Electroconvulsive Therapy

Seizure activity and threshold

- defined as the minimum amount of electrical energy that is required to induce cerebral seizure activity of a defined length
- higher in:
  - men
  - older people
  - bilateral ECT
- this results in an initial variation in threshold of up to 4000%
- ECT is anticonvulsant - in some patients there is a gradual reduction in the length of convulsive muscular activity, and a gradual rise in the seizure threshold which is more marked over the first few treatments
- the efficacy of unilateral ECT and the rate of improvement during a course of bilateral ECT correlate with the extent to which the dose of electrical energy exceeds the seizure threshold

<table>
<thead>
<tr>
<th>Factor</th>
<th>Effect on Seizure threshold</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increasing age</td>
<td>raise</td>
</tr>
<tr>
<td>Anti-convulsants</td>
<td>raise</td>
</tr>
<tr>
<td>Baldness</td>
<td>raise</td>
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<tr>
<td>Barbiturates</td>
<td>raise</td>
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<tr>
<td>Benzodiazepines</td>
<td>raise</td>
</tr>
<tr>
<td>Bilateral electrode placement</td>
<td>raise</td>
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<tr>
<td>Bones (thick)</td>
<td>raise</td>
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<tr>
<td>Caffeine</td>
<td>lower</td>
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<tr>
<td>CO₂ (low)</td>
<td>lower</td>
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<tr>
<td>Dehydration</td>
<td>raise</td>
</tr>
<tr>
<td>ECT (increasing number of treatments)</td>
<td>raise</td>
</tr>
<tr>
<td>ECT (previous course in last month)</td>
<td>raise</td>
</tr>
<tr>
<td>Electrode contact (poor)</td>
<td>raise</td>
</tr>
<tr>
<td>Hyperventilation</td>
<td>lower</td>
</tr>
<tr>
<td>Methohexitone in low dose</td>
<td>lower</td>
</tr>
<tr>
<td>Methohexitone dose &gt; 1.2 mg/ kg</td>
<td>raise</td>
</tr>
<tr>
<td>Oxygen saturation (low)</td>
<td>raise</td>
</tr>
<tr>
<td>Propofol</td>
<td>raise</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>raise</td>
</tr>
</tbody>
</table>

Electrical activity

- initially, high voltage high frequency spike waves occur simultaneously throughout the brain - correspond to the tonic phase of the convulsion
  - neocortical in origin (compared to epileptic activity which originates in the diencephalon)
• pattern then evolves into a characteristic polyspike and slow-wave complex often at 2-3 Hz - typical of generalized seizure activity
• seizure termination is often associated with abrupt flattening of the EEG, the ‘post-ictal suppression’ or fitswitch
• cerebral seizure activity measured by EEG last about 30 % longer than visible convulsive muscular activity

Effects on the brain
• increased cerebral blood flow

Systemic effects
• rise in body temperature - due to convulsive activity
• tachycardia - due to sympathetic activity

Long-term effects
• reduced frequency and increased amplitude of EEG
• bilateral ECT is associated with either symmetrical slowing or slowing more marked over the dominant hemisphere
• unilateral ECT may result in slowing more marked over the stimulated hemisphere
• these cumulative changes gradually disappear after the course of treatment
  • the time required for this varies inversely with the number of treatments
• in most people, these changes have disappeared by 1 month, and it is rare for changes to persist after 3 months

Endocrine effects
• ACTH and cortisol: increased release
• prolactin: increased release
  • simulated ECT doubles serum prolactin concentration
  • real ECT leads to a several fold rise that peaks 10-15 minutes after treatment
  • bilateral ECT is associated with a peak 25-50% higher than unilateral treatment
• Growth hormone: not affected
• TSH: not affected
• oxytocin and ADH released from the posterior pituitary
  • maximum release occurs within 2 minutes
  • suprathreshold ECT releases more oxytocin
Neurochemical activity

Noradrenergic transmission
Acute:
- increased plasma catecholamines, especially adrenaline
- increased cerebral plasma tyrosine hydroxylase activity
- increased cerebral noradrenaline
Chronic:
- decreased beta-adrenoceptor density

Serotonergic function
Acute:
- increased cerebral serotonin concentration
Chronic:
- increase in post-synaptic 5-HT2 receptors

Dopaminergic function
Acute:
- increased cerebral dopamine concentration
- increased cerebral concentration of dopamine metabolites
- increased behavioural responsiveness to dopamine agonists
Chronic:
- increased D1 receptor density
- increased second-messenger potentiation at dopamine D1 receptors

GABA function
- acute increase in the release of GABA – may be responsible for the neuroal hypometabolic rate subsequent to ECT
- acute increase in GABA<sub>B</sub> binding

Cholinergic function
- increased:
  - cerebral acetyltransferase activity
  - cerebral acetylcholinesterase activity
  - CSF acetylcholine concentration
- decreased:
  - cerebral acetylcholine concentration
Chronic:
- reduced muscarinic cholinergic receptor density in the cerebral cortex
- reduced muscarinic cholinergic receptor density in the hippocampus
- decreased second messenger response in the hippocampus
- ECT can reduce the signs of Parkinson’s disease (and has been used to treat PD)
Endogenous opioids

Chronic:
- increased cerebral met-enkephalin concentration and synthesis
- increased cerebral β-endorphin concentration and synthesis
- changes in opioid ligand binding

Brain Imaging studies
- no evidence of structural changes
- MRI:
  - small increase in T₁ relaxation that was maximal after two hours, and complete after 24 hours
  - may represent increased permeability to water (and perhaps other psychoactive peptides) in the blood brain barrier
- PET and SPET:
  - small reductions in uptake bilaterally in the inferior anterior cingulate cortex 45 minutes after a single treatment