Neuropsychiatry of Aggression

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Definition
- Any form of behaviour directed toward the goal of harming or injuring another living being who is motivated to avoid such treatment. (Baron & Richardson, 1994)
- The intentional use of physical force or power, threatened or actual, against oneself, another person, or against a group or community that either results in or has a high likelihood of resulting in injury, death, psychological harm, maldevelopment or deprivation. (WHO, Krug et al., 2002)
- Socially unacceptable behaviour that causes distress, harm or disadvantage to the persons themselves or to other people, and usually requires some intervention. (WP, Deb et al., 2009)

Related Concepts
- Violence
- Anger
- Hostility
- Impulsivity
- Urgency
- Irritability
- Anxiety

Aggression in NP Disorders

<table>
<thead>
<tr>
<th>Neuropsychiatric disorder</th>
<th>Prevalence</th>
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<tbody>
<tr>
<td>TBI</td>
<td>3%-71% (Deb, 1999; Silver, 2005)</td>
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<tr>
<td>Dementia</td>
<td>48%-82% (aggression + agitation) (Zuidema, 2007; Sadavoy, Deb, 2008)</td>
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<tr>
<td>ASD</td>
<td>10%-28% (ODD) (LL, 2014)</td>
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<tr>
<td>ADHD</td>
<td>&gt;50% (Saylor &amp; Aman, 2014)</td>
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<tr>
<td>ID</td>
<td>15%-33% (Spigoss, 1994; Hemmings, Deb, Chaplin, Hardy, Mukherjee, 2014)</td>
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<tr>
<td>Psychiatric outpatients (all ages)</td>
<td>6.3%; 3.1% (IED) (Coccaro, 2005)</td>
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<tr>
<td>Personality Disorder</td>
<td>14.4% (violence) (Johnson, 2000)</td>
</tr>
<tr>
<td>Drug and alcohol abuse</td>
<td>12-16 times higher vs. 5 times in Seizo + affective D. (Swanson, 1990)</td>
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<tr>
<td>Epilepsy</td>
<td>Controversial (Deb, 2007)</td>
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<tr>
<td>Children in the UK</td>
<td>8% (B); 3% (G) (CD) (NICE, 2013)</td>
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</tbody>
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EFFECTS OF AGGRESSION
- Hinders rehabilitation
- Causes major disability and impairment for patients
- Source of major stress for family, friends and carers
- Leads to social isolation and loss of placement
- May lead to unnecessary hospitalisation, use of medication and restraint
- Has financial implications for patients, family and the wider society

TYPES OF AGGRESSION
- Reactive/Affective/Defensive
  - Precipitated by stressful stimuli but is out of proportion (‘Fight or Flight’) (IED). (Somatic marker hypothesis)
- Proactive/Instrumental/Predatory
  - Pre-meditated, cold-blooded, goal directed action happens in calm and concentrated state of mind (CD, ODD). (Dysfunctional social learning)
Neurobiology of Aggression

Evidence (Animal + Human)

- Lesion studies (Phineas Gage)
- Structural neuroimaging (CT, CTA, MRI, VBM, DTI)
- Functional neuroimaging (PET-receptor studies, fMRI, MRS, MEG) (Facial expression, IAPS etc.)
- Neurosurgery (Klüver and Bucy)
- CSF, Peripheral and Genetic biomarkers

Phineas Gage

PATIENT’S LESIONS IDENTIFIED USING VBM method (SPM5)

SPM5 stats: one sample t-test with 3 covariates: healthy (140 brains aged 40+) v patient, age and sex
grey matter lesions (blue)
white matter lesions (red)

DTI-tractography

(Catani, 2006)
METABOLITES:

- **NAA**: N-acetylaspartate (marker of neuronal integrity and stability)
- **Cho**: choline (indicator of membrane activity, myelin breakdown)
- **INS**: myo-inositol (glial marker, myelin breakdown indicator)
- **Glx**: glutamine/glutamate (excitatory neurotransmitters)
- **Lac**: lactate (marker of cell death, ischemia)
- **Cre**: creatine (commonly used as internal neuronal metabolite reference)

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**Magnetic Resonance Spectroscopy (MRS)**

- **1H-MRS SV PRESS TE 35ms**

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**Head vs. Heart**

**Logic vs. Emotion**

**Pre-frontal cortex vs. Limbic system**

**Ventricular prefrontal cortex + Cingulate gyrus vs. Amygdala + Cingulate gyrus**
Early information processing/cognitive appraisal

Top-down "brakes":
- Suppression/regulation (orbital frontal cortex, anterior cingulate gyrus)
- Sensory distortions (drugs, alcohol, metabolic disturbances)
- Cultural/social factors (perception of aggressor)
- Sensory processing (perception of challenge)
- Cognitive impairment (e.g., paranoid ideation, conspiracy theories)
- Developmental stress/trauma (negative schema)
- Sensory deficits (hearing, vision loss)

Bottom-up "drive":
- Signal, trigger (amygdala, insula)
- Top-down "brakes":
- Frontal inhibition
- Frontal inhibition
- Frontal inhibition
- Frontal inhibition


**Brain Circuitry**

<table>
<thead>
<tr>
<th>Cortical</th>
<th>Neuromodulators</th>
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<tr>
<td>Cortical lesion (trauma, tumor)</td>
<td>Reduced serotonin</td>
</tr>
<tr>
<td>Decreased cortical volume (developmental)</td>
<td>Enhanced dopamine, norepinephrine</td>
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<tr>
<td>Orbitofrontal/cingulate cortex processing inefficiency</td>
<td>Reduced GABA</td>
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<table>
<thead>
<tr>
<th>Limbic</th>
<th>Neuromodulators</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amygdala, limbic system</td>
<td>Reduced GABA</td>
</tr>
<tr>
<td>Reduced amygdalar volume</td>
<td>Enhanced glutamate</td>
</tr>
<tr>
<td>Emotional hypersensitivity</td>
<td>Enhanced acetylcholine</td>
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**Neurobiological Applications: Pharmacotherapy**

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<tr>
<th>Pharmacologic Class</th>
<th>Target</th>
<th>Brake</th>
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<tbody>
<tr>
<td>Antiepileptics</td>
<td>(limbic irritability)</td>
<td>Frontal inhibition</td>
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<td>SSRIs</td>
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<tr>
<td>New APTs</td>
<td>(dopaminergic stimulation)</td>
<td>Frontal inhibition</td>
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<tr>
<td>Psychostimulants</td>
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<tr>
<td>Opioid antagonists</td>
<td>Opiates</td>
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**Neuropsychiatric Symptoms Overlap**

Psychosocial factors
- Cognitive deficits
- Physical impairment
- Psychiatric illness
- Behavioural problems

QUALITY OF LIFE

- Impact on employment
- Impact on finance
- Impact on family relationship
- Impact on leisure activities
- Impact on social relationship
- Impact on independent living
- Impact on physical health
- Impact on mental health
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