Point-of-Care Devices for Neurologic Emergencies

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UNIVERSITY OF Cincinnati

How did I get here?

- Why I studied Electrical Engineering:
  - Computers are “cool” (circa 1980 slang for hot new technology). Computers use Electricity → Electrical Engineers must know how to make computers → I will study Electrical Engineering
- Undergraduate Senior Design (CSU):
  - In mid 1980’s when I started my undergraduate studies CompE degree didn’t exist at many schools including CSU
  - Senior Project: Passivation of III-V semiconductors
- MS in EE completed in 1992 (still no CompE Degree):
  - Supported by NSF ERC focused on Optical Computing
  - MS Thesis: Optical NOR Gate Based on a Light Amplifying Optical Switch
- PhD in EE completed in 1995 (still no CompE Degree):
  - Dissertation: Design and Analysis of an Optoelectronic Recirculating Sorter

How did I get here?

- Post Doctoral Research (1995-1996 in Sheffield UK)
  - Optical Switching using a Piezoelectric Self Electro-optic Effect Device (P-SEED)
- UC – Early Years (1996 – 2003)
  - Photonic VLSI devices → *Photonics Systems Research*
  - Data Integrated Video Capture
- UC – Shift to Medical Devices (2003 – 2012)
  - Bilibox – Detection of Subarachnoid Hemorrhage → *Xanthostat*
  - B-KIN – Robotic Assisted Diagnosis of mTBI → *POC-CENT*
- UC – Current Research (2012 – Present)
  - Embedded Systems for Medical Diagnosis and Health Status Monitoring
  - Mobile EEG, Smart Inhaler, Smart Patch

Engineering Skills are far more important than Engineering Topics

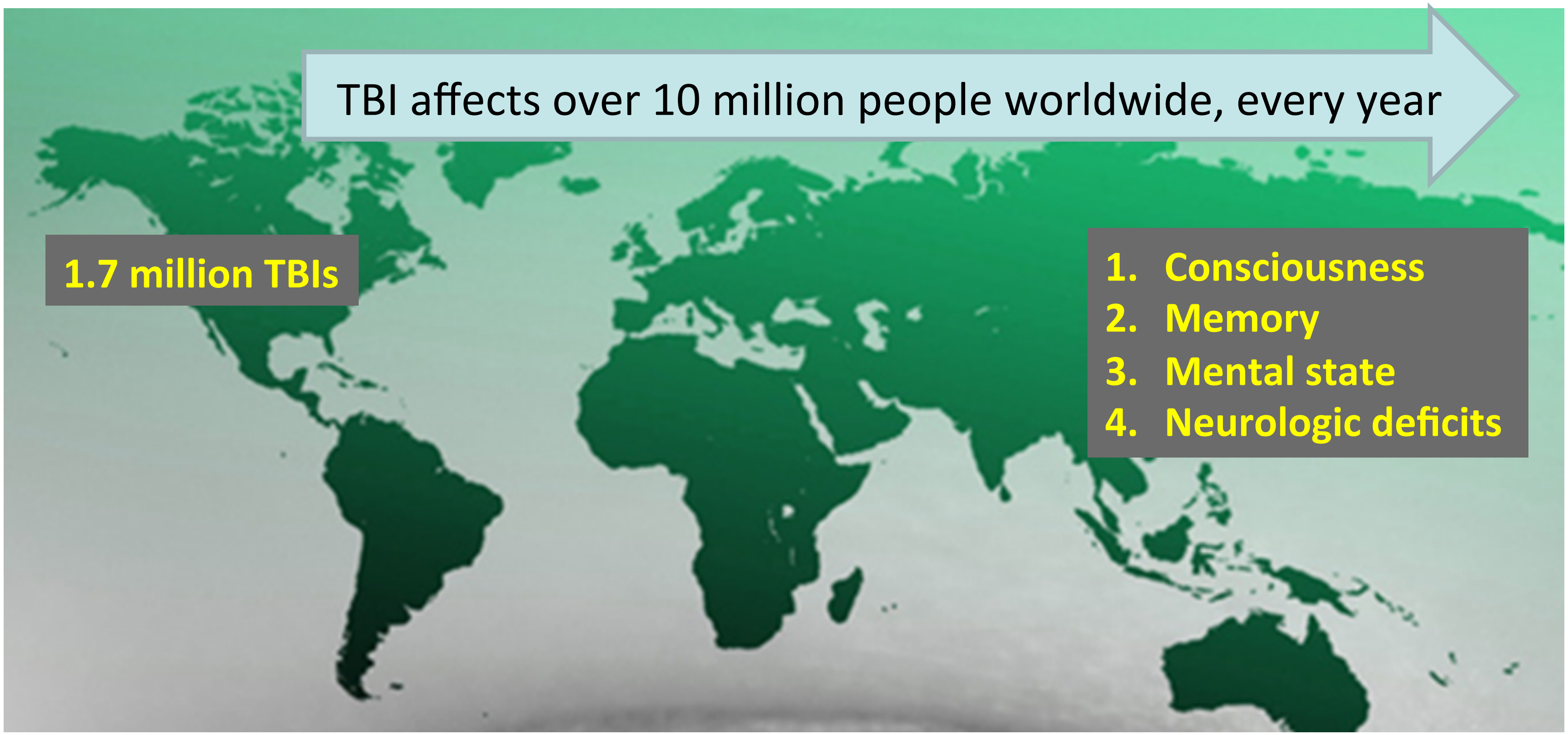
My Research Focus

My research group is focused on the development of Point-of-Care diagnostic and cutting edge health status monitoring devices that meet unmet needs for critical diagnostic and health monitoring information.

- There is a particular interest in developing technologies that can be introduced at the earliest possible point in the diagnostic paradigm (i.e. at the accident scene, in the Emergency Department or on the playing field).
- Current focus is on new and emerging technologies that address diagnostic needs for concussion/mild TBI
  - Robotic assisted assessment of injury severity.
  - Devices for quantifying changes in event related potentials (ERPs) immediately following injury.
- Emerging focus on wearable technologies that enhance understanding of our physiologic status.

Traumatic Brain Injury (TBI) – A global health problem

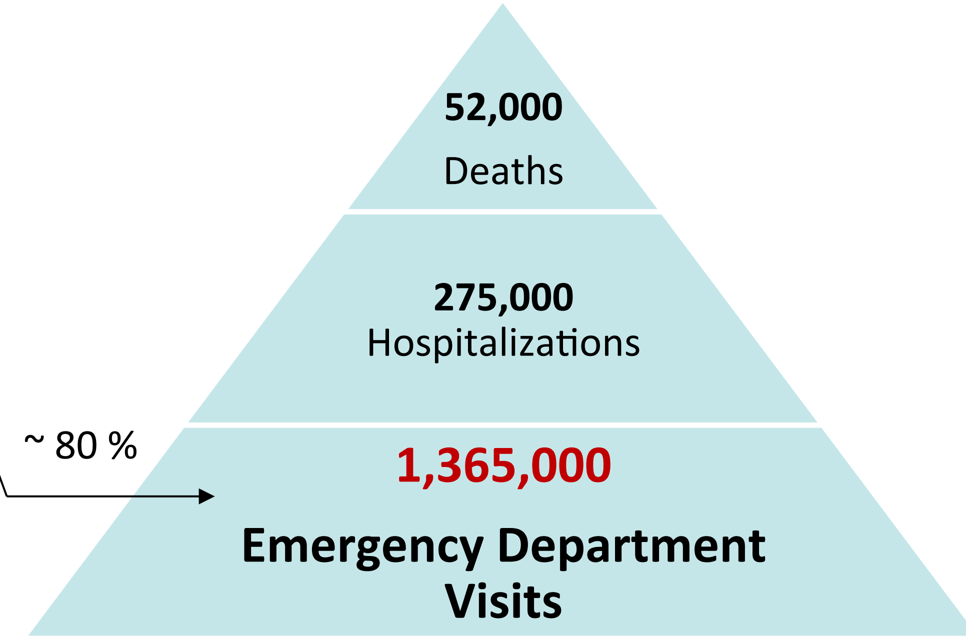
TBI is defined as an *alteration in brain function*, or other evidence of brain pathology, caused by an external force



A. A. Hyder, C. A. Wunderlich, P. Puvanachandra, G. Gururaj and O. C. Kobusingye, "The impact of traumatic brain injuries: a global perspective," *NeuroRehabilitation,* vol. 22, pp. 341-353, 2007.

Background

An estimated **1.7 million TBIs** occur in the US annually



Glasgow Coma Scale (GCS)

13-15	Mild
9-12	Moderate
3-8	Severe

The vast majority of all treated TBI cases (70 – 90%) are **mild**

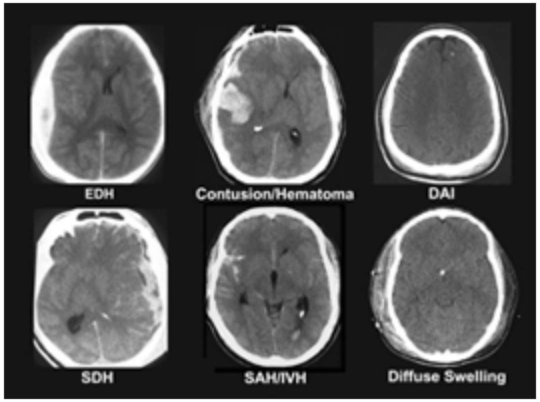
Traumatic brain injury in the United States: emergency department visits, hospitalizations, and deaths, 2002-2006. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Injury Prevention and Control, 2010.

Post-Concussion Syndrome (PCS)

- PCS: Constellation of emotional, physical, and psychological complaints
- **Rivermead** Post Concussion Symptoms Questionnaire
  - Presence of **3 or more symptoms**
- **50% of all mild TBI patients have PCS at 1 month**
- Up to 1/3rd of all mild TBI patients are functionally impaired at three months

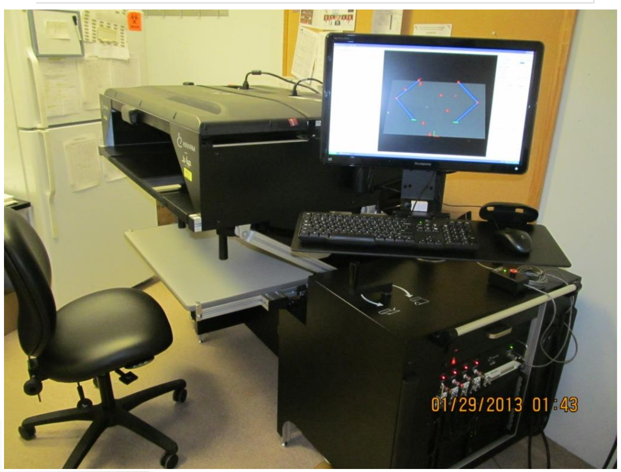
Study Rationale

The **need** for an objective test that can predict the likelihood of PCS at the initial point of care (ED)



McMahon PJ, Hricik A, Yue JK, et al. Symptomatology and functional outcome in mild traumatic brain injury: Results from the prospective TRACK-TBI study. *J Neurotrauma*. 2014;31(1):26-33. www.liebertpub.com/neu

Robotic Assessment of Neurologic Injury



- The robotic system developed by B-KIN Technologies was originally developed to study Neuromotor function.
- The system uses a large screen monitor to present “game-like” tasks to the subject.
- The sensitive position sensors in the robotic units allow for accurate assessment of subject response to both the visual stimuli and the position actuation of the robotic arms
- The technology can be used for both diagnosis and rehabilitation monitoring

✓ **Fully integrated into the ED clinical research workflow**

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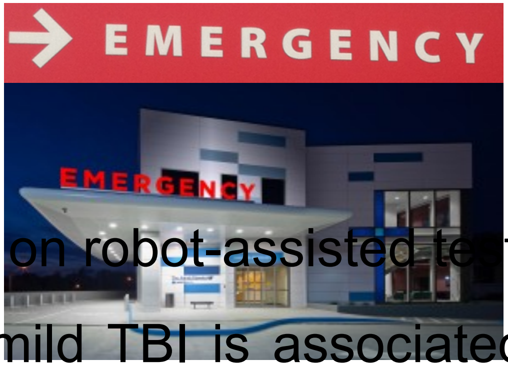
Research Goal: To assess the prognosticative value of robot-assisted neurologic testing in mild TBI patients

Study Design

Within 24-hours of **mild TBI**

head Injury



Eligible Patients

Informed Consent

Robot-assisted Testing

At 3 weeks

Assessment of **PCS** using Rivermead*

Hypothesis:

Performance on robot-assisted testing within 24-hours of mild TBI is associated with the prevalence of PCS, 3 weeks post injury.

UC IRB Approval #2012-3537 (Expires on Nov. 24, 2014)

RPQ = Rivermead Post Concussion Symptoms Questionnaire

University of Cincinnati

Image Source: Mercy Health, Cincinnati

Patient Inclusion/Exclusion Criteria

Inclusion Criteria:

1. Age: 18 years or greater
2. Diagnosis of mild TBI by the treating physician (within 24 hours of injury)
3. Blood Alcohol Level (BAL) of < 100 mg/dl

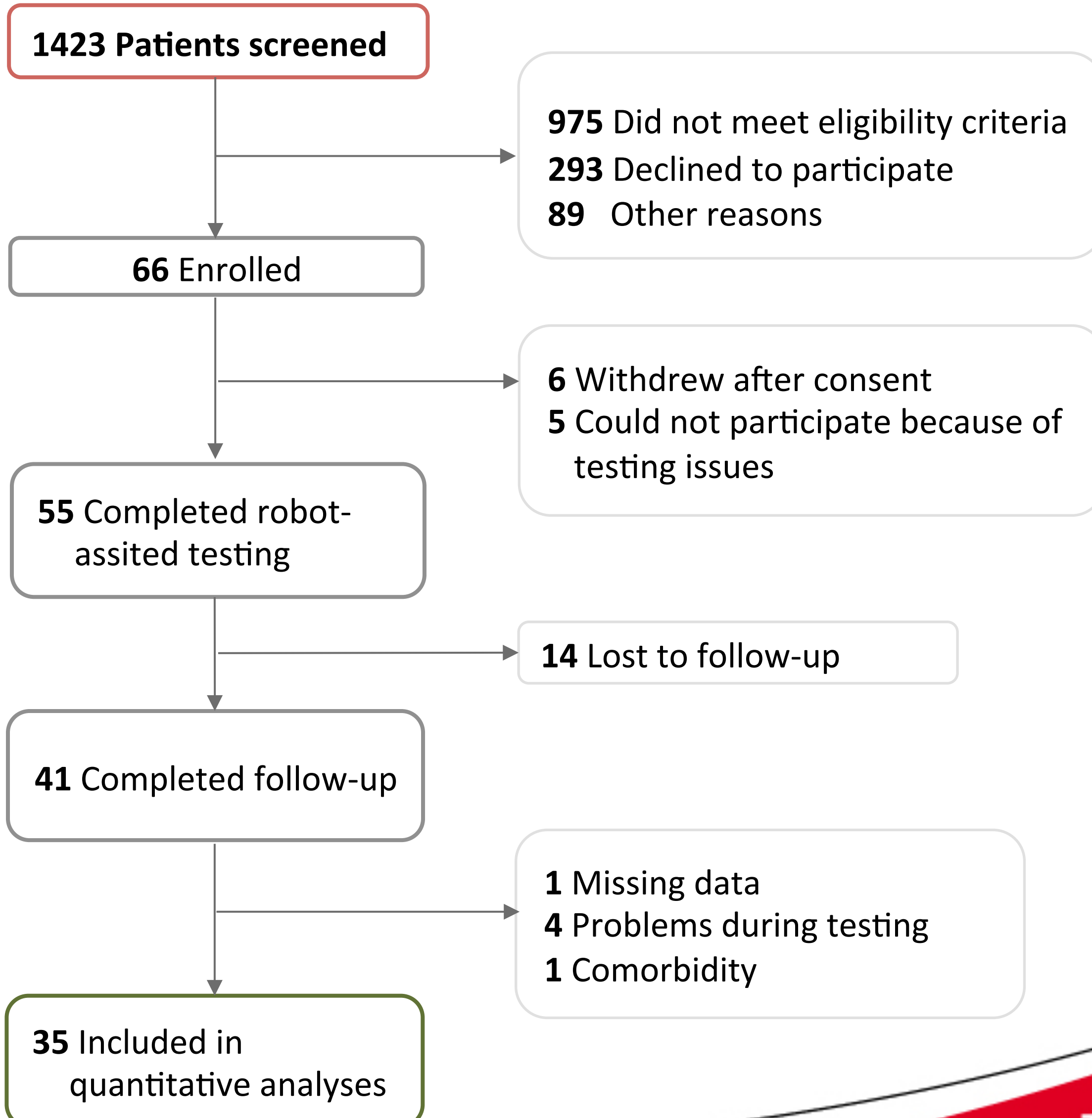
Exclusion Criteria:

1. Presence of focal neurologic deficit on standard neurological exam
2. Presence of co-morbidities that would affect test performance.
3. Vulnerable population

Study Participants

Enrollment Period:

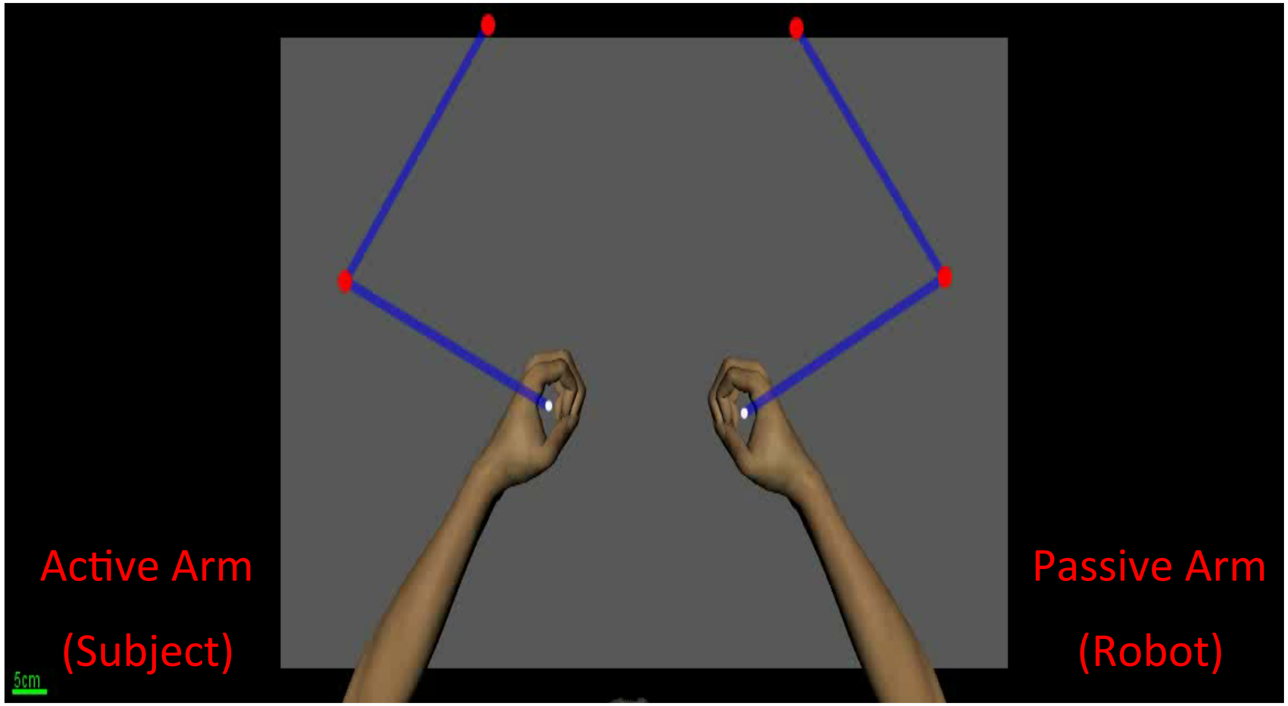
March 2013 to April 2014

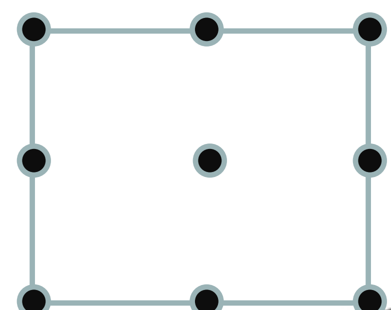


Neurologic Test Battery

Test	Primary Measurement
Arm-Position Matching	Proprioception
Visually-guided Reaching	Visual Reaction time
Trail-making	Visual search, cognition
Object-hit	Inter-limb coordination
Object hit & Avoid	Attention, rapid motor selection

Robot-Assisted Test of Proprioception



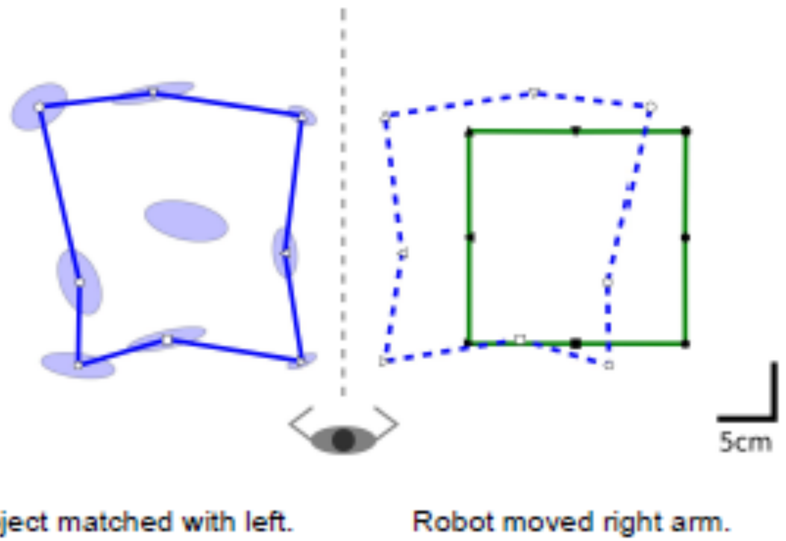


Proprioception: The awareness of position, orientation, and movement of one's body and its parts)

S. P. Dukelow, T. M. Herter, K. D. Moore, M. J. Demers, J. I. Glasgow, S. D. Bagg, K. E. Norman and S. H. Scott, "Quantitative assessment of limb position sense following stroke," *Neurorehabil. Neural Repair,* vol. 24, pp. 178-187, 2010.

Measures of Proprioception

- ✓ **Variability**: trial-to-trial consistency of the active hand.
- ✓ **Spatial Shift**: constant errors between the active and passive hands
- ✓ **Contraction/expansion ratio**: the area of the workspace matched by the active hand relative to that of the passive hand



S. P. Dukelow, T. M. Herter, K. D. Moore, M. J. Demers, J. I. Glasgow, S. D. Bagg, K. E. Norman and S. H. Scott, "Quantitative assessment of limb position sense following stroke," *Neurorehabil. Neural Repair,* vol. 24, pp. 178-187, 2010.

Quantitative Assessment of Proprioception

37 year old, Female, Struck on the head:

Parameters	Left	Right	Typical range		Unit
			Left	Right	
Variability X [1,3]	**7.5**	4.0	(1.7, 4.3)	(1.9, 4.7)	cm
Variability Y [1]	**2.34**	1.92	(0.98, 2.23)		cm
Variability XY [1,3]	7.9	4.4	(2.0, 4.8)	(2.3, 5.0)	cm
Contraction/Expansion ratio X [1]	**0.54**	0.71	(0.60, 1.12)		cm/cm
Contraction/Expansion ratio Y [1]	1.04	1.13	(0.81, 1.19)		cm/cm
Contraction/Expansion ratio XY [1]	0.62	0.80	(0.54, 1.21)		cm^2/cm^2
Shift X	**-8.5**	-3.1	(-6.5, 7.2)		cm
Shift Y [1,3]	2.2	1.5	(-4.6, 3.0)	(-4.2, 3.6)	cm
Shift XY [1]	**8.8**	3.5	(1.0, 8.1)		cm

Scale based on: [1]age, [2]gender, [3]handedness.

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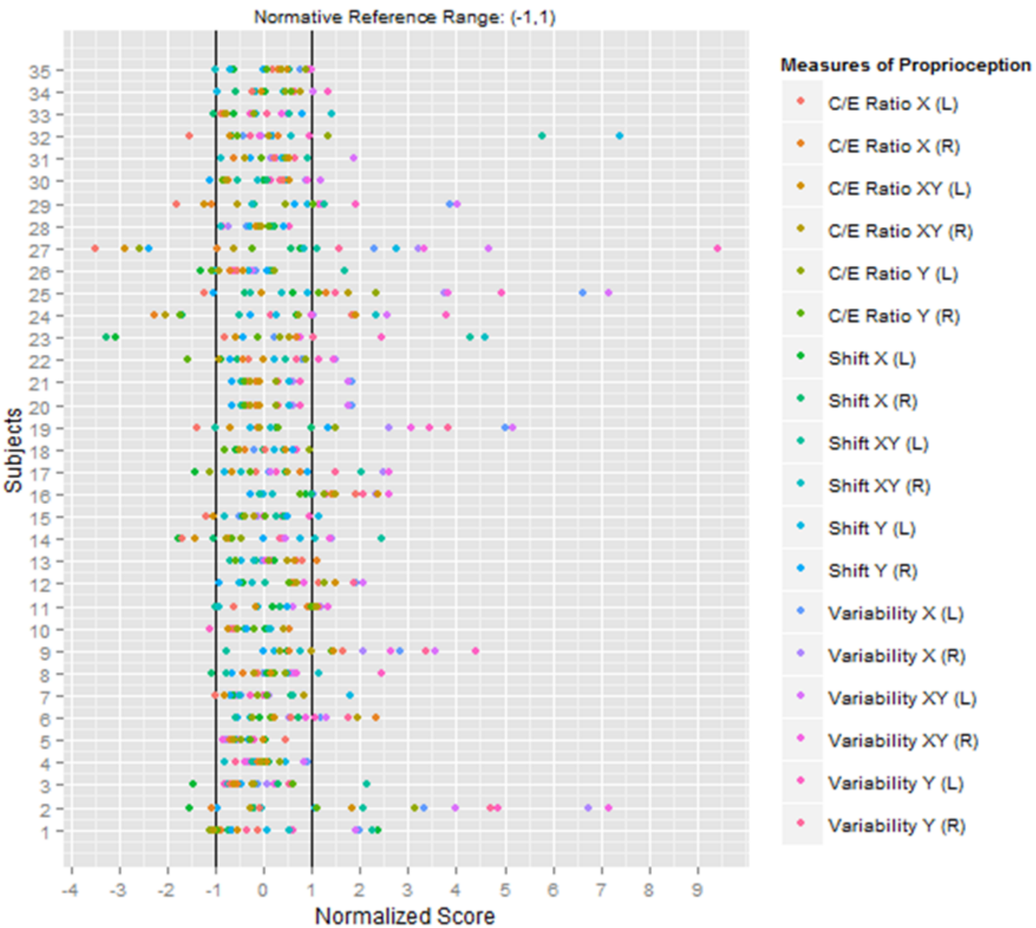
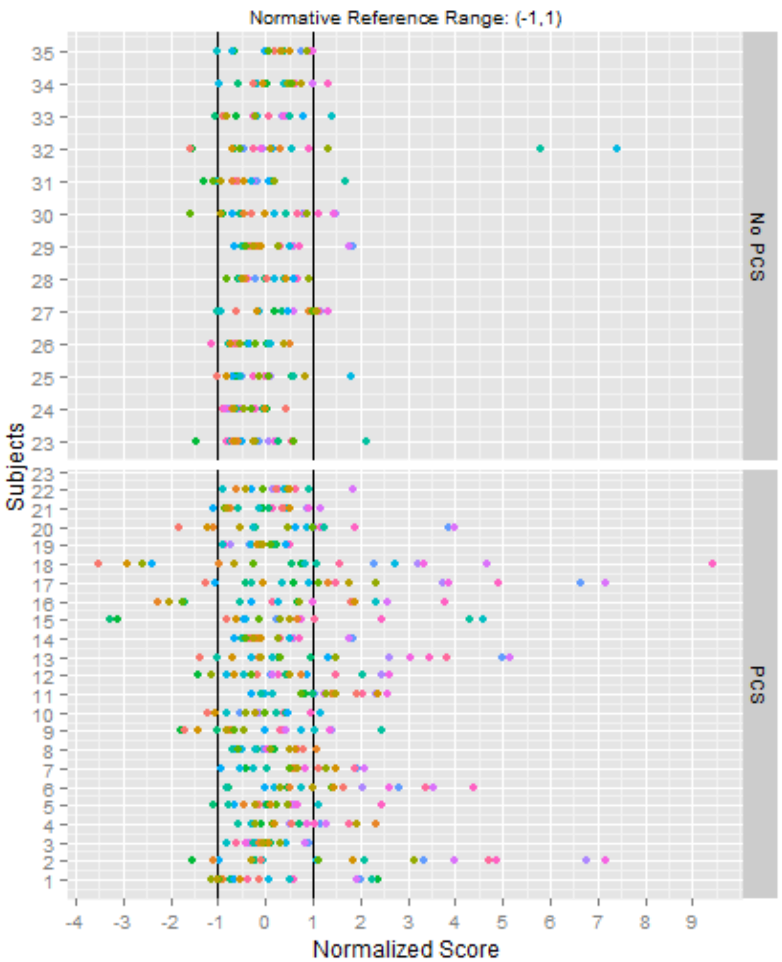
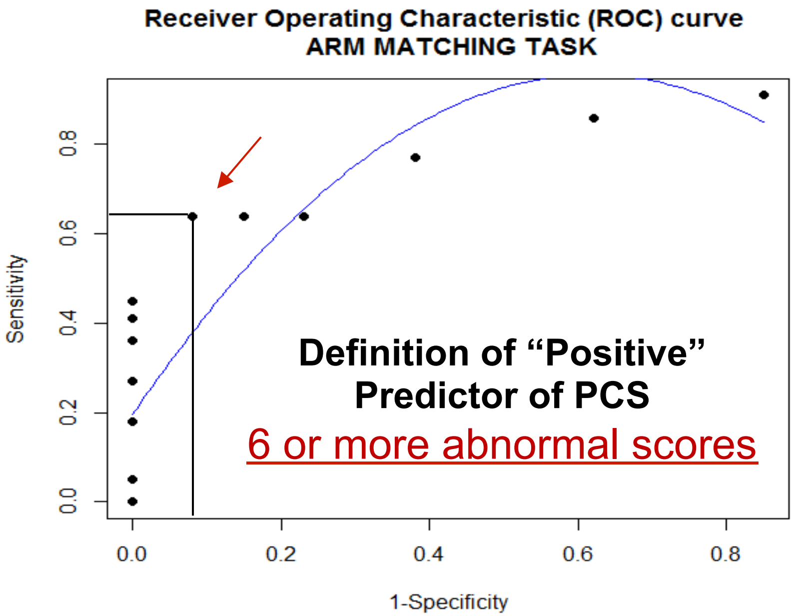
Results: Arm-Matching Task





Is Arm Matching Task a PCS Predictor?



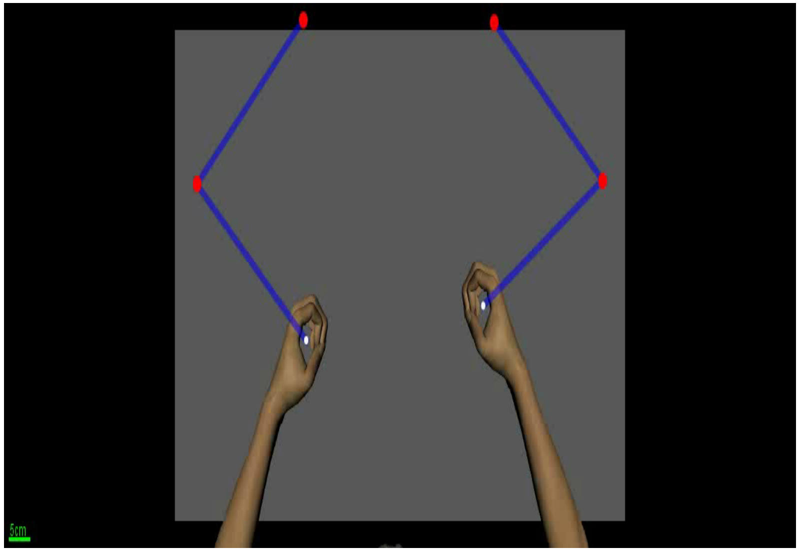
Arm Matching Task	Prevalence of PCS	
	PCS Present	PCS Absent
Positive	**14**	1
Negative	8	**12**

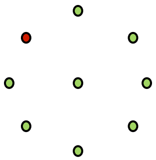
Validity Measure	Estimate	95% CI
Sensitivity	64%	41% -83%
Specificity	**92%**	64% - 100%
Positive Predictive Value	**93%**	68% - 100%
Negative Predictive Value	60%	36% - 81%

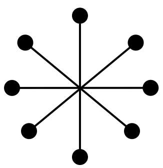
✓ **Risk Ratio = 2.33**, 95%CI: 1.29 – 2.83; Fisher's test: **p = 0.002**).

Other Tasks in the Test Battery

Unimanual Visuomotor Task (Visually Guided Reaching)



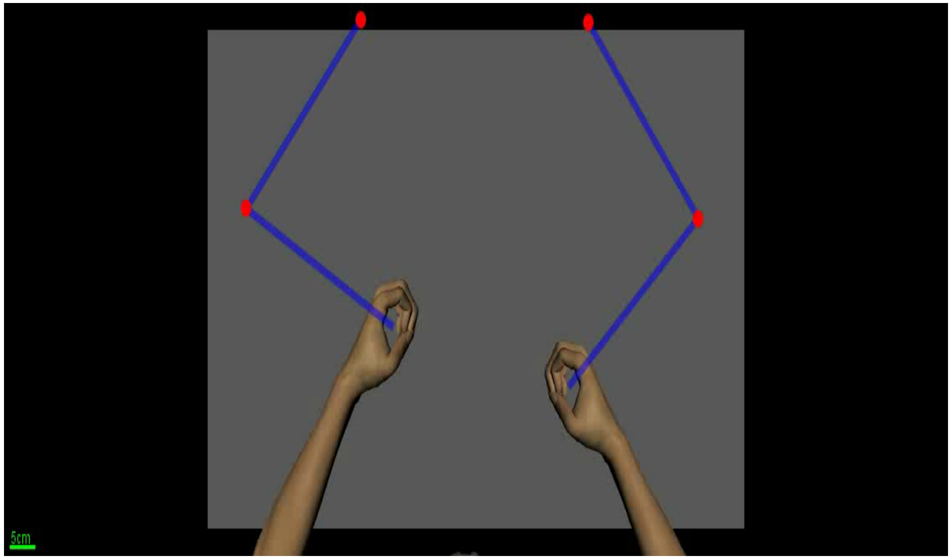




This test primarily quantifies

- Visual Reaction Time
- Movement control

Bimanual Visuomotor Task (Object-hit)



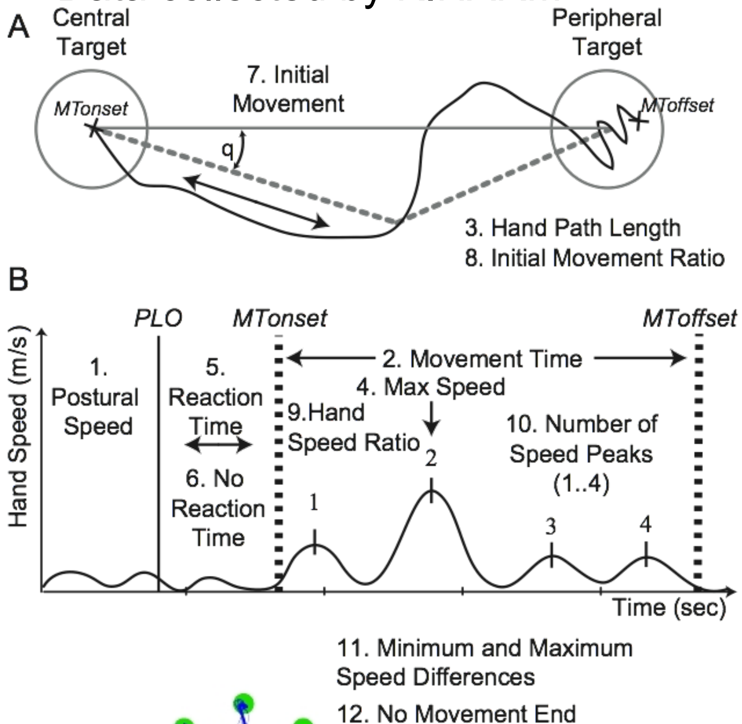
This test primarily quantifies

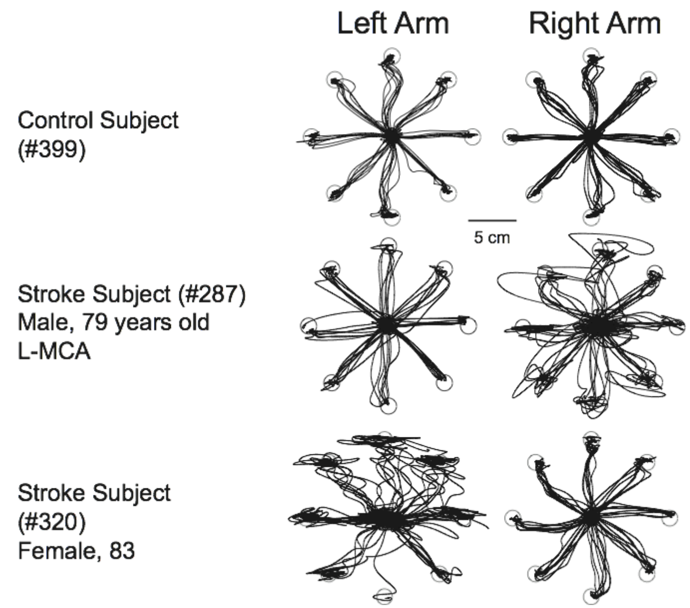
- Spatial awareness
- Asymmetries in the use of two limbs

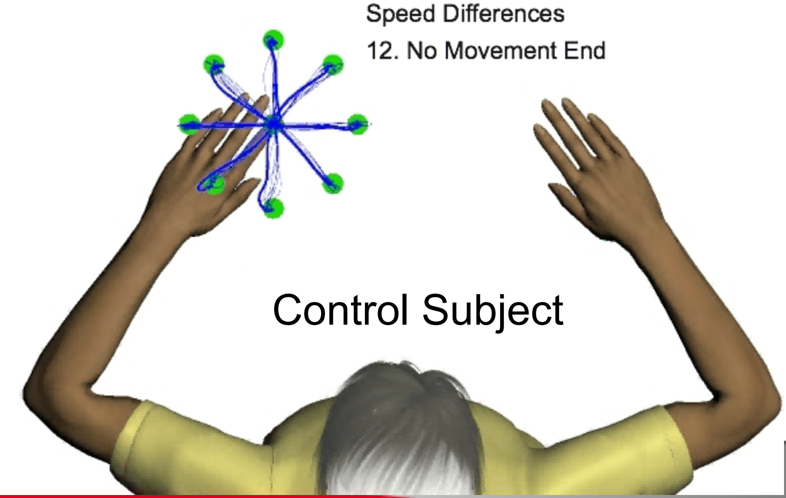
Example Test: Targeted Reach

Slide Content Provided by B•Kin Technologies

Data collected by KINARM™







- The device collects 10 different types of data as the subject move the handle from one target position to the next
- Overall performance is compared to a large normative database.

Where Are We Headed

- Working to complete analysis of the other 4 standard tasks.
  - Individual task analysis
  - Principle Component Analysis on the 88 parameters that make up the entire test battery.
- Initiating a study using the B-KIN system to assess concussed athletes looking at
  - Concussion diagnosis
  - Return-to-Play assessment
  - Impact of contact sport season on neuromotor function
- Developing a lightweight/portable system that would be affordable for use in assessment of high school athletes
- Developing Custom Tasks for Hemispatial Neglect
  - Quantitative assessment of hemispatial neglect
  - Integrated Assessment and Rehabilitation strategies

EEG Going Main Stream

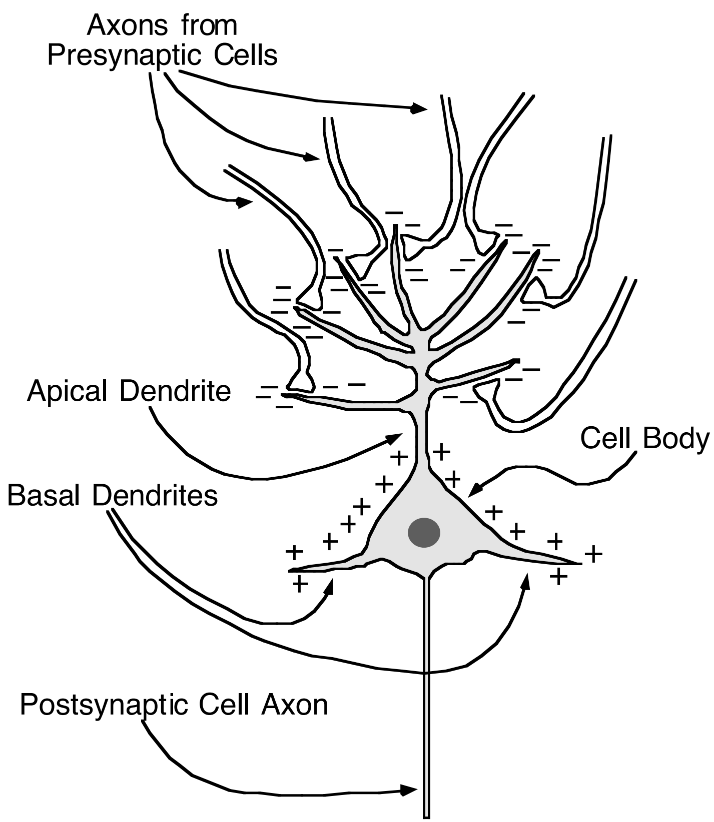
New dry electrode technologies and advanced signal processing techniques have enabled the development of EEG (brainwave measurement) systems that are:

- Easy to use (being incorporated into toys).
- Inexpensive (less that $100 for simple systems)
- Comfortable/Stable for continuous wear

We have been looking at the use of EEG and ERPs as potential biomarkers of Brain Injury and Neurological Impairment

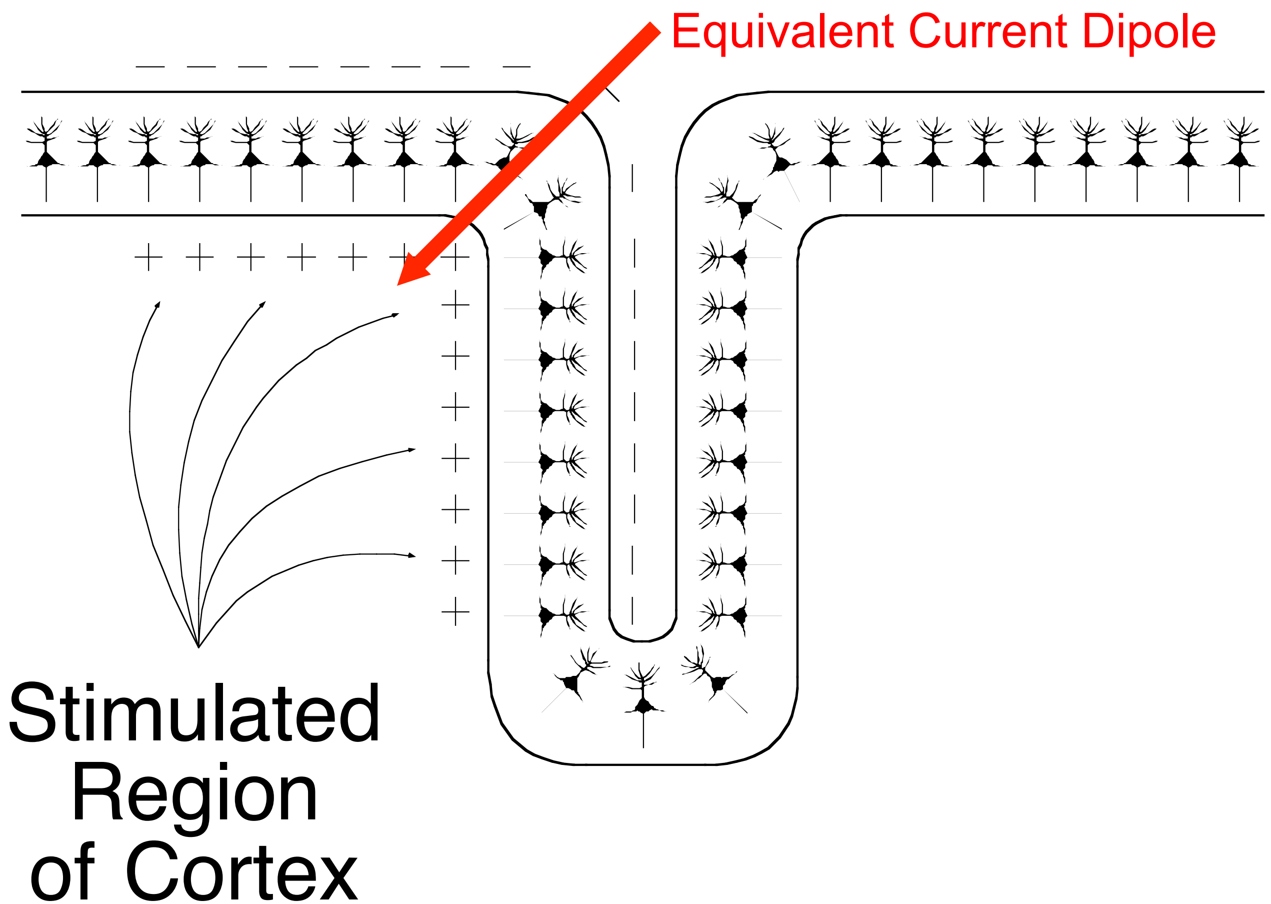
What is an ERP?

- An event related potential (ERP) is the measure of brain response that is the direct result of a specific sensory, cognitive or motor event.
- ERPs are part of the "brainwave" signal that are recorded with an EEG system.



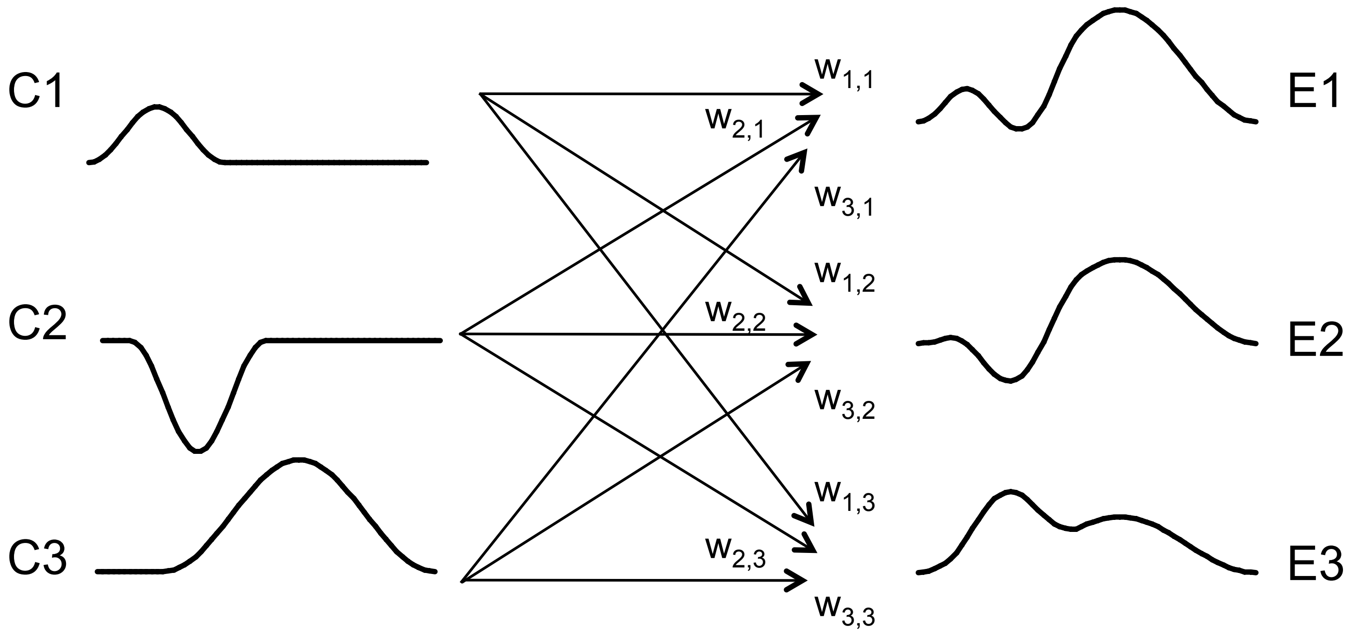
- Cortical pyramidal cell (basic input-output cell of cerebral cortex)
- Excitatory transmitter released on apical dendrites causes positive charges to flow into dendrites
- Net negative charge is left on the outside of cell creating a dipole.
- Polarity reverses with inhibitory transmitter
- Polarity at scalp also depends on orientation of the cortical surface and position of reference electrode

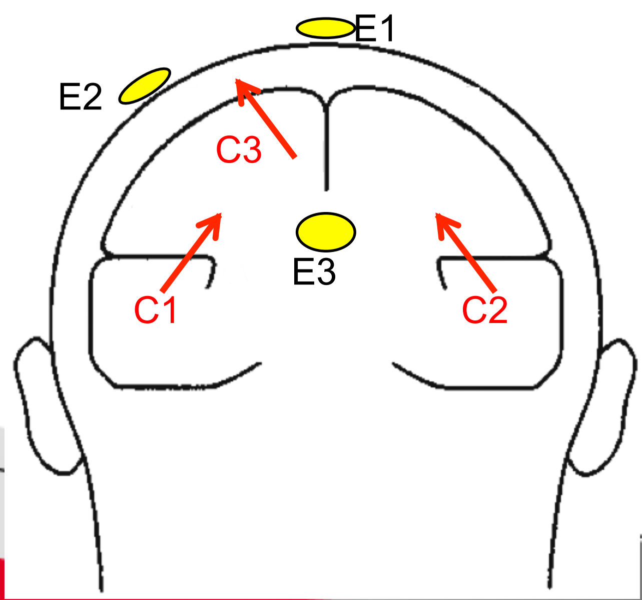
Where Do ERPs Come From?



To be recorded at a distance, large numbers of neurons must have similar voltage fields

The Superposition Problem

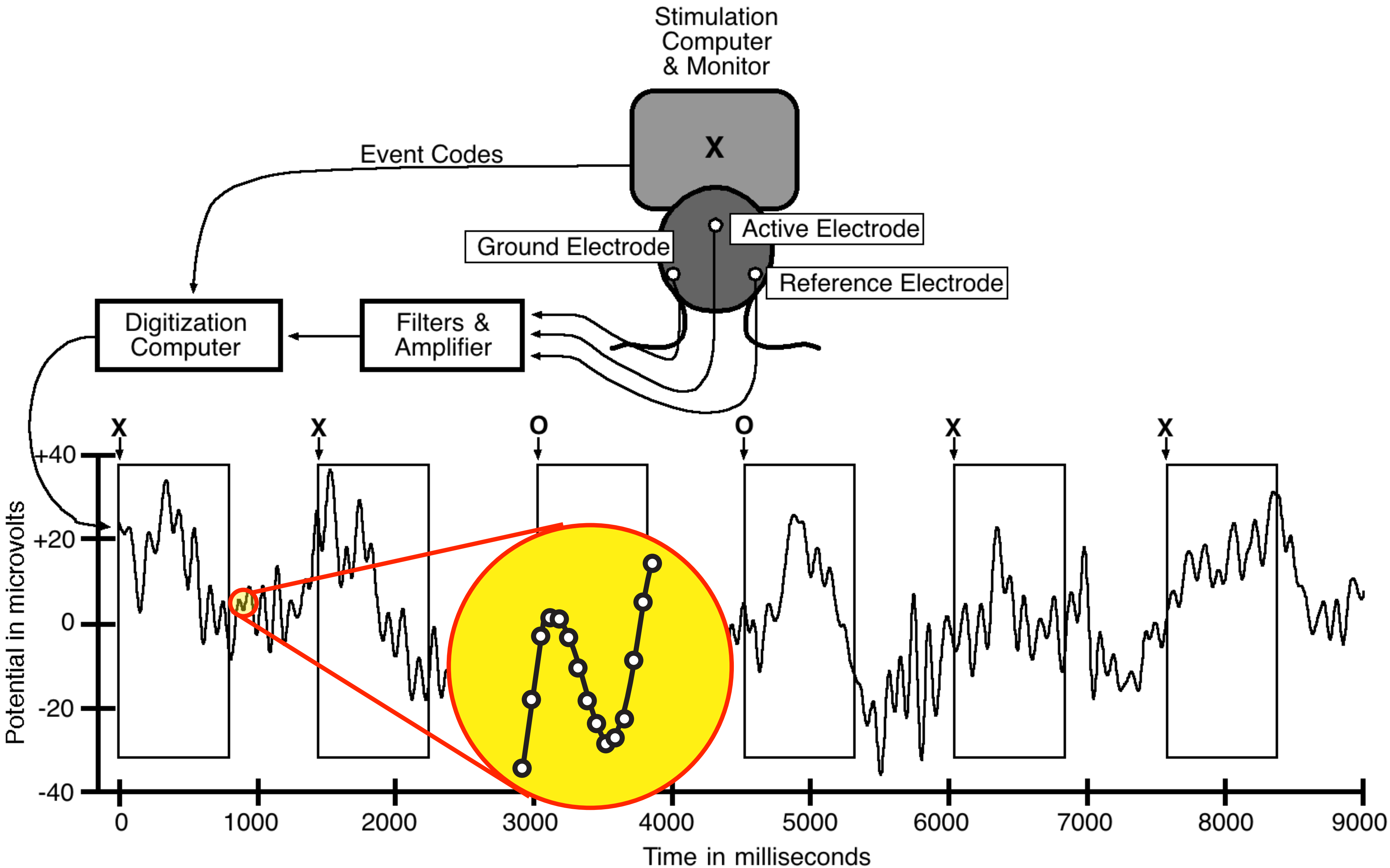




Voltage at an electrode at time *t* is a weighted sum of all components that are active at time *t*

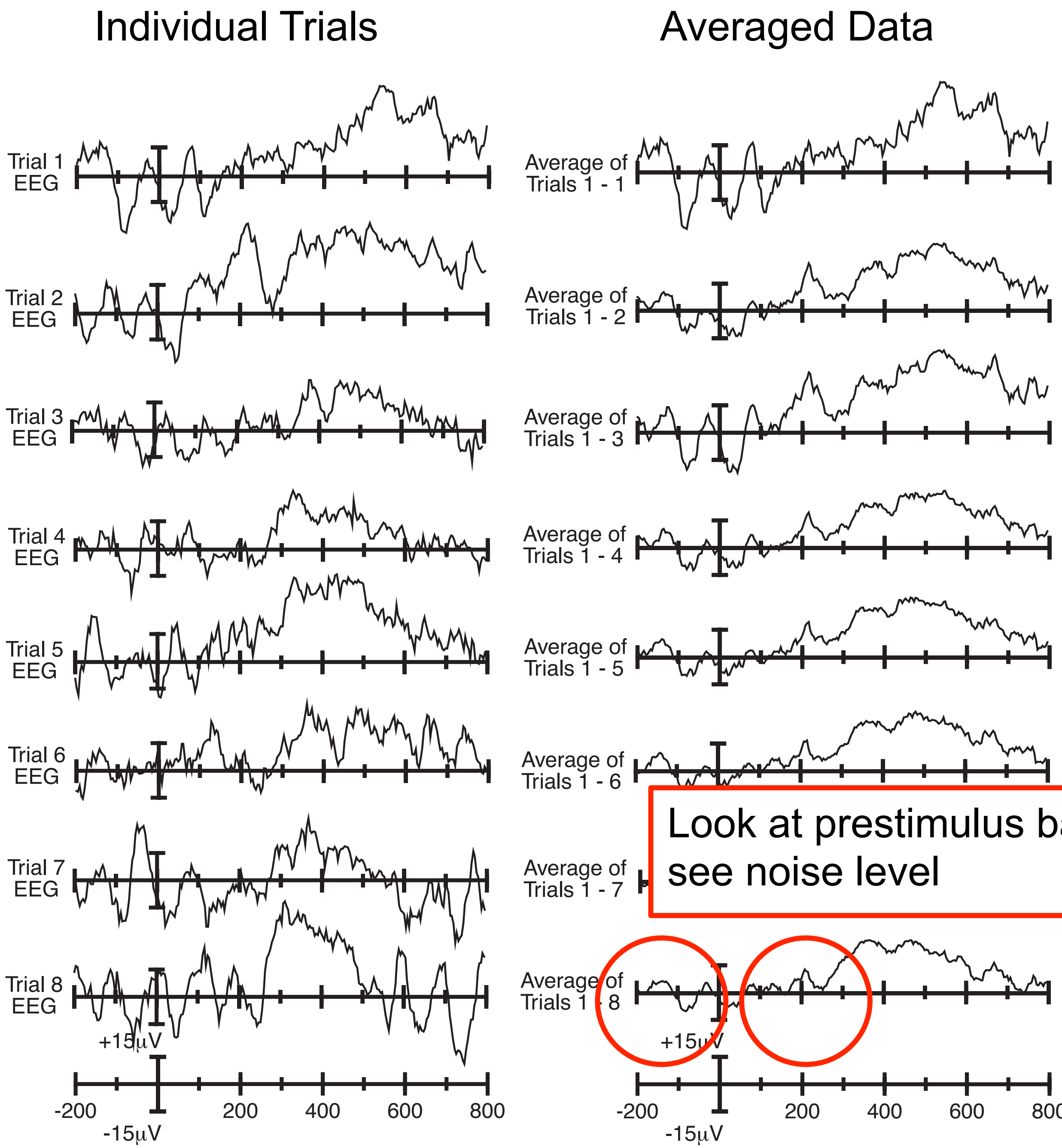
There is no foolproof way to recover the underlying components from the observed waveforms

Basic Recording Setup



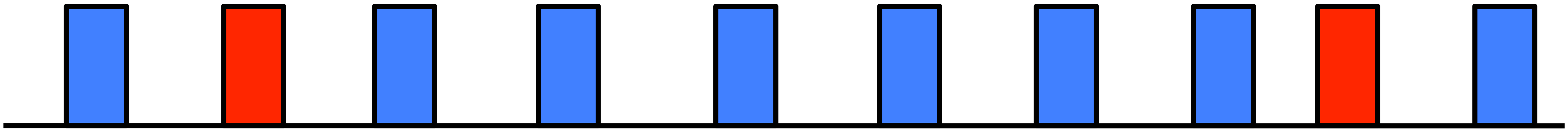
Importance of Clean Data

- ERPs are tiny
  - Many experimental effects are less than a millionth of a volt
- ERPs are embedded in noise that is 20-100 µV
- Averaging is a key method to reduce noise
  - S/N ratio is a function of sqrt(# of trials)
  - Doubling # of trials increases S/N ratio by 41% [sqrt(2)=1.41]
  - Quadrupling # of trials doubles S/N ratio [sqrt(4)=2]



Look at prestimulus baseline to see noise level

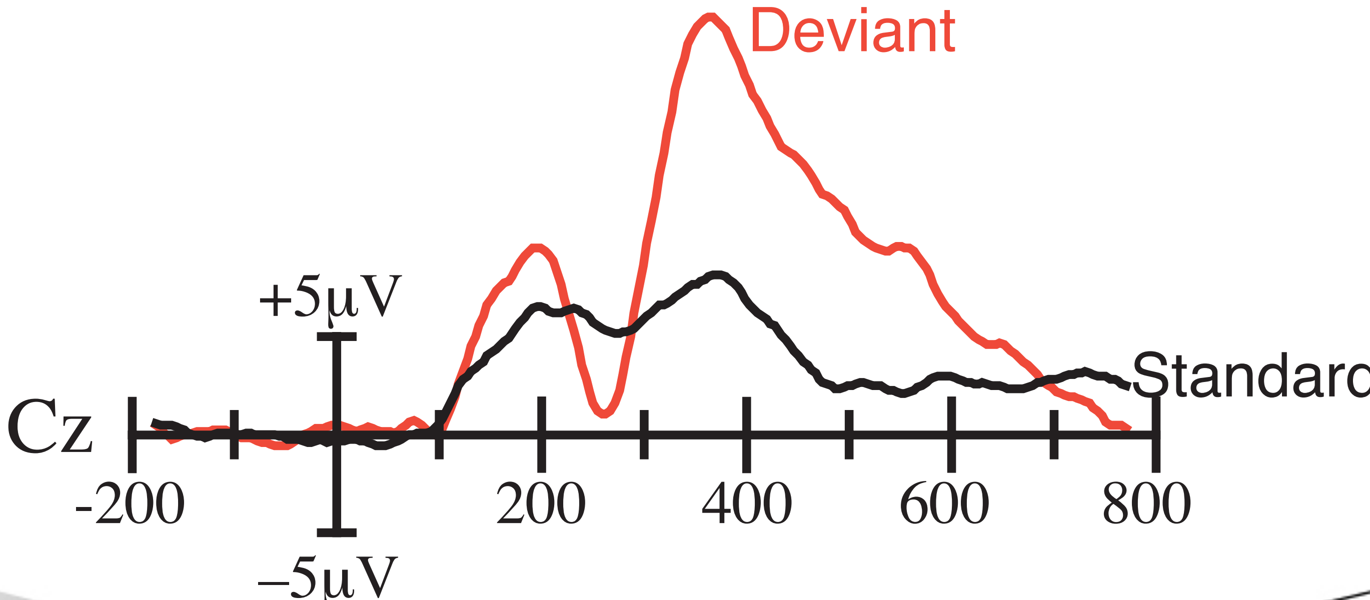
The Oddball Paradigm



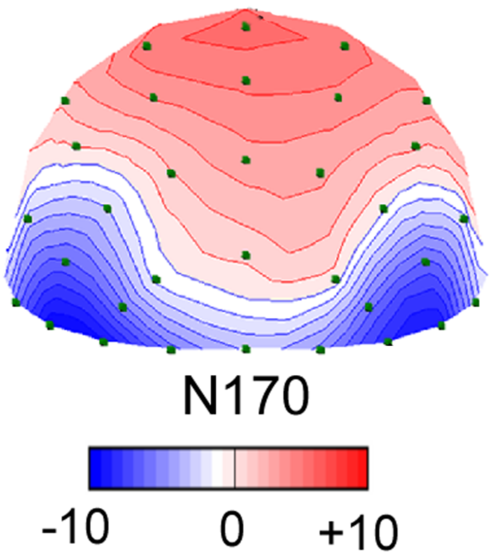
= Standard

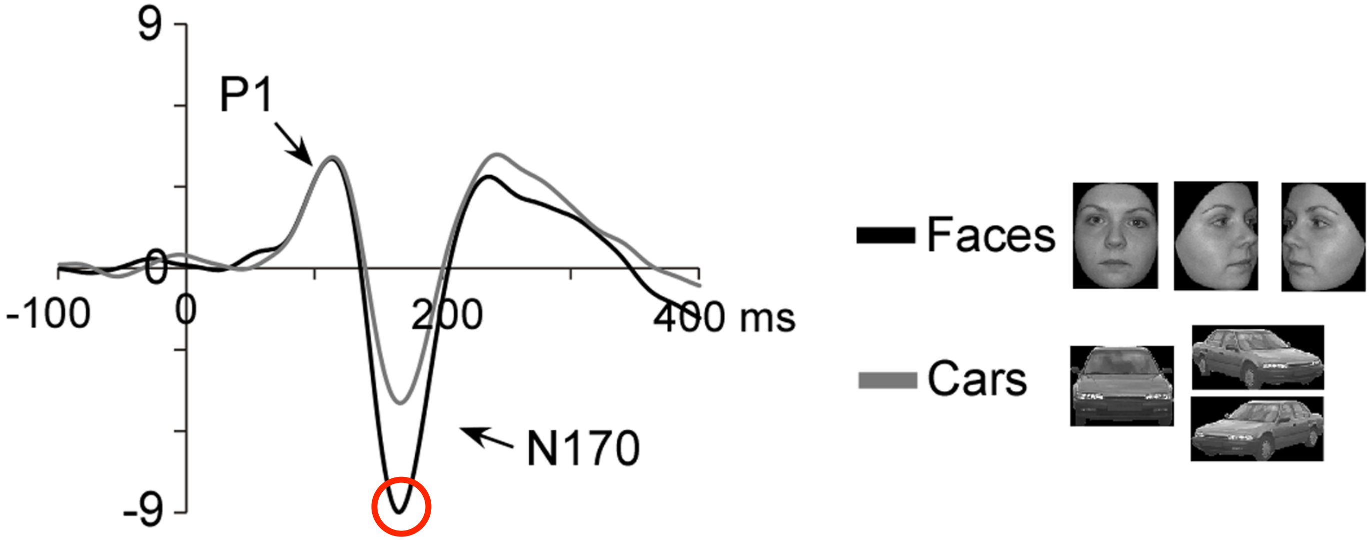
= Deviant/Oddball/Target

Typical Task Alternatives:
Count oddballs
Press only for oddballs
Different buttons for standard, oddball



Example: N170

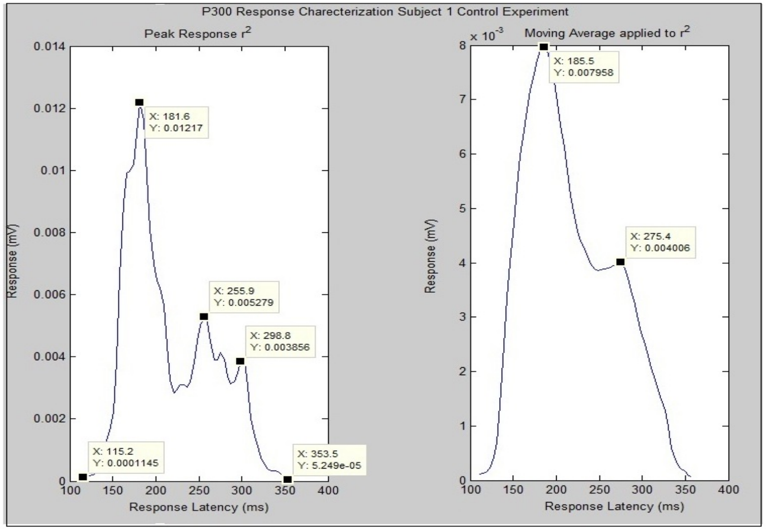




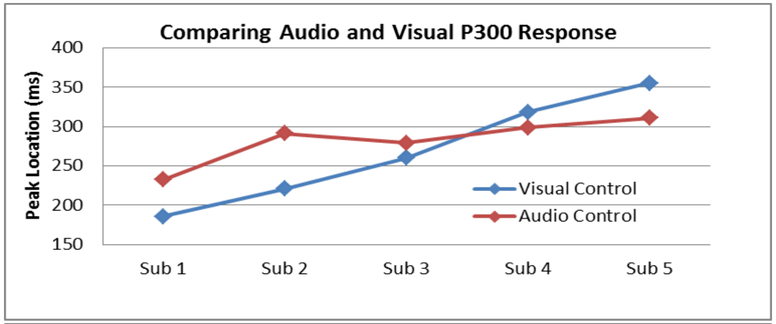
This voltage reflects face-related activity plus everything else that is active at 170 ms

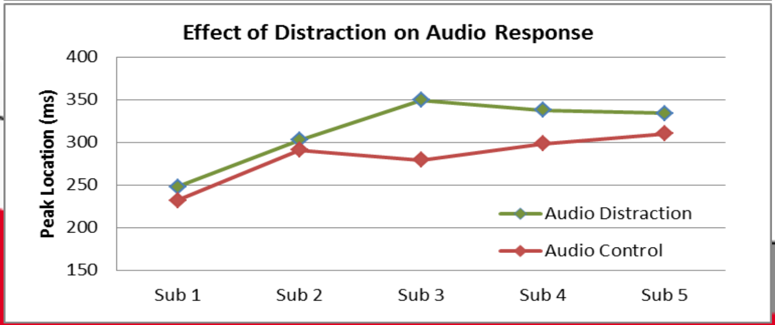
Rossion & Jacques (2009)

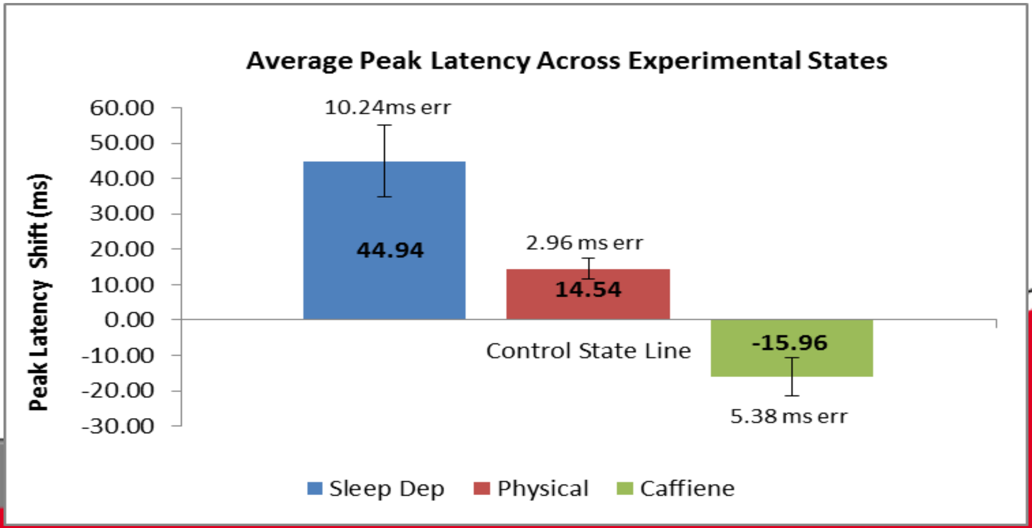
ERPs as a Biomarker of Injury or Fatigue



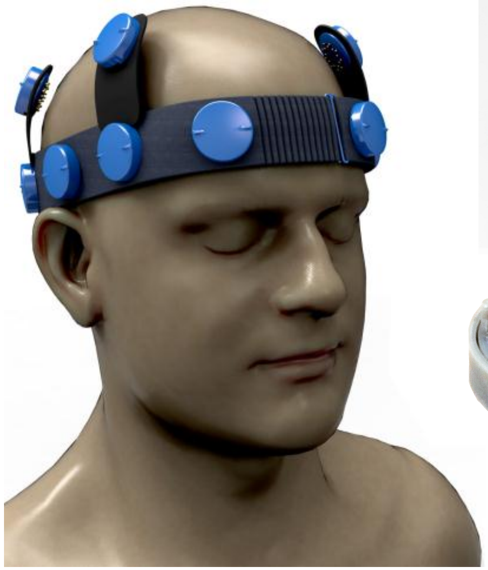
- Using the "oddball" paradigm with either visual or auditory stimuli produces a distinct response that is detectable within 200-500 ms (so called P300).
- While the timing of ERP response can vary between subjects, each persons response timing is self-consistent
- ERP timing will vary with neurologic state including sleep deprivation, fatigue, neurologic injury and with presence of stimulants (ex caffeine) or adrenaline
- ERPs are an inherent physiologic response that can not be "fooled" or "manipulated"
- In this study we looked at effects of exercise, caffeine and sleep deprivation on P300 timing.

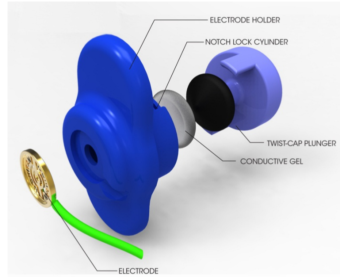


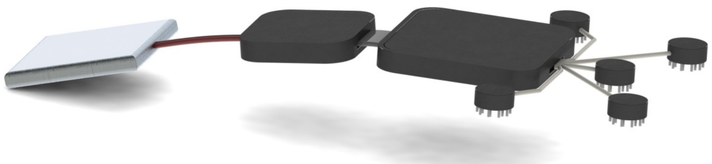


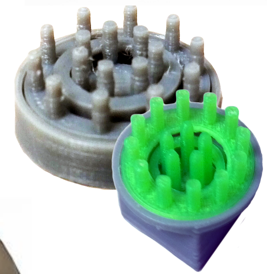


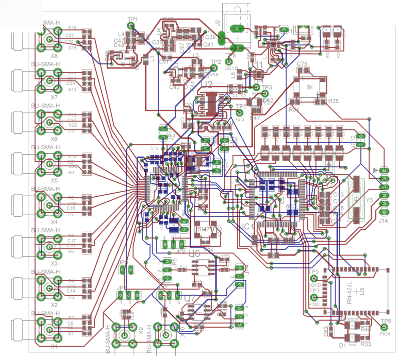
Our approach to EEG Capture

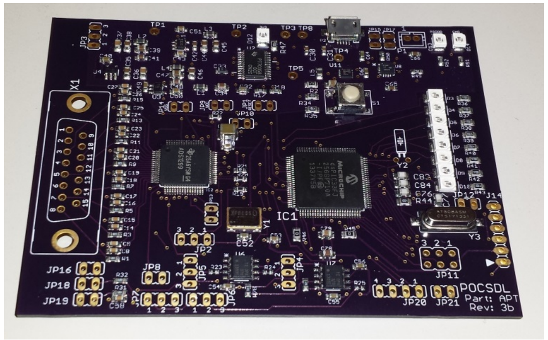








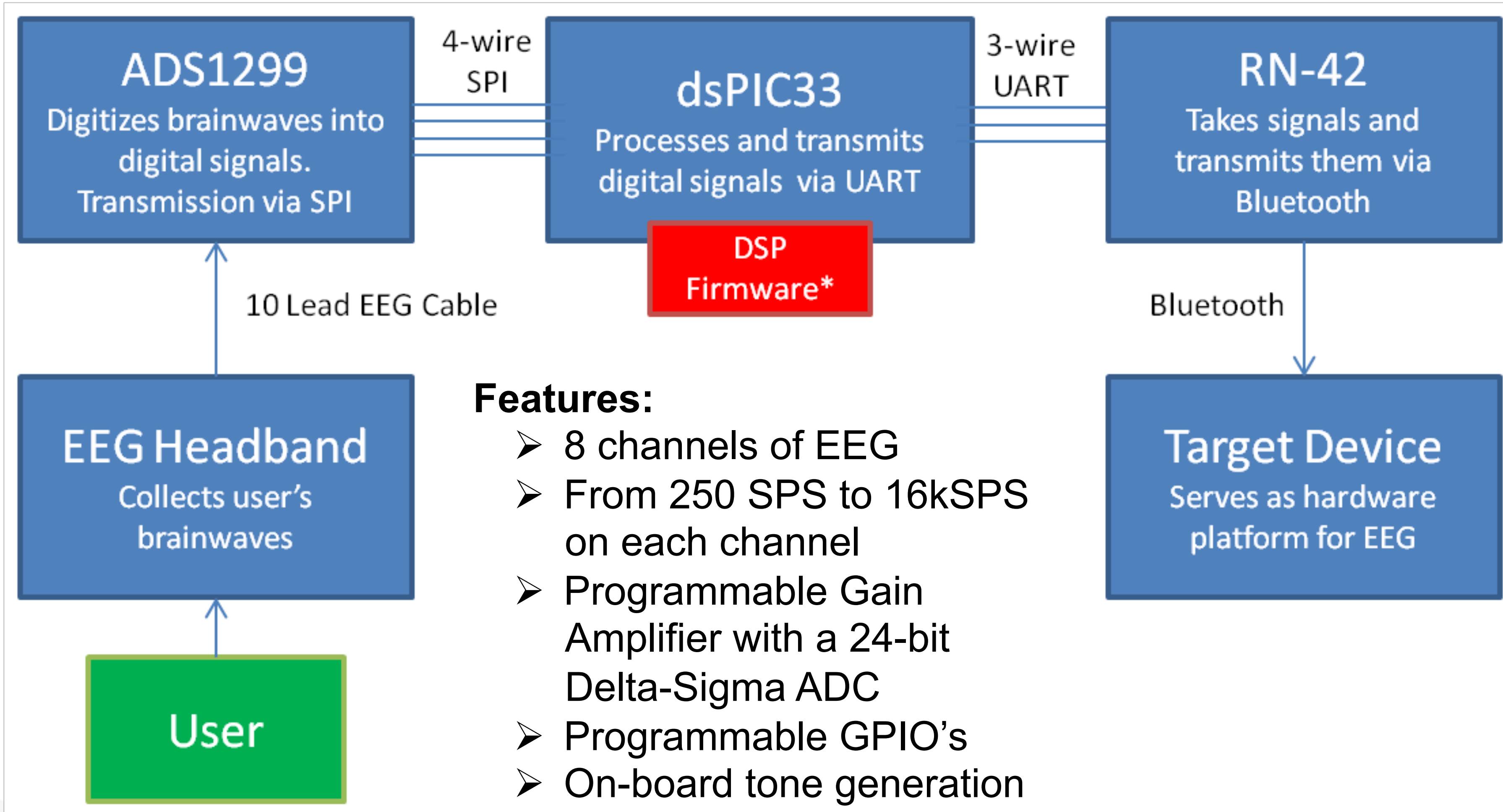




We have been developing a fully integrated wireless EEG system with the following features:

- 8-16 dry electrodes arranged to maximize signal evaluation for EEG or ERP work.
- Wireless communication using low power Bluetooth communication.
- Low power electronics for battery operation extending over several hours.
- Exploring options for embedding in helmets and other headgear.

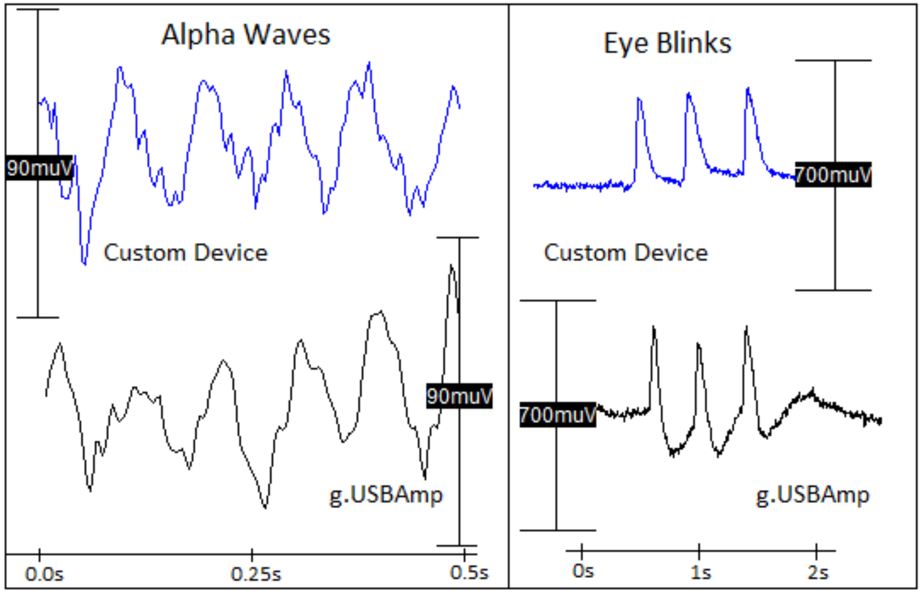
Custom Wireless EEG Platform



Features:

- 8 channels of EEG
- From 250 SPS to 16kSPS on each channel
- Programmable Gain Amplifier with a 24-bit Delta-Sigma ADC
- Programmable GPIO's
- On-board tone generation
- Board size: 2.5”x3.5”x.075”

Custom Device Compared to g.tec g.USBAMP



Performance comparison between our custom device and a clinically approved EEG system:

- Our device configured to match the g.tec system (i.e. basically low end of our system performance).
- Subject was asked to do standard EEG set-up verification tasks (i.e. resting with eyes closed and multiple eye blinks in quick succession)
- Look for similarity of shape, signal level and signal drift.

High Level Overview: EEG Platform

Hardware Frontend

Custom Device
- EEG Hardware
- EEG Cap
- Worn by the patient

Bluetooth

Software Backend

Python Server
- Device class encapsulating all communication to the H/W frontend
- Analysis class for filtering and manipulating data
- UI class encapsulating all communication with the S/W frontend

HTTP

Software Frontend

HTML UI
- Web based UI
- All configuration options and commands available

Firmware for the custom device is changed rarely, which means minimal reprogramming

Python server is easily manipulated to change basic functionality and design specific tests

Web interface is portable, robust, and easily adaptable in terms of layout and view

Future Direction

- Currently working to embed the technology in head gear typically worn by workers who are subject to disrupted decision making and/or injury related to mental/physical fatigue.
- Beginning to explore use of this technology as a diagnostic and/or rehabilitation assessment platform for concussion/mTBI
- Also exploring other application of EEG including a handheld device for seizure detection and a platform for security authentication.

Conclusions

- Electrical/Computer Engineers are playing a critical role in the development of novel technologies that can provided critical diagnostic information in clinical and health monitoring applications.
- Advances in sensors, hardware and software capabilities that are driving the consumer electronics market are also having a dramatic impact on the capabilities of POC medical devices that use embedded electronics.
- My research group has made significant progress with several technologies that are targeted towards the diagnosis and rehabilitation monitoring of brain injured patient.

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Collaborators:

EEG/Event Related Potentials Project

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Robotic Assisted Neurologic Assessment Project

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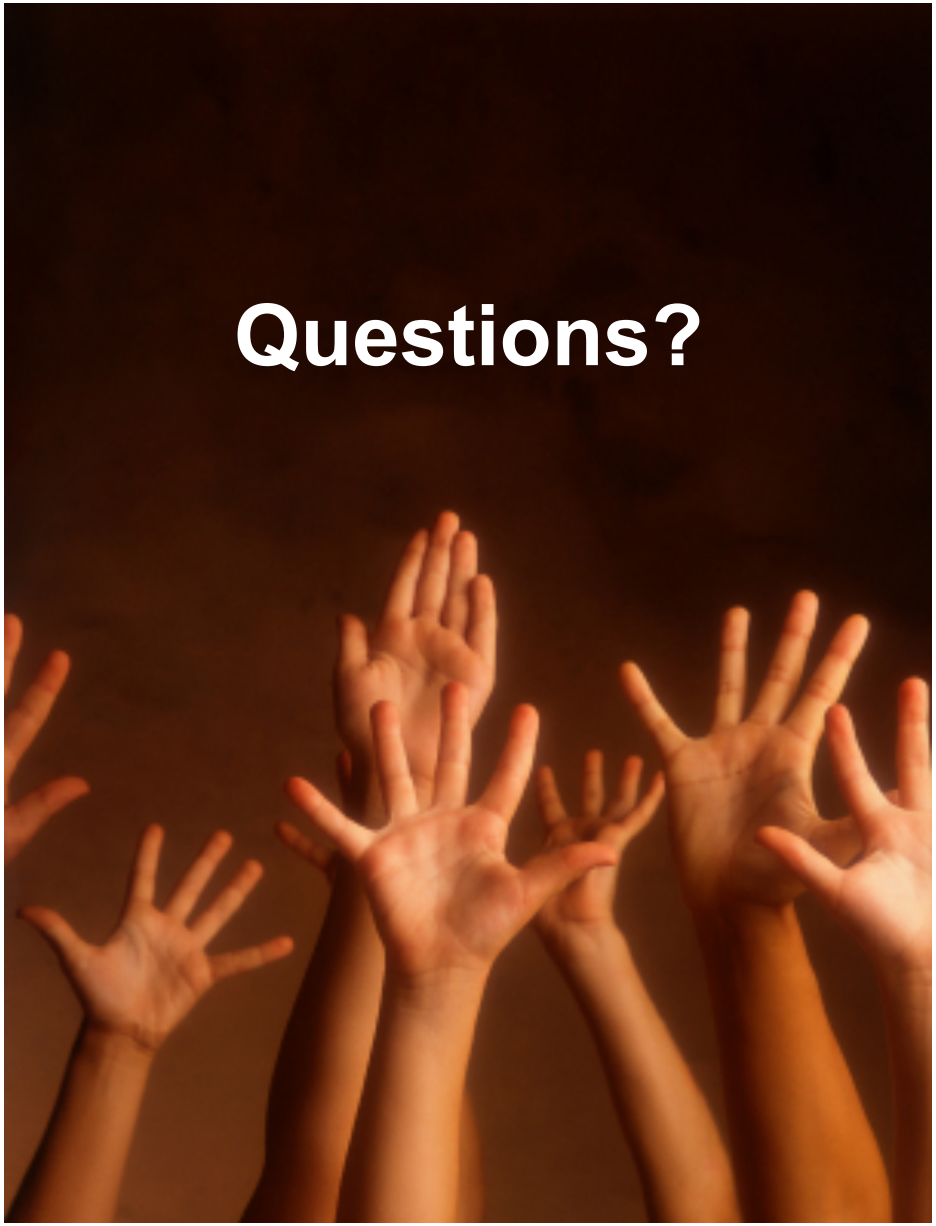
Questions?