Long known about psychological effects of war. Post trauma reactions documented as far back as 4000BC. In 1915 a clear account of PTSD described in The Lancet by Dr Forsyth. Experience of re-experiencing, reliving, arousal and grief.
1RAR 1960. At end of Malayan Emergency
The problem – In The USA

2000 - 2009: USA Department of Defence

767,290 diagnosed with a psychiatric condition

344,288 diagnosed in more than one category

Incidence of PTSD increased 6-fold, 2003-2008

Psychiatric disorders - leading cause of hospitalization for men in U.S. military
## Conditions of Interest

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjustment disorder</td>
<td>26.7%</td>
</tr>
<tr>
<td>Depression</td>
<td>17.7%</td>
</tr>
<tr>
<td>Alcohol or substance abuse</td>
<td>16.1%</td>
</tr>
<tr>
<td>Anxiety disorders</td>
<td>9.8%</td>
</tr>
<tr>
<td>Personality disorders</td>
<td>5.3%</td>
</tr>
<tr>
<td>PTSD</td>
<td>5.2%</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>1.1%</td>
</tr>
</tbody>
</table>
Active Combat Troops: 2007-2010 US Military

Actively deployed troops who had ever been diagnosed with a mental health disorder:
6.4% in 2007.
7.6% in 2010.

PTSD, major depression, bipolar disorder, alcohol dependence, substance dependence
USA - Medical Discharge

2002: 50% of service members hospitalized for a psychiatric condition medically discharged within 6 months.

Only 12% of service members hospitalized for other conditions discharged.

In the ADF it's probably much higher.
USA Medical Discharge

2003-2008, percentage of medical discharges related to a psychiatric condition:

Army 22%

Navy 24%

Marine Corps 42%
222,000 Iraq veterans:

35% sought psychiatric treatment in the year after returning home

-> Veteran’s Affairs Data
# Mental Health Epidemiology in Veterans

<table>
<thead>
<tr>
<th></th>
<th>Dohrenwend – 2006</th>
<th>O’Toole 1996</th>
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<tbody>
<tr>
<td><strong>Current</strong></td>
<td></td>
<td></td>
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<tr>
<td>PTSD</td>
<td>9.1</td>
<td>12</td>
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<tr>
<td><strong>Lifetime</strong></td>
<td></td>
<td></td>
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<tr>
<td>PTSD</td>
<td>18.7</td>
<td>21</td>
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<tr>
<td>Alcohol</td>
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<td>41</td>
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<tr>
<td>Depression</td>
<td>17</td>
<td>25</td>
</tr>
<tr>
<td>Anxiety</td>
<td>16</td>
<td>13</td>
</tr>
<tr>
<td>Antisocial Personality</td>
<td>10</td>
<td>6</td>
</tr>
</tbody>
</table>
2010 ADF Review

- ADF Vietnam veterans PTSD life time prevalence 21%
- ADF Gulf War Veterans, 10-15 years after Gulf War (1990), 5.4% of 1871 have current PTSD
- Royal Australian Navy (RAN) estimates of PTSD in the 1739 sailors deployed to the Middle East between 2001-2005 1.6%
In 2012 across all branches of the US military and reserves there were 349 recorded suicides.

In the same period 295 service members died in combat.

In the same period 6500 ex-military personnel killed themselves. One every 80 minutes.
Repent, sinners! The end is near. Spring is coming. They're snowmen, prophets of doom. You certainly take the pleasure out of waiting for daffodils.
Veteran Mental Health

Ward 17 incorporates several services for the management of psychiatric illness in veterans

- The Inpatient Unit
- Consultation Liaison Service which provides around 800 consultations a year to patients within RGH wards and to those who attend ARU.
- The Veterans Mental Health Rehabilitation Unit and Outpatients Clinics.
- The PTSD Unit.
Inpatient Unit

- Ward 17 is a 24 bed inpatient unit which manages acute and chronic psychiatric illness.
- Currently approximately 70% of inpatients are entitled veterans and serving members.
- The other 30% include veterans without entitlements, families of veterans (especially war widows) and community patients.
- Veterans have priority for admission.
Main diagnostic groups treated at Ward 17 include:

- PTSD
- Major Depression
- Anxiety Disorders
- Substance Use Disorders
- Ageing related disorders including early cognitive decline associated with psychological/psychiatric comorbidity
- Less commonly we manage Schizophrenia and Bipolar Disorder
Comorbid Issues

- Medical illness
- Age related frailty
- Substance use
- Pain disorders
- Social issues of relationship strain, financial stress, homelessness, social isolation

By themselves these are not usual indications for admission
I think we'd better get that kid to a psychologist.
PTSD

- The diagnosis of PTSD is made in the subset of people who have experienced trauma who are unable to cope with the consequences of trauma and whose well-being over time is greatly impacted by these consequences.
Military combat
Violent personal assault
Natural and man-made disasters
Severe motor vehicle accidents
Rape
Incest
Childhood sexual abuse
Diagnosis of a life-threatening illness
Severe physical injury
Hospitalization in an intensive care unit (ICU)
Posttraumatic stress disorder (PTSD) has been described as "the complex somatic, cognitive, affective and behavioural effects of psychological trauma".

PTSD is characterized by intrusive thoughts, nightmares and flashbacks of past traumatic events, avoidance of reminders of trauma, hypervigilance, and sleep disturbance, all of which lead to considerable social, occupational, and interpersonal dysfunction.
DSM IV

1. The person has been exposed to a traumatic event in which both of the following were present:
   - The person experienced, witnessed, or was confronted with an event or events that involved actual or threatened death or serious injury, or a threat to the physical integrity of self or others
   - The person’s response involved intense fear, helplessness, or horror

2. The traumatic event is persistently re-experienced in one (or more) of the following ways:
   - Recurrent and intrusive distressing recollections of the event, including images, thoughts, and perceptions
   - Recurrent distressing dreams of the event
   - Acting or feeling as if the traumatic event were recurring
   - Intense psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event
   - Physiological reactivity on exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event
AVOIDANCE

3. Avoidance of stimuli associated with the trauma and numbing of general responsiveness (not present before the trauma), as indicated by three (or more) of the following:

- Efforts to avoid thoughts, feelings, or conversations associated with the trauma
- Efforts to avoid activities, places, or people that arouse recollections of the trauma
- Inability to recall an important aspect of the trauma
- Markedly diminished interest or participation in significant activities
- Feeling of detachment or estrangement from others
- Restricted range of affect (e.g., unable to have loving feelings)
- Sense of foreshortened future (e.g., does not expect to have a career, marriage, children or a normal life span)
Hypervigilance

4. Persistent symptoms of increased arousal (not present before the trauma) as indicated by two (or more) of the following:
   - Difficulty falling or staying asleep
   - Irritability or outbursts of anger
   - Difficulty concentrating
   - Hypervigilance
   - Exaggerated startle response

5. Duration of the disturbance (symptoms in criteria 2, 3 and 4) is more than 1 month.

6. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning
DSM 5 – May 2013

- Criteria A2 removed (person does not need to experience fear or horror at the time).
- An extra symptom cluster will be added – the avoidance criteria will be divided into active avoidance and numbing.
- PTSD will be moved out of anxiety disorders into a new section “Trauma and stressor related disorders.”
- Extra symptoms will be added eg distorted blaming of others or self, persistent negative state, reckless or self-destructive behaviour.
The lifetime prevalence of PTSD ranges from 6.8 to 12.3 percent in the general adult population in the United States with one-year prevalence rates of 3.5 to 6 percent. In a study of 368 patients from a community primary care clinic, 65 percent reported a history of exposure to severe, potentially traumatic events; 12 percent went on to develop PTSD.

Personal and societal factors appear to affect both the likelihood of developing PTSD after a traumatic event and the clinical presentation of PTSD.

Risk factors for PTSD include lower socioeconomic status, parental neglect, family or personal history of a psychiatric condition, poor social support, and initial severity of reaction to the traumatic event.
The frequency with which PTSD occurs after a traumatic event is influenced by characteristics of the individual and the inciting event.

Overall, women are four times more likely to develop PTSD than men, after adjusting for exposure to traumatic events.

The rates of PTSD are similar among men and women after events such as accidents (6.3 versus 8.8 percent), natural disasters (3.7 versus 5.4 percent), or sudden death of a loved one (12.6 versus 16.2 percent). Although women are more than 10 times as likely as men to be raped, the incidence of PTSD after rape is higher in men (65 versus 46 percent).

The rate of PTSD is lower in men than in women after events such as molestation (12.2 versus 26.5 percent) and physical assault (1.8 versus 21.3 percent).
War-related PTSD has been associated with long-term consequences for mental health. A longitudinal cohort study compared a random sample of 450 Australian Vietnam veterans with matched subjects from the Australian general population. When assessed 36 years after the war, veterans with war-related PTSD were more likely than members of the general population to have depression, an anxiety disorder (e.g., social phobia, panic disorder, agoraphobia with or without panic disorder, and specific blood phobia), alcohol dependence, or persistent pain disorder.
Most individuals who develop PTSD experience its onset within a few months of the traumatic event. However, epidemiologic studies have found that approximately 25 percent experience a delayed onset after six months or more.

PTSD is commonly a chronic condition with only one-third of patients recovering at one year follow-up, and one-third still symptomatic ten years after the exposure to the trauma.

Individuals with one or more PTSD symptoms are more likely to experience occupational problems, have poorer social supports, and have more disability than controls. PTSD may increase the risk for attempted suicide. Individuals with PTSD have higher rates of problems in intimate relationships, including marital difficulties, compared to people without PTSD.
Clinical Administered PTSD Scale

- **Description**

  The CAPS is the gold standard in PTSD assessment. The CAPS is a 30-item structured interview that corresponds to the DSM-IV criteria for PTSD. The CAPS can be used to make a current (past month) or lifetime diagnosis of PTSD or to assess symptoms over the past week.

  Blake, Weathers, Nagy, Kaloupek, Chamey, & Keane, 1995
**Patient's name:**

**Instruction to patient:** Below is a list of problems and complaints that veterans sometimes have in response to stressful life experiences. Please read each one carefully, put an "X" in the box to indicate how much you have been bothered by that problem in the last month.

<table>
<thead>
<tr>
<th>No.</th>
<th>Responses</th>
<th>Not at all (1)</th>
<th>A little bit (2)</th>
<th>Moderately (3)</th>
<th>Quite a bit (4)</th>
<th>Extremely (5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Repeated, disturbing memories, thoughts, or images of a stressful experience from the past?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>Repeated, disturbing dreams of a stressful experience from the past?</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>3.</td>
<td>Suddenly acting or feeling as if a stressful experience were happening again (as if you were reliving it)?</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>4.</td>
<td>Feeling very upset when something reminded you of a stressful experience from the past?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>Having physical reactions (eg, heart pounding, trouble breathing, or sweating) when something reminded you of a stressful experience from the past?</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>6.</td>
<td>Avoid thinking about or talking about a stressful experience from the past or avoid having feelings related to it?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td>Avoid activities or situations because they remind you of a stressful experience from the past?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8.</td>
<td>Trouble remembering important parts of a stressful experience from the past?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9.</td>
<td>Loss of interest in things that you used to enjoy?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10.</td>
<td>Feeling distant or cut off from other people?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11.</td>
<td>Feeling emotionally numb or being unable to have loving feelings for those close to you?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12.</td>
<td>Feeling as if your future will somehow be cut short?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13.</td>
<td>Trouble falling or staying asleep?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14.</td>
<td>Feeling irritable or having angry outbursts?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15.</td>
<td>Having difficulty concentrating?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16.</td>
<td>Being &quot;superexcited&quot; or watchful on guard?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17.</td>
<td>Feeling jumpy or easily startled?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Total score: [ ]**
Diagnosis
Epidemiology

- Recent epidemiological studies indicate 12-month prevalence rates of 1.33% in Australia

Most individuals who develop PTSD do so without having suffered an ASD. (however ASD is associated with developing later PTSD)

Hyperarousal symptoms at the time of the trauma are most predictive of a later diagnosis of PTSD.

Severe combat associated stress is a predictor of PTSD. 30 years post Vietnam – 10% of veterans exposed to this form of stress continue to suffer severe PTSD.

Late onset PTSD can occur in 15-20% of sufferers – can occur many years later.
There has been considerable interest in finding effective psychopharmacological strategies for treating posttraumatic stress disorder (PTSD). It is assumed that biological treatment may have an important role, given the abnormalities in neurotransmitter, neuroendocrine, and neuroanatomical systems that have been identified in patients with PTSD.

So far, the mental health field has tended to focus on either biological or psychological targets. Maximizing treatment success may require an integrated approach that does not dichotomize biological and psychological aspects.
Neurobiological Aspects of PTSD.

- Autonomic Changes.
- Genetics
- Neuroimaging
- Neuroendocrine
- Epigenetics linked to neural changes.
**Increased neurological sensitivity**

- Alterations in fear conditioning, extinction learning, extinction retention and sensitization are likely to be involved in the development and/or maintenance of PTSD.
- One of the earliest and most replicated PTSD findings is that of heightened autonomic reactivity (such as heart rate and skin conductance) and facial EMG reactivity to external, trauma-related stimuli, such as combat sounds and film clips, as well as to internal, mental imagery of the traumatic event. Reactivity to trauma-related cues correlates with the severity of the disorder.

Genetics.

- Genetic influences account for 30% to 72% of vulnerability to PTSD. These estimates take into account genetic factors that may contribute to exposure to traumatic events, such as combat or interpersonal violence.
- Genetic influences on exposure to trauma are thought to largely function through heritable personality traits.
- Genetic risk factors that are common to major depression, generalized anxiety disorder and panic disorder also account for most of the genetic variation in PTSD identified to date. Thus, genes that affect the risk of developing PTSD also influence the risk of developing other psychiatric disorders, and vice versa.
- As with other mental disorders, influences on PTSD are probably polygenic; at least 17 gene variants have been associated with PTSD in at least one published study.
<table>
<thead>
<tr>
<th>Gene</th>
<th>Common name</th>
<th>Location</th>
<th>Total number of published reports</th>
<th>Significant findings</th>
<th>Null findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>DRD2 (also known as D2R and D2DR)</td>
<td>Dopamine receptor D2</td>
<td>11q23</td>
<td>6</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>DRD4 (also known as D4DR)</td>
<td>Dopamine receptor D4</td>
<td>11p15.5</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>SLC6A3 (also known as DAT1)</td>
<td>Dopamine transporter</td>
<td>5p15.3</td>
<td>4</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>DBH</td>
<td>Dopamine β-hydroxylase</td>
<td>9q34</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>SLC6A4 (also known as HTT, S-HTT, SERT and 5-HTTLPR)</td>
<td>5-hydroxytryptamine (serotonin) transporter</td>
<td>17q11</td>
<td>16</td>
<td>12</td>
<td>4</td>
</tr>
<tr>
<td>HTR2A (also known as 5-HT2A)</td>
<td>5-hydroxytryptamine receptor 2A</td>
<td>13q14-q21</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>FKBP5</td>
<td>FK506 binding protein 5</td>
<td>6p21</td>
<td>4</td>
<td>4</td>
<td>0</td>
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<tr>
<td>GCCR (also known as NR3C1)</td>
<td>Glucocorticoid receptor</td>
<td>5q31.3</td>
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<td>0</td>
<td>1</td>
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<tr>
<td>CRHR1</td>
<td>Corticotropin-releasing hormone receptor 1</td>
<td>17q12-22</td>
<td>1</td>
<td>1</td>
<td>0</td>
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<tr>
<td>RGS2</td>
<td>Regulator of G protein signalling 2</td>
<td>1q31</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>CNR1 (also known as CB1 and CNR)</td>
<td>Cannabinoid receptor 1 (brain)</td>
<td>6q14-q15</td>
<td>1</td>
<td>0</td>
<td>1</td>
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<tr>
<td>APOE</td>
<td>Apolipoprotein E</td>
<td>19q13</td>
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<td>1</td>
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<tr>
<td>BDNF</td>
<td>Brain-derived neurotrophic factor</td>
<td>11p13</td>
<td>3</td>
<td>0</td>
<td>3</td>
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<tr>
<td>NPY</td>
<td>Neuropeptide Y</td>
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<td>0</td>
<td>1</td>
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<tr>
<td>GABRA2</td>
<td>GABA type A receptor α2</td>
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<td>1</td>
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<td>COMT</td>
<td>Catechol-O-methyltransferase</td>
<td>22q11</td>
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<td>2</td>
<td>0</td>
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<tr>
<td>ADCYAP1R1</td>
<td>Receptor for adenylyl cyclase-activating polypeptide 1</td>
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<td>2</td>
<td>1</td>
<td>1</td>
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<tr>
<td>DTNBP1</td>
<td>Dystrobrevin-binding protein 1</td>
<td>6p22</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>CHRNA2</td>
<td>Cholinergic receptor</td>
<td>15q25.1</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>
Neuro imaging abnormalities

- Pioneering sMRI studies found significantly smaller hippocampi in subjects with PTSD compared to trauma-exposed and non-trauma-exposed subjects without PTSD. Since then, a large literature has emerged, most of which, along with meta-analyses, has provided empirical support for a lower hippocampal volume in PTSD.
- Does it exist pre-morbidly, is it associated with trauma regardless of PTSD development??
Dorsal anterior cingulate cortex (ACC). A cortical area that highly corresponds to Brodmann area 24. It may be called anterior the cingulate cortex.

 voxel-based morphometry (VBM) is an automated neuroimaging analytic technique that allows investigation of focal differences in brain anatomy using the statistical approaches and statistical parametric mapping and smoothing applied to structural images.

Fusion tensor imaging (shown in panels a and c) is involved in recognizing both conditioned and unconditioned stimuli signalling danger, as well as in expressing the fear response. Amygdala reactivity is exaggerated in individuals with post-traumatic stress disorder (PTSD) and is positively correlated with symptom severity. The insular cortex (a) and dorsal anterior cingulate cortex (b) are also hyper-reactive in PTSD; these structures may modulate (in these cases enhance) the amygdala’s expression of fear. By contrast, activation in the ventromedial prefrontal cortex (b), which also modulates (in this case reduces) the amygdala’s expression of the fear response, is diminished in PTSD; ventromedial prefrontal cortex activity is also negatively correlated with symptom severity. Functional neuroimaging findings in the hippocampus (c), which is involved in recognizing both safe and dangerous contexts, have been mixed in PTSD, with both hypo- and hyper-reactivity observed.

Ventral medial prefrontal cortex. Areas in the vmPFC (including the rostral ACC), subcallosal cortex and medial frontal gyri show decreased activation in subjects with PTSD during tasks that use either trauma-related or trauma-unrelated stimuli. Activation of those that are present during fear learning and extinction. Findings from functional neuroimaging in the hippocampus in patients with PTSD has been mixed, with some studies reporting less activation, others reporting more activation than in comparison
Neuroendocrine abnormalities

- **Catecholamines.** Numerous studies have provided compelling evidence for the presence of sympathetic nervous system hyper-reactivity in PTSD. It has been suggested that an excessively strong adrenergic response to the traumatic event may mediate the formation of the durable traumatic memories that in part characterize the disorder.

- **Indoleamines.** The 5-HT system also appears to be implicated in both the acute mediation of PTSD symptoms and the modulation of PTSD risk, as neuropharmacological, treatment and genetic epidemiological studies have indicated.

- **Neuropeptide Y**

- **Corticotropin-releasing hormone**
Epigenetics and neural changes.

- Increasing research into epigenetics
- Animal models mainly used.
- Focused on DNA hypermethylation of BDNF gene in hippocampal regions.
- Models in traumatised mice support the hypothesis that epigenetic marking of the BDNF gene may underlie hippocampal dysfunction produced by exposure to traumatic events.

A recent study has identified another gene prone to changes in hippocampal region methylation – Dlgap2.
Amygdala

- The transition of memories to a stable form is important for the persistence of PTSD and it is thus critical to understand the molecular mechanisms that underlie such memory stability in order to identify potential targets for pharmacological treatment.
- What changes in the amygdala are occurring to alter the way long term memories are stored?
- Epigenetic changes via methylation of several genes (including BDNF) implicated. Also changes in synaptic plasticity altered by epigenetic mechanisms.
A limitation of the currently available studies is the lack of direct evidence for the mechanism through which DNA methylation and histone modifications at the cellular level get translated into altered circuit and behavioral function. However, the reviewed studies give us mechanistic insights, such as evidence that DNA methylation controls fear memory stability and that changes in DNA methylation in the adult CNS regulate the expression of known fear conditioning-related genes.
PTSD as a Biological and psychological Entity?

- A number of biological abnormalities have been found statistically to discriminate PTSD from non-PTSD control groups in various studies; on this basis, they may loosely be regarded as biomarkers. However, none of them possesses the specificity and sensitivity that is necessary to be used as a stand-alone diagnostic test for PTSD.

- The current ‘gold standard’ for a PTSD diagnosis are the diagnostic criteria set forth in the fourth edition DSM IV.
Biological Management of PTSD

- Pharmacoprophylaxis
- Manage sleep disturbance.
- Treat comorbidities.
- Psychopharmacology including management of intrusions, anxiety and re-experiencing.
Pharmacoprophylaxis

- Does it mean administering medications to the many who will never develop a problem?
- Target the memory consolidation process which appears to occur in the presence of high levels of noradrenaline following a trauma.
- propanolol, morphine, gabapentine and hydrocortisone – limited evidence.
Comorbidity.

An estimated 79% of women and 88% of men diagnosed with PTSD have at least one other psychiatric disorder; and 49% of women and 59% of men have three or more concurrent psychiatric diagnoses.

Comorbidities

- Substance abuse
- Comorbidity of substance abuse is very high in PTSD patients. PTSD patients are at increased risk of abusing prescription medications.

Comorbidities

- Psychosis
- Psychotic symptoms in PTSD patients could indicate a comorbid psychotic disorder or could be part of the PTSD.
Comorbidities

- Major depressive disorder
  - History of major depression increases risk of developing PTSD, & PTSD diagnosis increases risk of depression.
  - Dysregulation of HPA axis may cause above associations. Responsiveness to antidepressants is diminished in PTSD patients with comorbid depression in some studies.

  - Gill J, Vythilingam M, Page GG. Low cortisol, high DHEA, and high levels of stimulated TNF-alpha, and IL-6 in women with PTSD. J Trauma Stress 2008;21:530–9.
Comorbidities

- Bipolar Disorder
- Pregnancy
- Dissociation (more serious pathology & less predictable response to pharmacotherapy)
- Sleep disturbance.
PTSD and Sleep

- Mounting evidence has implicated sleep impairment as a core symptom in PTSD and a primary source of distress and dysfunction for patients with this disorder.
- For many patients, sleep deprivation may exacerbate core daytime PTSD symptoms (hypervigilance, avoidance, reexperiencing), and these symptoms may improve when sleep improves.
- Another justification for treating sleep difficulties first is the availability of prazosin, a psychopharmacology option that targets impaired sleep in PTSD patients and that has demonstrated substantially larger effect sizes than medications commonly thought to be effective for the general symptom profile in PTSD.

Sleep disturbances common in PTSD include the following:
1. hyperarousal linked to difficulties initiating or maintaining sleep
2. trauma-related nightmares
3. Awakenings without nightmare recollection
4. prolonged sleep latency.
Increased noradrenergic activity during sleep and while trying to fall asleep is thought to be an important mechanism.
Other causes of insomnia may contribute to the sleep difficulties of patients with PTSD. These include sleep apnea, restless leg syndrome, periodic limb movements of sleep, sleep hygiene issues, nicotine withdrawal, and medical problems associated with sleep fragmentation (e.g., pain and nocturia). Caffeine, though frequently employed as a method of coping with daytime symptoms of sleep deprivation secondary to PTSD and other causes of insomnia, can at times become a major independent contributor.
Management of sleep

- Prazosin
- Sedating antidepressants
- Quetiapine
- Benzodiazepines – potential for abuse
- Zopiclone
SNOW SHARKS?

THAT GUY'S A GONER.
Pharmacotherapy of PTSD
The criteria for PTSD in the Diagnostic and Statistical Manual of Mental Disorders (4th ed.) (DSM-IV) include the symptom clusters of reexperiencing, avoidance, and hyperarousal.

These symptom clusters may differ in their responses to psychopharmacological treatment. It is less clear whether these differences depend on the nature of the trauma—for example, combat veterans versus survivors of rape or domestic abuse. Recently traumatized individuals may respond better than those with distant trauma, such as Vietnam veterans.
SSRIs

- SSRIs - FDA approval for paroxetine and sertraline. Mixed results in studies. Side effects often intolerable.
- Sertraline has weaker evidence than paroxetine but has less side effects (sexual dysfunction, constipation, sedation, drug interactions, withdrawal and pregnancy risks).
- Citalopram could be considered but has less literature evidence.
- 4-12 weeks for adequate trial.
Other Antidepressants

- Some evidence for
  - Venlafaxine, bupropion, mirtazepine and fluoxetine.
  - TCAs assisted with sleep and PTSD symptoms in some small studies.
Antipsychotics

- Intrusive flashbacks, olfactory and auditory experiences and paranoid thinking can respond to antipsychotic medication - both alone and as an augmenter of antidepressants.
- General hypervigilance and irritability/rage can also respond.
- Needs to be balanced against metabolic risks and other side effects.
- Evidence for quetiapine, risperidone and olanzapine.
Prazosin

- Prazosin is a generic alpha-1 adrenergic antagonist previously used to treat hypertension and symptoms of benign prostatic hyperplasia
- Well tolerated.
- Several small RCTs showing good effect size – especially for sleep improvement.
Mood Stabilisers

- Valproate – no evidence
- Lamotrigine – no evidence
- Topiramate – some limited evidence for re-experiencing and numbing phenomena, alcohol cravings, pain and weight loss. (PBS approval for epilepsy and migraine)

- A Double-Blind Randomized Controlled Trial To Study the Efficacy of Topiramate in a Civilian Sample of PTSD, Mary S. L. Yeh, et al CNS Neuroscience & Therapeutics 17 (2011) 305–310
Other therapies

- Beta blockers – limited studies
- Clonidine – assists hyperarousal and sleep
- MAOIs – evidence for improvement.
- Aripiprazole – early evidence for assistance with decreased CAPs scores.
- Modafanil
<table>
<thead>
<tr>
<th>Algorithm/guideline</th>
<th>Year</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expert consensus guidelines\textsuperscript{144}</td>
<td>1999</td>
<td>First-line: SSRIs, venlafaxine, &amp; nefazodone</td>
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<td></td>
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<td>Second-line: TCAs</td>
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<tr>
<td>Psychopharmacology Algorithm Project at Harvard South Shore Program\textsuperscript{4}</td>
<td>1999</td>
<td>Early use of hypnotic agent for sleep; trazodone first-line, followed by SSRIs for persistent daytime PTSD symptoms</td>
</tr>
<tr>
<td>The United Kingdom’s National Institute for Clinical Excellence\textsuperscript{7}</td>
<td>2005</td>
<td>SSRIs in PTSD are reviewed &amp; shown to have a more modest effect size then commonly considered</td>
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<td>Psychotherapy recommended as first-line treatment</td>
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<tr>
<td>Canadian clinical practice guidelines\textsuperscript{145}</td>
<td>2005</td>
<td>First-line: one agent among fluoxetine, paroxetine, sertraline, &amp; venlafaxine XR</td>
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<td>Second-line: mirtazapine, fluvoxamine, phenelzine, &amp; moclobemide, plus adjunctive olanzapine or risperidone</td>
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<tr>
<td>The International Psychopharmacology Algorithm Project\textsuperscript{5}</td>
<td>2005</td>
<td>Once diagnosis of PTSD established, SSRI trial recommended as first-line pharmacological intervention, followed by venlafaxine &amp; mirtazapine trials</td>
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<tr>
<td>The International Society of Traumatic Stress Studies\textsuperscript{6}</td>
<td>2008</td>
<td>SSRIs recommended as first-line intervention, followed by augmentation with atypical antipsychotics</td>
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<td></td>
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<td>Prazosin considered “promising”</td>
</tr>
<tr>
<td>APA Guidelines Watch\textsuperscript{10}</td>
<td>2009</td>
<td>Concludes new studies suggest SSRIs are less effective than previously assumed</td>
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<tr>
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<td></td>
<td>Prazosin considered a promising option for sleep disturbance in PTSD</td>
</tr>
<tr>
<td>VA/DoD clinical practice guideline for managing posttraumatic stress\textsuperscript{146}</td>
<td>2010</td>
<td>Strongest recommendation is for SSRIs &amp; SNRIs but suggests “some benefit” for prazosin, mirtazapine, &amp; adjunctive atypical antipsychotics</td>
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<td></td>
<td>Recommends consideration of prazosin for nightmares as adjunctive treatment if trazodone &amp; other hypnotics are insufficient</td>
</tr>
</tbody>
</table>

APA, American Psychiatric Association; DoD, Department of Defense; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant; VA, Veterans Administration.
The Psychopharmacology Algorithm Project at the Harvard South Shore Program: An Update on Posttraumatic Stress Disorder
Laura A. Bajor, DO, Ana Nectara Ticlea, MD, and David N. Osser, MD. Harv Rev Psychiatry September/October 2011, Vol 19, number 5.

A Double-Blind Randomized Controlled Trial To Study the Efficacy of Topiramate in a Civilian Sample of PTSD
Mary S. L. Yeh, Jair Jesus Mari, Mariana Caddrobi Pupo Costa, Sergio Baxter Andreoli, Rodrigo Affonseca Bressan & Marcelo Feijo. CNS Neuroscience & Therapeutics 17 (2011) 305-310

Australian Centre for Post Traumatic Health. Literature Reviews 2002-2012