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# De farmacologische behandeling van traumaklachten, ihb behandeling van nachtmerries en slaapproblemen

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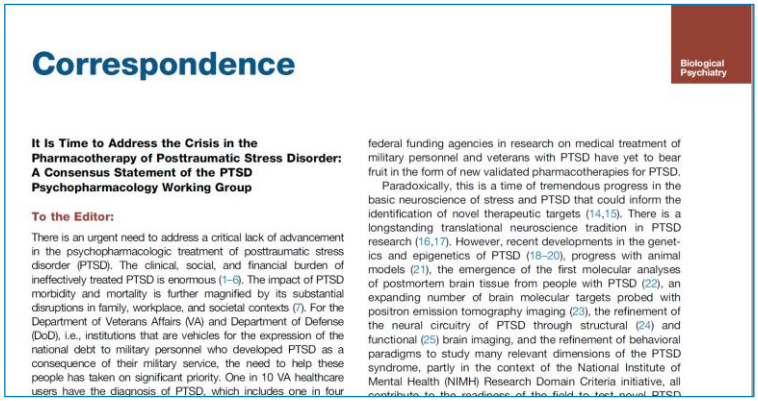
# Crisis in pharmacotherapy of PTSD

**# Only two medications approved**
**# Off label polypharmacy, little empirical evidence**
**# Research has stalled, void in new drug development**



Correspondence

Biological Psychiatry

**It Is Time to Address the Crisis in the Pharmacotherapy of Posttraumatic Stress Disorder: A Consensus Statement of the PTSD Psychopharmacology Working Group**

**To the Editor:**

There is an urgent need to address a critical lack of advancement in the psychopharmacologic treatment of posttraumatic stress disorder (PTSD). The clinical, social, and financial burden of ineffectively treated PTSD is enormous (1–6). The impact of PTSD morbidity and mortality is further magnified by its substantial disruptions in family, workplace, and societal contexts (7). For the Department of Veterans Affairs (VA) and Department of Defense (DoD), i.e., institutions that are vehicles for the expression of the national debt to military personnel who developed PTSD as a consequence of their military service, the need to help these people has taken on significant priority. One in 10 VA healthcare users have the diagnosis of PTSD, which includes one in four

federal funding agencies in research on medical treatment of military personnel and veterans with PTSD have yet to bear fruit in the form of new validated pharmacotherapies for PTSD.

Paradoxically, this is a time of tremendous progress in the basic neuroscience of stress and PTSD that could inform the identification of novel therapeutic targets (14,15). There is a longstanding translational neuroscience tradition in PTSD research (16,17). However, recent developments in the genetics and epigenetics of PTSD (18–20), progress with animal models (21), the emergence of the first molecular analyses of postmortem brain tissue from people with PTSD (22), an expanding number of brain molecular targets probed with positron emission tomography imaging (23), the refinement of the neural circuitry of PTSD through structural (24) and functional (25) brain imaging, and the refinement of behavioral paradigms to study many relevant dimensions of the PTSD syndrome, partly in the context of the National Institute of Mental Health (NIMH) Research Domain Criteria initiative, all

## Recommendations

Krystal et al., *Biol Psych*, 2017

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## Medications filed as prescriptions in 2004 -2013 after first diagnosis PTSD

| | Fiscal Year | | | | |
|---|---|---|---|---|---|
| | 2004 | 2007 | 2010 | 2013 | Overall |
| New PTSD Episodes | 51,750 | 69,604 | 84,850 | 82,546 | 731,520 |
| Mean Number of Psychotropics | 3.5 ± 2.5 | 3.5 ± 2.6 | 3.6 ± 2.7 | 3.5 ± 2.7 | 3.5 ± 2.7 |
| All Antidepressants | 85.1 (44,026) | 82.7 (57,544) | 80.1 (68,001) | 78.0 (64,394) | 81.0 (592,505) |
| Amitriptyline | 5.7 (2948) | 4.6 (3195) | 3.8 (3221) | 3.7 (3074) | 4.2 (31,019) |
| Mirtazapine | 12.4 (6392) | 12.3 (8578) | 12.9 (10,973) | 13.0 (10,722) | 12.6 (92,460) |
| Nefazodone | 1.2 (638) | 0.3 (237) | 0.1 (116) | 0.1 (50) | 0.3 (2097) |
| Phenelzine | 0.0 (20) | 0.0 (10) | 0.0 (8) | 0.0 (8) | 0.0 (92) |
| Trazodone | 33.4 (17,296) | 32.3 (22,484) | 30.5 (25,847) | 29.7 (24,489) | 31.0 (226,812) |
| Any SSRI or SNRI | 70.1 (36,290) | 67.6 (47,064) | 65.7 (55,740) | 63.1 (52,112) | 66.3 (485,194) |
| Fluoxetine | 13.9 (7212) | 11.8 (8246) | 9.5 (8022) | 11.5 (9481) | 11.3 (82,346) |
| Paroxetine | 10.3 (5331) | 7.0 (4842) | 5.0 (4266) | 6.0 (4951) | 6.6 (48,215) |
| Sertraline | 26.0 (13,449) | 16.3 (11,367) | 21.4 (18,145) | 31.2 (25,771) | 22.9 (167,613) |
| Venlafaxine | 9.2 (4770) | 8.5 (5882) | 8.4 (7121) | 11.7 (9680) | 9.1 (66,747) |
| All Anticonvulsants | 21.8 (11,267) | 22.8 (15,871) | 26.0 (22,080) | 29.1 (24,005) | 24.9 (182,077) |
| Gabapentin | 11.1 (5739) | 12.1 (8399) | 15.2 (12,851) | 18.2 (15,001) | 14.1 (102,791) |
| Topiramate | 2.1 (1072) | 2.6 (1832) | 3.3 (2764) | 4.3 (3517) | 3.1 (22,803) |
| Valproic acid | 7.3 (3794) | 6.8 (4723) | 6.8 (5732) | 6.2 (5152) | 6.7 (49,197) |
| Prazosin | 6.1 (3171) | 9.6 (6690) | 17.3 (14,641) | 25.8 (21,291) | 15.0 (110,048) |
| All Atypical Antipsychotics | 29.7 (15,390) | 23.8 (16,562) | 20.3 (17,185) | 16.9 (13,944) | 21.8 (159,757) |
| Olanzapine | 4.5 (2347) | 1.9 (1342) | 1.7 (1444) | 1.6 (1298) | 2.0 (14,691) |
| Quetiapine | 18.9 (9758) | 15.8 (10,970) | 11.5 (9728) | 9.0 (7426) | 13.3 (97,542) |
| Risperidone | 9.9 (5126) | 6.1 (4248) | 5.1 (4323) | 4.7 (3917) | 5.8 (42,311) |
| All Typical Antipsychotics | 1.8 (946) | 1.8 (1275) | 1.8 (1526) | 1.8 (1485) | 1.8 (13,304) |
| All Addiction Medicines[a] | 7.8 (4027) | 12.4 (8665) | 12.9 (10,984) | 12.9 (10,637) | 11.9 (87,361) |
| All Sedative Hypnotics | 38.2 (19,776) | 37.9 (26,353) | 41.3 (35,085) | 35.4 (29,262) | 38.9 (284,877) |
| Zolpidem | 4.6 (2404) | 7.9 (5532) | 18.2 (15,472) | 14.3 (11,837) | 13.0 (95,086) |
| Any benzodiazepine | 34.9 (18,066) | 32.9 (22,907) | 29.4 (24,979) | 25.1 (20,756) | 30.3 (221,309) |
| All Opioids[b] | 35.4 (18,325) | 37.8 (26,301) | 38.3 (32,473) | 34.6 (28,564) | 36.9 (270,103) |
| All Stimulants | 1.1 (592) | 1.5 (1060) | 2.3 (1991) | 3.3 (2702) | 2.1 (15,690) |
| Lithium | 1.8 (942) | 1.4 (951) | 1.4 (1162) | 1.5 (1254) | 1.4 (10,580) |
| Buspirone | 5.1 (2665) | 4.7 (3241) | 4.9 (4168) | 6.4 (5269) | 5.1 (37,614) |

Values are mean ± SD or % (n). Data from Shiner and Westgate (37). Cohort is described in detail elsewhere (38).
PTSD, posttraumatic stress disorder; SNRI, serotonin and norepinephrine reuptake inhibitors; SSRI, selective serotonin reuptake inhibitors.
[a]Includes acamprosate, buprenorphine, disulfuram, naltrexone, nicotine replacement, and varenicline.
[b]Includes all opioids in this class code (excluding methadone from methadone clinic) plus tramadol.

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**Table 4. Phase II Investigator-Initiated Drug Clinical Trials for PTSD in the United States Since 2006**

| Study Name | Intervention | Status | Funding Agency | Results |
|---|---|---|---|---|
| Pharmacogenetic Clinical Trial of Nepicastat for PTSD | SYN117 (nepicastat) vs. placebo | Completed (11/2009) | Department of Defense | Negative[a] |
| Risperidone Treatment for Military Service Related Chronic PTSD (CSP 504) | Risperidone vs. placebo | Completed (1/2011) | VA Office of Research & Development, Janssen provided drug | Negative (36) |
| Iloperidone for Symptoms of Arousal in PTSD | Iloperidone vs. placebo | Completed (2/2014) | University of Colorado, Novartis Pharmaceuticals (collaborator) | No published results |
| Ganaxolone in Posttraumatic Stress Disorder | Ganaxolone vs. placebo | Completed (3/2014) | Department of Defense, Marinus provided drug | Pending-results not published yet |
| Nepicastat for PTSD in OIF/OEF Veterans | Nepicastat vs. placebo | Completed (6/2014) | Department of Defense | Negative[a] |
| Evaluation of GSK561679 in Women With PTSD | GSK561679 vs. placebo | Completed (8/2014) | VA Office of Research & Development, National Institute of Mental Health | Negative |
| Glial Regulators for Testing Comorbid PTSD and Substance Use Disorders | *N*-acetylcysteine vs. placebo CPT | Completed (9/2014) | Medical University of South Carolina, Department of Defense, Institute for Translational Neuroscience | Participants treated with *N*-acetylcysteine compared with placebo evidenced significant improvements in PTSD symptoms (65). |
| Trial of Mifepristone in Combat Veterans With PTSD | Mifepristone vs. placebo | Recruiting | James J Peters VA Medical Center (Bronx, NY) | Ongoing |
| A Randomized Clinical Trial of Mifepristone in PTSD | Mifepristone vs. placebo | Recruiting | Bronx VA Medical Center, San Diego VA Medical Center, Durham VA Medical Center | Ongoing |
| Novel Therapeutics in PTSD: A Randomized Clinical Trial of Mifepristone | Mifepristone vs. placebo | Recruiting | VA Office of Research & Development | Ongoing |
| Repeated-Dose Intravenous Ketamine for PTSD | Ketamine vs. midazolam (active comparator) | Recruiting | Icahn School of Medicine at Mt. Sinai | Ongoing |
| CAP-Ketamine for Antidepressant Resistant PTSD | Ketamine vs. placebo | Recruiting | VA Office of Research & Development | Ongoing |
| Zonisamide in Addition to E-CPT-C for Veterans With PTSD and Comorbid Alcohol Dependence | Zonisamide vs. placebo E-CPT-C | Recruiting | Department of Defense | Ongoing |

CPT, Cognitive Processing Therapy; E-CPT-C, Enhanced Cognitive Processing Therapy-C; OEF, Operation Enduring Freedom; OIF, Operation Iraqi Freedom; PTSD, posttraumatic stress disorder; VA, Veterans Affairs.

[a]L. Davis, M.D., personal communication, Feb 17, 2017.

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**Phase III Investigator-Initiated Drug Clinical Trials for PTSD in the United States Since 2006**

| Study Name | Intervention | Status | Funding Agency | Results |
|---|---|---|---|---|
| Levetiracetam in PTSD | Levetiracetam vs. placebo | Completed (3/2008) | Duke University, UCB Pharma | No published results |
| CSP 563: Prazosin and Combat Trauma PTSD | Prazosin vs. placebo | Completed (5/2013) | VA Office of Research & Development | Negative [a] |
| Prazosin for Treatment of Patients With Alcohol Dependence and PTSD | Prazosin vs. placebo | Completed (10/2014) | Department of Defense and VA VISN 1 | Negative ( 59 ) |
| Prazosin for Nightmares and Sleep Disturbance | Prazosin vs. placebo | Completed (2/16/2006) | VA Office of Research and Development and NIMH | Positive ( 40 ) |
| Prazosin for Combat Trauma PTSD | Prazosin vs. placebo | Completed (8/29/2012) | VA Office of Research (VISN 20 MIRECC) | Positive ( 41 ) |

CSP, Cooperative Studies Program; MIRECC, Mental Illness Research, Education and Clini
Institute of Mental Health; PTSD, posttraumatic stress disorder; VA, Veterans Affairs; VISN
Network.
a M. Raskind, M.D., personal communication, Feb 1, 2017.


Prazosin and doxazosin for PTSD are underutilized and underdosed

Why is PTSD overlooked in substance use?

Prazosin and doxazosin, which have been used for PTSD, also can treat substance abuse; this "two birds with one stone" approach could become more common in clinical practice

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# Review studies pharmacotherapy in PTSD

Review article

## Pharmacotherapy for post-traumatic stress disorder: systematic review and meta-analysis

Mathew Hoskins, Jennifer Pearce, Andrew Bethell, Liliya Dankova, Corrado Barbui, Wietse A. Tol, Mark van Ommeren, Joop de Jong, Soraya Seedat, Hanhui Chen and Jonathan I. Bisson

**Background**
Pharmacological treatment is widely used for post-traumatic stress disorder (PTSD) despite questions over its efficacy.

**Aims**
To determine the efficacy of all types of pharmacotherapy, as monotherapy, in reducing symptoms of PTSD, and to assess acceptability.

**Method**
A systematic review and meta-analysis of randomised controlled trials was undertaken; 51 studies were included.

**Results**
Selective serotonin reuptake inhibitors were found to be statistically superior to placebo in reduction of PTSD symptoms but the effect size was small (standardised mean difference −0.23, 95% CI −0.33 to [illegible] pharmacological agents compared wit[illegible] more trials, we found small statistical[illegible] of efficacy for fluoxetine, paroxetine a[illegible]

**Conclusions**
Some drugs have a small positive impa[illegible] and are acceptable. Fluoxetine, parox[illegible] may be considered as potential treatm[illegible] For most drugs there is inadequate e[illegible] efficacy for PTSD, pointing to the nee[illegible] this area.

**Declaration of interest**
None.

Pharmacotherapy for post traumatic stress disorder (PTSD) (Review)

Stein DJ, Ipser JC, Seedat S

THE COCHRANE COLLABORATION®

| Study or Subgroup | Experimental Mean | SD | Total | Control Mean | SD | Total | Weight | Std. Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| Brady 2000 | -33 | 28.1 | 94 | -23.2 | 28.7 | 93 | 6.7% | -0.34 [-0.63, -0.05] |
| Brady 2004 | 32.56 | 15.69 | 49 | 32.7 | 28.75 | 45 | 4.5% | -0.01 [-0.41, 0.40] |
| Connor 1999 | 10.1 | 9.8 | 25 | 20.5 | 12.6 | 22 | 2.4% | -0.91 [-1.52, -0.31] |
| Davidson | -39.4 | 27.12 | 173 | -34.17 | 28.42 | 179 | 8.8% | -0.19 [-0.40, 0.02] |
| Davidson 2001c | -33 | 23.76 | 100 | -26.2 | 23.9 | 108 | 7.0% | -0.28 [-0.56, -0.01] |
| Friedman 2007 | -13.1 | 27.5 | 84 | -15.4 | 28.07 | 82 | 6.3% | 0.08 [-0.22, 0.39] |
| Hertzberg 2000 | 47 | 8 | 6 | 42 | 11 | 6 | 0.8% | 0.48 [-0.68, 1.64] |
| Marshall 2001 | -38.75 | 27.2 | 375 | -25.3 | 25.8 | 188 | 9.8% | -0.50 [-0.68, -0.32] |
| Marshall 2004 | 55.6 | 33.4 | 25 | 62.8 | 40.8 | 27 | 2.9% | -0.19 [-0.73, 0.36] |
| Martenyi 2002A | -34.6 | 28.1 | 226 | -26.8 | 26.1 | 75 | 7.3% | -0.28 [-0.54, -0.02] |
| Martenyi 2007 | -42.85 | 25.5 | 323 | -36.6 | 25.7 | 88 | 8.0% | -0.24 [-0.48, -0.01] |
| Panahi 2011 | -22.7 | 7.3 | 35 | -17.5 | 7.5 | 35 | 3.5% | -0.69 [-1.18, -0.21] |
| Pfizer588 | -27.4 | 27.12 | 94 | -27.9 | 28.42 | 94 | 6.7% | 0.02 [-0.27, 0.30] |
| Shalev 2011 | -31.12 | 29.63 | 23 | -27.8 | 20.13 | 23 | 2.6% | -0.13 [-0.71, 0.45] |
| SKB627 | -36.5 | 26.1 | 109 | -30.8 | 25.37 | 103 | 7.1% | -0.22 [-0.49, 0.05] |
| Tucker 2001 | -35.5 | 24.58 | 151 | -24.7 | 24.98 | 156 | 8.3% | -0.43 [-0.66, -0.21] |
| Tucker 2003 | -41.82 | 29.09 | 23 | -38.7 | 29.07 | 10 | 1.7% | -0.10 [-0.85, 0.64] |
| van der Kolk 2004 | -33.23 | 22.11 | 30 | -30.95 | 22.6 | 29 | 3.2% | -0.10 [-0.61, 0.41] |
| Zohar 2002 | -18.7 | 6.7 | 23 | -13.5 | 6.6 | 19 | 2.3% | -0.77 [-1.40, -0.14] |
| **Total (95% CI)** | | | **1968** | | | **1382** | **100.0%** | **-0.27 [-0.37, -0.16]** |

Heterogeneity: Tau² = 0.02; Chi² = 32.43, df = 18 (P = 0.02); I² = 45%
Test for overall effect: Z = 5.04 (P < 0.00001)

Std. Mean Difference IV, Random, 95% CI

-0.2 -0.1 0 0.1 0.2
Favours [experimental] Favours [control]

*Hoskins et al, British Journal of Psychiatry, 2015*

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Group (N = 27)
Top therapeutic Targets for PTSD from Expert Group

| | |
|---|---|
| NMDA Receptor Antagonists | 78 |
| Cannabinoid Receptor Modulators | 70 |
| Glucocorticoid Receptor Agonists | 58 |
| Non-SRI Antidepressants | 50 |
| Opioid Receptor Agonists | 25 |
| Alpha-1 Adrenergic Receptor Antagonists | 21 |
| 5HT2-D2 Receptor Antagonist (Other Than Risperidone) | 20 |
| Riluzole | 18 |
| Alpha-2 Adrenergic Receptor Agonists | 18 |
| NPY Receptor Modulators | 10 |
| Glucocorticoid Low-Activity Partial Agonists And/Or Antagonist | 10 |
| Orexin Receptor Antagonists | 9 |
| NMDA Receptor Coagonists | 9 |
| Anticonvulsants | 8 |
| D2 Receptor Agonists | 8 |

D2, dopamine type 2; NMDA, N-methyl-D-aspartate; NPY, neuropeptide Y; PTSD, posttraumatic stress disorder; SRI, serotonin reuptake inhibitor; 5-HT2, 5-hydroxytryptamine-2.

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# Recommendations

# The urgent need to find effective pharmacologic treatments for PTSD should be considered a national mental health priority.
# There is a need to increase the number of early phase clinical trials through novel collaborations among government, industry, and academia.
# There is a need to develop new trial designs and/or methodologies specifically in the area of PTSD psychopharmacology trials.
# Foundational studies are required to inform the optimal prescription of commonly prescribed medications for the treatment of PTSD.
# The development of a psychopharmacology clinical trials workforce and infrastructure for PTSD would advance the goal of increasing clinical trials in this area.
# Studies exploring the pathophysiology of PTSD will be critical to inform the rational development of novel pharmacologic interventions.
# There is a need to continue to invest in initiatives in translational neuroscience to enhance the expansion of the pipeline of new PTSD pharmacotherapeutics.

Krystal et al., BP, 2017

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**Brief Report**

# Reduction of Nightmares and Other PTSD Symptoms in Combat Veterans by Prazosin: A Placebo-Controlled Study

Murray A. Raskind, M.D.
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Ronald G. Thomas, Ph.D.
Miles M. McFall, Ph.D.

10mg dd for nightmares

**Objective:** Prazosin is a centrally active $\alpha_1$ adrenergic antagonist. The authors' goal was to evaluate prazosin efficacy for nightmares, sleep disturbance, and overall posttraumatic stress disorder (PTSD) in combat veterans.

**Method:** Ten Vietnam combat veterans with chronic PTSD and severe trauma-related nightmares each received prazosin and placebo in a 20-week double-blind crossover protocol.

**Results:** Prazosin (mean dose=9.5 mg/day at bedtime, SD=0.5) was superior to placebo for the three primary outcome measures: scores on the 1) recurrent distressing dreams item and the 2) difficulty falling/staying asleep item of the Clinician-Administered PTSD Scale and 3) change in overall PTSD severity and functional status according to the Clinical Global Impression of change. Total score and symptom cluster scores for reexperiencing, hyperarousal on the Clinician-Administered PTSD Scale were significantly more improved in the prazosin condition, and prazosin was well tolerated.

**Conclusions:** These data support the efficacy of prazosin for nightmares, sleep disturbance, and other PTSD symptoms.

*(Am J Psychiatry 2003; 160:371–373)*

| Case | Age | Optimum Prazosin Dose | CAPS-SX Nightmare Frequency + Severity | | | CAPS-SX Insomnia Frequency + Severity | | | CAPS-SX Total Score | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Baseline | Week 2 | Week 6 | Baseline | Week 2 | Week 6 | Baseline | Week 2 | Week 6 |
| 1 | 53 | 1 mg hs | 6 | | 2 | 6 | | 2 | 103 | | 81 |
| 2 | 45 | 1 mg a.m. and hs | 7 | 2 | 0 | 7 | 0 | 2 | 107 | 83 | 57 |
| 3 | 53 | 1 mg hs | 0 | 1 | 1 | 0 | 0 | 0 | 97 | 83 | 63 |
| 4 | 48 | 2 mg a.m. and hs | 5 | 0 | 1 | 7 | 0 | 3 | 102 | 82 | 71 |
| 5 | 40 | 1 mg hs | 7 | 0 | 1 | 7 | 3 | 3 | 106 | 84 | 69 |

[a]hs, at bedtime.

**The [alpha]1-Adrenergic Antagonist Prazosin Improves Sleep and Nightmares in Civilian Trauma Posttraumatic Stress Disorder.**
Taylor, Fletcher; Raskind, Murray

Journal of Clinical Psychopharmacology. 22(1):82-85, February 2002.

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Neurol Ther (2017) 6:247–257
DOI 10.1007/s40120-017-0078-4

ORIGINAL RESEARCH

# Use of Prazosin for Pediatric PTSD-Associated Nightmares and Sleep Disturbances: A Retrospective Chart Review

Brooks R. Keeshin · Qian Ding · Angela P. Presson · Steven J. Berkowitz · Jeffrey R. Strawn

Received: June 2, 2017 / Published online: July 28, 2017


ABSTRACT

***Introduction***: Youth exposed to trauma have an increased risk for developing posttraumatic stress disorder (PTSD) and associated sleep disturbances and nightmares. The alpha-1

**Enhanced Content** To view enhanced content for this article go to http://www.medengine.com/Redeem/A3E8F0602EF51F68.

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**Table 2** Posttraumatic stress disorder symptoms and vital signs at baseline and last time point, and change-over time

| Variable | Baseline, mean (SD) | Last time point, mean (SD) | Time estimate (95% CI) | Significance |
|---|---|---|---|---|
| Sleep score (range 0–8) | 7.32 (0.94) | 3.09 (2.40) | −0.939 (−1.219, −0.659) | <0.0001* |
| UCLA score | 51.65 (10.42) | 35.06 (14.52) | −4.5 (−5.821, −3.179) | <0.0001* |
| Intrusive | 13.65 (3.52) | 8.53 (4.41) | −1.241 (−1.691, −0.791) | <0.0001* |
| Avoidance | 6.03 (1.95) | 4.53 (1.95) | −0.35 (−0.565, −0.134) | 0.0019* |
| Negative mood | 16.71 (4.61) | 12.75 (5.27) | −1.217 (−1.682, −0.751) | <0.0001* |
| Arousal | 15.26 (3.33) | 9.78 (4.72) | −1.62 (−2.062, −1.178) | <0.0001* |
| Weight | 54.51 (17.16) | 55.80 (17.32) | 0.331 (0.15, 0.512) | 0.0005* |
| Systolic blood pressure | 104.64 (8.88) | 106.83 (11.81) | 0.103 (−0.901, 1.106) | 0.84 |
| Diastolic blood pressure | 61.30 (8.15) | 62.63 (8.30) | 0.565 (−0.269, 1.4) | 0.18 |
| Heart rate | 77.58 (13.03) | 81.83 (10.70) | 1.212 (−0.117, 2.541) | 0.07 |

* Significant difference between baseline and last time point at $p \leq 0.05$
CI, Confidence interval

headaches (6%). Prazosin treatment was associated with improved sleep and nightmares over time (pre-treatment $7.3 \pm 0.9$, post-treatment $3.1 \pm 2.4$; $p < 0.001$).

***Conclusion***: Prazosin was well-tolerated and associated with improvements in nightmares and sleep in youth with PTSD. Adverse events were consistent with the known side-effect profile of prazosin and included dizziness and nausea.

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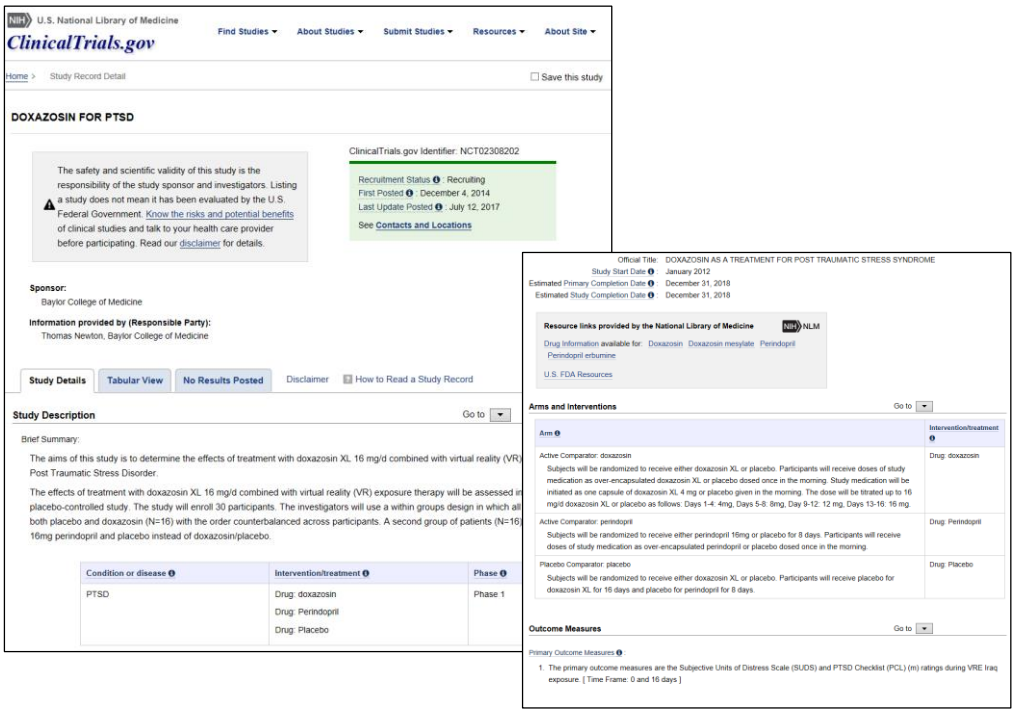

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**DOXAZOSIN FOR PTSD**

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Know the risks and potential benefits of clinical studies and talk to your health care provider before participating. Read our disclaimer for details.

ClinicalTrials.gov Identifier: NCT02308202

Recruitment Status : Recruiting
First Posted : December 4, 2014
Last Update Posted : July 12, 2017

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**Sponsor:**
Baylor College of Medicine

**Information provided by (Responsible Party):**
Thomas Newton, Baylor College of Medicine

Study Details | Tabular View | No Results Posted | Disclaimer | How to Read a Study Record

**Study Description** Go to

Brief Summary:

The aims of this study is to determine the effects of treatment with doxazosin XL 16 mg/d combined with virtual reality (VR) Post Traumatic Stress Disorder.

The effects of treatment with doxazosin XL 16 mg/d combined with virtual reality (VR) exposure therapy will be assessed in placebo-controlled study. The study will enroll 30 participants. The investigators will use a within groups design in which all both placebo and doxazosin (N=16) with the order counterbalanced across participants. A second group of patients (N=16) 16mg perindopril and placebo instead of doxazosin/placebo.

| Condition or disease | Intervention/treatment | Phase |
|---|---|---|
| PTSD | Drug: doxazosin<br>Drug: Perindopril<br>Drug: Placebo | Phase 1 |

Official Title: DOXAZOSIN AS A TREATMENT FOR POST TRAUMATIC STRESS SYNDROME
Study Start Date : January 2012
Estimated Primary Completion Date : December 31, 2018
Estimated Study Completion Date : December 31, 2018

**Resource links provided by the National Library of Medicine** NLM

Drug Information available for: Doxazosin Doxazosin mesylate Perindopril Perindopril erbumine

U.S. FDA Resources

**Arms and Interventions** Go to

| Arm | Intervention/treatment |
|---|---|
| Active Comparator: doxazosin<br>Subjects will be randomized to receive either doxazosin XL or placebo. Participants will receive doses of study medication as over-encapsulated doxazosin XL or placebo dosed once in the morning. Study medication will be initiated as one capsule of doxazosin XL 4 mg or placebo given in the morning. The dose will be titrated up to 16 mg/d doxazosin XL or placebo as follows: Days 1-4: 4mg, Days 5-8: 8mg, Day 9-12: 12 mg, Days 13-16: 16 mg. | Drug: doxazosin |
| Active Comparator: perindopril<br>Subjects will be randomized to receive either perindopril 16mg or placebo for 8 days. Participants will receive doses of study medication as over-encapsulated perindopril or placebo dosed once in the morning. | Drug: Perindopril |
| Placebo Comparator: placebo<br>Subjects will be randomized to receive either doxazosin XL or placebo. Participants will receive placebo for doxazosin XL for 16 days and placebo for perindopril for 8 days. | Drug: Placebo |

**Outcome Measures** Go to

Primary Outcome Measures

1. The primary outcome measures are the Subjective Units of Distress Scale (SUDS) and PTSD Checklist (PCL) (m) ratings during VRE Iraq exposure. [ Time Frame: 0 and 16 days ]

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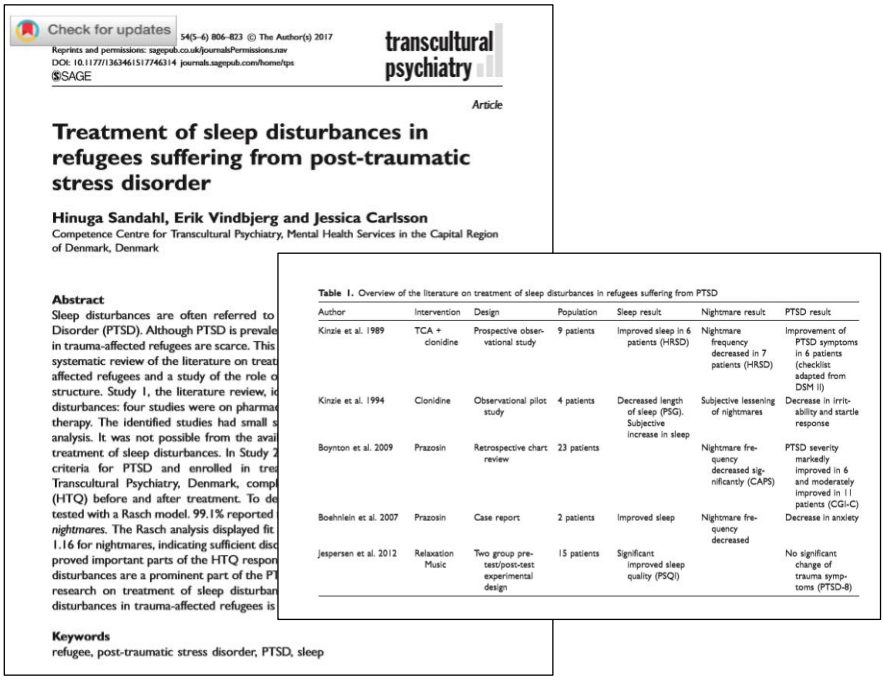



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DOI: 10.1177/1363461517746314 journals.sagepub.com/home/tps
SAGE

transcultural psychiatry

Article

## Treatment of sleep disturbances in refugees suffering from post-traumatic stress disorder

**Hinuga Sandahl, Erik Vindbjerg and Jessica Carlsson**
Competence Centre for Transcultural Psychiatry, Mental Health Services in the Capital Region of Denmark, Denmark

**Abstract**
Sleep disturbances are often referred to
Disorder (PTSD). Although PTSD is prevale
in trauma-affected refugees are scarce. This
systematic review of the literature on treat
affected refugees and a study of the role o
structure. Study 1, the literature review, i
disturbances: four studies were on pharma
therapy. The identified studies had small s
analysis. It was not possible from the avai
treatment of sleep disturbances. In Study 2
criteria for PTSD and enrolled in tre
Transcultural Psychiatry, Denmark, compl
(HTQ) before and after treatment. To de
tested with a Rasch model. 99.1% reported
*nightmares*. The Rasch analysis displayed fit
1.16 for nightmares, indicating sufficient disc
proved important parts of the HTQ respon
disturbances are a prominent part of the PT
research on treatment of sleep disturban
disturbances in trauma-affected refugees is

**Keywords**
refugee, post-traumatic stress disorder, PTSD, sleep

**Table 1.** Overview of the literature on treatment of sleep disturbances in refugees suffering from PTSD

| Author | Intervention | Design | Population | Sleep result | Nightmare result | PTSD result |
|---|---|---|---|---|---|---|
| Kinzie et al. 1989 | TCA + clonidine | Prospective observational study | 9 patients | Improved sleep in 6 patients (HRSD) | Nightmare frequency decreased in 7 patients (HRSD) | Improvement of PTSD symptoms in 6 patients (checklist adapted from DSM II) |
| Kinzie et al. 1994 | Clonidine | Observational pilot study | 4 patients | Decreased length of sleep (PSG). Subjective increase in sleep | Subjective lessening of nightmares | Decrease in irritability and startle response |
| Boynton et al. 2009 | Prazosin | Retrospective chart review | 23 patients | | Nightmare frequency decreased significantly (CAPS) | PTSD severity markedly improved in 6 and moderately improved in 11 patients (CGI-C) |
| Boehnlein et al. 2007 | Prazosin | Case report | 2 patients | Improved sleep | Nightmare frequency decreased | Decrease in anxiety |
| Jespersen et al. 2012 | Relaxation Music | Two group pre-test/post-test experimental design | 15 patients | Significant improved sleep quality (PSQI) | | No significant change of trauma symptoms (PTSD-8) |

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Psychoneuroendocrinology (2015) 51, 585–588

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/psyneuen

# The efficacy of nabilone, a synthetic cannabinoid, in the treatment of PTSD-associated nightmares: A preliminary randomized, double-blind, placebo-controlled cross-over design study

Rakesh Jetly[a,*], Alexandra Heber[a], George Fraser[b], Denis Boisvert[b]

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[b] Operational Trauma and Stress Support Centre, Canadian Forces Health Services Centre, Otta

Received 19 August 2014; received in revised form 30 October 2014; accepted 3 November 2014

KEYWORDS
PTSD;
Nightmares;
RCT;
Nabilone;
Treatment

Summary
*Objective:* Investigate the efficacy of nabilone capsules (N
intensity of nightmares in subjects with PTSD.
*Patients and methods:* Canadian male military personnel
treatment continued to experience trauma-related nightm
ment with 0.5 mg NAB or placebo (PBO), and then titrated
suppression) or reaching a maximum of 3.0 mg. Subjects we
following a 2-week washout period, were titrated with the c
for an additional 7 weeks. The modified intent-to-treat (mI
treated subjects that met inclusion/exclusion criteria, was
*Results:* Ten subjects were included in the mITT population.
as measured by the CAPS Recurring and Distressing Dream sco
in the NAB and PBO groups, respectively ($p = 0.03$). Mean
by the Clinical Global Impression of Change (CGI-C) was $1.9 \pm 1.1$ (i.e. much improved) and $3.2 \pm 1.2$ (i.e. minimally improved) in the NAB and PBO groups, respectively ($p = 0.05$). Five out of 10 (50%) were much improved on NAB versus 1 out of 9 (11%) on PBO. Results for the General Well Being Questionnaire (WBQ) were $20.8 \pm 22$ and $-0.4 \pm 20.6$ in the NAB and PBO groups, respectively ($p = 0.04$). The proportion of subjects who experienced a treatment-related occurrence of adverse events was 50% in the NBO group and 60% in the PBO group. No event was severe nor resulted in a drop-out. This study is registered with Health Canada.

Table 1 Change from baseline for both periods.

| | | Nabilone $n = 10$ | Placebo $n = 9$ | $p$-value[a] |
|---|---|---|---|---|
| CAPS[b] | Mean ± SD | −3.6 ± 2.4 | −1.0 ± 2.1 | 0.03 |
| | Median (P25, P75) | −3.5 (−6.0,−2.0) | 0.0 (−2.0,0.0) | |
| CGI-C[c] | Mean ± SD | 1.9 ± 1.1 | 3.2 ± 1.2 | 0.05 |
| | Median (P25, P75) | 1.5 (1.0,3.0) | 3.0 (3.0,4.0) | |
| WBQ[d] | Mean ± SD | 20.8 ± 22.1 | −0.4 ± 20.6 | 0.04 |
| | Median (P25, P75) | 18.0 (8.0,24.0) | −4.0 (−8.0,4.0) | |

[a] Wilcoxon Rank-Sum test.
[b] Clinician-Administered PTSD Scale (DSM-IV). Recurring and Distressing Dream Item, Frequency + Intensity.
[c] Clinical Global Impression of Change.
[d] General Well Being Questionnaire.

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DOI: 10.1002/da.22596

REVIEW

WILEY ADAA

# Marijuana and other cannabinoids as a treatment for posttraumatic stress disorder: A literature review

**Maria M. Steenkamp, PhD** | **Esther M. Blessing, MD PhD** | **Isaac R. Galatzer-Levy, PhD** | **Laura C. Hollahan, MA** | **William T. Anderson, MA**

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Posttraumatic stress disorder (PTSD) is common in the general population, yet there are limitations to the effectiveness, tolerability, and acceptability of available first-line interventions. We review the extant knowledge on the effects of marijuana and other cannabinoids on PTSD. Potential therapeutic effects of these agents may largely derive from actions on the endocannabinoid system and we review major animal and human findings in this area. Preclinical and clinical studies generally support the biological plausibility for cannabinoids' potential therapeutic effects, but underscore heterogeneity in outcomes depending on dose, chemotype, and individual variation. Treatment outcome studies of whole plant marijuana and related cannabinoids on PTSD are limited and not methodologically rigorous, precluding conclusions about their potential therapeutic effects. Reported benefits for nightmares and sleep (particularly with synthetic cannabinoid nabilone) substantiate larger controlled trials to determine effectiveness and tolerability. Of concern, marijuana use has been linked to adverse psychiatric outcomes, including conditions com-

**TABLE 1** Available outcome studies on marijuana and other cannabinoids for PTSD

| Source | Drug | Design | Sample | Length of Administration | PTSD Outcome | Findings |
|---|---|---|---|---|---|---|
| Greer et al. (2014) | Whole plant marijuana | Retrospective symptom report | 80 US civilian adults | NA | CAPS | Mean CAPS total score reduction of 76.3 points |
| Roitman et al. (2014) | THC | Uncontrolled pilot study | 10 Israeli adults | 3 weeks | CAPS | Mean CAPS total score reduction of 16.0 points |
| Fraser et al. (2009) | Nabilone | Uncontrolled pilot study | 47 Canadian civilian adults | NR | Self-report of nightmare intensity | 72% reported total cessation or lessening of nightmare severity |
| Cameron et al. (2014) | Nabilone | Chart review | 104 Canadian incarcerated adults | Average of 11.2 weeks | PCL-C | Mean PCL total score reduction of 15.9 points |
| Jetly et al. (2015) | Nabilone | Randomized placebo-controlled cross-over trial | 10 Canadian military personnel | 7 weeks | CAPS nightmare item | Mean reduction on item of 3.6 points |

CAPS, Clinician Administered PTSD Scale (range: 0–136); NR, not reported; NA, not applicable; PCL, PTSD Checklist—Civilian version (range: 17–85).

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1200 BAKER: USE OF LYSERGIC ACID DIETHYLAMIDE — Canad. Med. Ass. J. Dec. 5, 1964, vol. 91

# The Use of Lysergic Acid Diethylamide (LSD) in Psychotherapy

E. F. W. BAKER, M.D., F.R.C.P.[C], *Toronto*

**ABSTRACT**

**One hundred of 150 patients with non-psychotic functional psychiatric disorders were benefited by the use of LSD psychotherapy. The dosage of LSD employed was 25 to 2000 micrograms intramuscularly per session for from one to 10 sessions, On this regimen four patients became psychotic and required electroconvulsive therapy. None were permanently harmed.**

**Indications for and contraindications to this form of treatment and a procedure involving a doctor and a nurse as co-therapists are discussed. In particular, LSD is considered to permit "perceptualization of the transference".**

**LSD possibly extends the scope and value of the psychotherapeutic approach in such cases.**

**SOMMAIRE**

**Sur 150 malades atteints de troubles psychiatriques fonctionnels non psychotiques, l'emploi combiné de LSD et de psychothérapie a permis d'en améliorer 100. La posologie de LSD par voie I.M. a varié de 25 à 2000 microgrammes par séance, le nombre de séances ayant été d'un à 10. Sous l'influence de ce traitement, quatre malades présentèrent des réactions de psychose et durent être traités aux électrochocs. Les réactions de psychose ne furent permanentes dans aucun cas.**

**L'auteur expose les indications et les contre-indications de cette forme de traitement et d'une méthode où un médecin et une infirmière étaient co-thérapeutes. Le LSD est considéré en particulier comme capable de rendre "le transfert perceptible".**

**Il se peut que le LSD étende le champ d'action et la valeur de la psychothérapie dans ce genre de cas.**

LYSERGIC acid d… as an oxytocic s… in favour of ergotan… man, resurrected th… dentally discovered… LSD has been use… purposes since the e…

Two major reviev… published in 1957 b…

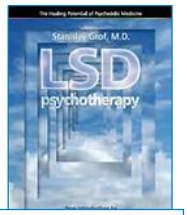
Over the past fou… the treatment of 150… chiatric disorders, ac… of the Toronto Wes… have received from… peutic sessions each… that LSD, judicious… to psychotherapy.

CLINICAL EFFECTS

Ingested or inject…

## Significance

**Lysergic acid diethylamide (LSD), the prototypical "psychedelic," may be unique among psychoactive substances. In the decades that followed its discovery, the magnitude of its effect on science, the arts, and society was unprecedented. LSD produces profound, sometimes life-changing experiences in microgram doses, making it a particularly powerful scientific tool. Here we sought to examine its effects on brain activity, using cutting-edge and complementary neuroimaging techniques in the first modern neuroimaging study of LSD. Results revealed marked changes in brain blood flow, electrical activity, and network communication patterns that correlated strongly with the drug's hallucinatory and other consciousness-altering properties. These results have implications for the neurobiology of consciousness and for potential applications of LSD in psychological research.**





## Neural correlates of the LSD experience revealed by multimodal neuroimaging

Robin L. Carhart-Harris[a,1], Suresh Muthukumaraswamy[b,c,d], Leor Roseman[a,e,f], Mendel Kaelen[a,f], Wouter Droog[a], Kevin Murphy[g], Enzo Tagliazucchi[h,i], Eduardo E. Schenberg[h,j], Timothy Nest[i], Csaba Orban[a,k], Robert Leech[a], Luke T. Williams[a], Tim M. Williams[a], Mark Bolstridge[a], Ben Sessa[a,l], John McGonigle[a], Martin I. Sereno[m], David Nichols[n], Peter J. Hellyer[a], Peter Hobden[a], John Evans[a], Krish D. Singh[b], Richard G. Wise[g], H. Valerie Curran[a], Amanda Feilding[a], and David J. Nutt[a]

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Edited by Marcus E. Raichle, Washington University in St. Louis, St. Louis, MO, and approved March 3, 2016 (received for review September 17, 2015)

**Lysergic acid diethylamide (LSD) is the prototypical psychedelic drug, but its effects on the human brain have never been studied before with modern neuroimaging. Here, three complementary neuroimaging techniques: arterial spin labelling (ASL), blood oxygen level-dependent (BOLD) measures, and magnetoencephalography (MEG), implemented during resting state conditions, revealed marked changes in brain activity after LSD that correlated strongly with its characteristic psychological effects. Increased visual cortex cerebral blood flow (CBF), decreased visual cortex alpha power, and a greatly expanded primary visual cortex (V1) functional connectivity profile correlated strongly with ratings of visual hallucinations, implying that intrinsic brain activity exerts greater influence on visual processing in the psychedelic state, thereby defining its hallucinatory quality. LSD's marked effects on the visual cortex did not significantly correlate with the drug's other characteristic effects on consciousness, however. Rather, decreased connectivity between the parahippocampus and**

be mediated by serotonin 2A receptor (5-$HT_{2A}$R) agonism (7). Previous neurophysiological research with LSD is limited to electroencephalography (EEG) studies in the 1950s and 1960s. These reported reductions in oscillatory power, predominantly in the lower-frequency bands, and an increase in the frequency of alpha rhythms (8). Broadband decreases in cortical oscillatory power have been observed in modern EEG and magnetoencephalography (MEG) studies with psilocybin (9, 10), with EEG and the dimethyltryptamine-containing brew "ayahuasca" (11), and with rodent brain local-field potential recordings and a range of different 5-$HT_{2A}$R agonists (12–14).

The effects of psychedelics (other than LSD) on human brain activity have also previously been investigated with positron emission tomography (PET) (15) and functional magnetic resonance imaging (fMRI) (16). fMRI studies with psilocybin revealed decreased cerebral blood flow (CBF) and blood oxygen level-dependent (BOLD) signal in connector hubs (16), decreased

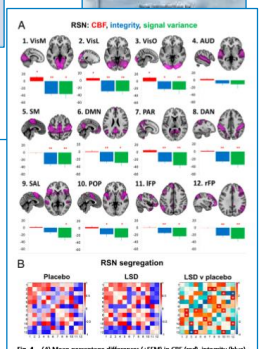


**Fig. 4.** (*A*) Mean percentage differences (±SEM) in CBF (red), integrity (blue), and signal variance (green) in 12 different RSNs under LSD relative to placebo (red asterisks indicate statistical significance, *$P < 0.05$; **$P < 0.01$, Bonferroni corrected). (*B*) Differences in between-RSN RSFC or RSN "segregation" under LSD vs placebo. Each square in the matrix represents the strength of functional connectivity (positive = red, negative = blue) between a pair of different RSNs (parameter estimate values). The matrix on the far right displays the between-condition differences in covariance (*t* values): red = reduced segregation and blue = increased segregation under LSD. White asterisks represent significant differences ($P < 0.05$, FDR corrected; $n = 15$).

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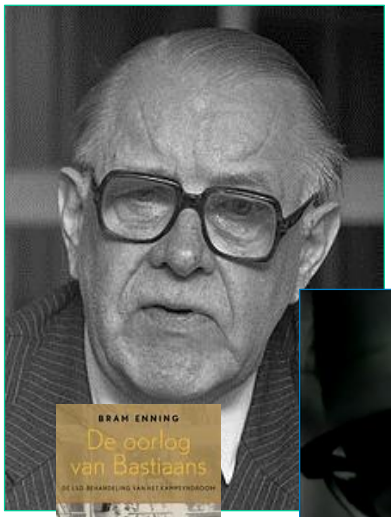
## Jan Bastiaans 1917-1997








D. DURRER

J. BASTIAANS, *Psychosomatische gevolgen van onderdrukking en verzet*. Oorspronkelijk als proefschrift (Amsterdam) verschenen. (Met een voorwoord van Prof. Dr. L. VAN DER HORST). 485 bl., 42 tabellen. N.V. Noord-Hollandsche Uitgevers Mij., Amsterdam 1957. Prijs: ingen. *f* 20,—.

Een voortreffelijk proefschrift, dat een zorgvuldige bewerking van de stof paart aan een grote rijkdom van inhoud. Na een inleiding en oriënterende probleemstelling wordt in een belangrijk hoofdstuk de verhouding van psychosomatiek en psychiatrie besproken. Het 3e hoofdstuk houdt zich bezig met het begrip „stress" en de gevolgen ervan. Op een literatuuroverzicht volgt dan een hoofdstuk over de psychosomato-traumatische gevolgtoestanden van oorlogs-„stress" bij ex-deelnemers aan het verzet in Nederland. In de hoofdstukken 6 tot en met 12 worden resp. longtuberculose, astma, adipositas, ulcus ventriculi et duodeni, musculoskeletale syndromen, hypertensie en enige andere syndromen beschreven als psychosomatische reactievormen na oorlogs-„stress". De beoordeling van de psychosomatische verzetsinvaliditeit, gevolgd door desiderata voor systematisch onderzoek, vormt het belangrijke 13e hoofdstuk. In het slothoofdstuk worden de resultaten van psychiatrische behandeling van ex-verzetslieden, benevens richtlijnen voor die behandeling vermeld. Ook hier eindigt het hoofdstuk met desiderata.

Elk hoofdstuk heeft een samenvatting en een opgave van literatuur. De samenvatting van het geheel is uitvoerig en goed. Terecht wijst de promotor, Prof. VAN DER HORST, in zijn voorwoord bij de handelsuitgave op het feit, dat de schrijver blijk geeft van een gedistancieerde beheersing der verschillende methoden van onderzoek en dat hij naast de hem vertrouwde psychoanalytische opvatting de fenomenologische methode en andere benaderingswijzen recht doet wedervaren.

Ik acht dit proefschrift een van de belangrijkste die er sedert de laatste wereldoorlog verschenen zijn, en ik kan het dan ook warm ter lezing aanbeveken als een belangwekkende en leerzame studie op het grensgebied van psychiatrie en psychosomatiek. Op vele plaatsen reikt dit boek bovendien ver over dit grensgebied heen.

P. A. H. BAAN

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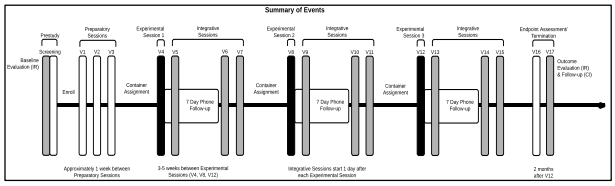


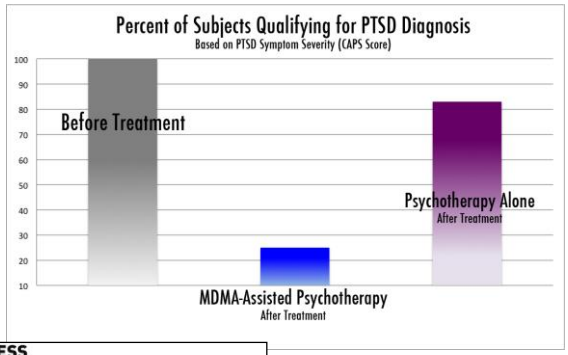


*Original Paper*

**The safety and efficacy of ±3,4-methylenedioxymethamphetamine-assisted psychotherapy in subjects with chronic, treatment-resistant posttraumatic stress disorder: the first randomized controlled pilot study**

Psychopharm

*Journal of Psychopharmacology*
25(4) 439–452
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DOI: 10.1177/0269881110378371

Michael C Mithoefer[1], Mark T Wagner[2], Ann T Mith
Lisa Jerome[3] and Rick Doblin[3]

**Abstract**

Case reports indicate that psychiatrists administered ±3,4-methylenedioxymeth
tional use of **MDMA** as 'Ecstasy' resulted in its criminalization in 1985. Over two-d
**MDMA** as a therapeutic adjunct. Twenty patients with chronic posttraumatic stress
were randomly assigned to psychotherapy with concomitant active drug ($n = 12$)
psychotherapy sessions. Both groups received preparatory and follow-up non-d
Administered **PTSD** Scale, administered at baseline, 4 days after each experimen
testing, blood pressure, and temperature monitoring were performed. After 2-mon
the experimental procedure with open-label **MDMA**. Decrease in Clinician-Adminis
group that received **MDMA** than for the placebo group at all three time points afte
treatment group versus 2/8 (25%) in the placebo group. There were no drug-relat
significant blood pressure increases. **MDMA**-assisted psychotherapy can be admin
harm, and it may be useful in patients refractory to other treatments.

**Keywords**
combat disorders, **MDMA**, Posttraumatic stress disorder, psychedelics, PTSD



Journal of Contemporary Psychotherapy
https://doi.org/10.1007/s10879-017-9379-2

ORIGINAL PAPER

**Current Perspective on MDMA-Assisted Psychotherapy for Posttraumatic Stress Disorder**

Sascha B. Thal[1] · Miriam J. J. Lommen[1]

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**Abstract**

The present paper discusses the current literature with regard to substance-assisted psychotherapy with Methylenedioxymethamphetamine (MDMA) for posttraumatic stress disorder (PTSD). The aim of the paper is to give a comprehensive overview of the development from MDMA's early application in psychotherapy to its present and future role in the treatment of PTSD. It is further attempted to increase the attention for MDMA's therapeutic potential by providing a thorough depiction of the scientific evidence regarding its theorized mechanism of action and potential harms of its application in the clinical setting (e.g., misattribution of therapeutic gains to medication instead of psychological changes). Empirical support for the use of MDMA-assisted psychotherapy, including the randomized, double-blind, placebo-controlled trails that have been conducted since 2008, is discussed. Thus far, an overall remission rate of 66.2% and low rates of adverse effects have been found in the six phase two trials conducted in clinical settings with 105 blinded subjects with chronic PTSD. The results seem to support MDMA's safe and effective use as an adjunct to psychotherapy. Even though preliminary studies may look promising, more studies of its application in a psychotherapeutic context are needed in order to establish MDMA as a potential adjunct to therapy.

**Keywords** PTSD · MDMA · MDMA-assisted therapy · Substance-assisted therapy · Overview

**PROGRESS**
in Neurology and Psychiatry

Opinion | MDMA for PTSD

**Could MDMA be useful in the treatment of post-traumatic stress disorder?**

Ben Sessa *BSc, MRCPsych*

In recent studies, 3,4-methylenedioxymethylamphetamine (MDMA) has shown promise in the treatment of post-traumatic stress disorder (PTSD) as an adjunct to post-trauma psychological therapy. However, because of historical associations with its use as the recreational drug ecstasy, MDMA research remains a controversial subject. Dr Sessa discusses these controversies and describes a UK-based MDMA/PTSD currently in development.

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| | |
|---|---|
| **Expert Consensus Guideline – 1999** | First choise: SSRI's, venlafaxine, & nefazodone<br>Second echelon: TCAs |
| **Psychopharmacology Algorithm Project at Harvard South Shore Program – 1999** | Early use of hypnotic agents for sleep; trazodone first choice, followed by SSRI for persistent PTSD symptoms |
| **UK NICE – 2005** | SSRI's bij PTSS revised → more modest effect demonstrated<br>Psychotherapy as first line treratment |
| **Canadian Clinical Practice Guideline – 2005** | Eerste choise: one choise from fluoxetine, paroxetine, sertraline, & venlafaxine XR<br>Second echelon: mirtazapine, fluvoxamine, phenelzine, moclobemide, plus adjuvant olanzapine of risperidone |
| **International Psychopharmacology Algoritm Project – 2005** | Once diagnosis of PTSD is made: SSRI first choise, followed venlafaxine & mirtazapine |
| **ISTSS- 2008** | SSRI's recommended as first choise intervention, followed up with addition with atypical antipsychotics<br>Prazosine considered "promising" |
| **APA guideline - 2009** | Concludes new studies suggest SSRI's are less effective than previously thought<br>Prazosine considered as promising option for sleep disturbance |
| **VA/DoD Clinical Practice guideline for PTSD- 2010** | Strongest recommendation SSRI's and SNRIs but give advantage to prazosine, mirtazapine, and adjuvant atypical antipsychotics<br>Prazosine for nightmares as adjuvant treatment when trazodone and other hypnotics are not sufficiently effective |

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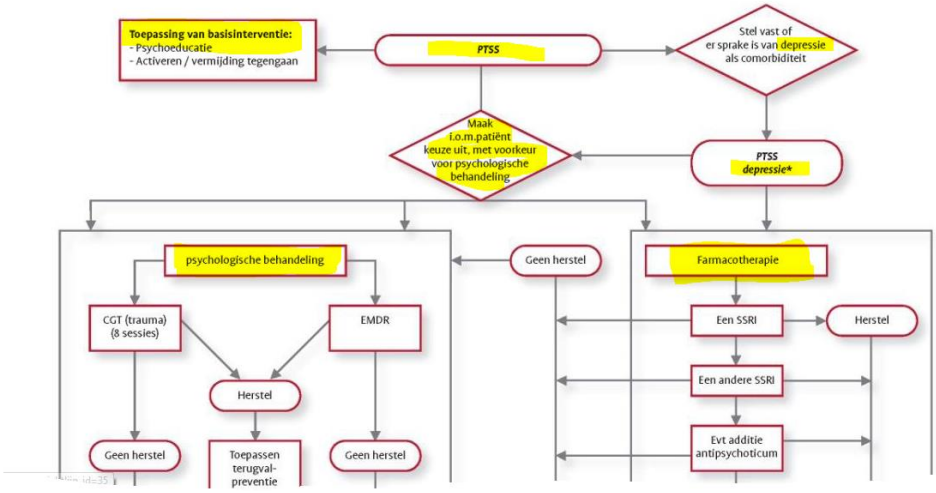
# Algoritme PTSS




Bij een ernstige co-morbide depressie is er een voorkeur om primair met medicatie te behandelen, ondanks de beperkte wetenschappelijke onderbouwing.
Wanneer de depressie voldoende is opgeklaard kan vervolgens CGT of EMDR worden toegevoegd

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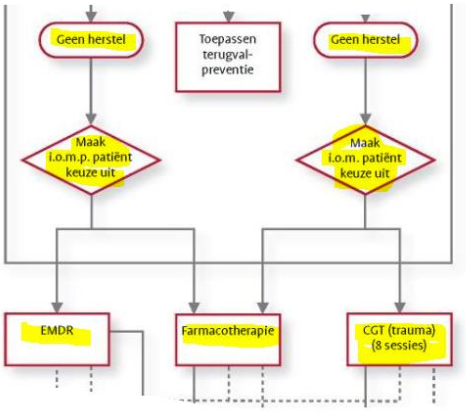
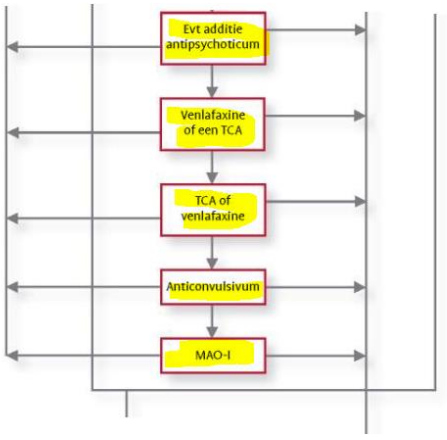
## MDR Trimbos 2009



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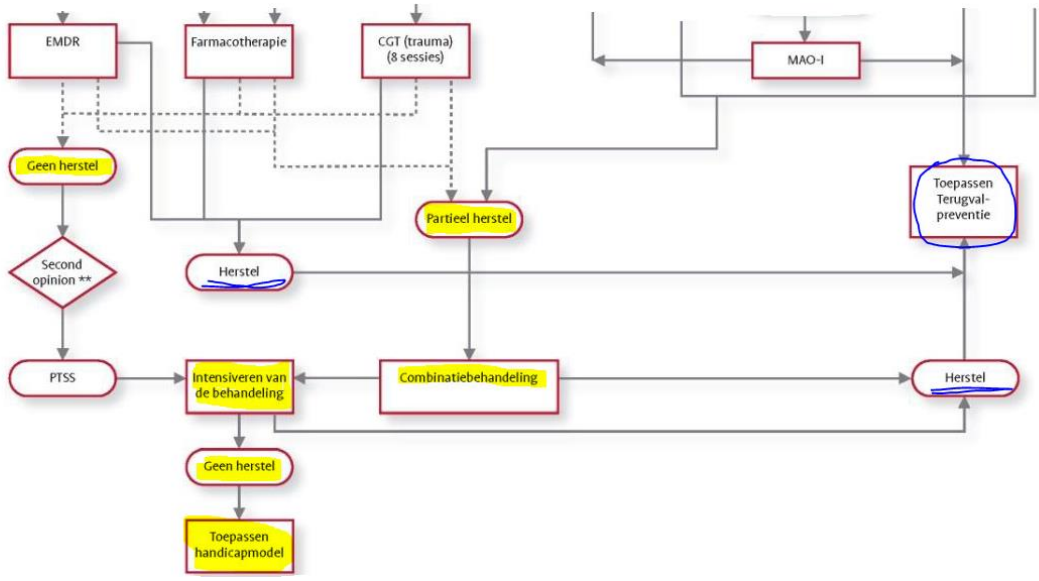
## MDR Trimbos 2009



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Kwaliteits-ontwikkeling GGz

Netwerk voor goede zorg

Zorgstandaard Psychotrauma- en stressorgerelateerde stoornissen

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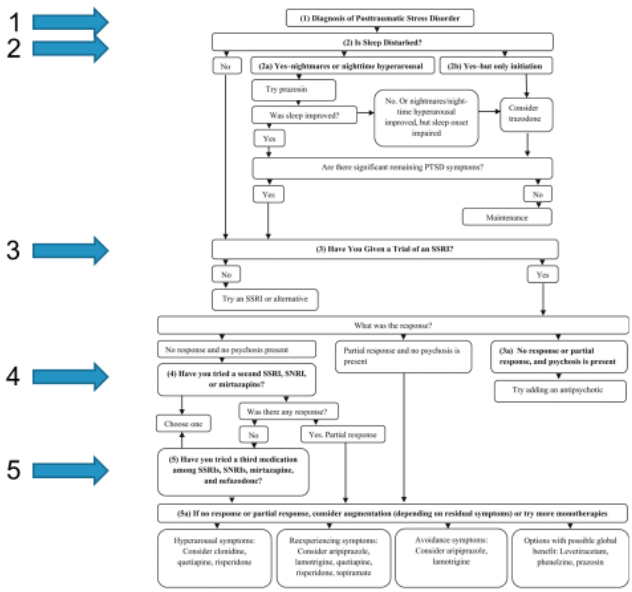
# Algorithm for PTSD



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Patient PTSS met comorbide cluster hoofdpijn.
Terug uit Afghanistan.
Behandeling 2 centra.
Cave polyfarmacie

| | 1-okt | 2-okt | 3-okt | 4-okt | 5-okt | 6-okt | 7-okt | 8-okt | 9-okt | 10-okt | 11-okt | 12-okt | 13-okt | 14-okt | 15-okt | 16-okt |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | ma | di | wo | do | vr | za | zo | ma | di | wo | do | vr | za | zo | ma | di |
| Geslapen | veel wakker | veel wakker | veel wakker | tot 3,5 | tot 3 | tot 3 | tot 3,5 | tot 3 | tot 3 | 24-3 / 5-8 | 07:45 | 6 | 07:30 | 07:30 | tot 4 | 07:30 |
| Cluster aanval | 4 a 5 | | | | 5 | | | | | 3 | 4 a 5 | 4 | 4a5 | | | |
| Cluster aanval | | | 7 | 5 a 6 | 5 | | 7 a 8 | 6 a 8 | | 4 | | 3 | 3 | | | |
| Cluster aanval | 8 | 7 | | pieken | 5 a 6 | | | | | | 4 a 5 | 5 | 5 | 6 | | |
| geslapen overdag | niet | niet | niet | niet | 1 u | niet | niet | niet | niet | niet | niet | put | niet | put | niet | niet |
| gevoel overdag | 6 en moe | 6 en moe | 7 erg moe | 7 moe | 7 | 6 a 7 | 6 a 7 | 6 a 7 | 6 a 7 | | 6 | minder | moe 6 | mnder | 6 | moe |
| Imigran6 | 21:30 | | 04:30 | | | | 18:00 | 22:00 | | | | diep | | diep | | |
| Verapamil | 480 mg | 480 mg | 480 mg | 480 mg | 480 mg | 480 mg | 480 mg | 480 mg | 480 mg | 480 mg | 480 mg | 480 mg | 480 mg | 480 mg | 480 mg | 480 mg |
| Lexapro | 1 | 1 | 1 | 1 | 1 | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Zopiclon | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 1 | 2 | 2 |
| diazepan | | | | | les | | | | | | lekker | | | | | |
| diverse | voetbal | verjaardag | prikkebaar | les | griepje | demo | bezoek | voetbal | boodschapjes | vermetter | in huis | bezoek | klussen | thuis | yvette | yvette |
| | op bezoek | | | | | | | | op pad geweest | | bezig | ouders | peter | bezig | werken | werken |
| naar bed | | | 23:00 | 00:30 | | 00:00 | 23:00 | 23:00 | 00:00 | 23:30 | 23:30 | 01:30 | 01:00 | 00:00 | | |
| | 17-okt | 18-okt | 19-okt | 20-okt | 21-okt | 22-okt | 23-okt | 24-okt | 25-okt | 26-okt | 27-okt | 28-okt | 29-okt | 30-okt | 31-okt | |
| | wo | do | vr | za | zo | ma | di | wo | do | vr | za | zo | ma | di | wo | |
| Geslapen | 07:30 | 07:30 | 06:00 | 05:00 | 08:30 | 07:30 | 07:00 | niet | 07:00 | 3:30/7:00 | 08:00 | 07:30 | 08:30 | ? | 3 | |
| Cluster aanval | | | 6 | om uur | 6 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 7 | 5 | 5 | |
| Cluster aanval | | steken | steken | wakker | 7 | 6 | 5 | 5 | 5 | 6 | 5 | 5 | 8 | 5 | | |
| Cluster aanval | 6 en steken | 6 a 7 | 6 a 7 | 7 | 7 | 8 | 5 | 6 | 5 | 6 | 6 | 6 | 7 | 5 | 6 | |
| geslapen overdag | niet | niet | niet | niet | niet | niet | niet | niet | niet | niet | | | | | | |
| gevoel overdag | 7 | 7 | 7,5 | 5 | 6 | 6,5 | 5 | 6,5 | 5 | 5 | 8 | 5 | 8 | ? | ? | |
| Imigran6 | | | | | | 21:45 | | | | | | | 17:15 | | | |
| Verapamil | 480 mg | 480 mg | 480 mg | 480 mg | 480 mg | 480 mg | 480 mg | 480 mg | 480 mg | 480 mg | 480 mg | 480 mg | 480 mg | 480 mg | | |
| Lexapro | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | |
| Zopiclon | 2 | 2 | 2 | 2 | 2 | 2 | 1x 3:30 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | |
| diazepan | | | yvette | | | | | | | | | | | telefonische | | |
| diverse | | | werken | geklust | examen | geklust | geklust | geklust | geklust | hele dag | | | aqfspraak | afspraak | | |
| | | | les | kamertje | hoorn | voetbal | karten | | | op pad | | | de vries | neuroloog | | |
| naar bed | 01:00 | 00:30 | 00:00 | | 23:30 | 23:00 | 23:30 | 23:30 | 00:00 | 01:00 | | | | | | |
| | 1-nov | 2-nov | 3-nov | 4-nov | 5-nov | 6-nov | 7-nov | 8-nov | 9-nov | 10-nov | 11-nov | 12-nov | 13-nov | 14-nov | 15-nov | 16-nov |
| | do | vr | za | zo | ma | di | wo | do | vr | za | zo | ma | di | wo | do | vr |
| Geslapen | 3 | 7 | 6 | 7 | 7 | 5 | 5 | 6 | 5 | 5 | 6 | 6 | 7 | 7 | 7 | 5 |
| Cluster aanval | 6 | 6 | 5 | 6 | 7 | 7 | 6 | 6 | 6 | 6 | 7 | 6 | 7 | 6 | 6 | 6 |
| Cluster aanval | 6 | 6 | 5 | 6 | 6 | 7 | 7 | 7 | 6 | 6 | 7 | 7 | 6 | 6 | 6 | 7 |
| Cluster aanval | 6 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 8 | 8 | 6 | 6 | 6 | 6 |
| geslapen overdag | | | | | | | | | | | | | | | | |
| gevoel overdag | 6 | 7,5 | 5 | 5 | 5 | 7 | ? | 6,5 | sloom niet | moe | 7 | 7 | 6 | 6,5 | 6,5 | 6,5 |
| Imigran6 | | | | | | | | | oplettend | | 20:45 | | | | | |
| Verapamil | 480 mg | 480 mg | 480 mg | 480 mg | 480 mg | 480 mg | 480 mg | 480 mg | 480 mg | 480 mg | 480 mg | 480 mg | 480 mg | 480 mg | 480 mg | 480 mg |
| Lexapro | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Zopiclon | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| diazepan | | boodschappen | | | | | | | | | | | | geklust | | |
| diverse | geklust | heel veel | klussen | feesje | yvette | yvette | de vries | meeting | tandarts | erg moe | | | | acda& | erg | |
| | kamertje | prikkels | bij peter | Sam | werken | werken | | texel | boodschappen | | | gesport | onrustig | de munick | onrustig | |
| naar bed | 00:00 | 00:00 | 01:00 | 00:00 | 23:30 | 23:30 | 00:00 | 00:00 | | 23:30 | | 23:30 | 23:00 | 23:30 | 00:15 | |

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***‘ For nearly every psychiatric disorder, it is common to distinguish between strategies applied to “firstline” treatments for unselected patients early in their course of illness and treatment approaches for more severe symptoms or symptoms that have not responded to first-line treatments, so-called treatment-resistant illness’ .***
***Krystal et al,., BP, 2017, p e53***

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Curr Psychiatry Rep (2017) 19: 10
DOI 10.1007/s11920-017-0761-2

DISASTER PSYCHIATRY: TRAUMA, PTSD, AND RELATED DISORDERS (E FOA AND A ASNAANI, SECTION EDITORS)

# The Need to Take a Staging Approach to the Biological Mechanisms of PTSD and its Treatment

**Alexander Cowell McFarlane[1] · Eleanor Lawrence-Wood[1] · Miranda Van Hooff[1] · Gin S. Malhi[2] · Rachel Yehuda[3]**

Published online: 7 February 2017


**Abstract** Despite the substantial body of neurobiological research, no specific drug target has been developed to treat PTSD and there are substantial limitations with the available interventions. We propose that advances are likely to depend on the development of better classification of the heterogeneity of PTSD using a staging approach of disease. A primary rationale for staging is to highlight the probability that distinct therapeutic approaches need to be utilised according to the degree of biological progression of the disorder. Prospective studies, particularly of military populations, provide substantial evidence about the emerging biological abnormalities that precede the full-blown disorder. These need to be targeted with tailored interventions to prevent disease progression. Equally, the neurobiology of chronic unremitting PTSD needs to be differentiated from the acute disorder which emerges across a spectrum of severity, and this range of presentations correspondingly needs to be addressed with differing therapeutic strategies. The staging approach also needs to take account of the range of somatic pathological outcomes that are being identified as a consequence of traumatic stress exposure.

This article is part of the Topical Collection on *Disaster Psychiatry: Trauma, PTSD, and Related Disorders*

✉ Alexander Cowell McFarlane
alexander.mcfarlane@adelaide.edu.au

PTSD should be
underpinned a rangs
abolic and altered i
rates of cardiovascu
ness of novel treatn
tiveness in addressir

**Keywords** PTSD
Inflammation · Me
Longitudinal cours

## Introduction

In contrast to most
significant levels of
traumatic stress di
be the front-line tr
tervention before t
makes this recomm
is now over quarter of a century's worth of research demonstrating alterations in neural circuitry, molecular biology, endocrinology and immune reactivity and other physiological domains in PTSD [2•, 3]. It therefore seems that at a time when there are more biological findings in PTSD than in almost any other psychiatric disorder, there are no drug targets,

**Table 1** Proposed staging model for PTSD

| Stage | Presentation | Example of possible neurobiological changes |
|---|---|---|
| Stage 0 | Trauma exposed asymptomatic but at risk | Down regulation of glucocorticoid receptor sensitivity, increased amygdala reactivity, 5FKH genotype |
| Stage 1a | Undifferentiated symptoms of mild anxiety and distress | Inflammatory cytokine activation, decreasing response inhibition in the frontal cognitive systems |
| Stage 1b | Subsyndromal distress with some behavioural and functional decline | Increased physiological reactivity to trauma-related stimuli and startle response, prolonged autonomic arousal on provocation |
| Stage 2 | First episode of full-threshold symptoms that has different trajectories | Early and potentially reversible neurobiological disinhibition of frontolimbic circuitry |
| Stage 3 | Persistent symptoms which may fluctuate with ongoing impairment: | Decreased anterior cingulate and hippocampal volume, hypertension and metabolic syndrome |
| | 3a Incomplete remission of first episode | |
| | 3b Recurrence or relapse of PTSD and persistent impairments | |
| | 3c Multiple relapses or worsening following incomplete treatment response | |
| Stage 4 | Severe unremitting illness of increasing chronicity with substantial disability | High allostatic load, high levels of inflammation, medical comorbidities, entrenched sensitization of a range of neurobiological systems |

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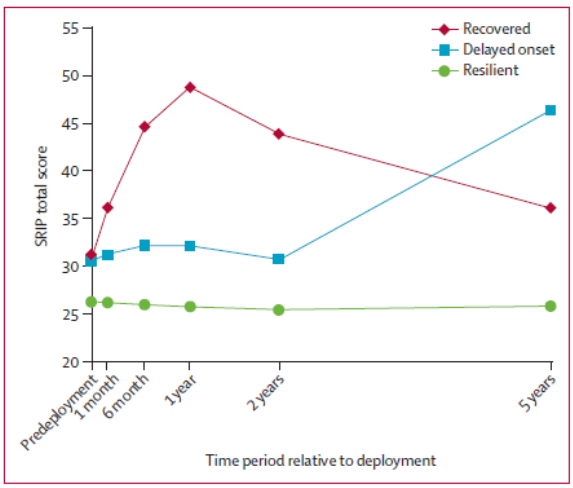
# Post-traumatic stress symptoms 5 years after military deployment to Afghanistan: an observational cohort study

Iris Eekhout, Alieke Reijnen, Eric Vermetten, Elbert Geuze




Delayed onset 9.4 %

Recovered 5.3%

Resilient 85.2%

| | Total number of participants with available data | Above cutoff* | Mean SRIP score |
|---|---|---|---|
| Pre-deployment | 680 | 27 (4%) | 26·76 (5·03) |
| 1 month | 753 | 62 (8%) | 27·62 (6·14) |
| 6 months | 737 | 63 (9%) | 27·73 (7·07) |
| 12 months | 562 | 38 (7%) | 27·02 (6·94) |
| 2 years | 528 | 29 (5%) | 26·64 (5·90) |
| 5 years | 559 | 72 (13%) | 28·30 (8·07) |

Data are n, n (%), or mean (SD), unless otherwise indicated. *We used an SRIP of 38 as our cutoff value. SRIP=Self-Rating Inventory for Post-traumatic Stress Disorder.

*Table 2:* **Dutch military personnel deployed to Afghanistan reporting post-traumatic stress symptoms at each timepoint**

Eekhout, Reijnen, Vermetten and Geuze, *Lancet Psychiatry*, 2016

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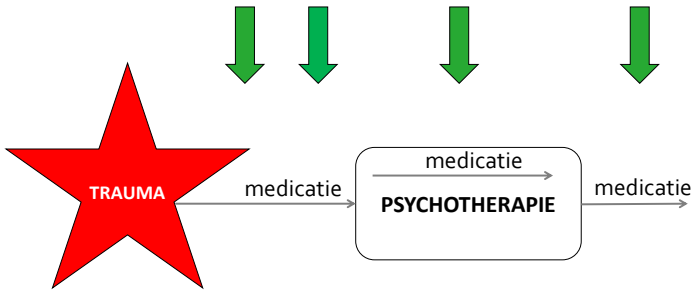
## Nieuw: Fasegericht Behandelen



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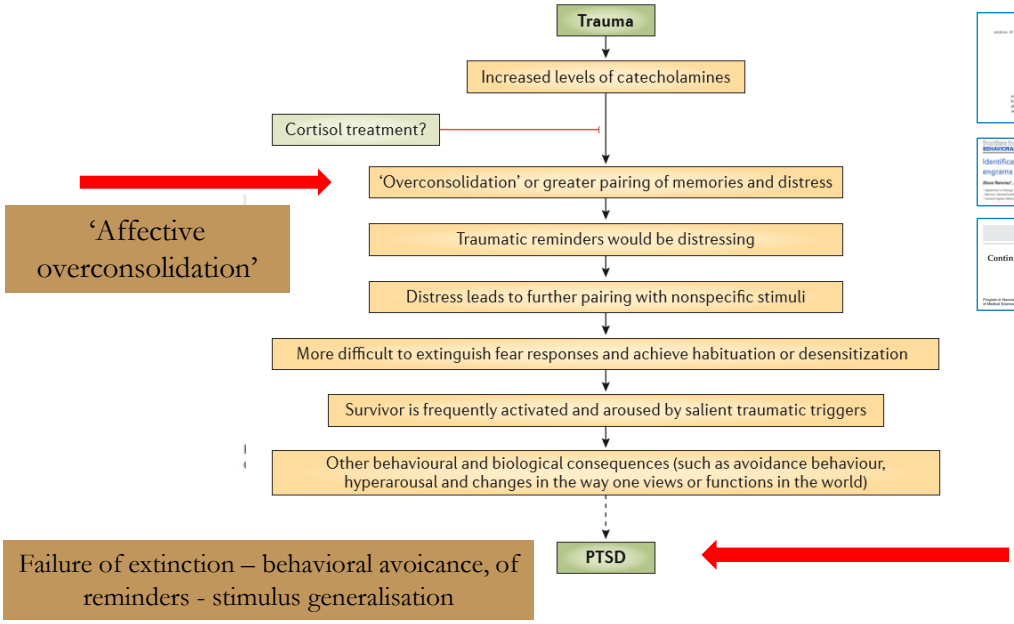
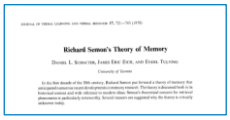
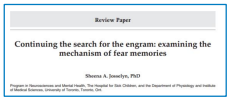
# *Pathophysiology of PTSD*





Richard Semon's Theory of Memory


Identification and optogenetic manipulation of memory engrams in the hippocampus


Review Paper

Continuing the search for the engram: examining the mechanism of fear memories

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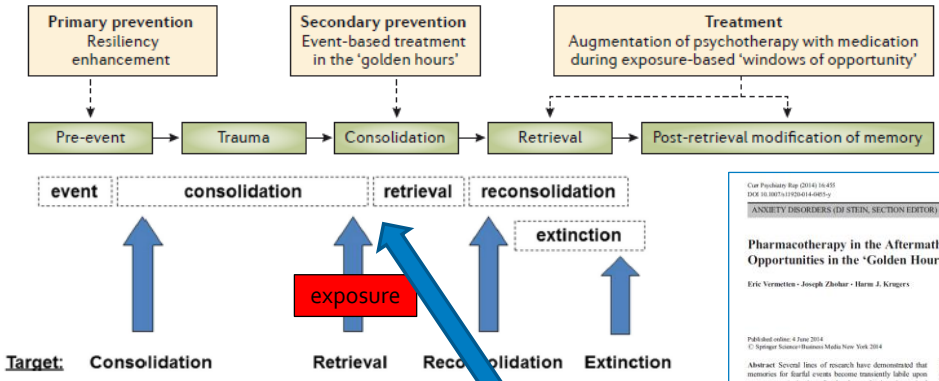
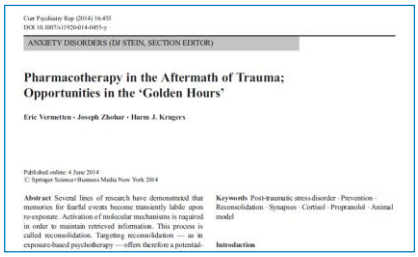
# Targeting fear memories: Golden hour opportunities

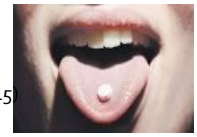


Pharmacotherapy in the Aftermath of Trauma; Opportunities in the 'Golden Hours'

Eric Vermetten · Joseph Zohar · Harm J. Krugers

**Compounds:**
- Oxytocin (Koch et al., 2015)
- D Cycloserin (de Kleine et al., 2015)
- Propanolol (Pitman, et al., 2015)
- Ketamine (Rasmussen, 2015)
- Corticosteroids (de Quervain et al., Mouthaan et al., 2015; Yehuda et al., 2015)
- Endocannabinoids, Nabilone, (Jetly et al., 2015)



*Roadmap: New initiative out of ECNP Traumatic Stress Network*

Vermetten, Zohar and Krugers, CPR, 2014

**Timed administration - two windows of opportunity - reduce fear memories - defined as 'golden hours' in treatment of PTSD symptoms: event-based golden hours and exposure-based golden hours.**

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TSN
TRAUMATIC STRESS NETWORK

**Integrating NIMH Research Domain Criteria (RDoC) into PTSD Research**

**Ulrike Schmidt and Eric Vermetten**

Curr Psychiatry Rep (2014) 16:455
DOI 10.1007/s11920-014-0455-y

ANXIETY DISORDERS (DJ STEIN, SECTION EDITOR)

**Pharmacotherapy in the Aftermath of Trauma; Opportunities in the 'Golden Hours'**

Eric Vermetten · Joseph Zhohar · Harm J. Krugers

Published online: 4 June 2014

**Abstract** Three and a half de
(PTSD) has produced substanti
and debilitating disease. Howev
has specifically targeted PTSD

Keywords Post-trau… disorder · Prevention · Reconsolidation · Sym… Cortisol · Propranolol · Animal model

…SD treatmen… today

Emerging Security Challenges Division

Science for Peace and Security Programme

Event Application

NATO Emerging Security Challenges Division, SPS Programme, Bd. Léopold III, B-1110 Brussels, Belgium
Submit applications in Microsoft Word format including scanned signatures along with all attachments to
sps.applications@hq.nato.int

| Event Title | Event Type |
|---|---|
| Risk Management of Terrorism Induced Stress - Guidelines for the Golden Hours (Who, What and When) | ARW |


**Eric Vermetten, Leiden University Medical Center, NETHERLANDS, chair**
**Joseph Zohar, Chaim Sheba Medical Center, ISRAEL, co-chair,**
**Carmen Lior, Chaim Sheba Medical Center, ISRAEL**
**Harm Krugers, University Amsterdam, NETHERLANDS**
**Ingrid Philippens, Biological Primate Research Center, NETHERLANDS**
**Ulrike Schmidt, Max Planck Institute of Psychiatry, GERMANY,**
**Elisabeth Binder, Max Planck Institute of Psychiatry, GERMANY,**
**Victor Spoormaker, Max Planck Institute of Psychiatry, GERMANY**
**David Nutt, Imperial College London, UNITED KINGDOM,**
**Jonathan Bisson, Cariff University, UNITED KINGDOM,**
**Dominique de Quervain, Basel, SWITZERLAND**
**Ben Sessa, Brisol University, UNITED KINGDOM**


GHO4CURE
ANXIETY DISORDERS & PTSD

Leiden University Medical Center

| Vragen | Juist antwoord | Feedback |
|---|---|---|
| **1. Wat is de eerste keus behandeling van PTSS?**<br>**A. Farmacotherapie met SSRI's**<br>**B. Farmacotherapie met anti-epileptica**<br>**C. Farmacotherapie met atypische antipsychotica**<br>**D. Psychotherapie** | D | Psychotherapie is de eerste keus behandeling van PTSS (A-C onjuist, D juist). Daarnaast kan farmacotherapeutische therapie voor bepaalde patiënten goede verbetering van PTSS klachten laten zien, maar dit is dus geen eerste keus behandeling. |
| **2. Mevrouw Stoel, 37 jaar, heeft een jeugd gehad met vanaf haar zesde jaar mishandeling door haar vader. Dit is nu nog steeds belastend voor haar. Ze komt bij u op het spreekuur nadat psychotherapie niet voldoende heeft gewerkt om haar van haar traumaklachten af te helpen. U bespreekt met mevrouw Stoel de mogelijkheden van een farmacotherapeutische behandeling. Ze stemt hiermee in. Ze heeft geen eerdere farmacotherapeutische behandelingen voor haar klachten ondergaan. U wilt haar graag conform de Nederlandse richtlijn voor de behandeling van PTSS behandelen met een geneesmiddel dat voor PTSS geregistreerd is. Welke twee middelen kunt u dan kiezen?**<br>**A. Fluoxetine en citalopram**<br>**B. Paroxetine en sertraline**<br>**C. Venlafaxine en mirtazapine**<br>**D. Topiramaat en lamotrigine** | B | Paroxetine en sertraline zijn de enige twee geneesmiddelen die geregistreerd zijn in Nederland voor de behandeling van PTSS (A, C en D onjuist, B juist). |
| **3. Op basis van de huidige onderzoeksgegevens is er geen plaats voor topiramaat bij de behandeling van PTSS. Deze stelling is:**<br>**A. Juist**<br>**B. Onjuist** | B | Topiramaat is nog niet in alle richtlijnen opgenomen, maar heeft goede resultaten laten zien bij RCTs met verschillende doelgroepen. Op basis van deze studies mag topiramaat niet als eerste keus middel worden gekozen maar zou het goed ingezet kunnen worden bij patiënten die niet in aanmerking komen voor een SSRI of die geen effect laten zien op een SSRI. Topiramaat kan ook goed gebruikt worden als additie bij een SSRI of bij het terugdringen van alcoholabusus bij mensen met een geschiedenis van misbruik. Topiramaat heeft dus wel degelijk een plaats bij de behandeling maar PTSS (stelling onjuist, A onjuist, B juist). Een meer definitieve plaatsbepaling van topiramaat in de richtlijnen is pas goed mogelijk als er meer onderzoeksgegevens beschikbaar komen. |

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| Tussentoetsvraag | Juist antwoord | Feedback |
|---|---|---|
| **De heer Bus (36 jaar) groeit op in een onveilige gezinssituatie waarin geweld en verslaving speelt. Op jonge leeftijd is hij er getuige van als vader in een ruzie moeder van de trap duwt. Ze belandt in het ziekenhuis, maar naar de buitenwereld zwijgt het gezin over wat er gebeurd is. Conflicten waarin geweld gebruikt blijven zijn hele jeugd spelen. Inmiddels heeft hij zelf kinderen en merkt hij onzekerheid in zijn vaderschap, bijvoorbeeld wanneer de kinderen zich moeilijk door hem laten troosten. De heer Bus heeft ook soms herbelevingen waarbij hij zijn moeder van de trap ziet vallen, wat angst oproept. De heer Bus vindt het vooral vervelend dat hij thuis steeds vaker geprikkeld en boos reageert. Nu de psychotherapie die hij afgelopen periode heeft ondergaan deze klachten niet heeft verminderd, wil hij graag met u in overleg over de volgende stap. Hij heeft op het internet gelezen dat pillen ook kunnen helpen. Welke groep geneesmiddelen zijn de eerste keus als farmacotherapeutische behandeling van PTSS?**<br>**A. SSRI's**<br>**B. SNRI's**<br>**C. TCA's**<br>**D. Anti-epileptica**<br>**E. Atypische antipsychotica** | A | De SSRI's zijn middelen van eerste keuze bij de farmacotherapeutische behandeling van PTSS (A juist, B-E onjuist). |

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Psyfar | juni 2017 | nummer 2

18 HOOFDARTIKEL

DEEL I, OVERZICHT EN UPDATE

# Stand van zaken van de farmacotherapie voor PTSS

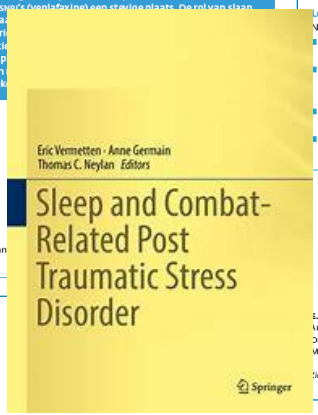
**Samenvatting**

Dit artikel geeft een overzicht van de opgebouwde kennis en huidige stand van zaken met betrekking tot de algemene farmacotherapie van PTSS (posttraumatisch stresssyndroom). Zowel omvang als kwaliteit van wetenschappelijk onderzoek naar behandelmogelijkheden voor PTSS is de laatste tien jaar enorm toegenomen. Er zijn geen nieuwe middelen voor de indicatie PTSS bijgekomen. De voorschrijver is aangewezen op off-labelproducten. Het algemene effect van farmacotherapie valt wat tegen. Psychotherapie is eerste keus in de meeste nieuwe richtlijnen, en behandeling van PTSS is meest gediend als deze gericht is op specifieke symptomen. De *golden hours* bieden een mogelijkheid voor secundaire preventie waarin sprake is van toenemend bewijs voor een rol voor corticosteroïden. In de algemene farmacotherapie van PTSS hebben SSRI's (paroxetine, sertraline, fluoxetine) en [illegible] een sterke plaats. De rol van slaap krijgt toenemend aandacht. Behandela[illegible] specifiek te interveniëren bij nachtmerri[illegible] prazosine. Het model van reconsolidati[illegible] aan op exposure gerichte psychotherap[illegible] benzodiazepines voor behandeling van [illegible] deel II zal worden ingegaan op specifiek[illegible]

**Leerdoelen**

Na het lezen van dit artikel

- kent u de betekenis van RDOC en NDN bij farmacotherapie
- is uw kennis over afweging tussen psychofarmaca en psychotherapie bij PTSS up-to-date
- hebt u inzicht in het belang van biologisch onderzoek bij farmacotherapie van PTSS
- hebt u kennis van de algemene principes van farmacotherapie bij PTSS

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16 HOOFDARTIKEL

DEEL II, SPECIFIEKE FARMACOTHERAPIE EN NIEUWE ONTWIKKELINGEN

# Stand van zaken van de farmacotherapie voor PTSS

**Samenvatting**

In 'Overzicht en update, deel I' (*Psyfar* 2017, nr. 2) zijn algemene principes van farmacotherapie bij PTSS beschreven. In dit deel wordt een overzicht gepresenteerd van de farmacotherapeutische behandelmogelijkheden bij PTSS en worden nieuwe ontwikkelingen beschreven. Psychotherapie is de behandeling van eerste keus voor PTSS. Indien gekozen wordt voor farmacotherapie, wordt geadviseerd te starten met een selectieve serotonineheropnameremmer (SSRI). Non-respons en/of aanwezige comorbiditeiten kunnen leiden tot de keuze voor andere psychofarmaca. De effectiviteit van deze mogelijkheden wordt beschreven. Ten slotte wordt een overzicht gegeven van mogelijke toekomstige opties voor de behandeling van PTSS.

**Leerdoelen**

Na het bestuderen van dit artikel

- weet u welke psychofarmaca *evidence-based* ingezet kunnen worden bij PTSS
- kent u behandelmogelijkheden bij PTSS en comorbiditeiten als middelenmisbruik en een bipolaire stoornis
- weet u hoe u nachtmerries bij PTSS kunt behandelen
- bent u op de hoogte van mogelijk toekomstige behandelmogelijkheden voor PTSS

**Inleiding**

Er bestaan diverse richtlijnen voor PTSS, verschillende (inter)nationale en wetenschappelijke verenigingen hanteren principes gebaseerd op *evidence-based medicine*. De beschikbare richtlijnen verschillen niet zoveel van elkaar.[1] Medio 2017 zal een hernieuwde Nederlandse richtlijn voor de behandeling van PTSS, die stamt uit 2009, worden gepubliceerd. Opnieuw blijkt daaruit dat medicatie ondersteunend is bij de behandeling van PTSS maar dat psychotherapie de eerstekeus-behandeling is voor PTSS. Er zijn natuurlijk specifieke indicaties en situaties waarbij daarvan kan worden afgeweken.

*Nooz* Bij onderstaande opsommingen van middelen valt op dat de geciteerde studies vaak klein zijn, niet altijd gerepliceerd worden en dat, als dat al zo is, er geen herhaling van het effect wordt gevonden. Dit is lang een probleem geweest bij studies op het gebied van PTSS, maar de laatste jaren worden de studies beter in design en worden metareviews gepubliceerd. Toch blijkt uit meerdere referenties dat kleine onderzoeken vaak onbetrouwbare resultaten leveren en dat replicatie echt nodig is om bijvoorbeeld een meta-analyse mogelijk te maken.

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*Zie voor het cv van de auteur: www.psyfar.nl.*

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Samenvattend

Crisis in psychofarmacologie?
Vintage drugs
Nieuwe ideeën over psychotherapie –
    vroeg, dan wel ondersteunend/katalyserend voor psychotherapie
Veranderende vormen van psychotherapie
Medicatie is ondersteunend
Symptom-based approach, slaap, RDOC
Slaap: Prazosine, doxazosine, medicinale cannabis
Slaapregistratie: horloge, objectivering slaap