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# Immediate Treatment with Propranolol Decreases Posttraumatic Stress Disorder Two Months after Trauma

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**Background:** *This study investigated the efficacy of propranolol prescribed shortly after trauma exposure in the prevention of posttraumatic stress disorder (PTSD) symptoms and diagnosis.*

**Methods:** *Eleven patients received 40 mg of propranolol 3 times daily for 7 days, followed by a taper period of 8–12 days. They were compared with eight patients who refused propranolol but agreed to participate in the study. Though nonrandomized, the two groups did not differ on demographics, exposure characteristics, physical injury severity, or peritraumatic emotional responses.*

**Results:** *Posttraumatic stress disorder rates were higher in the group who refused propranolol (3/8) compared with those who received the medication (1/11), as were the levels of PTSD symptoms ( $U = 85, p = .037$ ).*

**Conclusions:** *Our results are consistent with earlier findings and suggest that propranolol may be useful for mitigating PTSD symptoms or perhaps even preventing the development of PTSD. Biol Psychiatry 2003;54:947–949 © 2003 Society of Biological Psychiatry*

**Key Words:** Posttraumatic stress disorder, immediate treatment, propranolol, peritraumatic distress, short-term outcome

## Introduction

Victims of traumatic events display a number of reactions and symptoms during the trauma and in its immediate aftermath. These immediate reactions are re-

lated in part to the release of catecholamines (adrenalin and noradrenalin), as a consequence of activation of the central nucleus of the amygdala and the locus coeruleus, key components of the neurocircuitry of fear (Goddard and Charney 1997). A subgroup of trauma victims experiences a peritraumatic panic-like state that can include hyperventilation, trembling, sweating, and tachycardia, which suggest an immediate adrenergic activation at the time of traumatic exposure. Police officers with elevated peritraumatic arousal and emotional distress during critical incident exposure, including panic reactions, have greater levels of subsequent posttraumatic stress symptoms (Brunet et al 2001). Prolonged adrenergic activation, as reflected by greater peritraumatic tachycardia, was prospectively shown to increase the risk for posttraumatic stress disorder (PTSD) (two positive studies: Bryant et al 2000; Shalev et al 1998; and one negative study: Blanchard et al 2002). Prolonged states of adrenergic activation are believed to increase the risk for PTSD through increased fear conditioning (Orr et al 2000) and the overconsolidation of the memories related to the traumatic event (Southwick et al 1999).

Propranolol is a  $\beta$ -adrenergic antagonist that is used in the treatment of hypertension and also for the treatment of anxiety disorders (Laverdure and Boulenger 1991). Based on pilot data, Pitman et al (2002) have suggested that propranolol given within 6 hours of the traumatic event for 10 days was superior to a placebo for reducing PTSD symptoms 1 month posttrauma.

In France, propranolol can be prescribed for symptoms of tachycardia after temporarily distressing situations. We therefore studied the influence of propranolol prescribed shortly after a traumatic event in survivors who presented with tachycardia. Based on a model of adrenergic dysregulation in PTSD proposed by Southwick et al (1999) and findings linking hyperarousal to increased fear conditioning (Orr et al 2000), we hypothesized that propranolol would counter the hyperadrenergic state and decrease PTSD symptoms and diagnosis 2 months posttrauma.

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## Methods and Materials

### Participants

The trauma victims were recruited at the Emergency Departments of the Douai and Lille hospitals (France) shortly after their admission (2–20 hours posttrauma) after motor vehicle accidents or physical assault. The participants included 21–30-year-old individuals in good physical health with tachycardia of at least 90 beats/min after 20 min of rest in a lying position. Participants were excluded if they had lost consciousness during the trauma, had sustained important physical or traumatic brain injuries, had a cardiovascular or active asthma disease, or in case of past or present PTSD at baseline.

### Measures

The subjective severity of the traumatic event was assessed using the Peritraumatic Distress Inventory (Brunet et al 2001). Physical injury severity was assessed with the Trauma Score (Smith 1990). The Treatment Outcome PTSD scale (Davidson and Colket 1997) and the DSM-IV criteria were used to assess PTSD symptoms and diagnosis, respectively. Posttraumatic stress disorder at baseline and prior trauma history were assessed with the Mini International Neuropsychiatric Interview (Lecrubier et al 1997). After the study protocol was fully explained, the participants provided informed consent.

### Procedure

Patients received a monotherapy of 40 mg of propranolol 3 times daily for 7 days. The first pill was prescribed immediately after the 20-min baseline heart rate recording period. Treatment termination included the measure of heart rate at day 7, with an 8–12-day taper period (a drop of 40 mg every 4 days). Two months after trauma exposure, a psychiatrist, blind to the treatment status of the participants, assessed them for PTSD symptoms and diagnosis.

### Statistical Analyses

Analyses were conducted with SPSS 10.0 software (SPSS, Chicago, IL). Because of the small sample size, we used the Wilcoxon rank test to compare means and Fisher exact test to compare rates. The  $\alpha$  was set at .05 (two-sided tests). There were no missing data.

## Results

Over a 6-month period, 54 victims presenting to the Emergency Department met the DSM-IV criteria A1 and A2 for trauma exposure. Nineteen patients were excluded because of injury severity and four because of age. Of 31 potential participants, 23 had a resting heart rate greater than 90 beats/min. Among those 23, 11 agreed to take the propranolol, 8 refused but agreed to participate in the study, and 4 refused to be study participants. As can be seen in Table 1, the two study groups did not differ on age,

Table 1. Between-Group Comparisons of Participants Who Agreed Versus Refused to Take Propranolol in the Aftermath of Trauma

	Propranolol (n = 11)	No Propranolol (n = 8)	p
Age (years)			
Mean (median)	23.90 (10.59)	23.00 (9.19)	.58
SD	3.80	3.70	
Gender			
Male	7	4	.50
Female	4	4	
Type of Event			
Traffic accident	7	6	.61
Aggression	4	2	
Trauma Score			
Mean (median)	.72 (9.59)	.87 (10.56)	.69
SD	.78	.83	
PDI Score			
Mean (median)	14.36 (10.05)	14.62 (9.94)	.97
SD	7.80	6.60	
Heart Rate Baseline (beats/min)			
Mean (median)	102.80 (9.78)	100.30 (8.13)	.50
SD	8.20	6.70	
Propranolol (mg/day)			
M	101.80	–	–
SD	20.00		
Heart Rate at Day 7 (beats/min)			
Mean	61.90	79.40	–
SD	5.00	9.30	
PTSD Score			
Mean (median)	6.18 (7.73)	11.75 (13.13)	.037
SD	5.20	6.40	W = 85
PTSD Diagnosis	1	3	.012
			$\chi^2 = 6.4$

PDI, Peritraumatic Distress Inventory; PTSD, posttraumatic stress disorder.

gender, employment, marital status, baseline heart rate, or on the type of event, injury severity score, and peritraumatic distress.

Propranolol was delivered 2–20 hours after the trauma (mean = 9.5, SD = 6). Compliance was good, as evidenced by the resting heart rate obtained 1 week posttrauma (mean = 62, SD = 5). As shown in Table 1, 2 months after the traumatic event, PTSD rates were higher among subjects who refused propranolol (3/8) compared with those who received the medication (1/11), as were the PTSD symptom scores ( $U = 85, p = .037$ ). Treatment tolerance was deemed satisfactory among the participants who, for the most part, had never previously taken any medication. Despite the prescribed taper period, two patients discontinued propranolol abruptly after 1 week. After he discontinued the propranolol without taper period, one of these individuals presented with a marked anxiety reaction, without any cardiovascular complications. Three patients were slightly bothered by a sensation of sedation or lethargy.

## Discussion

Recent work on the pathogenic effects of traumatic stress has focused on adrenergic activation, associated with states of terror at the time of exposure. Traumatic events are hypothesized to be followed by a critical period of increased brain plasticity, during which long-lasting neuronal changes may occur in those who develop traumatic stress disorders (Shalev 2000). Physiologic arousal during the traumatic event and in the post-immediate phase may trigger the neurobiological processes that lead to PTSD. Propranolol has been shown to reduce memory for emotional events through a central adrenergic blockade (Cahill et al 1994). Propranolol is a  $\beta$ -adrenergic antagonist that binds to peripheral and central  $\beta$ -adrenergic receptors and readily crosses the blood–brain barrier. At the clinical level, it counters trembling, sweating, and palpitations. Central nervous system effects of traumatic exposure are mediated by cognitive appraisals of threat. Greater perceived threat influences the release of central catecholamines by activating the central nucleus of the amygdala, locus coeruleus, and other structures that constitute the neurocircuitry of fear.

This pilot study suggests that administering propranolol to young healthy individuals with tachycardia is effective in mitigating PTSD symptoms and perhaps in preventing PTSD. Contrary to other studies, our study controlled for the level of peritraumatic distress, ensuring that both the experimental and control groups were exposed to equally distressing events. The study also has limitations, notably a small sample size of nonrandomized participants followed for a relatively brief period.

Our results are consistent with those of Pitman et al (2002), who reported encouraging findings in a pilot, double-blind, controlled trial. Large-scale controlled trials are warranted with diverse trauma groups and longer follow-up, to determine the value of propranolol in the secondary prevention of PTSD.

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