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REGULAR ARTICLE

Alleviating Social Pain: A Double-Blind, Randomized, Placebo-Controlled Trial of Forgiveness and Acetaminophen

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Abstract

Background Research has suggested that physical pain (e.g., caused by injury) and social pain (e.g., caused by social rejection) are modulated by some of the same biological systems. Consequently, it is possible that acetaminophen, which is commonly used to alleviate physical pain through neurochemical pathways, may have social pain-relieving effects that interact with forgiveness, which reduces social pain through psychological pathways. To date, however, only a few studies have examined how experiences of social pain change over time, and none have examined how acetaminophen and forgiveness interact to influence these effects.

Purpose We addressed these issues by investigating how acetaminophen administration and daily forgiveness are associated with experiences of social pain over 21 days. We hypothesized that acetaminophen-related reductions in social pain across the 21-day study period would be greatest on days following high levels of forgiveness.

Method To test this hypothesis, we conducted a double-blind, randomized, placebo-controlled trial in which we randomly assigned 42 healthy young adults to an acetaminophen condition (1,000 mg of acetaminophen daily), placebo-control condition (400 mg of potassium daily), or empty-control (no pill) condition. We then assessed their levels of forgiveness and social pain for 20 consecutive days.

Results As hypothesized, acetaminophen reduced participants' social pain levels over time but only for those exhibiting high levels of forgiveness (i.e., 18.5% reduction in social pain over 20 days).

Conclusions These data are the first to show that forgiveness and acetaminophen have interactive effects on experiences of social pain, which is one of the most common and impactful of all human experiences.

Keywords Social pain • Physical pain • Forgiveness • Acetaminophen • Randomized controlled trial • Health

Forming and maintaining close social bonds is critical for survival and has been called a *fundamental human motivation* [1, 2]. When this basic need is threatened, individuals can experience a constellation of negative emotions collectively referred to as *hurt feelings* [3]. Such feelings are typically triggered by negative interpersonal interactions or events involving social rejection or exclusion that thwart a person's desire for closeness and indicate a potential lessening of the individual's social status, value, or regard [4]. The distress that a target individual experiences during such situations correlates strongly with feelings of social rejection, and this rejection is hypothesized to give rise to *social pain* [5], defined as "a specific emotional reaction to the perception that one is being excluded from desired relationships or being devalued by desired relationship partners or groups" (6, p. 202).

Experiences of social pain are notable as they have been found to strongly impact human health and behavior [7]. For example, experiencing even one social pain-inducing life event can increase a person's risk for major depressive disorder (MDD) in adolescence [8] and hasten the development of MDD in adulthood [9]. Prolonged experiences of social pain, in turn, have been associated with increased spending [10] and higher rates of mental and physical health problems

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[7]. In addition, socially rejected individuals exhibit decreased cognitive functioning and self-regulatory ability and increased aggression and engagement in a variety of self-defeating behaviors, including risk taking and procrastination [7, 11]. In contrast, individuals with stronger social bonds tend to have better health outcomes [12, 13] as well as lower levels of physical pain related to pregnancy, cancer, and surgery [14].

Links between Social and Physical Pain

Given this latter evidence linking experiences of social rejection and connection with physical pain, studies have begun investigating cognitive, emotional, and neural processes that may underlie associations between social and physical pain (e.g., [15–17]). It has been observed, for example, that people often use physical pain-related terms, such as "broke," "hurt," and "burn," to describe situations involving social pain and rejection—for example, "He broke my heart" or "She hurt my feelings" [18, 19]. Beyond simply adding richness to descriptions of socially painful events, this linguistic overlap may make adaptive sense if physical and social pain share a common evolutionary function, as has been suggested [20].

From this evolutionary perspective, separation or exclusion from a group of protective conspecifics would have historically represented a life-threatening challenge [6]. Consequently, animals that were able to form and maintain strong social bonds were more likely to survive and reproduce than those who were excluded, and the motivation to maintain strong social bonds was thus conserved [5, 6]. As animals became increasingly social over the course of evolution, instead of creating a new system for detecting social pain and exclusion, it has been hypothesized that the brain began using the response system designed for physical pain to respond to social rejection and exclusion [7]. Consistent with this formulation, research has indicated that the social attachment system grew out of existing regulatory systems that were used for attachment, thermoregulation, and physical pain (for a review, see [6]).

Several lines of research have examined these ideas and the resulting evidence suggests that physical pain and social pain appear to share some of the same neurobiological, immunologic, and genetic roots. At the level of the brain, for example, neuroimaging studies have shown that social and physical pain engage some of the same neural regions, including the anterior insula, dorsal anterior cingulate cortex, thalamus, and periaqueductal gray [21, 22], although these patterns of activation can also be distinguished depending on the neuroimaging analysis performed [17]. In addition, positron emission tomography studies have shown that thinking about interpersonal loss and rejection alters central μ-opioid signaling, which also modulates experiences of physical pain [23, 24]. At the level of the immune system, in turn, inflammation is known as one of the body's primary responses to physical pain and injury [25, 26], but studies have shown that social evaluation and rejection also strongly activate inflammatory processes at the level of both proteins [27] and gene expression [28, 29]. Finally, at the genetic level, a functional single nucleotide polymorphism that is well-known to regulate the experienced intensity of physical pain (i.e., the A/G transition [A118G] within *OPRM1*) has also been found to influence neural responses to social rejection in the laboratory [30] as well as emotional responses to social rejection in daily life [8].

Antidotes for Social Pain

Given these effects, researchers have sought to identify strategies that may help reduce social pain and its associated risk for negative emotional and physical health. These strategies have included both social-psychological interventions and psychopharmacological approaches. One popular social-psychological intervention has involved reducing experiences of social pain by promoting *forgiveness*, which is commonly defined as having both decisional and emotional dimensions. Whereas decisional forgiveness is a cognitive process motivated by a principle or religious belief, emotional forgiveness involves the reduction of negative emotions related to an offense or offender and the possible replacement of negative emotions with positive ones.

We focused on emotional forgiveness in the present study, which is one strategy that individuals can use to help reduce unforgiveness and potentially increase positive, altruistic emotions toward an offense or offender [31, 32]. Emotional forgiveness is thought to promote better health by reducing negative emotions involved in stress and by inducing positive emotions that enhance well-being [33]. For example, given that forgiveness mitigates the effects of both weekly perceived stress and lifetime stress exposure on mental health problems [34, 35], researchers have examined whether interventions that boost forgiveness might reduce negative effects caused by social pain and rejection. The consensus from this body of work is that forgiveness interventions can be effective for lessening levels of perceived stress, anger, negative feelings, and myocardial perfusion defects induced by hurtful interpersonal transgressions [36, 37]. Therefore, forgiveness may help people manage feelings of anger and resentment toward an offender and may, therefore,

be beneficial for reducing negative emotional and health consequences associated with social pain.

Researchers have also tested the efficacy of psychopharmacological interventions for reducing social pain that are informed by the mechanistic research described above. Most notably, several studies have examined whether acetaminophen, which is commonly used to treat physical pain, also alleviates social pain [22]. Although the exact mechanisms underlying acetaminophen's effect on physical pain are not fully understood, cyclooxygenase enzyme inhibition and serotonergic, cannabinoid, and opioidergic neural pathways have been implicated [38, 39]. Moreover, acetaminophen appears to modulate central nervous system pathways that mediate physical pain and social pain [38, 39]. Consistent with these effects, daily consumption of acetaminophen for 3 weeks has been found to reduce daily experiences of social pain, as well as neural responding to a brief, laboratory-based episode of social rejection in brain areas previously associated with processing the affective component of physical pain [40]. Acetaminophen has also been shown to reduce individuals' emotional reactions to others' social and physical pain [41], suggesting that it broadly modulates social pain-related responding.

Interactive Effects of Forgiveness and Acetaminophen

If forgiveness reduces social pain through psychological processes and acetaminophen through neurochemical pathways, one possibility is that the greatest reductions in social pain over time may be evident for individuals taking acetaminophen who also exhibit positive psychological characteristics, such as being highly forgiving. Several lines of research converge to support this possibility. First, both forgiveness and acetaminophen have independently been shown to reduce social pain [37, 40]. Second, acetaminophen may help blunt negative emotions that could prevent the development of forgiveness [42, 43]—and/or reduce the ability for unforgiveness to promote rumination about socially painful events—thereby making forgiveness-related reductions in social pain more possible [32, 44]. Third, experiences of social pain and forgiveness of others appear to have some of the same neural substrates. For example, both social pain and forgiveness have been associated with insular engagement [40, 45]. Additionally, the anterior cingulate cortex has been implicated in both social pain and forgiveness [40, 46, 47], and ruminating on experiences of social pain appears to activate the medial prefrontal cortex, as does forgiveness [46–50]. Considered together, then, it is possible that the greatest reductions in social pain over time may be evident for individuals taking acetaminophen who also possess positive attributes, such as being highly forgiving.

Present Study

To test this hypothesis, we conducted a double-blind, randomized, placebo-controlled trial in which we randomly assigned participants to an acetaminophen condition (two 500 mg doses of acetaminophen daily), placebo-control condition (two 200 mg doses of potassium daily), or empty-control (no pill) condition. Given prior studies showing that social pain and forgiveness both fluctuate on a daily basis [40, 51], we followed participants longitudinally for 21 days and assessed how their levels of forgiveness changed over time and predicted their next-day feelings of social pain. Based on the research summarized above, we hypothesized that acetaminophen-related reductions in social pain across the 21-day study period would be greatest on days that were preceded by high levels of forgiveness. We specifically examined the effects of forgiveness on next-day social pain to ensure temporal precedence (i.e., forgiveness reducing social pain).

Method

Participants and Procedure

Participants were 42 healthy young adults attending a mid-sized college who ranged in age from 18 to 22 years old (M = 19.48; SD = 1.27) and who were recruited for a study of perception. This target sample size was preset in advance based on an *a priori* power analysis using data from the effect size estimate reported by DeWall et al. [40]. A power curve was generated using an effect size of f = .215, α = .01, and this curve revealed that power was in excess of .95 for a total sample of 30 participants (i.e., 10 per condition). To provide protection against attrition, missing data, and noncompliance, we recruited and randomly assigned 45 individuals in total (i.e., 15 per condition), yielding a power of >.99. One participant was lost in the placebo-control condition and two were lost in the empty-control condition due to noncompliance with study protocols. Individuals were excluded from participation if they reported a history of liver problems or any other major illnesses, or if they consumed any nonstudy-related pain medication or consumed more than two alcoholic beverages on any given day during the 21-day trial.

On Day 1 of the trial, participants were consented and informed that they may be asked to take acetaminophen twice daily for the next 20 days. They were then randomly assigned to the acetaminophen, placebo-control,

or empty-control (no pill) condition. Beginning on Day 2, those in the acetaminophen condition (n = 15) took 500 mg of acetaminophen immediately upon waking and 1 hr before going to bed. Participants in the placebo-control condition (n = 14) took 200 mg of potassium immediately upon waking and 1 hr before going to bed. We used a 200 mg potassium pill because it is a low-cost, convenient supplement; is identical in size, shape, and taste to the acetaminophen pill; and does not have known effects on pain levels at such a low dosage. Finally, those in the empty-control condition (n = 13) took no pills during the study. For participants in the first two conditions, the acetaminophen and potassium pills were provided by the researchers to ensure consistency and proper dosage.

Regardless of experimental condition, all participants completed online measures at home, 1 hr before going to bed, to assess their forgiveness and social pain levels each day for 20 consecutive days (see below). To ensure that these surveys were filled out on the correct (i.e., current) day, the surveys opened and closed each day. In addition, daily email notifications were sent to participants reminding them to complete their daily survey (all groups) and to take their morning and evening pills (acetaminophen and placebo groups). Given these daily reminders and the brevity of the surveys, there were no missing follow-up data for any participants in the study.

Overall self-reported adherence to the prescribed pill regiment (acetaminophen or placebo pill) was excellent. More specifically, all participants adhered perfectly to their prescribed pill regiment for 13 out of the 20 treatment days. On the remaining 5 days, only one participant failed to adhere to the morning schedule; on an additional day, two participants failed to adhere to the morning schedule; and on an additional day, three participants failed to adhere to the morning schedule, yielding an overall morning pill adherence rate of 96.55%. With respect to the evening pill schedule, there was perfect adherence for 15 out of the 20 days. On the remaining 5 days, only one participant failed to adhere to the treatment regiment, yielding an overall evening pill adherence rate of 98.28%. No participant missed more than one scheduled administration (acetaminophen or placebo), and no demographic factors (i.e., age, gender) were associated with missing a scheduled administration. All participants were mailed a written debriefing statement immediately following completion of the study, at which point they were paid $10 for their time. All procedures were approved by the Institutional Review Board.

Measures

Daily state forgiveness

Daily levels of state forgiveness were assessed with the Offense-Specific Forgiveness Measure (OSFM) [52]. The OSFM is a seven-item scale that assesses a person's level of forgiveness toward a specific person who has wronged the individual (see Supplementary Material). Instructions for this scale on Day 1 read, "For the next set of questions, consider a person that has wronged you recently. Please take note of this event, as you will be referring to it throughout the duration of the study." Instructions on the following days read, "For the next set of questions, consider a person who wronged you recently. Please answer with regard to the same incident as you recalled yesterday." An example item is, "I hope this person gets what's coming to them for what he/she did to me." Participants rated their agreement or disagreement on a 1 (*strongly disagree*) to 7 (*strongly agree*) scale. The OSFM has shown good reliability and construct validity with other measures of forgiveness [52]. The average internal consistency of the OSFM over 20 days was excellent, α = .91.

Social pain

Daily levels of social pain were assessed with the Hurt Feelings Scale (HFS) [3]. The HFS is a six-item instrument designed to measure levels of hurt feelings (see Supplementary Material) [3]. Consistent with prior research [40], the items on the HFS were altered slightly to focus on a daily levels of hurt feelings—for example, "Today, my feelings are easily hurt." Participants are asked to rate how characteristic each item is of them on a 1 (*not at all characteristic of me*) to 5 (*extremely characteristic of me*) scale. The HFS has shown good reliability and validity; moreover, it has been shown to measure aspects of social pain that are not confounded by other negative emotions [3]. The average internal consistency of the HFS over 20 days was good, α = .82.

Analyses

The intraclass correlation coefficients for forgiveness and social pain were .80 and .59, respectively. Hence, 20% and 41% of the variance in forgiveness and social pain, respectively, was due to day-to-day fluctuations in these constructs over time. Bolger and Laurenceau [53] recommend the use of multilevel models even when modest effects of nonindependence exist because multilevel modeling provides unbiased estimates when nested data structures are used. Muthen and Satorra [54], in turn, suggest that multilevel models should be employed when the design effect is greater than 2. In the present study, the design effects are 16 and 12 for forgiveness and social pain, respectively, thus suggesting that a multilevel approach should be used.

Following the multilevel modeling guidelines provided by Finch, Bolin, and Kelley [55], therefore, the primary analysis was a multilevel model ANOVA conducted in R using the defaults in the lmerTest package, with Forgiveness

as a time-varying continuous predictor (i.e., values of forgiveness the day prior predicting next-day social pain), Experimental Condition as a between-subjects factor, and Time as a time-varying continuous predictor (i.e., the linear trend in social pain over time). Forgiveness and Time were grand mean centered, and all three variables were allowed to interact in the model. Because Forgiveness was grand mean centered, effects involving Forgiveness incorporate variance at both Level 1 (i.e., within persons) and Level 2 (i.e., between persons). We assumed that, across participants, the same level of forgiveness would contribute to the same level of social pain on the next day, regardless of how extreme of a level that forgiveness is for a person on a given day (i.e., absolute levels of forgiveness predict absolute levels of social pain). Using the nlme package in R, we tested whether an autoregressive covariance matrix was a better fit to the data than an unstructured covariance matrix that is default in lme4. However, the model with an unstructured covariance matrix was a slightly better fit to the data (Bayesian Information Criterion [BIC] = 4083.84) than the model with an autoregressive covariance matrix (BIC = 4085.36), so we used the former. Importantly, though, the results came out very similarly in both circumstances.

Values decomposing effects were model-estimated marginal means and trends, estimated using the lsmeans package in R. Analyses utilized the Satterwaite approximation to calculate the degrees of freedom, which is more robust to violations of assumptions than the typical approach but entails that the degrees of freedom contain noninteger numbers. Because the models were constructed with lagged effects, with forgiveness predicting social pain on the *subsequent* day, these models successfully address the important issue of temporal precedence (i.e., forgiveness prospectively predicting subsequent changes in social pain over time). Finally, data were graphed using estimated marginal trends (also called least-squares trends) to depict model estimates for persons exhibiting "high" versus "low" forgiveness across the three experimental conditions (i.e., Fig. 2).

Results

Descriptive statistics for the sample and main study variables are presented in Table 1. As shown, participants did not differ with respect to their sex or age distribution across the three experimental conditions (i.e., acetaminophen, placebo-control, and empty-control group). They also did not differ with respect to their levels of forgiveness or social pain at baseline or averaged across the trial (all ps > .27). Similarly, with forgiveness as the outcome in a multilevel model, there was no effect of Experimental Condition, $F(2, 42.5) = 1.02$, $p = .371$, nor was there an Experimental Condition × Time interaction, $F(2, 795.0) = 2.01$, $p = .134$, indicating that there were no differences in levels of forgiveness by experimental condition, either on average or over time.

Turning to the primary analysis, there was a significant main effect of Forgiveness on changes in social pain over time, $F(1, 707.2) = 19.12$, $p < .0001$, such that higher levels of forgiveness on the preceding day predicted less social pain on the subsequent day, $B = -.104$. There was also a marginally significant main effect of Time on social pain, $F(2, 748.7) = 3.05$, $p = .081$, indicating that, overall, participants exhibited marginal decreases in social pain over the course of the study, $B = -.035$ (see Fig. 1). The Forgiveness × Time interaction effect was not significant, $p = .639$, indicating that the effect of forgiveness on next-day social pain levels did not differ over time. In addition, no Experimental Condition, Experimental Condition × Time, or Experimental Condition × Forgiveness effect was observed, ps > .667. Consistent with our primary hypothesis, however, there was a significant Forgiveness × Experimental Condition × Time interaction, $F(2, 753.4) = 4.72$, $p = .009$, indicating that the association between participants' daily forgiveness levels and their next-day social pain levels differed across the three experimental conditions.

Decomposing this three-way Forgiveness × Experimental Condition × Time interaction revealed that the social pain-reducing effects of acetaminophen

Table 1 Descriptive characteristics of the sample across the three experimental conditions

Experimental Condition	Acetaminophen (n = 15)		Placebo-Control (n = 14)		Empty-Control (n = 13)		Difference Test
Sex	6 males, 9 females		5 males, 8 females		3 males, 11 females		$p = .51$
	M	*SD*	*M*	*SD*	*M*	*SD*	
Age	19.40	1.35	19.15	1.35	19.86	1.35	$p = .35$
Forgiveness at baseline	32.40	11.71	38.31	7.78	34.57	7.78	$p = .27$
Forgiveness mean across assessments	34.72	8.93	39.53	10.58	36.37	10.58	$p = .33$
Social pain at baseline	16.07	3.58	14.77	3.03	15.43	3.03	$p = .54$
Social pain mean across assessments	14.69	5.03	13.32	4.27	14.13	4.27	$p = .64$

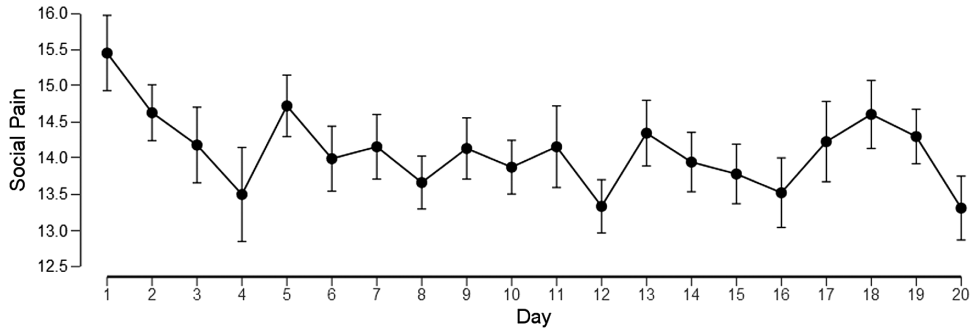

Fig. 1. Levels of social pain across 20 days. On average, participants' levels of social pain decreased marginally over time, $p = .08$. This effect did not differ by experimental condition (i.e., acetaminophen, placebo-control, and empty-control group), $p > .66$ ($n = 42$).

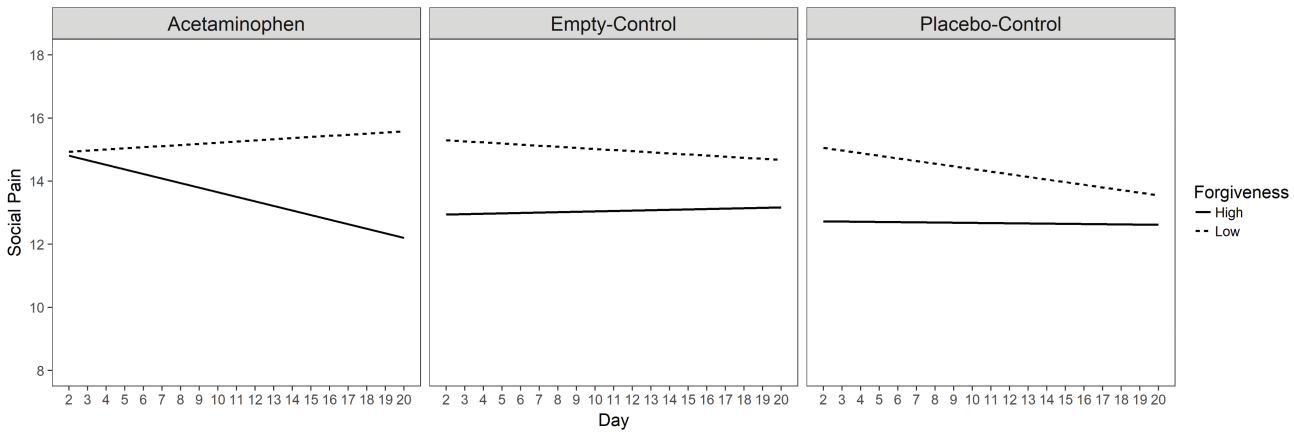

Fig. 2. Forgiveness × Experimental Condition × Time effect on levels of social pain over 20 days. Acetaminophen reduced participants' levels of social pain over time, and this effect was significantly greater in persons exhibiting high levels of forgiveness ($B = -.14$, $p = .003$) than for those exhibiting low levels of forgiveness ($B = .03$, $p = .18$), $p = .003$. In contrast, forgiveness was not related to changes in social pain over time in the placebo-control or empty-control condition, ps > .344. The lines for high and low forgiveness represent model estimates, not distinct participant groups ($n = 42$).

were observed but only for individuals exhibiting high levels of forgiveness (see Fig. 2). As hypothesized, only participants taking acetaminophen who reported higher levels of forgiveness (i.e., 1 *SD* above the mean) exhibited decreases in social pain over time, $B = -.137$, $p = .003$; no other group at high or low levels of forgiveness decreased in social pain over time, ps > .100. Confirming the potential of a forgiveness-acetaminophen interactive effect on social pain, these longitudinal reductions in social pain were significantly greater for participants exhibiting high levels of forgiveness in the acetaminophen condition than for those exhibiting high levels of forgiveness in either the placebo-control condition ($B = -.005$), $t(749.5) = 1.99$, $p = .047$ or the empty-control condition ($B = .012$), $t(748.4) = 2.22$, $p = .027$.

In contrast, forgiveness-related reductions in social pain over time did not differ between participants exhibiting mean levels or low levels (i.e., 1 *SD* below the mean) of forgiveness (ps > .118). Moreover, among participants taking acetaminophen, those exhibiting higher levels of forgiveness (i.e., 1 *SD* above the mean) showed greater reductions in social pain over time ($B = -.137$) as compared to those reporting mean levels of forgiveness ($B = -.051$), $p = .003$, or low levels of forgiveness (i.e., 1 *SD* below the mean; $B = .034$), $p = .003$. Therefore, acetaminophen reduced participants' levels of social pain over time but only for persons exhibiting higher levels of forgiveness.

Finally, for descriptive purposes, we evaluated how much social pain was alleviated, on average, among participants exhibiting low versus high forgiveness across the three experimental conditions. Participants who were generally low in forgiveness across assessments (i.e., 1 *SD* below the mean) reported similar levels of social pain at the end of the study as they did at the beginning, and this was true regardless of experimental condition (4.58% increase in social pain for the acetaminophen group, and 4.32% and 10.54% decrease in social pain, respectively, for the empty-control and placebo-control group). Likewise, participants in the placebo-control and empty-control (no pill) conditions who were high in forgiveness

(i.e., 1 *SD* above the mean) reported only minimal reductions in social pain over time (0.91% decrease and 1.83% increase in social pain, respectively). In comparison, participants in the acetaminophen condition exhibiting high levels of forgiveness across the assessments exhibited a 18.50% decrease in social pain over time, therefore suggesting an interactive benefit of acetaminophen and forgiveness in reducing social pain.

Discussion

Prior research has found that forgiveness and acetaminophen independently alleviate experiences of social pain frequently caused by hurtful interpersonal interactions (e.g., [37], [40]). The goal of this study was to extend this work by examining for the first time how forgiveness and acetaminophen interact to reduce social pain in the context of a 21-day double-blind, randomized, placebo-controlled trial. Consistent with prior studies linking forgiveness [37] and acetaminophen [40] to reductions in social pain, the present data revealed that exhibiting a more forgiving attitude toward others and taking acetaminophen together reduced levels of social pain over time. Based on these data, we conclude that acetaminophen helps alleviate social pain, but these effects may be evident only for individuals who cultivate forgiveness in their lives.

The ability for acetaminophen to reduce social pain is consistent with a growing body of research demonstrating that social and physical pain are represented by some of the same brain areas [20, 22]. One possibility, therefore, is that acetaminophen reduces social pain by modulating the activity of neural networks that are involved in processing experiences of pain. Although neuroimaging data were not collected in this study, prior research has shown that acetaminophen decreases neural responses to social rejection in brain regions that represent the affective component of physical pain [40]. The present results are novel in this context as they show that acetaminophen's social pain-relieving effects may occur only in highly forgiving individuals who have the ability to more easily move past anger and resentment caused by social rejection and interpersonal conflict.

Several possibilities exist for how forgiveness and acetaminophen might have an interactive effect on social pain. First, whereas acetaminophen may help reduce the amount of social pain caused by situations involving interpersonal conflict or social rejection, forgiveness may help prevent such events from recurring or becoming chronic. This possibility is consistent with the present data, which showed that acetaminophen and forgiveness were not associated with lower levels of social pain overall but rather with longitudinal reductions in social pain over time. Second, acetaminophen may dampen the severity of social pain, thus making forgiveness easier. In this case, acetaminophen would act as a catalyst for forgiveness, which is in turn responsible for reducing social pain. In the present data, however, acetaminophen did not increase participants' forgiveness levels, making this explanation unlikely. Finally, acetaminophen and forgiveness may exert an interactive, social pain-reducing effect by modulating the activity of brain areas involved in social pain [40, 46, 56].

Clinically speaking, the present data may give rise to the idea of prescribing forgiveness therapy or acetaminophen for persons experiencing difficult interpersonal situations (e.g., targeted rejection, divorce) as a means of reducing their risk for emotional disorders such as depression. In support of this possibility, forgiveness interventions have been found to reduce depression, anger, hostility, and stress [37]. Because most studies have not specifically selected individuals presently going through interpersonal turmoil, additional research is needed to determine whether forgiveness interventions are effective for *preventing* emotional disorders associated with socially painful life events. Similar caveats apply to acetaminophen: although the idea of prescribing acetaminophen to individuals undergoing difficult interpersonal situations may be attractive, we are not aware of any studies that have shown acetaminophen to be an effective prophylactic against psychiatric disorders for persons currently experiencing socially stressful circumstances. Moreover, long-term acetaminophen use can increase risk of kidney, heart, and blood pressure problems that require careful monitoring. In sum, therefore, additional research is needed to examine how and when forgiveness therapy and acetaminophen are safe and effective for persons experiencing social stress. Likewise, it is important to remember that negative emotions such as anger and sadness are natural responses that serve adaptive functions and help people make sense out of social situations [57]. Artificially augmenting experiences of such situations should thus be done with caution regardless of the abovementioned effectiveness and safety issues.

Despite being the first double-blind, randomized, placebo-controlled trial of forgiveness, acetaminophen, and social pain, several limitations of this study should be noted. First and foremost, the present sample was relatively homogeneous and the sample size was limited. Therefore, the present results should be regarded as preliminary until future studies are conducted using larger and more diverse samples—for example, to examine the robustness of these effects, examine their generalizability, and test for possible gender differences. Second, we manipulated participants' acetaminophen levels by random assignment, but forgiveness was assessed longitudinally. Therefore, all results involving forgiveness are correlational. Future research should thus employ

experimental manipulations of forgiveness, such as forgiveness training, to provide evidence of potential causality. Studies that conduct such interventions while employing neuroimaging methods could be particularly useful in that they could help clarify neural pathways that are influenced by forgiveness and acetaminophen and related to social pain. Third, since we focused specifically on the social pain-relieving benefits of forgiveness, future research is needed to examine the extent to which other positive psychological characteristics (e.g., gratitude, hope, optimism) might have similar effects.

Fourth, we did not assess the specific interpersonal transgressions that were causing participants social pain in this study, and the effects described here could have differed based on the severity or type of social situation to which people were responding [58, 59]. These social situations should thus be assessed in future studies—for example, using state-of-the-art life stress interviews—in order to better understand whether the effects observed here differ by the specific types of situations experienced [60–62]. Fifth, we controlled for the potential confounding effects of daily stressors and other factors (e.g., sleep, diet, exercise) that could have influenced participants' social pain levels by randomly assigning participants to the experimental conditions, but future research should assess these factors to estimate their relative impact on changes in social pain longitudinally. Indeed, negative factors such as continued contact with an offender could have helped sustain individuals' social pain levels over time, but positive factors could have also exerted an influence, such as uplifting social events that could have made forgiving another person easier. Finally, we have shown that acetaminophen reduces social pain over time, but at least one study has shown that acetaminophen also appears to reduce emotional reactions to positive stimuli [63]. Therefore, the effects of acetaminophen on social experiences may not be specific to social pain.

In conclusion, it is well-known that socially painful life events can increase risk for several negative health outcomes, including anxiety disorders, depression, and certain somatic and physical health problems [64, 65]. To date, however, it has remained unclear whether psychological and psychopharmacological factors interact to reduce social pain. We addressed this issue here in the context of a double-blind, randomized, placebo-controlled trial and found that two factors that have previously been shown to reduce social pain—namely, forgiveness and acetaminophen—were interactively associated with reductions in social pain over time. More specifically, we found that the social pain-reducing effects of acetaminophen over 21 days were observed but only for individuals exhibiting high levels of daily forgiveness. Given the limited sample size, additional studies are needed to examine the robustness and generalizability of these effects. Additional research is also needed to elucidate psychological, neural, and physiologic processes linking forgiveness and acetaminophen with social pain. Experimental studies that manipulate both forgiveness and acetaminophen would be particularly beneficial in this context, as they could clarify issues of causality and help inform the development of interventions for reducing social pain and improving human health.

Supplementary Material

Supplementary material for this article is available on the *Annals of Behavioral Medicine* website.

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Compliance with Ethical Standards

Authors' Statement of Conflict of Interest and Adherence to Ethical Standards The authors declare that they have no conflicts of interest with regard to this study. All study procedures were carried out in accordance with the ethical standards of the University's Institutional Review Board, and with the 1964 Helsinki declaration and its later amendments.

Authors' Contribution This study was designed by GMS and LLT, who supervised GSS, BDD, and AG in conducting the research. Analyses were performed by GSS and LLT. The manuscript was written by GMS and subsequently edited by all authors who read and approved the final version for publication.

Ethical Approval This study was approved by the Institutional Review Board.

Informed Consent Written informed consent was obtained from all participants in this study.

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