# Prepulses Reduce the Pain of Cutaneous Electrical Shocks

TERRY D. BLUMENTHAL, PHD, TRAVERSE T. BURNETT, AND CHARLES D. SWERDLOW, MD

**Objective:** Both the startle reflex elicited by an intense acoustic or tactile stimulus and the perceived intensity of that stimulus can be diminished by a weak "prepulse" that precedes the startling stimulus. The present study examined whether prepulses can also diminish the pain produced by an intense electrical stimulus similar to that used to treat life-threatening cardiac arrhythmias in conscious patients with implantable cardioverter/defibrillators or transcutaneous pacemakers. **Methods:** Perceptual and pain thresholds for electrical shocks to the arm were determined in 20 adults. Participants then rated the painfulness of 25 electrical shocks that were 1.5 times the pain threshold (mean shock intensity, ≈160 V) and either presented alone or preceded (at 40–60 ms) by weak electrical prepulses equal to or 25% above the perceptual threshold. **Results:** Prepulses significantly reduced the pain produced by the intense shocks. Individuals with the lowest pain thresholds experienced the greatest pain reduction with prepulses. In these more sensitive individuals, the most effective prepulses reduced perceived pain by 26% across the entire test session and by 54% in the initial block of five shocks. **Conclusions:** Prepulses may be useful in diminishing the pain associated with the therapeutic electrical shocks used to treat cardiac arrhythmias. **Key words:** implantable cardioverter/defibrillator, prepulse inhibition, pain, startle.

ANOVA = analysis of variance; ICD = implantable cardioverter/defibrillator; T = perception threshold; VAS = visual analog scale.

## INTRODUCTION

Painful electrical stimuli may be necessary to treat life-threatening cardiac arrhythmias in conscious patients. For example, ICDs deliver intense shocks to terminate tachyarrhythmias (1–3). Pain and startle caused by ICD shocks are important problems for ICD therapy because they reduce patient acceptance of therapeutic shocks and may contribute to severe anxiety and mood disorder (4–8).

Abrupt, intense stimuli can trigger the startle reflex, and both the magnitude of the reflex and the perceived intensity of the stimulus can be reduced if the startling stimulus is preceded by a weak prepulse delivered 30 to 500 ms earlier (9–12). For example, acoustic prepulses can reduce both the magnitude of the startle reflex elicited by an intense noise or air puff and the perceived intensity of the startling stimuli (11, 12). Electrical prepulses have been reported to inhibit the startle reflex elicited by intense electric stimuli (13).

On the basis of these observations, we hypothesized that electrical prepulses could reduce the pain of a sudden, intense electrical shock. The major aim of the present study was to test this hypothesis for cutaneous shocks as a first step in evaluating the possible utility of prepulses as a method to reduce the pain of therapeutic electrical shocks.

From the Department of Psychology (T.D.B., T.T.B.), Wake Forest University, Winston-Salem, North Carolina; and Cedars Sinai Medical Center (C.D.S.), Los Angeles, California.

Address reprint requests to: Terry D. Blumenthal, PhD, Department of Psychology, Wake Forest University, Winston-Salem, NC 27109. Email: blumen@wfu.edu

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## METHODS

### Participants

Twenty-nine undergraduate students participated in this study for extra course credit. They gave written, informed consent according to a protocol approved by the Wake Forest University Institutional Review Board. Individuals were excluded if they had specific medical problems, such as unexplained fainting or loss of consciousness, heart disease or heart problems, heart palpitations or unexplained periods of rapid heartbeats lasting longer than 1 minute, epilepsy, any other seizure disorder, panic or anxiety disorder, or hypersensitivity to pain. Nineteen participants completed the protocol. One participant completed all but the last six shocks. We analyzed data for these 20 participants (10 men and 10 women; age = 19 years, 10 months–20 years 2 months). The remaining nine participants were unable to tolerate the painful shocks and terminated the tests before sufficient data could be collected.

### Instrumentation

Prepulses and shocks were delivered through two electrodes placed 5 to 6 cm apart and taped to the skin overlaying the biceps muscle on the nondominant arm. We delivered shocks to the arm rather than the torso to prevent the possibility of initiating a cardiac arrhythmia. Although the risk of inducing ventricular arrhythmias may be minimized by synchronizing shocks to the QRS complex of the electrocardiogram, synchronization may fail. Also, QRS-synchronized shocks have nearly optimal timing to induce atrial arrhythmias. Shocks delivered to the arm create a sufficiently weak electrical field in the chest so that there is no risk of initiating arrhythmias. Electrical pulses with a duration of 0.5 ms were produced by a Biopac MP100 stimulator and a StimIsoB stimulus-isolation unit. The experimenter controlled the amplitude of the stimulus over a range of 0 to 200 V. The interval between shocks was approximately 20 seconds. To record eye-blink response as a measure of startle, two recording electrodes were taped to the skin overlaying the orbicularis oculi muscle below the left eye, with an interelectrode distance of 1.5 cm. A third (reference) electrode was taped to the left temple area. Eye-blink responses (periorbital electromyographs from orbicularis oculi) were recorded using a Coul-



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bourn Bioamplifier with filters passing 90 to 250 Hz to a Biopac Systems MP100 interface.

## Procedure

*Perception threshold.* First we determined the perception threshold for a stimulus to the arm. The amplitude of the initial stimulus was 10 V with a duration of 0.5 ms. The stimulus amplitude was increased by 2-V increments until the participant reported feeling something. Then the stimulus amplitude was reduced by 2 V per trial until the participant no longer reported feeling the stimulus. Stimulus amplitude was then increased again by 2-V increments until the participant reported feeling something. This value was defined as the perception threshold (T) (Table 1).

*Pain threshold.* Next we determined the pain threshold. The amplitude of the initial stimulus was twice the perception threshold. The stimulus amplitude was increased by 4-V increments on each trial until the participant reported that the stimulus was painful. This value was defined as the pain threshold (Table 1). On each trial, participants placed a mark on a 100-mm VAS that ranged from "can't feel it" to "painful."

*Effect of prepulses on perception of shock pain.* We then delivered a sequence of five blocks of five constant-amplitude, painful shocks for a total of 25 shocks. The shock intensity was set at a value equal to 1.5 times the pain threshold but no higher than 200 V. Thus, shock amplitude was 200 V whenever the pain threshold was >133 V.

Each trial block included a control shock without a prepulse and four test shocks with prepulses. We used two prepulse amplitudes, each delivered at two prepulse intervals (time from onset of prepulse to onset of painful shock). The two prepulse amplitudes were perceptual threshold (T) and 1.25 times perceptual threshold (1.25T). The two prepulse intervals were 40 and 60 ms. The order of stimulus conditions (control, 40 ms/1.0T, 60 ms/1.0T, 40 ms/1.25T, 60 ms/1.25T) was randomized independently for each trial block.

After each trial, the participant was asked to assess the perceived intensity of the intense shock using a 100-mm VAS that ranged from "can't feel it" to "intolerable pain." VAS ratings were measured in millimeters from the left end of the scale. The VAS value on each trial was converted to a "relative pain score," which was the VAS rating expressed as a percentage of the total range for that participant: $(P_x - P_{min})/(P_{max} - P_{min})$, where $P_x$ = the rating on this trial, $P_{min}$ = the minimum rating for all trials, and $P_{max}$ = the maximum rating for all trials. We also recorded eye-blink electromyographs for each trial.

**TABLE 1. Perceptual and Pain Thresholds**

| Participant | Sex | Perceptual Threshold (Volts) | Pain Threshold (Volts) |
|---|---|---|---|
| 1 | Female | 10 | 108 |
| 2 | Female | 12 | 88 |
| 3 | Male | 8 | 140 |
| 4 | Male | 14 | 100 |
| 5 | Female | 16 | 52 |
| 6 | Male | 8 | 200 |
| 7 | Male | 10 | 160 |
| 8 | Female | 12 | 112 |
| 9 | Male | 12 | 76 |
| 10 | Male | 18 | 110 |
| 11 | Male | 20 | 140 |
| 12 | Female | 6 | 76 |
| 13 | Female | 10 | 72 |
| 14 | Male | 16 | 80 |
| 15 | Female | 12 | 128 |
| 16 | Female | 8 | 48 |
| 17 | Male | 52 | 182 |
| 18 | Female | 20 | 148 |
| 19 | Female | 44 | 200 |
| 20 | Male | 50 | 198 |

## Statistical Analyses

Relative pain scores were analyzed by ANOVA. VAS values were not recorded on 14 of 500 trials (2.8%). Almost half of these were from a single participant who terminated the study after 19 trials; the remaining 8 missing trials occurred in four other participants. Because any single missing cell resulted in the loss of the entire participant from a within-participant analysis, several strategies were taken to minimize the statistical impact of these missing cells. In the most conservative strategy, values were collapsed within a stimulus condition across the five trial blocks to yield an average VAS rating for each stimulus condition across the entire test. These data were analyzed by an ANOVA with repeated measures on stimulus condition (no prepulse, 40 ms/1.0T, 40 ms/1.25T, 60 ms/1.0T, 60 ms/1.25T). To permit assessment of the effects of repeated stimulus presentations on pain and prepulse effects, missing cells were replaced with the average value for that stimulus condition for that participant. Data were then analyzed by ANOVA with repeated measures on stimulus condition and trial block. Similar results were obtained if missing values were replaced by a value derived by extrapolation/interpolation of the previous and subsequent trials of the same stimulus condition for that participant. Finally, exploratory analyses were undertaken by dividing the participants into two groups using a median split of pain thresholds, based on the known impact of pain threshold on pain-reducing effects of anesthetic interventions (14). In these cases, pain threshold (low vs. high) was used as a grouping factor. For all analyses, $\alpha$ was 0.05.

# RESULTS

## Perceptual and Pain Thresholds

Perceptual and pain thresholds are shown in Table 1. Values for both perceptual and pain thresholds were normally distributed. The mean perceptual threshold was 17.9 V (range = 6–52 V), and the mean pain threshold was 120.9 V (range = 48–200 V). Neither perceptual nor pain thresholds differed significantly between men and women (perceptual threshold: $F < 1$; pain threshold: $F = 2.89$; $df = 1,18$; $p$ = NS). A significant correlation between perceptual and pain threshold was found within participants ($r\,(20) = +0.62$, $p < .005$) despite the fact that two participants exceeded the maximal measured pain threshold (ie, the assigned value of 200 V underestimated their true pain threshold).

Based on pain thresholds, the mean amplitude of test shocks was 158.75 V (range = 72–200 V). Overall, 12 participants with pain thresholds ≤128 V received test shocks that were 1.5 times their pain thresholds, and 8 participants with pain thresholds ≥140 V re-

ceived 200 V shocks that were <1.5 times their pain thresholds.

### Startle Eye-Blink Response

Shocks presented to the arm elicited eye-blink startle on 35% of the control (no prepulse) shock trials, averaged across trial blocks for the entire session. Eye-blink response probability was 27, 24, 18, and 22% on the 40 ms/1.0T, 40 ms/1.25T, 60 ms/1.0T, and 60 ms 1.25T trials, respectively. Therefore, prepulse seemed to inhibit blink probability, but this probability was very low even without prepulses. In contrast, shocks elicited pronounced contractions of the arm musculature, resulting in occasional large, flailing movements of the arm and in some cases more generalized skeletal motor responses.

### Overall Prepulse Effects on Pain

ANOVA of relative VAS ratings for all shocks revealed a significant effect of stimulus condition ($F = 3.10$; $df = 4,19$; $p < .025$). Post hoc comparisons revealed a significant 17.5% reduction in pain with 60 ms/1.0T trials compared with control trials ($F = 18.45$; $df = 1,19$; $p < .0005$) as well as lesser but significant pain reduction with 40 ms/1.25T and 60 ms/1.25T prepulses ($p < .05$ and $p < .005$, respectively) (Figure 1, *inset*). Similar outcomes were obtained when missing VAS values were replaced by participants' average values for that trial condition (17.5% reduction with 60 ms/1.0T trials; effect of trial type: $F = 3.11$; $df = 4,76$; $p < .025$; control vs. 60 ms/1T trials: $F = 18.49$; $df = 1,19$; $p < .0005$).

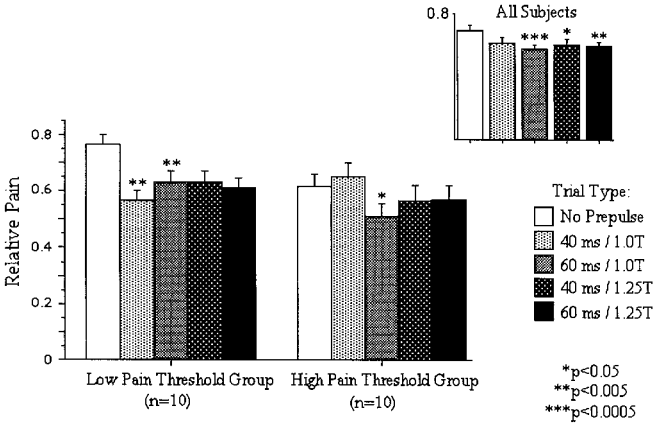


Fig. 1. Relative pain ratings (mean and SEM) as a function of prepulse condition by pain threshold group. *Inset*, Relative pain ratings as a function of prepulse condition for all subjects.

### Effect of Pain Threshold

The following analyses examined whether the effectiveness of prepulses or optimal prepulse parameters in the ranges tested differed in individuals with low vs. high pain thresholds (Figure 1). A median split analysis revealed that individuals with low pain thresholds reported higher relative VAS scores in the control condition than individuals with high pain thresholds (mean (SEM) relative VAS: low pain threshold = 0.64 (0.02); high pain threshold = 0.58 (0.02); $F = 7.51$; $df = 1,18$; $p < .025$). ANOVA of VAS scores averaged across the session, with low vs. high pain threshold as a grouping factor, revealed a significant effect of stimulus condition ($F = 3.47$; $df = 4,72$; $p < .025$) and a significant interaction of stimulus condition by pain threshold ($F = 3.21$; $df = 4,72$; $p < .025$). Post hoc comparisons revealed that the low pain threshold group experienced a significant 25.9% pain reduction across the session with 40 ms/1.0T prepulses ($F = 21.66$; $df = 1,9$; $p < .005$) and a significant 18.2% pain reduction with 60 ms/1.0T prepulses ($F = 14.24$; $df = 1,9$; $p < .005$). In contrast, the high pain threshold group (eight of whom received less than "full-strength" test shocks) experienced no significant pain reduction across the session with 40 ms/1.0T prepulses ($F < 1$) but did experience a significant 17.7% pain reduction with 60 ms/1.0T prepulses ($F = 5.71$; $df = 1,9$; $p < .05$).

A prepulse "impact" value for each stimulus condition was calculated by subtracting the relative VAS score for that stimulus condition from the relative VAS score for the no-prepulse condition. There was a significant negative correlation between the mean prepulse impact for each participant and that participant's pain threshold ($r(20) = -0.45$, $p < .05$). Thus, the pain-reducing impact of prepulses for any participant was inversely related to their pain threshold: Participants who were most sensitive to pain benefited most from prepulses.

Because participants were told that they could terminate the session at any time, the sample population for this study included only individuals who were relatively insensitive to pain. The nine individuals who withdrew from the study before delivery of intense test shocks (1.5 times pain threshold) had lower pain thresholds (mean = 65.8 V, range = 36–158 V) than did the remaining 20 participants (mean = 120.9 V, range = 48–200 V) ($F = 8.91$; $df = 1,27$; $p < .01$). Although one of these nine participants was a relatively stoic "outlier" (pain threshold = 158 V), the pain thresholds of the remaining eight participants (mean = 54.3 V, range =36–90 V) were significantly lower than those of participants in the low pain thresh-

old group who completed testing ($F = 8.01$; $df = 1,16$; $p < .025$).

### Effect of Trial Block

The pain-reducing effects of prepulses were examined across the five trial blocks in the 19 participants who completed the test session (Figure 2). Pain ratings for all stimulus conditions increased substantially across the session, with mean (SEM) relative VAS ratings on no-prepulse trials increasing from 0.45 (0.06) (block 1) to 0.83 (0.06) (block 5). In the low pain threshold group, these values approached the maximal level of 1.0 by block 5 (mean = 0.95, SEM = 0.03), indicating a "ceiling effect" that might diminish the sensitivity of detecting prepulse effects on pain perception. ANOVA with trial block as a within-participant factor and pain threshold as a between-groups factor revealed a significant effect of trial block ($F = 15.33$; $df = 4,68$; $p < .0001$) and stimulus condition ($F = 2.73$, $df = 4,68$; $p < .05$) and significant interactions of stimulus condition by pain threshold ($F = 3.34$; $df = 4,68$; $p < .025$) and stimulus condition by pain threshold by trial block ($F = 1.88$; $df = 16,272$; $p < .025$).

### First Block of Shocks

The pain ratings in the initial trial block are most relevant to ICD therapy, which usually consists of one or a few shocks. Based on the above-mentioned, significant three-way interaction, data from the initial trial block were examined separately (Figure 3). Because only a single trial from each stimulus type was included in this ANOVA, power was greatly reduced, and there was no main effect of stimulus condition ($F = 1.60$; $df = 4,72$; $p$ = NS). However, a significant interaction of pain threshold by stimulus condition was found ($F = 4.30$; $df = 4,72$; $p < .005$). Post hoc analyses in the low pain threshold group revealed a significant 54.2% reduction in relative VAS rating with 40 ms/1.0T trials ($F = 8.26$; $df = 1,9$; $p < .025$).

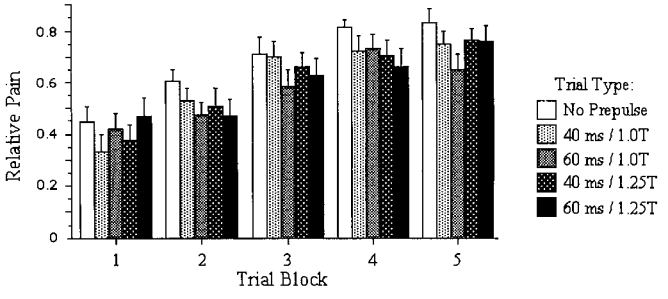


Fig. 2 Relative pain ratings (mean and SEM) as a function of prepulse condition by trial block.

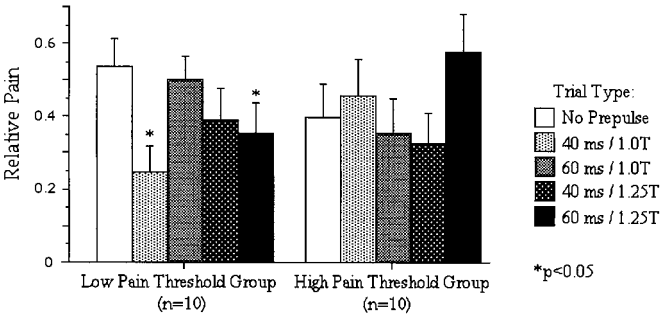


Fig. 3. Relative pain ratings (mean and SEM) as a function of prepulse condition in the first trial block.

The maximal pain reduction in the high pain threshold group also occurred with 40 ms/1.0T prepulses (18.8%), but this effect was not statistically significant ($F < 1$). Among the 12 participants whose painful shocks were 1.5 times their pain thresholds, relative VAS scores in this initial trial block were reduced by 42.6% in the 40 ms/1.0T prepulse condition and by 22.2% in the 60 ms/1.25T prepulse condition.

Interestingly, 60 ms/1.25T prepulses significantly reduced relative VAS scores in the low pain threshold group by 34.2% ($F = 6.45$; $df = 1,9$; $p < .05$) but increased relative VAS scores by 44.9% in the high pain threshold group, although this latter effect did not reach significance ($F = 3.06$; $df = 1,9$; $p < .15$).

## DISCUSSION

The principal finding of this study is that the pain associated with an intense (mean = 160 V) cutaneous electrical shock can be reduced by delivering a weak prepulse 40 or 60 ms before the shock. In the initial trial block, among individuals most sensitive to the painful effects of shocks (low pain threshold group), prepulses at the perceptual threshold, presented 40 ms before the shock, reduced pain ratings by >50%. Similarly, among all participants who received a full-strength shock, these prepulses reduced relative VAS scores by >40%.

### Mechanism of Pain Reduction by Prepulses

A reduction in pain on prepulse trials relative to control trials could be due to one or more of several processes, including prepulse inhibition, sensory assimilation, and refractoriness. Prepulse inhibition is the normal inhibition of a startle reflex that occurs when the startling stimulus is preceded by a weak prepulse (15). Prepulse inhibition stimulated by acoustic prepulses seems to be mediated by the effects of the acoustic prepulse on brain circuitry within the

pontine tegmentum (16, 17), resulting in suppression of activity within the "primary" startle circuit at the level of the caudal pons (18, 19). If this same circuitry mediates the startle-inhibiting effects of electrical prepulses, the pontine circuitry activated by the prepulse may also project to other brainstem pain pathways, inhibiting the perception of painful stimuli.

A less likely mechanism by which a prepulse might decrease the pain of a shock to the arm might involve the process of perceptual averaging, referred to in the auditory system as "loudness assimilation," wherein the perception of an intense stimulus can be modulated by a weaker stimulus presented just before the intense stimulus (20). Loudness assimilation involves a shift in the perceptual attributes of both stimuli toward each other, so that the weak prepulse sounds louder and the intense pulse sounds weaker. If an analogous process regulates the perception of electrical stimuli in the present situation, the perception of the electrical prepulse would lead to the subsequent intense stimulus being perceived as less intense and therefore less painful. Such a process could be relevant to the present findings only if perceptual averaging does not require a conscious awareness of the prepulse stimulus, because the prepulse intervals in this study (40–60 ms) do not typically permit the detection of two distinct stimuli. With acoustic stimuli these prepulse intervals are too short to detect the effects of attentional allocation on prepulse inhibition (21), suggesting that separate attentional mechanisms are not engaged by lead stimuli with this stimulus configuration.

Refractoriness of pain sensation caused by the prepulse is an unlikely explanation for the present findings, because prepulse amplitude was well below pain threshold.

### Ancillary Findings

We note two additional results of this study. The first is that pain ratings increased temporally across the session for all stimulus conditions. This sensitization to painful stimuli was also found by Duker et al. (22) and may be due to depletion of endorphins with repeated presentation of painful stimuli. The fact that participants attended to the painful stimulus (to provide VAS scores) also probably contributed to the increased painfulness of those stimuli across trials (23).

A second ancillary finding is the low probability of eye-blink responses to the intense shocks presented to the arm, although prepulses seemed to inhibit response probability slightly. If shocks of considerably lower intensity had been presented to the forehead, eye blinks would have occurred on most trials (11). Given the fact that ascending sensory projections arising in the arm eventually pass through the pons, these data suggest that most, but not all, of these projections bypass the pontine startle center or the nucleus of the facial nerve, which drives the orbicularis oculi and causes the eye-blink response (24, 25). Sarno et al. (26) have suggested that the electrically elicited blink response may not be an example of a startle response, and the present study shows that the location of the electrical stimulus is one factor that determines the degree to which an eye-blink response will be activated.

### Potential Clinical Application

Prepulses may reduce the pain of intense therapeutic electrical stimuli such as those used to treat cardiac arrhythmias in conscious patients. Although ICDs have become first-line therapy for some patients with life-threatening ventricular tachycardia or fibrillation (1–3), shock-induced pain is an important problem and may cause psychiatric morbidity (4–8). Recently ICDs have been used to treat atrial fibrillation (27). Shock-induced pain severely limits patient acceptance of ICD treatment of atrial fibrillation, which is not life-threatening (27, 28). Furthermore, startle is an important component of shock-related psychiatric morbidity (7). In the present study, we did not strongly confirm inhibition of eye-blink startle responses by weak electrical prepulses because of the relative insensitivity of the eye-blink measures to the startling effects of arm shocks. However, a substantial amount of literature supports the notion that a startle reflex elicited by electrical, acoustic, or tactile stimuli can be reliably suppressed by appropriate prestimuli (11, 15, 19, 29). Thus, prepulses delivered before ICD shocks may reduce both pain and startle.

The pain of electrical pulses also limits patient acceptance of transcutaneous (30, 31) and esophageal (32) cardiac pacing. An important difference between ICD shocks and cardiac pacing is that ICD shocks usually are single, but pacing consists of a series of stimuli. The present findings suggest that optimal prepulse parameters for reducing pain from a single shock may not be optimal for reducing pain elicited by a series of electrical pulses. Thus, the optimal prepulse interval for pain reduction may differ for ICD shocks and transcutaneous or esophageal pacing.

There are important differences between the present study and actual use of therapeutic electrical shocks in patients: 1) Subjects in this study were healthy college students; most ICD recipients are older and have serious cardiac disease. 2) Shocks in this study were delivered to the skin of the arm through small electrodes; ICD shocks are delivered through intrathoracic electrodes with 25 to 50 times more surface area. 3) Sub-

jects in this study received more shocks than ICD recipients receive. 4) The characteristics of the shock waveforms differ. 5) Before receiving the initial test shock, subjects received multiple high-intensity shocks to measure pain threshold. This contrasts with the usual clinical situation, in which patients receive single ICD shocks. Given these differences, the possible utility of prepulses in reducing pain associated with therapeutic electrical pulses should, in future studies, be tested under conditions that more accurately model clinical use of these therapies.

### Limitations

Participants in this study were self-selected for relatively high pain thresholds. Because the pain-reducing impact of prepulses was inversely related to pain threshold, the present findings may underestimate the pain-reducing effect of prepulses in an unselected population. Also, the present study was not designed to assess the wide range of stimulus parameters that might influence prepulse inhibition of perceived pain. Based on the fact that prepulse inhibition of startle is highly sensitive to variations in stimulus conditions (15), prepulse effects on pain perception may be similarly sensitive to stimulus conditions. Careful parametric studies are needed to identify the experimental conditions that will yield maximal pain reduction by prepulses.

## SUMMARY

An electrical prepulse delivered shortly before an intense shock to the arm can reduce the pain elicited by that shock. Individuals who are most sensitive to pain experience the greatest prepulse-induced reduction in pain. Additional studies will be necessary to determine whether, and to what extent, prepulses may improve patient acceptance of ICD shocks or transcutaneous or esophageal pacing.

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## REFERENCES

1. Zipes DP, Wyse DG, Friedman PL, Epstein AE, Halstrom AP, Greene HL, Schron EB, Domanski M. A comparison of antiarrhythmic-drug therapy with implantable defibrillators in patients resuscitated from near-fatal ventricular arrhythmias. N Engl J Med 1997;337:1576–83.
2. Buxton AE, Lee KL, Fisher JD, Josephson ME, Prystowsky EN, Hafley G. A randomized study of the prevention of sudden death in patients with coronary artery disease. Multicenter Unsustained Tachycardia Trial Investigators. N Engl J Med 1999;341:1882–90.
3. Moss AJ, Hall WJ, Cannom. DS, Daubert JP, Higgins SL, Klein H, Levine JH, Saksena S, Waldo AL, Wilber D, Brown MW, Heo M. Improved survival with an implanted defibrillator in patients with coronary disease at high risk for ventricular arrhythmia. N Engl J Med 1996;335:1933–86.
4. Morris P, Badger J, Chmielewski C, Berger E, Goldberg RJ. Psychiatric morbidity following implantation of the automatic implantable cardioverter defibrillator. Psychosomatics 1991;32:58–64.
5. Luderitz B, Jung W, Deister A, Manz M. Patient acceptance of implantable cardioverter defibrillator devices: changing attitudes. Am Heart J 1994;127:1179–84.
6. Dougherty C. Psychological reactions and family adjustment in shock versus no shock groups after implantation of internal cardioverter defibrillator. Heart Lung 1995;24:281–91.
7. Dunbar SB, Warner CD, Percell JA. Internal cardioverter defibrillator device discharge: experiences of patients and family members. Heart Lung 1993;22:494–501.
8. Dunbar S, Summerville J. Cognitive therapy for ventricular dysrhythmia patients. J Cardiovasc Nursing 1997;12:33–44.
9. Graham FK. The more or less startling effects of weak prestimulation. Psychophysiology 1975;12:238–48.
10. Peak H. Time order in successive judgements and in reflexes: inhibition of the judgement and the reflex. J Exp Psychol 1939;25:535–65.
11. Blumenthal TD, Schicatano EJ, Chapman JG, Norris CM, Ergenzinger ER. Prepulse effects on magnitude estimation of startle-eliciting stimuli and startle responses. Percept Psychophysics 1996;58:73–80.
12. Swerdlow NR, Geyer MA, Blumenthal TD, Hartman PL. Effects of discrete acoustic prestimuli on perceived intensity and behavioral responses to startling and tactile stimuli. Psychobiology 1999;27:547–56.
13. Ison JR, Foss JA, Falcone P, Sakovits L, Adelson AA, Burton RI. Reflex modification: a method for assessing cutaneous dysfunction. Percept Psychophysics 1986;40:164–70.
14. Lipman JJ, Blumenkopf B. Comparison of subjective and objective analgesic effects of intravenous and intrathecal morphine in chronic pain patients by heat beam dolorimetry. Pain 1989;39:249–56.
15. Blumenthal TD. Short-lead-interval startle modification. In: Dawson ME, Schell A, Boehmelt A, editors. Startle modification: implications for neuroscience, cognitive science, and clinical science. Cambridge, UK: Cambridge University Press; 1999. p. 51–71.
16. Swerdlow NR, Geyer MA. Prepulse inhibition of acoustic startle in rats after lesions of the pedunculopontine nucleus. Behav Neurosci 1993;107:104–17.
17. Koch M, Kungel M, Herbert H. Cholinergic neurons in the pedunculopontine tegmental nucleus are involved in the mediation of prepulse inhibition of the acoustic startle response in the rat. Exp Brain Res 1993;97:71–82.
18. Koch M, Schnitzler H. The acoustic startle response in rats: circuits mediating evocation, inhibition, and potentiation. Behav Brain Res 1997;89:35–49.
19. Swerdlow NR, Geyer MA. Neurophysiology and neuropharmacology of short lead interval startle modification. In: Dawson ME, Schell A, Boehmelt A, editors. Startle modification: implications for neuroscience, cognitive science, and clinical science. Cambridge, UK: Cambridge University Press; 1999. p. 114–33.
20. Massaro DW, Kahn BJ. Effects of central processing on auditory recognition. J Exp Psychol 1973;97:51–8.
21. Bohmelt AH, Schell AM, Dawson ME. Attentional modulation of short- and long-lead-interval modification of the acoustic

startle response: comparing auditory and visual prestimuli. Int J Psychophysiol 1999;32:239–50.
22. Duker PC, van den Bercken J, Foekens MA. Focusing versus distraction and the response to clinical electric shocks. J Behav Ther Exp Psychiatry 1999;30:199–204.
23. Arntz A, Dreessen L, Merckelbach H. Attention, not anxiety, influences pain. Behav Res Ther 1991;29:41–50.
24. Lee Y, Lopez DE, Meloni EG, Davis M. A primary acoustic startle pathway: obligatory role of cochlear root neurons and the nucleus reticularis pontis caudalis. J Neurosci 1996;16:3775-89.
25. Evinger C. A brain stem reflex in the blink of an eye. News Physiol Sci 1995;10:147–53.
26. Sarno AJ, Blumenthal TD, Boelhouwer AWJ. Modification of the electrically-elicited startle response by visual stimuli. Psychobiology 1997;25:253–65.
27. Wellens HJ, Lau CP, Luderitz B, Akhtar M, Waldo AL, Camm AJ, Timmermans C, Tse HF, Jung W, Jordaens L, Ayers G. Atrioverter: an implantable device for the treatment of atrial fibrillation. Circulation 1998;98:1651–6.
28. Griffin JC. Indications for an atrial defibrillator. J Cardiovasc Electrophysiol 1998;9(8 Suppl):S187–92.
29. Cohen C. Sensory magnitude estimation in the context of reflex modification. J Exp Psychol 1981;7:1363–70.
30. Klein LS, Miles WM, Heger JJ, Zipes DP. Transcutaneous pacing: patient tolerance, strength-interval relations and feasibility for programmed electrical stimulation. Am J Cardiol 1988;62:1126–9.
31. Altamura G, Toscano S, Bianconi L, Lo Bianco F. Transcutaneous cardiac pacing for termination of tachyarrhythmias. Pacing Clin Electrophysiol 1990;13(12 Pt 2):2026–30.
32. Chung DC, Kerr CR, Cooper J. Termination of spontaneous atrial flutter by transesophageal pacing. Pacing Clin Electrophysiol 1987;10:1147–53.