EE 795 LECTURE 11

Functional Electrical Stimulation

LECTURE OUTLINE

We will look at:

- Design of FES
- Electrodes and electrode-tissue behavior
- Nerve excitation
- Recruitment
- Clinical applications

Design of functional electrical stimulation:

In *functional electrical stimulation* (FES), nerve stimulation is achieved by passing current between two or more electrodes implanted in or on the body.

In order for this system to produce *functional* nerve activation, the appropriate spatial and temporal patterns of stimulation must be determined for the desired stimulus response. This requires an understanding of both the stimulus properties and the resulting nerve response properties.

Design of FES (cont.):

Stimulus design considerations include electrode properties such as:

- number and positions of electrodes,
- material,
- size,
- shape, and

stimulating current properties such as:

- strength, and
- waveform.

Design of FES (cont.):

Example stimulus waveform shapes:

- monophasic,
- biphasic,
- chopped,
- triphasic, and
- asymmetric,

and parameters:

- pulse amplitude,
- pulse width,
- interphase gap, and
- pulse rate.

(From Shepherd & Javel, *Hear. Res.* 1999)

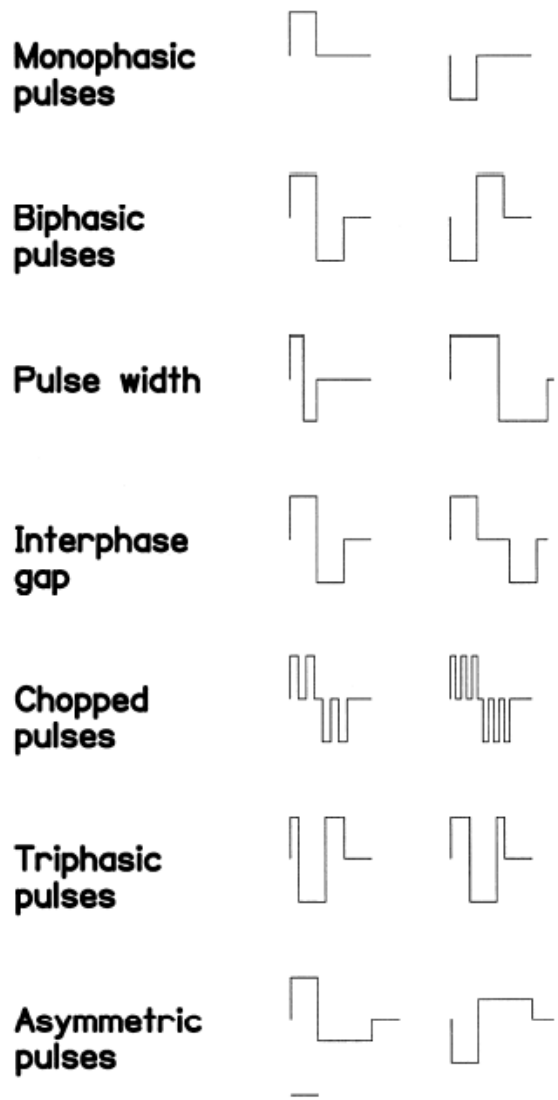


Fig. 1. Diagram illustrating the range of stimulus waveforms used in the present study. Note that all stimuli in the first column deliver an initially anodic current pulse to the most apical electrode.

Stimulator

- Constant Current or Constant Voltage
- Early stimulators were constant voltage (easier design)
- Modern stimulators mostly constant current
- Electrode/neural tissue interface has a complex impedance Z, which is unknown and can change over time, constant current provides set stimulus strength and desired response regardless of Z

Stimulus Parameters

- Pulse durations <50 μsec to 1 msec.
- Pulse trains for most FES applications, i.e. 20 – 30 Hz for muscle stimulation.
- Waveforms mostly rectangular with monophasic or balanced biphasic shapes.
- Intra-corporeal electrode (implanted) stimulators need only deliver I_S = several 10's of mamps., with subsequent voltages $V_S = ZI_S$ several volts (all electronics)
- Surface electrode stimulators must deliver up to 100 ma with subsequent voltages of several hundred volts (step-up transformers or DC-DC converters necessary)

Electrodes and electrode-tissue behavior:

When a closed current loop is created by implanting stimulating electrodes in body tissue, the *current carriers* in the wires and electrodes are *electrons*, whereas current within the tissue is carried by *ions*, primarily sodium, potassium and chloride.

An *electrochemical reaction* must therefore take place at the *electrode-tissue interface* that (in part) *exchanges metal electrons for ions in solution*.

Electrodes and electrode-tissue behavior (cont.):

For extracellular metal electrodes:

- **anode** $\equiv$ **positive** net charge in the electrode, and
- **cathode** $\equiv$ **negative** net charge in the electrode.

In the extracellular electrolyte, an opposite charge develops that is separated from the electrode by a molecular layer of water adsorbed on the metal surface.

Electrodes and electrode-tissue behavior (cont.):

This charged layer corresponds to a charged capacitance.

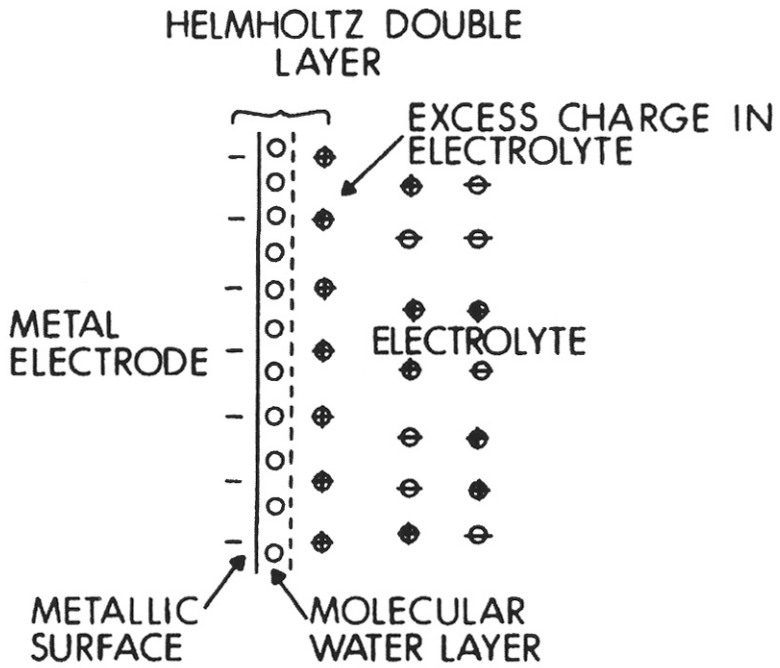


Figure 12.1. Idealized cross-sectional view of the metal–tissue interface of an electrode (cathode) under very low (zero) current conditions. [From A. M. Dymond, Characteristics of the metal–tissue interface of stimulation electrodes. *IEEE Trans. Biomed. Eng.* **BME-23**:274–280 (1976), copyright 1976, IEEE.]

Electrodes and electrode-tissue behavior (cont.):

The equivalent electrical circuit of the electrode-tissue interface will therefore incorporate this capacitance in parallel with a resistance that reflects the electrode-electrolyte charge movement that results from both *reversible* and *irreversible* electrochemical *Faradaic* reactions.

An experimental set-up for analysing this behaviour is shown on the next slide.

Electrodes and electrode-tissue behavior (cont.):

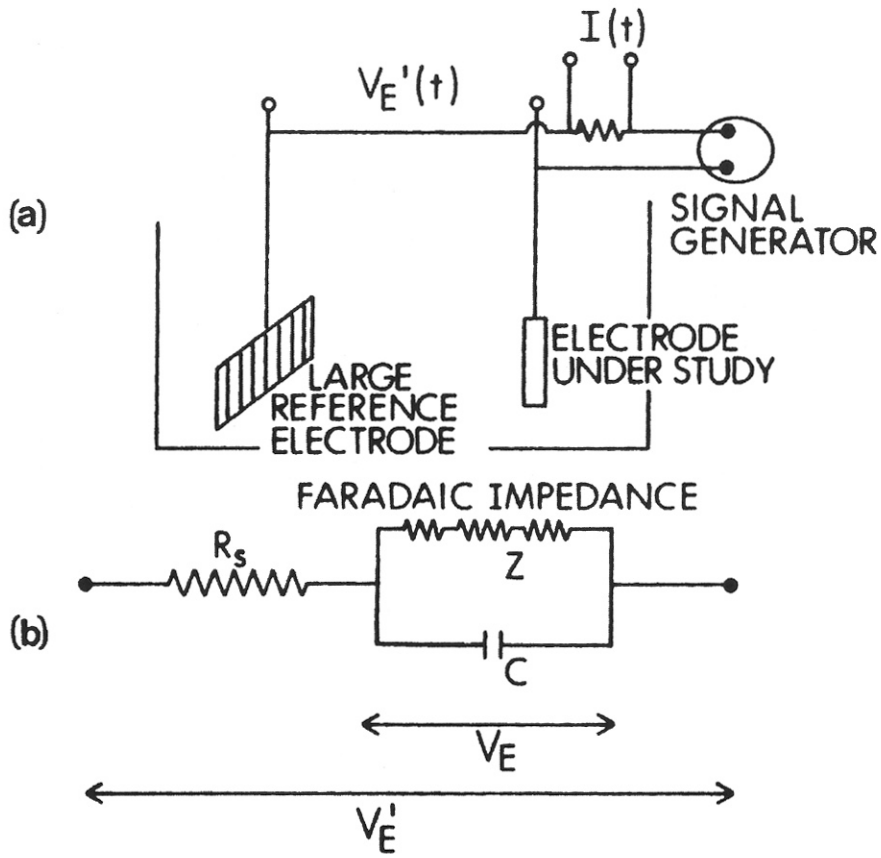


Figure 12.2. (a) Apparatus used in biomedical studies of electrode impedance where current $I(t)$ and total electrode voltage $V_E'(t)$ are monitored. (b) Equivalent circuit for system in (a). R_s is the solution resistance, C is the double-layer capacitance, and Z is the Faradaic impedance (the latter consisting of charge-transfer resistance, diffusional impedance, and reaction impedance). [From A. M. Dymond, Characteristics of the metal–tissue interface of stimulation electrodes, *IEEE Trans. Biomed. Eng.* **BME-23**:274–280 (1976), copyright 1976, IEEE.]

Electrodes and electrode-tissue behavior (cont.):

An RC voltage response is consequently observed in the electrode-tissue interface response to a current step.

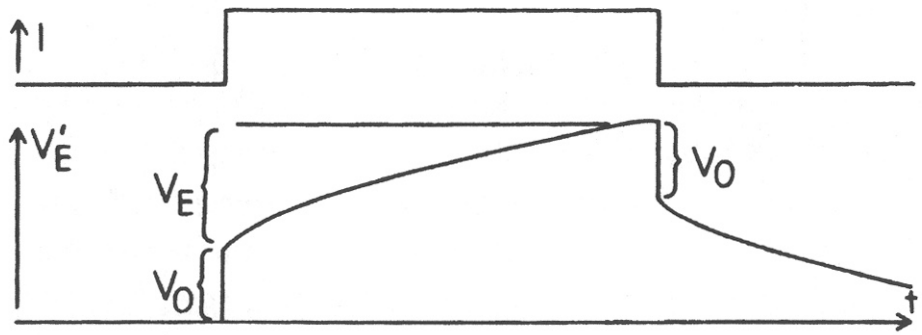


Figure 12.3. Voltage waveform observed between test electrode and reference electrode in response to the constant current pulse shown. V_0 is the voltage across the electrolyte path (IR_s) while V_E is that across the electrode–electrolyte capacitive interface. (From J. T. Mortimer, Motor prostheses, in *Handbook of Physiology*, Sec. I: *The Nervous System*, Vol. II, *Motor Control*, Part I, American Physiological Society, Bethesda, Maryland, 1981, pp. 155–187.)

Electrodes and electrode-tissue behavior (cont.):

The operating characteristics of an electrode depend on:

- the effective capacitance C and R per unit area, and (C,R = f(I_S, Freq) when I_S > 1 ma/cm^2
- the reversible or irreversible electrochemical reaction between the electrode and electrolyte.

A graphical scheme for analysing electrode performance is shown on the next slide.

Electrodes and electrode-tissue behavior (cont.):

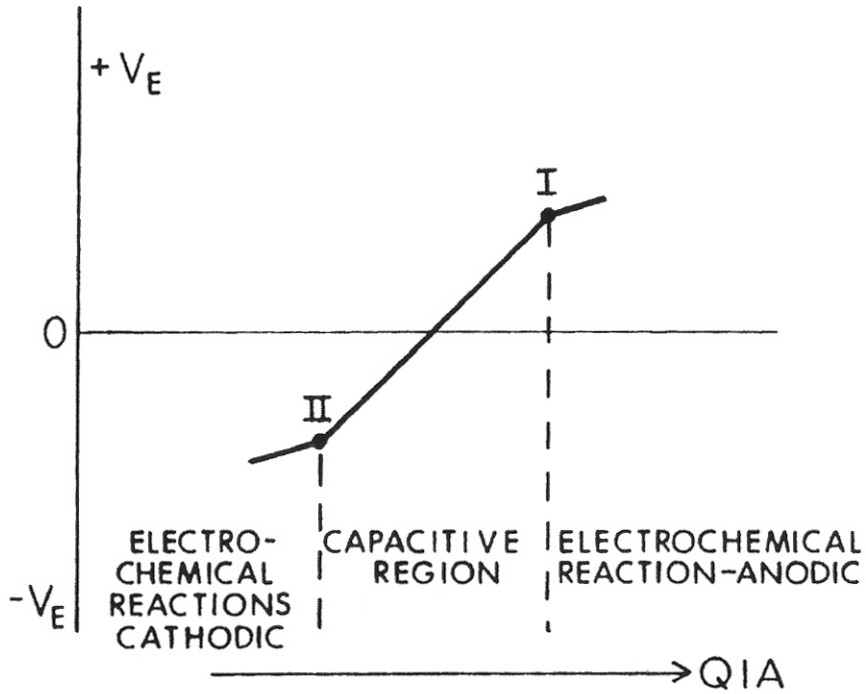


Figure 12.4. Idealized representation of relationship between electrode potential V_E and charge density (charge per unit of real electrode area, Q/A). Charge injection in the central region involves processes that are capacitive and therefore completely reversible. Charge injection in regions to right of point I or left of point II involve electrochemical reactions. These are reversible if, by driving current in the opposite direction, no new species are introduced. Irreversibility involves diffusion of new chemical species away from the electrode. (Modified from J. T. Mortimer, Motor prostheses, in *Handbook of Physiology*, Sec. I: *The Nervous System*, Vol. II, *Motor Control*, Part I, American Physiological Society, Bethesda, Maryland, 1981, pp. 155–187.)

Electrodes and electrode-tissue behavior (cont.):

In the central region, the capacitance of the electrode-electrolyte interface dominates. It is desirable to operate within this region and thus avoid Faradaic reactions at the interface, but the charge delivered may not be sufficient to achieve nerve activation.

Exceeding the limits of the linear region, i.e., delivering charge beyond points I or II (or both), introduces Faradaic conditions (i.e., electrochemical reactions).

Electrodes and electrode-tissue behavior (cont.):

For example, a *stainless steel* electrode that is driven beyond point I by an *anodic* potential may experience the *irreversible* reaction:

$$\mathrm{Fe} \longrightarrow \mathrm{Fe}^{++} + 2e^{-}\,, \qquad (12.2)$$

which leads to dissolution of the iron.

For *cathodic* potentials beyond point II the reaction may be of the form:

$$2\mathrm{H_2O} + 2e^{-} \longrightarrow \mathrm{H_2} \uparrow \mathrm{OH}^{-}\,, \qquad (12.3)$$

which is again irreversible and produces a pH increase that could cause tissue damage.

Electrodes and electrode-tissue behavior (cont.):

On the other hand, for a *platinum* electrode the *anodic* reaction may be:

$$\mathrm{Pt} + \mathrm{H_2O} \rightarrow \mathrm{PtO} + 2\mathrm{H}^+ + 2e^- \,, \quad (12.4)$$

which is *reversible*.

For *cathodic* potentials the reaction may be of the form:

$$\mathrm{Pt} + \mathrm{H}^+ + e^- \longrightarrow \mathrm{Pt\text{-}H} \,, \quad (12.5)$$

which is again reversible. Note that neither of these reactions introduces new chemical species.

Electrodes and electrode-tissue behavior (cont.):

For *monophasic* stimulation, the charge continually builds up at the electrode interface.

For anodic pulses, the build-up reaches point I, after which electrochemical reactions take place that result in the loss of charge.

For cathodic pulses, the build-up reaches point II.

Consequently, monophasic stimuli are rarely used for indwelling electrodes.

Electrodes and electrode-tissue behavior (cont.):

- The build up of charge is normally avoided by using *charge-balanced biphasic* current pulses.
- Charge balance is usually ensured by the use of a capacitor in series with the electrode.
- In the ideal case, the operating point does not drift from charge build-up, and the range of charges delivered stays within the linear (capacitive) region of the V_E versus Q/A curve, so that Faradaic charge losses are not incurred.

Electrodes and electrode-tissue behavior (cont.):

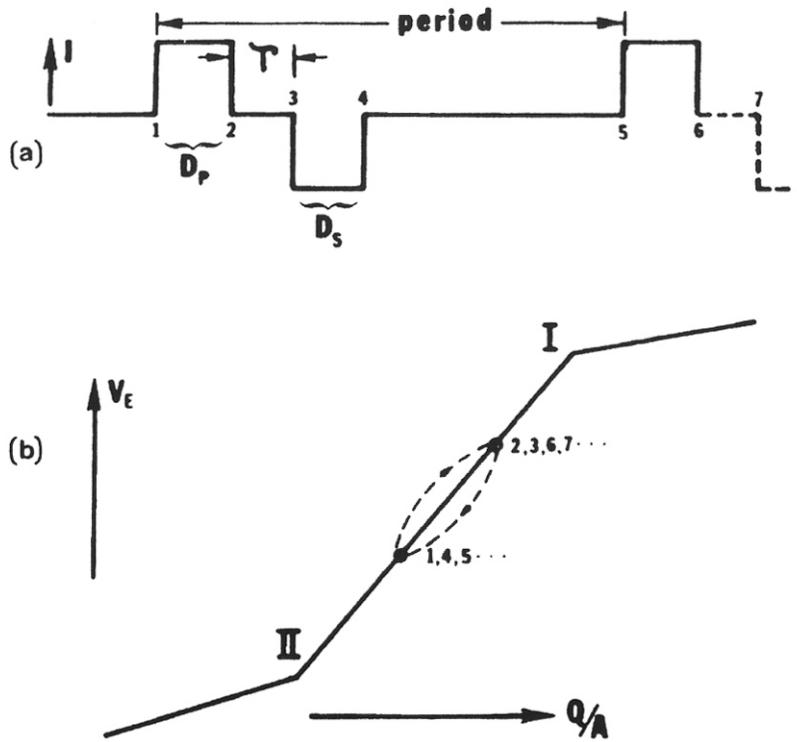


Figure 12.5. Balanced-charge biphasic stimulation. (a) Stimulus waveform with zero net charge transfer per cycle ["period" >> $(D_p + \tau + D_s)$]. (b) Variation in electrode potential, for conditions where charge is accommodated entirely within capacitive region. *I* and *D* refer to current pulse amplitude and pulse duration. Subscripts *P* and *S* refer to primary and secondary stimulus pulses, respectively. Parameter τ is the time delay between the end of the primary pulse and the beginning of the secondary pulse. Balanced charge requires that $I_P D_P = I_S D_S$. Points 1–7 in (a) correspond to points in (b). (From J. T. Mortimer, Motor prostheses, in *Handbook of Physiology*, Sec. I: *The Nervous System,* Vol. II, *Motor Control*, Part I, American Physiological Society, Bethesda, Maryland, 1981, pp. 155–187.)

Electrodes and electrode-tissue behavior (cont.):

If $Q_P \neq -Q_S$, then steady-state operation must involve some irreversible behaviour.

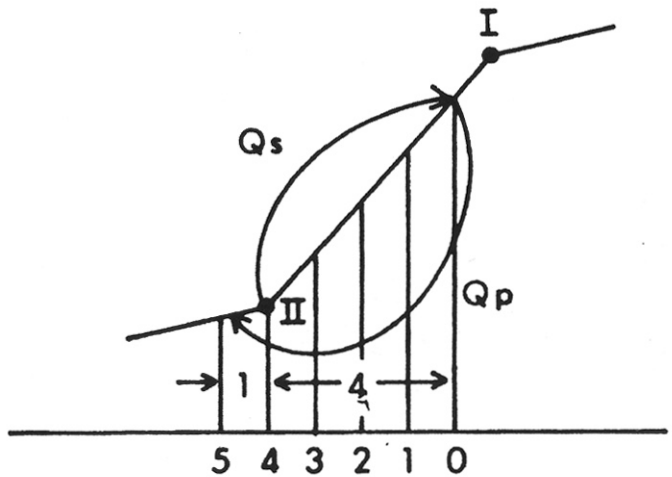


Figure 12.6. Behavior when $Q_p = -5$ units and $Q_s = 4$. Owing to charge imbalance 1 cathodic unit is lost beyond II.

If the irreversible reaction produces OH^-, as per Eqn. (12.3), this process may be tolerable, because the blood can buffer some OH^-.

Electrodes and electrode-tissue behavior (cont.):

Note:

- Comparable anodic irreversibility is never tolerated, because the result is irreparable electrode damage.
- The capacitive region may be expanded by:
  1. coating the electrode with a dielectric (i.e., insulator) or,
  2. roughening the electrode surface to increase its effective surface area.

Electrodes and electrode-tissue behavior (cont.):

Factors to consider when choosing electrode material include:

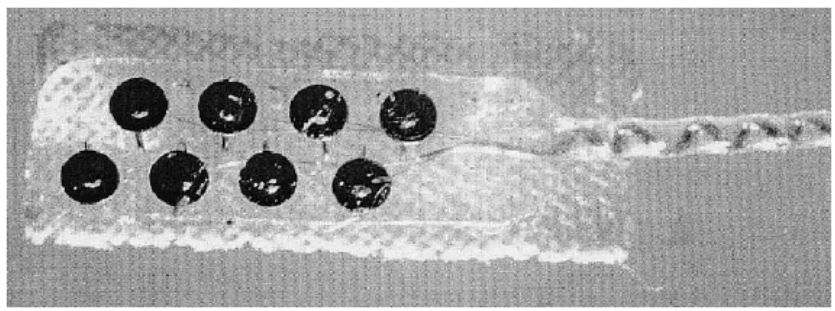
1. passive *biocompatibility* with the tissue,
2. extent of reversible behaviour (capacitive region + region of reversible electrochemical reactions), and
3. mechanical compatibility with the tissue.

The most widely used electrode materials are platinum, platinum-iridium and 316 stainless steel (SUS 316L).

Electrodes and electrode-tissue behavior (cont.):

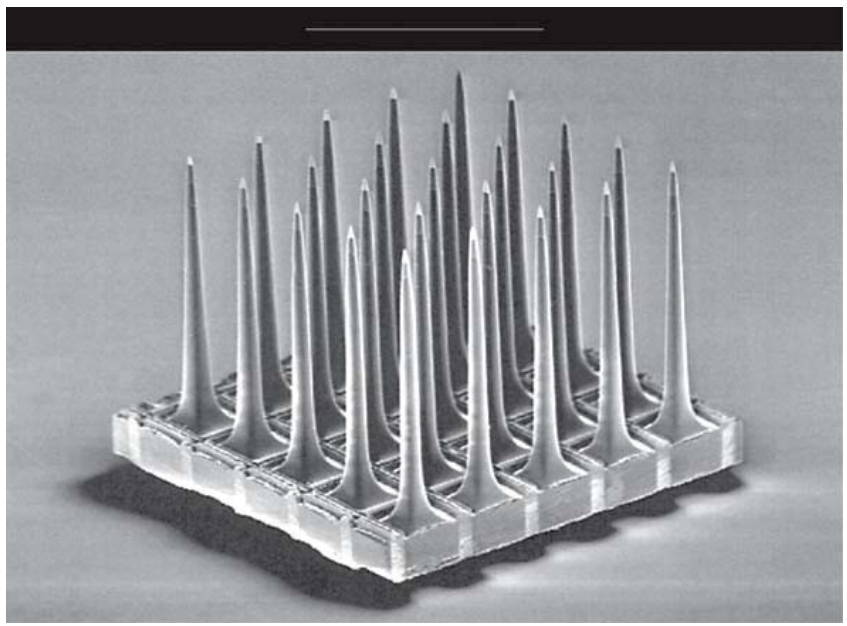
Types of electrodes for specific applications:

1. A — Brain: surface electrodes
    a. Passive implants – minimal trauma to brain tissue; become encapsulated mainly on the superficial side.
    b. Active implants – mainly platinum is used; only low-intensity charged-balanced biphasic stimulation is safe.



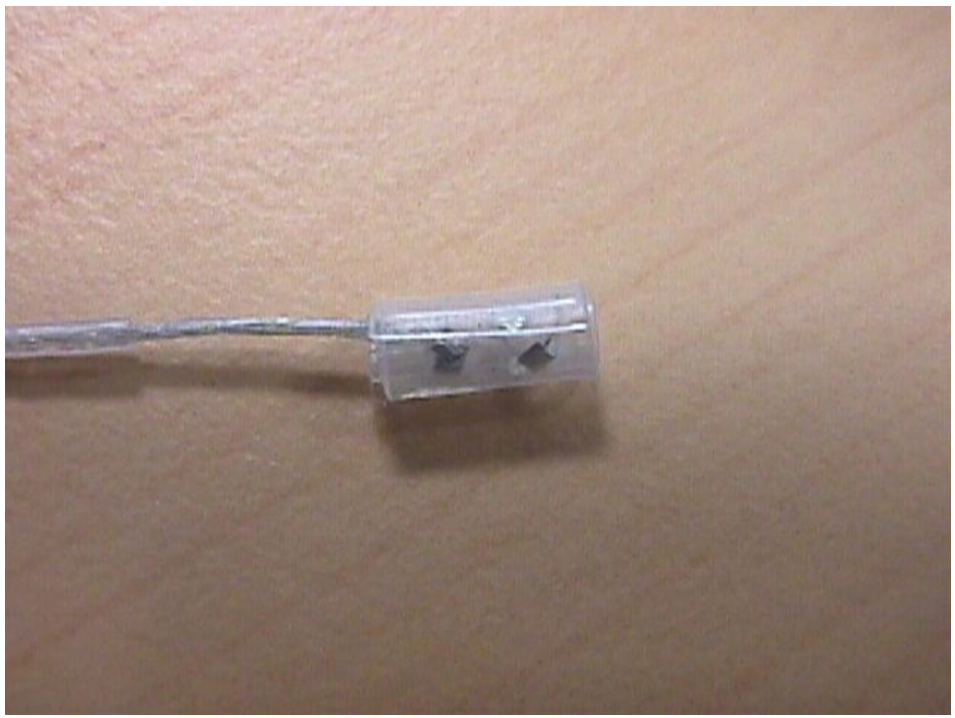
Electrodes and electrode-tissue behavior (cont.):

1. B — Brain: penetrating electrodes
    a. Passive implants – can cause trauma to brain tissue.
    b. Active implants – mainly silicon based.



Electrodes and electrode-tissue behavior (cont.):

2. Nerve (cuff electrodes)
   Surround nerve bundle for confined stimulation, reducing the required current.



Electrodes and electrode-tissue behavior (cont.):

3. Intramuscular (coiled-wire electrodes)
    a. Passive implants – subjected to mechanical strains; become encapsulated.
    b. Active implants – actually stimulate motor axons, *not* muscle fibers.
        i. monophasic: some irreversible cathodic processes tolerated for low currents;
        ii. balanced biphasic: moderate-high currents can be used without degrading electrode;
        iii. imbalanced biphasic: moderate currents are permissible because of blood buffering.

Clinical applications:

Because of the problems involved with spatial selectivity and recruitment, FES has been most successful in clinical applications where these two issues are not so crucial, for example:

- heart pacemakers, cochlear implants, bladder control, respiratory control, gross motor movements.

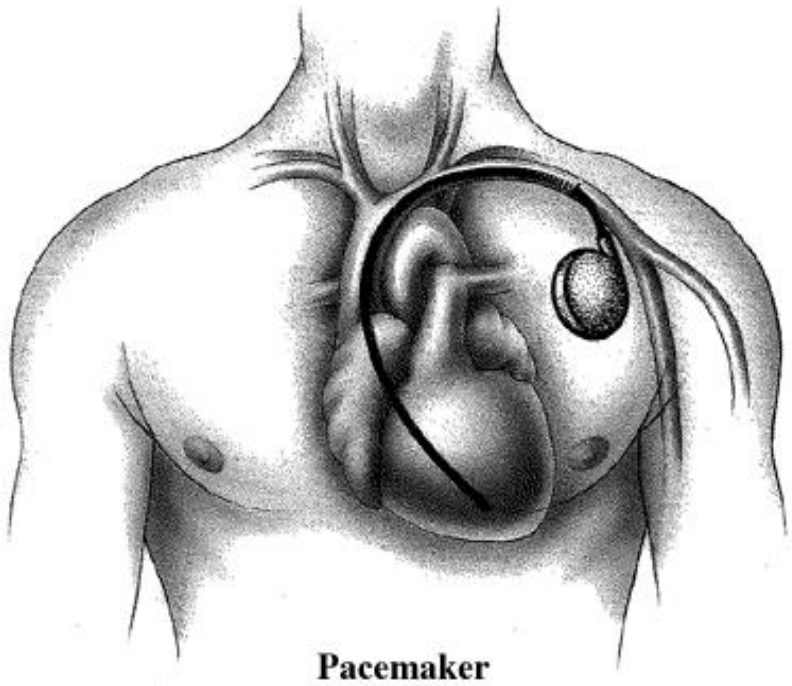
More challenging for clinical application are:

- fine motor control, retinal implants, etc.

Pacemakers:

- First major application of electrical stimulation of excitable cells
- Stimulate just ventricles, or atria and ventricles (dual-chamber)
- Typically platinum or platinum-iridium electrodes, monopolar or bipolar
- Monophasic or biphasic waveforms used
- Both cathode make excitation and anode break excitation are likely to occur

Cardiac Pacing



Pacemaker

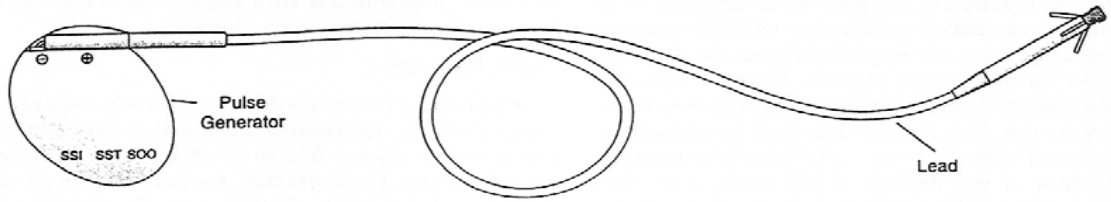


Figure 1. Implantable pacemaker.

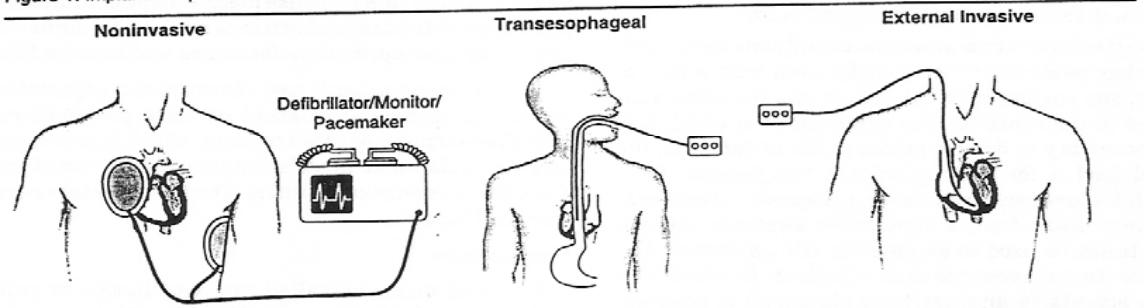


Figure 2. The three types of external pacemakers.

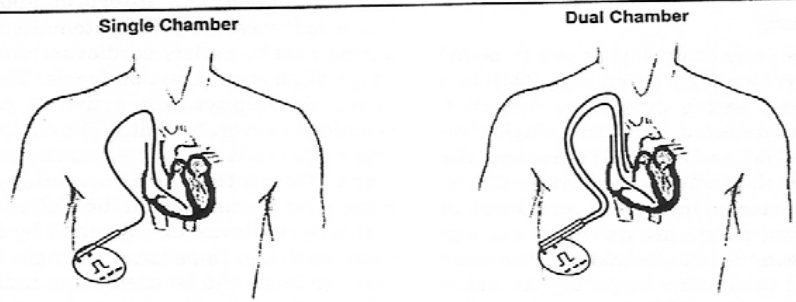


Figure 3. Single-chamber and dual-chamber pacemakers.

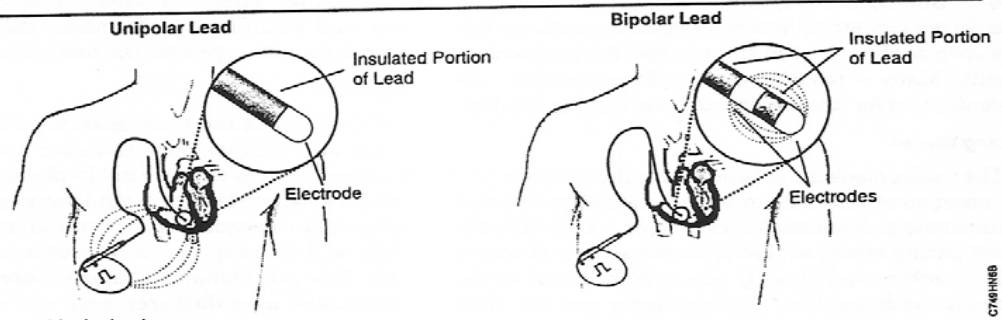
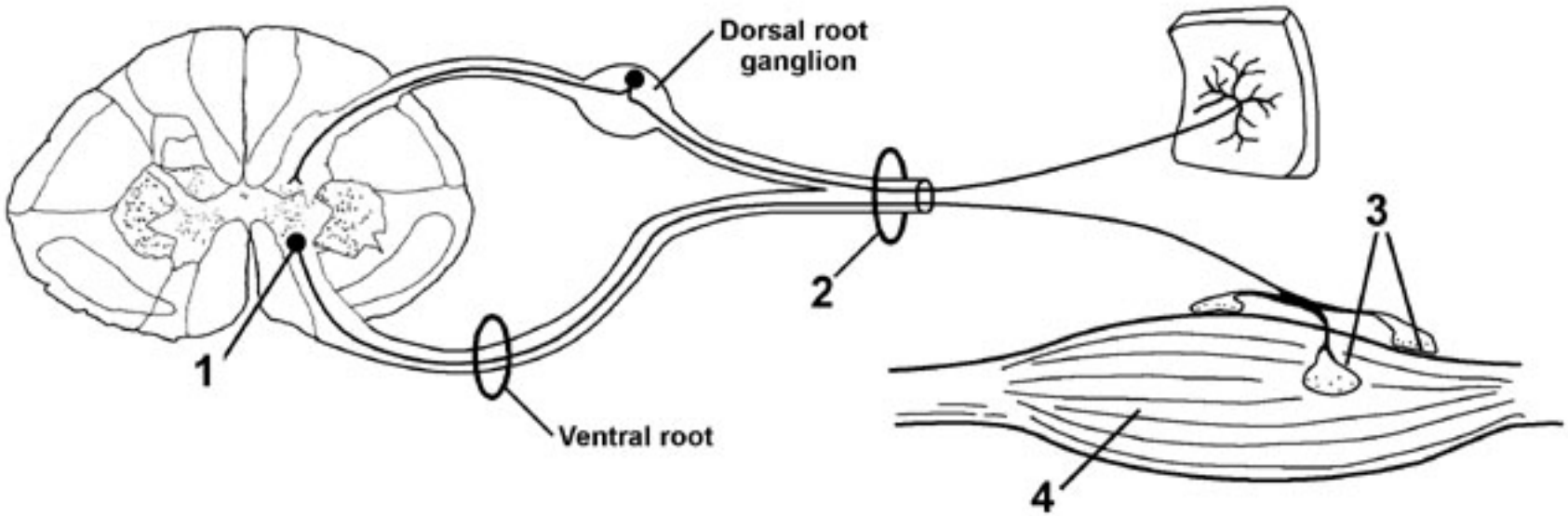


Figure 4. Unipolar and bipolar leads.

Functional electrical stimulation (FES)



To where should the electrical stimulus be applied?

Some electrode types:

1. Cuff electrode around nerve bundle

   pros: activates all the motor units in a muscle

   cons: simultaneous activation of all motor units; activates more than one muscle; stimulates afferent (ascending) sensory nerve fibers

2. Surface electrodes over muscle

   pros: only activates some motor units in a muscle; only activates one muscle or muscle group

   cons: simultaneous activation of all muscle fibers in a motor unit; stimulates *afferent* (ascending) sensory nerve fibers

Motor Unit Recruitment:

For nerve cuff electrodes, larger motor units tend to be recruited first. For surface electrodes MU proximity and size affect recruitment order.

However, under physiological conditions for *motor units*, small diameter fibers innervating slow oxidative (SO) muscle fibers tend to be recruited *before* larger diameter fibers innervating fast glycolytic (FG) muscle fibers.

Thus, the natural order of recruitment is reversed in FES.

Recruitment (cont.):

One approach to combat this recruitment-order problem is to utilize two electrodes.

The *first* electrode supplies a *large depolarizing current* that excites fibers with a large range of diameters.

The *second* electrode supplies a *small hyperpolarizing current* that *prevents action potential propagation* on the *large diameter fibers* excited by the first electrode.

The hyperpolarizing pulse must be designed with a ramp that prevents anode-break excitation.

Effects of Pulse Width

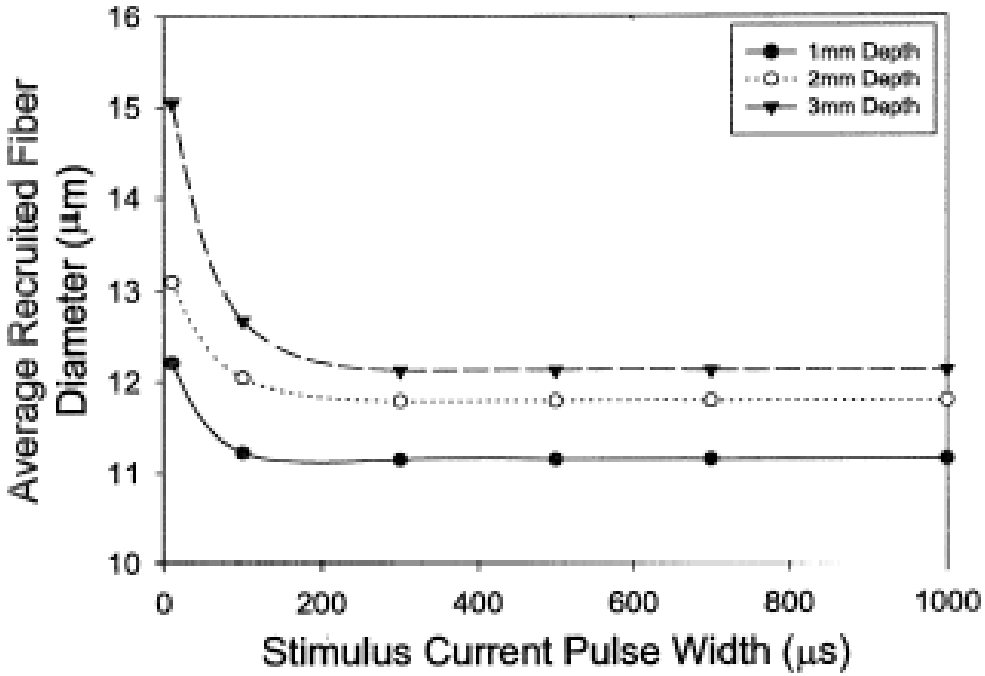


Fig. 4. Plot of simulations of average recruited nerve fiber diameter under conditions of variable stimulus current pulse width.

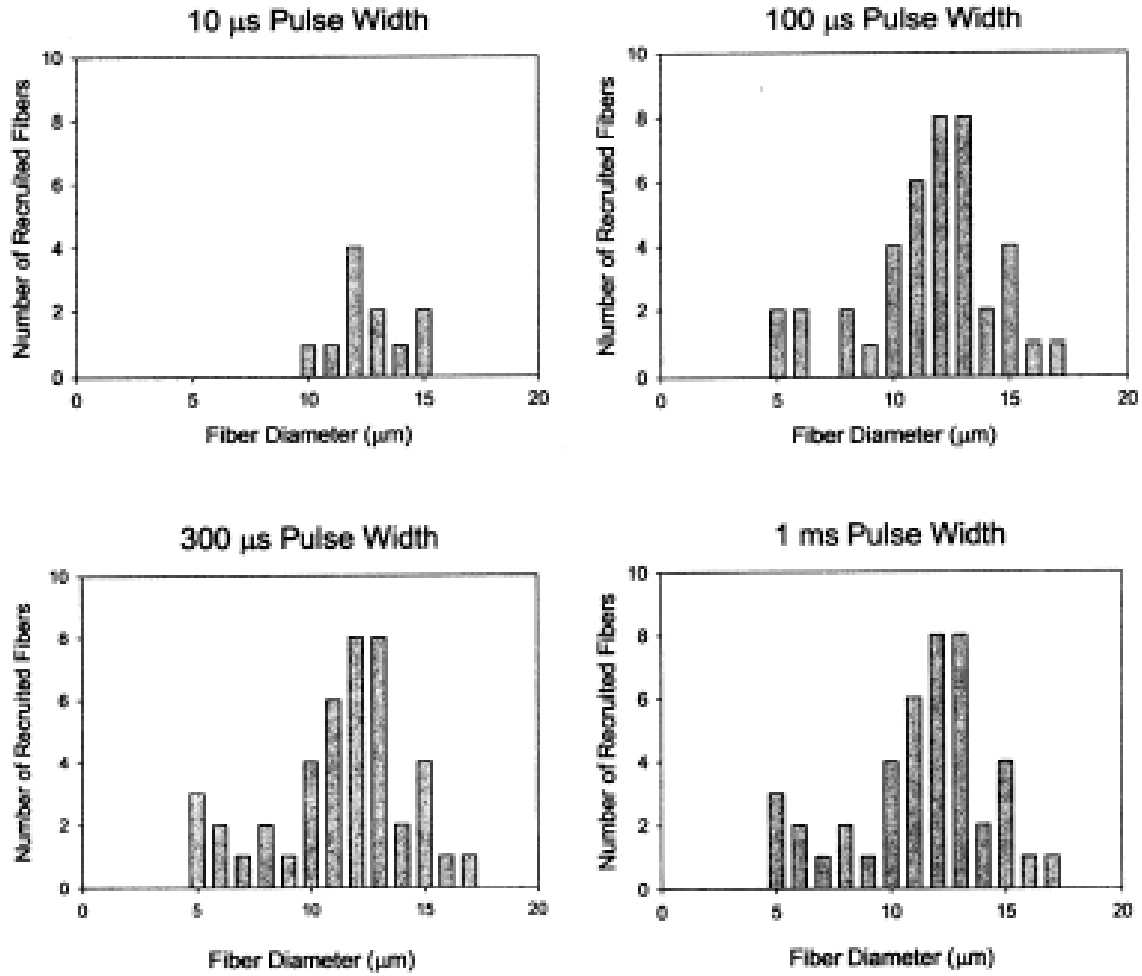
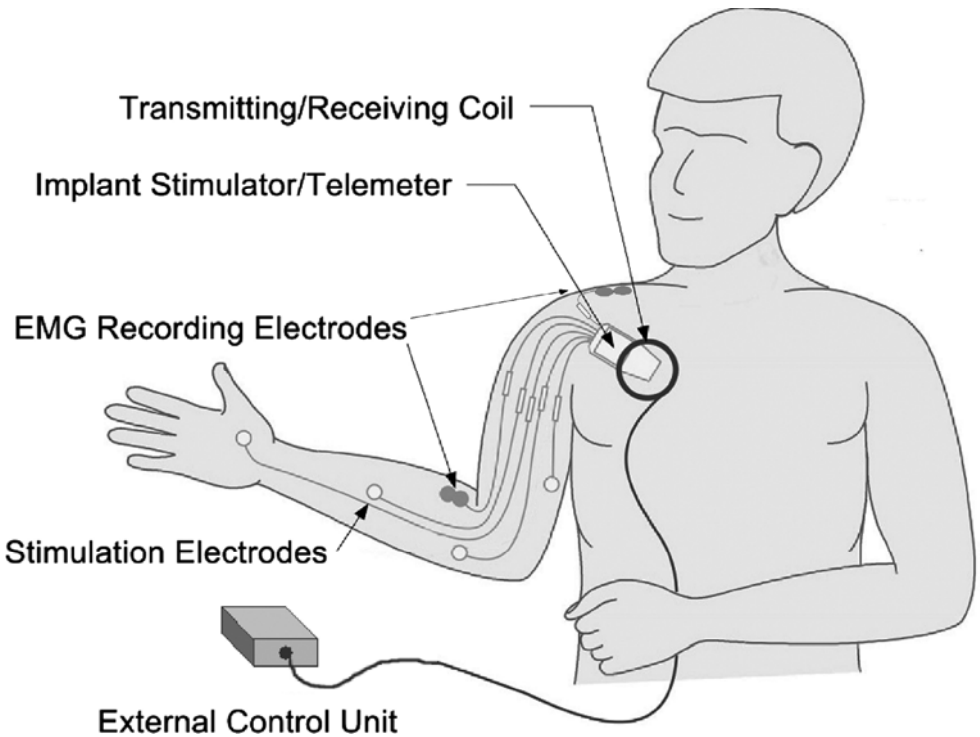


Fig. 6. Histograms of the recruitment order of nerve fibers in the 2 mm electrode fiber group spacing simulations. As can be seen from the histograms, the distribution or recruited nerve fibers remains the same for pulse widths between 300 μs and 1 ms.

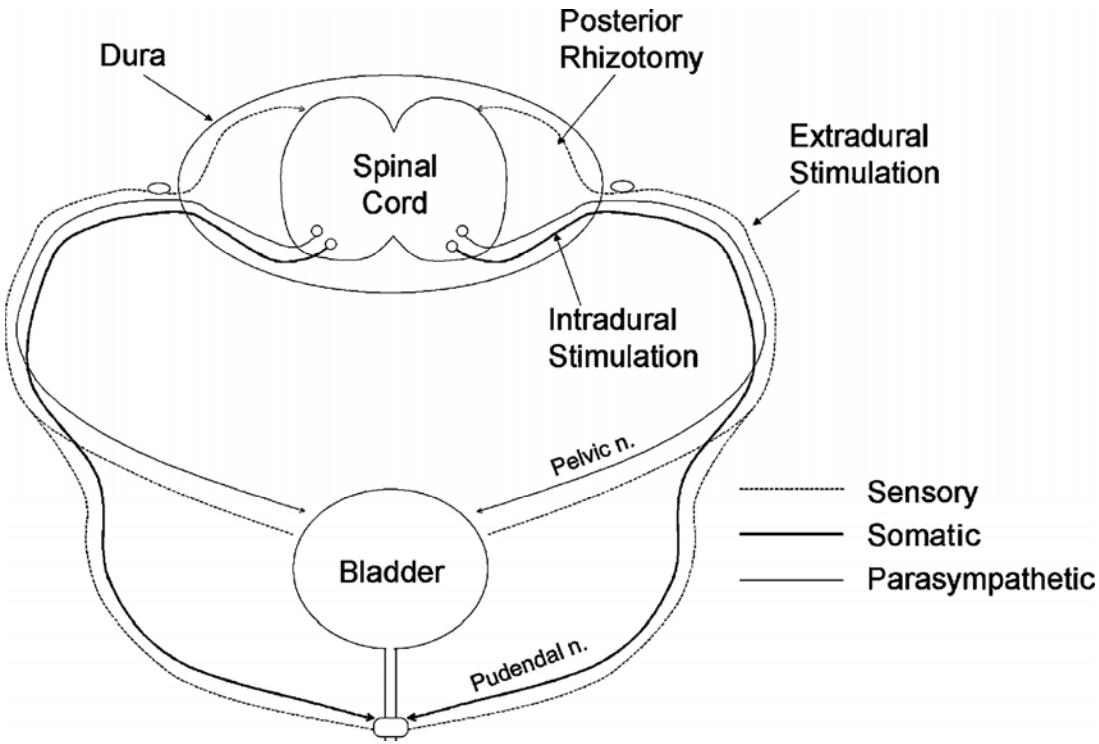
Upper limb stimulation:

- Stimulates peripheral nerve fibers of motor neurons
- Used in spinal cord injury or stroke patients



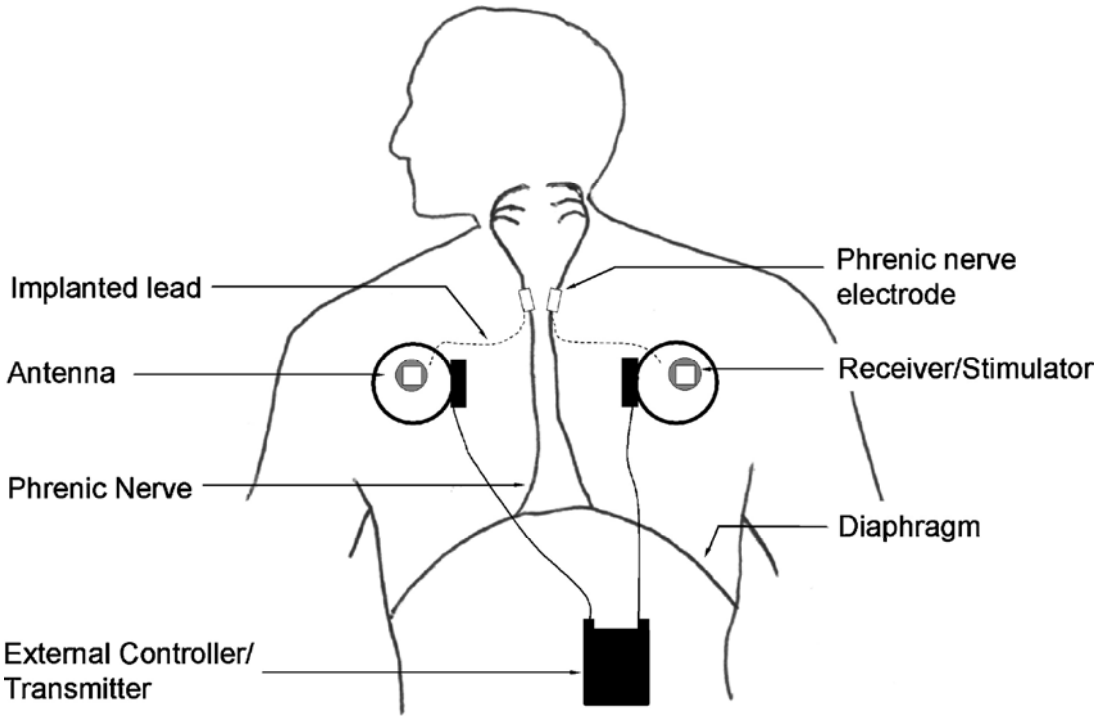
Bladder control:

- Intradural or extradural electrodes
- Stimulation can lead to bladder *and* sphincter contraction – intermittent stimulation can overcome this problem



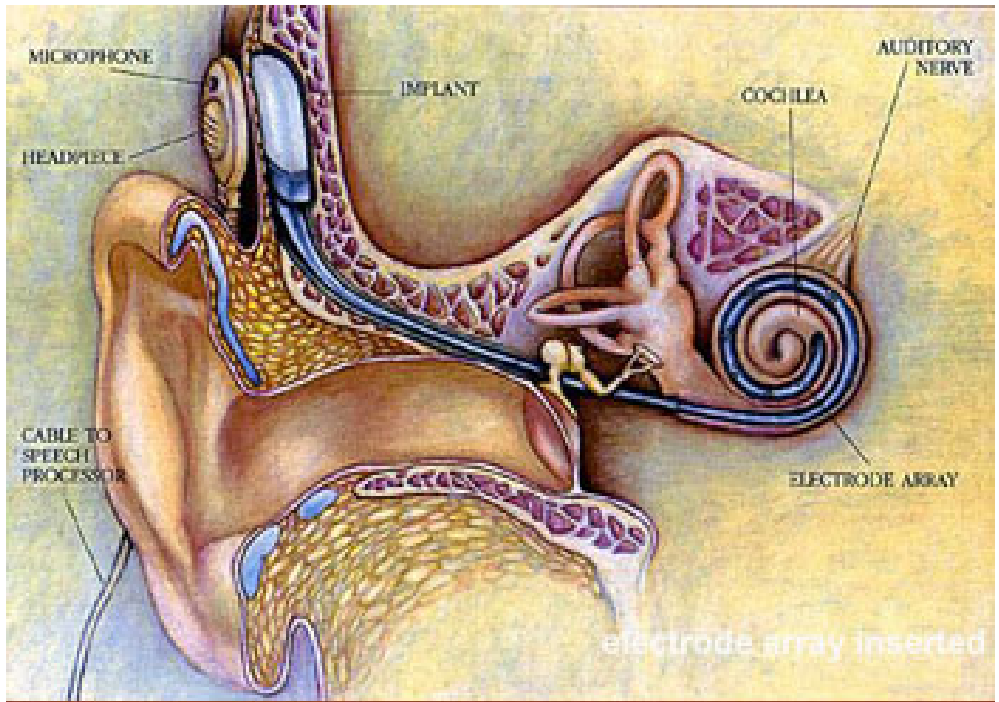
Phrenic nerve stimulator:

- Provides diaphragm pacing to aid respiration
- Bilateral stimulation for symmetrical activation of the diaphragm



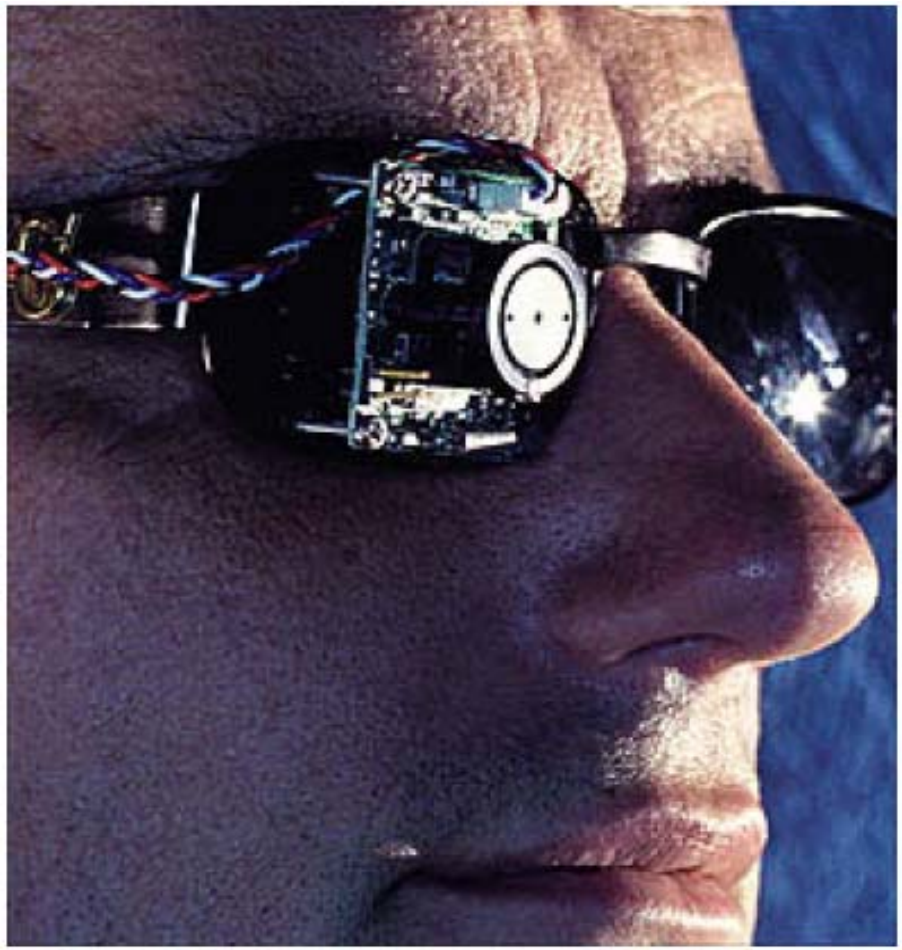
Stimulating Electrode

Cochlear Implant



Schematic of cochlear implant; note electrode array inserted into cochlea.

Prosthetic Advances
(Visual – Artificial Retina)



Direct Brain Stimulation

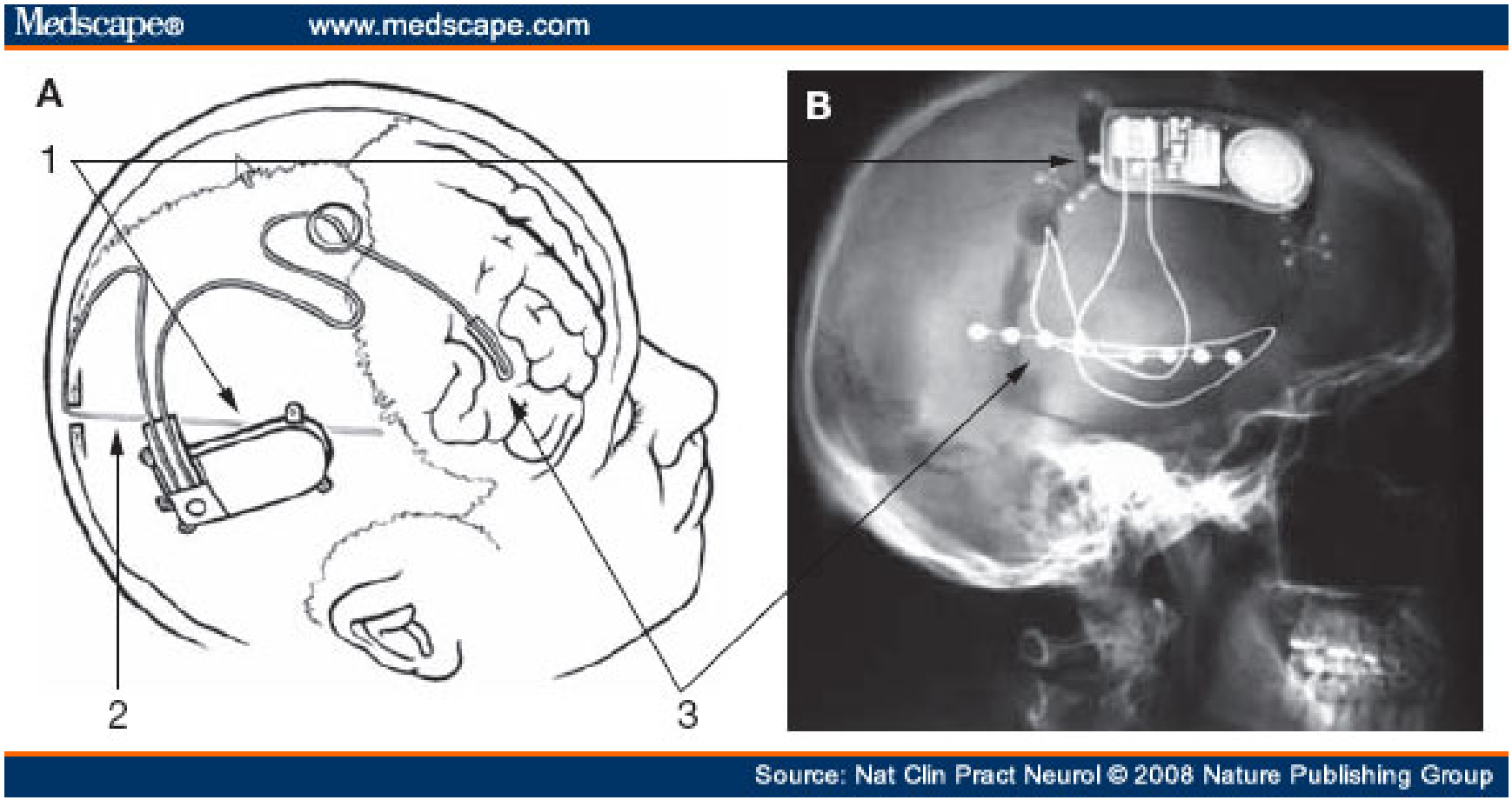
Therapeutic Brain Stimulation

- Intracranial cortical stimulation (e.g. epilepsy)
- ECT (transcranial electrical stimulation e.g. depression)
- Deep brain stimulation (e.g. Parkinsonism)
- Vagal stimulation (epilepsy, depression)*
- Transcranial magnetic stimulation (depression, schizophrenia)*

Problems Encountered

- Complexity of Brain (anatomical, neurophysiological) especially of frontal lobes
- Treatment mechanisms little understood (animal research suggests some mechanisms but human mostly hypotheses)
- Hardware well developed and flexible but treatment protocols either too rigid or too flexible
- Patient selection

Closed Loop Epilepsy Treatment



Movement Disorders
(Parkinsonism)

- Resulting from loss of neurons in substantia nigra (SNc) which produces dopamine
- Treated with dopamine agonist (short lived), monoamine oxidase inhibitor (less effective), dopamine precursor L-DOPA (gold standard)
- Biggest challenge is dose regulation (half-life of L-DOPA is 90 min)
- Less and less effective as deterioration of

Basal Ganglia

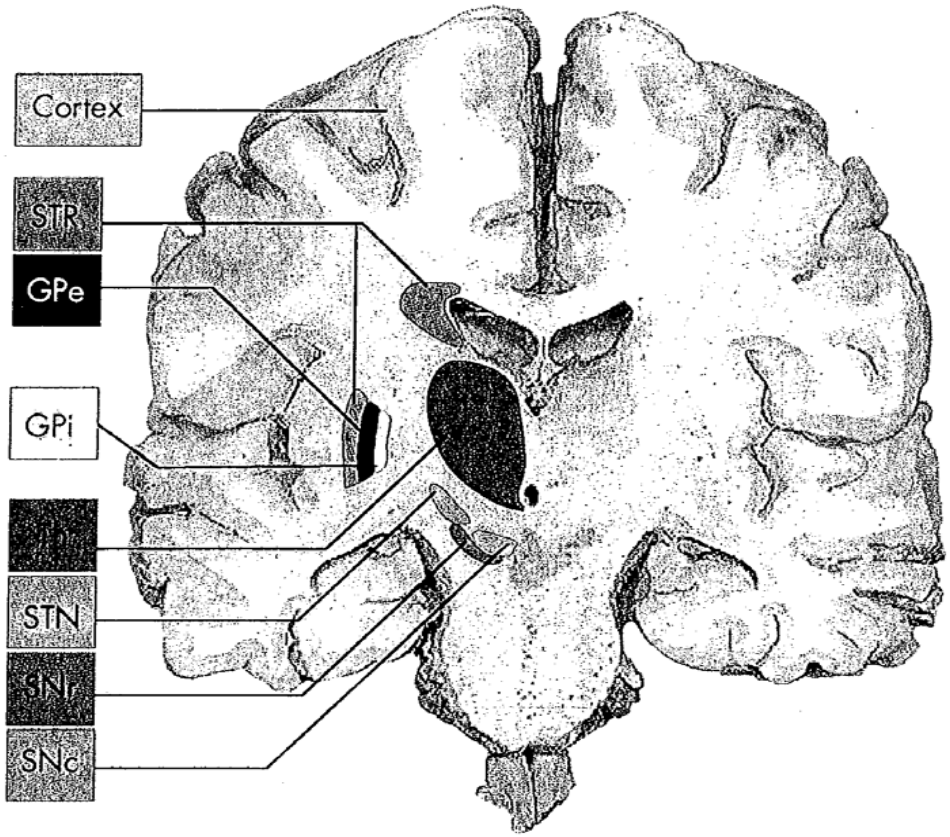
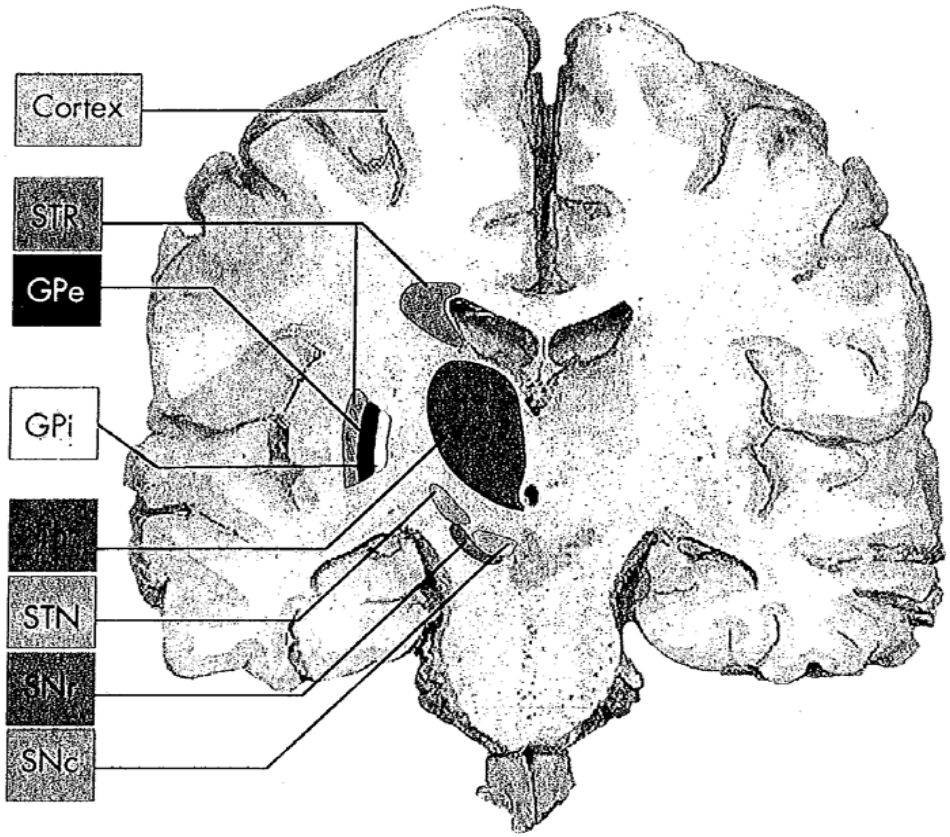


Figure 1 - Coronal (frontal) section of the brain showing the different structures in the basal ganglia. STR, striatum; GPe, globus pallidus pars externa; GPi, globus pallidus pars interna; Th, thalamus; STN, subthalamic nucleus; SNc, substantia nigra pars compacta; SNr, substantia nigra pars reticulata[14].

Deep Brain Stimulation

- Instead of ablation (to relieve tremor)
- First reported in 1987 with thalamus stimulation
- Globus pallidus next site with some success
- Subthalamic nucleus (1998) most successful with immediate relief of symptoms when stimulator turned on
- Stimulation of 60–200 μs pulses at >100 Hz
- Hypothesized result is inhibition, same as ablation

Basal Ganglia



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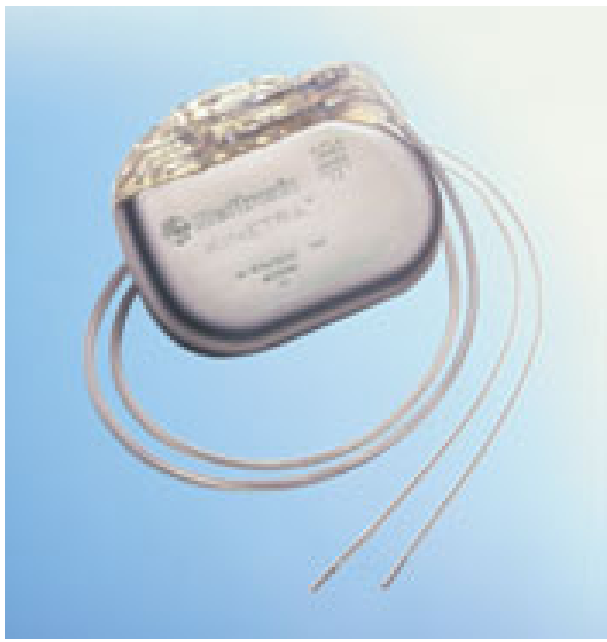
Basic Stimulator

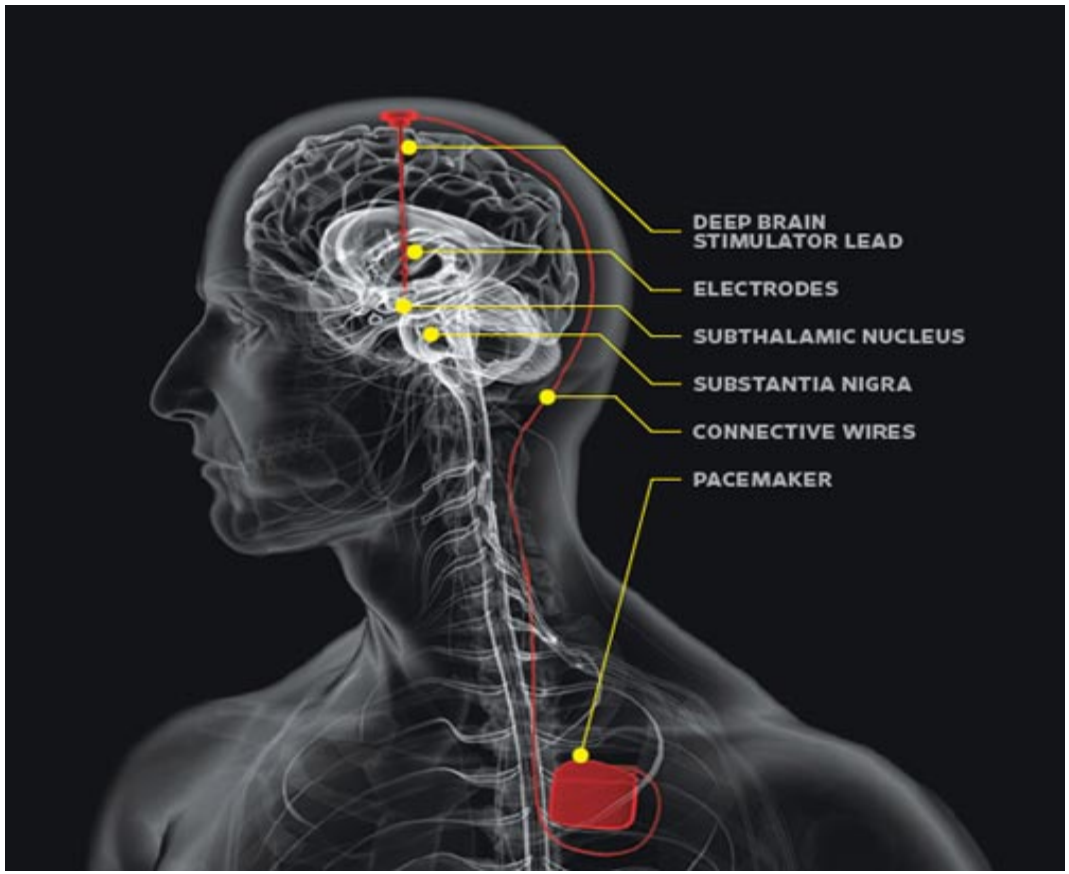
- Medtronic Kinetra Stimulator
- Treat Parkinson or other Movement Disorders



Deep brain stimulation (cont.):

- Stimulator and lead system

System to Control Movement Disorders



Deep brain stimulation (cont.):

- Example electrode placement

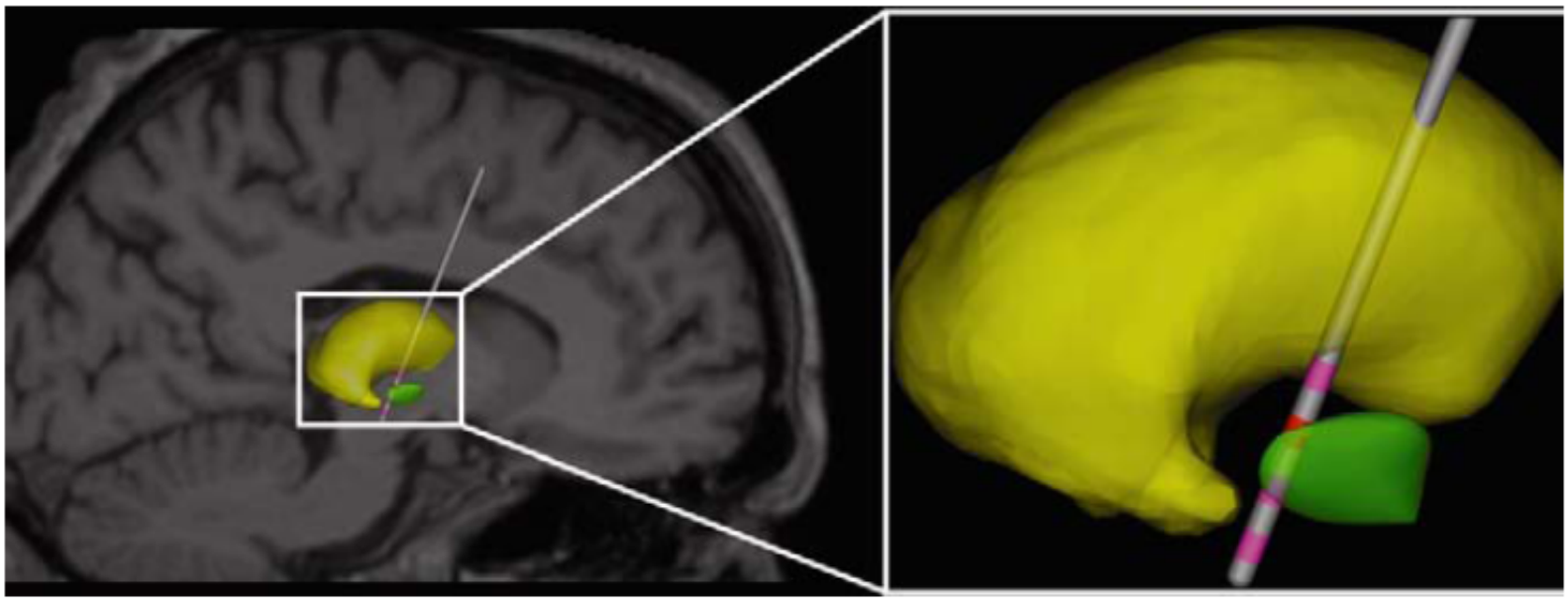
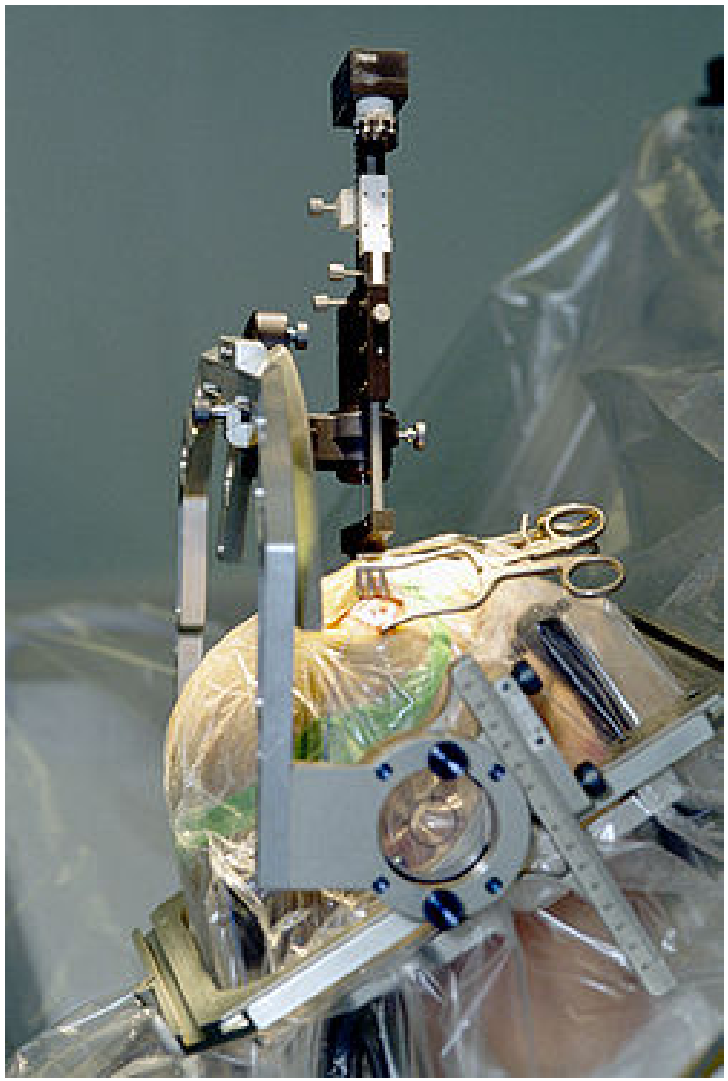


Fig. 1. Patient MRI scan with a 3D brain atlas warped to fit the thalamus (yellow) and STN (green). Right panel shows the position of the surgically implanted DBS electrode relative to the anatomical nuclei.

Electrode Insertion



Electrodes for Depression

Problems Encountered

- Complexity of Brain (anatomical, neurophysiological) especially of frontal lobes
- Treatment mechanisms little understood (animal research suggests some mechanisms but human mostly hypotheses)
- Hardware well developed and flexible but treatment protocols either too rigid or too flexible
- Patient selection

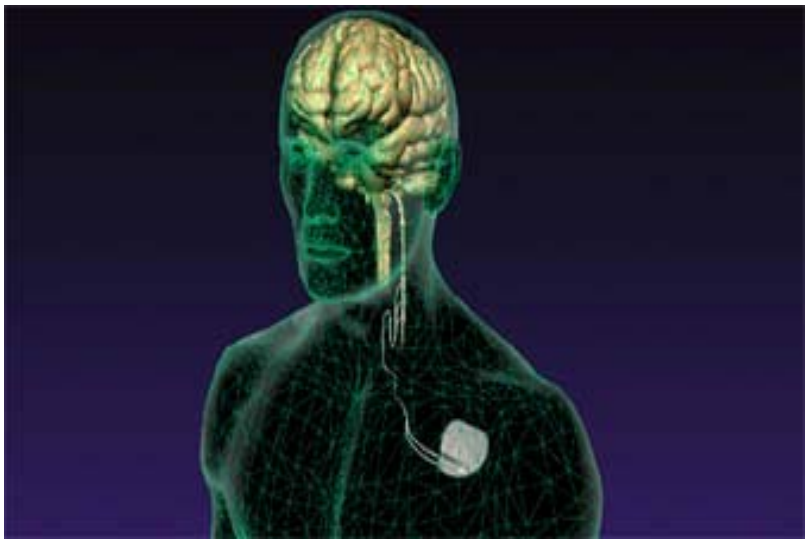
VNS: Vagal Nerve Stimulation Possible Mechanisms

- Alters CSF concentrations of neurotransmitters (e.g. GABBA) or their metabolites
- Alters functional activity of orbital frontal cortex, insula, thalamus, hypothalamus, etc.
- Anticonvulsants have been shown to have therapeutic value in mood disorders

VNS: Vagal Nerve Stimulation Clinical Results

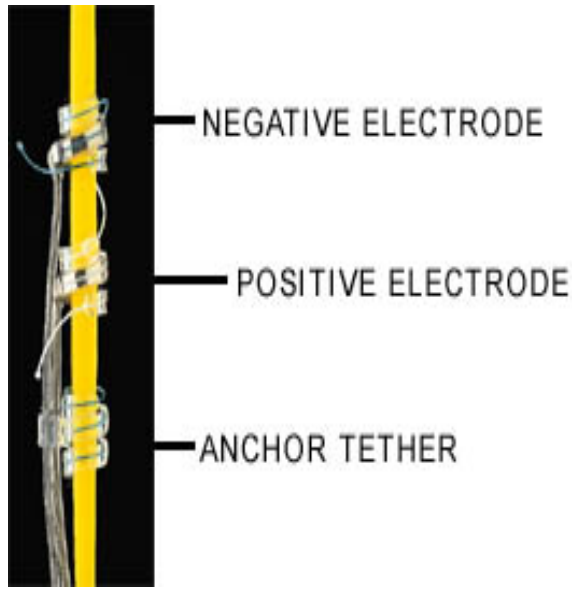
- Reduction in epileptic seizures (29,000 Cyberonics implants by 2005) few side effects
- 21 centre trial for major treatment-resistant depression 222 patients (Rush et al, Biol Psychiatry 2005)
- After 10 weeks 15% responded ($\geq$ 50% improvement in HRSD) in treatment group vs 10% responded in sham group (not sig.)
- Longer term response rates more encouraging

Cyberonics VNS System



- Pacemaker similar to cardiac pacemaker
- Cuff electrodes on left vagal nerve
- Patient or caregiver parameter adjustment via magnetic field

Pacemaker and Electrodes



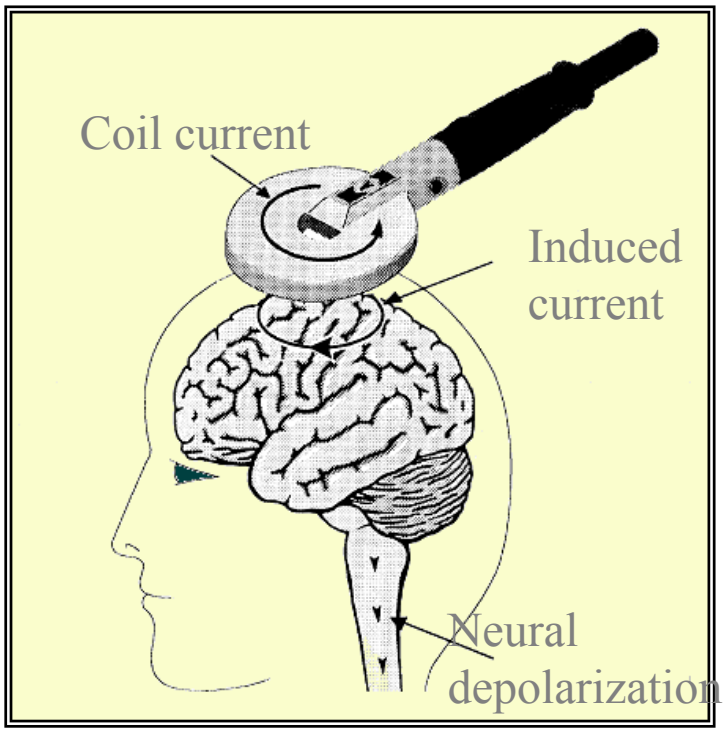
Treatment Settings

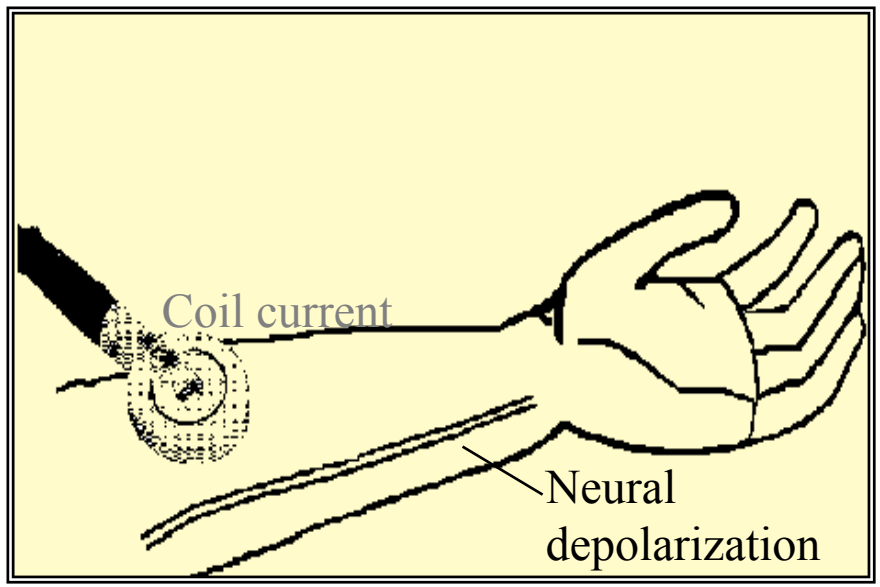
- Output current 0 -3.5mA: median last visit .75 ma, range .00 – 1.5 mA; start .25 mA (Rush)
- Signal frequency 1 – 30 Hz: median 20 Hz, range 10 – 20 Hz; start 20 Hz (Rush)
- Pulse width 130 – 1000 μsec: median 500 μsec, range 130 – 500 μsec; start 500 μsec (Rush)
- On time 7 – 60 sec, median 30 sec, range 14 – 30; start 30 sec (Rush)
- Off time .2 – 180 min: median 5 min; start 5 min (Rush)

rTMS: Repetitive Trans-Cranial Magnetic Stimulation

- Treat severely depressed patients who are resistant to pharmacology
- Alternative is periodic applications of electro-shock (ECT) treatment
- 30% of patients respond
- Would like to increase percentage of responders

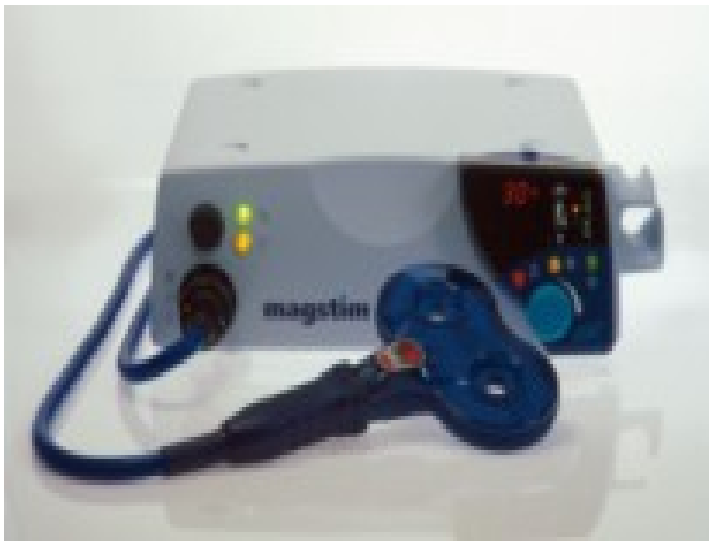
Magnetic Nerve Stimulation (MNS)



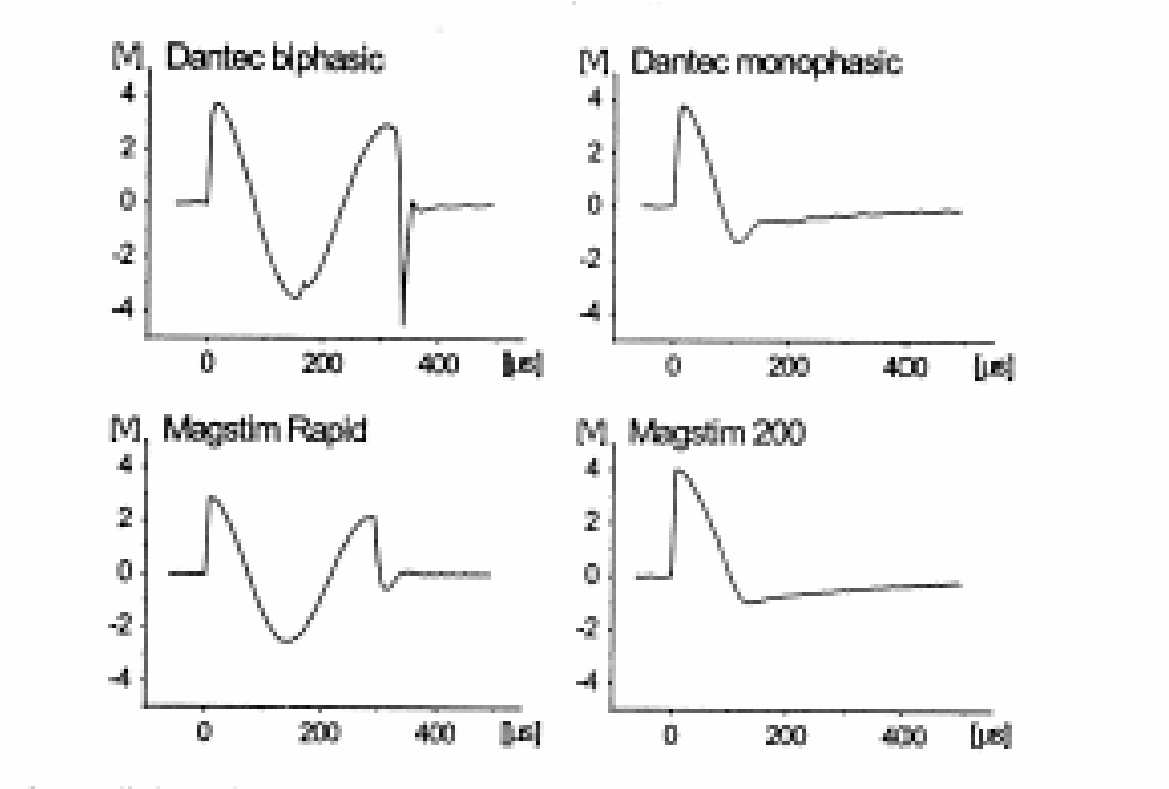


Current Commercial Machines

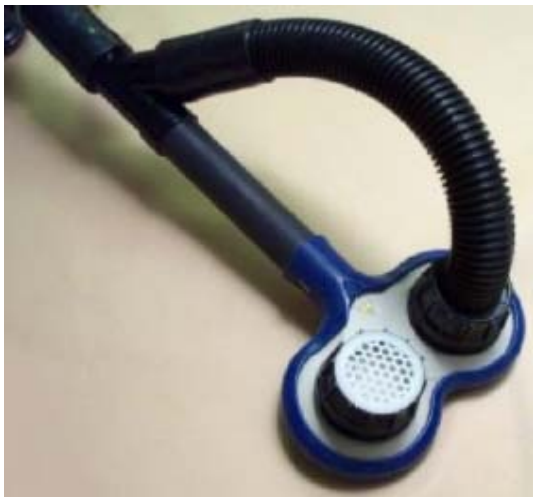
- Example Magstim



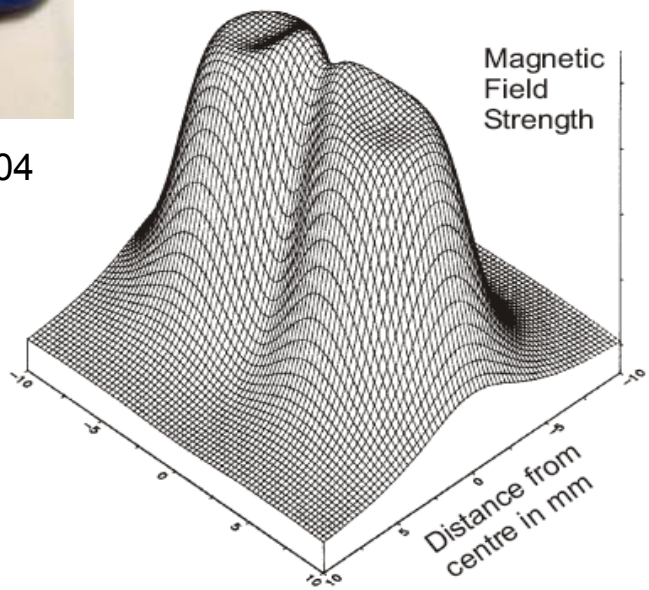
Stimulus Waveforms

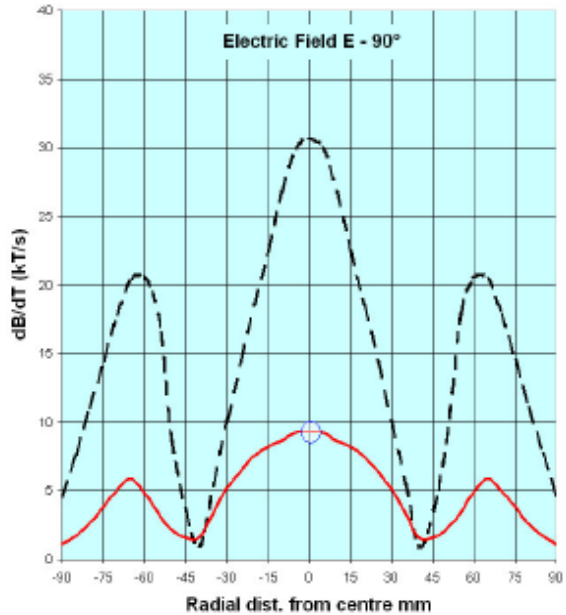


Magnetic Field



Source: Medtronic, 2004





Source: Medtronic, 2004

Source: Medtronic, 2004

Treatment Protocol

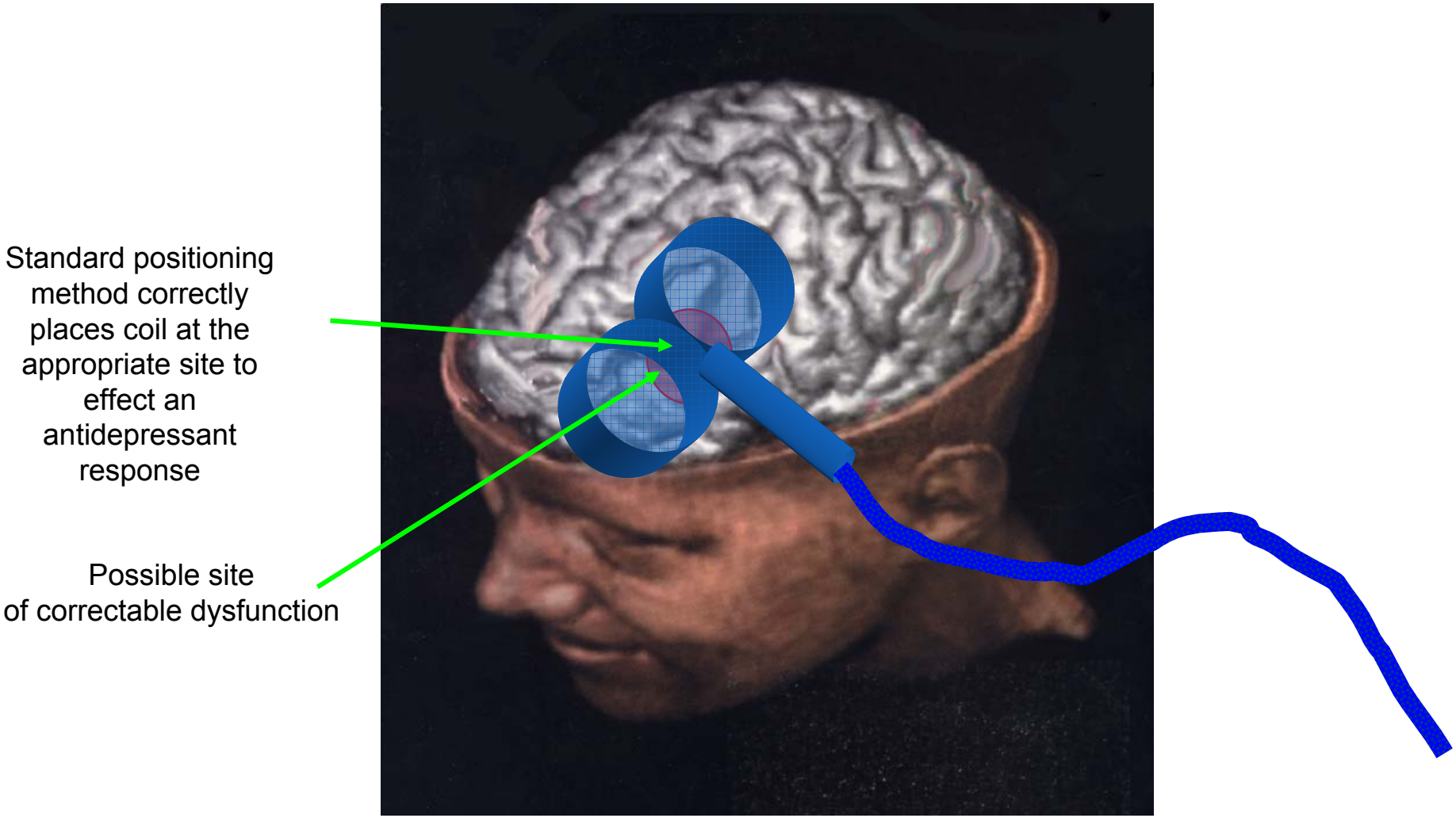
- Find left thenar (abductor pollicis brevis) motor cortex stimulation point by monitoring M-wave of right thenar muscle
- Stimulate left frontal lobe (F3) at point 5 cm anterior to this site on a sagittal line
- Using a fixed % (80 – 120) of thenar threshold amplitude stimulate at 8 to 10 Hz for fixed periods up to 1800 stimuli; several clinics 3000 stimuli
- Repeat 4 to 5 times/week for 5 weeks

Clinical Treatment

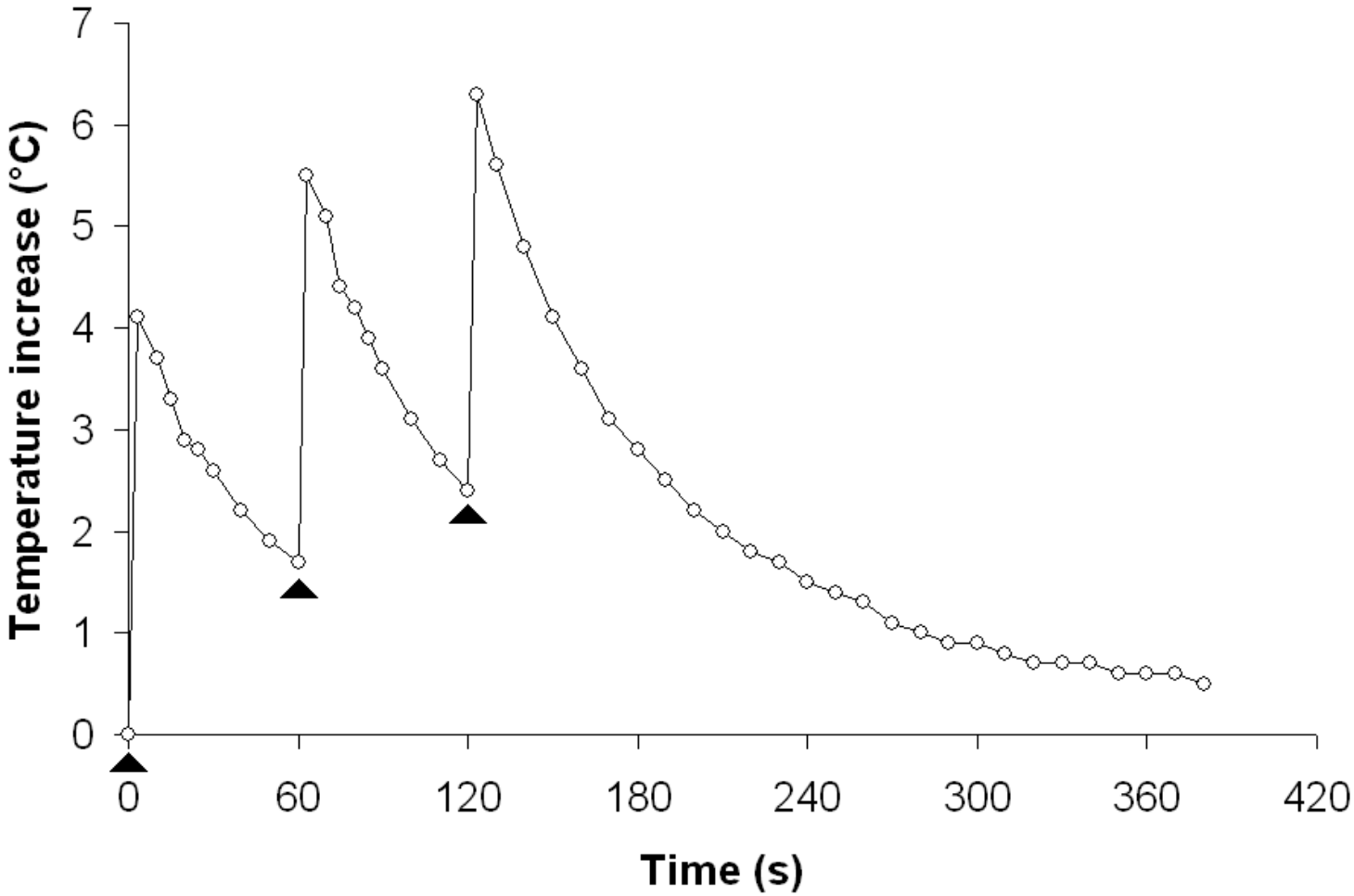
Research Challenges (Objectives)

- Develop quantitative method for predicting which patients will respond to rTMS (use pre treatment EEG parameters, QEEG)
- Develop quantitative method for determining best site of stimulation
- Determine effects of changing stimulus amplitude and frequency

Figure 11
Other subjects respond as their head size is such that standard methods place the coil over the site of possible dysfunction (detectable using QEEG)



rTMS Trains of Stimuli

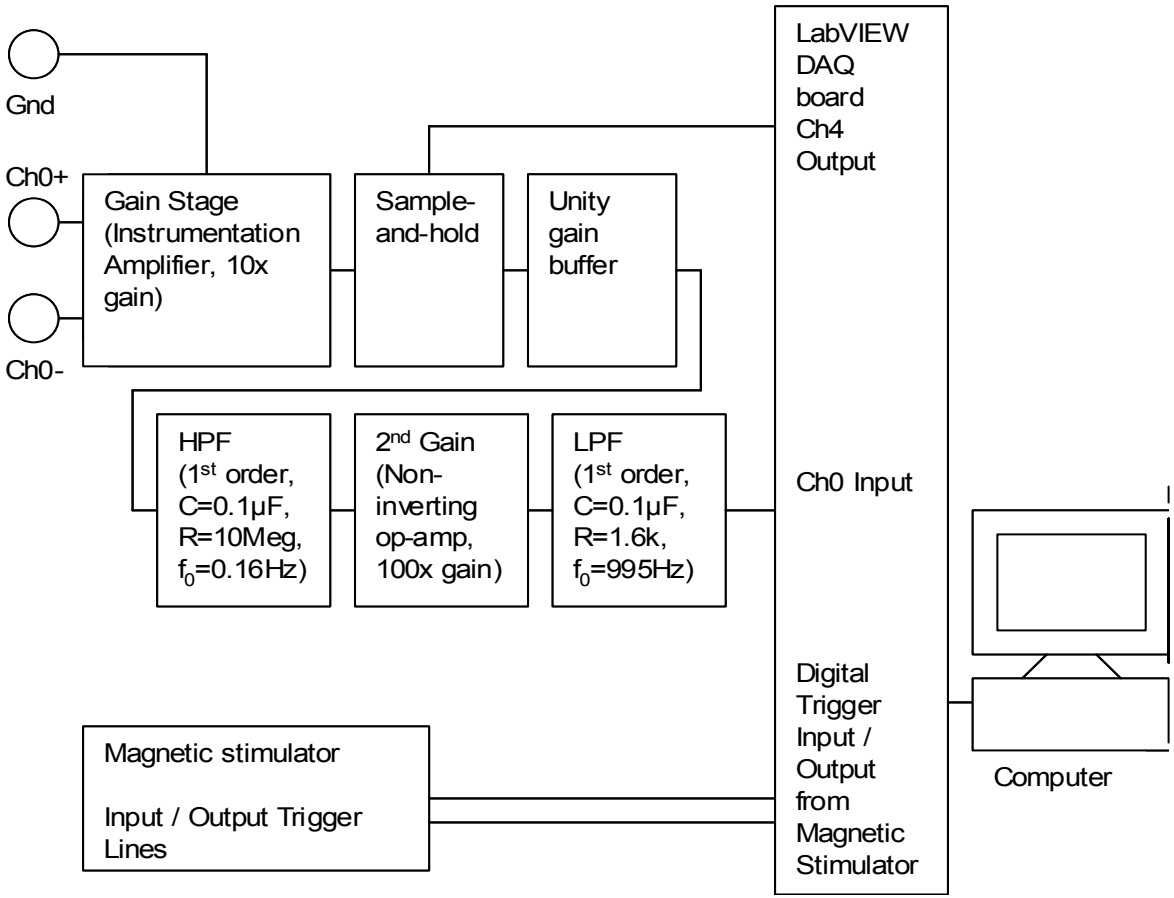


Au electrode, 3s at 20Hz at 85% intensity, trains at 0, 60, 120s

Artifact Blocking

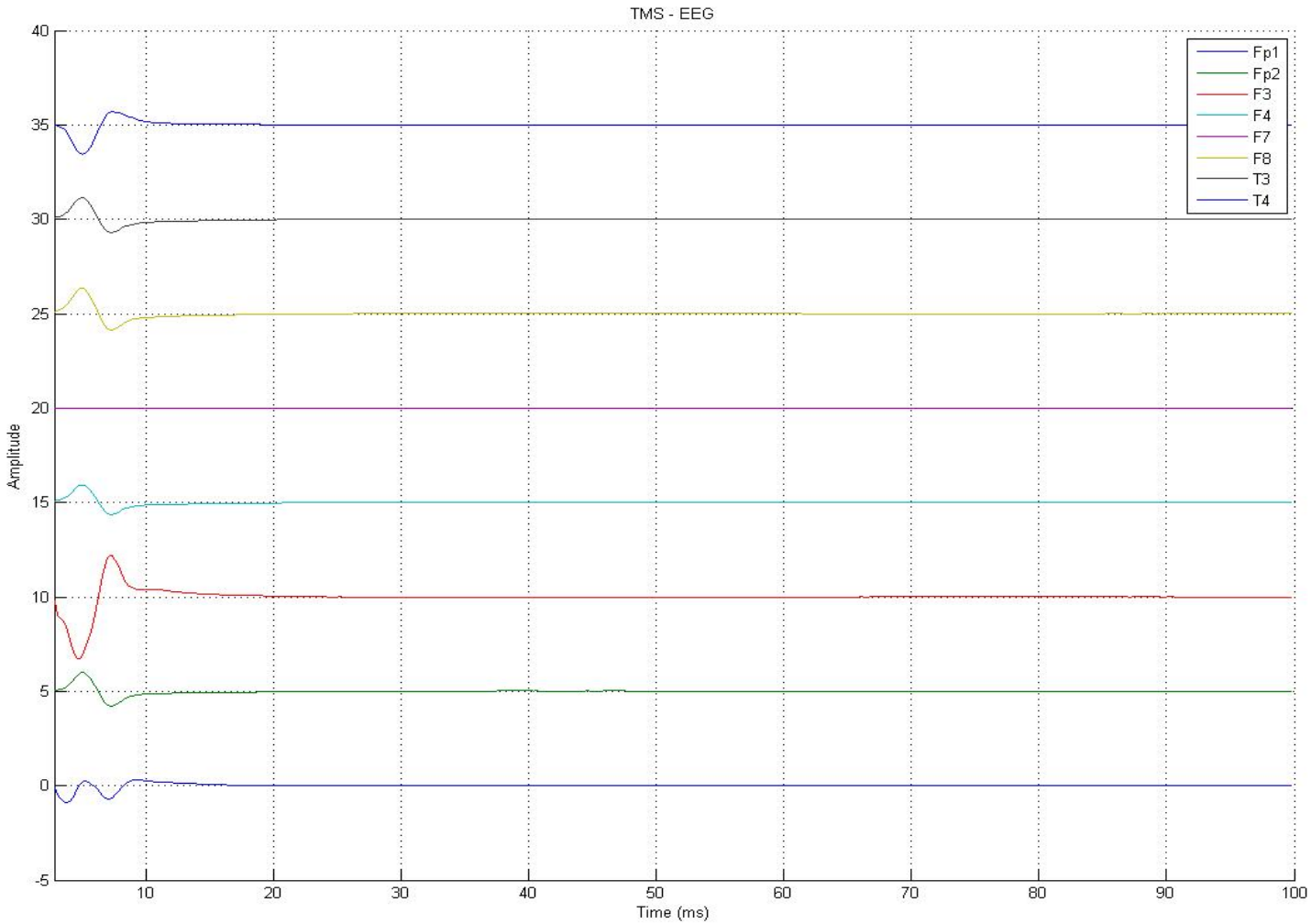
- Various methods have been used:
  - Low slew rate amplifiers (Thut, 2005, Ives, 2006)
    - First 30ms of signal lost and bandwidth reduced
  - High bandwidth amplifiers (Fuggetta, 2005)
    - First 15ms of signal lost
  - Switching off the amplifiers (Shutter, 2006)
    - First 200ms of signal lost
  - Sample-and-hold circuit (Ilmoniemi, 1997)
    - Works, published results ignore or mask first 10 ms

Systems Approach



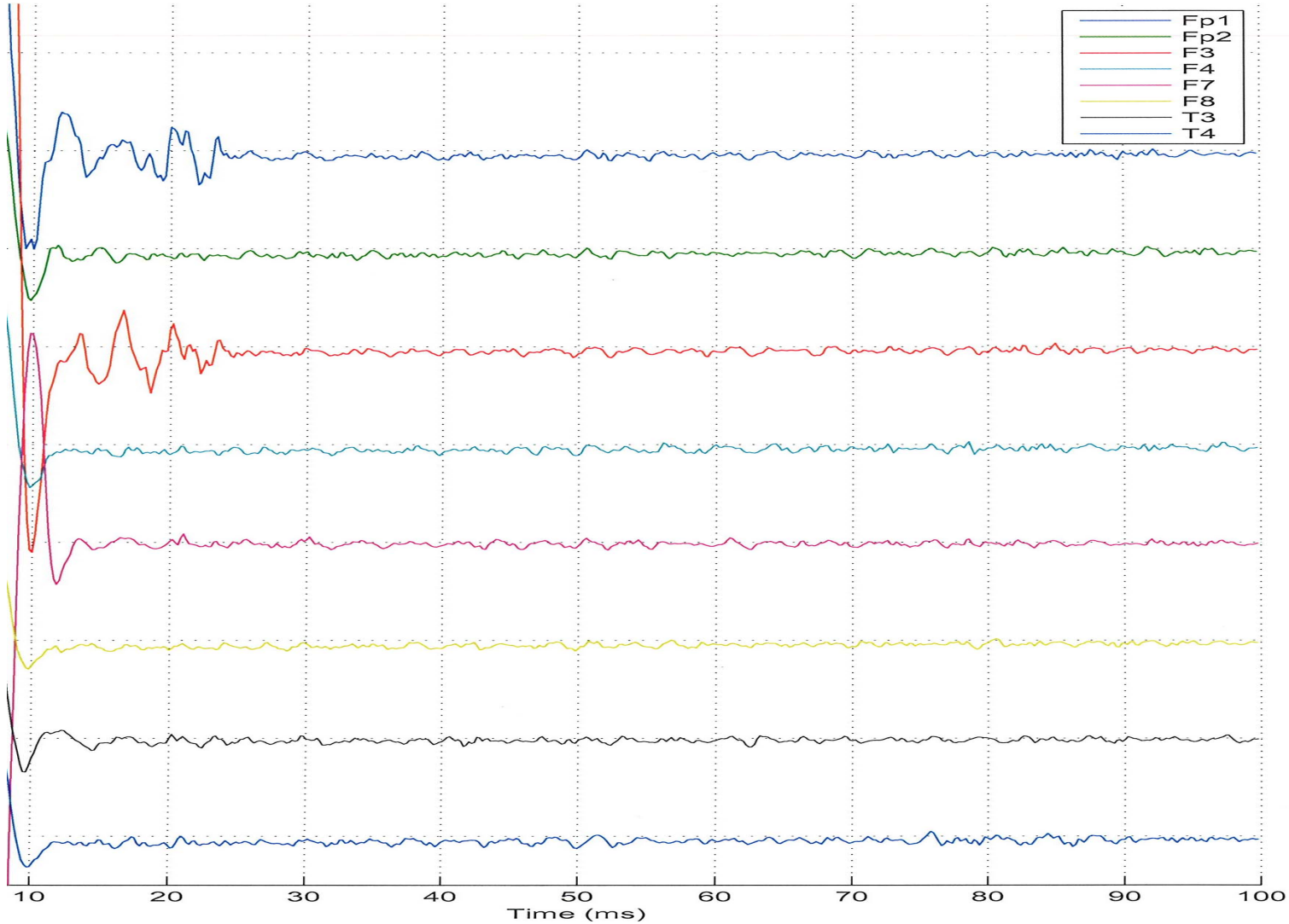
8 Channel Average Results

8 Hz, 10 sec, Brodmann 46, 69% max, scale mv



Brain Response Left Side

(20 μV between traces)



Brain Response Right Side

(20 μV between traces)