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Can Over-the-Counter Pain Medications Influence Our Thoughts and Emotions?

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Abstract

Recent research at the intersection of social psychology and psychopharmacology is raising new questions about some of our favorite over-the-counter (OTC) pain medications. This work suggests that drugs like acetaminophen and ibuprofen might influence how people experience emotional distress, process cognitive discrepancies, and evaluate stimuli in their environment. These studies have the potential to change our understanding of how popular pain medications influence the millions of people who take them. However, this research is still in its infancy. Further studies are necessary to address the robustness of reported findings and fully characterize the psychological effects of these drugs.

Keywords

physical pain, social pain, evaluation, cognitive conflict, acetaminophen, ibuprofen, NSAIDs

Tweet

New research finds that over-the-counter (OTC) analgesics influence more than pain. What should policymakers and the public know?

Key Points

- Brain imaging research suggests that social and physical pain might have overlapping biological mechanisms.
- A handful of findings suggest that OTC pain medications modulate social pain.
- Other research indicates that these medications influence affective and cognitive processes more generally.
- More research is needed to confirm existing findings and address the many lingering questions.
- Policymakers should be aware of this research but wait for further studies before taking action.

Introduction

Over the past several years, these headlines have captured the public's attention: "Feeling the Pain of Rejection? Try Taking a Tylenol" (Stix, 2010), "A Common Painkiller May Inhibit Your Ability to Detect Mistakes" (Arlotta, 2016), and "Study: Acetaminophen Dulls Your Pain—But Also Your Empathy" (Ahmed, 2016). Such claims are newsworthy because they challenge the conventional wisdom that over-the-counter (OTC) pain medications simply relieve physical discomfort. However, what is the actual state of the evidence? Should policymakers revise their understanding of these drugs?

This review discusses the small body of scientific research behind the headlines. We explain why researchers began investigating whether OTC pain medications might do more than dull physical sensations and detail the methodologies that researchers used to arrive at their conclusions. We then turn our attention to societal implications and advocate for further research to address important unanswered questions.

OTC Pain Medications

Various medications help people manage pain. Many belong to a class of drugs called analgesics. Opioids are typically viewed as the most effective analgesics for severe pain, but they are addictive and require a prescription (Ballantyne, 2017; Ventafridda, Saita, Ripamonti, & De Conno, 1985). In contrast, OTC analgesics are nonaddictive and can be purchased from a wide range of stores without the approval of a physician. Popular OTC analgesics include acetaminophen (paracetamol, Tylenol) and nonsteroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen (Advil, Motrin), aspirin (Bayer), and naproxen (Aleve). As an indicator of how important these drugs are to the public, acetaminophen tops the chart of frequently used OTC and prescription medications. NSAIDs are also high on the list (Kaufman, Kelly, Rosenberg, Anderson, & Mitchell, 2002).

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How Do They Work?

Although a full description of the pharmacological mechanisms of these drugs is beyond the scope of this review, in brief, NSAIDs are cyclooxygenase (COX) inhibitors. COX is an enzyme that synthesizes prostaglandins from a polyunsaturated omega-6 fatty acid called arachidonic acid. Arachidonic acid is found in many meats, fish, and dairy products and is also derived from essential fatty acids in plants and other food sources (Calder, 2007). Prostaglandins are important signaling molecules in the immune system's inflammatory response. It is through this role that prostaglandins are associated with pain sensitivity and fever. Thus, by inhibiting COX, NSAIDs decrease inflammation by reducing the formation of prostaglandins (Cashman & McAnulty, 1995). As many people know, a side effect of NSAIDs is stomach irritation and even ulcers in extreme cases. This occurs because COX is also involved with maintaining the mucosal lining of the stomach and intestines. Because NSAIDs inhibit COX, these drugs can weaken the gastrointestinal lining by making it less resistant to corrosive digestive acids (Wallace, 2001).

Acetaminophen is not an NSAID and is better tolerated by people with gastrointestinal sensitivity. The mechanisms of action for acetaminophen are less clear than those of NSAIDs. There is some evidence that a metabolite of acetaminophen called AM404 is associated with COX inhibition in the central nervous system but has a lesser effect on COX in the periphery. However, the role of AM404 in pain reduction is complex. For instance, it also operates as a capsaicin receptor agonist and blocks the reuptake of an endogenously produced cannabinoid called anandamide. Interestingly, chili peppers also activate capsaicin receptors and cannabinoids found in marijuana mimic anandamide and influence anandamide levels. Capsaicin receptors, anandamide, and COX are all part of a complicated web of neurochemical systems that regulate multiple bodily states, including body temperature, inflammation, and feelings of pain (Bertolini et al., 2006).

Despite ambiguity about neurochemical mechanisms, particularly those of acetaminophen, OTC analgesics provide millions of people relief from headaches and from moderate pain due to injury. These physical painkilling effects have been well recognized for decades. However, a potential impact of these drugs on affective and cognitive processing is not part of the typical understanding of these medications.

Acetaminophen, Ibuprofen, and Social Pain

As is often the case in science, the possibility that OTC pain medications could influence more than physical pain occurred while researchers were investigating a separate, albeit related, research question. In the early 2000s, a team of investigators working at the intersection of social psychology and cognitive neuroscience conducted an influential brain imaging study that investigated whether neural regions involved with physical pain perception also responded to experiences of social exclusion (Eisenberger, Lieberman, & Williams, 2003). To measure participants' brain activity, they used a technique called functional magnetic resonance imaging (fMRI). Participants played a virtual ball tossing game called Cyberball in an MRI scanner. During this game, participants were told that they were playing with two other people who were also in MRI scanners and that players could toss the ball to whomever they desired.

In actuality, participants played with a computer program that determined the behavior of the supposed other ball throwers. During the inclusion part of the study, the participants were thrown the ball as often as was normally appropriate in a game of catch. Toward the end of the study, however, the two other players stopped throwing the participant the ball. This surprise exclusion made the participants report social distress. Critically, a region of the brain called the dorsal anterior cingulate cortex (dACC) was more responsive during social exclusion compared with inclusion. This same brain region is linked to the affective experience of pain (Rainville, Duncan, Price, Carrier, & Bushnell, 1997; Sawamoto et al., 2000).

The above social exclusion finding was consistent with the possibility that neural mechanisms which evolved to help organisms respond to physical pain were co-opted by social attachment systems because both physical injury and social isolation can have dire consequences for an organism's survival (Eisenberger & Lieberman, 2004; Harlow, Dodsworth, & Harlow, 1965; Macdonald & Leary, 2005; Panksepp, 1998). Given that social exclusion is a form of social pain, this brain imaging work provided empirical evidence that metaphors linking physical and social pain (e.g., feeling "stabbed in the back" when one is betrayed by a friend) may be rooted in overlapping biological processes. This possibility is contentious, and over a decade later, the relationship between social pain and physical pain continues to be debated (Eisenberger, 2015; Iannetti, Salomons, Moayedi, Mouraux, & Davis, 2013; Kross, Berman, Mischel, Smith, & Wager, 2011; Lieberman & Eisenberger, 2015; Wager et al., 2016).

OTC pain medications initially drew the interest of social psychologists as a tool for testing social and physical pain overlap. The logic was that if perceptions of social pain involve similar neural mechanisms to physical pain, then medications used to reduce physical pain should blunt feelings of social rejection. DeWall and colleagues (2010) were the first to test this possibility. In their initial study, participants were randomly assigned to ingest acetaminophen or placebo pills daily for 3 weeks, 500 mg in the morning and 500 mg 1 hr before bed. Each night the participants also completed several scales that assessed hurt feelings and daily positive emotions. Starting on Day 9 of the study and continuing to the study conclusion on Day 21, participants in the acetaminophen condition reported fewer hurt feelings than those in the placebo condition. The two conditions did not

statistically differ on the positive emotions measure, which suggested that acetaminophen effects were specific to social pain and not driven by positive emotions.

A second study directly examined whether these acetaminophen effects could be tied to brain regions previously associated with social pain. The acetaminophen dose was doubled to 2,000 mg daily for 3 weeks, and then the authors used the same Cyberball paradigm as the original study by Eisenberger and colleagues. The researchers specifically focused their analyses on the dACC and another region called the anterior insula. When comparing social exclusion with social inclusion, participants in the acetaminophen condition showed less neural response in those regions than did participants in the placebo condition. When the whole brain was analyzed, a similar pattern emerged, and effects were observed bilaterally in the posterior insula and the right amygdala, brain areas also implicated in the affective response to physical pain.

Despite these intriguing findings, this initial work did leave some open questions. For instance, in Study 2, neural responses differed between conditions but self-reported distress did not. The study also had no physical pain condition to directly compare the drug's influence on physical pain and social pain. Furthermore, as the authors acknowledge, the half-life of acetaminophen is only a couple hours, and no evidence indicates that the drug accumulates over multiple dosage periods (Forrest, Clements, & Prescott, 1982; Sahajwalla & Ayres, 1991). As a result, specifying the neurochemical mechanisms through which acetaminophen might have been operating in these studies remains to be done. Note also that the sample sizes in these studies, although not uncommon when the studies were conducted, are low by current standards. Nonetheless, this work raised the possibility that acetaminophen influences responsiveness to social pain, and it set into motion a flurry of studies to understand OTC analgesic effects on emotions and cognition.

The aforementioned research by DeWall and colleagues involved more female than male participants. This is relevant to the generalizability of the work because of reported gender differences in physical pain and analgesic response (Berkley, 1997; Walker & Carmody, 1998) and experiences of social pain (Miller & Roloff, 2005). A separate research team, this time using ibuprofen instead of acetaminophen, examined gender differences in analgesic influences on social pain (Vangelisti, Pennebaker, Brody, & Guinn, 2014). Male and female participants were given 400 mg capsules of ibuprofen (equivalent to an extra strength dose) or placebo. After waiting 45 min for the drug to metabolize and absorb into the blood, they measured hurt feelings in response to Cyberball; participants also wrote separately about experiences of social pain (betrayal by a close other) and physical pain. The order of Cyberball and the writing task was counterbalanced across participants.

For both Cyberball and the writing task, female participants in the ibuprofen condition reported less social pain than those in the placebo condition. These effects reversed for men. Moreover, consistent with previous evidence of first-person pronoun use when people are experiencing emotional pain, content analyses showed that women in the ibuprofen condition used fewer first-person pronouns compared with the placebo condition. Again, men demonstrated the opposite pattern. The authors concluded that ibuprofen blunted women's sensitivity to social pain because of ibuprofen's painkilling properties. However, they suggested that men responded in the opposite manner because the drugs disrupted their default tendency to suppress emotional pain.

To the extent that pain medications affect people's ability to perceive their own social pain, the question emerges: What about empathy for others' pain? In two studies, 1,000 mg of acetaminophen or placebo in oral suspension (similar to how children typically take OTC medications) were administered to participants, and experimental tasks began after a 60-min delay for drug absorption (Mischkowski, Crocker, & Way, 2016). In the first study, participants read multiple scenarios that each described a person experiencing physical pain (e.g., a finger laceration) or social pain (e.g., rejection from college). Participants rated their personal distress while reading the scenarios and their perceptions of the protagonist's pain. In a second study, new participants responded to the scenarios from the first study and completed two other tasks. During one of these tasks, participants evaluated painful noise blasts for loudness and unpleasantness from their perspective and that of an imagined study participant. They also witnessed a game of Cyberball during which two people excluded an unknown third person.

In regard to the hypothetical scenarios in both studies, acetaminophen reduced personal distress and perceived pain. In the second study, participants who took acetaminophen reported less empathic concern for the protagonist. The noise blast and Cyberball results showed a similar pattern; acetaminophen was associated with less sensitivity to the painful noise and less regard for the victim of social exclusion. Notably, general mood was not affected by acetaminophen, which suggested that empathy effects were not due to differences in mood.

Summary

Together, these studies provide preliminary evidence that acetaminophen and ibuprofen do not just dull physical pain sensations, but they also influence sensitivity to social experiences that are interpreted as painful. This work suggests that social pain and physical pain share a phenomenology that is deeper than common linguistic descriptors. The gender difference effects indicate that the psychological influence of these drugs might not be uniform across people and how an individual was socialized to experience emotional distress could matter. To the extent that these medications blunt reactivity to pain, they could also hinder people's ability to put themselves in another person's shoes and feel that

individual's emotional and physical pain. Given the complex ways that modulating pain sensitivity could influence how people make sense of the world around them, this work raises many questions that require further research.

Effects Beyond Pain

Studies on social and physical pain overlap have led researchers to consider the cognitive and affective processes that could underlie both experiences. This thinking has given rise to new hypotheses about how OTC analgesics influence psychology.

Pain as an Alarm Signal?

One possibility is that the feeling of pain is an "alarm signal" that alerts attention to physical injury and damage to social relationships that could threaten well-being (Eisenberger & Lieberman, 2004). By drawing attention to these threats, such an alarm marshals physiological and social resources to mitigate the damage. The finding that the dACC seems to respond to both social and physical pain serves as a lynchpin in this argument. Although opinions differ about the function of this brain region, a respected theory argues that the dACC generally responds to conflicts in information processing, such as discrepant perceptual representations, action tendencies that do not match task goals, and violations of expectations and outcomes (Botvinick, Cohen, & Carter, 2004). From this vantage, the sensation of pain can be viewed as a specialized case of a discrepancy between a desired state and reality.

If pain can be construed as an alarm signal triggered by psychological discrepancies, then acetaminophen might generally blunt reactions to cognitive conflict (Randles, Heine, & Santos, 2013). Testing this possibility in the context of dissonant life experiences, one study took advantage of the fact that people find thoughts of death to be jarring, at least in part, because of the incongruence of mortality cognitions with desires to plan for the future and continue social relationships. Consistent with the prediction that acetaminophen blunts reactivity to dissonant cognitions, participants given a 1,000 mg pill of the drug demonstrated less reactivity to thinking about their own mortality than those in the placebo condition. In a follow-up study, expectancies were violated with a film clip that did not abide by standard movie conventions and social values. Again, acetaminophen was associated with less reactivity to information that conflicted with typical patterns of thought.

Although these findings were provocative, the paradigms were complex, and the effects were interpretable according to various theoretical frameworks. Follow-up work (Randles, Kam, Heine, Inzlicht, & Handy, 2016) sought a more direct test by measuring neural signals using a technique called electroencephalography (EEG). Participants completed a Go/No Go task that required them to respond to a frequent stimulus type ("Go" trials) but avoid responding when a less frequent second stimulus type appeared ("No Go" trials). This task creates cognitive conflict because participants develop a default action tendency to respond, but this tendency is not appropriate on the trials that require response inhibition. Participants received 1,000 mg of acetaminophen or placebo in pill form.

Acetaminophen was associated with higher errors of omission (failing to respond to Go trials) but not errors of commission (inappropriately responding to No Go trials). Moreover, the Pe, an EEG signal linked to the evaluation of errors, decreased in the acetaminophen condition compared with the placebo condition. Acetaminophen apparently blunted evaluative processing, which manifested in less attentional engagement during the frequently repeated Go trials, perhaps because participants were less concerned about errors.

These findings are consistent with other work (DeWall, Chester, & White, 2015), which showed acetaminophen blunting cognitive conflict during a classic dissonance paradigm. As has become standard for recent experimental studies investigating acetaminophen effects on psychological outcomes, participants received either 1,000 mg of acetaminophen or placebo. Then they were exposed to a cognitive dissonance spreading-of-alternative paradigm (Harmon-Jones, Schmeichel, Inzlicht, & Harmon-Jones, 2011). That is, they rated seven cognitive tasks according to their desirability. Then after the experimenter narrowed the list to two equivalently rated tasks, the participants chose the one they wanted to complete. Finally, the participants rated all the cognitive tasks a second time. The classic dissonance finding is post-choice spreading of the otherwise equivalent alternatives in favor of the chosen one and disfavoring the nonchosen other. Participants who received acetaminophen versus placebo demonstrated less cognitive dissonance as evidenced by less change in their rating of the task they rejected.

In a second study using the same drug protocol, acetaminophen reduced the endowment effect—people valuing an object just because they own it. Specifically, participants were told a mug was either theirs to keep or the property of the lab. Then all participants were asked to set a selling price for the mug. Of the participants endowed with the mug, those who received acetaminophen chose a lower selling point. The authors reasoned that the endowment effect can result from the discomfort of losing an item that one owns. Thus, a smaller endowment effect for people given acetaminophen is consistent with the cognitive dissonance finding to the extent that acetaminophen was minimizing cognitive discomfort in each case.

Just Negativity?

Acetaminophen's evaluative blunting effects could be specific to negative psychological experiences or independent

of valence (Durso, Luttrell, & Way, 2015). Research on differential susceptibility (Belsky & Pluess, 2009) suggests that people who are insensitive to negative stimuli in their environment are also insensitive to positive stimuli. From this perspective, the key variable is not whether the stimulus is good or bad but whether the perceivers respond to their environment. In two separate experiments (Durso et al., 2015), participants were given 1,000 mg of acetaminophen or placebo in oral suspension. Participants viewed images from the International Affective Picture System (IAPS) that ranged from unpleasant to pleasant. They rated the valence of the images and how much the images elicited an emotional reaction. In Study 2, participants also provided nonevaluative rating of how much the color blue was represented in the images.

Consistent with a general evaluative dampening effect, participants in the acetaminophen condition rated both the positive and negative IAPS images less extremely than did control participants. The acetaminophen participants also reported the images as less arousing. No differences appeared on the color ratings, which goes against the possibility that participants in the acetaminophen condition were simply encoding the images to a lesser extent.

Evaluations of Social Groups?

Perhaps, then, acetaminophen could influence evaluations that occur outside of the domains of pain and psychological discomfort. This possibility inspired our own research (unpublished to date) on OTC pain medications and evaluations of social groups. Key to our work is the observation that attitudes toward social groups are rooted in basic neurocognitive mechanisms involved in evaluation and motivation (Amodio & Ratner, 2011; Phelps et al., 2000; Van Bavel, Packer, & Cunningham, 2008). As a result, drugs that blunt responsiveness to evaluative images might also alter biases favoring ingroup members and negativity toward stereotyped outgroup members.

All our studies gave participants 1,000 mg of acetaminophen or placebo in oral suspension and waited 45 min before starting the experimental tasks. The first study used a classic minimal group paradigm to create groups in the lab. That is, participants were randomly assigned to one of two novel social groups. A computer task then generated a visual rendering of how participants imagined ingroup and outgroup faces. This task can reveal an ingroup positivity bias (Ratner, Dotsch, Wigboldus, van Knippenberg, & Amodio, 2014). Consistent with acetaminophen blunting ratings of positive images, the typical ingroup positivity effect was lessened in the acetaminophen condition.

A second study used a similar measure to assess bias in what participants thought a typical African American face looked like. We were interested in representations of the social category African American because this racial group has historically been the target of negative stereotypes in the United States. In line with a general evaluative blunting effect of acetaminophen, the face representations generated by participants in the acetaminophen condition revealed less negativity bias than those created by participants in the placebo group.

A third study returned to ingroup positivity. Two monetary allocation tasks examined whether acetaminophen's apparent evaluative blunting effects would generalize to behavior in an intergroup context. It did not. Observing no drug effect suggested to us that our earlier evaluative blunting effects were either task specific or masked in deliberate choice behavior. Given this null effect, we ran a preregistered replication of our initial study with a larger sample size. We also added an ibuprofen condition to examine whether any effects generalized to another OTC pain medication. To our surprise, preliminary analyses indicate a significant effect in the *opposite* direction: Both acetaminophen and ibuprofen increased ingroup positivity. We currently do not have an explanation for this flipped effect.

These preliminary intergroup perception results indicate that extending OTC psychological effects—beyond social pain, discrepancy alarm signals, and general valence—will require programmatic research. Our results also highlight the importance of replication and the complexity of interpreting results from drug studies.

Summary

Basic cognitive and affective processes might be influenced by acetaminophen, and possibly also ibuprofen. Although the paradigms and topics of these studies are diverse, the common ingredient seems to be evaluation. In some cases, evaluative responses were triggered by cognitive discrepancies, and in other cases, evaluative responses resulted from emotionally evocative stimuli. With the exception of our own unpublished work, the results consistently showed an evaluative blunting effect of acetaminophen.

Policy Considerations

In many ways, the reviewed findings are alarming. Consumers assume that when they take an OTC pain medication, it will relieve their physical symptoms, but they do not anticipate broader psychological effects. Are more regulations needed? Should warnings be expanded on drug labels? At this point, drawing strong conclusions from the existing studies would be premature. Nonetheless, policymakers might start thinking about potential public health risks and benefits.

One place to begin is OTC analgesic use in pregnant women and children. It is possible that these drugs do not simply ease pain but also dampen psychological discomfort. If this is the case and these drugs are administered frequently,

what are the long-term consequences of blunting emotional processing during early brain development?

Some epidemiological research might already provide clues. A handful of studies have linked attention deficit hyperactivity disorder (ADHD) and autism to acetaminophen exposure in utero and during childhood (e.g., Schultz et al., 2008; Ystrom et al., 2017). Although these possibilities are worth investigation, they are limited by correlational research methods, so consumers should not overreact. Stoking concern about acetaminophen or other common painkillers could have adverse effects on people's ability to manage their own pain. Awaiting more extensive investigation on psychological side effects of OTC analgesics, the well-established advantages of these drugs seem to outweigh the potential risks.

On the flipside of apprehensions is the intriguing possibility that these drugs could have therapeutic benefits for dealing with transient hurt feelings, much in the way they help minimize minor aches and pains. One could imagine taking acetaminophen after a flubbed work presentation or a spousal disagreement. It is also natural to wonder whether these drugs could be incorporated into treatments for more enduring psychological problems, such as depression, social anxiety disorder, and borderline personality disorder. Repurposing these drugs to combat emotional pain is appealing because they are well tolerated; research and development are dramatically expedited when new uses are found for old medications (Collins, 2011).

However, tempering this excitement might be wise because not all effects could be beneficial. For instance, individuals who suppress emotions might experience increased emotional sensitivity on these drugs (Vangelisti et al., 2014). In addition, if these medications blunt reactivity to pain, they could impede people's ability to empathize with others (Mischkowski et al., 2016). Also, clinical disorders are heterogeneous. Some people who are depressed, for instance, exhibit anhedonia—difficulty experiencing pleasure (Pizzagalli, 2014). For these people, medications that blunt evaluative reactions could worsen their condition.

Another critical consideration is that OTC pain medications can be dangerous if taken in large doses or in combination with alcohol and various other medications. As mentioned, NSAIDs in high concentrations result in severe gastric problems. Perhaps less known is that a by-product of acetaminophen called NAPQI (N-acetyl-p-benzoquinone imine) is toxic to the liver. For this reason, acetaminophen is a leading cause of calls to poison control and emergency room visits (Lee, 2004). In fact, many overdoses that result in death from combination opioid/acetaminophen drugs can be attributed to acetaminophen (Michna, Duh, Korves, & Dahl, 2010). Although a large number of acetaminophen deaths are unintentional, suicidal acetaminophen overdoses have been on the rise in the United States (Schiødt, Rochling, Casey, & Lee, 1997). People suffering from mental anguish might be desperate to self-medicate and not adequately weigh the negative consequences of taking too large a dose. All this adds to the complexity of considering acetaminophen and NSAIDs as treatments for emotional distress.

Any changes in policy should be grounded in robust research findings. Large-scale replications by independent laboratories need to confirm existing results. Although such efforts are time-consuming, proper safety precautions and the necessary ethics approval are not difficult. In addition to replications, further studies need to examine the generalizability of inferences made thus far. For instance, most of the research has focused on acetaminophen. Do NSAIDs—such as ibuprofen, aspirin, and naproxen—show effects similar to acetaminophen? This matters because NSAIDs are popular. Furthermore, this research could shed light on neurochemical mechanisms because OTC analgesics have overlapping and distinct influences on physiology.

Policymakers should also be aware that drugs at low and high dosages can have different effects. Methylphenidate (Ritalin), a drug used to treat ADHD, is a good example. The effects of this drug on learning and social behavior depend on the dose that is given (Sprague & Sleator, 1977). Are the reported psychological effects of OTC analgesics also dose dependent? Factors that influence drug absorption also matter, affecting concentrations of the drug in the body.

Future work should also understand how psychological effects might differ for those who are taking these drugs to relieve physical pain and those who are not currently experiencing physical pain. The reviewed studies administered OTC analgesics to people who were not taking the drugs for physical pain. As a result, the reported effects may or may not apply to the typical person who takes these medications for pain.

Researchers have only begun to understand OTC analgesic effects on psychological processing. Clarifying these relationships could have tremendous societal benefits. Found in medicine cabinets across the world and used multiple times per week by people of all ages, genders, and ethnic backgrounds, these drugs are woven into modern life. Policymakers should take note of existing findings but not rush to judgment. Given this research topic's novelty and suggested complexity, further research is needed before policy recommendations are warranted.

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References

Ahmed, S. (2016, May 13). Study: Acetaminophen dulls your pain—but also your empathy. *CNN*. Retrieved from http://www.cnn.com/2016/05/12/health/study-acetaminophen-dulls-empathy

Amodio, D. M., & Ratner, K. G. (2011). A memory systems model of implicit social cognition. *Current Directions in Psychological Science*, *20*, 143-148.

Arlotta, C. J. (2016, April 13). A common painkiller may inhibit your ability to detect mistakes. *Forbes*. Retrieved from https://www.forbes.com/sites/cjarlotta/2016/04/13/common-painkiller-may-be-inhibiting-brain-response-associated-with-error-detection

Ballantyne, J. C. (2017). Opioids for the treatment of chronic pain: Mistakes made, lessons learned, and future directions. *Anesthesia & Analgesia*, *125*, 1769-1778.

Belsky, J., & Pluess, M. (2009). Beyond diathesis stress: Differential susceptibility to environmental influences. *Psychological Bulletin*, *135*, 885-908.

Berkley, K. J. (1997). Sex differences in pain. *Behavioral and Brain Sciences*, *20*, 371-380.

Bertolini, A., Ferrari, A., Ottani, A., Guerzoni, S., Tacchi, R., & Leone, S. (2006). Paracetamol: New vistas of an old drug. *CNS Drug Reviews*, *12*, 250-275.

Botvinick, M. M., Cohen, J. D., & Carter, C. S. (2004). Conflict monitoring and anterior cingulate cortex: An update. *Trends in Cognitive Sciences*, *8*, 539-546.

Calder, P. C. (2007). Dietary arachidonic acid: Harmful, harmless or helpful? *British Journal of Nutrition*, *98*, 451-453.

Cashman, J., & McAnulty, G. (1995). Nonsteroidal anti-inflammatory drugs in perisurgical pain management: Mechanisms of action and rationale for optimum use. *Drugs*, *49*, 51-70.

Collins, F. S. (2011). Mining for therapeutic gold. *Nature Reviews Drug Discovery*, *10*, Article 397.

DeWall, C. N., Chester, D. S., & White, D. S. (2015). Can acetaminophen reduce the pain of decision-making? *Journal of Experimental Social Psychology*, *56*, 117-120.

DeWall, C. N., Macdonald, G., Webster, G. D., Masten, C. L., Baumeister, R. F., Powell, C., . . . Eisenberger, N. I. (2010). Acetaminophen reduces social pain: Behavioral and neural evidence. *Psychological Science*, *21*, 931-937.

Durso, G. R. O., Luttrell, A., & Way, B. M. (2015). Over-the-counter relief from pains and pleasures alike: Acetaminophen blunts evaluation sensitivity to both negative and positive stimuli. *Psychological Science*, *26*, 750-758.

Eisenberger, N. I. (2015). Social pain and the brain: Controversies, questions, and where to go from here. *Annual Review of Psychology*, *66*, 601-629.

Eisenberger, N. I., & Lieberman, M. D. (2004). Why rejection hurts: A common neural alarm system for physical and social pain. *Trends in Cognitive Sciences*, *8*, 294-300.

Eisenberger, N. I., Lieberman, M. D., & Williams, K. D. (2003). Does rejection hurt? An FMRI study of social exclusion. *Science*, *302*, 290-292.

Forrest, J. A., Clements, J. A., & Prescott, L. F. (1982). Clinical pharmacokinetics of paracetamol. *Clinical Pharmacokinetics*, *7*, 93-107.

Harlow, H. F., Dodsworth, R. O., & Harlow, M. K. (1965). Total social isolation in monkeys. *Proceedings of the National Academy of Sciences of the United States of America*, *54*, 90-97.

Harmon-Jones, C., Schmeichel, B. J., Inzlicht, M., & Harmon-Jones, E. (2011). Trait approach motivation relates to dissonance reduction. *Social Psychological and Personality Science*, *2*, 21-28.

Iannetti, G. D., Salomons, T. V., Moayedi, M., Mouraux, A., & Davis, K. D. (2013). Beyond metaphor: Contrasting mechanisms of social and physical pain. *Trends in Cognitive Sciences*, *17*, 371-378.

Kaufman, D. W., Kelly, J. P., Rosenberg, L., Anderson, T. E., & Mitchell, A. A. (2002). Recent patterns of medication use in the ambulatory adult population of the United States: The Slone survey. *JAMA*, *287*, 337-344.

Kross E., Berman, M. G., Mischel, W., Smith, E. E., & Wager, T. D. (2011). Social rejection shares somatosensory representations with physical pain. *Proceedings of the National Academy of Sciences of the United States of America*, *108*, 6270-6275.

Lee, W. M. (2004). Acetaminophen and the U.S. acute liver failure study group: Lowering the risks of hepatic failure. *Hepatology*, *40*, 6-9.

Lieberman, M. D., & Eisenberger, N. I. (2015). The dorsal anterior cingulate cortex is selective for pain: Results from large-scale reverse inference. *Proceedings of the National Academy of Sciences of the United States of America*, *112*, 15250-15255.

Macdonald, G., & Leary, M. R. (2005). Why does social exclusion hurt? The relationship between social and physical pain. *Psychological Bulletin*, *131*, 202-223.

Michna, E., Duh, M. S., Korves, C., & Dahl, J. L. (2010). Removal of opioid/acetaminophen combination prescription pain medications: Assessing the evidence for hepatotoxicity and consequences of removal of these medications. *Pain Medicine*, *11*, 369-378.

Miller, C. W., & Roloff, M. E. (2005). Gender and willingness to confront hurtful messages from romantic partners. *Communication Quarterly*, *53*, 323-337.

Mischkowski, D., Crocker, J., & Way, B. M. (2016). From painkiller to empathy killer: Acetaminophen (paracetamol) reduces empathy for pain. *Social Cognitive and Affective Neuroscience*, *11*, 1345-1353.

Panksepp, J. (1998). *Affective neuroscience: The foundations of human and animal emotions*. New York, NY: Oxford University Press.

Phelps, E. A., O'Connor, K. J., Cunningham, W. A., Funayama, E. S., Gatenby, J. C., Gore, J. C., & Banaji, M. R. (2000). Performance on indirect measures of race evaluation predicts amygdala activation. *Journal of Cognitive Neuroscience*, *12*, 729-738.

Pizzagalli, D. A. (2014). Depression, stress, and anhedonia: Toward a synthesis and integrated model. *Annual Review of Clinical Psychology*, *10*, 393-423.

Rainville, P., Duncan, G. H., Price, D. D., Carrier, B., & Bushnell, M. C. (1997). Pain affect encoded in human anterior cingulate but not somatosensory cortex. *Science*, *277*, 968-971.

Randles, D., Heine, S. J., & Santos, N. (2013). The common pain of surrealism and death: Acetaminophen reduces compensatory affirmation following meaning threats. *Psychological Science*, *24*, 966-973.

Randles, D., Kam, J. W. Y., Heine, S. J., Inzlicht, M., & Handy, T. C. (2016). Acetaminophen attenuates error evaluation in cortex. *Social Cognitive and Affective Neuroscience*, *11*, 899-906.

Ratner, K. G., Dotsch, R., Wigboldus, D. H. J., van Knippenberg, A., & Amodio, D. M. (2014). Visualizing minimal ingroup and outgroup faces: Implications for impressions, attitudes, and

behavior. *Journal of Personality and Social Psychology*, *106*, 897-911.

Sahajwalla, C. G., & Ayres, J. W. (1991). Multiple-dose acetaminophen pharmacokinetics. *Journal of Pharmaceutical Sciences*, *80*, 855-860.

Sawamoto, N., Honda, M., Okada, T., Hanakawa, T., Kanda, M., Fukuyama, H., . . . Shibasaki, H. (2000). Expectation of pain enhances responses to nonpainful somatosensory stimulation in the anterior cingulate cortex and parietal operculum/posterior insula: An event-related functional magnetic resonance imaging study. *Journal of Neuroscience*, *20*, 7438-7445.

Schiødt, F. V., Rochling, F. A., Casey, D. L., & Lee, W. M. (1997). Acetaminophen toxicity in an urban county hospital. *New England Journal of Medicine*, *337*, 1112-1118.

Schultz, S. T., Klonoff-Cohen, H. S., Wingard, D. L., Akshoomoff, N. A., Macera, C. A., & Ji, M. (2008). Acetaminophen (paracetamol) use, measles-mumps-rubella vaccination, and autistic disorder: The results of a parent survey. *Autism: The International Journal of Research and Practice*, *12*, 293-307.

Sprague, R. L., & Sleator, E. K. (1977). Methylphenidate in hyperkinetic children: Differences in dose effects on learning and social behavior. *Science*, *198*, 1274-1276.

Stix, G. (2010, September 1). Feeling the pain of rejection? Try taking a tylenol. *Scientific American*. Retrieved from https://www.scientificamerican.com/article/social-analgesics

Van Bavel, J. J., Packer, D. J., & Cunningham, W. A. (2008). The neural substrates of in-group bias: A functional magnetic resonance imaging investigation. *Psychological Science*, *19*, 1131-1139.

Vangelisti, A. L., Pennebaker, J. W., Brody, N., & Guinn, T. D. (2014). Reducing social pain: Sex differences in the impact of physical pain relievers. *Personal Relationships*, *21*, 349-363.

Ventafridda, V., Saita, L., Ripamonti, C., & De Conno, F. (1985). WHO guidelines for the use of analgesics in cancer pain. *International Journal of Tissue Reactions*, *7*, 93-96.

Wager, T. D., Atlas, L. Y., Botvinick, M. M., Chang, L. J., Coghill, R. C., Davis, K. D., . . . Yarkoni, T. (2016). Pain in the ACC? *Proceedings of the National Academy of Sciences of the United States of America*, *113*, E2474-E2475.

Walker, J. S., & Carmody, J. J. (1998). Experimental pain in healthy human subjects: Gender differences in nociception and in response to ibuprofen. *Anesthesia and Analgesia*, *86*, 1257-1262.

Wallace, J. L. (2001). Pathogenesis of NSAID-induced gastroduodenal mucosal injury. *Best Practice & Research. Clinical Gastroenterology*, *15*, 691-703.

Ystrom, E., Gustavson, K., Brandlistuen, R. E., Knudsen, G. P., Magnus, P., Susser, E., . . . Reichborn-Kjennerud, T. (2017). Prenatal exposure to acetaminophen and risk of ADHD. *Pediatrics*, *140*, e20163840.