The α_1-Adrenergic Antagonist Prazosin Ameliorates Combat Trauma Nightmares in Veterans With Posttraumatic Stress Disorder: A Report of 4 Cases

Murray A. Raskind, M.D.; Dorcas J. Dobie, M.D.; Evan D. Kanter, M.D., Ph.D.; Eric C. Petrie, M.D.; Charles E. Thompson, M.D.; and Elaine R. Peskind, M.D.

Background: Central nervous system (CNS) adrenergic hyperresponsiveness may be involved in the pathophysiology of posttraumatic stress disorder (PTSD). Two Vietnam combat veterans with PTSD prescribed the centrally active α_1-adrenergic antagonist prazosin for symptoms of benign prostatic hypertrophy unexpectedly reported elimination of combat trauma nightmares. This observation prompted an open-label feasibility trial of prazosin for combat trauma nightmares in chronic combat-induced PTSD.

Method: Four consecutively identified combat veterans with chronic DSM-IV PTSD and severe intractable combat trauma nightmares participated in an 8-week open trial of escalating-dose prazosin. Nightmare severity response was rated using the nightmare item of the Clinician Administered PTSD Scale and the Clinical Global Impressions-Change scale.

Results: The 2 patients who achieved a daily prazosin dose of at least 5 mg were markedly improved, with complete elimination of trauma nightmares and resumption of normal dreaming. The 2 subjects limited to 2 mg of prazosin to avoid excessive blood pressure reduction were moderately improved with at least 50% reduction in nightmare severity.

Conclusion: These clinical observations, together with neurobiological evidence for α_1-adrenergic regulation of CNS neurobiological systems relevant to PTSD, provide rationale for placebo-controlled trials of prazosin for PTSD combat trauma nightmares.

(J Clin Psychiatry 2000;61:129–133)

Received Feb. 17, 1999; accepted Aug. 5, 1999. From the Department of Veterans Affairs Northwest Network Mental Illness Research, Education and Clinical Center (MIRECC), and the University of Washington, Department of Psychiatry and Behavioral Sciences, Seattle.

Supported by the Department of Veterans Affairs and the Veterans Affairs Northwest Network Mental Illness Research, Education and Clinical Center (MIRECC). The authors appreciate the logistic support of Ms. Susan Martin and Ms. Kitty Smith.

Reprint requests to: Murray A. Raskind, M.D., VA Puget Sound Health Care System, Mental Health Service (116), 1660 S. Columbian Way, Seattle, WA 98108 (e-mail: raskind.murray@seattle.va.gov).

A substantial number of studies are consistent with adrenergic hyperresponsiveness in posttraumatic stress disorder (PTSD).[1] Such adrenergic hyperresponsiveness suggests that pharmacologic blockade of central nervous system (CNS) postsynaptic adrenergic receptors could be effective in the treatment of PTSD.[2] The α_1-adrenergic receptor subtype and the β-adrenergic receptor subtype constitute the majority of postsynaptic adrenergic receptors in the mammalian CNS.[3] These 2 receptor subtypes mediate various downstream effects of CNS norepinephrine and epinephrine,[4] and both receptor subtypes are widely distributed in human brain.[5] Although both α_1- and β-adrenergic receptor subtypes theoretically could be involved in the pathophysiologic processes underlying PTSD symptoms, only the possible therapeutic efficacy of β-adrenergic receptor antagonists has been explored in open case report studies.[6,7] The preferential distribution of human α_1 receptors in hippocampus, amygdala, and other brain areas relevant to PTSD[8,9] and the involvement of brain α_1-adrenergic receptors in the modulation of sleep and startle[10,11] provide the neurobiological rationale for exploring the efficacy of α_1-adrenergic antagonist therapy in this disorder. The possibility that pharmacologic blockade of CNS α_1-adrenergic receptors could provide symptomatic relief in PTSD has not, to our knowledge, been addressed.

In addition to these theoretical considerations, a clinical observation in 2 Vietnam combat veterans with chronic PTSD suggested potential efficacy of α-adrenergic blockade for an important PTSD symptom, the combat trauma nightmare. Frequent combat trauma nightmares occur in 15% of Vietnam combat veterans with PTSD, appear specific for PTSD, and are the sleep disturbance symptom most related to combat trauma exposure.[12] These 2 veterans spontaneously and unexpectedly reported marked reduction in combat trauma nightmare severity and resumption of normal dreams after the α_1 antagonist prazosin had been prescribed for symptomatic relief of benign prostatic hypertrophy. Because peripherally administered prazosin crosses from blood into brain and can affect behavior,[13] it seemed possible that prazosin blockade of CNS α_1-adrenergic receptors could have accounted for this observation. α_1-Adrenergic agonist administration severely

disrupts sleep in laboratory animals,[10] and indirect measures of nocturnal CNS noradrenergic activity negatively correlate with total sleep time in persons with PTSD.[14]

As the first step in testing the hypothesis that pharmacologic blockade of α_1-adrenergic receptors reduces combat trauma nightmares, we conducted a preliminary open-label, 8-week feasibility trial of prazosin in 4 additional consecutively identified veterans with PTSD and severe, chronic combat trauma nightmares.

SUBJECTS AND METHOD

Four combat veteran outpatients consecutively identified as meeting inclusion criteria for this study were assessed over 8 weeks for combat trauma nightmare severity prior to and during treatment with the α_1-adrenergic antagonist prazosin. Informed consent was obtained from each patient after the nature of the treatment trial had been fully explained. Inclusion criteria were as follows: (1) combat veteran with PTSD using DSM-IV criteria, (2) chronic and severe combat trauma nightmares that were the primary PTSD symptom motivating treatment, (3) no alcohol or other substance abuse for at least 6 months, and (4) a score of at least 6 (of a maximum of 8) on the nightmare item of the Clinician Administered PTSD Scale for DSM-IV, One Week Symptom Version (CAPS-SX).[15] This measure combines a 4-point nightmare frequency scale based on response to the question, "In the past week have you had unpleasant dreams about [event]?" ranging from 0 ("never") to 4 ("daily or almost every day"), and a 4-point nightmare intensity scale based on response to the question, "How much distress or discomfort did these dreams cause you?" ranging from 0 ("no distress") to 4 ("extreme, incapacitating stress, did not return to sleep").

Although not an inclusion criterion, all 4 subjects at trial entry had mild-to-moderate hypertension (systolic blood pressure greater than 140 mm Hg and/or diastolic blood pressure greater than 90 mm Hg) despite ongoing antihypertensive treatment regimens. No subject had been receiving sympatholytic drugs as part of their antihypertensive regimens. Thus, a therapeutic trial of prazosin was a reasonable adjunct to these patients' antihypertensive regimens as well as a potentially helpful agent for combat trauma nightmares.

Each veteran was receiving disability compensation for PTSD from the Department of Veterans Affairs. Three patients (cases 1, 2, and 3) were treated and rated by the lead author (M.A.R.). These patients were assigned a CAPS-SX nightmare severity score at pretreatment baseline, and at weeks 2, 4, and 8 of prazosin treatment. The fourth patient was treated and rated by the second author (D.J.D.). He was assigned a CAPS-SX nightmare severity score at baseline and at weeks 4 and 8. In addition, all patients were assigned a Clinical Global Impressions-Change scale (CGI-C)[16] score for nightmare severity at week 8.

Table 1. Reduction in CAPS-SX Nightmare Severity Score Over 8 Weeks of Treatment With Prazosin in 4 Combat Veterans With Posttraumatic Stress Disorder[a]

		Prazosin Dose	CAPS-SX Nightmare Severity Score			
Case	Age	Reached (mg/d)	Baseline	Week 2	Week 4	Week 8
1	51	10	8	5	4	0
2	52	5	7	4	0	0
3	50	2	8	4	4	4
4	75	2	7	…	5	3

[a]Abbreviation: CAPS-SX = Clinician Administered PTSD Scale for DSM-IV, One Week Symptom Version.

For cases 1, 2, and 3, prazosin was started at 1 mg at bedtime during week 1 and increased to 2 mg at bedtime during week 2. If trauma nightmares persisted and there were no apparent adverse effects of prazosin, the dose was increased to 5 mg at bedtime during weeks 3 and 4. If trauma nightmares persisted, prazosin was further increased to 10 mg in divided doses of 5 mg in the afternoon and 5 mg at bedtime during weeks 5 through 8. Because of the fourth patient's advanced age, his prazosin dose was increased only to 2 mg at bedtime (see below).

RESULTS

Subjects' ages, maximum prazosin dose achieved, and CAPS-SX severity scores over the 8-week trial are presented in Table 1. Case descriptions are presented to appreciate symptom phenomenology prior to the prazosin trial and to give details of clinical management and response during the trial.

CASE REPORTS

Case 1

Mr. A, a 51-year-old African American veteran, had participated in the defense of the Marine Corps base at Khe Sanh during the entire harrowing siege by North Vietnamese forces. He had experienced distressing combat trauma–content nightmares since returning from Vietnam. Nightmares were described as "like being in a horror videotape I can't turn off." Psychotherapy and a trial of sertraline had been ineffective.

At trial entry, Mr. A's CAPS-SX nightmare severity score was 8. Baseline medications (glyburide, 5 mg q.d., and enalapril, 20 mg q.d.) were continued during the trial. His blood pressure was 150/110 mm Hg and his heart rate was 96 beats per minute (b.p.m.). His CAPS-SX nightmare score decreased to 5 at the week 2 rating, and decreased further to 4 at the week 4 rating, at which point trauma content dreams continued to occur but were described as "like I was observing the battle from a high observation tower. It was interesting and only mildly distressing." Prazosin was increased to 5 mg in the afternoon and 5 mg h.s. At week 8, Mr. A's CAPS-SX nightmare

score was 0, with no recollected trauma dreams. His blood pressure was 145/95 mm Hg, and his heart rate was 96 b.p.m. Transient lethargy experienced during week 3 resolved during week 4. His CGI-C rating was "markedly improved."

Case 2

Mr. B, a 52-year-old African American veteran, had experienced extensive combat trauma during multiple firefights and enemy rocket and mortar attacks during his tour in Vietnam. Terrifying combat trauma nightmares had become increasingly frequent for approximately 5 years and became nightly during the year prior to the current trial. Courses of nortriptyline, trazodone, sertraline, valproate, temazepam, and zolpidem had failed to reduce nightmare severity. A trial of the β-adrenergic antagonist propranolol was associated with even further increased nightmare intensity. Because vivid dreams are a reported adverse effect of propranolol,[17] this drug had been discontinued.

Mr. B's baseline CAPS-SX nightmare severity score was 7. His blood pressure was 150/105 mm Hg, and his heart rate was 112 b.p.m. Baseline medications (enalapril, 10 mg q.d., and alprazolam, 0.5 mg b.i.d.) were continued during the trial. His CAPS-SX nightmare score decreased to 4 at week 2 and to 0 at weeks 4 and 8. His CGI-C rating of trauma nightmare treatment response at week 8 was "markedly improved." Mr. B continued to experience dreams, but the contents of the dreams did not involve trauma and were "normal . . . like before Vietnam."

In contrast to trauma nightmares, hypervigilance and low anger threshold, as well as mild hypertension (blood pressure = 150/90 mm Hg), persisted during Mr. B's prazosin treatment. Continued sinus tachycardia (108 b.p.m.) suggested β-adrenergic receptor–mediated cardiovascular hyperreactivity. Although a prior trial of propranolol had been associated with nightmare exacerbation, it was reasoned that propranolol in the presence of α_1-adrenergic blockade by prazosin might reduce β-adrenergic–mediated behavioral and cardiovascular symptoms without exacerbating trauma nightmares. This argument relied on analogy with the symptomatic treatment of pheochromocytoma cardiovascular symptoms with adrenergic antagonists.[18] Treatment of this catecholamine-producing adrenal tumor with a β antagonist in the absence of α_1 blockade exacerbates hypertension, whereas a β antagonist instituted in the presence of α_1 blockade reduces tachycardia without elevating blood pressure. Two days after propranolol, 40 mg b.i.d., had been added to prazosin, 5 mg q.d., Mr. B reported substantially reduced irritability and hypervigilance without return of trauma content nightmares. His heart rate decreased to 78 b.p.m. and his blood pressure to 130/80 mm Hg. Other than occasional mild orthostatic dizziness, Mr. B reported no adverse effects related to either prazosin or propranolol.

Case 3

Mr. C, a 50-year-old African American Vietnam veteran, suffered multiple episodes of combat trauma as an Army infantryman. Terrifying trauma nightmares had become more frequent and distressing during the 2 years prior to the current trial. Courses of nortriptyline, trazodone, sertraline, clonazepam, and valproate had not relieved nightmare severity. Temazepam hastened sleep onset, but had no beneficial effect on nightmares.

Mr. C's baseline CAPS-SX nightmare severity score was 8. His blood pressure was 140/100 mm Hg, and his heart rate was 78 b.p.m. Baseline medications (hydrochlorothiazide, 25 mg q.d., and temazepam, 30 mg h.s.) were continued during the trial. Mr. C's CAPS-SX nightmare severity had decreased to 4 at week 2, but he also reported mild lethargy and occasional dizziness. His blood pressure at week 2 was 125/80 mm Hg in the sitting position and decreased to 115/70 after 2 minutes of upright posture. To avoid potentially problematic hypotension, his prazosin dose was kept at 2 mg for the remainder of the 8-week trial, without recurrence of lethargy or dizziness. At week 8, Mr. C's CAPS-SX nightmare severity ratings continued at 4 and his CGI-C assessment of nightmare severity was "moderately improved." For the first time in many years, Mr. C reported having "normal dreams about my childhood that were not frightening."

Case 4

Mr. D, a 75-year-old African American veteran, had served as a "Red Ball Express" truck driver and combat infantryman in World War II. He had participated in prolonged life-threatening combat and witnessed terrible carnage in the European theater. For 5 years prior to the current treatment trial, combat trauma dreams had become increasingly distressing despite courses of buspirone, trazodone, doxepin, paroxetine, and clonazepam. Nefazodone, 150 mg b.i.d., had been prescribed. Although nefazodone produced modest improvement in mood, severely distressing combat trauma nightmares persisted.

Mr. D's baseline CAPS-SX nightmare severity score was 7. His blood pressure was 160/85 mm Hg, and his pulse was 78 b.p.m. Nefazodone and hydrochlorothiazide, 25 mg q.d., were continued during the treatment trial. Mr. D's prazosin dose reached 2 mg h.s. at week 2 and was not increased further, given reduction of blood pressure to 140/75 mm Hg. At week 8, his CAPS-SX nightmare severity score was 3 and his CGI-C score was "moderately improved." After the 8-week trial, Mr. D "ran out" of prazosin capsules for 2 weeks. During this period, combat trauma nightmare severity increased to pretreatment levels. When prazosin was reinstituted, nightmare severity rapidly subsided.

DISCUSSION

The association between prazosin administration and improvement in severe and chronic combat trauma nightmares in 4 consecutively treated combat veterans suggests possible efficacy of α_1-adrenergic blockade for this distressing PTSD symptom. In 2 patients who tolerated a prazosin dose of at least 5 mg, combat trauma nightmares were completely eliminated. Although nightmare reduction could have resulted from psychotherapeutic effects of trial participation or a placebo effect,[19] all patients had undergone psychotherapy and courses of other psychotropic medications prior to the prazosin trial without reduction in nightmare severity. If double-blind placebo-controlled trials of prazosin for trauma nightmares in combat veterans with PTSD demonstrate efficacy, prazosin would be a welcome addition to the therapeutic armamentarium for PTSD. The beneficial effects of prazosin on hypertension[20] and symptomatic benign prostatic hypertrophy[21] would be added benefits for many older male veterans.

The rationale for the potential efficacy of α_1-adrenergic blockade in PTSD is strengthened by human and animal studies. In humans, the highest concentrations of α_1-adrenergic receptors are observed in hippocampus, amygdala, and neocortex.[8,9] These areas are likely involved in the neurobiology of PTSD.[22] In the rat, electrophysiologic recordings demonstrate α_1-adrenergic stimulatory regulation of the startle response,[11] a behavior reminiscent of some PTSD symptoms.[23] Release of corticotropin-releasing hormone from the hypothalamus during restraint stress in rats is stimulated by the α_1-adrenergic agonist methoxamine and blocked by prazosin.[24] Hypothalamic corticotropin-releasing hormone release in humans also is regulated by α_1 stimulation.[25]

Animal studies demonstrate sleep disruption by α_1-adrenergic stimulation. In dogs, the α_1-adrenergic agonist methoxamine markedly disrupts sleep architecture, and this sleep disruption can be blocked by prazosin.[10] In cats, acute administration of the norepinephrine reuptake blocker desipramine suppresses rapid eye movement (REM) sleep, presumably by increasing intrasynaptic norepinephrine. This desipramine effect is reversed by prazosin, but not by the β-adrenergic antagonist propranolol.[26] These animal studies suggest that REM sleep is under α_1-adrenergic inhibitory regulation and suppressed by α_1 receptor stimulation. That "normal" dreaming, characteristic of REM sleep, increased in the 4 PTSD patients during prazosin treatment is consistent with this model. How reduction in trauma nightmares can be reconciled with this model is unclear. It is possible that combat trauma nightmares are not REM sleep stage phenomena. Except for REM sleep, stage 1 (light) sleep is the sleep stage most associated with nightmares.[27] In contrast to REM sleep, stage 1 sleep is increased by α_1-adrenergic stimulation with methoxamine, and this effect is blocked by prazosin.[10] A hypothesis has been presented that phasic CNS noradrenergic outflow might underlie non-REM nightmares, and if so, such nightmares should emerge preferentially from stage 1 sleep.[27] It also may be possible that what are called nightmares by these veterans are actually non-REM night terrors arising from slow-wave sleep.[28]

The complex nature of adrenergic postsynaptic receptor distribution and function in the brain is consistent with possible differential effects of α_1 and β-blockers on PTSD symptoms. That optimal management of the second patient's PTSD symptoms appeared to occur during combined prazosin and propranolol administration supports this possibility. α_1-Adrenergic receptors and β-adrenergic receptors are differentially distributed on postsynaptic targets of adrenergic neurons in both the CNS and the periphery.[4] In addition, α_1 and β receptors often mediate different and even opposite effects on CNS regulation of stress-responsive neuroendocrine systems. For example, stimulation of α_1-adrenergic agonists stimulates release of the stress-responsive neuropeptide vasopressin, whereas stimulation of β-adrenergic agonists inhibits vasopressin release.[29] In sympathetic nervous system regulation of vascular resistance, α_1-adrenergic receptor stimulation produces vasoconstriction, whereas β-adrenergic receptor stimulation produces counter-regulatory vasodilation.[30]

These complexities raise the possibility of multifaceted pharmacotherapeutic approaches to modifying adrenergic activity in PTSD. Anecdotal reports suggest reduction of PTSD symptoms by either the β-adrenergic antagonist propranolol[6,7] or by the α_2-adrenergic agonists clonidine and guanfacine.[6,31,32] As suggested by case 2, a combination of antiadrenergic agents might offer greater symptomatic relief than any single agent alone. Placebo-controlled trials are needed to definitively assess the efficacy of prazosin and other antiadrenergic drugs in the symptomatic management of PTSD.

Drug names: alprazolam (Xanax and others), buspirone (BuSpar), clonazepam (Klonopin and others), clonidine (Catapres and others), desipramine (Norpramin and others), doxepin (Sinequan and others), enalapril (Vasotec and others), methoxamine (Vasoxyl), nefazodone (Serzone), nortriptyline (Pamelor and others), paroxetine (Paxil), prazosin (Minipress and others), propranolol (Inderal and others), sertraline (Zoloft), temazepam (Restoril and others), trazodone (Desyrel and others), zolpidem (Ambien).

REFERENCES

1. Charney DS, Deutch AY, Krystal JH, et al. Psychobiologic mechanisms of posttraumatic stress disorder. Arch Gen Psychiatry 1993;50:294–305
2. Friedman MJ, Southwick SM. Towards pharmacotherapy for posttraumatic stress disorder. In: Friedman MJ, Charney DS, Deutch AY, eds. Neurobiological and Clinical Consequences of Stress: From Normal Adaptation to PTSD. Philadelphia, Pa: Lippincott-Raven; 1995:465–481
3. Insel PA. Adrenergic receptors: evolving concepts on structure and function. Am J Hypertens 1989;2:112S–118S
4. Al-Damluji S. Measuring the activity of brain adrenergic receptors in man. J Endocrinol Invest 1991;14:245–254
5. Palacios JM, Probst A, Cortes R. Mapping receptors in the human brain. Trends Neurosci 1986;9:284–289

6. Kolb LC, Burris BC, Griffiths S. Propranolol and clonidine in the treatment of the chronic posttraumatic stress disorders of war. In: van der Kolk BA, ed. Post Traumatic Stress Disorder: Psychological and Biological Sequelae. Washington, DC: American Psychiatric Press; 1984:97–107
7. Famularo R, Kinscherff R, Fenton T. Propranolol treatment for childhood posttraumatic stress disorder, acute type: a pilot study. Am J Dis Child 1988;142:1244–1247
8. Gross-Isseroff R, Dillon KA, Fieldust SJ, et al. Autoradiographic analysis of α_1-noradrenergic receptors in the human brain postmortem. Arch Gen Psychiatry 1990;47:1049–1053
9. Palacios JM, Hoyer D, Cortes R. α_1-Adrenoceptors in the mammalian brain: similar pharmacology but different distribution in rodents and primates. Brain Res 1987;419:65–75
10. Pickworth WB, Sharpe LG, Nozaki M, et al. Sleep suppression induced by intravenous and intraventricular infusions of methoxamine in the dog. Exp Neurol 1977;57:999–1011
11. Stevens DR, McCarley RW, Greene RW. The mechanism of noradrenergic α_1 excitatory modulation of pontine reticular formation neurons. J Neurosci 1994;14:6481–6487
12. Neylan TC, Marmar CR, Metzler TJ, et al. Sleep disturbances in the Vietnam generation: findings from a nationally representative sample of male Vietnam veterans. Am J Psychiatry 1998;155:929–933
13. Van Zwieten PA. Antihypertensive drugs interacting with alpha- and beta-adrenoreceptors: a review of basic pharmacology. Drugs 1988;35:6–19
14. Mellman TA, Kumar A, Kulick-Bell R, et al. Nocturnal/daytime urine noradrenergic measures and sleep in combat-related PTSD. Biol Psychiatry 1995;38:174–179
15. Blake DD, Weathers FW, Nagy LM, et al. The development of a Clinician Administered PTSD Scale. J Trauma Stress 1995;8:75–80
16. Lehmann E. Practicable and valid approach to evaluate the efficacy of nootropic drugs by means of rating scales. Pharmacopsychiatry 1984;17:71–75
17. Yamada Y, Shibuya F, Hamada J, et al. Prediction of sleep disorders induced by beta-adrenergic receptor blocking agents based on receptor occupancy. J Pharmacokinet Biopharm 1995;23:131–145
18. Werbel SS, Ober KP. Pheochromocytoma: update on diagnosis, localization, and management. Med Clin North Am 1995;79:131–153
19. Coalson B. Nightmare help: treatment of trauma survivors with PTSD. Psychotherapy 1995;32:381–388
20. Lund-Johansen P, Hjermann I, Iversen BM, et al. Selective alpha-1 inhibitors: first- or second-line antihypertensive agents? Cardiology 1993;83:150–159
21. Hieble JP, Ruffulo RR Jr. The use of alpha-adrenoreceptor antagonists in the pharmacological management of benign prostatic hypertrophy: an overview. Pharmacol Res 1996;33:145–160
22. Charney DS, Deutch AY, Southwick SM, et al. Neural circuits and mechanisms of post-traumatic stress disorder. In: Friedman MJ, Charney DS, Deutch AY, eds. Neurobiological and Clinical Consequences of Stress: From Normal Adaptation to PTSD. Philadelphia, Pa: Lippincott-Raven; 1995:271–287
23. Davis M, Falls WA, Campeau S, et al. Fear-potentiated startle: a neural and pharmacological analysis. Behav Brain Res 1993;58:175–198
24. Kiss A, Aguilera G. Participation of alpha 1 adrenergic receptors in the secretion of hypothalamic corticotropin-releasing hormone during stress. Neuroendocrinology 1992;56:153–160
25. Al-Damluji S, Francis D. Activation of central alpha-1 adrenoreceptors in humans stimulates release of prolactin and TSH, as well as ACTH. Am J Physiol 1993;264:E208–E214
26. Ross RJ, Gresch PJ, Ball WA, et al. REM sleep inhibition by desipramine: evidence for an α_1 adrenergic mechanism. Brain Res 1995;701:129–134
27. Woodward SH. Neurobiological perspectives on sleep in post-traumatic stress disorder. In: Friedman MJ, Charney DS, Deutch AY, eds. Neurobiological and Clinical Consequences of Stress: From Normal Adaptation to PTSD. Philadelphia, Pa: Lippincott-Raven; 1995:315–333
28. Llorente MD, Currier MB, Norman SE, et al. Night terror in adults: phenomenology and relationship to psychopathology. J Clin Psychiatry 1992;53:392–394
29. Day TA, Randle JCR, Renaud LP. Opposing alpha- and beta-adrenergic mechanisms mediate dose-dependent actions of noradrenaline on supraoptic vasopressin neurones in vivo. Brain Res 1985;358:171–179
30. Graham RM. Adrenergic receptors: structure and function. Cleve Clin J Med 1990;57:481–491
31. Kinzie JD, Leung P. Clonidine in Cambodian patients with posttraumatic stress disorder. J Nerv Ment Dis 1989;177:546–550
32. Horrigan JP, Barnhill LJ. The suppression of nightmares with guanfacine [letter]. J Clin Psychiatry 1996;57:371