PTSD: Treatment Opportunities

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• exposure to: actual or threatened death, serious injury, or sexual violence, as follows: (1 required)

• Via:
  1. directly experiencing
  2. Witnessing in person the event occurring to others
  3. Learning that it occurred to a family member or close friend – events violent or accidental
  4. Repeated or extreme exposure to aversive details of traumatic events e.g. first responders; other occupational exposures
PTSD

- How many Australians have been exposed to a potentially traumatic event?
- Females - 50%
- Males – 65%

Examples of PTEs:
- combat
- other violent crimes
- torture
- severe accidents
- rape victims
- natural disasters
Mental Health Responses To Trauma

- Most people recover with no long term effects
- Some people report long term, extreme distress and social / occupational impairment
- Diagnoses:
  - Depression
  - Substance abuse
  - Anxiety, including panic, phobias, and post-traumatic stress disorder (PTSD)
PTSD (DSM-5)

- A: Objective experience of trauma
- B: Intrusive memories (images, smells, etc.) (1/5)
- C: Active attempts to avoid reminders (1/2)
- D: Negative alterations in cognitions and mood (2/7)
- E: Hyperarousal, tense, on edge, jumpy (2/6)
- F: Duration > 4 weeks
- G: Functional impairment and/or distress
COMMON PATTERNS OF RESPONSE FOLLOWING TRAUMA OR DISASTER (BONNANO)
Epidemiology of PTSD

• Australian 12 Month Prevalence
  • 6.4% (Commonest Anxiety Disorder)

• Global Prevalence
  • 1.3-8.8% World Mental Health Survey using Worst Event Methodology
FIGURE 2  Lifetime PTSD Prevalence Rates: Specified Canadian Populations.
Sources: Van Ameringen, Mancini, Paterson et al. (2008); Boulos & Zamorski (2013); Marchand, Boyer, Martin et al. (2010); Asmundson & Stapleton (2008); Rosine (1992); Stadnyk (2004); Corneil, Beaton, Murphy et al. (1999); Regehr, Goldberg & Hughes (2002).
Micro to Macro Effects

Trauma

Genetic vulnerability

Injury

‘Network’ level: dysregulation of neural circuitry
Functional and structural changes

Neuroendocrine, autonomic and immune dysregulation

Cellular and subcellular level impact on:
Intracellular signaling
Gene transcription
Neurotrophic support

Neuropsychiatric symptoms
Emotional
Cognitive
Behavioral
Physical
Systemic manifestations
Medication Classes Utilised in PTSD

• Antidepressants
  • SSRIs
    • Fluoxetine
    • Paroxetine
    • Sertraline
    • Citalopram
    • Fluvoxamine
  • SNRIs
    • Venlafaxine
  • Atypical Antidepressants
    • Mirtazapine
Meta-analysis of selective serotonin reuptake inhibitors v. placebo (SMD, standardised mean difference).

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Experimental Mean</th>
<th>s.d.</th>
<th>Total</th>
<th>Control Mean</th>
<th>s.d.</th>
<th>Total</th>
<th>Weight</th>
<th>SMD IV, random, 95% CI</th>
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</thead>
<tbody>
<tr>
<td>Brady (2000)</td>
<td>-33</td>
<td>28.1</td>
<td>94</td>
<td>-23.2</td>
<td>28.7</td>
<td>93</td>
<td>5.8%</td>
<td>-0.34 (-0.63, -0.05)</td>
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<tr>
<td>Brady (2005)</td>
<td>32.56</td>
<td>15.69</td>
<td>49</td>
<td>32.7</td>
<td>28.75</td>
<td>45</td>
<td>4.1%</td>
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<td>Connor (1999)</td>
<td>10.1</td>
<td>9.8</td>
<td>25</td>
<td>20.5</td>
<td>12.6</td>
<td>22</td>
<td>2.4%</td>
<td>-0.91 (-1.52, -0.31)</td>
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<tr>
<td>Davidson</td>
<td>-39.4</td>
<td>27.12</td>
<td>173</td>
<td>-34.17</td>
<td>28.42</td>
<td>179</td>
<td>7.3%</td>
<td>-0.19 (-0.40, 0.02)</td>
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<td>Davidson (2001)</td>
<td>-33</td>
<td>23.76</td>
<td>100</td>
<td>-26.2</td>
<td>23.9</td>
<td>108</td>
<td>6.1%</td>
<td>-0.28 (-0.56, -0.01)</td>
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<tr>
<td>Eli Lilly</td>
<td>-10.42</td>
<td>7.5</td>
<td>323</td>
<td>-10.59</td>
<td>10.21</td>
<td>88</td>
<td>6.8%</td>
<td>0.02 (-0.21, 0.26)</td>
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<td>Friedman (2007)</td>
<td>-13.1</td>
<td>27.5</td>
<td>86</td>
<td>-15.4</td>
<td>28.07</td>
<td>83</td>
<td>5.6%</td>
<td>0.08 (-0.22, 0.38)</td>
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<tr>
<td>Hertzberg (2009)</td>
<td>47</td>
<td>8</td>
<td>6</td>
<td>42</td>
<td>11</td>
<td>6</td>
<td>0.8%</td>
<td>0.48 (-0.68, 1.64)</td>
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<td>Marshall (2001)</td>
<td>-38.75</td>
<td>27.2</td>
<td>375</td>
<td>-25.3</td>
<td>25.8</td>
<td>188</td>
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<td>Marshall (2004)</td>
<td>55.6</td>
<td>33.4</td>
<td>25</td>
<td>62.8</td>
<td>40.8</td>
<td>27</td>
<td>2.8%</td>
<td>-0.19 (-0.73, 0.36)</td>
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<td>Martenyi (2002)</td>
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<td>75</td>
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<td>Martenyi (2007)</td>
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<td>25.5</td>
<td>323</td>
<td>-36.6</td>
<td>25.7</td>
<td>88</td>
<td>6.8%</td>
<td>-0.24 (-0.48, -0.01)</td>
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<td>Penahni (2011)</td>
<td>-22.7</td>
<td>7.3</td>
<td>35</td>
<td>-17.5</td>
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<td>3.3%</td>
<td>-0.69 (-1.18, -0.21)</td>
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<tr>
<td>Pfizer 585</td>
<td>-27.4</td>
<td>27.12</td>
<td>94</td>
<td>-27.9</td>
<td>28.42</td>
<td>94</td>
<td>5.9%</td>
<td>0.02 (-0.27, 0.30)</td>
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<td>Pfizer 589</td>
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<td>27.12</td>
<td>84</td>
<td>-15.4</td>
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<td>82</td>
<td>5.6%</td>
<td>0.08 (-0.22, 0.39)</td>
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<td>Shaleve (2011)</td>
<td>-31.12</td>
<td>29.63</td>
<td>23</td>
<td>-27.8</td>
<td>20.13</td>
<td>23</td>
<td>2.5%</td>
<td>-0.13 (-0.71, 0.45)</td>
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<tr>
<td>SKB627</td>
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<td>109</td>
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<td>25.37</td>
<td>103</td>
<td>6.2%</td>
<td>-0.22 (-0.49, 0.05)</td>
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<td>Tucker (2001)</td>
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<td>24.58</td>
<td>151</td>
<td>-24.7</td>
<td>24.98</td>
<td>156</td>
<td>7.0%</td>
<td>-0.43 (-0.66, -0.21)</td>
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<td>Tucker (2003)</td>
<td>-41.82</td>
<td>29.09</td>
<td>23</td>
<td>-38.7</td>
<td>29.07</td>
<td>10</td>
<td>1.7%</td>
<td>-0.10 (-0.85, 0.64)</td>
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<td>Van der Kolk (2007)</td>
<td>-33.23</td>
<td>22.11</td>
<td>30</td>
<td>-30.95</td>
<td>22.6</td>
<td>29</td>
<td>3.0%</td>
<td>-0.10 (-0.61, 0.41)</td>
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<td>Zohar (2002)</td>
<td>-18.7</td>
<td>6.7</td>
<td>23</td>
<td>-13.5</td>
<td>6.6</td>
<td>19</td>
<td>2.2%</td>
<td>-0.77 (-1.40, -0.14)</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>2377</td>
<td></td>
<td>1553</td>
<td>100.0%</td>
<td>0.23(-0.33, -0.12)</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Heterogeneity: $\chi^2 = 0.03; \; \chi^2 = 42.90, \; d.f. = 20 \; (P = 0.002); \; I^2 = 53%$

Test for overall effect: $Z = 4.23 \; (P < 0.0001)$

Mathew Hoskins et al. BJP 2015;206:93-100

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Medication Classes Utilised in PTSD

• Antipsychotics
  • Risperidone
  • Olanzapine
  • Quetiapine

• Benzodiazipenes
• Prazosin
• Topiramate
Evidence Based Use of medication in PTSD

• Only SSRIs have the highest level evidence
  • Benefit is variable and modest in size
  • Only first line treatment in certain circumstances
• Other Antidepressants may be helpful
• Benzodiazepenes are for short term use wherever possible
• Atypical Antipsychotics may be useful but with a difficult risk benefit equation
Systematic Reviews & Guidelines:

- RANZCP AGREE II Survey 2013

Average Scores of the Guidelines
Australian PTSD Guidelines - 2013

Developed in consultation with experts and people affected by PTSD

Supported by the Australian Government and approved by peak health research body - NHMRC

Endorsed by professional associations – RACGP, RANZCP, APS

Available from www.acpmh.unimelb.edu.au
NHMRC Guideline Recommendations: Adults

• Trauma focussed CBT or EMDR is the treatment of choice for PTSD:
  ○ Trauma focused CBT included
    ○ In vivo and imaginal exposure
    ○ Cognitive therapy or cognitive processing therapy

• Medication should not be used as routine 1st line in preference to TF psychological treatment

• Where prescribed:
  ○ SSRIs
  ○ Other newer antidepressants, tricyclics, phenelzine
Outcomes of Trauma Focussed Therapy

Clinical Bottom Line

• Posttraumatic stress disorder (PTSD) is a disabling psychiatric condition common among military personnel and veterans

• A range of psychotherapies are available, but military-PTSD is complex and difficult to treat

• The available evidence supports the use of structured trauma-focused or non–trauma-focused approaches

• Although trauma-focused and non–trauma-focused interventions often improve symptoms, many patients continue to meet criteria for PTSD after treatment

• There is an urgent need for innovative treatment strategies, whether trauma-focused or non–trauma-focused

Steenkamp et al JAMA 2015
Pharmacotherapy and prevention

- Covers the use of pharmacological agents post trauma to prevent development of symptoms
- Limited high level evidence
- ACPMH Guidelines (ACPMH, 2013)
  - Should not be used for all those exposed as a preventative intervention
Pharmacotherapy and Prevention

- Pitman et al (Biol. Psychiatry 2002)
  - Propranolol (N= 18) V Placebo (23)

- Stein et al (J. Traumatic Stress 2007)
  - Propranolol (n=17) V Gabapentin(14) V Placebo (17)
  - No impact on severity of PTSD or depressive Symptoms

  - Treatment with Clonazepam/Alprazolam (N= 10) V Placebo (N= 13)
  - No impact of treatment on anxiety or PTSD symptom scores

  - Variable dose hydrocortisone V Placebo (N=91)
  - Significant reduction in chronic stress, but not PTSD symptoms in Steroid treated group (p<.05)
Conclusion

• PTSD is a common, complex and disabling disorder
• PTSD is particularly common in certain subgroups
• PTSD is a cause of high personal and economic burden
• Currently only Level 1 evidence for SSRIs
  • Effect size small-medium
• Most guidelines recommend psychotherapy as first line treatment but not always appropriate
• Marked unmet need