Electro-Convulsive Therapy (ECT)

An update
Depression

Meanings and implications

Social

Cultural

Medical
Depression

Medical Models

Continuum Model
Mild ------------ Severe
ICD.10

Discreet Illness Model
Reactive---------Endogenous
ICD.9
Depression
A Possible Hierarchical Approach

- Depressed Mood
- Reactive Depression
- Mild Depression
- Moderate Depression
- Puerperal Psychosis
- Manic Depressive Psychosis
- Psychotic Depression
- Agitated Depression
- Severe Depression
- Retarded Depression

Mild to Severe
Depression
Signs and Symptoms

Normal to Mild
- Anxiety
- Appetite changes
- Sleep-Initial insom
- Depressed mood
- Mood Swings p.m.
- Conc. Poor.
- Cognition intact
- Soft mood and memory dysfunction
- If pushed, can function OK
- More Subjective

Moderate
- Appetite reduced,
- Sleep- E.M.W
- CV changes, temp
- Conc/cognition
- Memory- O.C
- Mood Swings a.m.
- Delusions/Halls
- Agit/Retardation
- Speech dysfunction
- General Function impaired
- Social functioning impaired
- More Objective

Severe
Depression (Severe) (Right column)

Signs/Symptoms---Clustering

- Executive/Social Functioning
  - Social interaction
  - Inter/intra personal skills
- Perception of SELF
  - Thought/Delusions of guilt and worthlessness
- Emotion Memory
  - Memory issues
  - Flattening of emotions
  - Poor concentration
- Sleep, digestion, CVS, temp arousal
  - Bodily functions
  - Agitation, retardation
- Thought Processes
  - Reasoning, problem solving
Depression (Severe) 
Signs/Symptoms---Brain Regions

- Social interaction
  - Intra/inter personal skills
- Thoughts/Delusions of guilt and worthlessness
- Memory issues
- Flattening of emotions
- Concentration
- Bodily functions
- Agitation, retardation
- Reasoning, problem solving, language problems

Frontal Cortex

Ventricular medial PFC

Limbic System

Brain Stem, Autonomic Sym

General Cortex
Depression (Severe)
Signs/Symptoms---Brain Regions---Common Factor?

Frontal Cortex

Ventricular-medial PFC

Limbic System

Brain Stem, Autonomic Sym

General Cortex

Ventricular-lateral pre-frontal cortex
Depression (Severe)  
Pre-Frontal Cortex Dysfunction

Evidence from:

- Cerebral Blood Flow Studies (Drevets et al 1997)
- Functional PET scans (Increased frontal metabolism and connectivity, Y.L. Sheline PNAS April 2010)
- EEG Studies (Frontal over-activity and hyperconnectivity with other areas, Andrew F. Leucher. Feb 2012)
Sites of abnormal blood flow in depression
Drevets et al 1997
regions, although the patterns of connectivity involving these nodes differed by frequency: in the alpha band, these nodes were involved in significantly longer distance edges than in the beta band. Examination of the most significant edges in the alpha band showed that the connections were between the frontopolar or DLPFC regions and the temporal or parieto-occipital regions, whereas in the beta band, the connections were most often found between the prefrontal, temporal, or less often the parieto-occipital regions.
Depression (Severe)

Over activity in V.L. pre-frontal cortex can be seen as a diagnostic pointer for depressive illness
Depression (Severe)  
Pathways/Connections in Dep. Illness

- Over activity of VLPFC
- Excessive (white noise) output to other areas
- Dysfunctional result

Executive/Social decisions

Perception of SELF

Emotion Memory

Sleep, digestion, CVS, temp arousal

Thought processes
Depression
Theories of Depressive Illness

Neurobiological causes
- Neurotransmitters and neuromodulators
- Endocrine Factors
- Neurogenesis
- Gene expression

Systems Level
- Areas involved: Pre-frontal cortex with connections to frontal cortex, limbic system and hypothalamic pituitary adrenal axis
- Result is the clinical presentation (Final Common Pathway)
Depression (Severe)
Theories of Depressive Illness

No longer thought to be due to single neurotransmitter deficit but now a systems level disruption. Now considered to be a combination of:

- loss of regional brain volume
- reduction in neuroplasticity
- over activity of ‘default mode’ network
  GABA reduction and increase in hyperconnectivity
Working Model of Depressive Illness

Loss of ‘braking effect’
?? GABA reduction

‘Default Network’
overactive, includes VLPFC.

Dysfunction

Signs and Symptoms resulting

Loss of social skills

Dels. of guilt, nihilism and worthlessness

Sleep/bowel/temp/appetite

Slow ponderous thinking, retardation

Flat mood, memory issues

Frontal cortex

VM PFC

Autonomic system

Cortex

Limbic system

‘Default Network’

VLPFC

?Primary ?Secondary Effects
Electro-convulsive therapy

The induction of a controlled epileptiform seizure in an anaesthetised and paralysed patient, by the passage of a titrated electric current though the cerebral hemispheres.
BBC Video Clip

bbc.co.uk/news/health-23453426

3.25 minutes to end of treatment phase at 6 minutes
Clinical Global Impression of change post ECT

Episode entry  Episode exit
CGI score (entry)
1
2
3
4
5
6
7
Mean CGIC score (exit)
Normal; not at all ill
Borderline mentally ill
Mildly ill
Moderately ill
Markedly ill
Severely ill
Extremely ill
Capacity                                      No capacity

Very much improved
Much improved
Minimally improved
No change
Minimally worse
Much worse
Very much worse
HRSD 50% reduction after 3 treatments
How does ECT work?

- Anticonvulsant (1)
- Receptor modulator (2)
- Neurotrophic (BDNF) (3)
- Changes in gene expression(4)

1) Sackeim, The anticonvulsant hypothesis of the mechanisms of action of ECT: Current Status
2) Sattin A, The role of TRH and related peptides in the mechanism of action of ECT
3) Krystal A & Weiner R, EEG correlates of the response to ECT

All in The Journal of ECT vol 15 1999
4) Fochtmann LJ, Genetic approaches to the neurobiology of ECT. J of ECT 1998;14:206-19
Mechanism of action of ECT

- Normalisation of ventro-lateral PFC
- ECT may affect structure of hippocampus
- ECT may reduce CBF and CMR in PFC
- Normalisation of reduced GABA-ergic and Glutamate in PFC
- Normalisation of the HPA axis and central cortisol feedback
- Affects gene expression, neurogenesis (increase in BDNF) and synaptic plasticity
After ECT

- Decreased blood flow frontal areas
- Upregulation of genes producing BDNF
- Increased hippocampal neurogenesis
- Increased hippocampal plasticity
- 5% increase hippocampal volume
- Reinstatement of negative feedback loop for cortisol
- Increased GABA function
- Reduced 5HT2 receptor activity (excitatory)
- Increased DA receptor numbers and DA levels
Concerns of ECT today

- Efficacy of treatment
- Cognitive side effects
- Risks of treatment
- Consenting issues
ECT Variables

- Electrode position
- Stimulus current
- Wave/Pulse details
- Treatment frequency
Electrode position

- Bi-Lateral position
  a) Bi-temporal
  b) Bi-frontal

- Uni-lateral position
  a) Right side (default)
  b) Left side
Stimulus current

- Dosage measured in milli-coulombs (mcs)
- Dosage varies 25 – 504 mcs
Wave form and frequency

- Square pulse form, 0.5 to 1.5m/s
- Frequency. dose dependent
Recent research

‘Bifrontal, bitemporal and right unilateral electrode placement in ECT: randomised trial’
Kellner C.H. et al
BJPsych (2010) 196, 226-234

Recent research / article by Kellner et al, resolved issues and established treatment protocols regarding electrode position and stimulus dose and relates them to efficacy and cognitive issues.
Research findings

- To be therapeutic the stimulus current must exceed the seizure threshold by 1.5-2X (Bil) or 6-8X (Uni)
- All positions reduced HRSD score by 50%+ after 3 treatments, Bi-temp > Bi-front > R-unilat
- After 10 treatments, HRSD scores show Bi-temp = Bi-f ront > R-unilat
- Bi-front showed sl. more memory problems (short term) than Bi-temp and R-unilat
- Time to reorientation best for R-unilat < the other two
- Memory testing at 2/52 post-treatment shows no difference
Treatment protocols

• For ECT to be therapeutic, seizure must be of a finite intensity and duration (EEG = 3 stages)
• Seizure threshold needs to be identified for each patient
• Therapeutic seizure follows a stimulus current of 1.5 - 2 times threshold current for Bilateral and 6 - 8 times for Uni-lateral
• EEG shows
  a) low amp spike/wave (cortex)
  b) 7-10 sec run of delta waves (deep structures)
  c) post-ictal suppression
ECT procedure

Diagnosis
Consent etc
Work up
Anaesthetic
Treatment
Recovery
Review
ECT procedure (treatment)

- Set/ monitoring for basics
- I.V access
- Anaesthetic
- Set up for ECT
- Muscle paralysis
- Treatment and review (EEG)
- Anaesthetic recovery
- General follow up and monitoring
EEG recording therapeutic seizure
Risks/Adverse effects of ECT

- Pre-treatment risks
- Risk effects of stimulus current
- Risk effects of seizure
- Post-treatment adverse effects/risks
  a) Short term
  b) Medium term
  c) Long term
These are the risks

- Consent issues (capacity and status)
- Stimulus current:
  a) Teeth and jaw injury (direct stimulation)
  b) Muscle / bone injury (un-modified)
  c) Bradycardia / Asystole, Hypotension (Vagal Nerve effect)
These are the risks

• Seizure:-
  a) Tachycardia / Hypertension (Symp ++)
  b) Non-therapeutic seizure
  c) Prolonged seizure

• Post-treatment:-
  a) Confusion, headache etc (an+ elec+ fit)
  b) Short term memory issues (an+ elec+ fit)
  c) Long term, ?Auto-Biographical  ??None. Other causes (depr, meds, organic brain dis.)
Indications for ECT

• Clinical indicators
• NICE guidelines
• Patient’s choice
• Patient’s past history
Predictors of outcome

- Retardation and psychosis predictive of better outcome (Buchan et al 1992, Petrides et al 2001)

- Poorer response in antidepressant-resistant patients, who also have a higher relapse rate (Prudic et al 1996, Sackheim et al 2001)

Today ECT – Tomorrow TMS??

- TMS (Trans-cranial Magnetic Stimulation)
- Can be directed to specific sites (PFC)
- Pulsed magnetic fields depolarises/hyperpolarises neurones, like ECT
- No seizure
- No anaesthetic
- At moment, only 5pt reduction in HRSD
THE END