1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26

This preprint has been published in Psychological Science (<https://doi.org/10.1177/09567976221119727>)

Placebo analgesia reduces costly prosocial helping to lower another’s pain

Helena Hartmann^{1,2}, Paul Forbes¹, Markus Rütgen¹, & Claus Lamm^{1*}

¹ Social, Cognitive and Affective Neuroscience Unit, Department of Cognition, Emotion, and Methods in Psychology, Faculty of Psychology, University of Vienna, Vienna, Austria

² Social Brain Laboratory, Netherlands Institute for Neuroscience, Royal Netherlands Academy of Arts and Sciences, Amsterdam, The Netherlands

* Corresponding author: claus.lamm@univie.ac.at, +43-1-4277-47130, Social, Cognitive and Affective Neuroscience Unit, University of Vienna, Liebiggasse 5, 1010 Vienna, Austria

Keywords

Empathy, prosocial behavior, decision-making, placebo analgesia, pain, effort

Abstract

Painkiller administration lowers pain empathy, but whether this also reduces prosocial behavior is unknown. In this preregistered study, we investigated whether inducing analgesia through a placebo painkiller reduced effortful helping. When given the opportunity to reduce the pain of another person, individuals experiencing placebo analgesia ($n = 45$ adults from Austria, 21 male, 24 female) made fewer prosocial choices at the lowest helping level and exerted less physical effort when helping, compared to controls with unaltered pain sensitivity ($n = 45$, 21 male, 24 female). Self-reported empathic unpleasantness positively correlated with prosocial choices across the whole sample. Despite not replicating group differences in empathy, a mediation analysis revealed that the level of unpleasantness to others' pain fully mediated the effect of placebo analgesia on prosocial choices. Given the importance of prosociality for social cohesion, these findings have broad potential implications for both individuals under the influence of painkillers and for society at large.

Statement of Relevance

The increased and widespread use of opioids has been recognized as a major individual and public health threat, with a global average prevalence around 0.7% (28.6-30 million people). One under-investigated aspect is how the intake of painkillers affects our social interactions. Previous studies highlighted detrimental effects of psychopharmacological interventions targeting the opioidergic system on empathic abilities. However, it is unclear whether reduced pain sensitivity also leads to changes in prosocial behavior. In this experimental behavioral study, we tested whether lowering pain sensitivity by means of placebo analgesia lowers helping behavior, measured by exerting physical effort to reduce another's pain. Placebo analgesia not only decreased the willingness to invest effort, but also decreased the actual effort exerted when helping. These detrimental effects of analgesia on prosociality may have far-reaching implications, for individuals under the influence of painkillers, but also for social cohesion in societies with regular consumption of analgesics.

1 Introduction

The frequent use of opioid painkillers has been recognized as a global health concern, with negative effects on individuals and society (Bolshakova et al., 2019 for a review). Pain medication has widespread effects on our own pain perception, but some studies show that it also impacts how we emotionally resonate with conspecifics (Mischkowski et al., 2016, 2019; Ratner et al., 2018 for a review). Past research using a systemic placebo administration route (oral placebo pill) has causally linked an upregulation of the opioidergic system to reduced affective pain empathy, suggesting that the intake of painkillers may have detrimental effects on social motivation and subsequent behaviors (Rütgen, Seidel, Silani, et al., 2015; de Pascalis & Vecchio, 2022; Vecchio & de Pascalis, 2021). While the effects of psychopharmacological manipulations on first-hand and empathy for pain have been demonstrated, their potential downstream effects on prosociality remain to be established. Understanding these effects is fundamentally important, as these processes are not only key drivers of group bonding and social cohesion, but also strongly contribute to individual and societal wellbeing (de Waal, 2008 for a review; Rameson et al., 2012).

A series of experimental studies has shown that individuals whose first-hand pain was reduced by placebo analgesia (i.e., belief that an inert treatment acts as a potent painkiller) showed reductions in self-reported pain empathy and decreased activation in key areas of the brain's affective 'pain empathy network' (Rütgen et al., 2021; Rütgen, Seidel, Riečanský, et al., 2015; Rütgen, Seidel, Silani, et al., 2015; Vecchio & de Pascalis, 2021). Importantly, follow-up studies investigating whether these effects extend to the somatosensory system (using administration of a placebo gel to a selected body part rather than a pill affecting pain processing in a systemic fashion) did not find effects (Hartmann, Riva, et al., 2021; Hartmann, Rütgen, et al., 2021). Of note here is that placebo mechanisms in first-hand pain (Petrovic et al., 2002; Zubieta et al., 2005; Zubieta & Stohler, 2009) and pain empathy (Rütgen et al., 2018, 2021; Rütgen, Seidel, Silani, et al., 2015) have been linked to an upregulation of the endogenous opioid system. Single-dose administration of acetaminophen, a non-opioidergic painkiller (i.e., Paracetamol, Tylenol), also reduced self-

81 reported empathy (Mischkowski et al., 2016, 2019). Thus, psychopharmacological
82 manipulations of our own pain state causally and selectively influence how we share the
83 affective-motivational component of others' pain.

84 Empathy and prosociality are closely linked, with evidence both for somatosensory,
85 cognitive, and affective domains (Yin & Wang, 2022 for a meta-analysis). High trait and state
86 empathy can act as powerful drivers of prosocial tendencies and behaviors (Brethel-Haurwitz
87 et al., 2018; Crockett et al., 2015; Lockwood et al., 2014, 2017; Morelli et al., 2014; Story et
88 al., 2020; see de Waal & Preston, 2017; Eisenberg & Giunta, 2011; Eisenberg & Miller, 1987;
89 Lamm et al., 2019 for reviews). Gallo et al. (2018) found that disrupting primary
90 somatosensory cortex altered the coupling between pain perceived in another person and
91 monetary donations to reduce that pain, Morelli et al. (2014) linked septal activity during
92 empathy to daily helping and Lockwood et al. (2014) identified emotion regulation as a
93 moderator. Contrarily, it has been pointed out that more empathy may not always lead to
94 more prosociality, but that aspects connected to the former (such as personal distress) may
95 also impair the latter (Bloom, 2018; Decety & Cowell, 2014; Lamm & Majdandžić, 2015 for
96 reviews).

97 However, whether altering first-hand pain sensitivity also impacts helping has not been
98 systematically investigated. Answering this question will have major implications, as it could
99 demonstrate that painkillers not only interfere with how we represent others' emotions, but
100 also how we behave towards others. The objective of this study was, thus, to investigate how
101 reducing pain sensitivity through a well-established placebo analgesia manipulation
102 influences helping. We preregistered that placebo analgesia would modulate prosocial
103 behavior. This would show in a reduced willingness to choose an effortful helping option,
104 longer reaction times when making such choices, and a reduced amount of actual force
105 exerted. However, we also considered the possibility that placebo analgesia could increase
106 prosocial behavior in the preregistration (for further details regarding this hypothesis, see the
107 [preregistration](#))

2 Materials and Methods

2.1 Open Practices Statement

As suggested by Simmons et al. (2012), we report how we determined our sample size, all data exclusions, all manipulations, and all measures in the study. This study was preregistered on the Open Science Framework (OSF) prior to data collection (Hartmann & Lamm, 2019; [preregistration](#) and [addendum](#), deviations listed in the Supplement). All data and code to analyze the data and reproduce the figures are available on the [OSF](#).

2.2 Procedure

Session overview. Participants took part in one behavioral session in pairs, with the other participant being a gender-matched confederate posing as the second participant (Figure 1 for an overview and Supplement for more detailed procedure). All participants received the same financial compensation, and the ethics committee of the University of Vienna approved all procedures (application number 00412).

Role assignment and calibrations. The participant and confederate were asked to complete an “random role assignment procedure” determining the roles of ‘Receiver’ and ‘Decider’ in the prosocial effort task, as per previous studies (Crockett et al., 2015; Lockwood et al., 2017). While the participant who was always chosen as the Decider would make choices involving the other person receiving pain, the confederate as the Receiver would receive electrical stimulation. All subsequent steps relate to the real participant as the Decider. Anonymity (except for gender and name) was ensured over the whole session to limit the effects of reputation and reciprocity (as per Lockwood et al., 2017, participants might act more prosocial just because they think they might meet the other person later again). Then, we employed a pain calibration as in Rütgen, Seidel, Silani, et al. (2015) where electrical stimulation was given to the dorsum of the non-dominant, left hand to gain average stimulation intensities between 0 (not perceivable) and 8 (extremely painful) using a Digitimer DS5 Isolated Bipolar Constant Current Stimulator (Digitimer Ltd, Clinical & Biomedical Research Instruments). Calculated intensities for the average ratings of 1 (perceivable, but not painful) and 4 (medium painful) were later used for the conditioning, while 1 and 7 (very

136 painful) were used for the pain task. After this, effort was calibrated using maximum voluntary
 137 contraction (MVC), whereby participants were asked to grip a handheld dynamometer
 138 (Vernier, Beaverton, OR, USA) in their dominant, right hand with as much force as possible.
 139 This ensured the effort levels used in the task were relative to each participants' individual
 140 strength. The maximum of four MVC trials (two before and two after the placebo induction)
 141 was taken to calculate the effort levels (30-70% of that value) in the prosocial effort task. The
 142 effort calibration was completed three times (before and after the placebo induction and at
 143 the end of the session). To measure changes in motivation and fatigue over time, we also
 144 measured each participant's MVC twice in a row at the same three time points as the NASA
 145 ratings.

Figure 1. Overview of the experimental session for each group. Real participants were always chosen as the “Decider”. Participants in both groups underwent the same steps, except for the placebo analgesia induction. During this time, the control group had an equally long waiting time. Belief ratings about the effectiveness of the pill were only collected from the placebo group. PANAS = Positive and Negative Affect Schedule (Krohne et al., 1996); MVC = maximum voluntary contraction.

Placebo analgesia induction. Next, the placebo group underwent a placebo analgesia induction using an inert pill presented as an “effective and powerful painkiller” and similar verbal suggestions by a medical student acting as the study’s medical doctor. After a waiting time of 10 minutes for the pill “to take effect”, classical conditioning was performed to amplify the placebo effect. Participants received stimulation with a medium intensity (rated as 4 in the pain calibration), coupled with corresponding feedback suggesting substantial pain reduction by the pill (e.g., “This stimulus was rated as very/extremely painful before”). To measure placebo responding over the course of the session, we collected three belief ratings about the effectiveness of the “medication”. The control group did not undergo any such manipulations but had equally long waiting times to keep the overall session length the same. We additionally collected positive and negative mood ratings from both groups at three times using the Positive and Negative Affect Schedule (PANAS; Krohne et al., 1996).

Prosocial effort task. A major challenge in measuring prosocial behavior is that many existing paradigms involve one-shot tasks, such as picking up dropped pens or donating part of a monetary endowment (Thielmann et al., 2020 for an overview). These tasks may not capture moment-by-moment decisions necessary in everyday life. Moreover, they largely rely on self-report, which is prone to social desirability and often measures hypothetical intentions rather than actual behavior (Martí-Vilar et al., 2019; Pfattheicher et al., 2022 for reviews). To overcome these limitations, recently developed experimental paradigms require participants to invest physical effort over multiple trials (Cameron et al., 2021; Contreras-Huerta et al., 2020 for reviews). These tasks show that individuals vary their helping based on how much effort they need to put in, and how rewarding that helping is (Lockwood et al., 2017, 2020). Furthermore, participants’ decision-making in the form of choice behavior has been increasingly used in addition to subjective indicators such as ratings to more comprehensively measure the full extent of prosocial behavior (Crockett et al., 2015;

Lockwood et al., 2016; Story et al., 2020). We therefore developed a paradigm to test whether placebo analgesia affects the effort individuals exert to reduce another's pain. The prosocial effort task was adapted from Lockwood et al. (2017) and Crockett et al. (2015): Each trial, participants were asked to make a choice between a baseline "rest" offer (no effort necessary) where the confederate received a fixed amount of six shocks, and a "work" offer involving exertion of physical effort (30, 40, 50, 60 or 70 % of their MVC) to help the other participant (reducing the number of shocks the confederate would receive by either 1, 2, 3, 4 or 5 shocks; Figure 2). Every work offer combination (5 effort levels x 5 shock reduction levels = 25 levels) was presented three times, leading to 75 choices. If the participants chose to help, but failed to reach the chosen effort level, or when they did not respond within 3 seconds, the confederate received 10 shocks (see Supplement for more information on these 'fail trials', which did not differ between groups, all p 's > .055). The participants were told that the other participant would receive shocks they had rated as very painful (i.e., in the upper range of the rating scale) in their pain calibration. In fact, the 'Receiver' never received pain in this task. This deception was used to create a believable and realistic social situation where decisions of the participants would ostensibly have real and live consequences for another person, to induce a conflict between costly investing of effort and helping to reduce another's pain. At the end of the prosocial effort task, MVC was measured again, but this time it was incentivized to determine participant's personal effort motivation to earn a financial bonus for themselves. We used this one-trial measure as a control to assess whether the placebo influenced self-related motivation. Of note, while other studies have used a more closely matched self-related control (Contreras-Huerta et al., 2020 for review), we opted against this for practical and theoretical constraints of our study - balancing length, duration, believability, other-focus in terms of resource, and possible carry-over effects between experimental and control conditions. As per our preregistration, if placebo analgesia acted exclusively on prosocial motivation, we would expect no group differences on this task. If, on the other hand, placebo analgesia modulates motivation to exert effort in general, we would expect a group difference.

Figure 2. In the prosocial effort task, the real participant as the “Decider” had to make a choice between a baseline rest option (no effort exertion) and a more effortful prosocial option: In the latter case, participants were asked to exert either 30, 40, 50, 60 or 70% of their maximum voluntary contraction (MVC; the more filled the circle the greater the effort level and 1/6th filled as the baseline option and each additional slice representing a higher effort level) to reduce the number of shocks the other participant was going to receive in that trial by 1, 2, 3, 4 or 5 (indicated below the circle). This led to 5 x 5 = 25 possible combinations, each of which was presented three times. After the choice, participants immediately exerted their chosen effort while receiving visual real-time feedback to show how much effort they were exerting in comparison to the effort they had to reach (indicated by a yellow line, which had to be reached for at least 1 out of 3 sec). After the 3 seconds had elapsed, they received feedback on the shocks the other participant (allegedly) got. The feedback included text and red lightning-shapes, which appeared one after the other to reinforce the belief that shocks were given to the Receiver in real time. All information given on-screen in the task was in German.

First-hand and empathy for pain task. To evaluate analgesic effects on first-hand and empathy for pain, participants rated painful and non-painful electrical stimulation (rated as 1 = 'noticeable but not painful' or 7 = 'very painful' in the pain calibration) that they either received themselves (self trials) or that the confederate received (other trials; Figure 3; Rütgen, Seidel, Riečanský, et al., 2015). Participants completed a short pre-effort empathy for pain task (two pain and two no-pain trials) before the prosocial effort task (as per the “Other” condition in Figure 3) and the full, post-effort first-hand and empathy for pain task afterwards. This structure was purposefully chosen to avoid first-hand pain experience before the prosocial effort task and to avoid counteracting any effects by delaying the effort task. This allowed us to assess transfer effects of placebo analgesia to empathy for pain before and after the effort task, at two different time points in the session.

Figure 3. Participants completed measures of empathy for pain before and after the prosocial effort task. Post-effort, the participants either received electrical stimulation themselves (Self) or observed the second participant seemingly receiving such stimulation (Other). Afterwards, participants were asked to rate the pain intensity and unpleasantness of these stimulations. Pre-effort, participants only supplied empathy ratings and did not receive first-hand stimulation.

Post-experimental questions. At the end of the session, we assessed any doubts regarding the cover story (whether participants believed their anonymity was kept, whether their decisions were kept secret from the other participant, and whether they felt their decisions were monitored by the experimenters) and the placebo manipulation to identify non-responders (section Participants in the Supplement). We also measured how painful they remembered the average painful and non-painful stimulation in the pain task.

2.3 Participants

Participants were German-speaking, right-handed young university students with normal or corrected-to-normal vision who reported no history of neurological or psychiatric disorders. Our sample had the final preregistered size of $N = 90$ participants (45 participants per group, mean age $\pm$ standard deviation = 23.56 ± 2.90 (placebo group) and 24.00 ± 4.32 (control group)). We based our group sizes on previous studies using tasks involving either effort or pain, as our task was a combination of the two (Crockett et al., 2015; Lockwood et al., 2017). All exclusion criteria were determined *a priori* in the preregistration. Placebo analgesia non-responders were determined as in Rütgen, Seidel, Silani, et al. (2015; Supplement for more information): First, we recorded verbally expressed doubts about the analgesic effects of the pill or the cover story. Second, differences of the belief scores about the effectiveness of the placebo before and after the induction procedure were analyzed. Third, we took the number of conditioning trials needed to suggest pain relief into account. Dropouts and exclusions in

each group were replaced until the group sizes of 45 were reached. These exclusion criteria were not related in any way to our two outcomes of interest, empathy for pain and prosocial behavior, but served to establish a reliable first-hand placebo analgesia effect as a prerequisite for the group comparisons. The two final groups were comparable regarding age and trait measures of socio-cognitive and emotional abilities (Table S1 in the Supplement).

2.4 Data collection and analysis

Tasks were implemented in [Cogent 2000](#) Version 1.33 running in MATLAB R2018a (Mathworks, 2018). Data were processed and analyzed using MATLAB R2016a and RStudio 4.1.0 (2021-05-18; R Core Team, 2020). All p values were interpreted two-sided. Wherever Mauchly's Test for Sphericity was violated, we report p values using Greenhouse-Geisser correction (^{GG}). The final manuscript was checked for statistical reporting errors using [statcheck](#) (Rife et al., 2016) and for reference errors using [reciteworks](#) (4cite Labs).

2.4.1 Manipulation checks

We conducted five manipulation checks, some of which were preregistered, and others were added post hoc due to the novelty of the design, as indicated below: First, we evaluated the correct performance of the prosocial effort task (1) and the cover story in both groups (2) (see Supplement). Then we tested the effectiveness of the placebo analgesia induction procedure (3-5): The placebo groups' belief in the effectiveness of the medication (3) was analyzed by calculating three paired t -tests comparing two of the three time points (pre-conditioning/post-conditioning/post-session). While these analyses were preregistered as "exploratory", they were also employed in our previous studies using a very similar placebo analgesia induction with a gel instead of a pill (Hartmann, Riva, et al., 2021; Hartmann, Rütgen, et al., 2021). Based on these studies, we expected a strong belief in the medication and an increased belief from pre- to post-conditioning (Supplement for exact criteria). (4) We aimed to evaluate whether the placebo analgesia induction influenced a) first-hand pain as well as b) other-related pain intensity and unpleasantness ratings with the goal of replicating the placebo analgesia effect reported in Rütgen, Seidel, Silani, et al. (2015). As in that study, we expected placebo analgesia to downregulate participants' first-hand pain as well as their

pain empathy. We thus preregistered that placebo analgesia would lead to lowered empathic responses. We calculated two ANOVAs using the pre-effort empathy ratings, with the other pain intensity or the unpleasantness ratings as the dependent variables, and the independent variables *treatment* (placebo/control) and *intensity* (pain/no pain). We then calculated an additional two ANOVAs using the post-effort first-hand and empathy for pain ratings: the first ANOVA compared the self- and other-related pain intensity ratings on the independent variables *treatment* (placebo/control), *target* (self/other) and *intensity* (pain/no pain); the second ANOVA compared the unpleasantness ratings on *treatment* (placebo/control) and *intensity* (pain/no pain). The pre-effort empathy for pain analyses were not preregistered but mirrored the preregistered post-effort ones. (5) To measure whether the placebo effect lasted until the end of the session, we compared the post-experimental rating about how much pain was felt on average in the pain task using a *t*-test, using the index of pain – no pain ratings as the dependent variable and *group* (placebo/control) as a factor. This check had not been preregistered, but was also employed in our previous studies (Hartmann, Riva, et al., 2021; Hartmann, Rütgen, et al., 2021).

2.4.2 Preregistered core analyses

We calculated a mixed ANOVA with the ‘proportion of work offers chosen’ as the dependent variable, and the factors *effort level* (1-5), *shock reduction / helping* (1-5) and *group* (placebo/control) as independent variables. We then repeated this analysis with reaction time as the dependent variable. As preregistered, both of these analyses were repeated using LMMs to detect more subtle differences using single-trial data, adopting a ‘multiverse’ analysis approach (see e.g., Silberzahn et al., 2018 for behavior or Botvinik-Nezer et al, 2020 for imaging analyses). Lastly, we ran a LMM with area under the curve (AUC) of the force data as the dependent variable and group, effort level, shock reduction and their interactions as fixed effects, and included a subject-level random intercept (as well as exploratory mixed models for the single trial choice and RT data). To check whether placebo analgesia influenced general motivation, we calculated a *t*-test to compare the two groups on the MVC and exerted force in the one-shot self-trial.

2.4.3 Post hoc analyses

To evaluate the effects of the placebo induction on participant's general strength and mood, we calculated three ANOVA with the dependent variables MVC, positive or negative mood, with *time* (pre-induction/post-induction/post-session) and *group* (placebo/control) as factors. We also investigated correlations between the two tasks, i.e., empathy for pain and prosocial behavior. To this end, we correlated the first-hand pain, other-related pain intensity and unpleasantness ratings in the first-hand and empathy for pain task with the proportion of prosocial choices in the prosocial effort task. Moreover, we explored associations between prosocial choices and reaction time in the prosocial effort task. Lastly, individuals differ in how much they value other people's rewards relative to their own (prosocial/altruistic vs. individualistic oriented). We explored the relationship between prosocial choices in the prosocial effort task and social value orientation (SVO) by correlating the proportion of prosocial choices to each participants' social value angle from the SVO by Murphy et al. (2011), which was calculated as the arc tangent of the ratio for other- vs. self-related payoffs as an angle in degrees (with higher values meaning higher prosocial/other-related orientation). These correlations were not preregistered and are therefore exploratory and reported uncorrected for multiple comparisons. Lastly, we calculated an exploratory mediation analysis to investigate the role of affect sharing in mediating the effect of placebo analgesia on prosocial choices. As the independent variable, we operationalized the placebo effect by subtracting the first-hand pain rating from the value 7 (i.e., the rating corresponding to the pain intensity delivered, as determined during prior individual pain calibration). The mediator variable consisted of the other-related unpleasantness rating in response to painful stimuli and the dependent variable was again the proportion of prosocial choices.

3 Results

3.1 Both groups show correct task performance, cover story belief as well as similar strength, motivation, and mood

There were no significant group differences regarding correct performance of the prosocial effort task and believability of the cover story (manipulation checks 1 and 2; Figure S1 and Tables S2-S4 in the Supplement for details). We also did not observe any group or

time differences in participants' general strength measured as MVCs over the course of the session (all $p > .561$; Figure S2 and Table S5 in the Supplement). In the analysis of participants' effort exertion when aiming to win an additional monetary bonus for themselves, we observed no group differences, neither in participant's MVC ($p = .432$) nor in the AUC of the exerted force ($p = .175$; Figure S3A for MVC and Figure S3B for force data). Evaluating the participants' mood at three time points over the whole session, we observed that both positive and negative mood decreased significantly over the course of the session (both p 's $< .001$), but these effects were similar for both groups (Figure S4A for positive, Figure S4B for negative mood, and Tables S6 and S7 in the Supplement).

3.2 Placebo vs. control group differ in first-hand pain but not in other-related pain intensity or unpleasantness ratings

In assessing the placebo analgesia effect, we observed a significant increase in the belief about the effectiveness of the pill in the placebo group from pre- to post conditioning ($t(44) = 3.92$, $p < .001$, mean of the differences (M_{diff}) = 13.58, 95% CI [6.59, 20.57], Cohen's $d_z = 0.58$; pre-conditioning: $M \pm SEM = 65.44 \pm 3.24$; post-conditioning: 79.02 ± 2.21 ; manipulation check 3; Figure 4A). From post-conditioning to post-session (67.27 ± 3.71), the belief ratings decreased significantly ($t(44) = -4.05$, $p < .001$, $M_{diff} = -11.76$, 95% CI [-17.60, -5.91], Cohen's $d_z = 0.60$), while the post-session ratings did not differ significantly from the ones measured pre-conditioning ($t(44) = 0.34$, $p = .735$, $M_{diff} = 1.82$, 95% CI [-8.97, 12.62], Cohen's $d_z = 0.05$). Importantly, the average belief rating was generally very high ($M \pm SEM = 70.58 \pm 2.06$ on a scale from 0-100), indicating a generally high belief in the medication's effectiveness.

Figure 4. Manipulation checks 3, 4 and 5 evaluating the first-hand placebo analgesia effect. A) We observed high belief ratings in general and a significant increase in the belief in the effectiveness of the medication from before to after the conditioning procedure. Although this belief significantly decreased towards the end of the session, it did not drop lower than the initial belief before the conditioning. B) In the first-hand and empathy for pain task, participants of the placebo group rated the electrical stimulation they received on the back of their hand as significantly less painful compared to the control group. C) Finally, participants in the placebo group indicated even at the end of the session that they remembered the stimulations in the first-hand and empathy for pain task to be significantly less painful compared to participants in the control group.

Next, we analysed the pre- and post-effort ratings in our first-hand and empathy for pain task (manipulation check 4; Figure 4B for first-hand pain, Figure 5 for other-related pain intensity and unpleasantness, Supplement for more detailed results). Analyses confirmed a significant placebo effect for first-hand pain, as shown by general lower ratings in the placebo compared to the control group (main effect of group, $p = .008$) independent of intensity or target as well as a bigger rating difference in the index (pain – no pain stimulation) between self- and other-related stimulation (i.e., control ($\text{self}_{\text{pain} - \text{no pain}} - \text{other}_{\text{pain} - \text{no pain}}$) > placebo ($\text{self}_{\text{pain} - \text{no pain}} - \text{other}_{\text{pain} - \text{no pain}}$)) for the control compared to the placebo group (group x intensity x target interaction, $p = .020$), but no group differences regarding other pain intensity or unpleasantness ratings (p 's > .128), neither in the pre- nor post-effort pain task data. While the hypothesized group differences in other pain intensity and unpleasantness ratings went into the expected direction (placebo < control), they were not significant, and their effect sizes (Cohen's d 's between 0.04 and 0.15) were much smaller compared to previous studies that had also used a between-subjects design and very similar setup (e.g., Rütgen, Seidel, Silani, et al., 2015, Cohen's d 's of first-hand analgesia effect between 0.62 and 0.79, and empathy analgesia effect between 0.44 and 0.76).

Figure 5. Manipulation check 4 evaluating the effect of placebo analgesia on other pain intensity and unpleasantness ratings. Participants completed A) pre-effort empathy for pain task (Tables S8 and S9 in the Supplement) and B) the full post-effort first-hand and empathy for pain task afterwards (Tables S10 and S11 in the Supplement). They rated pain intensity as well as their own unpleasantness when the other participant (allegedly) received electrical stimulation in both instances. We observed no effect of placebo analgesia on other pain intensity or unpleasantness, neither in the pre- nor in the post-effort data.

We further observed a significant difference between the average index for first-hand pain – no pain ratings in the task when asked to remember the pain at the end of the session ($t(83.12) = 2.68, p = .009, 95\% \text{ CI } [-0.20, 1.36], \text{Cohen's } d = 0.57$; manipulation check 5; Figure 4C). In this context, the placebo group (3.69 ± 0.23) remembered the self-directed electrical stimulation as significantly less painful compared to the control group (4.47 ± 0.18).

Taken together, manipulation checks 3-5 showed the success of the placebo analgesia induction. Replicating previous studies, placebo analgesia downregulated first-hand pain ratings in the placebo compared to the control group, and this effect lasted until the end of the session and thus beyond the part in which the prosocial effort task was performed. Contrary to previous research and our preregistered hypothesis, other pain intensity and unpleasantness ratings did not seem to be affected by the placebo analgesia manipulation, neither when measured directly after the placebo analgesia manipulation nor in the ratings given after the prosocial effort part of the experiment.

3.3 Placebo group displays reduced prosocial behavior compared to the control group in their choices and exerted force

In the ANOVA analyzing the proportion of work offers chosen (Figure 6 here and Table S12 in the Supplement) we observed main effects of effort level and shock reduction (see Supplement for further details). Both of these effects were expected from previous studies and predicted by our preregistered, directional hypotheses, while any interactions were left exploratory. Intriguingly, we observed a group x shock reduction interaction ($F(4,352) = 4.10$, $p = .020^{\text{GG}}$, $\hat{\eta}_G^2 = .01$), showing that the placebo group showed reduced prosocial behavior compared to the control group, dependent on the number of shocks the other would receive, but independent of effort level (Figure 6A). Post hoc tests confirmed that this group difference was true only for a shock reduction of 1, i.e., the lowest helping level ($p < .001$, value adjusted using Tukey). Lastly, we observed an effort level x shock reduction interaction ($F(16,1408) = 13.11$, $p < .001^{\text{GG}}$, $\hat{\eta}_G^2 = .03$), whereby the differences in the proportion of prosocial choices between the five effort levels increased with decreasing possibility to help, independent of group (Figure 6B). In other words, participants differentiated their helping behavior less at the effort levels when they could help more compared to less. No other effects were significant. The generalized LMM of the same data largely mirrored the ANOVA results (Table S13 in the Supplement).

A

B

Figure 6. A) Participants of the placebo group (orange) chose the prosocial option significantly less often compared to the control group (blue) when the possibility to help was highest, i.e., a reduction of 5 shocks, while the groups did not differ for the other shock reduction amounts (reduction of 1-4 shocks; group x shock reduction interaction). B) Participants differentiated their helping behavior less over the five effort levels when they could help more compared to less (effort level x shock reduction interaction).

The same ANOVA analyzing reaction time during the choice phase revealed faster RTs for choices involving lower effort exertion as well as higher possibility to help over both groups (Table S14 in the Supplement). In other words, participants were faster in their decisions when they needed to put in less effort and could help more. Furthermore, we observed an effort level x shock reduction interaction, whereby the differences in RTs between the five effort levels decreased with increasing possibility to help, independent of group (all p 's < .001). Regarding our preregistered hypotheses, no other effects were significant, showing no group differences in the choice RTs. The LMM of the same data mirrored the ANOVA results (Table S15 in the Supplement).

In the LMM analyzing the exerted force (Table S16 in the Supplement), we found a main effect of group ($\chi^2_{(1)} = 5.21$, $p = .022$), whereby the placebo group (0.43 ± 0.002) exerted less force compared to the control group (0.44 ± 0.002), after having chosen to put in effort to help the other. Moreover, we again observed a main effect of effort ($\chi^2_{(4)} = 3844.73$, $p < .001$), showing that participants exerted more force with increasing effort level. We additionally found an effort x shock reduction interaction ($\chi^2_{(16)} = 77.39$, $p < .001$).

3.4 Prosocial behavior correlates with choice reaction times and unpleasantness but not pain intensity when observing others' pain

We observed a significant positive association between the amount of prosocial choices and unpleasantness ratings across all participants (Spearman's $\rho = .22$, $p = .035$ uncorrected), whereby higher levels of unpleasantness were associated with increased prosocial behavior (choosing the prosocial option more often; Figure S5A in the Supplement). We did not find a significant association between prosocial behavior and first-hand pain ($\rho = .03$, $p = .768$ uncorrected) or other pain intensity ratings ($\rho = .01$, $p = .920$ uncorrected; Figure S5B in the Supplement). Moreover, we found a significant negative correlation between participants' reaction times when making their choice and the proportion of prosocial choices in the prosocial effort task ($\rho = -.58$, $p < .001$ uncorrected), showing that faster reaction times were associated to increased prosociality, and vice versa (Figure S5C in the Supplement). Lastly, there was a significant positive correlation between participants'

trait SVO and their prosocial behavior in the prosocial effort task ($p = .23$, $p = .028$ uncorrected), showing that participants who ascribed themselves to be more other-oriented also had a higher proportion of prosocial choices, or vice versa (Figure S5D in the Supplement).

3.5 Affect sharing mediates the effect of placebo analgesia on prosocial choices

As previous studies found downregulating effects of placebo analgesia on affect sharing, we then aimed to show the effect of placebo analgesia on prosocial behavior in our study was mediated by the level of affect sharing using an exploratory mediation analysis. This showed that the effect of placebo analgesia on prosocial choices was fully mediated via the level of affect sharing in response to others' pain (see Figure S6 in the Supplement). While the direct effect between the placebo response and proportion of prosocial choices was not significant and reduced from $b_{DE} = -0.02$ ($p = .181$) to $b_{ADE} = -0.01$ ($p = .686$), the regression coefficient between affect sharing and prosocial choices was significant ($b = 0.04$, $p = .043$), and so was the effect of placebo responses on affect sharing ($b = -0.37$, $p < .001$). The indirect effect (average causal mediation effect; ACME) was $b_{ACME} = (.04 * -.37) = -.01$. We tested the significance of this indirect effect using bootstrapping procedures and the 95% confidence interval was computed by determining the indirect effects at the 2.5th and 97.5th percentiles. Standardized indirect effects were computed for each of 1000 bootstrapped samples in the R package mediation (Tingley et al., 2014). The bootstrapped standardized ACME was $b = -0.01$, and the 95% confidence interval ranged from $b = -.03$ to $.00$. Thus, the indirect effect, which is the main effect of interest in our mediation analysis, was significant ($p = .032$).

4 Discussion

We investigated the causal effects of a placebo painkiller on prosociality. Participants under placebo analgesia showed reduced willingness to put in effort to help others at the lowest helping level, and exerted less force when putting in effort to help.

Our design revealed that placebo participants' drop in helping behavior scaled with the amount of shock reductions: While it most strongly differed in low-shock conditions, it was virtually identical for maximum shock reduction. This pattern seems counterintuitive, as one might expect effects to be strongest in more intense situations, but could be explained in terms of saliency and social norms: If there is high need for and effectiveness of helping, the incentive to help may be so high that placebo analgesia is not able to modulate behavior; conversely, if stakes are lower, placebo analgesia has leverage to exert its effects. In other words, while high-shock-situations are very salient and produce a strong (moral) urge to help without question, low-shock situations are more ambiguous and may prompt a more open-ended decision. This is in line with prior work by Gallo et al. (2018) who showed that participants donate more money on trials in which a confederate expresses more pain. Furthermore, Fehr & Fischbacher (2004) posit that prosocial norms depend on the expected beliefs and desires of the recipient, which, according to our results, may be perceived differently in high vs. low pain conditions. As per the norm activation model (Steg & de Groot, 2010), participants might be more aware of adverse consequences of their behavior in exactly those high pain conditions, feel a stronger moral obligation, and thus prevent them more readily. This interpretation is supported by our RT data whereby all participants were quicker to help in high-shock reduction situations. However, this hypothesis will have to be systematically tested in future studies. Even when choosing to help, the placebo group exerted less energy compared to controls (this effect was only found in the LMM and not the ANOVA). Lockwood et al. (2017) reported similar findings when participants exerted effort for others compared to themselves. Our results suggest that placebo analgesia could exacerbate this 'prosocial apathy'.

Although placebo analgesia successfully reduced first-hand pain, we did not replicate previous studies of reduced other-related pain intensity and unpleasantness (Mischkowski et al., 2016; Rütgen, Seidel, Riečanský, et al., 2015; Rütgen, Seidel, Silani, et al., 2015; de Pascalis & Vecchio, 2022; Vecchio & de Pascalis, 2021). One explanation could be that our placebo induction was not strong enough to affect pain empathy. What speaks against this is

that we found no group differences in empathy for pain measured directly after the induction showing that placebo analgesia lasted until the end of the session. Furthermore, there were several differences between our and previous studies reporting placebo or painkiller effects on empathy, e.g., task length, anonymity of participants towards each other, varying study doctors between sessions, and framing (the focus being on the prosocial effort task here and on the pain task previously), which could all have influenced the way placebo analgesia affects pain empathy on a group level. Importantly, when considering individual differences in placebo responses and affect sharing in an exploratory mediation analysis, the two were not only significantly related, but affect sharing also fully mediated the effects of placebo responding on prosocial choices. Our results thus highlight the importance of individual differences, as well as that altering first-hand pain may additionally influence prosociality via routes beyond empathy and affect sharing. What routes those are and how differences in perception (“what we feel”) and placebo responsiveness are linked to actions (“what we do”) are important avenues for further research.

Unpleasantness ratings when observing others in pain are usually seen as a marker of affect sharing, while pain intensity ratings are thought to measure cognitive-evaluative components of empathy (Lamm & Majdandžić, 2015 for a review). Interestingly, exploratory analyses showed that the proportion of prosocial choices was positively associated with higher unpleasantness ratings when observing others in pain, but not with self- or other-related pain intensity ratings. Our post-hoc mediation analysis extended this finding by showing that the effects of individual differences in placebo analgesia on prosocial choices were fully mediated by the level of affect sharing in response to others’ pain. This resonates well with prior work linking affect sharing, empathic concern, and prosocial behavior (Eisenberg & Fabes, 1990 for a review; Lengersdorff et al., 2020; Lockwood et al., 2016): Hein et al. (2010) found that self-reported trait empathic concern for another’s suffering predicted later costly helping (enduring physical pain to reduce the other’s pain). Gallo et al. (2018), however, stressed a connection between cognitive-evaluative ratings of the pain intensity observed in others and subsequent donation behavior to reduce their pain. Taken

together, the multi-faceted nature of these findings shows that certain aspects of empathy-related responses may influence different aspects of prosociality (exerting effort, enduring pain, donating money). It also reminds us that empathy is not the only driver of prosocial behavior (Bloom, 2018; Decety & Cowell, 2014; Lamm & Majdandžić, 2015 for reviews). To tease apart these various influences, future studies could connect different ways to induce and measure facets of empathy and prosociality.

A higher proportion of prosocial choices was associated with faster reaction times. This is in line with studies associating quicker decisions to greater prosociality (Chen & Krajbich, 2018; Rand et al., 2012). The proportion of prosocial choices also correlated with increased prosocial tendencies in trait social value orientation (SVO). This nicely links prosocial traits people ascribe themselves with their actual behavior, complementing studies demonstrating that the level of cooperativeness in SVO relates to contributing more hours for a prosocial cause (McClintock & Allison, 1989) and greater donations (Lange et al., 2010).

The present study had strengths and limitations worth discussing. We preregistered our study, clearly distinguishing confirmatory from exploratory findings and reducing the risk of type-I errors (Nosek et al., 2018). We aimed to exclude alternative explanations such as social norms, reciprocity, or reputation, as participants never met face-to-face (Crockett et al., 2015). Belief in our cover story highlighted that participants' behavior was likely not influenced by these concerns. Anonymity may still have reduced empathic responses, through mechanisms such as objectification (Eklund, 2006), dehumanization (Cameron et al., 2015), or distancing (Cameron et al., 2019; Story et al., 2020). However, such effects would likely be independent of the placebo manipulation. As in Lockwood et al. (2021), we operationalized prosocial behavior using costly choices and exertion of physical effort, and kept this behavior independent of monetary gains, group allocation or study time. This setup grasped both peoples' explicit choice behavior as well as the implicit energization of their actions, disentangling 'true' from 'superficial' helping behaviors. With this, we aimed to measure prosocial behavior in an ecologically more valid way, which may better translate to real-world prosocial acts. Nevertheless, future research should translate our laboratory-

based findings to real-life measures of prosociality, e.g., using ecological momentary assessment or diaries (Morelli et al., 2014; Rameson et al., 2012). And although the present study gives insights into effects of altered pain sensitivity on social emotions and behavior, generalizations to people affected by pain-related disorders and frequent painkiller use will require different study designs and participants.

In sum, placebo analgesia decreased people's willingness to exert effort to reduce others' pain as well as their actual effort. Downregulation of one's own pain sensitivity changes not only how we experience pain but also affects our decisions to help others. Notwithstanding independent validation and extension to more ecological settings, and especially to use of painkillers, this study has important implications for the social interactions of people under the influence of analgesics and with chronic pain conditions.

5 Acknowledgements

We thank Lei Zhang for input on the study design, Magdalena Banwinkler, Elisabeth Löffler and numerous interns for supporting the data collection, Federica Riva for supervision, and Valeria Gazzola, Jonas Nitschke, and Max Eder for feedback on the manuscript/code.

6 Funding

The present study was financially supported by the uni:docs scholarship of the University of Vienna, the Marietta-Blau scholarship of the Agency for Education and Internationalisation Austria (OeaD) (both awarded to H.H.), the Austrian Science Fund (FWF W1262-B29 and P32686), and the Vienna Science and Technology Fund (WWTF VRG13-007). None of the funders had any role in study design, data collection and analysis, interpretation, writing or decision to publish.

7 Declarations of Interest

H.H. works as a researcher and psychologist for MyMind GmbH, a company developing a neurofeedback training game for children with autism spectrum disorder and attention deficit hyperactivity disorder, but this work is in no way related to the present research. The

remaining authors declare that they have no financial interests or potential conflicts of interest.

8 References

- Bloom, P. (2017). Empathy and its discontents. *Trends in Cognitive Sciences*, 21(1), 24–31. <https://doi.org/10.1016/j.tics.2016.11.004>
- Bolshakova, M., Bluthenthal, R., & Sussman, S. (2019). Opioid use and misuse: health impact, prevalence, correlates and interventions. *Psychology & Health*, 34(9), 1105–1139.
- Botvinik-Nezer, R., Holzmeister, F., Camerer, C. F., Dreber, A., Huber, J., Johannesson, M., ... & Rieck, J. R. (2020). Variability in the analysis of a single neuroimaging dataset by many teams. *Nature*, 582(7810), 84–88.
- Brethel-Haurwitz, K. M., Cardinale, E. M., Vekaria, K., Robertson, E., Walitt, B., VanMeter, J., & Marsh, A. (2018). Extraordinary altruists exhibit enhanced self-other overlap in neural responses to distress. *Psychological Science*, 29(10), 1631–1641.
- Cameron, C. D., Conway, P., & Scheffer, J. A. (2021). Empathy regulation, prosociality, and moral judgment. *Current Opinion in Psychology*. <https://doi.org/10.1016/J.COPSYC.2021.09.011>
- Cameron, C. D., Harris, L. T., & Payne, B. K. (2015). The emotional cost of humanity: Anticipated exhaustion motivates dehumanization of stigmatized targets. *Http://Dx.Doi.Org/10.1177/1948550615604453*, 7(2), 105–112. <https://doi.org/10.1177/1948550615604453>
- Cameron, C. D., Hutcherson, C. A., Ferguson, A. M., Scheffer, J. A., Hadjiandreou, E., & Inzlicht, M. (2019). Empathy is hard work: People choose to avoid empathy because of its cognitive costs. *Journal of Experimental Psychology: General*, 148(6), 962–976. <https://doi.org/10.1037/xge0000595>
- Chelnokova, O., Laeng, B., Eikemo, M., Riegels, J., Løseth, G., Maurud, H., Willoch, F., & Leknes, S. (2014). Rewards of beauty: the opioid system mediates social motivation in humans. *Molecular Psychiatry*, 19(7), 746–747. <https://doi.org/10.1038/mp.2014.1>
- Chen, F., & Krajbich, I. (2018). Biased sequential sampling underlies the effects of time pressure and delay in social decision making. *Nature Communications* 2018 9:1, 9(1), 1–10. <https://doi.org/10.1038/s41467-018-05994-9>
- Contreras-Huerta, L. S., Pisauro, A., & Apps, M. A. J. (2020). Effort shapes social cognition and behaviour: a neuro-cognitive framework. *Neuroscience & Biobehavioral Reviews*, 118, 426–439.
- Crockett, M. J., Kurth-Nelson, Z., Siegel, J. Z., Dayan, P., & Dolan, R. J. (2015). Harm to others outweighs harm to self in moral decision making. *Proceedings of the National Academy of Sciences*, 112(4), E381–E381. <https://doi.org/10.1073/pnas.1424572112>
- Decety J., & Cowell J.M. (2014). The complex relation between morality and empathy. *Trends Cogn Sci.*, 18(7), 337–9. <https://doi.org/10.1016/j.tics.2014.04.008>. PMID: 24972506
- De Pascalis, V., & Vecchio, A. (2022). The influence of EEG oscillations, heart rate variability changes, and personality on self-pain and empathy for pain under placebo analgesia. *Scientific Reports*, 12(1), 1–18.
- De Waal, F. B. M. (2008). Putting the altruism back into altruism: the evolution of empathy.

- 593 *Annual Review of Psychology*, 59, 279–300.
594 <https://doi.org/10.1146/annurev.psych.59.103006.093625>
- 595 De Waal, F. B. M., & Preston, S. D. (2017). Mammalian empathy: Behavioural manifestations
596 and neural basis. *Nature Reviews Neuroscience*, 18(8), 498–509.
597 <https://doi.org/10.1038/nrn.2017.72>
- 598 Decety, J. (2021). Why empathy is not a reliable source of information in moral decision
599 making. *Current Directions in Psychological Science*, 096372142110319.
600 <https://doi.org/10.1177/09637214211031943>
- 601 Eisenberg, N., & Fabes, R. A. (1990). Empathy: Conceptualization, measurement, and
602 relation to prosocial behavior. *Motivation and Emotion*, 14(2), 131–149.
603 <https://doi.org/10.1007/BF00991640>
- 604 Eisenberg, N., & Giunta, L. Di. (2011). Empathy-related responding: Association with
605 prosocial behavior, aggression and intergroup relations. *National Institutes of Health*,
606 4(1), 1–32. <https://doi.org/10.1111/j.1751-2409.2010.01020.x> Empathy-related
- 607 Eisenberg, N., & Miller, P. A. (1987). The Relation of Empathy to Prosocial and Related
608 Behaviors. *Psychological Bulletin*, 101(1), 91–119. [https://doi.org/10.1037/0033-](https://doi.org/10.1037/0033-2909.101.1.91)
609 2909.101.1.91
- 610 Eklund, J. H. (2006). Empathy and viewing the other as a subject. *Scandinavian Journal of*
611 *Psychology*, 47(5), 399–409. <https://doi.org/10.1111/J.1467-9450.2006.00521.X>
- 612 Fehr, E., & Fischbacher, U. (2004). Social norms and human cooperation. *Trends in*
613 *Cognitive Sciences*, 8(4), 185-190.
- 614 Gallo, S., Paracampo, R., Müller-Pinzler, L., Severo, M. C., Blömer, L., Fernandes-
615 Henriques, C., Henschel, A., Lammes, B. K., Maskaljunas, T., Suttrup, J., Avenanti, A.,
616 Keysers, C., & Gazzola, V. (2018). The causal role of the somatosensory cortex in
617 prosocial behaviour. *ELife*, 7(May), e32740. <https://doi.org/10.7554/eLife.32740>
- 618 Hartmann, H., & Lamm, C. (2019). *Another's Pain in my Social Brain: The Effects of Placebo*
619 *(Empathy) Analgesia on Social Behavior | OSF Registries*. <https://osf.io/g3acp>
- 620 Hartmann, H., Riva, F., Rütgen, M., & Lamm, C. (2021). Placebo analgesia does not reduce
621 empathy for naturalistic depictions of others' pain in a somatosensory specific way.
622 *Cerebral Cortex Communications*, tgab039. <https://doi.org/10.1093/TEXCOM/TGAB039>
- 623 Hartmann, H., Rütgen, M., Riva, F., & Lamm, C. (2021). Another's pain in my brain: No
624 evidence that placebo analgesia affects the sensory-discriminative component in
625 empathy for pain. *NeuroImage*, 224, 117397.
626 <https://doi.org/https://doi.org/10.1016/j.neuroimage.2020.117397>
- 627 Hein, G., Silani, G., Preuschoff, K., Batson, C. D., & Singer, T. (2010). Neural responses to
628 ingroup and outgroup members' suffering predict individual differences in costly helping.
629 *Neuron*, 68(1), 149–160. <https://doi.org/10.1016/J.NEURON.2010.09.003>
- 630 Krohne, H. W., Egloff, B., Kohlmann, C.-W., & Tausch, A. (1996). Untersuchungen mit einer
631 deutschen Version der Positive and Negative Affect Schedule (PANAS). *Diagnostica*,
632 42(2), 139–156. <https://doi.org/10.1037/t49650-000>
- 633 Lamm, C., & Majdandžić, J. (2015). The role of shared neural activations, mirror neurons,
634 and morality in empathy - A critical comment. *Neuroscience Research*, 90, 15–24.
635 <https://doi.org/10.1016/j.neures.2014.10.008>
- 636 Lamm, C., Rütgen, M., & Wagner, I. C. (2019). Imaging empathy and prosocial emotions.
637 *Neuroscience Letters*, 693, 49–53. <https://doi.org/10.1016/j.neulet.2017.06.054>
- 638 Lange, P. A. M. Van, Bekkers, R., Schuyt, T. N. M., & Vugt, M. Van. (2010). From games to

- 639 giving: Social value orientation predicts donations to noble causes.
640 <https://doi.org/10.1080/01973530701665223>, 29(4), 375–384.
641 <https://doi.org/10.1080/01973530701665223>
- 642 Lengersdorff, L. L., Wagner, I. C., Lockwood, P. L., & Lamm, C. (2020). When implicit
643 prosociality trumps selfishness: the neural valuation system underpins more optimal
644 choices when learning to avoid harm to others than to oneself. *Journal of Neuroscience*,
645 40(38), 7286–7299.
- 646 Lockwood, P., Abdurahman, A., Gabay, A., Drew, D., Tamm, M., Husain, M., & Apps, M.
647 (2021). Ageing increases prosocial motivation for effort. *Psychological Science*, 32(5),
648 668–681. <https://doi.org/10.31234/osf.io/8c5ra>
- 649 Lockwood, P. L., Ang, Y.-S., Husain, M., & Crockett, M. J. (2017). Individual differences in
650 empathy are associated with apathy-motivation. *Scientific Reports*, 7(1), 17293.
651 <https://doi.org/10.1038/s41598-017-17415-w>
- 652 Lockwood, P. L., Apps, M. A. J., Valton, V., Viding, E., & Roiser, J. P. (2016).
653 Neurocomputational mechanisms of prosocial learning and links to empathy.
654 *Proceedings of the National Academy of Sciences*, 113(35), 9763–9768.
655 <https://doi.org/10.1073/pnas.1603198113>
- 656 Lockwood, P. L., Hamonet, M., Zhang, S. H., Ratnavel, A., Salmony, F. U., Husain, M., &
657 Apps, M. A. J. (2017). Prosocial apathy for helping others when effort is required.
658 *Nature Human Behaviour*, 1(7), 1–10. <https://doi.org/10.1038/s41562-017-0131>
- 659 Lockwood, P. L., Seara-Cardoso, A., & Viding, E. (2014). Emotion regulation moderates the
660 association between empathy and prosocial behavior. *PLoS ONE*, 9(5).
661 <https://doi.org/10.1371/journal.pone.0096555>
- 662 Martí-Vilar, M., Corell-García, L., & Merino-Soto, C. (2019). Systematic review of prosocial
663 behavior measures. *Revista de Psicología*, 37(1), 349–377.
- 664 Mathworks. (2018). *MATLAB*. The MathWorks Inc.
- 665 McClintock, C. G., & Allison, S. T. (1989). Social value orientation and helping behavior.
666 *Journal of Applied Social Psychology*, 19(4), 353–362. <https://doi.org/10.1111/J.1559->
667 1816.1989.TB00060.X
- 668 Mischkowski, D., Crocker, J., & Way, B. M. (2016). From painkiller to empathy killer:
669 Acetaminophen (paracetamol) reduces empathy for pain. *Social, Cognitive and Affective*
670 *Neuroscience*, 11(9), 1345–1353. <https://doi.org/10.1093/scan/nsw057>
- 671 Mischkowski, D., Crocker, J., & Way, B. M. (2019). A social analgesic? Acetaminophen
672 (Paracetamol) reduces positive empathy. *Frontiers in Psychology*, 10(March), 1–8.
673 <https://doi.org/10.3389/fpsyg.2019.00538>
- 674 Morelli, S. A., Rameson, L. T., & Lieberman, M. D. (2014). The neural components of
675 empathy: Predicting daily prosocial behavior. *Social Cognitive and Affective*
676 *Neuroscience*, 9(1), 39–47. <https://doi.org/10.1093/SCAN/NSS088>
- 677 Murphy, R. O., Ackermann, K. A., & Handgraaf, M. J. J. (2011). Measuring social value
678 orientation. *Judgment and Decision Making*, 6(8), 771–781.
- 679 Nosek, B. A., Ebersole, C. R., DeHaven, A. C., & Mellor, D. T. (2018). The preregistration
680 revolution. *Proceedings of the National Academy of Sciences of the United States of*
681 *America*, 115(11), 2600–2606. <https://doi.org/10.1073/pnas.1708274114>
- 682 Nummenmaa, L., & Tuominen, L. (2017). Opioid system and human emotions. *British*
683 *Journal of Pharmacology*, 175(14), 2737–2749. <https://doi.org/10.1111/bph.13812>
- 684 Petrovic, P., Kalso, E., Petersson, K. M., & Ingvar, M. (2002). Placebo and opioid analgesia -

- 685 imaging a shared neuronal network. *Science*, 295(5560), 1737–1740.
686 <https://doi.org/10.1126/science.1067176>
- 687 Pfattheicher, S., Nielsen, Y. A., & Thielmann, I. (2022). Prosocial behavior and altruism: A
688 review of concepts and definitions. *Current Opinion in Psychology*, 44, 124–129.
689 <https://doi.org/10.1016/J.COPSYC.2021.08.021>
- 690 R Core Team. (2020). *R: A language and environment for statistical computing*. R
691 Foundation for Statistical Computing. <https://www.r-project.org/>
- 692 Rameson, L. T., Morelli, S. A., & Lieberman, M. D. (2012). The neural correlates of empathy:
693 Experience, automaticity, and prosocial behavior. *Journal of Cognitive Neuroscience*,
694 24(1), 235–245. https://doi.org/10.1162/JOCN_A_00130
- 695 Rand, D. G., Greene, J. D., & Nowak, M. A. (2012). Spontaneous giving and calculated
696 greed. *Nature* 2012 489:7416, 489(7416), 427–430. <https://doi.org/10.1038/nature11467>
- 697 Ratner, K. G., Kaczmarek, A. R., & Hong, Y. (2018). Can over-the-counter pain medications
698 influence our thoughts and emotions? *Policy Insights from the Behavioral and Brain*
699 *Sciences*, 5(1), 82–89. <https://doi.org/10.1177/2372732217748965>
- 700 Rife, S. C., Nuijten, M. B., & Epskamp, S. (2016). *statcheck: Extract statistics from articles*
701 *and recompute p-values [web application]*. Retrieved from <http://statcheck.io>.
- 702 Rütgen, M., Eidel, E. M., Pletti, C., Riečanský, I., Gartus, A., Eisenegger, C., & Lamm, C.
703 (2018). Psychopharmacological modulation of event-related potentials suggests that
704 first-hand pain and empathy for pain rely on similar opioidergic processes.
705 *Neuropsychologia*, 116, 5–14. <https://doi.org/10.1016/j.neuropsychologia.2017.04.023>
- 706 Rütgen, M., Seidel, E.-M., Riečanský, I., & Lamm, C. (2015). Reduction of empathy for pain
707 by placebo analgesia suggests functional equivalence of empathy and first-hand
708 emotion experience. *Journal of Neuroscience*, 35(23), 8938–8947.
709 <https://doi.org/10.1523/JNEUROSCI.3936-14.2015>
- 710 Rütgen, M., Seidel, E.-M., Silani, G., Riečanský, I., Hummer, A., Windischberger, C.,
711 Petrovic, P., & Lamm, C. (2015). Placebo analgesia and its opioidergic regulation
712 suggest that empathy for pain is grounded in self pain. *Proceedings of the National*
713 *Academy of Sciences of the United States of America*, 112(41), E5638–E5646.
714 <https://doi.org/10.1073/pnas.1511269112>
- 715 Rütgen, M., Wirth, E.-M., Riečanský, I., Hummer, A., Windischberger, C., Petrovic, P., Silani,
716 G., & Lamm, C. (2021). Beyond sharing unpleasant affect – evidence for pain-specific
717 opioidergic modulation of empathy for pain. *Cerebral Cortex*, bhaa385.
718 <https://doi.org/10.1093/cercor/bhaa385>
- 719 Scott, D. J., Stohler, C. S., Egnatuk, C. M., Wang, H., Koeppe, R. A., & Zubieta, J. K. (2007).
720 Individual differences in reward responding explain placebo-induced expectations and
721 effects. *Neuron*, 55(2), 325–336. <https://doi.org/10.1016/J.NEURON.2007.06.028>
- 722 Silberzahn, R., Uhlmann, E. L., Martin, D. P., Anselmi, P., Aust, F., Awtrey, E., ... & Nosek, B.
723 A. (2018). Many analysts, one data set: Making transparent how variations in analytic
724 choices affect results. *Advances in Methods and Practices in Psychological Science*,
725 1(3), 337–356.
- 726 Simmons, J. P., Nelson, L. D., & Simonsohn, U. (2012). A 21 Word Solution. *SSRN*
727 *Electronic Journal*, 1–4. <https://doi.org/10.2139/ssrn.2160588>
- 728 Steg, L., & De Groot, J. (2010). Explaining prosocial intentions: Testing causal relationships
729 in the norm activation model. *British Journal of Social Psychology*, 49(4), 725–743.
- 730 Story, G. W., Kurth-Nelson, Z., Crockett, M., Vlaev, I., Darzi, A., & Dolan, R. J. (2020). Social

- 731 discounting of pain. *Journal of the Experimental Analysis of Behavior*, 1–18.
732 <https://doi.org/10.1002/jeab.631>
- 733 Thielmann, I., Böhm, R., & Hilbig, B. E. (2021). Economic games: An introduction and guide
734 for research. *Collabra*, June.
- 735 Thielmann, I., Spadaro, G., & Balliet, D. (2020). Personality and prosocial behavior: A
736 theoretical framework and meta-analysis. *Psychological Bulletin*, 146(1), 30–90.
737 <https://doi.org/10.1037/bul0000217>
- 738 Tingley, D., Yamamoto, T., Hirose, K., Keele, L., & Imai, K. (2014). Mediation: R package for
739 causal mediation analysis.
- 740 Vecchio, A., & de Pascalis, V. De. (2021). ERP indicators of self-pain and other pain
741 reductions due to placebo analgesia responding: The moderating role of the fight-flight-
742 freeze system. *Brain Sciences*, 11(9). <https://doi.org/10.3390/BRAINSKI11091192>
- 743 Yin, Y., & Wang, Y. (2022). Is empathy associated with more prosocial behaviour? A meta-
744 analysis. *Asian Journal of Social Psychology*. <https://doi.org/10.1111/AJSP.12537>
- 745 Zubieta, J.-K., Bueller, J. A., Jackson, L. R., Scott, D. J., Xu, Y., Koeppe, R. A., Nichols, T.
746 E., & Stohler, C. S. (2005). Placebo effects mediated by endogenous opioid activity on
747 mu-opioid receptors. *Journal of Neuroscience*, 25(34), 7754–7762.
748 <https://doi.org/10.1523/JNEUROSCI.0439-05.2005>
- 749 Zubieta, J.-K., & Stohler, C. S. (2009). Neurobiological mechanisms of placebo responses.
750 *Annals of the New York Academy of Sciences*, 1156, 198.
751 <https://doi.org/10.1111/J.1749-6632.2009.04424.X>