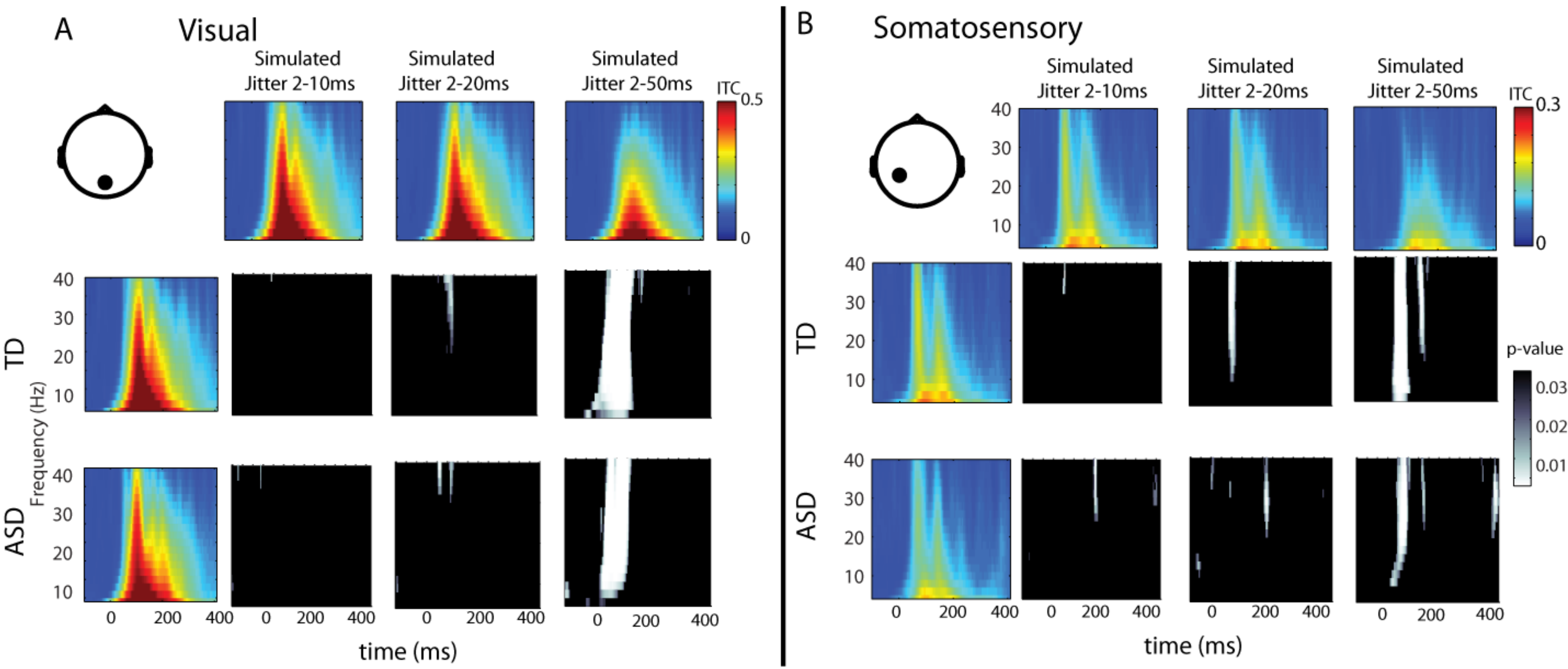
- Temporal Jitter
- Simulation
  - 0-10ms
  - 0-20ms
  - 0-50ms

Temporal Jitter Simulation



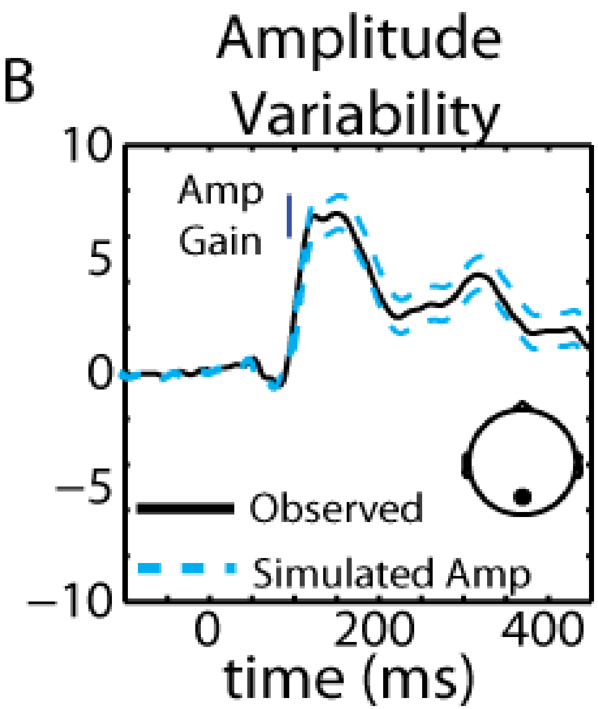
Temporal Jitter Simulation

Inter-Trial Coherence

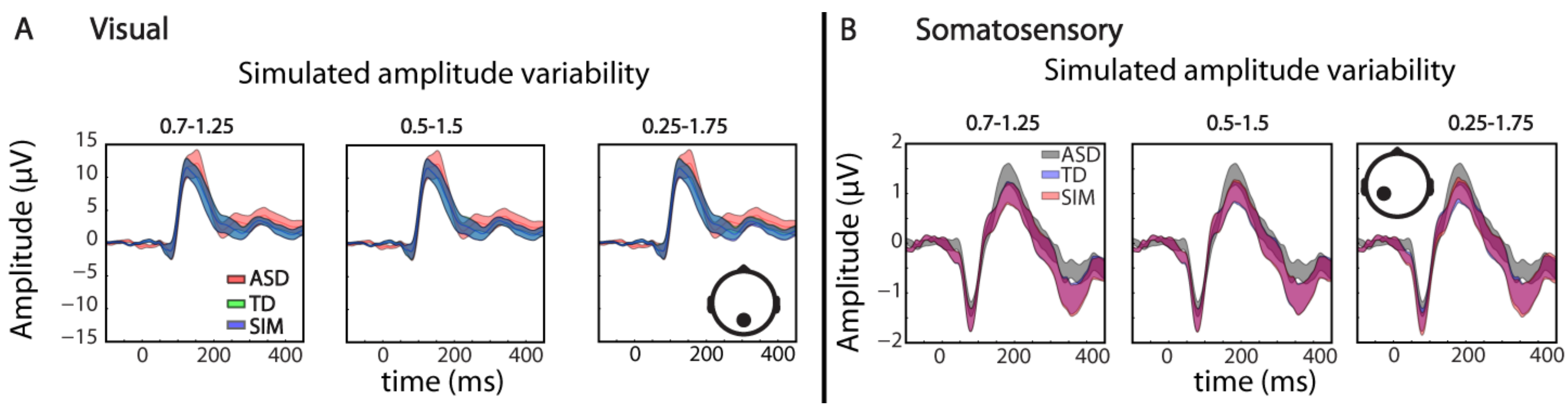


Amplitude Jitter Simulation

- Amplitude Jitter
- Range
  - 0.75-1.25
  - 0.5-1.5
  - 0.25-1.75

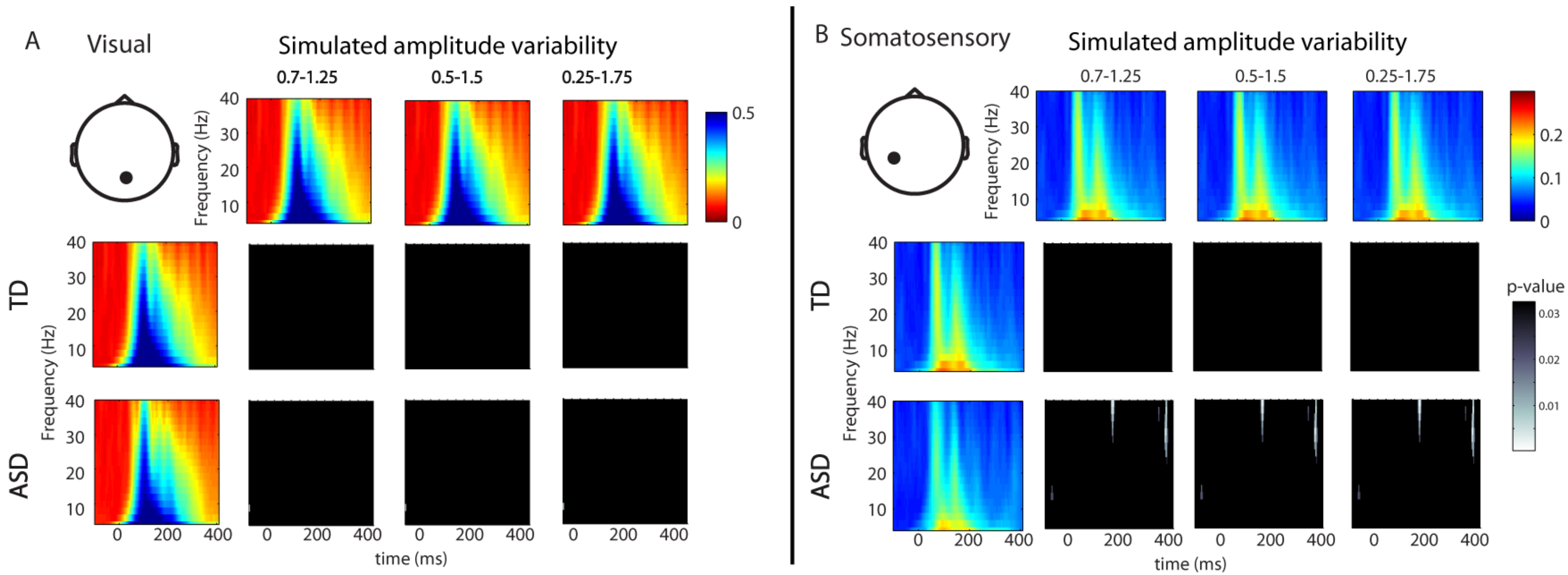


Amplitude Jitter Simulation



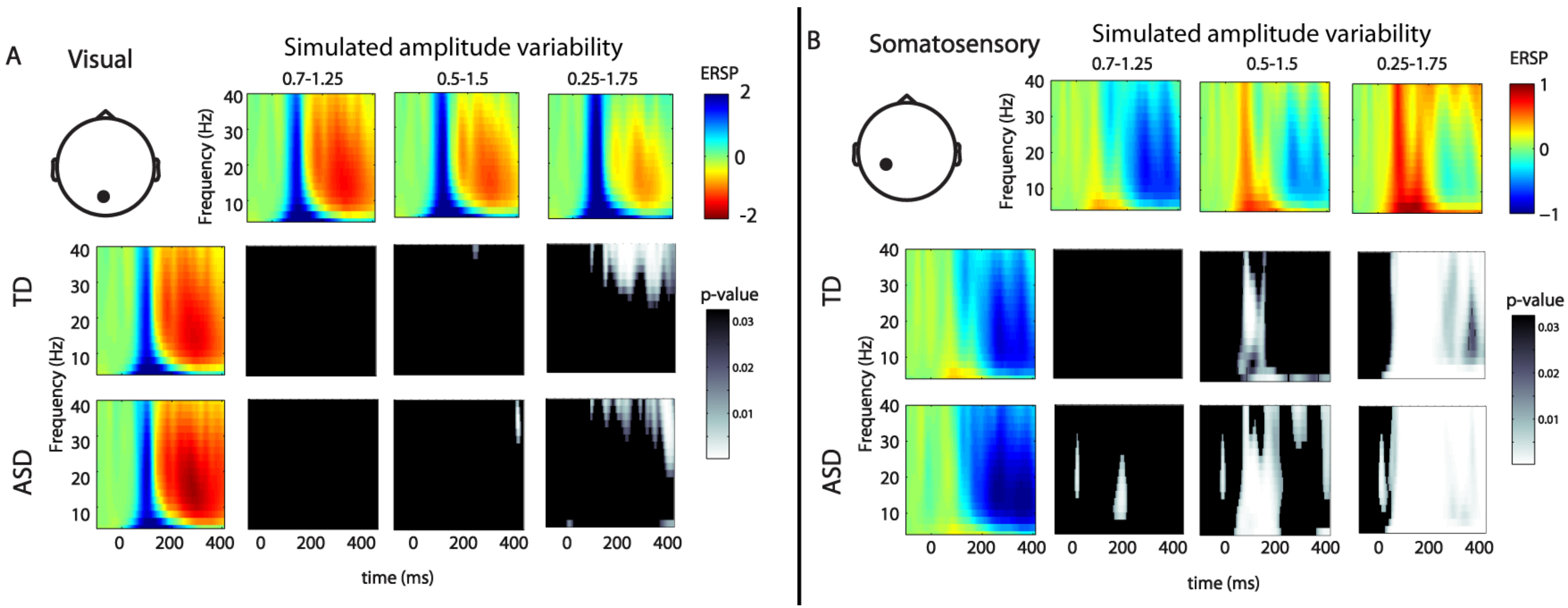
Amplitude Jitter Simulation

ITC



Amplitude Jitter Simulation

ERSP



Simulations Overview

- The simulations shows the sensitivity of the measures to single trial variability
- These differences were not exhibited in the group comparison

What are the considerations

- The significance of significance
- The importance of attention (task)
- The role of connectivity
- Mismatching groups
- Diagnosis as a continuous variable

The significance of significance

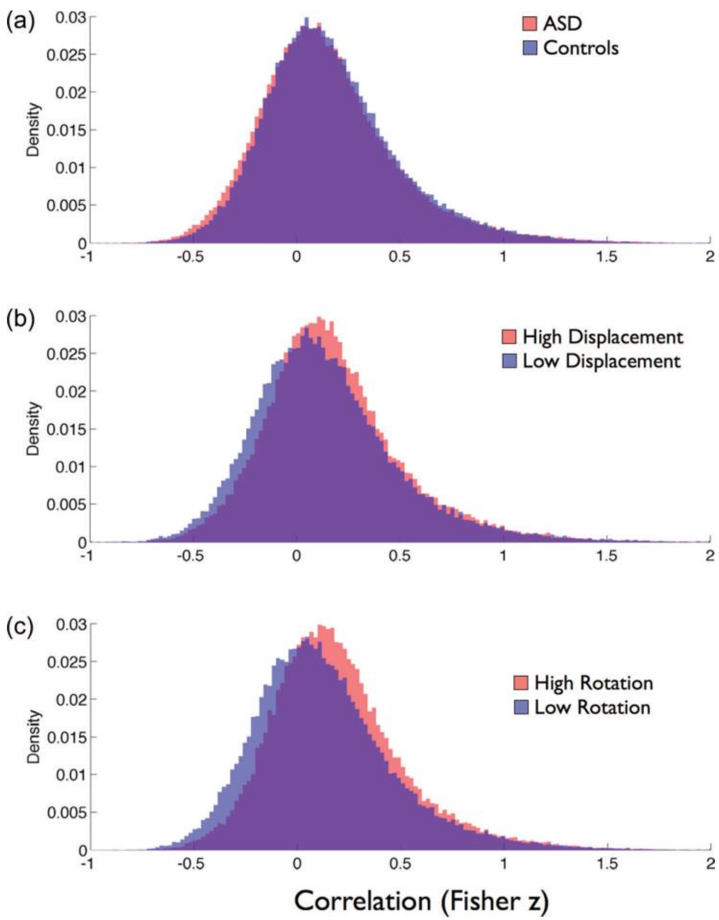
Largely Typical Patterns of Resting-State Functional Connectivity in High-Functioning Adults with Autism

J. Michael Tyszka[1], Daniel P. Kennedy[2,3], Lynn K. Paul[2] and Ralph Adolphs[1,2]

[1]Division of Biology and [2]Division of Humanities and Social Sciences, California Institute of Technology, Pasadena, CA, USA and [3]Department of Psychological and Brain Sciences, Indiana University, Bloomington, IN, USA

- Difference between the ASD and Controls

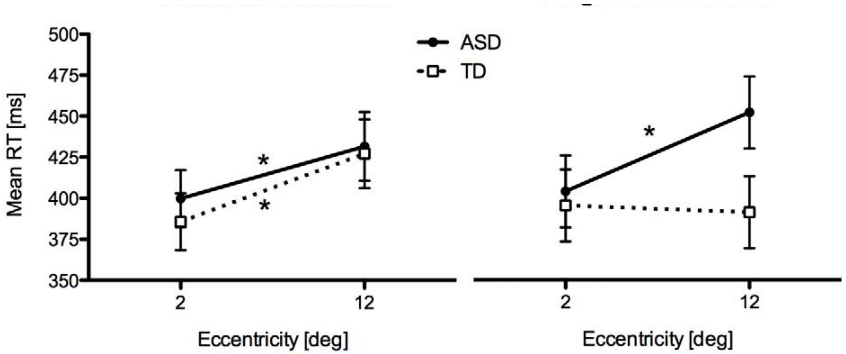
- Larger differences between movers and non-movers independent of diagnosis



Tyszka, (2013). Cereb Cortex.

The importance of attention (task)

Decreased Coherent Motion Discrimination in Autism Spectrum Disorder: The Role of Attentional Zoom-Out Deficit



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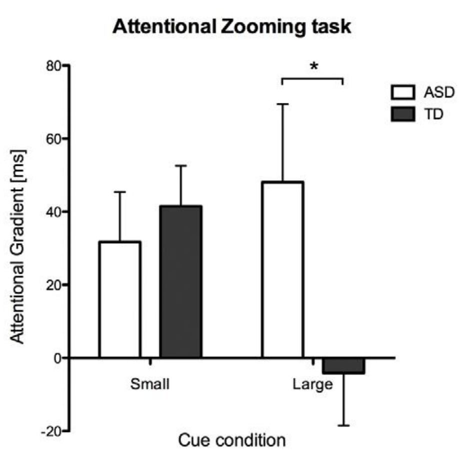
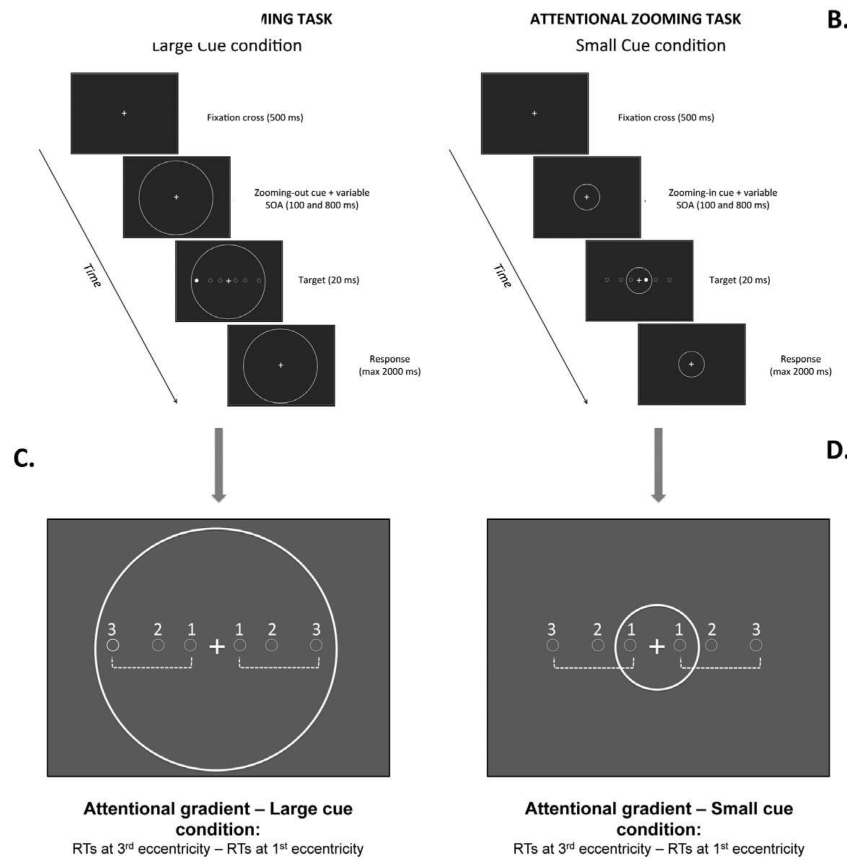
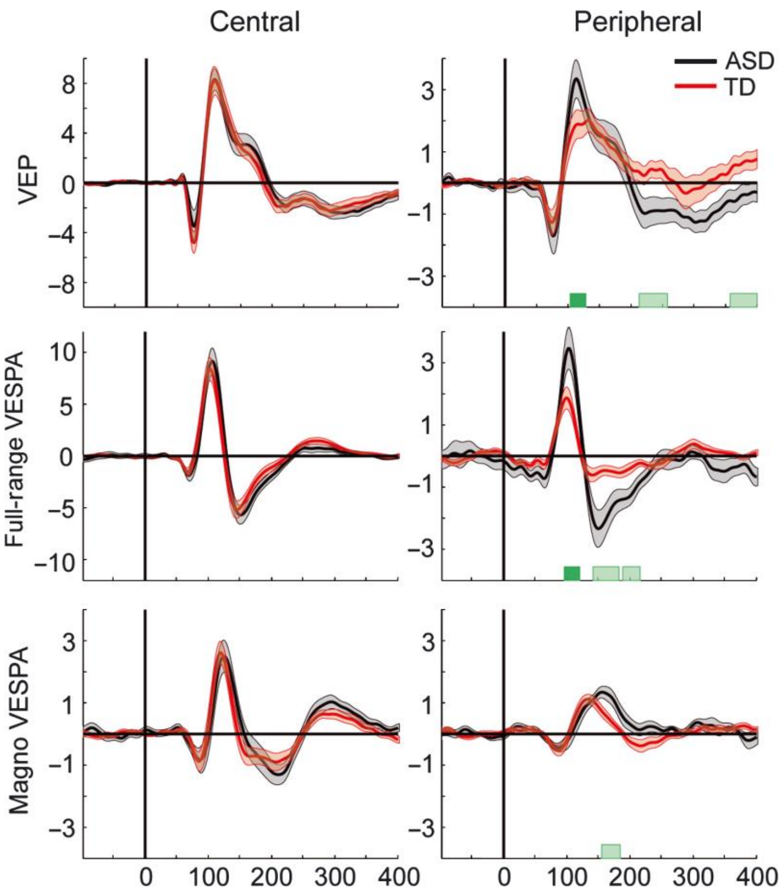




Ronconi et al. 2012, PloS One

The role of connectivity

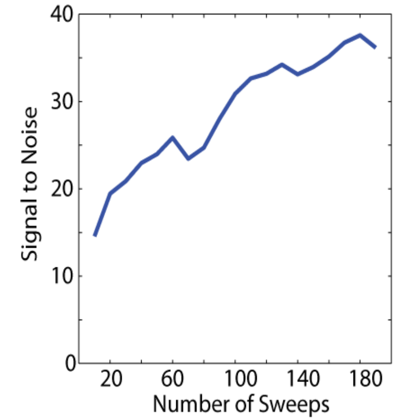
- Imbalance in connectivity
  - Larger local response
  - Smaller global response

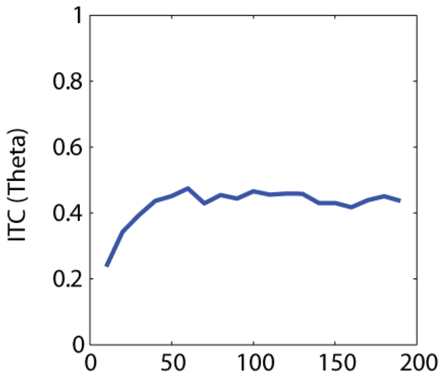


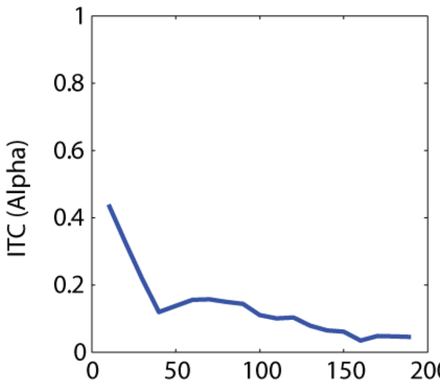
Frey et al. 2013 EJN

Mismatching groups

- Gender match
- IQ match
- Number of trials match
- Number of participants

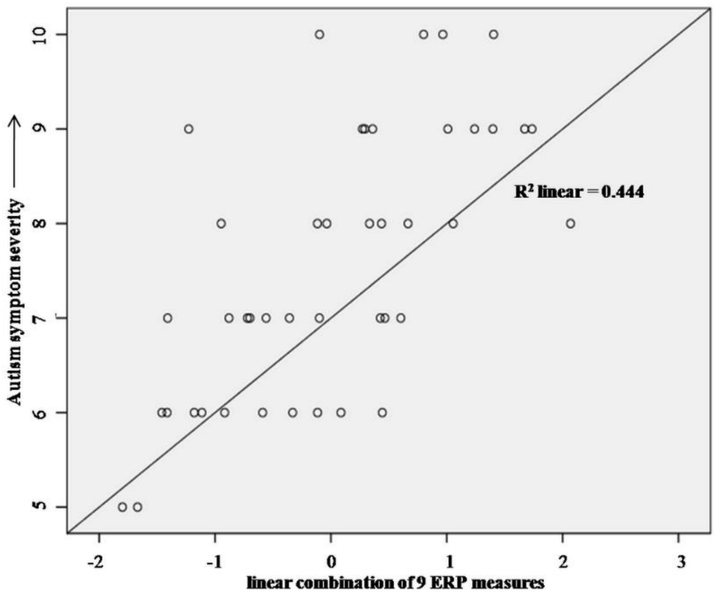


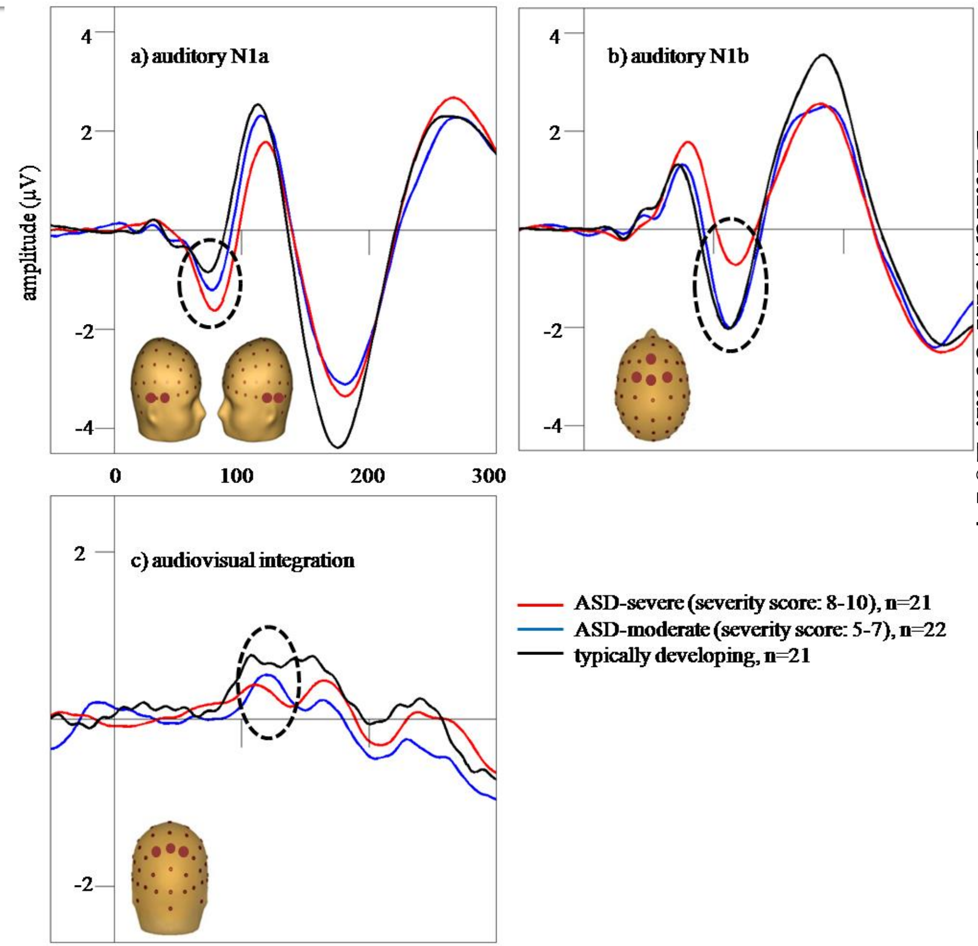




Diagnosis as a continuous variable

- Severity of diagnosis



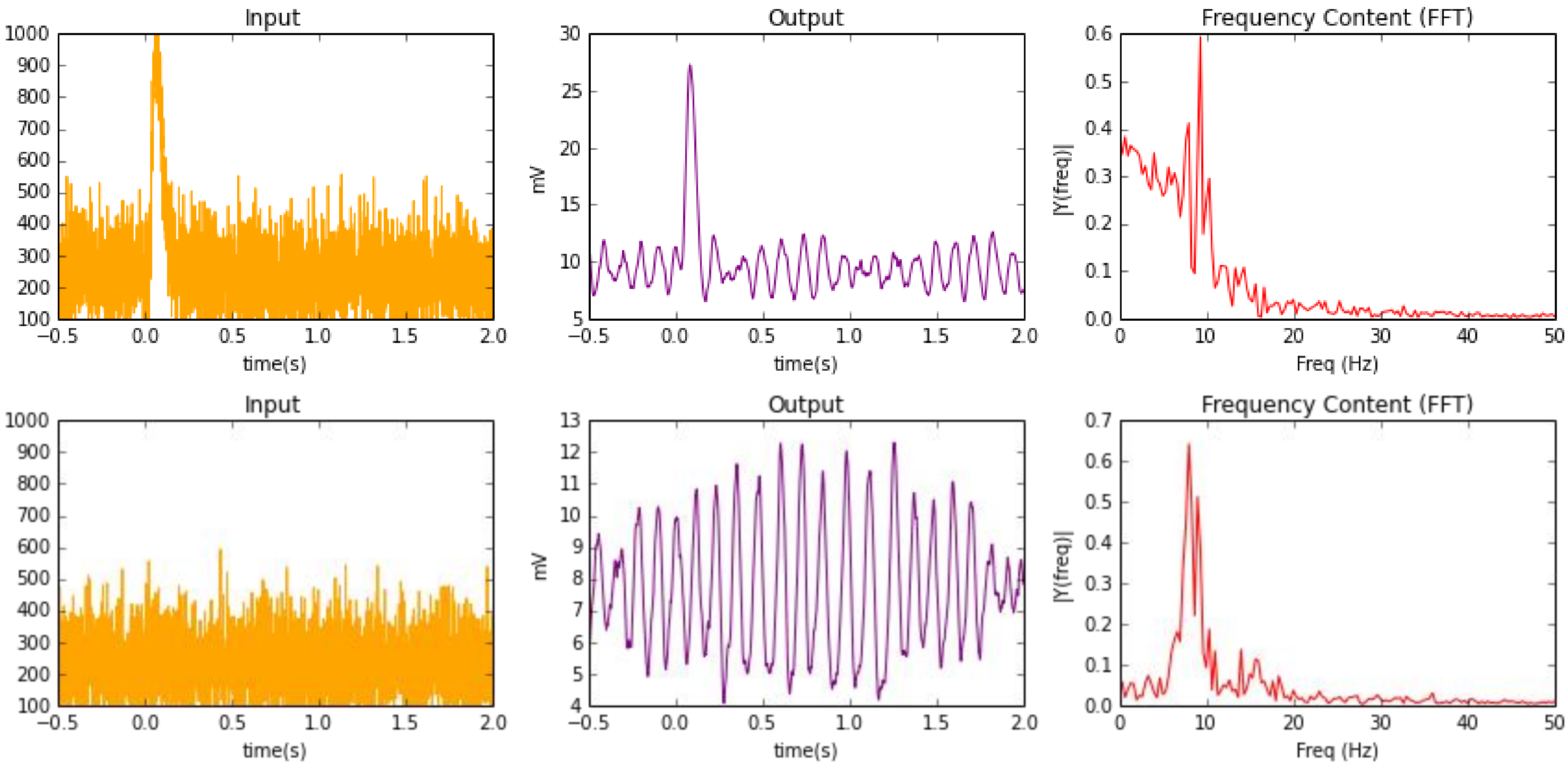


Brandwein et al. 2014

Conclusions

- ASD and TD groups exhibited similar evoked response
- While the unreliability thesis might hold for unique situations it does not hold for all
- ASD is a more subtle and complex disorder
- Null results are important to understand when something breaks down

Future Directions



https://somsdit.ie:8000/user/jbutler/notebooks/Neural%20Mass%20Model/Neural%20Mass%20Model%20Double%20Column-RK4.ipynb

Any questions

Sophie Molholm
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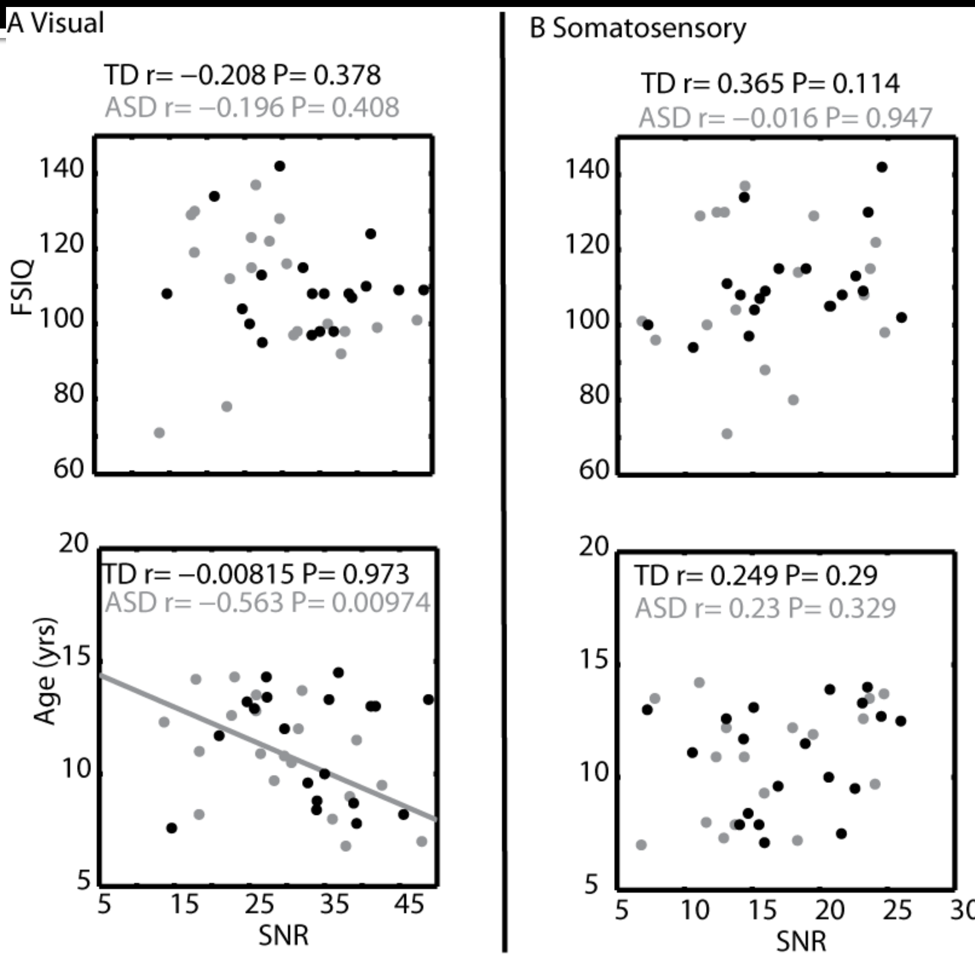
Authors	Journal	Year	Stimuli	Clinical	Controls	Age (yrs)	Difference
(Bertone, Mottron et al. 2003)	J Cogn. Neuroscience	2003	Visual motion	20	20	mean 13.3 and 12.18	Similar first order, reduced second order motion discrimination
(Bertone, Mottron et al. 2005)	Brain	2005	Visual orientation	13	13	mean 22.3 and 20.5	Improved first order, reduced second order orientation
(Pellicano, Gibson et al. 2005)	Neuropsychologia	2005	Visual motion	20	20	8 to 12	Higher coherence thresholds no flicker difference
(Blakemore, Tavassoli et al. 2006)	Brain and Cognition	2006	Tactile detection	10	9	18 to 45	Similar for 30Hz stimuli different for 200Hz
(Milne and Scope 2008)	Brit J Dev Psychol	2008	Contour illusions	18	20 (TD) 16 (SpNeeds)	7 to 13	Similar across groups
(Cascio, McGlone et al. 2008)	J Autism Dev Disord	2008	Tactile detection	8	8	20 to 45	Some enhanced perception on the forearm
(Cook, Saygin et al. 2009)	Neuropsychologia	2009	Biological motion	16	16	34.4	ASD group were worse at detecting biological motion
(Tavassoli, Latham et al. 2011)	Vision Res	2011	Visual acuity	20	20	30.4	Similar visual acuity
(Milne, Scope et al. 2012)	J Autism Dev Disord	2012	Visual detection	11	21	10 to 17	Imbalance in Nasal and temporal hemifield sensitvity
(Robertson, Kravitz et al. 2013)	Journal of Neuroscience	2013	Visual	20	20	19 to 50	Sharper Spatial attention
(Ronconi, Gori et al. 2012)	Cortex	2012a	Attentional Zoom	11	12	9-18 ASD 11-18 TD	ASD performance was worse for the large attenational cue condition
(Ronconi, Gori et al. 2012)	Plos One	2012b	Coherent Motion	11	11	9-18 ASD 11-18 TD	Central different, peripheral Same

Authors	Journal	Year	Stimuli	Clinical	Controls	Age (yrs)	Early sensory
(Milne 2011)	Frontiers in Psychology	2011	Gabor Grating 8 cycles	13	12	8 to 15.4	X
(Milne, Scope et al. 2009)	Biol Psychiatry	2009	Gabor Grating (0.5, 1, 4, 8), Zebra	20	20	ASD 12.2 TD 13.5	~
(Jemel, Mimeault et al. 2010)	JoV	2010	Gratings	16	14	18-33	~
(Magnee, de Gelder et al. 2011)	Plos One	2011	Stimuli on faces	23	24	22.7	X
(Constable, Gaigg et al. 2012)	Doc Ophthalmol	2012	Motion and pattern	9	7	ASD 36.6 TD 48.9	~
(McPartland, Crowley et al. 2012)	J. Neurodevelompental Disorders	2012	Ballons	26	28	TD 10-13.5 ASD 7.7-15.0	X
(Fiebelkorn, Foxe et al. 2012)	Cortex	2012	Dogs, Cars, Guitars	17	21	8 to 13yrs	X
(Frey, Molholm et al. 2013)	Euro. J. Neuroscience	2013	VEP, VESPA	22	29	7 to 17 yrs	~
(Brandwein, Foxe et al. 2012)	Ceberal Cortex	2012	Audio Visual Response task	72	46	7 to 10 11 to 16	~
(Russo, Foxe et al. 2010)	Autism Research	2010	Somatosensory Auditory	17	17	6 to 16	~



A Visual
B Somatosensory
TD r= −0.208 P= 0.378
ASD r= −0.196 P= 0.408
TD r= 0.365 P= 0.114
ASD r= −0.016 P= 0.947
FSIQ
140
120
100
80
60
20
15
10
5
Age (yrs)
TD r= −0.00815 P= 0.973
ASD r= −0.563 P= 0.00974
TD r= 0.249 P= 0.29
ASD r= 0.23 P= 0.329
5 15 25 35 45
5 10 15 20 25 30
SNR
SNR