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# Toward a Deeper Understanding of the Mechanisms of Animal-Assisted Interventions: How Important is the Animal?

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**Erklärung zur wissenschaftlichen Lauterkeit**

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- **Study I:**

  **Wagner, C.,** Gaab, J., Locher, C., Hediger, K. (2021): Lack of Effects of the Presence of a Dog on Pain Perception in Healthy Participants - a Randomized Controlled Trial. *Frontiers in Pain Research*
- **Study II:**

  **Wagner, C.,** Gaab, J., Hediger, K. (2022): The Importance of the Treatment Rationale for Pain in Animal-Assisted Interventions: A Randomized Controlled Trial in Healthy Participants *(submitted for publication)*
- **Study III:**

  **Wagner, C.,** Grob, C., Hediger, K. (2022): Specific and Nonspecific Factors of Animal-Assisted Interventions: A Systematic Review *(submitted for publication)*

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## TABLE OF CONTENTS

**APPENDICES**

A. Study I

B. Study II

C. Study III

D. Curriculum Vitae

**Abstract**

There is an ever-increasing interest in animal-assisted interventions, and while its effects seem promising, little is known about the underlying mechanisms. The literature on animal-assisted interventions generally assumes that the animal itself is responsible for the effects of the interventions. However, evidence from placebo research suggests that a significant portion of treatment effects can be explained by contextual factors that are not specific to a treatment itself. Regarding animal-assisted interventions, this would suggest that the effects are not due to the animal but to contextual factors.

In order to better understand the role of the animal and contextual factors in animal-assisted interventions, this thesis pursued two aims. First, it investigated to what extent the effects of animal-assisted interventions on pain can be attributed to the presence of an animal or to how the animal is embedded in the treatment rationale. Second, it identified the hypotheses previous studies have pursued regarding the underlying mechanisms of animal-assisted interventions and what factors have been considered as specific and nonspecific. Two different approaches were applied to address these two aims. For the first aim, we conducted two randomized controlled trials with healthy participants in a heat-pain placebo paradigm (Study I and Study II). For the second aim, a systematic review was conducted to assess factor hypotheses that researchers have presented in previous studies on animal-assisted interventions and to identify what specific and nonspecific factors have been considered in animal-assisted interventions (Study III).

In the two experimental heat-pain studies, we did not find any analgesic effects in healthy participants compared to the control group when the dog was not part of the treatment rationale (Study I). Instead, participants experienced heat-pain to be more intense at the limit of their tolerance in the presence of the dog compared to the control group (i.e., self-reported pain intensity at the limit of pain tolerance, $p = 0.041$). When the dog was part of the treatment rationale (Study II), it did have a positive effect on pain perception in healthy participants compared to the control group (i.e., self-reported ratings of pain unpleasantness at the limit of pain tolerance, $p = 0.010$). The systematic review (Study III) found that a majority of studies did not define specific hypotheses regarding potential mechanisms of animal-assisted interventions. Further, most studies controlled for the animal or the interaction with the animal as specific factors.

Based on the findings of this thesis, it is urgent to reconsider the explanatory model for the effectiveness of animal-assisted interventions. More precisely, instead of only focusing on *the animal* in animal-assisted interventions, researchers and practitioners should start to include contextual factors in their explanatory models. A better understanding of the relevant factors in animal-assisted interventions might also reveal how important the animal is and whether these effects can be facilitated through other factors.

# 1. Introduction

Animal-assisted interventions are currently gaining increased attention from the public as well as from practitioners and researchers (Fine et al., 2019). For example, animals are increasingly being incorporated in interventions in various healthcare settings, such as in hospitals (Linder et al., 2017; Uglow, 2019), psychotherapeutic settings (Templin et al., 2018; Wagner et al., 2019), rehabilitation clinics (Hediger et al., 2021; Theis et al., 2020), emergency departments (Kline et al., 2019), and nursing homes (Banks & Banks, 2002; Majic et al., 2013; Schuurmans et al., 2016; Wu et al., 2002).

Further, while the research field of animal-assisted intervention is rather young, there has been a rapid growth in studies in the past decades (López-Cepero, 2020). Although the results are mixed, the evidence suggests that animal-assisted interventions are a promising way to treat a variety of health conditions (Babka et al., 2021; Borgi et al., 2020; Chang et al., 2021; Cotoc et al., 2019; Klimova et al., 2019; Nieforth et al., 2021; Park et al., 2020; Waite et al., 2018). Most relevant for a great part of this thesis is evidence suggesting that animal-assisted interventions can be an effective intervention for clinical pain management (Feng et al., 2021; Waite et al., 2018; Zhang et al., 2021).

An animal-assisted intervention is defined as “a goal oriented and structured intervention that intentionally includes or incorporates animals in health, education and human services (e.g., social work) for the purpose of therapeutic gains in humans" (cited from IAHAIO, 2018, p. 5). The term *animal-assisted intervention* is used as an umbrella term that includes different types of interventions, such as animal-assisted therapy (AAT), animal-assisted education (AAE), animal-assisted activity (AAA), and animal-assisted coaching (AAC) (IAHAIO, 2018).

Although the effects of animal-assisted interventions seem promising, little is known about their underlying mechanisms (López-Cepero, 2020). The majority of studies on animal-assisted interventions have been designed to examine *if* animal-assisted interventions are effective, but they have neglected exploring *how* animal-assisted interventions work. Despite this lack of understanding, the literature on animal-assisted intervention consists of numerous anecdotes, theories, and hypotheses that assume that the animal itself is responsible for the effects of animal-assisted interventions (Marino, 2012). In other words, the animal is considered to be the specific factor of animal-assisted interventions (Marino, 2012). As a result, the effects of animal-assisted interventions are rarely attributed to other factors besides the animal.

Evidence from intervention research, however, suggests that a large part of treatment responses can be explained by contextual or nonspecific factors rather than by specific factors of the intervention itself (Wager & Atlas, 2015). Much of what is known about contextual factors comes from placebo research, since it is these contextual factors that are responsible for the effectiveness of placebos (Ashar et al., 2017; Miller et al., 2009; Price et al., 2008). With only a few exceptions, the possibility that contextual factors also play an important role in animal-assisted interventions has not been considered.

For this reason, the aim of this thesis is to explore the mechanisms of animal-assisted interventions. More precisely, this thesis aims to implement knowledge from placebo research in order to better understand how animal-assisted interventions might work and whether the animal itself truly is a specific factor. To do so, the thesis focuses on the effects of animal-assisted interventions on pain. This is motivated by the fact that there already exists a considerable amount of placebo research on pain (placebo analgesia) that has investigated the role of contextual factors. There has not yet been investigation on whether the effects of animal-assisted interventions on pain are due to the presence of the animal or to contextual factors.

Further, since contextual factors have not been widely acknowledged in the literature on animal-assisted interventions, another part of this thesis aims to explore what hypotheses previous authors have pursued regarding potential mechanisms and how they have controlled for specific and nonspecific, hence contextual, factors in previous studies on animal-assisted interventions.

Chapter 2 will provide a theoretical background including an overview of the current evidence and research gaps with regard to animal-assisted interventions and also present the most prominent theories about the mechanisms of animal-assisted interventions. Additionally, an overview of the mechanisms from placebo research will be presented. Chapter 3 will introduce the aims of this thesis and the research questions. In chapter 4, an overview of the methods of each study will be presented, and chapter 5 will summarize the results of each study. Since the article behind each study can be found in the appendix, chapter 4 and 5 will only provide short summaries of the studies. In chapter 6, the main findings of the thesis will be discussed and future implications will be outlined.

# 2. Theoretical background

## 2.1 Animal-assisted interventions

### *2.1.1 Current evidence and research gaps*

Numerous studies have suggested that animal-assisted interventions are clinically effective (Hediger et al., 2019) and have demonstrated that they can be an effective in treating behavioral, mental, and neurological disorders and in rehabilitating from them (Babka et al., 2021; Bernabei et al., 2013; Borgi et al., 2020; Kamioka et al., 2014; Lundqvist et al., 2017; Maujean et al., 2015; Nimer & Lundahl, 2007; O'Haire et al., 2015; Souter & Miller, 2007). For example, there is evidence that animal-assisted interventions can reduce depressive symptoms in different populations (Borgi et al., 2020; Souter & Miller, 2007), positively affect psychological, cognitive and psychosocial and behavioral aspects in older adults (Babka et al., 2021; Chang et al., 2021; Klimova et al., 2019; Park et al., 2020), improve social interaction and communication in patients with autism-spectrum disorders (Nieforth et al., 2021; O'Haire, 2013), and be effective in treating trauma-related symptoms (Germain et al., 2018; Hediger et al., 2021; O'Haire et al., 2015). Furthermore, and especially important for this thesis, recent meta-analyses and systematic reviews have concluded that animal-assisted interventions can be a promising complementary treatment approach for clinical pain management in adult, child, and adolescent patients (Feng et al., 2021; Waite et al., 2018; Zhang et al., 2021).

While these results are promising, contradictory findings and methodological limitations make it difficult to determine the true effectiveness of animal-assisted interventions. A number of studies and meta-analyses have not found any important clinical effects of animal-assisted interventions with regard to depression (Feng et al., 2021; Zafra-Tanaka et al., 2019), anxiety (Barker et al., 2015; Feng et al., 2021), stress (Feng et al., 2021), or pain (Barker et al., 2015). Further, previous meta-analyses have also noted that their findings are based on a very small sample of studies (Borgi et al., 2020; Hediger et al., 2021; Hu et al., 2018; Waite et al., 2018; Zafra-Tanaka et al., 2019), which are also often very heterogenous (Borgi et al., 2020; Zafra-Tanaka et al., 2019). For example, Borgi et al. (2020) conducted a meta-analysis of ten studies and reported a heterogeneity of 71% between the studies. While analyzing a small sample of studies already limits the measurability of effectiveness (Feng et al., 2021), a high heterogeneity between the studies makes their comparability questionable (Zafra-

Tanaka et al., 2019). Moreover, several meta-analyses have noted the low-quality study design of the included studies (Charry-Sánchez et al., 2018; Diniz Pinto et al., 2021; Hediger et al., 2021; Waite et al., 2018). Previous studies have also only had a small sample size (Zafra-Tanaka et al., 2019), incorporated inadequate control conditions (Waite et al., 2018), or provided insufficient information regarding the study design and interventions (Hediger et al., 2021). A lack of good control groups seems to be one of the biggest challenges in research on animal-assisted interventions and represents a threat to the internal validity of the studies (López-Cepero, 2020; Marino, 2012). Good control groups are necessary in order to disentangle specific effects from nonspecific effects and to identify what makes animal-assisted interventions effective (Marino, 2012).

In the light of these challenges the effectiveness of animal-assisted interventions should be questioned (Serpell et al., 2017). In addition, there remains an even greater lack of evidence regarding the mechanisms of animal-assisted interventions, which I will discuss in the next section—to date it is still unclear *how* animal-assisted interventions work.

#### *2.2.1. Possible mechanisms*

The field of animal-assisted interventions is currently lacking investigations on the underlying mechanisms that explain the beneficial outcomes of animal-assisted interventions (Kruger & Serpell, 2006; López-Cepero, 2020). Even though little empirical research has been conducted regarding the mechanisms of animal-assisted interventions, the literature on animal-assisted interventions presents several theories and hypotheses for the underlying mechanisms (Serpell et al., 2017). In the following, the main theories and hypotheses will be summarized.

Some have suggested that the bond or attachment between humans and animals is what makes animal-assisted intervention effective (Fine & Beck, 2015; O'Haire et al., 2015). For example, in one study, stroking and talking to dogs led to lower blood pressure and increased dopamine levels (Odendaal & Meintjes, 2003). Further, there is evidence that interacting and also simply having eye contact with an animal can activate the oxytocin system in humans (Handlin et al., 2011; Nagasawa et al., 2015; Odendaal, 2000; Odendaal & Meintjes, 2003). The release of oxytocin can reduce stress, anxiety, and depression, increase pain tolerance (Beetz & Bales, 2016; Moberg & Moberg, 2003), and foster social interactions and relationships (see Beetz

& Bales, 2016; Uvnäs-Moberg, 2003). In addition, it has also often been assumed that animals can provide humans with social support (Barker & Wolen, 2008).

Another well-known theory regarding the mechanisms of animal-assisted interventions derives from Wilson (1984) biophilia hypothesis. This hypothesis assumes that humans are attracted to nature and animals in order to survive. Perceiving nature or an animal as calm allows a person to consider an environment safe (Julius et al., 2012).

Finally, one of the most commonly proposed theories is that animals can function as social mediators and increase interactions between humans (Kruger & Serpell, 2010). For example, studies have shown that humans are more likely to interact positively with a stranger in public when they are accompanied by a dog compared to when they are unaccompanied (Guéguen & Ciccotti, 2008; Mader et al., 1989; McNicholas & Collis, 2000; Wells, 2004). Some have speculated that animals may increase the interaction between humans because they provide a neutral conversation theme or because they help promote positive social qualities (Guéguen & Ciccotti, 2008; Wells, 2004). Different kinds of evidence suggest that people are perceived more positively when an animal is present compared to when no animal is present. The evidence stems from studies in which people were asked to evaluate others in photographs or videos in the presence or absence of animals (Creary, 2017; Lockwood, 1983; Schneider & Harley, 2006; Wells & Perrine, 2001). People were perceived as friendlier and less threatening when they were depicted with animals than when the same people were depicted without animals (Lockwood, 1983; Wells & Perrine, 2001). Furthermore, psychotherapists were perceived to be more attractive (Creary, 2017; Schneider & Harley, 2006) and more trustworthy (Schneider & Harley, 2006) when they were pictured with an animal compared to when the animal was absent. Similarly, participants were also more willing to disclose personal information when a psychotherapist was accompanied by a dog (Schneider & Harley, 2006). However, other studies found no evidence of such effects (Goldmann et al., 2015). Nevertheless, the consensus seems to be that animals enhance the therapeutic alliance by positively influencing our perception and relationship building (Creary, 2017; Kruger & Serpell, 2010; Schneider & Harley, 2006).

These theories support the idea that animals contribute to the effects of animal-assisted interventions as the specific factor. Yet none of these theories have been adequately empirically tested (López-Cepero, 2020). Moreover, even though it has been noted that “animal-assisted interventions are potentially vulnerable to placebo effects” (cited from Marino, 2012, p. 142), the possibility that animal-assisted interventions work through same mechanisms found in other interventions such as placebos has not been widely acknowledged. For this reason, the next section will present an overview of the mechanisms that placebo research has identified as they could have important implications for examining the mechanisms of animal-assisted interventions.

### 2.2. Context matters

It is assumed that the effects of a treatment can be summed up by natural, specific, or contextual effects (Wampold, 2021). Natural effects are defined as the change of the condition of the disease as a result of the natural progress of the disease. This can either lead to improvements or to deterioration. The term *specific effects* suggest that the effects are caused by a specific intervention (Wampold, 2021). Besides natural and specific effects, contextual effects are also known to impact treatment outcomes (Wampold, 2021). As a matter of fact, evidence suggests that a large part of our treatment response can be explained by contextual effects rather than by the specific effects of an intervention (Wager & Atlas, 2015). For this reason, contextual effects will be discussed in more detail.

Contextual effects are composed of various factors commonly known as contextual factors. Contextual factors provide the context that surrounds any health intervention (Rossettini et al., 2018). These contextual factors are actively interpreted by patients and can evoke a reaction that can influence the outcome of an intervention (Wager & Atlas, 2015). This also highlights that an intervention is never administered in a neutral setting (Rossettini et al., 2018). Contextual factors are thus important for every type of treatment since they make up the context (Rossettini et al., 2018).

Much of what we know about contextual factors derives from placebo research, as it is commonly thought that these factors are what make placebos effective (Benedetti, 2021; Miller et al., 2009). We can distinguish between different kinds of contextual factors. There are internal (i.e., the memories, emotions, expectations, and psychological traits of patients, previous experiences, gender, age), relational (i.e., verbal communication, nonverbal communication, emotional resonance), and external (i.e., physical aspects of the treatment, type of treatment, environment, carrier) contextual factors (Rossettini et al., 2018; Wager & Atlas, 2015).

Of the various contextual factors that have already been studied and substantiated in placebo research, expectation and conditioning are considered to be the core mechanisms that evoke placebo effects (Colloca & Benedetti, 2006; Elsenbruch, 2014; Kirsch, 1985; Murray & Stoessl, 2013). Especially in the area of placebo analgesia, the influence of treatment expectations has been well studied and demonstrated (Fields, 2018). For this reason, I will discuss treatment expectations in more detail in the following section.

### *2.2.1. Treatment expectations*

In recent decades, evidence from placebo research has demonstrated that patients' expectations toward a treatment are an important factor for the outcome of the intervention. Especially in the field of placebo analgesia, the influence of treatment expectations has been well studied (Fields, 2018). Placebo analgesia occurs when the administration of an inert treatment leads to pain reduction (Case et al., 2019) and can be demonstrated in healthy individuals (Lyby et al., 2010; Matre et al., 2006) and in patients (Lee et al., 2012; Levine & Gordon, 1984). Several studies have found that the expectation of pain relief can lead to placebo analgesia (Cormier et al., 2016; Price et al., 2008; Vase et al., 2003), and treatment expectations are considered the main contributor to placebo analgesia (Benedetti et al., 2016; De Tommaso et al., 2017; Price et al., 1999). For example, Cormier et al. (2016) investigated the relation between expectations and clinical outcomes in patients with chronic pain. The authors found several significant relations between expectations and outcomes mediated by patients' global impressions of change, such as changes in pain intensity ($r = 0.46$), changes in pain interferences ($r = 0.33$), or changes in pain catastrophizing ($r = 0.37$), and emphasized the importance of patients' expectations in treating pain (Cormier, Lavigne, Choinière, & Rainville, 2016). These and other findings indicate that interventions that evoke expectations of pain relief are likely to contribute to improving the effectiveness of standard analgesic treatments in clinical practice (Peerdeman et al., 2016).

Many different factors can influence expectations. But the most efficient way to influence expectations is through verbal suggestions, such as treatment rationales (Rossettini et al., 2020; Wampold, 2021). Treatment rationales will be elucidated in the following section.

### *2.2.2. Treatment rationales*

The impact of treatment rationales on treatment responses has been demonstrated in diverse interventions, for example, in psychotherapy (Tondorf et al., 2017), placebo treatments (Gaab et al., 2019), and open-label placebo treatments (Carvalho et al., 2016; Hoenemeyer et al., 2018; Kaptchuk et al., 2010; Locher et al., 2017).

Treatment rationales explain the effects and mechanisms of a particular intervention (Kam-Hansen et al., 2014; Kaptchuk et al., 2010; Kelley et al., 2012). These explanations can influence patients' belief that the intervention that she or he is receiving has a therapeutic effect, which can also result that the intervention becomes meaningful to that person (Liu, 2022). This also supports the meaning model where it has been argued that we respond to the meaning given to the intervention (Moerman, 2006; Moerman & Jonas, 2002). Moerman and Jonas (2002) introduced the concept of *meaning response* to replace the term *placebo response*. In their paper, they argued that placebos are by definition inert and so cannot be the cause of anything, which means that there is no placebo effect. Instead, they suggested that while a placebo cannot cause anything, the meaning ascribed to an intervention can (Moerman & Jonas, 2002). Based on the premise that even inactive interventions can be meaningful and have effects, (Moerman, 2006) suggested that *meaning response* happens in every intervention. The more persuasive the treatment rationale, the stronger the meaning response may be (Trachsel & grosse Holtforth, 2019).

Further, depending on the meaning attributed to the intervention, the treatment response may be different. For example, the administration of a pain intervention with a positive meaning can induce positive expectations and lead to a positive analgesic response, whereas the administration of a pain intervention with no meaning or a negative meaning may induce no expectations or negative expectations, which can lead to an exacerbation or perpetuation of the pain (Bingel et al., 2011).

Moreover, there is also evidence that in addition to the information and explanations offered by the healthcare provider with the treatment rationale, *how* the treatment rationale is provided can affect the treatment response and the outcome of the intervention. This includes, for example, whether the healthcare provider is more or less empathic (Annoni & Miller, 2016; Caspi & Bootzin, 2002; Gaab et al., 2019).

This is in line with psychotherapy research, which has shown that the therapeutic relationship, also known as the therapeutic alliance between the therapist and the patient is crucial to the effects of interventions. This relationship includes a cognitive element, in which information is communicated, and an emotional element, which includes empathy, warmth, caring, and understanding (Di Blasi et al., 2001; Howe et al., 2019; Kelley et al., 2014). It is well-established that the therapeutic alliance is a consistent predictor of outcomes in psychotherapy (Flückiger et al., 2018; Horvath et al., 2011). The importance of the therapeutic alliance has also been demonstrated in placebo research. It is believed that a good therapeutic alliance between the therapist and the patient can potentially enhance the patient's expectations of receiving an effective treatment (Howe et al., 2017; Price et al., 1999). While placebo effects can also occur without a therapeutic alliance, evidence shows that placebo effects are enhanced by the therapeutic alliance (Wampold, 2021). A meta-analysis showed that a good relationship between the healthcare provider and the patient enhances placebo analgesia (Vase et al., 2015).

While this is not a complete review of the research, one can say in summary that the literature on animal-assisted interventions assumes that the animals are responsible for the specific effects of animal-assisted interventions. The most common hypothesis is that the animal can act as a social mediator through its presence, can positively influence our social perception, and can thus facilitate the therapeutic alliance. Intervention research indicates that contextual factors are responsible for a significant portion of our treatment responses and that they play a greater role than the specific treatment itself. Findings on placebo analgesia especially consider treatment expectations evoked by verbal suggestions such as treatment rationales as a crucial context factor for the outcome of an intervention. This supports the idea that the meaning we ascribe to a treatment based on the treatment rationale may have an influence on the effects of the treatment. In addition, the evidence suggests that the therapeutic alliance may enhance these effects.

## 3. Aims of thesis

The main objective of this thesis was to explore the mechanisms of animal-assisted interventions and, relatedly, to identify how important the animal itself is to the effects of the intervention.

To that end, the thesis pursued two aims. One was to investigate to what extent the effect of animal-assisted interventions on pain in healthy participants can be attributed to the presence of an animal and to what extent it can be attribute to other mechanisms. More specifically, this thesis wanted to distinguish whether the potential analgesic effects of animal-assisted interventions are due to the presence of an animal or whether they are due to how the animal is embedded in the treatment rationale in such a way that the animal is imbued with a meaning that can evoke treatment expectations. According to the literature on animal-assisted interventions, the animal itself is considered to be the relevant factor for the effects. In contrast, placebo research strongly supports the impact of contextual factors, such as treatment expectations, on pain.

In light of the impact of contextual factors and the common assumption that animals are the specific factor in animal-assisted interventions, the second aim of this thesis was to investigate whether studies on animal-assisted interventions really consider the animal to be the specific factor and which factors have been considered specific and which have been considered nonspecific based on the experimental and control conditions. The aim was to give an overview of the researchers' assumptions regarding the mechanisms of animal-assisted interventions and to draw implications for future research.

Two different approaches were applied to address these two aims. For the first aim, we conducted two randomized controlled trials with healthy participants. For the second aim, a systematic review was conducted.

The three research projects described in this thesis were designed to provide insight into the following primary questions:

1. *Can the effects of animal-assisted interventions on pain be explained by the animal itself or by contextual factors? (Two experimental studies)*

**Study I.** The aim of study I was to examine if the mere presence of a dog leads to pain relief by its presence or by enhancing the therapeutic alliance. This would indicate that the analgesic effects of animal-assisted interventions can be attributed to the animal.

**Study II.** The aim of study II was to investigate if embedding the presence of a dog in the treatment rationale gives the animal a meaning that affects the treatment response, for example, by leading to pain relief. This would suggest that the analgesic effects of animal-assisted interventions can be attributed to contextual factors.

2. *Which factors are considered specific and which are considered nonspecific in animal-assisted interventions? (Systematic review)*

**Study III.** The aim of study III was to identify factor hypotheses that researchers have presented in previous studies on animal-assisted interventions and to identify which factors have been considered specific and which have been considered nonspecific. The goal was to provide an overview of which hypotheses are most common and which factors are considered specific or nonspecific.

## 4. Methods

### 4.1 Sample and procedures

**Study I.** We conducted a randomized controlled trial with four experimental conditions that employed a standardized experimental heat-pain placebo paradigm in healthy participants. The study was conducted between April 2019 and July 2019. We compared participants in four conditions who received either an animal-assisted intervention or no animal-assisted intervention in a pain assessment or in a pain-therapy context. First, baseline measurements of heat pain and self-reported ratings of pain were collected. After that, the treatment phase was conducted. Participants in the conditions with an animal-assisted intervention were introduced to the dog and deceived by the real reason for the dog's presence (to suppress possible expectation effects). After this introduction, the study investigator applied an inert white cream on the participants in all four conditions. After the treatment phase, posttreatment heat-pain measurements and self-reported ratings of pain were recorded in an identical manner to the baseline assessments. Participants had a mean age of 26.2 (*SD* = 8.3). Eighty-eight were females, and 44 were males.

**Study II.** We conducted a randomized controlled trial with four experimental conditions that employed a standardized experimental heat-pain placebo paradigm in healthy participants. The study was conducted between June 2020 and November 2020. We compared participants in the four conditions who received either an animal-assisted intervention, a placebo, both, or no treatment. First, baseline measurements of heat-pain and self-reported ratings of pain were collected. After that, the treatment phase was conducted, and all the conditions, except for the no-treatment condition, received a positive treatment rationale. After this treatment phase, posttreatment measurements of heat-pain and self-reported ratings of pain were assessed identically to baseline. Participants had a mean age of 28.82 (*SD* = 10.78). Eighty-four participants were female, and 44 were male.

**Study III.** We conducted a systematic literature search of the following databases: PsychINFO, PSYNDEX, ERIC, MEDLINE, Embase, PubMed, Cochrane Library, Web of Science, Scopus, CINAHL, PTSDpubs, and Dissertations & Theses. The date of the last search was 13 January 2022. The systematic review included all studies on animal-assisted interventions with an active control group. Our inclusion criteria were met by 172 studies that were included in this systematic review. These 172 studies were published in 176 reports.

### 4.2. Measurements

**Study I.** Participants' heat-pain tolerance, their perception of the unpleasantness and intensity of pain at the limit of their heat-pain tolerance, and their perception of the study investigator were collected. Heat-pain tolerance was determined using a thermal sensory analyzer (Medoc, Ramatishai, Israel; TSA 2). Participants were asked to stop the increasing heat stimulus at the moment they could not stand the heat any longer. This procedure was repeated three times in a row. Heat-pain tolerance was defined as the average of the three measurements (Hermann et al., 2006). Self-reported ratings of unpleasantness and intensity at the limit of heat-pain tolerance were measured with a visual analogue scale (VAS). The VAS ranged from 1–10 (1 = "not intense at all" or "not unpleasant at all"; 10 = "the most intense pain I have ever experienced" or "the most unpleasant pain I have ever experienced"). Participants were asked to evaluate subjective pain intensity and unpleasantness after each objective pain measurement. Participants' perception of the study investigator was assessed with the Counselor Rating Form–Short Version (CRF-S) (Corrigan & Schmidt, 1983). The CRF-S is a 12-item questionnaire for measuring an individual's perception of a therapist on the following three subscales: *trustworthiness*, *expertness*, and *attractiveness*. The questionnaire contains items on a 7-point Likert scale, ranging from 1 (not very) to 7 (very). For this study, only the subscale *trustworthiness* was analyzed because it is most central to the therapeutic alliance.

**Study II.** Heat-pain tolerance and the corresponding self-reported ratings of the unpleasantness and intensity of pain at participants' limits of heat-pain tolerance were defined as primary outcomes. We assessed heat-pain tolerance and the self-reported ratings of unpleasantness and intensity at their limit of heat-pain tolerance following the design of study I (Wagner et al., 2021).

**Study III.** Factor hypotheses and specific and nonspecific factors of each study were extracted. Factor hypotheses were defined as the factors that authors mention in the introduction regarding potential mechanisms of animal-assisted interventions. Specific and nonspecific factors were identified by comparing the experimental and control interventions. To extract the factor hypotheses and the specific and nonspecific factors, we used structured content analysis following Mayring (2014).

### 4.3. Statistical analyses

**Study I.** The primary outcome (posttreatment heat-pain tolerance) was analyzed using linear models (analysis of covariance, ANCOVA) with the corresponding baseline outcome of heat-pain tolerance as a covariate. We wanted to investigate how the dog affects pain perception in the two different contexts—pain assessment and pain therapy—by comparing “pain” with “pain + dog” and “pain + placebo” with “pain + placebo + dog.” For the corresponding self-reported ratings of pain intensity and unpleasantness at participants’ limits of heat-pain tolerance, we also conducted linear models (ANCOVAs) comparing “pain” with “pain + dog” and “pain + placebo” with “pain + placebo + dog.” In each model, the respective corresponding baseline outcomes were used as covariates. To analyze the subscale *trustworthiness* of the CRF-S questionnaire, we conducted a linear model (analysis of covariance, ANCOVA) to investigate whether the presence of the dog affected the perception of the participants. The dog was used as an independent factor and the corresponding baseline outcome of the subscale *trustworthiness* was used as a covariate.

**Study II.** The primary outcomes (posttreatment heat-pain tolerance and the corresponding self-reported ratings of pain unpleasantness and intensity at participants’ limits of heat-pain tolerance) were analyzed using linear models (analysis of covariance, ANCOVA) with the corresponding baseline outcomes as a covariate. For each outcome, we calculated prespecified separate models to analyze the dog effect, the placebo effect, and the interaction effect of the dog and the placebo. We quantified the dog effect by comparing the dog-treatment condition with the no-treatment condition. The placebo effect was quantified by comparing the placebo-treatment condition with the no-treatment condition. The interaction effect of the dog and the placebo was estimated in a model that included all four conditions and that employed the placebo and the dog as between-subject factors.

**Study III.** The frequencies of the categories for factor hypotheses, specific factors, and nonspecific factors were analyzed. Descriptive analyses were carried out using R for Mac, version 1.4.1103.

## 5. Summary of the results

**Study I.** The results of study I show that the dog had no effect on posttreatment heat-pain tolerance or on the self-reported ratings of pain unpleasantness at participants' limits of heat-pain tolerance. However, regarding the self-reported ratings of pain intensity at participants' limits of heat-pain tolerance, there was a difference between participants in the animal-assisted condition in the pain-assessment context compared to participants with no animal-assisted intervention in the pain-assessment context. Participants in the animal-assisted condition experienced higher pain intensity at their limits of heat-pain tolerance with a mean of 7.57 compared to the mean of 6.83 in the condition "pain" (difference = 0.40, CI = 0.02 to 0.79, $p$ = 0.041). Participants also did not perceive the study investigator to be more trustworthy in the presence of the dog compared to when no dog was present.

**Study II.** Study I did not reveal any differences in the means of posttreatment heat-pain tolerance between the conditions. Regarding the self-reported ratings of pain, we found differences comparing the dog-treatment with the no-treatment conditions. Participants in the dog-treatment condition experienced heat-pain tolerance to be less unpleasant with a mean of 6.39 compared to participants in the not-treatment condition, who had a mean of 7.75. Further, we found a significant interaction of the dog and the placebo in the unpleasantness ratings, which were higher in the combined dog and placebo-treatment than in the separate dog-treatment and placebo-treatment (difference = 1.19, CI = 0.33 to 2.05, $p$ = 0.007). Finally, we found a trend in the self-reported ratings of pain intensity at participants' limits of heat-pain tolerance at posttreatment. Participants in the dog-treatment condition rated pain intensity to be less intense with a mean of 7.17 compared to a mean of 7.96 for the ratings by participants in the no-treatment condition (difference = -0.44, CI = -0.89 to 0.02, $p$ = 0.060). There was a trend for an interaction of the dog and the placebo in the intensity ratings, which were higher in the combined dog and placebo-treatment than in the separate dog-treatment and placebo-treatment (difference = 0.71, CI = -0.05 to 1.47, $p$ = 0.077).

**Study III.** This systematic review identified eleven categories describing hypotheses about factors, nine categories describing specific factors of animal-assisted interventions, and 14 categories for nonspecific factors.

**Factor hypotheses:** 1) human–animal interaction (32.56%), 2) not specified (16.86%), 3) movement by the animal (13.95%), 4) social facilitator or catalyst (12.21%), 5) relationship with an animal (9.3%), 6) other (8.72%), 7) presence of animal (6.98%), 8) physical contact (5.81%), 9) social or emotional support (3.49%), 10) taking care of an animal (2.91%), 11) physical activity (2.91%).

**Specific factors**: 1) animal (88,37%), 2) interaction with an animal (46.51%), 3) movement by the animal (17.44%), 4) physical contact (12.79%), 5) taking care of an animal (12.21%), 6) training an animal (6.39%), 7) other (6.39%), 8) social interaction (5.81%), 9) relationship with an animal (2.32%).

**Nonspecific factors**: 1) therapeutic aspects (37.21%), 2) social interaction (33.14%), 3) physical activity (29.65%), 4) activity, distraction, or absorption (27.91%), 5) education or training (15.17%), 6) plush or toy animal (11.63%), 7) animal (8.72%), 8) environment (8.14%), 9) interaction with something like an animal (6.35%), 10) movement or rhythm (5.81%), 11) relaxation (5.23%), 12) watching or seeing animal (4.65%), 13) other (4.65%), and 14) novelty (1.74%).

## 6. Discussion

Although an increasing number of studies are investigating the effects of animal-assisted interventions and showing promising results, the mechanisms potentially responsible for these effects remain underexplored (López-Cepero, 2020). The literature on animal-assisted interventions assumes that the animal is the specific factor that contributes to these effects (Marino, 2012). In contrast, evidence from placebo research suggests that contextual rather than specific factors contribute to the outcome to a larger extent (Wager & Atlas, 2015).

The three studies that make up this thesis explored the mechanisms of animal-assisted interventions. The first aim of this thesis was to explore the mechanisms of animal-assisted intervention on experimentally induced pain in healthy participants to distinguish whether the analgesic effects are due to the presence of a dog (Study I) or due how the dog is embedded into the treatment rationale (Study II). The second aim of this thesis was to explore which factors were named as possible mechanisms of animal-assisted interventions in previous research and which factors were defined as specific or nonspecific (Study III).

The two aims of the thesis will be discussed separately in the following. The role of the animal and contextual factors in animal-assisted interventions will be discussed first. Then, based on the results of the systematic review, I will discuss which factors were named as possible mechanisms of animal-assisted interventions in previous research and which factors were defined as specific or nonspecific. Finally, I will summarize the strengths and limitations, offer a conclusion and detail the implications for future research.

### 6.1. Exploring the role of the animal in animal-assisted interventions for pain

The findings of study I show that the mere presence of a dog had no positive analgesic effect on experimentally induced pain in healthy participants when the dog was not part of the treatment rationale. Participants' heat-pain tolerance did not increase when a dog was present. Instead, self-reports show that participants experienced pain to be more intense at the limits of heat-pain tolerance when the dog was present compared to when no dog was present. Further, participants did not perceive the study investigator to be more trustworthy when a dog was present compared to when no dog was present.

Study II found that when a positive treatment rationale was provided for the presence of the dog, the dog had a positive effect on participants' pain perception. While no differences were found in posttreatment heat-pain tolerance between participants receiving the dog treatment or no treatment, the results of the self-reported ratings show that participants experienced pain to be significantly less unpleasant and tendentially less intense at the limits of heat-pain tolerance in the presence of the dog compared to participants in the no-treatment group.

The findings from Study I and Study II contradict the assumption that the analgesic effects of animal-assisted interventions are mediated by the animal's providing direct social support or strengthening the alliance between the participant and the treatment provider. Instead, they suggest that the analgesic effects of animal-assisted interventions are not due to the animal but rather due to how the animal is embedded in the treatment rationale.

In the context of pain treatment, these findings contradict previous studies on animal-assisted interventions suggesting that the animal is responsible for the analgesic effects of animal-assisted interventions (Calcaterra et al., 2015; Harper et al., 2015; Silva & Osório, 2018; Zhang et al., 2021), but they are in line with evidence from research on placebo analgesia showing that treatment rationales that evoke positive treatment expectations are crucial for pain management (Skyt et al., 2020; Vase et al., 2003). Depending on the information provided in the treatment rationale, the same pain treatment can lead to different analgesic outcomes (Bingel et al., 2011). This has been demonstrated in open and hidden paradigms. It is well known that the hidden administration (unexpected) of a treatment is less effective than open administration (expected) in analgesic treatments. Several studies have shown that the effects of analgesic treatments decrease when patients are not aware that they are receiving a treatment (Amanzio et al., 2001; Benedetti, Maggi, et al., 2003; Benedetti, Pollo, et al., 2003; Colloca et al., 2004; Levine & Gordon, 1984).

In a broader context, these findings underline that treatment rationales lead us to attribute a meaning to interventions and that we respond to those meanings (Moerman, 2006; Moerman & Jonas, 2002). In Study I, the dog was intentionally given no meaning related to pain management. In Study II, the dog was embedded in the treatment rationale and given a meaning that suggested that the dog can lead to pain reduction. By stating that the dog had nothing to do with the study, it is possible that participants attributed no meaning or a negative meaning to the dog (e.g., that the dog is disturbing). It is known that the administration of an analgesic intervention without any expectations, with negative expectations (Bingel et al., 2011), or without verbal suggestions (Bąbel et al., 2017) can result in a negative treatment response and negative pain maintenance. This would also explain why the presence of the dog had no analgesic effect or even a negative effect on pain perception in Study I. These findings thus suggest that participants responded to the meaning given to the dog and not to the dog per se.

This also gives us reason to assume that it is important to integrate animals into treatment rationales in order to enhance the effects of interventions. This presents a challenge, however, for animal-assisted interventions. It has been suggested that effective treatment rationales should be understandable, credible, and compelling (Trachsel, 2019). Further, treatment rationales have to be evidence-based and conform to research findings (Beutler, 1998; Blease et al., 2016; Blease et al., 2018). Given the lack of available evidence regarding the mechanisms of animal-assisted interventions, it is impossible for practitioners to provide patients with evidence-based treatment rationales in animal-assisted interventions.

In addition, the findings the studies presented here suggest that—like a placebo—it might not be the animal *per se* that contributes to pain relief but rather the meaning given to the animal. Considering that meaning is relevant in every treatment (Moerman, 2006), it seems likely that the meaning given to the animal might generally be important for treatment response in animal-assisted interventions and not only for pain management. While it has been acknowledged that animal-assisted interventions might be susceptible to placebo effects (Marino, 2012), the possibility that animals could function like placebos has not been considered. Studies of placebo effects have demonstrated that psychosocial and contextual factors related to patients' perceptions of the intervention—such as information about the intervention, expectations, and the context of the intervention—can contribute to the overall effect of intervention (Bingel et al., 2011; Vase et al., 2002; Vase et al., 2003).

The possibility that an animal could share the same mechanisms as a placebo would also contradict and question the general assumption in the field of animal-assisted interventions that animals are responsible, as specific factors, for the effects of animal-assisted interventions. However, this does not necessarily mean that other factors related to the animal are not relevant, but there is currently a lack of evidence for this. It therefore seems to be important to pursue this question specifically in order to understand how animal-assisted interventions work and what role the animal plays in them.

If the animal itself is not as important as generally believed in the field of animal-assisted interventions, this would have implications for the design of these interventions—especially when taking into account that animal-assisted interventions can be stressful and challenging for the animals (Ng et al., 2021). If the meaning given to the animal and not the animal itself is crucial for the effect, then it seems reasonable to question to what extent it is justified to incorporate living animals in interventions. Further research should address whether the animal can be substituted, for example, by using robots. The reason for this suggestion comes from a study that showed that both a living dog and a robot dog significantly decreased loneliness in elderly patients, which suggests that a living animal is not necessary (Banks et al., 2008).

### 6.2. Specific and nonspecific factors in animal-assisted interventions

The results of the systematic review (Study III) showed that a substantial portion (16%) of the analyzed studies did not specify factor hypotheses referring to the concrete working mechanisms of animal-assisted interventions in their introduction or methods. The majority of the studies (84%) did, however, provide a hypothesis. The most frequently mentioned factor hypothesis was that human–animal interaction (HAI) leads to the effects of animal-assisted interventions, followed by the movement of the animals, animals as social facilitators or catalysts, and the presence of an animal. Regarding the specific factors, we identified that “animal” and “interaction with animal” were the most frequent categories when comparing the experimental and control conditions of previously published studies on animal-assisted interventions. By using different control conditions, the studies also controlled for specific factors such as movement, physical contact, or the relationship with the animal. This finding confirms that the majority of studies considered the animal as a specific factor of animal-assisted interventions. The analysis of the nonspecific factors revealed that previous studies already controlled for several nonspecific factors, such as therapeutic aspects and social interactions. Some of the studies also controlled for specific elements of the animal, for example, by defining the presence of the animal (Tepper et al., 2021) or simply walking with a dog (Syzmanski et al., 2018) as nonspecific factors.

These findings are not surprising and reflect some of the current problems within the research field of animal-assisted interventions. First, they show that with a few exceptions, authors largely do not explain *how* animal-assisted interventions work. Second, they reveal that studies simply assume that the animal or the interaction with the animal is responsible for the specific effects—without specifying which components of the animal or of the interaction possibly contribute to the outcome. The majority of researchers thus still support the general concept that animals are the panacea of animal-assisted interventions (López-Cepero, 2020). This leads to a rather exaggerated and probably unrealistic view, namely, that the animal itself is sufficient to generate positive effects (Fine et al., 2019). This also neglects the fact that the animal is a complex stimulus and that interaction with animals has many different components (Marino, 2012). Because animals are complex, it seems reasonable to require that researchers explicitly define which factors of the animal or the interaction with the animal positively affect the intervention (López-Cepero, 2020). By avoiding determining specific factors, animals can be perceived as passive tools rather than as active factors in the therapeutic process (Kruger & Serpell, 2010). It is worth mentioning that some of the included studies in the systematic review controlled for specific elements of the interaction with the animal or the animal itself as nonspecific factors, for example, walking with a dog (e.g., Syzmanski et al., 2018) or the sound of the animal (e.g.,Park et al., 2019). While this is promising, these studies currently represent the minority in the field of animal-assisted interventions. More studies are needed that systematically control for specific factors.

Moreover, animal-assisted interventions take place in very complex settings. While, strictly defined, there is no animal-assisted intervention without *the animal* (Marino, 2012), such interventions do not only consist of the animal but also of the handler, the patient, and the larger therapeutic setting itself (Menna et al., 2019). It is evident that researchers should take all these factors into account when addressing the question of *how* animal-assisted interventions work, rather than assuming that the animal is central for the effects of animal-assisted interventions and ignoring all other factors.

This also addresses the need to consider contextual factors. It is interesting that while animal-assisted interventions are thought to be vulnerable to placebo effects because the nature of the treatment is usually evident to the subjects (Marino, 2012), we did not identify a single study that controlled for potential placebo effects.

Based on the results of study I and II and evidence showing that contextual factors explain a significant portion of the effects of interventions rather than the specific intervention itself (Wager & Atlas, 2015), it seems likely that these factors also explain a significant portion of the effects of animal-assisted interventions. For this reason, it appears essential for the field of animal-assisted interventions to focus more on the influence of contextual factors.

### 6.3. Strengths and limitations

There is an acknowledged need for animal-assisted interventions to increase their internal validity (López-Cepero, 2020), and there is a recognized lack of high-quality studies on the effects of animal-assisted interventions on pain and the mechanisms involved (Waite et al., 2018). In Study I and Study II, we conducted a randomized control trial with a highly standardized study procedure to systematically control for confounding variables and increase the internal validity. The study design of Study I and II ensured internal validity, but the external validity is limited: only healthy participants were included, so the results cannot be generalized to patients. While experimentally induced pain in healthy participants is regarded as a good model for clinical pain (Peerdeman et al., 2016), the results may not be generalizable to a clinical population. However, research on placebo analgesia has found “that studies on healthy individuals may underestimate the magnitude of the placebo analgesic effect in patients" (cited from Forsberg et al., 2017, p. 394), so our findings could also be relevant for patients.

Furthermore, the standardized study procedure and the limited interaction between participants and the dog might not represent a typical animal-assisted intervention. However, the aim of Study I and Study II was to investigate whether and how the presence of a dog can have an analgesic effect. Furthermore, only one dog was included in both studies, so the effects with other animals or dog species are unclear. Moreover, another limitation is that we did not directly compare groups receiving different treatment rationales for the presence of the dog. Instead, we compared the results of one of our previous studies (Wagner et al., 2021) with the findings of the current study. It is thus possible that other unknown factors—other than including the dog in the treatment rationale or not—led to the differences between the two studies.

Regarding Study III, a strength of this systematic review was that we included all animal-assisted intervention studies with an active control group. This allowed us to analyze studies as broadly as possible. Further, we also included dissertations and therefore counteracted publication bias. Nevertheless, the results of the third study must also be interpreted with caution. We only included studies published in German and English, so we did not include all studies. Further, the information about conditions was often restricted, so it is possible that not all potential specific and nonspecific factors were assessed in the review. Finally, studies without an active control group were excluded, but it is possible that these studies defined factor hypotheses more specifically, so the results of this systematic review are only applicable to studies that used an active control group.

### 6.4. Conclusions and implications for future research

Despite limitations, this thesis has determined that analgesic effects in animal-assisted interventions are likely caused by contextual factors, which makes the relevance of the animal and animal-related factors uncertain. More specifically, the evidence indicates that a treatment rationale that gave the dog a meaning led to an analgesic effect. Based on evidence showing that contextual factors can explain a significant portion of our treatment responses (Rossettini et al., 2020; Wager & Atlas, 2015), it can be assumed that contextual factors are important not only for the effects of animal-assisted interventions on pain but probably also for animal-assisted interventions more generally.

This thesis has also shown that the majority of previous studies on animal-assisted interventions have continued to assume that the animal or the interaction with the animal are the specific factors of animal-assisted interventions and to account and control for the effects of animal-assisted interventions accordingly.

Although the evidence from Study I and Study II suggests that contextual factors are relevant, this does not mean that other animal-specific factors, such as the animal or the interaction with the animal, are not also relevant in animal-assisted interventions, but there is a lack of evidence to establish if this is the case. It therefore seems necessary that supporters of the idea that animal-specific factors are important in animal-assisted interventions should provide this evidence.

Based on the findings of this thesis, it is urgent to reconsider the explanatory model for the effectiveness of animal-assisted interventions. More precisely, instead of only focusing on *the animal* in animal-assisted interventions, researchers and practitioners should start to include contextual factors in their explanatory models. Future research should thus pursue the following objectives: a) define and investigate more explicitly which factors of the animal or the interaction with the animal contribute to the beneficial effects of animal-assisted interventions, and b) investigate the influence of contextual factors in animal-assisted interventions.

It is necessary to describe and investigate the mechanisms of animal-assisted interventions explicitly, so studies should define exactly what about the animal or the interaction with the animal lead to an improvement (López-Cepero, 2020). A better understanding of which factors about the animal or the interaction with the animal are important might also be relevant in determining whether we should use animals at all or whether we can facilitate these factors in some other way. For example, it could be helpful if studies incorporate control conditions that specifically control for certain factors of the animal or the interaction with the animal. To systematically control for certain factors of the animal, animal-like objects (e.g., robots) could be an informative approach. For the interaction, it could be helpful to compare different types of interactions in different conditions and explicitly describe what was done in which condition.

Further, researchers and practitioners should perceive the context as a potential amplifier and as a key contributor to therapeutic outcomes (Di Blasi & Kleijnen, 2003).

Systematically investigating the impact of contextual factors that are known to influence patients' perceptions of animal-assisted interventions can help us better understood how important the animal is and also how to enhance the effects of animal-assisted interventions. Based on the findings of this thesis, an open-and-hidden experimental study design, for example, could be helpful to disentangle potential expectation effects from the effects of the intervention (Zion & Crum, 2018). Studies could compare the effects of different treatment rationales in which animals are given different meanings (e.g., a positive meaning, a negative meaning, or no meaning). Further, it would also be interesting to investigate if the manner in which the healthcare provider supplies the treatment rationale also affects the outcome of the intervention (Annoni & Miller, 2016; Caspi & Bootzin, 2002; Gaab et al., 2019). This could help us better understand the role of the animal and also the role of contextual factors in animal-assisted interventions.

Portraying animals as a panacea only reinforces the fantasized image of animal-assisted interventions (López-Cepero, 2020) and prevents animal-assisted interventions from being considered an evidence-based intervention (Kruger & Serpell, 2010; López-Cepero, 2020) and the field from moving forward. Because the current evidence does not support the conclusion that animals are a panacea, researchers and practitioners must be more realistic in their explanations of the efficacy of animal-assisted interventions (Fine et al., 2019) and more transparent about the fact that it remains unclear how important the animal truly is in animal-assisted interventions (Marino, 2012).

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# Appendices

## Appendix A

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### Study I

**Wagner, C.,** Gaab, J., Locher, C., Hediger, K. (2021): Lack of Effects of the Presence of a Dog on Pain Perception in Healthy Participants - a Randomized Controlled Trial. *Frontiers in Pain Research*

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# Lack of Effects of the Presence of a Dog on Pain Perception in Healthy Participants—A Randomized Controlled Trial

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Animal-assisted interventions (AAIs) have been shown to be effective in the treatment of pain. Studies suggest that relationships with animals can have comparable qualities to relationships with humans and that this enables animals to provide social support. Further, the presence of an animal can strengthen the therapeutic alliance between patients and treatment providers. This suggests that the analgesic effects of AAI might be mediated by social support from an animal or by strengthening the alliance between the patient and the treatment provider. To test these assumptions, we examined the effects of the presence of a dog on experimentally induced pain in a pain assessment and a pain therapy context. Hundred thirty-two healthy participants were randomly assigned to the conditions "pain," "pain + dog," "pain + placebo," or "pain + placebo + dog." We collected baseline and posttreatment measurements of heat-pain tolerance and the heat-pain threshold and of the corresponding subjective ratings of heat-pain intensity and unpleasantness as well as of participants' perceptions of the study investigator. The primary outcome was heat-pain tolerance. The presence of the dog did not influence the primary outcome ("pain" vs. "pain + dog": difference = 0.04, CI = −0.66 to 0.74, $p$ = 0.905; "pain + placebo" vs. "pain + placebo + dog": difference = 0.43, CI = −0.02 to 0.88, $p$ = 0.059). Participants did also not perceive the study investigator to be more trustworthy in the presence of the dog ("pain" vs. "pain + dog": difference = 0.10, CI = −0.67 to 0.87, $p$ = 0.796; "pain + placebo" vs. "pain + placebo + dog": difference = 0.11, CI = −0.43 to 0.64, $p$ = 0.695). The results indicate that the mere presence of a dog does not contribute to pain reduction and that the analgesic effects of AAI that previous studies have found is not replicated in our study as AAI did not increase perceived social support and had no effect on the alliance between the participant and the treatment provider. We assume that the animal most likely needs to be an integrated and plausible part of the treatment rationale so that participants are able to form a treatment-response expectation toward AAI.

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**Clinical Trial Registration:** This study was preregistered as a clinical trial on www.clinicaltrials.gov (Identifier: NCT0389814).

**Keywords:** pain, animal-assisted intervention, expectation, treatment rationale, placebo, social support

## INTRODUCTION

Animal-assisted interventions (AAIs) are "goal-oriented and structured interventions that intentionally incorporate animals in health, education and human service for the purpose of therapeutic gains in humans" (1). AAIs have a wide range of clinically relevant effects, such as lowering symptoms in patients with depressive and anxiety disorders (2–7), improving neurohormone levels in adult patients diagnosed with advanced heart failure (8), and reducing cortisol levels in adult healthcare professionals as well as in children with insecure attachment (9, 10). Moreover, a recent meta-analysis has suggested that AAI can be an effective therapy for relieving pain in patients across all age groups (7). For example, children exhibited a significant reduction in pain perception and experience after an AAI compared to a control intervention without an animal present both in an acute pediatric setting (11) and after surgery (12). Similar effects have been reported in AAI studies on pain syndromes in adults. Patients who had 15-min visits with a therapy dog before receiving standard postoperative treatment had significantly lower perceptions of pain after total joint arthroplasty than patients who only received standard postoperative treatment (13). Adult patients with chronic pain perceived significantly less pain when they spent their waiting time with a therapy dog compared to patients in a waiting room without a dog present (14). Further, patients with fibromyalgia showed a greater decrease in pain when they were in a group that received a 20-min session with a therapy dog and its handler compared to a group that received the session with only the handler (15). However, not all studies found that AAI leads to pain reduction (16, 17). Further, previous studies differed with regard to the study design and also showed methodological weakness, such as lack of no randomization or insufficient control groups (7). Thus, the evidence base for the effects of AAI on pain is still weak, and high-quality studies are warranted to investigate the effects and the mechanisms by which AAI leads to pain reduction (7).

Although these results are promising, the mechanisms by which AAI leads to pain relief are yet to be fully understood, since it is still unclear how animals contribute to pain relief (7). Research on social support can suggest possible explanations. The mere presence of another person has been shown to lead to a reduction of perceived pain (18). This effect on pain can be found in both active (19, 20) and passive forms of social support (18), and it does not seem to depend on the degree of the relationship, that is, on whether the person is a partner, friend, or stranger (18, 21). Previous research has highlighted that relationships with animals can have comparable qualities to relationship with humans (22, 23) and that pets can provide social support for their owners (24). Furthermore, the presence of an animal can also positively influence how we perceive others and strengthen the therapeutic alliance between the patient and the treatment provider (25–27). This is of relevance since the therapeutic alliance is an important determinant of treatment outcomes in medical interventions (28), psychotherapy (29), and placebo interventions (30, 31).

The analgesic effects of AAI could thus be mediated by providing direct social support for the patient or by strengthening the alliance between the patient and the treatment provider. To test these assumptions, we examined the effects of AAI with a dog on experimentally induced pain in healthy participants, mimicking two different clinical settings: pain assessment and pain therapy. We hypothesized that participants would show increased heat-pain tolerance in both settings when a dog is present based on the assumption that the mere presence of a dog can act as direct social support. We also hypothesized that participants would show increased heat-pain threshold and decreased subjective ratings of pain intensity and unpleasantness of heat-pain tolerance and threshold in both settings where a dog is present. Moreover, we also hypothesized that the presence of a dog would strengthen the alliance between participant and the treatment provider. To examine possible effects of the presence of an animal on the therapeutic alliance, we assessed participants' perception of the study investigator in all pain assessments.

## METHODS

### Design

We conducted a randomized controlled trial with four experimental conditions and healthy participants. In the pain assessment context, experimental pain was induced and assessed with a standardized experimental heat-pain paradigm, simulating a setting in which persons experience pain without treatment. In the pain therapy context, experimental pain was induced, assessed with a standardized experimental heat-pain paradigm, and, in addition, we employed an established expectation-induced placebo paradigm. In this context, we introduced placebo as therapeutic intervention for the experimentally induced pain to simulate a setting in which persons experience pain and get a treatment. A positive verbal suggestion was administered to induce expectation in relation to the placebo intervention. No positive verbal suggestion was administered in relation to the dog's presence to suppress possible expectation effects. Participants were randomly assigned to pain assessment ("pain"), pain assessment in the presence of a dog ("pain + dog"), pain assessment and a placebo intervention only ("pain + placebo"), or pain assessment and a placebo intervention in the presence of a dog ("pain + placebo + dog").

The study protocol ensured the dog's welfare at any time. We conducted all dog sessions according to the guidelines of the International Association for Human-Animal Interaction Organizations (1).

The study was conducted between April 2019 and July 2019. The study protocols and the informed consent of the study were approved by the Ethics Committee of the Faculty of Psychology at the University of Basel, Switzerland.

## Participants

Through online advertisements, 284 participants were recruited for a study on pain perception at the University of Basel. The online advertisement did not contain any information about the possible presence of a dog to prevent attracting participants with an affinity for dogs. The online advertisement contained a link to a short questionnaire. Participants interested in participating had to complete this questionnaire first to check for eligibility and inclusion and exclusion criteria. Participants had to be (a) right-handed (32) and (b) 18 years or older to be included in the study. Exclusion criteria were (a) any acute or chronic disease as well as skin pathologies, (b) current medications or current psychological or psychiatric treatment, (c) pregnancy, (d) nursing, (e) current or regular drug consumption, (f) insufficient German language skills, (g) a fear of dogs, (h) dog-hair allergies, and (i) previous participation in studies using a heat-pain paradigm.

Of the total 284 screened participants, 201 met the inclusion criteria. All eligible participants received the study information, which contained the whole study procedure, aims, participants' rights, notification of the possible presence of a dog, and a selection of study appointments. After receiving all information about the study, a total of 159 participants were willing to participate in the study (a detailed overview of the enrollment can be found in the **Supplementary Material**, F1). Participants who were still willing to participate were asked to sign in for a study appointment. As soon as the scheduled $N = 132$ participants confirmed their study appointments, the remaining people were informed that there were no further appointments available. Participants attended one appointment that took about 70 min. The study compensation was CHF 80. Psychology students had the opportunity to obtain credit points for study.

Participants were blinded regarding the aims of our study and the placebo intervention. At the end of the study, all participants provided delayed informed consent, which debriefed them about the aims of the study. Participants were able to withdraw data from the study if they did not consent to participate anymore.

## Randomization

We used an adaptive randomization to apportion male participants over all four conditions because we expected more women than men to participate in the study. This approach automatically considered the previous gender allocation in the four conditions and influenced the probability of the next gender allocation. This ensured that gender was equally represented in all four conditions ("pain," "pain + dog," "pain + placebo," "pain + placebo + dog," each $N = 33$). The randomization was conducted with Microsoft® Excel for Mac, version 16.16.17. The first author entered participant's code and gender into the Excelfile which then automatically allocated participants to one of the four study conditions. Participants did not know in which condition they were until the treatment phase. The study investigators, however, were not blinded as they knew in which condition the participant was.

## Procedure

After guiding a participant into the room, the study investigator explained the study procedure to the participant and asked them to fill in the sociodemographic questionnaire, which took about 10 min. Then baseline measurements of heat-pain tolerance and threshold as well as subjective pain ratings were collected for each participant. This baseline procedure lasted 20 min.

After these baseline measurements, the treatment phase was conducted; it took a total of 15 min. Participants in the AAI conditions were introduced to the dog. They were deceived about the real reason for the dog's presence (to investigate the effect of the mere presence of a dog) so as to suppress possible expectation effects. Participants were informed that the dog had to be acquainted with the study procedure to be able to participate in a future study. They were told that the dog would rest quietly on a blanket and would not disturb the study procedure. To standardize the interaction between the participants and the dog, all participants were asked to greet and pet the dog as soon as it entered the room. We explained that it would be easier for the dog to relax on a blanket when allowed to greet the new person in the room. The duration of the interaction between the participant and the dog was kept to minimum, that is, under 1 min. During the greeting phase the study investigator also interacted with the dog, if the dog approached the investigator. After this greeting phase, the dog was asked to lie on its blanket, which was always next to the participant so that participants could still see the dog. Participants did not touch the dog during the further procedure. The study investigator also did not interact with the dog during the further procedure. The dog was a one-and-a-half-year-old female Golden Retriever used interacting with unfamiliar people. All conditions without a dog were carried out by three other female study investigators. All dog conditions were performed by the same female study investigator, who was the dog's owner. The reason for this was to ensure that the dog is not stressed. Leaving the dog in a setting with unfamiliar individuals without the dog's owner would have been inappropriate from an ethical standpoint. All study investigators were instructed to follow a study manual describing all the procedures and the instructions of the participants.

After this introduction, the study investigator applied an inert white cream on the participants in all four conditions. However, the rationale differed in the four conditions. Participants in the two placebo conditions ("pain + placebo" and "pain + placebo + dog") were told: "You will receive a generic analgesic cream with the active ingredient lidocaine. Lidocaine is the main ingredient of the analgesic cream Stilex (a local anesthetic commonly used in Switzerland). The cream prevents and treats itchy and painful skin problems, such as light burns, sunburns, or insect bites. The efficacy of lidocaine has been evidenced in several high-quality studies." Participants in the two pain-assessment conditions ("pain" and "pain + dog") were told: "You will receive a cream (hand cream) to moisturize the skin. This allows accurate pain measurements."

After the treatment phase, posttreatment heat-pain measurements and subjective ratings of pain intensity and unpleasantness were performed in an identical manner to the baseline assessments and lasted 20 min. At the end of the study, all participants provided delayed informed consent (see **Figure 1** for the timeline of the study procedure).

# MEASURES

## Pain Ratings

We assessed heat-pain tolerance and heat-pain threshold following the design of previous trials (33–35). We defined posttreatment heat-pain tolerance as the primary outcome. Heat-pain tolerance is related to affective and motivational aspects (33, 36) and implies experiencing maximum discomfort, which results in greater subjective stress (33). In addition, it has been associated with pathological pain, as there is an inverse relationship between ischemic pain tolerance and the perceived severity of clinical pain (37). Posttreatment heat-pain threshold was defined as a secondary outcome. Both, the heat-pain threshold and heat-pain tolerance were determined using the Thermal Sensory Analyser (Medoc, Ramatishai, Israel; TSA 2). The heat-pain threshold was measured prior to heat-pain tolerance in order to minimize interference between the two outcomes (34, 35). The TSA 2 is a pain management system for qualitative assessment of pain and measures sensory thresholds such as heat-induced pain. The employed heat stimuli did not entail any significant danger and have already been used in previous studies in our lab (30, 34, 35, 38, 39). Participants were able stop the stimuli at any time during each experimental run.

The study investigator administered the heat stimuli to the right volar forearm of the participant using a 30 × 30 mm Peltier device (Medoc, Ramatishai, Israel; TSA 2). The thermode of the TSA 2 was fixed at two different locations (locations Y and X, determined using a positioning device). Location Y was placed one-third away from the elbow, while location X was placed two-thirds away from the elbow. Half of the participants were randomly assigned to start with location Y for the baseline heat-pain measurement and to switch then to location X for the posttreatment heat-pain measurement. The other half of the participants started with the opposite location, location X first for the baseline heat-pain measurement followed by location Y for the posttreatment measurement. The reason for moving the thermode was to avoid effects of sensitization or habituation (40).

Before starting with the actual heat-pain measurement, participants performed a practice round to experience how the heat stimuli work and how to handle the device including how to stop the heat stimuli. After this practice round, we started with the baseline measurements. We first assessed heat-pain threshold which was determined by the method of limits. Participants were instructed to press the button to determine the turning point from perceiving warmth to perceiving pain. The temperature was increased from the baseline (32°C) at a rate of 0.5°C/s. When participants indicated that the pain threshold had been reached, the device resumed from its baseline (32°C) with a rise of 0.5°C/s. This procedure was repeated three times in a row (35). The heat-pain threshold was defined as the average of the three measurements.

Afterward, heat-pain tolerance was determined using the method of limits. Participants were asked to stop the increasing heat stimulus at the moment they could not stand the heat any longer. The temperature increased from the baseline (32°C) at a rate of 0.5°C/s. As soon as participants indicated that their pain tolerance had been reached, the device resumed from its baseline (32°C) with a rise of 0.5°C/s. Again, this procedure was repeated three times in a row (35). To avoid physical injury, the pain tolerance measurement stopped at a temperature of 52°C (41). Heat-pain tolerance was defined as the average of the three measurements (42).

The secondary outcomes were the subjective pain-intensity rating of heat-pain tolerance, the subjective pain-intensity rating of the heat-pain threshold, the subjective unpleasantness rating of heat-pain tolerance, the subjective unpleasantness rating of the heat-pain threshold, and pain expectation.

Subjective pain-intensity and unpleasantness ratings of heat-pain tolerance and of the heat-pain threshold were measured with a visual analogue scale (VAS). The VAS ranged from 1 to 10 (1 = "not intense at all" or "not unpleasant at all"; 10 = "the most intense pain I have ever experienced" or "the most unpleasant pain I have ever experienced"). Participants were asked to evaluate subjective pain intensity and unpleasantness after each objective pain measurement. Subjective pain intensity and unpleasantness are assessed pain parameters in heat pain paradigm studies (43). Intensity refers to cognitive dimensions of pain, whereas unpleasantness refers to the affective dimension of pain (44).

After the treatment phase and before conducting the posttreatment heat-pain measurements, participants were asked to indicate on a VAS how intense they expect pain to be after the treatment phase. These expectation ratings were made on the same VAS (ranging from 1 to 10) as those for pain intensity and pain unpleasantness (35). Pain expectation was assessed to control if the expectation-induced placebo intervention was successful.

## Participants' Perception of the Study Investigator

Participants' perception of the study investigator was assessed with the Counselor Rating Form–Short Version (CRF-S) (45). The CRF-S is a 12-item questionnaire for measuring an individual's perception of the therapist on the following three subscales: *trustworthiness*, *expertness*, and *attractiveness*. The questionnaire contains items on a 7-point Likert scale, ranging from 1 (not very) to 7 (very). For this study, only the subscale *trustworthiness* was analyzed because it is most central to the therapeutic alliance. Studies indicate that patient trust in the physician is of particular importance in clinical practice (46–48). The subscale *trustworthiness* included the following four items: *honest, reliable, sincere and trustworthy.* The CRF-S was used twice in the study: first after the baseline assessments and second after the posttreatment assessments. Due to an

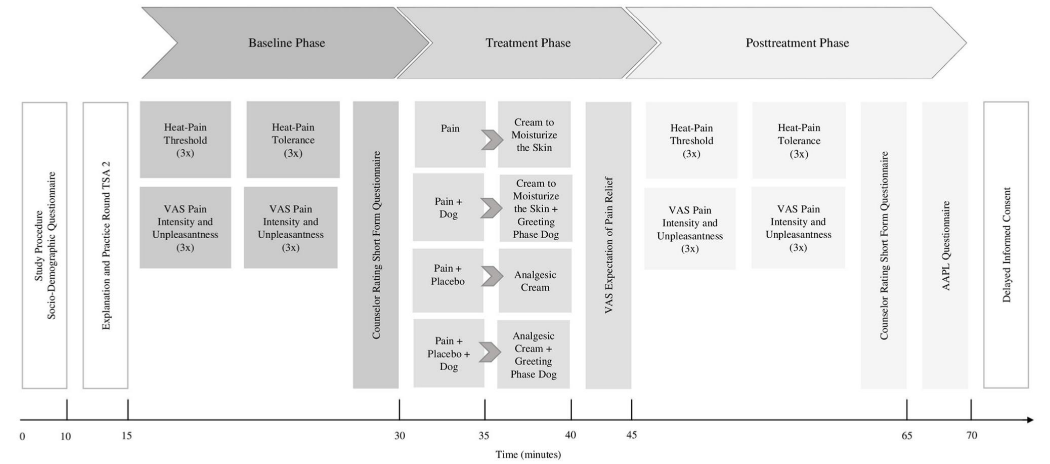


**FIGURE 1** | Timeline of the study procedure.

online survey programming error the item *honest* of the subscale *trustworthiness* has not been collected within the first 31 participants. As the other tree items of the subscale *trustworthiness* were completed, this has been defined as item-level missingness (49). To treat these missing items, the mean across available items was taken, as recommended by Roth et al. (50).

## Demographic Variables

Before the study start, we assessed demographic variables (i.e., age, sex, nationality, family status, educational level, employment situation, and income) with the sociodemographic questionnaire.

## Dog Related Variables

The study investigator quantified the intensity of the contact between participant and dog during the greeting phase with a 5-stage Likert scale. The Likert scale ranged from 1 = "no contact at all" to 5 = "very high intensity of contact." Further, we assessed the participants affinity for dogs at the end of the study with a short self-developed questionnaire. We used a 5-stage Likert scale, with 1 indicating that participants like dogs "not at all" and 5 indicating "very much."

## Data Analysis

We estimated that a sample size of $N = 128$ with a power of 0.8, an alpha error of 5% and a beta error of 20% would be necessary to detect a medium size effect of $f = 0.25$ between the four conditions, as well as interaction between them (7). We decided to add $N = 4$ (one person in each condition) in case of dropouts during the study or data loss due to technical problems. We therefore included 132 participants.

The primary outcome (posttreatment heat-pain tolerance) was analyzed using linear models (analysis of covariance, ANCOVA) with the corresponding baseline outcome of heat pain tolerance as a covariate. We wanted to investigate how the dog affects pain perception in the two different contexts—pain assessment and pain therapy—by comparing "pain" with "pain + dog" and "pain + placebo" with "pain + placebo + dog." We also run both models for the primary outcome twice, including gender and once including age (not pre-specified).

For the secondary outcomes (the posttreatment heat-pain threshold and the corresponding subjective pain-intensity and unpleasantness ratings of heat-pain tolerance and of the heat-pain threshold), we also conducted linear models (ANCOVAs) comparing "pain" with "pain + dog" and "pain + placebo" with "pain + placebo + dog." In each model, the respective corresponding baseline outcomes were used as covariates.

With regard to the subjective expectation ratings, we conducted a linear model (analysis of variance, ANOVA) using the four treatment conditions ("pain," "pain + dog," "pain + placebo," and "pain + placebo + dog") as an independent between-subject factor.

To analyze the subscale *trustworthiness* of the CRF-S questionnaire, we conducted a linear model (analysis of covariance, ANCOVA) to investigate whether the presence of the dog affected the perception of the participants. Dog was used as an independent factor and the corresponding baseline outcome of the subscale *trustworthiness* was used as a covariate. In a second step, the same model was run with the four study investigators as a covariate. To control whether there was a difference between the four study investigators, another model was calculated including the study investigator as a factor.

The requirements for the analyses were tested using Levene's test to determine the variance homogeneity of the four conditions, the homogeneity of the regression slopes, and the

**TABLE 1** | Sociodemographic characteristics of participants.

| Condition | *N* | Age mean (*SD*) | *N* (%) female | Family status *N* | Highest educational level *N* (%) | Employment level *N* (%) |
|---|---|---|---|---|---|---|
| Pain | 33 | 26.58 (10.03) | 23 (69.69%) | Single: 32<br>Married: 0<br>Registered partnership: 0<br>Divorced: 0<br>Other: 1 | Primary school: 0<br>Secondary school: 1 (3.03%)<br>High school: 19 (57.57%)<br>University: 13 (39.39%) | Full time: 3 (9.09%)<br>Part time: 8 (24.24%)<br>None or student: 22 (66.66%) |
| Pain + Dog | 33 | 26 (6.13) | 22 (66.66%) | Single: 31<br>Married: 1<br>Registered Partnership: 0<br>Divorced:0<br>Other: 1 | Primary school: 0<br>Secondary school: 0<br>High school: 17 (51.52%)<br>University: 16 (48.48%) | Full time: 5 (15.15%)<br>Part time: 14 (42.42%)<br>None or student: 14 (42.42%) |
| Pain + Placebo | 33 | 24.64 (7.06) | 23 (69.69%) | Single: 31<br>Married: 2<br>Registered partnership: 0<br>Divorced:0<br>Other: 0 | Primary school: 0<br>Secondary school: 3 (9.09%)<br>High school: 18 (54.55%)<br>University: 12 (36.36%) | Full time: 2 (6.06%)<br>Part time: 8 (24.24%)<br>None or student: 23 (69.70%) |
| Pain + Placebo + Dog | 33 | 27.39 (9.38) | 20 (60.60% | Single: 29<br>Married: 3<br>Registered partnership: 0<br>Divorced: 0<br>Other: 1 | Primary school: 0<br>Secondary school: 1 (3.03%)<br>High school: 20 (60.60%)<br>University: 12 (36.36%) | Full time: 8 (24.24%)<br>Part time: 6 (18.18%)<br>None or student: 19 (57.58%) |

*SD, standard deviation.*

normal distribution of the variables were tested using Shapiro-Wilk's test and quantile-quantile plot (Q-Q plot). All variables were normally distributed and all requirements were met. The prerequisites of ANCOVA were also met. There were no significant differences in baseline pain scores and in the CRF-S questionnaire between the four conditions. Further, there was a linear relationship between each covariate, in our case the corresponding baseline value, and the dependent variable, in our case the corresponding posttreatment value. We reported our outcomes according to the Consolidated Standards of Reporting Trials (CONSORT) guidelines that suggest using the estimate with the confidence interval. The mean difference (estimate) was used as effect size, the confidence interval was defined at 95% and the significance level was set at 0.05. All statistical analyses were carried out using R for Mac, version 1.4.1103.

# RESULTS

## Sample Characteristics

All 132 participants were included in the analysis. Participants had a mean age of 26.2 ($SD = 8.3$). Eighty-eight participants were females, and 44 were males. Participants in the four conditions did not differ regarding age (pain: mean age = 26.58, SD = 10.03; pain + dog: mean age = 26, SD = 6.13; pain + placebo: mean age = 24.62, SD = 7.06; pain + placebo + dog: mean age = 27.39, SD = 9.38), gender, family status, educational level, or employment level (see **Table 1**). In addition, we also analyzed if there were differences between the conditions "pain" and "pain + dog" and the condition "pain + placebo" and "pain + placebo + dog" separately. No differences were found; detailed outcomes can be found in the (**Supplementary Materials 1**, **2**). Moreover, we also analyzed potential differences between the conditions "pain + dog" and "pain + placebo + dog" regarding the intensity of interaction between the participants and the dog or regarding the participants' dog affinity. No differences were found; detailed results can be found in the (**Supplementary Material 3**).

## Primary Outcome: Heat-Pain Tolerance

We observed a mean posttreatment heat-pain tolerance of 47.64 in the "pain" condition which did not differ significantly from 48.02 in the "pain + dog" condition (difference = 0.04, CI = −0.66 to 0.74, $p$ = 0.905). The posttreatment heat-pain tolerance mean value in the "pain + placebo" condition was 48.01 and did also not significantly differ from 48.38 in the "pain + placebo + dog" condition (difference = 0.43, CI = −0.02 to 0.88, $p$ = 0.059) (see **Table 2**; **Figure 2**). Baseline heat-pain tolerance was associated with $p < 0.001$ in both models.

When including age in the model comparing the conditions "pain" and "pain + dog," age has no effect on posttreatment heat-pain tolerance (difference = 0.58, CI = −0.03 to 0.05, $p$ = 0.701) and the conditions "pain" and "pain + dog" did not differ regarding posttreatment heat-pain tolerance (difference = 0.05, CI = −0.66 to 0.75, $p$ = 0.891). In the comparison "pain + placebo" with "pain + placebo + dog" there was an age effect (difference = −0.04, CI = −0.07 to 0.01, $p$ = 0.002) and the conditions "pain + placebo" and "pain + placebo + dog" significantly differed (difference= 0.54, CI = 0.12–0.97, $p$ = 0.013).

**TABLE 2 |** Heat-pain tolerance and corresponding subjective intensity and unpleasantness ratings [mean, standard deviation (SD)].

| | | Condition | | | |
|---|---|---|---|---|---|
| | | Pain (*N* = 33) | Pain + Dog (*N* = 33) | Pain + Placebo (*N* = 33) | Pain + Placebo + Dog (*N* = 33) |
| Baseline | Heat-pain tolerance (mean, SD) | 48.06 (2.12) | 48.41 (1.51) | 48.29 (1.22) | 48.22 (1.70) |
| | Subjective heat-pain intensity (mean, SD) | 6.83 (1.52) | 7.24 (1.45) | 7.06 (1.43) | 6.96 (1.45) |
| | Subjective heat-pain unpleasantness (mean, SD) | 6.72 (1.73) | 7.07 (1.30) | 6.73 (1.85) | 6.53 (1.79) |
| Posttreatment | Heat-pain tolerance (mean, SD) | 47.64 (2.63) | 48.02 (1.84) | 48.01 (1.58) | 48.38 (1.69) |
| | Subjective heat-pain intensity (mean, SD) | 6.83 (1.49) | 7.57 (1.36) | 7.04 (1.75) | 7.01 (1.66) |
| | Subjective heat-pain unpleasantness (mean, SD) | 6.89 (1.87) | 7.14 (1.41) | 6.64 (2.12) | 6.63 (1.91) |

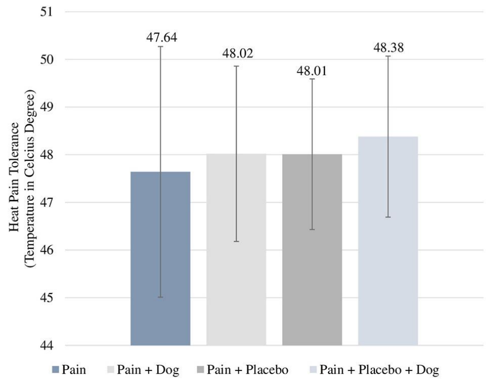


**FIGURE 2 |** Posttreatment mean scores of heat-pain tolerance. For each condition, the respective mean and standard deviation are displayed.

Baseline heat-pain tolerance was associated with $p < 0.001$ in both models.

When including gender into the model no changes to the original model were found. Gender had no effect on posttreatment heat-pain tolerance when comparing the conditions "pain" and "pain + dog" (difference = −0.10, CI = −0.87 to 0.66, $p = 0.785$). There was no difference between "pain" and "pain + dog" in posttreatment heat-pain tolerance (difference = 0.04, CI = −0.66 to 0.75, $p = 0.902$). When comparing the conditions "pain + placebo" and "pain + placebo + dog," we found no effect of gender (difference = 0.20, CI = −0.28 to 0.67, $p = 0.407$) and no group differences in posttreatment heat-pain tolerance (difference= 0.41, CI = −0.04 to 0.86, $p = 0.073$). Baseline heat-pain tolerance was associated with $p < 0.001$ in both models.

## Secondary Outcomes

### The Heat-Pain Threshold, Subjective Pain Intensity and Unpleasantness of Heat-Pain Tolerance, Subjective Pain Intensity and Unpleasantness of the Heat-Pain Threshold

There was no significant effect of the dog on the posttreatment heat-pain threshold; detailed outcomes can be found in the (**Supplementary Material 4**, T1).

With regard to the subjective intensity rating of heat-pain tolerance the "pain" had a mean value of 6.83 which was significantly lower than 7.57 in the "pain + dog" condition. This indicates that participants in the "pain + dog" condition experienced higher pain intensity of heat-pain tolerance compared to participants in the condition "pain" (difference = 0.40, CI = 0.02–0.79, $p = 0.041$) (see **Table 2**; **Figure 3**). Further, "pain + placebo" had a mean value of 7.04 which did not significantly differ from 7.01 in "pain + placebo + dog" condition (difference = 0.07, CI = −0.38 to 0.52, $p = 0.754$) (see **Table 2**). Baseline subjective ratings of pain intensity of heat-pain tolerance was associated with $p < 0.001$ in both models.

With regard to the subjective unpleasantness rating of heat-pain tolerance, the dog had no effect. There was no significant difference between mean value of 6.89 in the "pain" condition compared to the mean value of 7.14 in "pain + dog" condition (difference = −0.03, C = −0.59 to 0.53, $p = 0.913$) or between the mean value of 6.64 in the "pain + placebo" condition and the mean value of 6.63 in the "pain + placebo + dog" condition (difference = 0.19, CI = −0.29 to 0.67 $p = 0.44$). Baseline subjective ratings of pain unpleasantness of heat-pain tolerance was associated with $p < 0.001$ in both models.

With regard to the subjective intensity and unpleasantness rating of the heat-pain threshold there were no differences among the conditions; detailed outcomes can be found in the (**Supplementary Material 5**, T1).

### Expectation of Pain Reduction

We found no differences between the four conditions regarding their expectation of pain reduction after treatment (difference

**TABLE 3 |** Counselor Rating Short Form Questionnaire (CRF-S): Subscale Trustworthiness [mean, standard deviation (SD)].

| | | Condition | | | |
|---|---|---|---|---|---|
| | | Pain (*N* = 33) | Pain + Dog (*N* = 33) | Pain + Placebo (*N* = 33) | Pain + Placebo + Dog (*N* = 33) |
| Trustworthiness | Baseline (mean, SD) | 25.42 (3.25) | 26.58 (2.18) | 25.70 (3.10) | 26.58 (2.19) |
| | Posttreatment (mean, SD) | 25.94 (2.90) | 26.76 (2.28) | 25.52 (3.26) | 26.48 (2.36) |

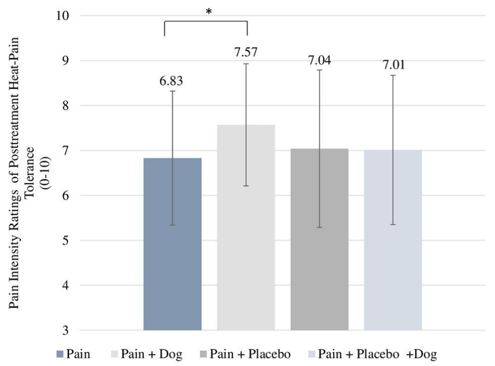


**FIGURE 3 |** Posttreatment scores of subjective intensity ratings for heat-pain tolerance. For each condition, the respective mean and standard deviation are displayed. **p*-value < 0.05.

= −0.17, CI = −0.45 to 0.11, $p = 0.241$). Separate analysis of the conditions also showed no difference regarding pain expectation between the conditions "pain" with a mean value of 5.41 and the mean value of 5.36 in the "pain + dog" condition (difference = 0.04, CI = −0.88 to 0.97, $p = 0.927$) or the conditions "pain + placebo" with a mean value of 4.81 and the mean value of 5.03 in the "pain + placebo + dog" condition (difference = −0.22, CI = −1.09 to 0.66, $p = 0.620$).

### Perception of the Study Investigator

There was no significant effect of the dog on the trustworthiness of the study investigators (see **Table 3**). The ratings of trustworthiness of the study investigators in the condition "pain" with a mean value of 25.94 did not differ from the mean value of 26.76 in the condition "pain + dog" (difference = 0.10, CI = −0.67 to 0.87, $p = 0.796$). The ratings of trustworthiness of the study investigators in the condition "pain + placebo" with 25.52 did not differ from 26.48 in the condition "pain + placebo + dog" (difference = 0.11, CI = −0.43 to 0.64, $p = 0.695$). Baseline trustworthiness ratings of the study investigators was associated with $p < 0.001$ in both models. When we controlled for study investigator, there was still no significant difference in the subscale *trustworthiness* of the study investigators between the four different investigators comparing the conditions "pain" with "pain + dog" (difference = −0.06, CI = −1.46 to 1.35, $p = 0.936$) or between the conditions "pain + placebo" and "pain + placebo + dog" (difference = 0.26, CI = −0.74 to 1.27, $p = 0.601$). Baseline trustworthiness ratings of the study investigators was associated with $p < 0.001$ in both models.

The results of the subscales attractiveness and expertness can be found in the (**Supplementary Materials 6**).

## DISCUSSION

AAIs have been shown to be effective in the treatment of pain, but the mechanisms of this analgesia have not yet been elucidated. This study investigated whether the analgesic effects of AAI could be mediated by providing direct social support through the presence of a dog or by strengthening the alliance between the patient and the treatment provider. We tested these hypotheses with established paradigms for pain assessment and pain therapy, i.e., expectancy-induced placebo analgesia.

The results of our randomized controlled trial show that participants heat-pain tolerance did not increase in both pain assessment and pain therapy when a dog was present. Instead, subjective measures show that participants experienced heat-pain tolerance to be more intense when the dog was present compared to when no dog was present in the pain assessment condition where no treatment was offered. Further, participants did not perceive the study investigator to be more trustworthy when a dog was present compared to when no dog was not present. These results contradict our assumption that the analgesic effects of AAI could be mediated by providing direct social support or by strengthening the alliance between the participant and the treatment provider.

These findings also contradict previous observations of analgesia in the presence of a dog in a clinical setting (11–14, 51) but are in line with studies that found no effect of AAI in pain (16, 17). Moreover, we did not only find no analgesic effect of the dog but instead a negative effect in the subjective pain intensity of heat-pain tolerance. To our knowledge, this is the first study that found a negative effect of AAI on pain. There are several possible explanations for this discrepancy between our findings and previous studies.

These contradict results could be a consequence of differences in the study setting as we employed an experimentally induced acute pain paradigm in healthy participants, whereas previous studies reported pain reduction in patients in the presence of a dog compared to patients without a dog present in a clinical setting (11–14, 51).

Further, it is possible that for AAI to be effective, the animal (in our case, a dog) needs to be actively involved in giving social support to modulate pain, for example, through direct physical contact or a clear attentional focus of the animal toward the human. This would be in line with a previous meta-analysis on the analgesic effects of human social support suggesting that the mere presence of another person is not sufficient to affect pain perception and experience and that social support needs to be expressed clearly in order to reduce pain, for example, through verbal communication or holding hands (19). It is therefore possible that a dog also needs to be actively involved in the therapeutic process in order to modulate pain. Accordingly, in previous studies that have suggested that dogs affect patients' pain perception, patients typically interacted with the dogs for 10–20 min (11–13, 51). This would also be in line with previous studies showing that physical contact between a human and an animal is important to stimulate biological reactions in humans (52–54). Notably, these effects might not only rely on physical contact since both physically interacting with and just seeing a dog increases oxytocin level in humans (23). Based on these findings as well as on our results, we assume that the mere presence of a dog is not sufficient to affect pain perception and that at least a longer interaction phase and some form of contact between the human and the animal might be needed. Further, it can be important whether the person knows or owns the animal. Support for this assumption comes from a study that examined the effect of the presence of friends, spouses and pet on cardiovascular responses to psychological and physical stress. The authors showed that pet owners perceive their pets as an important, supportive part of their lives, and significant cardiovascular and behavioral benefits are associated with this perception (55, 56). In our study, participants did not know the dog. So, it is possible that a relationship needs to exists between human and animal for the presence of an animal to have a positive effect. Future studies should investigate if the relationship to the animal mediates a possible analgesic effect.

Another explanation is based on findings from placebo and psychotherapy research. Studies have shown that a treatment rationale is an important prerequisite for a treatment response (30, 35, 39). In our experiment, we used a deceptive rationale for the dog's presence, and we intentionally avoided a therapeutic narrative for the dog. However, research has indicated that interventions evoking expectations of pain reduction—either by verbal suggestion, conditioning, or imagery techniques—are likely to contribute to improving the effectiveness of standard analgesic treatments in clinical practice (57). Further, depending on the information given in verbal suggestions, the verbal suggestion of an analgesic treatment can lead to different magnitudes of analgesia (58–61). For example, a positive expectation leads to significant pain reduction, whereas a verbal suggestion inducing negative expectations can even block a painkiller's analgesic effect. This leads to the assumption that positive and negative expectations can have an impact on the outcome of an intervention (62). Hence, it is possible that we did not find an analgesic effect of the dog because participants lacked the grounds to incorporate the dog in their treatment expectations. Moreover, it is even possible that the dog was then perceived as a negative distraction. This would also explain why participants in the "pain + dog" condition experienced greater pain intensity compared to participants in the "pain" condition. This would also mean that the effect of AAI on pain reduction cannot be explained solely by the animal but is rather influenced by contextual factors, such as expectation.

Further, it could be that by not providing any information regarding the presence of a dog during the recruitment process, we might have attracted participants with no specific attitudes toward dogs. In our study dog affinity was only collected to check that groups did not differ regarding their dog affinity. However, it has been suggested that individuals with an affinity for animals may be more likely to benefit from their presence (14). It is possible that people with an affinity for dogs would more strongly benefit from a dog's presence. Thus, not limiting the study to people with an affinity for dogs could have led to a smaller effect of the dog's presence on pain perception and experience.

Last, the presence of a dog did not positively affect how participants perceived the study investigator. These results do not support findings of previous studies suggesting that the presence of an animal positively influences how we perceive others (25, 63). In both studies, participants perceived psychotherapists in images or videos with an animal present to be more attractive, and in a study by Schneider et al. (63), participants perceived the same psychotherapists as more trustworthy when an animal was present. However, our results are in line with the study by (26), who also found that the presence of a dog had no effect on participants' perception. A plausible explanation for the difference in results between, on the one hand, previous studies supporting a positive effect of animals on our perception (25, 63) and, on the other, our study and Goldmann et al.'s study is the study setting. In our study and in Goldmann's study, the effect of the presence of a dog on participants' perception was investigated *in vivo*. In both studies, there was direct interaction between the participant and the study leader, whereas in the previous studies the participants had to judge an image or video of a person with or without an animal and the participants did not interact with an animal or study leader. It is therefore possible that through this direct interaction between participant and study investigator, the dog was not the focus of participants and had no effect on their perception of the study investigator (26). However, since the dog conditions were only performed by one study investigator, these results must be interpreted with caution. With our design, it is difficult to compare the study investigator that worked with the dog with the other three study investigators.

Overall, the results of this study are not only interesting for research on AAIs but also for placebo research, especially from a methodological perspective. In this study, we used a placebo as an intervention paradigm to examine whether the presence of a dog could amplify the placebo effect. The placebo was thus not used as a control intervention to eliminate specific factors as is usually the case. Using a placebo as an intervention paradigm has been implemented in a few previous studies, for example, in those by (30, 31) investigated the effect of the patient–practitioner relationship on patients with irritable-bowel syndrome using a placebo acupuncture intervention; they suggested that an enhanced relationship with a practitioner is the most robust component in therapy. Further, Gaab et al. (30) examined the impact of expectation and relationships in healthy participants using a placebo intervention consisting of animated videos. The authors showed that placebos with a psychological treatment rationale are effective when provided in a trustworthy, friendly, and empathic relationship. In our study, we used the presence of a dog to examine whether the presence of a dog could amplify the placebo effect and found that the mere presence of a dog has no impact on the placebo effect.

However, it should also be emphasized that in this study, we did not succeed in inducing placebo effects. This finding contradicts results from previous studies (34, 35). A possible explanation for the lack of placebo effect might be that in this study, the expectation induction was not successful. As known from previous research treatment response expectation is generally seen as the main contributor to placebo-induced analgesia (64–66). Hence, we may not have been able to produce placebo effects since participants had no expectation of pain relief. Another possible explanation might be that the dog and not the placebo was the focus in our study. We used a placebo as an intervention paradigm and not to study placebo effects like in previous studies. As a result, it is possible that the study investigators did not have a placebo allegiance in this study. As known from psychotherapy research there exists a robust relationship between researcher allegiance and outcome (67). Hence, a potential missing placebo allegiance could lead to a lower expectation of pain reduction among participants and explain the lack of placebo effect in this study.

The findings of this study have to be seen in light of some limitations. Our sample consisted of young and healthy people who were not suffering from acute or chronic pain. While valuable evidence can be provided from studies in healthy participants, it is important to stress that short-term experimentally induced or acute pain in healthy participants differs from chronic pain in patients (68). Hence, our results only provide information about how the presence of a dog affects experimentally induced acute pain of healthy participants. Therefore, our results need to be treated with caution in the context of acute or chronic pain. Future studies should apply this design also with patients with pain disorders or patients experiencing acute pain in clinical settings. Further, the dog conditions were performed by the same person, while the other interventions were performed by different people. The results of the CRF-S questionnaire showed, however, that even when controlling for the investigator, there was no significant difference in how participants rated the study investigators. Finding no difference can lead to the assumption that all four investigators performed the intervention in the same standardized manner according to the manual. However, even though this analysis made us assume that all our study investigators performed the conditions in the same manner we need to highlight that with our design, it is not possible to distinguish between the effects of the dog and the study investigator. Future studies should make sure that the study investigators carry out both conditions with and without an animal present to entangle the effects of the animal and the effects of the study investigator. Further, participants had only limited contact with the dog since the aim of this study was to investigate whether the mere presence of a dog had an analgesic effect.

Last but not least, the intensity as well as dog affinity were collected in this study, but only to roughly investigate if the dog groups differ regarding the intensity of contact and their dog affinity. It would have been interesting to investigate whether dog affinity and intensity of the contact between the participants and the dog mediates the effect. We therefore suggest that future studies should specifically address the affinity of participants for animals in general as well as for the animal that is presented.

Considering the findings and limitations of this current study, future studies are warranted that would investigate whether animals need to be integrated in the treatment rationale in order to have effects on pain. Further, it is important to examine whether physical contact with a dog is needed for an analgesic effect or not and whether affinity toward dogs mediates this effect.

In conclusion, our results indicate that the mere presence of a dog does not contribute to pain reduction and that the previously reported analgesic effects of AAI is not replicated in our study. The presence of a dog did not seem to provide social support or had an effect on the alliance between the participants and the treatment provider. We assume that the animal might need to be an integrated and plausible part of the treatment rationale so that participants are able to form a treatment-response expectation toward AAI.

## DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

## ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethics Committee of the Faculty of Psychology at the University of Basel, Switzerland. The patients/participants provided their written informed consent to participate in this study.

## AUTHOR CONTRIBUTIONS

JG had the idea for the study. CW, KH, JG, and CL designed the study. CW contributed to acquiring the data. CW and CL carried out the analysis. CW, KH, JG, and CL wrote the manuscript, which was revised by all authors. All authors contributed to the article and approved the submitted version.

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## SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpain.2021.714469/full#supplementary-material

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**Lack of Effects of the Presence of a Dog on Pain Perception in Healthy Participants - a Randomized Controlled Trial**

## SUPPLEMENTARY MATERIALS

**Table of Contents**

**Lack of Effects of the Presence of a Dog on Pain Perception in Healthy Participants - a Randomized Controlled Trial**

**S1: Results: Sample characteristics "Pain" vs. "Pain + Dog"**

| | **Difference** | **95% confidence interval** | **p-value** |
|---|---|---|---|
| Age | 0.58 | -3.5 – 4.68 | 0.779 |
| Gender | -0.03 | -0.26 – 2.0 | 0.795 |
| Family status | -0.03 | -0.46 – 0.40 | 0.888 |
| Education level | -0.12 | -0.72 – 0.47 | 0.685 |
| Employment level | 0.33 | 0.04 – 0.71 | 0.078 |

**S2: Results: Sample characteristics "Pain + Placebo" vs. "Placebo + Dog"**

| | **Difference** | **95% confidence interval** | **p-value** |
|---|---|---|---|
| Age | -2.76 | -6.84 – 1.33 | 0.182 |
| Gender | -0.09 | -0.33 – 0.15 | 0.446 |
| Family status | -0.18 | -0.51 – 0.15 | 0.271 |
| Education level | -0.39 | -0.99 – 0.20 | 0.192 |
| Employment level | 0.33 | -0.06 – 0.73 | 0.094 |

**S3: Results: Intensity Interaction with the Dog and Dog Affinity in "Pain + Dog" vs. "Pain + Placebo + Dog"**

| | **Difference** | **95% confidence interval** | **p-value** |
|---|---|---|---|
| Interaction contact | 0.09 | -0.67 –0.49 | 0.755 |
| Dog affinity | -0.28 | -0.14 – 0.69 | 0.193 |

**S4: Results: Heat-Pain Threshold**

We observed a man posttreatment heat-pain threshold of 42.95 in the "pain" condition which did not differ significantly from 43.15 in the "pain + dog" condition (difference = 0.17, CI = -1.0 – 1.35, p = 0.772). The posttreatment heat-pain threshold mean value in the "pain + placebo" condition was 42.47 which did also not differ significantly from 43.61 in the "pain + placebo + dog" condition (difference = 0.93, CI = -0.05 – 1.90, p = 0.061). Baseline heat-pain threshold was associated with p < .001 in both models.

### S5: Results: Subjective Ratings for Heat-Pain Threshold

Analysis showed no dog effect in pain intensity of heat-pain threshold between the condition's "pain" and "pain + dog" (difference = 0.13, CI = -0.31– 0.57, p = 0.556) or between "pain + placebo only" and "placebo + dog" (difference = 0.30, CI = -0.06 – 0.67, p = 0.105). Baseline subjective ratings for pain intensity of heat-pain threshold was associated with p < .001 in both models. Further, there were also no significant differences in pain unpleasantness of heat-pain threshold between the condition's "pain" and "pain + dog" (difference = 0.12, CI = -0.39 – 0.62, p = 0.643) or between "pain + placebo" and "pain + placebo + dog" (difference = 0.20, CI = -0.16 – 0.56, p = 0.267). Baseline subjective ratings for pain unpleasantness of heat-pain threshold was associated with p < .001 in both models.

### S6: Results: Perception of the Study Investigator (Counselor Short Form Questionnaire)

There was no significant dog effect on the subscale's *attractiveness* and *expertness.* The ratings of *attractiveness* of the study investigators with 25.53 in the "pain" condition did not differ from the rating of 25.39 in the "pain + dog" condition (difference = 0.46, CI = -0.19 –1.11, p = 0.160) or between the ratings of 25.64 in the "pain + placebo" condition and the ratings of 26.06 in the "pain + placebo + dog" condition (difference = 0.12, CI = -0.39 – 0.63, p = 0.630). Baseline ratings of *attractiveness* was associated with p < .001 in both models. Further, no significant differences were found in the ratings of *expertness* of the study investigators between 25.09 in the "pain only" and 25.82 in the "pain + dog condition (difference = 0.29, CI = -0.38 – 0.97, $p = 0.393$) or between the ratings of 24.33 in the "pain + placebo" condition and the ratings of 25.58 in the "pain + placebo + dog" condition (difference= -0.36, CI = -1.06 –0.33, $p = 0.295$). Baseline ratings of *expertness* was associated with $p < .001$ in both models.

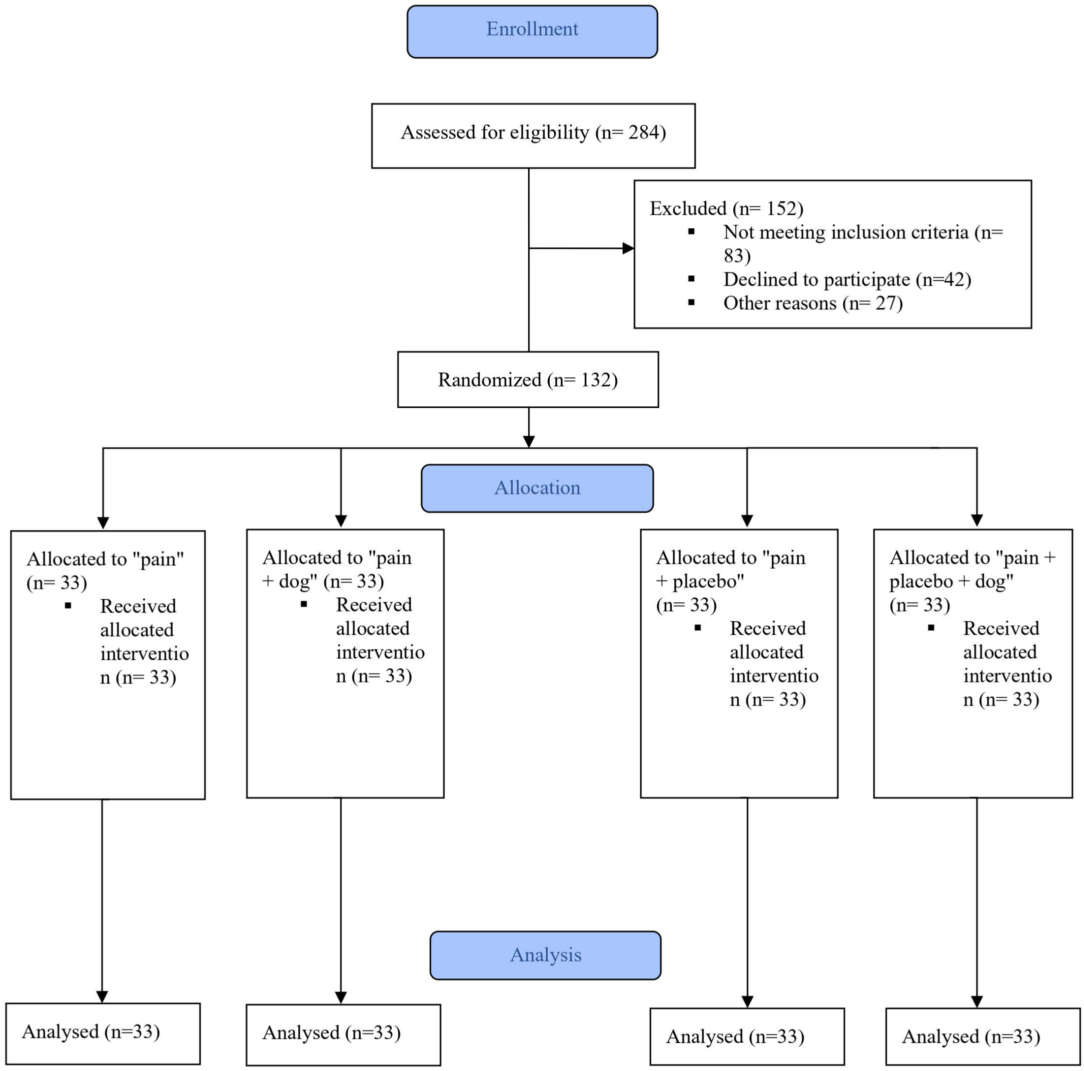
**ST1: Heat-Pain Threshold and Corresponding Subjective Intensity and Unpleasantness Ratings**

*Heat-pain threshold and corresponding subjective intensity and unpleasantness ratings (mean, standard deviation [SD])*

| | | Condition | | | |
|---|---|---|---|---|---|
| | | **Pain** (N = 33) | **Pain + Dog** (N = 33) | **Pain + Placebo** (N = 33) | **Pain + Placebo + Dog** (N = 33) |
| **Baseline** | **Heat-pain threshold** (mean, SD) | 43.86 (2.95) | 43.89 (2.77) | 43.77 (2.82) | 44.05 (2.68) |
| | **Subjective heat-pain intensity** (mean, SD) | 4.46 (1.77) | 4.10 (1.92) | 4.34 (2.13) | 3.99 (1.84) |
| | **Subjective heat-pain unpleasantness** (mean, SD) | 4.12 (1.77) | 3.90 (2.06) | 3.56 (1.86) | 3.60 (1.84) |
| **Posttreatment** | **Heat-pain threshold** (mean, SD) | 42.95 (3.07) | 43.15 (3.42) | 42.47 (2.72) | 48.38 (3.00) |
| | **Subjective heat-pain intensity** (mean, SD) | 3.94 (1.62) | 3.77 (1.90) | 3.60 (1.87) | 3.57 (1.88) |
| | **Subjective heat-pain unpleasantness** (mean, SD) | 3.52 (1.55) | 3.4 (1.88) | 3.04 (1.57) | 3.25 (1.94) |

**Lack of Effects of the Presence of a Dog on Pain Perception in Healthy Participants - a Randomized Controlled Trial**

**SF1: Flow Chart**



## Appendix B

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### Study 2

**Wagner, C.,** Gaab, J., Hediger, K. (2022): The Importance of the Treatment Rationale for Pain in Animal-Assisted Interventions: A Randomized Controlled Trial in Healthy Participants *(submitted for publication)*

# The Importance of the Treatment Rationale for Pain in Animal-Assisted Interventions: A Randomized Controlled Trial in Healthy Participants

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## ABSTRACT

Animal-assisted intervention (AAI) is a promising treatment approach for pain, but possible mechanisms still need to be elucidated. This study set out to investigate the analgesic effects of an animal provided with a treatment rationale in a randomized controlled trial employing a standardized experimental heat-pain paradigm. We randomly assigned 128 healthy participants to: dog treatment (DT), placebo treatment (PT), dog and placebo treatment (DPT), and no treatment (NT). Primary outcomes were heat-pain tolerance and the corresponding self-reported ratings of pain unpleasantness and intensity. Results revealed no differences in heat-pain tolerance between the conditions. However, participants in the DT condition experienced heat-pain as significantly less unpleasant at the limit of their tolerance compared to participants in the NT condition (estimate = -0.96, CI = -1.58 to 0.34, $p$ = 0.010). Participants in the DT condition also showed lower ratings of pain intensity at the limit of their tolerance compared to participants in the NT condition (estimate = -0.44, CI = -0.89 to 0.02, $p$ = 0.060). This study indicates that a dog has analgesic effects on pain perception when integrated into the treatment rationale. We assume that providing a treatment rationale regarding the animal is important in AAI on pain.



**Trial registration**: Clinical Trials NCT04361968.

**Keywords:** pain, animal-assisted intervention, expectation, treatment rationale, placebo,


**Perspective:** The presence of an animal is not sufficient for animal-assisted intervention to have an analgesic effect on pain unless it is provided with a treatment rationale.

## 1. INTRODUCTION

Animal-assisted interventions (AAIs) are "goal-oriented and structured interventions that intentionally incorporate animals in health, education and human service for the purpose of therapeutic gains in humans" (IAHAIO, 2018). While it is assumed that AAI could be a promising treatment approach for pain management in different settings and populations (Waite et al., 2018), the evidence base for the analgesic effects of AAI is weak.

First, the results about the effects of AAI on pain are mixed: While some studies have shown promising effects of AAI on pain in adults as well as in children and adolescent patients (Braun et al., 2009; Calcaterra et al., 2015; Harper et al., 2015; Marcus et al., 2013; Rodrigo-Claverol et al., 2019; Silva & Osório, 2018), other studies have not found any analgesic effects in children and adolescent patients (Barker et al., 2015; Havener et al., 2001; Vagnoli et al., 2015) or in healthy adults (Wagner et al., 2021). Second, it has been widely hypothesized that the animal is responsible for the reported analgesic effects, but the factors responsible for the potential analgesic effects of AAI have not been investigated (Waite et al., 2018).

Findings from intervention research highlight the importance of a treatment rationale, that is, a verbal suggestion, to treatment responses (Carvalho et al., 2016; Gaab et al., 2019; Hoenemeyer et al., 2018; Kaptchuk et al., 2010; Locher et al., 2017; Tondorf et al., 2017). With the treatment rationale, a meaning is attributed to the intervention at hand, which in turn affects the expectations and outcomes of the treatment (Moerman, 2006). Expectations are especially powerful with regard to pain, as they predict the outcomes of analgesic treatments (Cormier et al., 2016; Mondloch et al., 2001; Peerdeman et al., 2016) and have been identified as a core mechanism in placebo analgesia (Vase et al., 2003; Vase et al., 2015).

To date, the role of the treatment rationale has not been investigated in AAI. In a previous study, we demonstrated that the mere presence of an animal, i.e., without a treatment rationale, does not contribute to pain relief in a standardized experimental heat-pain placebo paradigm (Wagner et al., 2021). It therefore might not be the animal itself that contributes to pain relief but rather *how* the animal is embedded in the treatment rationale.

The aim of the present study was to examine the effect of the treatment rationale on pain in an AAI. Using an experimentally induced heat-pain placebo paradigm, we compared participants in four conditions receiving either an AAI and/or a placebo or no treatment. Expect for the no-treatment condition, all conditions received a treatment rationale. Primary outcomes were posttreatment heat-pain tolerance and the corresponding self-reported ratings of unpleasantness and intensity at the limit of heat-pain tolerance.

We hypothesized that providing an AAI with a treatment rationale has similar effects as a placebo and would thus lead to increased heat-pain tolerance and to decreased self-reported ratings of unpleasantness and intensity at the limit of their heat-pain tolerance at posttreatment compared to no treatment.

## 2. METHODS

### 2.1 Design

We conducted a randomized controlled trial on healthy participants, which were randomly assigned to one of four conditions (for details, see below). The study was conducted between June 2020 and November 2020. The study protocols and the informed consent of the study were approved by the Ethics Committee of Northwest and Central Switzerland (ID number: 2020-00642). Since the study was conducted during the Covid-19 pandemic, the study's protective protocol measures were approved by the Ethics Committee of the Faculty of Psychology at the University of Basel, Switzerland. The study protocol ensured the dog's welfare at all times. We conducted all sessions with a dog according to the guidelines of the International Association for Human–Animal Interaction Organizations (IAHAIO, 2018). The study was preregistered as a clinical trial on www.clinicaltrials.gov (Identifier: NCT04361968).

### 2.2. Participants

Through online advertisements, 363 persons were recruited for "an efficacy study of a new innovative treatment method on individual pain perception of healthy participants" on the website of the University of Basel. The online advertisement did not contain any information about the possible presence of a dog to prevent attracting only participants with an affinity for dogs. The advertisement contained a link to a short questionnaire. Persons interested in participating had to complete this questionnaire first to check for eligibility and inclusion and exclusion criteria. In order to participate in the study, participants had to be right-handed (Oldfield, 1971) and between 18 and 65 years old. Exclusion criteria were (a) any acute or chronic disease as well as skin pathologies, (b) current medications or current psychological or psychiatric treatment, (c) pregnancy, (d) nursing, (e) current or regular drug consumption, (f) insufficient German-language skills, (g) a fear of dogs, (h) dog-hair allergies, and (i) previous participation in studies using a heat-pain paradigm.

Of the total 363 screened persons, 206 met the inclusion criteria (see Figure 1). All eligible persons received the study information, which contained the whole study procedure, the mandatory Covid-19 safety measures, the aims, participants' rights, notification of the possible presence of a dog, and a selection of study appointments. Of the 206 persons, 63 declined to participate in the study after receiving the study information. One hundred forty-three persons who were still willing to participate were asked to sign in for a study appointment. As soon as the predefined number of participants ($N$ = 128) was included, the remaining persons were informed that there were no further appointments available. All participants attended one appointment with a duration of 70 minutes. The study compensation was CHF 50. Psychology students had the opportunity to obtain credit points for their bachelor's program.

Participants were blinded regarding the aims of our study and the placebo treatment. At the end of the study, all participants provided written delayed informed consent, in which they were debriefed about the aims of the study. Participants had the possibility to withdraw data from the study if they did not consent to participate after being debriefed.

### 2.3 Randomization

We used an adaptive randomization to apportion male participants over all four conditions because we expected more women than men to participate in the study. This approach automatically considered the previous gender allocation in the four conditions and influenced the probability of the next gender allocation to ensure equal representation in all four conditions (each $N$ = 32). The randomization was conducted with Microsoft® Excel for Mac, version 16.58. The first author entered each participant's code and gender into an Excel file that then automatically allocated participants to one of the four conditions. Participants did not know in which condition they were until the treatment phase. The study investigators, however, knew in which condition each participant was.

### 2.4 Procedure

To comply with mandatory Covid-19 safety measures, participants had to wash their hands and put on a mask before entering the lab room. Upon arrival, study investigators explained the study procedure and participants were told that the study's aim was to investigate if the presence of a dog has a similar effect on pain perception and experience as an established analgesic cream. Then baseline measurements of participants' heat-pain tolerance and threshold as well as their corresponding self-reported ratings of pain unpleasantness and intensity were collected. After these baseline measurements, we conducted the treatment phase. Participants were allocated to one of the following four conditions: no treatment (NT), dog treatment (DT), placebo treatment (PT), or dog and placebo treatment (DPT). Except for participants in the NT condition, all participants received a positive treatment rationale for pain relief (see chapter 2.5 for a detailed description of the four conditions).

After the treatment phase, posttreatment heat-pain measurements and the corresponding self-reported ratings of pain unpleasantness and intensity were performed in an identical manner to the baseline assessments (see Figure 2 for the timeline).

### 2.5 Conditions

Participants were allocated to one of the following four conditions:

- No treatment (NT): In the NT condition, participants were told that they were in the no-treatment group and that they would not receive any treatment.
- Dog treatment (DT): In the DT condition, participants were informed that they were in the dog treatment. After this information, the study investigators shortly left the room to retrieve the dog. The dog was a 2-year-old female Golden Retriever that was experienced in interacting with strangers. To standardize the interaction between the participants and the dog, all participants were asked to greet and pet the dog as soon as the dog entered the room. We explained that it would be easier for the dog to relax on a blanket when allowed to greet the new person in the room. The duration of the interaction between the participant and the dog was kept to a minimum, that is, under three minutes. During the greeting phase, study investigators also interacted with the dog if the dog approached the investigator. While participants interacted with the dog, the study investigators gave participants the treatment rationale for the dog's

presence. They explained that previous studies had showed that the presence of a dog could lead to pain reduction in patients and that we wanted to examine if the presence of a dog could also lead to pain reduction in this study. After giving the treatment rationale for the dog’s presence, the dog was asked to lie on her blanket, which was always in the participants’ field of vision. The participants did not touch the dog during the further procedure. The study investigators also did not interact with the dog during the further procedure.

- Placebo treatment (PT): In the PT condition, participants were told that they were in the analgesic-cream-treatment condition, which was in fact a placebo provided with a treatment rationale. The study investigators explained that the cream contains the active ingredient lidocaine and that the efficacy of lidocaine has been proven in several high- quality studies. Then the study investigators applied the placebo cream on participants’ left volar forearms.
- Dog and placebo treatment (DPT): In the DPT, participants received the placebo provided with a treatment rationale while in the presence of the dog with a treatment rationale for the dog’s presence. Participants were introduced to the dog and received the treatment rationale for the dog, then the treatment rationale for the placebo cream, and the cream application.

**2.6 Study investigators**

Four study investigators carried out the 128 study appointments. Appointments were randomly distributed across all four investigators, with study investigator CW conducting 44 appointments (11 per condition) and study investigators AH, MR, and MB each conducting 28 appointments (7 per condition). CW was the owner of the study dog and performed all dog appointments on her own (DT and DPT). The other three study investigators each performed the dog appointments (DT and DPT) in the presence of the dog owner to ensure that the dog was not stressed. Leaving the dog in a setting with unfamiliar individuals without the dog’s owner would have been inappropriate from an ethical standpoint. In these cases, the dog owner sat quietly in a chair, did not interact with participants (except for greetings and goodbyes), and avoided being in the participants’ field of vision.

### 2.7 Heat-pain tolerance and threshold and the corresponding self-reported ratings of unpleasantness and intensity

Posttreatment heat-pain tolerance and the corresponding self-reported ratings of unpleasantness and intensity at the limit of the heat-pain tolerance (see below for more information) were defined as primary outcomes. Heat-pain tolerance is related to affective and motivational aspects (Harris & Rollman, 1983) and has been associated with pathological pain, as there is an inverse relationship between ischemic pain tolerance and the perceived severity of clinical pain (Edwards et al., 2001).

We assessed heat-pain tolerance and heat-pain threshold following the design of a previous study (Wagner et al., 2021). Both heat-pain tolerance and threshold were determined using a Thermal Sensory Analyser (TSA 2, Medoc, Ramatishai, Israel). Heat-pain threshold were measured prior to heat-pain tolerance in order to minimize interference between the two outcomes (Krummenacher et al., 2014; Locher et al., 2017). The TSA 2 is a pain management system for the qualitative assessment of pain and measures sensory threshold such as heat-induced pain. The employed heat stimuli did not entail any significant danger and have already been used in previous studies in our lab (Gaab et al., 2016; Gaab et al., 2019; Krummenacher et al., 2014; Locher et al., 2017; Locher et al., 2019). Participants were able stop the stimuli at any time during each experimental run.

The study investigator administered the heat stimuli to the right volar forearm of the participant using a 30 × 30 mm Peltier device. The thermode of the TSA 2 was fixed at two different locations (locations Y and X, determined using a positioning device). Location Y was placed one-third of the way down the forearm from the elbow, while location X was placed two-thirds of the way down the forearm from the elbow. Half of the participants were randomly assigned to start with location Y for the baseline heat-pain measurement and to switch then to location X for the posttreatment heat-pain measurement. The other half of the participants started with the opposite location, location X, for the baseline heat-pain measurement and then switched to location Y for the posttreatment measurement. The reason for moving the thermode was to avoid effects of sensitization or habituation (Emerson et al., 2014).

Before starting with the actual heat-pain measurement, participants performed a practice round to experience how the heat stimuli work and how to handle the device including how to stop the heat stimuli. After this practice round, we started with the baseline measurements. We first assessed participants' heat-pain threshold by determining limits. Participants were instructed to press the button to determine the turning point from perceiving warmth to perceiving pain. The temperature was increased from the baseline (32 °C) at a rate of 0.5 °C/s. When participants indicated that the pain threshold had been reached, the device returned to its baseline (32 °C) and began to rise again at a rate of 0.5 °C/s. This procedure was repeated three times in a row (Locher et al., 2017). The heat-pain threshold was defined as the average of the three measurements.

Afterward, heat-pain tolerance was determined using limits. Participants were asked to stop the increasing heat stimulus at the moment they could not stand the heat any longer. The temperature increased from the baseline (32 °C) at a rate of 0.5 °C/s. As soon as participants indicated that their pain tolerance had been reached, the device returned its baseline (32 °C) and began to rise again at a rate of 0.5 °C/s. This procedure was again repeated three times in a row. To avoid physical injury, the pain-tolerance measurement stopped at a temperature of 52 °C (Krummenacher et al., 2010). Heat-pain tolerance was defined as the average of the three measurements (Hermann et al., 2006).

Further, we assessed self-reported ratings of unpleasantness and intensity at the heat-pain threshold and limit of heat-pain tolerance, which represent common pain parameters in heat-pain-paradigm studies (Petersen et al., 2012). Unpleasantness refers to the affective dimension of pain, whereas intensity refers to cognitive dimensions of pain (Price, 2000). After each heat-pain tolerance and threshold measurement, participants had to rate pain unpleasantness and intensity on a visual analogue scale (VAS). The VAS ranged from 1–10 (1 = "not unpleasant at all" or "not intense at all"; 10 = "the most unpleasant pain I have ever experienced" or "the most intense pain I have ever experienced").

### 2.8 Measures and questionnaires

After the baseline measurements and again after the posttreatment measurements, we assessed participants' perception of the study investigator with the Counselor Rating Form—Short Version (CRF-S) (Corrigan & Schmidt, 1983). The CRF-S is a 12-item questionnaire for measuring an individual's perception of the therapist on the following three subscales: *trustworthiness*, *expertness*, and *attractiveness*. The questionnaire contains items on a 7-point Likert scale, ranging from 1 (not very) to 7 (very). For this study, only the subscale *trustworthiness* was analyzed, because it seems most central to the therapeutic alliance. For example, studies have indicated that patient trust in the physician is of particular importance in clinical practice (Birkhäuer et al., 2017; Coulter, 2002; Mechanic & Schlesinger, 1996). The subscale *trustworthiness* included the following four items: *honest*, *reliable*, *sincere*, and *trustworthy.*

Previous studies have shown that the presence of an animal positively influences how we perceive others and have suggested that this could strengthen the therapeutic alliance between the patient and the treatment provider (Creary, 2017; Goldmann et al., 2015; Kruger & Serpell, 2010). Since the therapeutic alliance is important for the treatment outcome, we used the CRF-S to control for whether a possible change in the perception of the study investigator could also explain the analgesic effects.

After the treatment phase and before conducting posttreatment heat-pain measurements, we assessed demographic variables (i.e., age, sex, nationality, family status, education level, employment situation, and income) with a sociodemographic questionnaire. At this point, we also asked participants to rate using a VAS how unpleasant and intense they expected heat-pain to be at the limit of their tolerance after the treatment. These self-reported ratings of their expectations of pain unpleasantness and intensity were made with a similar VAS (ranging from 1 to 10) as those for pain unpleasantness and intensity (Locher et al., 2017; Pollo et al., 2001). The self-reported ratings of expected heat-pain at the limit of their tolerance were assessed to control for whether the expectation induction was successful.

The study investigator quantified the intensity of the contact between participant and dog during the greeting phase on a 5-stage Likert scale ranging from 1 = “no contact at all” to 5 = “very high intensity of contact.” We also assessed participants’ affinity for dogs at the end of the study with a short self-developed questionnaire. For that, we used a 5-stage Likert scale, with 1 indicating that participants liked dogs “not at all” and 5 indicating “very much.” Both outcomes were used to investigate if participants in the DT and DPT conditions differed regarding the intensity of the contact with the dog during the greeting and regarding their general affinity to dogs.

### 2.9 Statistical analyses

We estimated that a sample size of $N$ = 128 with a power of 0.8, an alpha error of 5%, and a beta error of 20% would be necessary to detect a medium size effect of $f$ = 0.25 between the four conditions (Waite et al., 2018).

The primary outcomes (posttreatment heat-pain tolerance and the corresponding self-reported ratings of pain unpleasantness and intensity at the limit of their heat-pain tolerance) were analyzed using linear models (analysis of covariance, ANCOVA) with the corresponding baseline outcomes as a covariate. For each outcome, we calculated prespecified separate models to analyze the dog effect, the placebo effect, and the interaction effect of the dog and the placebo. We quantified the dog effect by comparing the DT with the NT. The placebo effect was quantified by comparing the PT with the NT. The interaction effect of the dog and the placebo was estimated in a model with all four conditions included in which the placebo and the dog served as between-subject factors.

For the secondary outcomes (the posttreatment heat-pain threshold and the corresponding self-reported ratings of unpleasantness and intensity at the heat-pain threshold, expectations of pain unpleasantness and intensity at the limit of their tolerance after the treatment, and the subscale from the CRF-S for trustworthiness, we also conducted linear models (ANCOVAs) to assess the dog, the placebo, and the interaction effects. In each model, the respective baseline outcome was used as a covariate.

The requirements for the analyses were tested using Levene's test to determine the variance homogeneity of the four conditions and the homogeneity of the regression slopes. The normal distribution of the variables and residuals was tested using Shapiro-Wilk's test and a quantile–quantile plot (Q–Q plot). All variables and residuals were normally distributed, and all prerequisites were met. We report our outcomes according to the Consolidated Standards of Reporting Trials (CONSORT). The mean difference (estimate) was used as the effect size, the confidence interval was defined at 95%, and the significance level was set at 0.05. We decided a priori to treat results with a probability error equal to or lower than 10% ($p < 0.10$) as indicating a trend. All statistical analyses were carried out using R for Mac, version 1.4.1103.

## 3. RESULTS

### 3.1 Sample characteristics

All 128 participants were included in the analysis. Participants had a mean age of 28.82 years (*SD* = 10.78). Eighty-four participants were female, and 44 were male (see Table 1).

### 3.2 Primary outcome

Our analysis found no differences in the means of posttreatment heat-pain tolerance between the conditions. The mean of 48.32 °C in the NT condition did not statistically differ from the mean of 48.52 °C in the DT condition (difference = 0.09, CI = - 0.27 to 0.44, $p$ = 0.634) or from the mean of 47.99 °C in the PT condition (difference = -0.06, CI = - 0.56 to 0.43, $p$ = 0.800). Further, there was no interaction effect of the dog and the placebo (difference = 0.09, CI = -0.53 to 0.71, $p$ = 0.786) on posttreatment heat-pain tolerance (see Table 2).

We found a statistically relevant difference in the self-reported ratings of pain unpleasantness at the limit of heat-pain tolerance at posttreatment between the conditions DT and NT (difference = -0.96, CI = -1.58 to 0.34, $p$ = 0.010). Participants in the DT condition experienced heat-pain tolerance to be less unpleasant with a mean of 6.39 compared to participants in the NT condition, who had a mean of 7.75. There was no significant difference between the conditions PT and NT, as participants in the PT condition rated the unpleasantness of heat-pain tolerance with a mean of 7.01 and participants in the NT condition with a mean of 7.75 (difference = -0.40, CI = -0.97 to 0.17, $p$= 0.168). Further, we found a significant interaction of the dog and the placebo in the unpleasantness ratings, which were higher in the combined DPT than in the separate DT and PT (difference = 1.19, CI = 0.33 to 2.05, $p$ = 0.007) (see Table 2 and Figure 3).

Finally, we found a trend in the self-reported ratings of pain intensity at the limit of heat-pain tolerance at posttreatment. Participants in the DT condition rated pain intensity to be less intense with a mean of 7.17 compared to the mean of 7.96 of the ratings by participants in the NT condition (difference = -0.44, CI = -0.89 to 0.02, $p$ = 0.060). Again, no differences were found in the self-reported ratings of pain intensity between participants in the PT group with a mean of 7.25 and participants in the NT condition with a mean of 7.96 (difference = -0.33, CI = -0.79 to 0.13, $p$ = 0.153). There was a trend for an interaction of the dog and the placebo in the intensity ratings, which were higher in the combined DPT than in the separate DT and PT (difference = 0.71, CI = -0.05 to 1.47, $p$ = 0.077) (see Table 2 and Figure 4).

### 3.3 Secondary outcomes

We found no significant differences in the posttreatment heat-pain threshold between the conditions. The mean of 43.47 °C in the NT condition did not statistically differ from the mean of 43.02 °C in the DT condition (difference = -0.27, CI = -1.62 to 1.08, $p$ = 0.688) or the mean of 42.53 °C in the PT condition (difference = -0.22, CI = -1.53 to 1.09, $p$ = 0.739). Further, there was no interaction effect of the dog and the placebo on the posttreatment heat-pain threshold (difference = 0.90, CI = -0.97 to 2.76, $p$ = 0.342) (see Table 3).

With regard to the self-reported ratings of pain unpleasantness at the heat-pain threshold, we found a trend for a significant difference between the DT and NT conditions (difference = -0.54, CI = -1.16 to 0.08, $p$ = 0.088). Participants in the DT condition reported a lower rating of pain unpleasantness with a mean of 2.74 compared to those in the NT condition with a mean of 2.74. However, we found no significant differences between the ratings of participants in the PT condition with a mean of 2.54 and the ratings of participants in the NT condition with a mean of 3.97 (difference = -0.41, CI = -0.93 to 0.12, $p$ = 0.128). There was a significant interaction of the dog and the placebo in the unpleasantness ratings at the heat-pain threshold, which were higher in the combined DPT than in the separate DT and PT (difference = 0.99, CI = 0.12 to 0.187, $p$ = 0.027) (see Table 3).

The analyses of the self-reported ratings of pain intensity at the heat-pain threshold revealed no statistically relevant findings. The mean rating of 4.16 in the NT condition did not differ statistically from the mean of 3.48 in the DT condition (difference = -0.03, CI = -0.72 to 0.66, $p$ = 0.939) or from the mean of 3.16 in the PT condition (difference = -0.24, CI = -0.81 to 0.32, $p$ = 0.391). There was also no interaction effect of the dog and the placebo (difference = 0.39, CI = -0.59 to 1.37, $p$ = 0.430) (see Table 3).

With regard to expected pain unpleasantness, the findings show that participants in the DT and PT conditions expected heat-pain to be less unpleasant at the limit of their tolerance at posttreatment compared to participants in the NT condition. Participants in the NT condition had a mean of 6.78, which did significantly differ from the mean of 4.91 in the DT condition (difference = 0.83, CI = 0.60 to 1.05, $p$ < 0.001) or from the mean of 4.28 in the PT condition (difference = -2.18, CI = -2.96 to 1.40, $p$ < 0.001). Additionally, we found a significant interaction effect of the dog and the placebo regarding expected pain unpleasantness, which was lower in the combined treatment than in the separate DT and PT (difference = 2.19, CI = 1.09 to 3.28, $p$ < 0.001) (see Table 4 and Figure 5).

Similar results were found for expected pain intensity. Participants in the DT condition expected heat-pain to be less intense at the limit of their tolerance at posttreatment with a mean of 5.53 compared to those in the NT condition with a mean of 6.72 (difference = 0.82, CI = -1.73 to 0.01, $p$ = 0.051). Further, we found that participants in the PT condition expected heat-pain to be significantly less intense at the limit of their tolerance with a mean of 4.47 than participants in the NT condition who had a mean of 6.72 (difference = 0.83, CI = 0.59 to 1.07, $p$ < 0.001). Moreover, we also found a significant interaction effect of the dog and the placebo for expected pain intensity, which was lower in the combined treatment compared to the PT (difference = -1.71, CI = 0.61 to 2.80, $p$ = 0.003) (see Table 4 and Figure 6).

### 3.4 Perception of the study investigator

Analyses of the CRF-S showed differences among the conditions regarding perceptions of the study investigator. Participants in the DT condition tended to rate the study investigator to be more trustworthy with a mean of 26.53 compared to a mean of 25.94 for participants in the NT condition (difference = 0.45, CI = -0.08 to 0.99, $p$ = 0.096). Further, we also found that participants in the PT condition rated the study investigator to be significantly more trustworthy with a mean of 26.81 than participants did in the NT condition with a mean of 25.94 (difference = 0.66, CI = 0.18 to 1.14, $p$ = 0.008). Analysis showed no interaction effect of the dog and the placebo on the trustworthiness of the study investigator (difference = -0.41, CI = -1.19 to 0.40, $p$ = 0.327) (see Table 5).

### 3.5 Interaction with the dog and dog affinity

We found no difference between the intensity of interaction with the dog between participants (difference = -0.12, CI = -0.58 to 0.33, $p$ = 0.586). Further, there was no difference regarding the participants' dog affinity between the DT and the DPT conditions (difference = -0.12, CI = -0.50 to 0.25, $p$ = 0.507) (see Table 6).

## 4. DISCUSSION

The aim of this study was to examine the effect of the treatment rationale in AAI on experimentally induced pain in healthy participants.

While no differences in posttreatment heat-pain tolerance were found, participants rated the heat-pain experienced at the limit of their tolerance to be significantly less unpleasant and tendentially less intense posttreatment when the employed AAI was provided with a treatment rationale compared to participants in the no treatment condition. Further, they expected heat-pain at the limit of their tolerance to be significantly less unpleasant and tendentially less intense after posttreatment compared to participants that received no treatment. With regard to participants' posttreatment heat-pain threshold, the same pattern was observed, i.e., participants did not differ in their heat-pain threshold, but participants in the dog treatment experienced the pain at their heat-pain threshold to be significantly less unpleasant compared to participants in the no-treatment group. No differences were found in the ratings of pain intensity at participants' heat-pain threshold.

In a previous study we conducted on AAI with a dog in which the dog was not included in the treatment rationale, the presence of the dog had no positive analgesic effects on healthy participants. Instead, participants experienced heat-pain to be more intense at the limit of their tolerance in the presence of the dog compared to when no dog was present (Wagner et al., 2021). Taken together with the findings of the present study, this leads us to suggest that AAI needs to provide a treatment rationale to have analgesic effects.

This hypothesis is in line with previous research stressing the importance of treatment contexts to be effective (Wager & Atlas, 2015). The treatment rationale is considered to be an important factor in providing therapeutic meaning and in shaping the overall treatment context (Moerman & Jonas, 2002). The impact of the treatment rationale on treatment response has been demonstrated in diverse interventions, for example in psychotherapy (Tondorf et al., 2017), placebo treatments (Gaab et al., 2019), and open-label placebo treatments (Carvalho et al., 2016; Hoenemeyer et al., 2018; Kaptchuk et al., 2010; Locher et al., 2017). Interestingly, the effect of the treatment rationale can go in either direction: it can elicit a positive treatment response or a negative one (Rossettini et al., 2018). For example, the administration of a pain intervention with a positive meaning can induce positive expectations and lead to a positive analgesic response, whereas the administration of a pain intervention with no meaning or a negative meaning can induce no expectations or negative expectations that lead to an exacerbation or perpetuation of pain (Bingel et al., 2011). "Meaning making is central to every treatment" (Trachsel, 2019, p. 3), and our results suggest that this is also the case in AAIs for pain.

This understanding expands the common belief in AAI that animals are solely responsible for the analgesic effects. Previous studies have proposed direct neuroendocrine responses (Braun et al., 2009; Calcaterra et al., 2015; Harper et al., 2015; Silva & Osório, 2018; Zhang et al., 2021), cognitive distraction (Rodrigo-Claverol et al., 2019; Silva & Osório, 2018; Zhang et al., 2021), or social support (Zhang et al., 2021) as explanatory mechanisms for AAI. However, based on our findings and evidence stressing the importance of the treatment context (Wager & Atlas, 2015) it seems important to reevaluate the idea that animals are the panacea in AAI. Instead, it should be acknowledged that the effects in AAIs are also influenced by contextual factors, such as the provision of a treatment rationale.

We found that participants rated the study investigator as more trustworthy in the presence of a dog compared to when no dog was present. This is in line with previous in vitro studies (Creary, 2017; Schneider & Harley, 2006), which suggests that animals positively influence how we perceive others but contradicts the results from two studies with a real dog where no such effect was found (Goldmann et al., 2015; Wagner et al., 2021). But in those two studies, the presence of the dog was not part of the rationale. It is thus possible that including the animal in the treatment rationale is again important, in this case for positively impacting our perception of other people. Based on the mixed evidence, however, further research is needed to better understand if and how animals influence our perception.

Interestingly, we found no placebo effect in this study. While this result was unexpected considering the fact that we employed a well-established and standardized paradigm, which has elicited placebo effects in previous studies in our lab (Gaab et al., 2016; Gaab et al., 2019; Krummenacher et al., 2014; Locher et al., 2017; Locher et al., 2019), it is possible that the strict COVID measures impacted the interaction between study personnel and participants but not between the dog and participants. This might not only have reduced possible placebo effects but also have led to the observed negative interaction effects in self-reported unpleasantness at the limit of participants' heat-pain tolerance and at their heat-pain threshold posttreatment as well as in the expected unpleasantness at the limit of their heat-pain tolerance at posttreatment when both the dog and the placebo were administered.

### 4.1 Strengths and limitations

Other researchers have stated that there is a need to increase the internal validity of AAIs (López-Cepero, 2020, p. 1), and there is a recognized lack of high-quality studies on the effects and the mechanisms of AAI on pain (Waite et al., 2018). We therefore conducted a randomized controlled trial with a highly standardized study procedure to systematically control for confounding variables and to increase the internal validity. Further, this is the first study that investigated the impact of the treatment rationale on pain in an AAI. Hence, our findings bring new and important insights for future research on the mechanisms regarding pain in AAIs.

However, our study has several limitations. Our sample consisted of healthy participants that were not suffering from acute or chronic pain. While experimentally induced pain in healthy participants is regarded as a good model for clinical pain (Peerdeman et al., 2016), the results may not be generalizable to a clinical population. Further, the effects were only present in the self-reported pain ratings and not in heat-pain tolerance or threshold. This is in line, however, with previous placebo studies (Foddy, 2009; Locher et al., 2017; Schwarz & Büchel, 2015; Wechsler et al., 2011). Further, the dog owner performed dog appointments on her own while the other three study investigators only performed dog appointments in the presence of the dog owner. It is possible that the dog owner also had an impact on the results, but we surmise that the impact was very small since findings from meta-analysis of the analgesic effects of human social support suggest that the mere presence of a person is not sufficient to affect pain perception (Che et al., 2018). Moreover, only one dog participated in the study. This makes the dog treatment in this study highly comparable, but the results cannot be generalized to other dogs or other animal species.

### 4.2 Implications for future research

Our findings show that contextual factors matter in AAI, and further research is required to better understand the impact of contextual factors in AAI and to make these potential benefits available in the clinical application of AAI. Since AAI is increasingly being accepted and used clinical practice, we also see both the need and the potential to examine the impact of the treatment rationale and other contextual factors on the effects of AAI in clinical conditions.

## 5. CONCLUSION

The results of our study show that the treatment rationale can significantly impact the analgesic effects of AAI. When provided with a treatment rationale, AAI resulted in less unpleasant and tendentially less intense pain at the limit of heat-pain tolerance, both in participants’ experience and in their expectations.

This corresponds with the findings of a previous study, where the presence of a dog had no positive analgesic effects when it was not part of the treatment rationale.

We thus conclude that the presence of an animal is not sufficient for AAI to have an analgesic effect on pain unless it is provided with a treatment rationale.

**6. Conflicts of interest**

The authors declare no conflicts of interest.

**7. Author contributions**

J. G., C. W. and K. H. conceived the study. C. W., K. H., and J. G designed it. C. W. acquired the data, carried out the analyses, and drafted the manuscript. K. H. and J. G. provided critical advice and revised the manuscript. All authors read and approved the final manuscript.

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## 11. Figure legends

**Figure 1.** Flow Chart

**Figure 2.** Timeline of the study procedure

**Figure 3.** Self-reported ratings of pain unpleasantness at the limit of heat-pain tolerance. For each condition (NT = no treatment, DT = dog treatment, PT = placebo treatment, DPT = dog and placebo treatment), the respective mean and standard deviation are displayed. ** = p - value <.01

**Figure 4.** Self-reported ratings of pain intensity at the limit of heat-pain tolerance. For each condition (NT = no treatment, DT = dog treatment, PT = placebo treatment, DPT = dog and placebo treatment), the respective mean and standard deviation are displayed.

**Figure 5.** Self-reported ratings of expected pain unpleasantness at the limit of heat-pain tolerance. For each condition (NT = no treatment, DT = dog treatment, PT = placebo treatment, DPT = dog and placebo treatment), the respective mean and standard deviation are displayed. ** = p - value <.01

**Figure 6.** Self-reported ratings of expected pain intensity at the limit of heat-pain tolerance. For each condition (NT = no treatment, DT = dog treatment, PT = placebo treatment, DPT = dog and placebo treatment), the respective mean and standard deviation are displayed. ** = p - value <.01

**Table 1.** *Sociodemographic characteristics of participants*

| **Condition** | ***N*** | **Age mean (*SD*)** | ***N* (%) female** | **Family status *N*** | **Highest educational level *N* (%)** | **Employment level *N* (%)** |
|---|---|---|---|---|---|---|
| NT | 32 | 29.22 (12.51) | 20 (62.5%) | Single: 27<br>Married: 5<br>Registered partnership: 0<br>Divorced: 0<br>Other: 0 | Primary: 0<br>Secondary: 19 (59.38%)<br>Tertiary: 13 (40.62%) | Full-time: 10 (31.25%)<br>Part-time: 16 (50%)<br>None or student: 6 (18.75%) |
| DT | 32 | 31.03 (12.55) | 21 (65.63%) | Single: 29<br>Married: 2<br>Registered partnership: 0<br>Divorced:1<br>Other: 0 | Primary: 0<br>Secondary: 15 (46.88%)<br>Tertiary: 17 (53.12%) | Full-time: 6 (18.75%)<br>Part-time: 11 (34.38%)<br>None or student: 15 (46.88%) |
| PT | 32 | 29.06 (10.19) | 21 (65.3%) | Single: 28<br>Married: 4<br>Registered partnership: 0<br>Divorced:0<br>Other: 0 | Primary: 0<br>Secondary: 18 (56.25%)<br>Tertiary: 14 (43.75%) | Full-time: 3 (9.38%)<br>Part-time: 11 (34.38%)<br>None or student: 18 (56.25%) |
| DPT | 32 | 25.97 (6.66) | 22 (68.75%) | Single: 29<br>Married: 2<br>Registered partnership: 0<br>Divorced: 0<br>Other: 1 | Primary: 0<br>Secondary: 15 (46.88%)<br>Tertiary: 17 (53.12%) | Full-time: 4 (12.5%)<br>Part-time: 7 (21.88%)<br>None or student: 21 (65.63%) |

*SD* = standard deviation, *N* = number of participants, NT = no treatment, DT = dog treatment, PT = placebo treatment, DPT = dog and placebo treatment

**Table 2.** *Primary outcomes: Limit of heat-pain tolerance and corresponding self-reported ratings of pain intensity and unpleasantness. Values for heat-pain tolerance are presented in °C.*

| | | Condition | | | |
|---|---|---|---|---|---|
| | | **NT** ($N$ = 32) | **DT** ($N$ = 32) | **PT** ($N$ = 32) | **DPT** ($N$ = 32) |
| **Baseline** | **Heat-pain tolerance** (mean, *SD*) | 48.42 (1.56) | 48.58 (1.05) | 48.11 (1.55) | 48.14 (1.51) |
| | **Self-reported pain intensity** at the limit of tolerance (mean, *SD*) | 7.90 (1.61) | 7.5 (1.52) | 7.48 (1.64) | 7.44 (1.54) |
| | **Self-reported pain unpleasantness** at the limit of tolerance (mean, *SD*) | 7.62 (1.95) | 7.1 (1.83) | 7.22 (1.83) | 7.38 (1.55) |
| **Posttreatment** | **Heat-pain tolerance** (mean, *SD*) | 48.32 (1.36) | 48.52 (1.10) | 47.99 (1.88) | 48.18 (1.48) |
| | **Self-reported pain intensity** at the limit of tolerance (mean, *SD*) | 7.96 (1.60) | 7.17 (1.72) | 7.25 (1.72) | 7.48 (1.90) |
| | **Self-reported pain unpleasantness** at the limit of tolerance (mean, *SD*) | 7.75 (1.93) | 6.39 (1.91) | 6.39 (1.96) | 7.39 (1.82) |

*SD* = standard deviation, *N* = number of participants, NT = no treatment, DT = dog treatment, PT = placebo treatment, DPT = dog and placebo treatment

**Table 3.** *Heat-pain threshold and corresponding self-reported ratings of pain intensity and unpleasantness. Values for heat-pain threshold are presented in °C.*

| | | Condition | | | |
|---|---|---|---|---|---|
| | | **NT** (*N* = 32) | **DT** (*N* = 32) | **PT** (*N* = 32) | **DPT** (*N* = 32) |
| **Baseline** | **Heat-pain threshold** (mean, *SD*) | 44.43 (2.24) | 44.17 (2.31) | 43.37 (2.88) | 43.40 (2.92) |
| | **Self-reported pain intensity** at threshold (mean, *SD*) | 4.98 (2.11) | 4.19 (1.88) | 4.06 (1.80) | 4.38 (2.03) |
| | **Self-reported pain unpleasantness** at threshold (mean, *SD*) | 4.88 (2.11) | 4.01 (1.96) | 3.67 (1.67) | 4.20 (2.07) |
| **Posttreatment** | **Heat-pain threshold (**mean, *SD*) | 43.47 (2.78) | 43.02 (3.33) | 42.53 (3.37) | 43.18 (3.18) |
| | **Self-reported pain intensity** at threshold (mean, *SD)* | 4.16 (2.26) | 3.48 (1.98) | 3.16 (1.59) | 3.71 (2.22) |
| | **Self-reported pain unpleasantness** at threshold (mean, *SD*) | 3.97 (2.38) | 2.74 (1.59) | 2.54 (1.22) | 3.34 (2.21) |

*SD* = standard deviation, *N* = number of participants, NT = no treatment, DT = dog treatment, PT = placebo treatment, DPT = dog and placebo treatment

**Table 4.** *Self-reported ratings of expected unpleasantness and intensity at the limit of heat-pain tolerance*

| | Condition | | | |
|---|---|---|---|---|
| | **NT** (*N* = 32) | **DT** (*N* = 32) | **PT** (*N* = 32) | **DPT** (*N* = 32) |
| **Expected intensity** at limit of heat-pain tolerance (mean, *SD*) | 6.72 (2.25) | 5.53 (2.02) | 4.47 (1.8) | 5.22 (1.26) |
| **Expected unpleasantness** at limit of heat-pain tolerance (mean, *SD*) | 6.78 (2.46) | 4.91 (2.13) | 4.28 (1.76) | 5.05 (1.35) |

*SD* = standard deviation, *N* = number of participants, NT = no treatment, DT = dog treatment, PT = placebo treatment, DPT = dog and placebo treatment

**Table 5.** *Counselor Rating Form—Short Version (CRF-S): Subscale trustworthiness*

| | | Condition | | | |
|---|---|---|---|---|---|
| | | **NT** (*N* = 32) | **DT** (*N* = 32) | **PT** (*N* = 32) | **DPT** (*N* = 32) |
| **Trustworthiness** | **Baseline** (mean, *SD*) | 26.19 (2.61) | 26.34 (1.70) | 26.44 (1.88) | 26.06 (2.56) |
| | **Posttreatment** (mean, *SD*) | 25.94 (2.51) | 26.53 (1.95) | 26.81 (1.75) | 26.59 (2.03) |

*SD* = standard deviation, *N* = number of participants, NT = no treatment, DT = dog treatment, PT = placebo treatment, DPT = dog and placebo treatment

**Table 6.** *Interaction with the dog and dog affinity*

| | Condition | |
|---|---|---|
| | **DT**<br>(*N* = 32) | **DPT**<br>(*N* = 32) |
| **Dog affinity** (mean, *SD*) | 4.56 (0.88) | 4.69 (0.59) |
| **Dog interaction** (mean, *SD*) | 2.91 (1.00) | 3.03 (0.82) |

*SD* = standard deviation, *N* = number of participants, DT = dog treatment, DPT = dog and placebo treatment

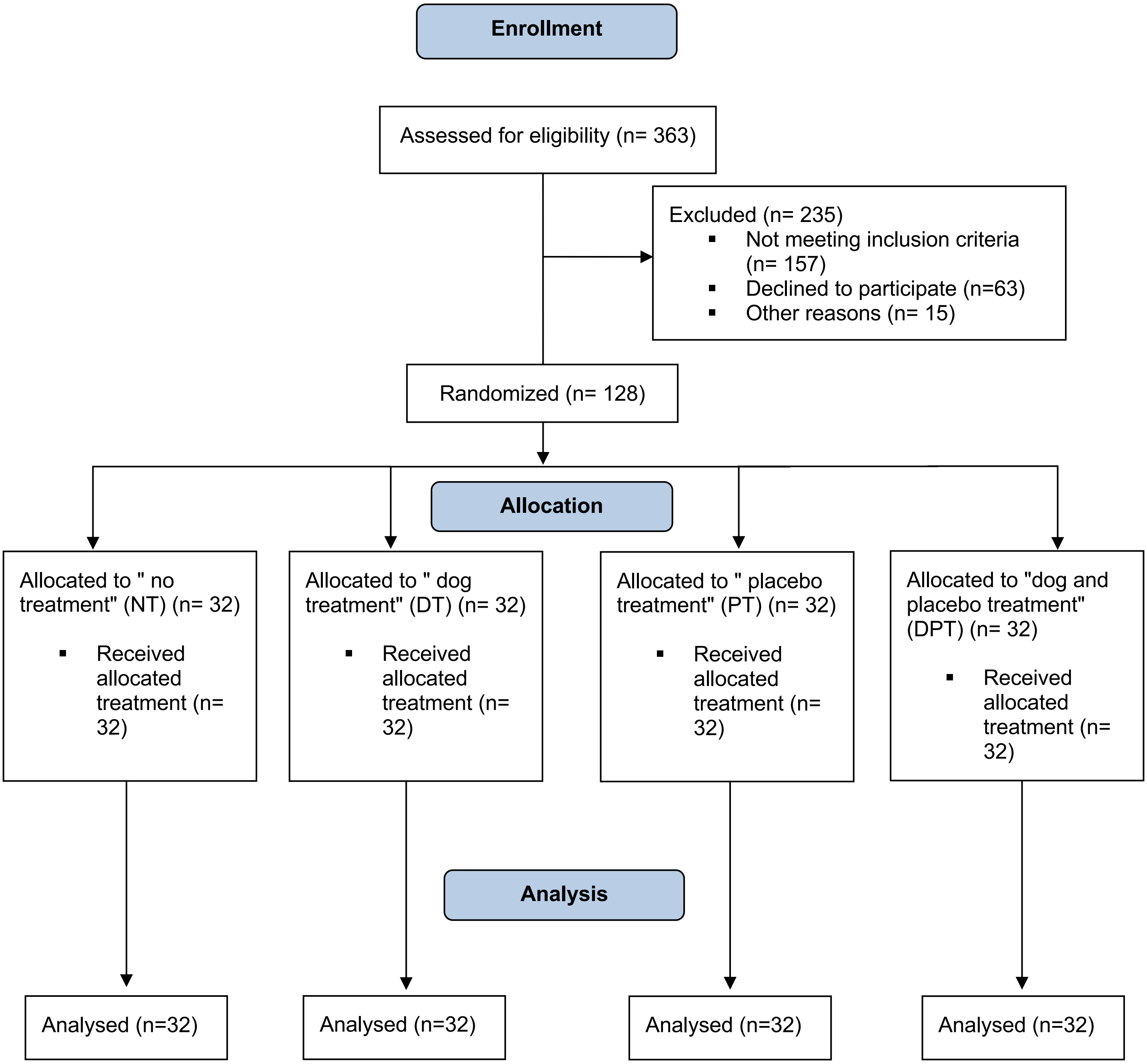
Enrollment
Assessed for eligibility (n= 363)
Excluded (n= 235)
Not meeting inclusion criteria (n= 157)
Declined to participate (n=63)
Other reasons (n= 15)
Randomized (n= 128)
Allocation
Allocated to " no treatment" (NT) (n= 32)
Received allocated treatment (n= 32)
Allocated to " dog treatment" (DT) (n= 32)
Received allocated treatment (n= 32)
Allocated to " placebo treatment" (PT) (n= 32)
Received allocated treatment (n= 32)
Allocated to "dog and placebo treatment" (DPT) (n= 32)
Received allocated treatment (n= 32)
Analysis
Analysed (n=32)
Analysed (n=32)
Analysed (n=32)
Analysed (n=32)

**Figure 1.**

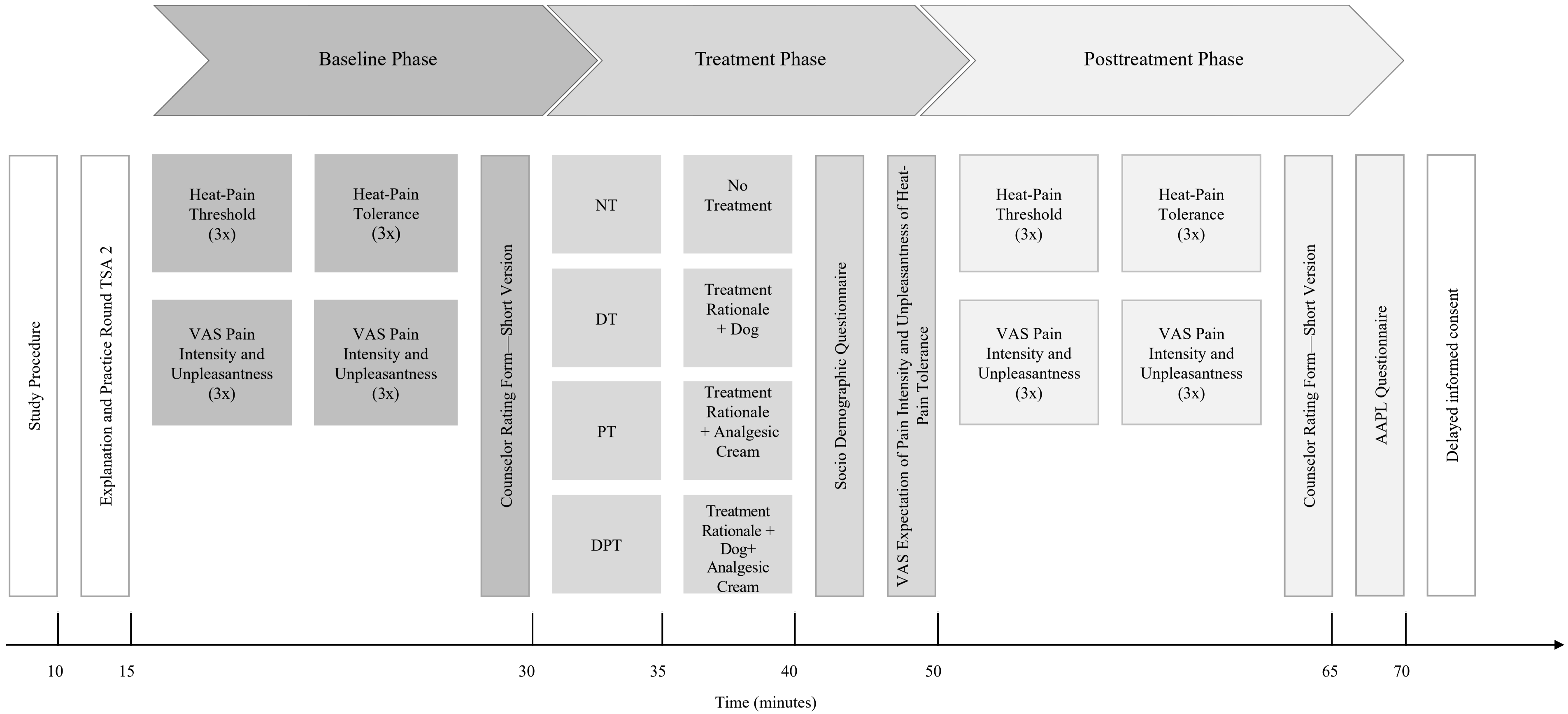
Baseline Phase
Treatment Phase
Posttreatment Phase
Study Procedure
Explanation and Practice Round TSA 2
Heat-Pain Threshold (3x)
VAS Pain Intensity and Unpleasantness (3x)
Heat-Pain Tolerance (3x)
VAS Pain Intensity and Unpleasantness (3x)
Counselor Rating Form—Short Version
NT
DT
PT
DPT
No Treatment
Treatment Rationale + Dog
Treatment Rationale + Analgesic Cream
Treatment Rationale + Dog+ Analgesic Cream
Socio Demographic Questionnaire
VAS Expectation of Pain Intensity and Unpleasantness of Heat-Pain Tolerance
Heat-Pain Threshold (3x)
VAS Pain Intensity and Unpleasantness (3x)
Heat-Pain Tolerance (3x)
VAS Pain Intensity and Unpleasantness (3x)
Counselor Rating Form—Short Version
AAPL Questionnaire
Delayed informed consent
10
15
30
35
40
50
65
70
Time (minutes)

**Figure 2.**

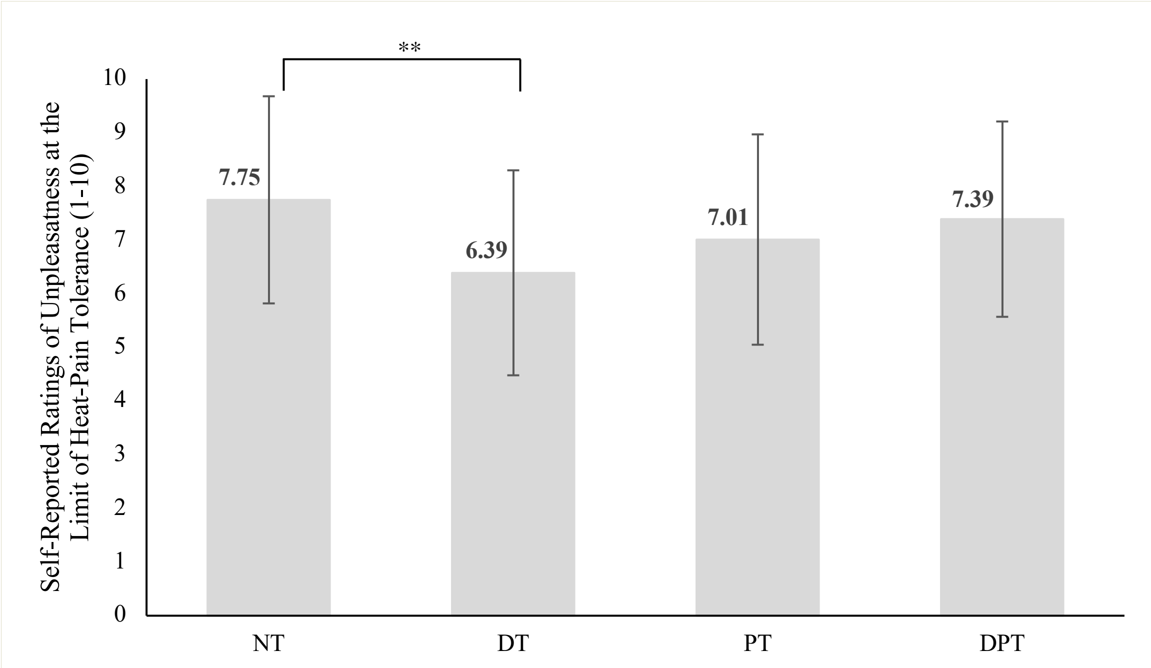


**Figure 3.**

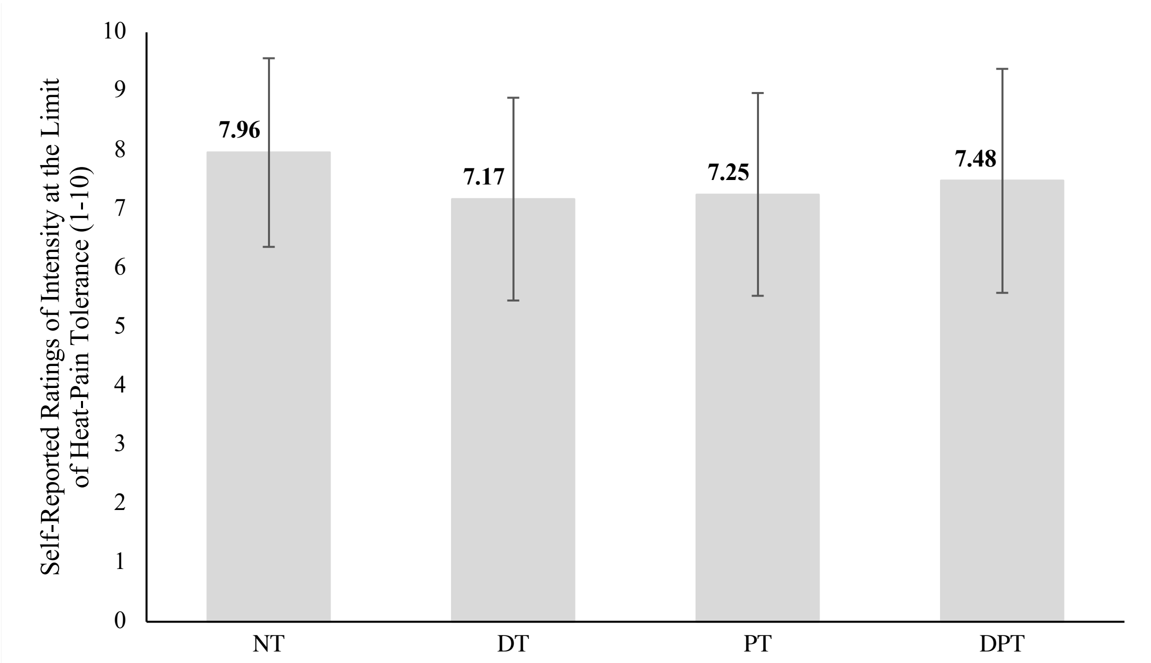


**Figure 4.**

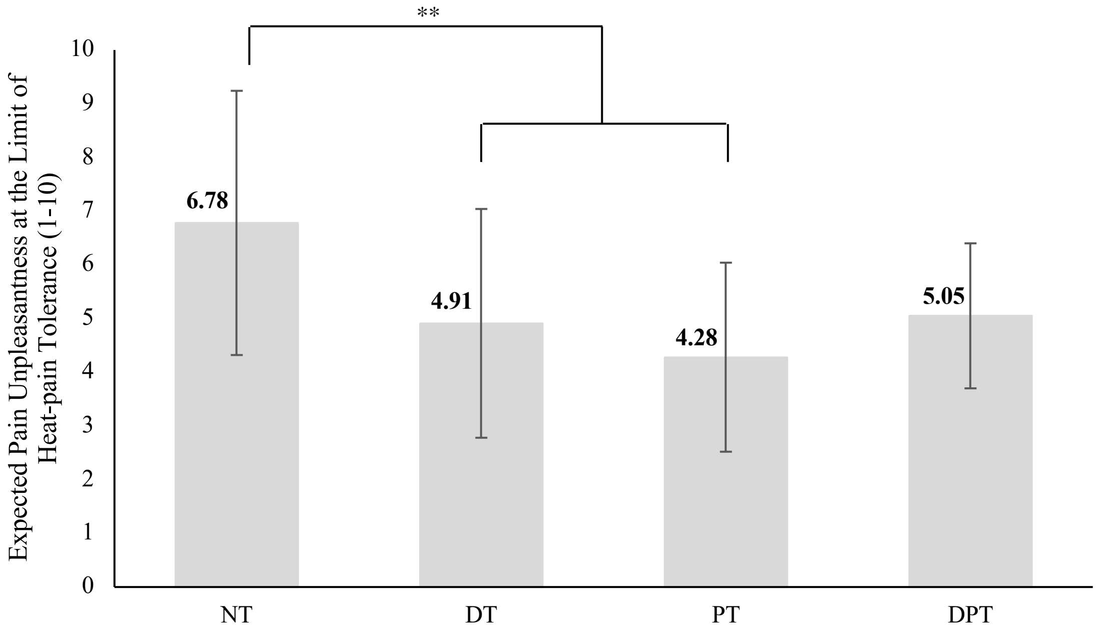


**Figure 5.**

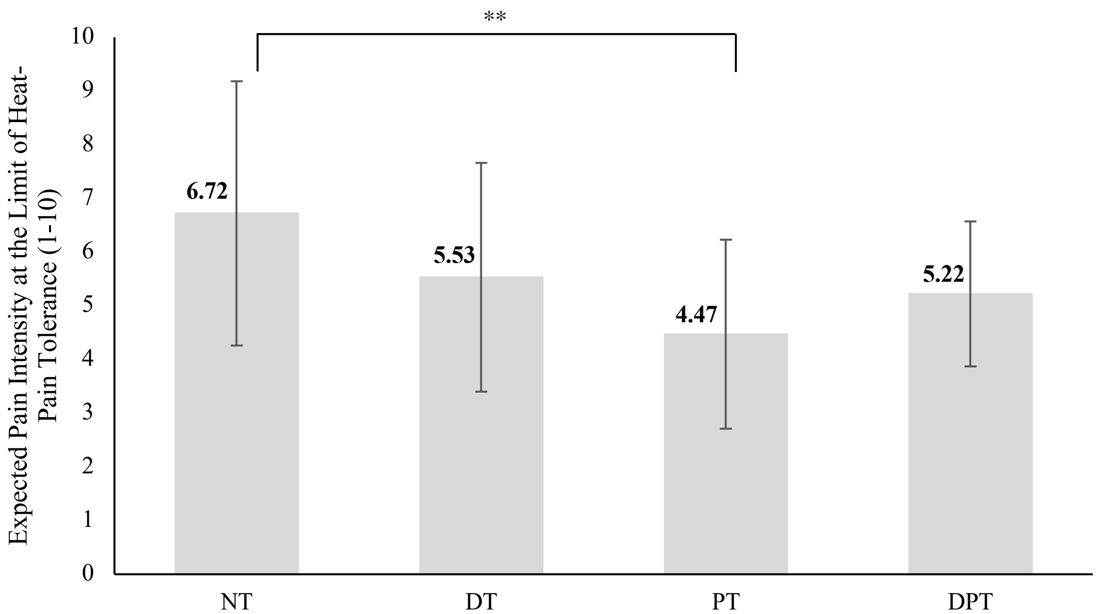


**Figure 6.**

## Appendix C

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### Study 3

**Wagner, C.,** Grob, C., Hediger, K. (2022): Specific and Non-Specific Factors of Animal-Assisted Interventions: A Systematic Review *(submitted for publication)*

# Specific and Nonspecific Factors of Animal-Assisted Interventions: A Systematic Review

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## ABSTRACT

Research on animal-assisted interventions (AAIs) has increased massively in the last few years. But it is still not clear how AAIs work and how important the animal is in such interventions. The aim of this systematic review was to compile the existing state of knowledge about the working mechanisms of AAIs. We searched 12 major electronic databases for previous AAI studies with active control groups. Of 2001 records identified, we included 172 studies in the systematic review. We extracted previously published hypotheses about working mechanisms and factors that have been implicitly considered specific or nonspecific in AAI research by categorizing control conditions using content analysis following Mayring. We found that 84% of the included studies mentioned a hypothesis of working mechanisms, but 16% did not define specific hypotheses. By analyzing their control conditions, we found that in most controlled studies, the animal or the interaction with the animal was implicitly considered as a specific factor for the effects of the AAI. Nonspecific factors such as therapeutic aspects, social interactions, or novelty have also been controlled for. We conclude that AAI research still cannot answer the question of how and why AAIs work. To address this important research gap, we suggest using component studies with innovative control conditions and results from placebo research to address both the specific and nonspecific, contextual factors of AAIs to disentangle its mechanisms.

**Keywords:** animal-assisted intervention; specific factor; contextual factor; mechanism

## 1. INTRODUCTION

Research on animal-assisted interventions (AAIs) has increased massively in the last few years (Rodriguez et al., 2021). But it is still not clear how important the animal is in such interventions. In 2012, Marino addressed construct validity in AAIs and concluded in a review that it is a hugely neglected topic (Marino, 2012). One decade later, the evidence of the effectiveness of AAIs is increasing (Waite et al., 2018; Wood and Fields, 2019; Borgi et al., 2020; Babka et al., 2021; Chang et al., 2021; Diniz Pinto et al., 2021; Hediger et al., 2021; Nieforth et al., 2021), but the question of construct validity is still unresolved. Previous research has mainly focused on investigating *if* AAIs work but almost entirely ignored the question of *how* it works. The claim that the underlying mechanisms of AAIs are not clear is not new, but it is intensifying, and researchers are debating the internal validity of a broad range of different interventions that are all subsumed under the umbrella term of AAI (Kazdin, 2017; Serpell et al., 2017; López-Cepero, 2020; Rodriguez et al., 2021).

AAIs are based on the assumption that the animal is the key relevant component for the effects of such interventions. It has been proposed that an animal adds something different to a therapeutic setting compared to a human or another stimulus. The literature has therefore claimed that a live animal is a highly specific component of AAIs (Marino, 2012). It is, however, still unclear if the living animal itself—and if so, what specific characteristics of the animal—leads to the documented effects of AAIs. Specificity is a major challenge in current AAI research, so it is crucial to identify if the effects of AAIs are due to the presence of an animal specifically.

López-Cepero (2020) proposed a component-centered approach to investigate how AAIs work. AAIs consist of a complex mixture of components such as being confronted with a novel stimulus and situation, receiving increased attention from a therapist, engaging in increased physical activity and physical contact, or sometimes even being in a different environment. AAI should thus be seen as a treatment (such as psychotherapy, speech therapy or physiotherapy) or even as a specific manualized therapy (such as cognitive behavioral therapy, for example) with the addition of a specific component: the animal. We agree with this approach of disentangling the effect of different treatment components, but we propose going even a step further by using a component-centered approach to look at the animal, the added component. The animal itself is a complex stimulus with different characteristics (Marino, 2012;

Rodriguez et al., 2021): for example, animals react to clients' behavior, move proactively, have fur or feathers, come in different shapes and colors, and have varying temperaments and personalities. All of these characteristics could lead to different effects.

Component studies are the best method for examining the active components of a treatment (Cuijpers et al., 2019). Their study designs can decompose multicomponent treatments by comparing the complete intervention with an intervention in which one component is left out (dismantling studies) or with an intervention with an additional component (additive studies) (Bell et al., 2013; Mira et al., 2019). The effects of an intervention can be distinguished into specific effects and contextual, or nonspecific, effects (Wampold, 2021). Specific effects are effects that are caused by the specific intervention, while contextual, or nonspecific, effects result from factors that are not specific to the intended intervention and that appear in every intervention, such as treatment expectations, the therapeutic alliance (Rossettini et al., 2018; Wampold, 2021), novelty, demand characteristics, and effects from experimenters' expectations (Marino, 2012). Such nonspecific effects are considered as confounding variables that can affect internal and external validity (Carlino et al., 2011; Geers and Miller, 2014).

It is crucial that we begin to understand what makes AAIs effective. To pursue this goal, we must know what mechanisms, specific factors, and nonspecific factors have been investigated so far. While older studies usually did not control for nonspecific effects, recent studies have started to dismantle the potential components of AAIs and even of the animal by using more specific and rigorous controls. Investigating the used control conditions in previous AAI studies makes it possible to infer the authors' assumptions about the specific and nonspecific effects of AAIs.

The aim of this systematic review was to compile the existing state of knowledge about how AAIs work. To do so, we collected the explicitly stated hypotheses about the working mechanisms of AAIs in previous studies and inferred which factors were implicitly considered specific or nonspecific by categorizing the control conditions.

## 2. METHODS

### 2.1 Search strategy

We conducted a systematic literature search in the following databases: PsychINFO, PSYNDEX, ERIC, MEDLINE, Embase, PubMed, Cochrane Library, Web of Science, Scopus, CINAHL, PTSDpubs, and Dissertations & Theses. We also used other sources to identify studies. A summary of the applied search strategies can be found in the Appendix, Table 1.

We imported all the records into Covidence, a systematic review software (Veritas Health Innovation, Melbourne, Australia), where duplicates were identified and removed. The screening was also performed in Covidence. The titles and abstracts of the included records were screened by two independent researchers in duplicate to exclude obvious irrelevant references and duplicates. Full texts were again screened by two independent researchers in duplicate to examine the records in more detail for inclusion and exclusion criteria. Conflicts were resolved by consensus among all the researchers involved in the screening process (CW, KH, and CG).

Identifying, screening, and determining the eligibility of the studies was done according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (McInnes et al., 2018). The study procedure was defined a priori, and the protocol was preregistered with PROSPERO (registration number: CRD42020158103). The date of the last search was 13 January 2022.

**2.2 Study selection**

To be eligible for inclusion, studies had to (1) investigate an AAI, (2) include an active control group, and (3) be written in English or German.

We included all studies that examined a type of AAI (e.g., animal-assisted therapy, animal-assisted activity, animal-assisted education, hippotherapy, pet therapy) with a live animal. We followed the terminologies of the IAHAIO (2018) and included every study with an intervention that can be considered an AAI according to the IAHAIO definition. We excluded studies on pet ownership. We included all forms of active control conditions in all types of study designs. Active control was defined as a condition in which the participants received a specific intervention offered by the study team. We excluded studies where participants in the control condition received standard care (i.e., care that was not offered by the study team), where they were on a waiting list, or where the study was a pre–post design with only one group. Further, we excluded records that were only registered as clinical trials and abstracts or poster presentations, because they did not provide sufficient information for our review. We contacted the study authors if a record was not available through university libraries. Studies were excluded if we were not able to receive the full text (see Figure 1 for the flow chart).

We first screened the titles and abstracts of the records. During full-text screening we excluded all records that did not fulfill all our inclusion criteria.

## 2.3 Data extraction

Prior to the data extraction, all researchers received training in using the form for extracting information on the following categories: first author's name and country, publication year, the characteristics of the experimental and control intervention, factor hypotheses, and the animal included in the study.

In a first step, all the data were independently extracted and coded in duplicate by a team of five research assistants in Microsoft Office Excel 2016. In a second step, all disagreements between the two raters were identified independently by two researchers, and conflicts were resolved by consensus among all the researchers involved in the screening process (CW, KH, and CG).

## 2.4 Data analyses

To extract the factor hypotheses, the specific factors, and the nonspecific factors, we used structured content analysis following Mayring (2014). Two independent raters analyzed the manuscripts independently in a first step and extracted the hypotheses, the specific factors, and the nonspecific factors. In a second step, the two coding schemes were compared, disagreements were discussed with two authors (CW and HK), and consensus was reached on one scheme. All hypotheses and factors that were not mentioned more than twice and did not fit into any existing category were classified as "other." The base rate for the study characteristics, factor hypotheses, and specific and nonspecific factors was the total number of the included studies ($N$ = 172). Descriptive analyses were carried out using R for Mac, version 1.4.1103.

### *2.4.1. Factor hypotheses*

We defined factor hypotheses as hypotheses, factors, or mechanisms that authors mentioned in the introductions of their studies to explain how AAIs work. It was possible for a study to mention several hypotheses. Two independent raters independently extracted factor hypotheses in the studies. All disagreements were solved by two authors (CW and KH). After that, two authors (CW and KH) reviewed the categories of the factor hypotheses and subsumed them into 11 main categories.

*2.4.2. Specific factors of AAIs*

We defined a factor as specific if it was present in the experimental condition but not in the control condition. Two raters independently compared the characteristics of the experimental interventions and the control interventions. All factors that were not present in the control conditions were coded as specific factors. The two raters extracted the factors independently. After that, they independently summarized the factors into categories. All disagreements were resolved by a third rater (CW). Then two researchers (CW and KH) reviewed the categories and subsumed then into nine main categories.

Items were listed in several categories if they were applicable. For example, the item *training in animal care* was included in category 5, “taking care of an animal,” because aspects of taking care of an animal were present and in category 8, “education about an animal,” because subjects received training.

*2.4.3. Nonspecific factors of AAIs*

All factors that existed in both the experimental and the control interventions were defined as nonspecific factors. Two independent raters compared the experimental and control conditions from each study and independently listed all the factors that occurred in both interventions. In a second step, they independently categorized the factors. All disagreements were then resolved by a third rater (CW). After the disagreements were resolved, two authors (CW and KH) reviewed the categories of nonspecific factors and subsumed them into 14 main categories.

It was possible for an item to be listed in several categories. *Physiotherapy*, for example, was included in category 1, “physical activity,” but also in category 2, “therapeutic aspects.”

## 3. RESULTS

### 3.1 Search results

We identified 2001 reports and screened 1893 titles and abstracts after we had removed duplicates. We assessed the full text of 525 reports for eligibility. In the end, 172 studies, which were published in 176 reports, fulfilled our inclusion criteria and were included in this systematic review (see Figure 1).

### 3.2 Study characteristics

The included studies were published in records between 1987 and 2022. Of these, 76.14% (*n* = 134) were published between 2014 and 2021; 164 were peer-reviewed and published as journal articles, and only six were not published.

The majority of the reports (*n* = 116) were conducted in the USA (*n* = 74), Germany (*n* = 13), South Korea (*n* = 12), Spain (*n* = 9), or Italy (*n* = 8). Regarding the animals, a large majority of the studies used dogs (*n* =107) or horses (*n* = 50), followed by cats (*n* = 7), guinea pigs (*n* = 6), or farm animals (*n* = 6) such as donkeys, goats, sheep, chickens, pigs, and rabbits (see Table 1 for an overview of the study characteristics).

### 3.3 Factor hypotheses

We defined the following eleven categories, sorted by frequency: (1) human–animal interaction, (2) not specified, (3) movement by the animal, (4) social facilitator or catalyst, (5) relationship with an animal, (6) other, (7) presence of an animal, (8) physical contact, (9) social or emotional support, (10) taking care of an animal, (11) physical activity (see Table 2 and Figure 2). Detailed information about each factor-hypothesis category can be found in the Supplement, S2.

**Human–animal interaction.** This category subsumed hypotheses that held the positive impact of human–animal interaction in general as responsible for the effects of AAIs. For example, authors stated that the interaction with an animal can reduce human stress (e.g., Barker et al., 2016; Fiocco and Hunse, 2017) or anxiety (e.g., Crossman et al., 2015; Foerder and Royer, 2021) or increase oxytocin levels (e.g., Chen et al., 2021). We found that 32.56% (*n* = 56) of the analyzed studies hypothesized human–animal interaction to be the working mechanism of AAIs.

**Not specified.** This category contained studies where the authors did not specify possible mechanisms, made general assumptions, or mentioned different mechanisms in their introduction without specifying in the end what they hypothesized to be the working mechanism. For example, if authors mentioned that AAIs can lead to stress relief but did not specify what leads to this stress relief (such as interacting with the animal), the hypothesis was categorized as not specified (e.g., Gocheva et al., 2018; Bunketorp-Kall et al., 2019; An and Park, 2021). The results show that 16.86% (*n* = 29) of the studies did not specify factor hypotheses.

**Movement by the animal**. In this category, we subsumed hypotheses that assumed that movement by the animal is crucial for the effects of AAIs. This includes, for example, the movement or rhythm of a horse when riding (e.g., Ambrozy et al., 2017; Hession et al., 2019; Kraft et al., 2019). We found that authors of 24 studies mentioned movement as a mechanism for the effects of AAIs, which accounted for 13.95% of the analyzed studies.

**Social facilitator or catalyst.** In this category, we included studies that hypothesized that animals' ability to act as social facilitators or catalysts has positive effects on humans. For example, authors hypothesized that animals enhance social learning in humans (Schuck et al., 2015) or foster human social communication and interaction skills (e.g., Barak et al., 2001; Flynn et al., 2019). The analyses revealed that 12.21% ($n$ = 21) of the analyzed studies mentioned the animal as a social facilitator or catalyst as a possible mechanism for the effects of AAIs.

**Relationship with an animal.** In this category, we subsumed hypotheses addressing the positive effect of relationships, attachment, or companionship between humans and animals. For example, some authors mentioned the positive effect of an attachment (e.g., Crump and Derting, 2015) or relationship established over time between a patient and an animal (Lanning et al., 2014). The results show that 16 studies mentioned the relationship between humans and animals as an explanation for the mechanisms of AAIs. This accounted for 9.3% of the analyzed studies.

**Other.** In this category, we summarized hypotheses that were not mentioned more than twice and did not match any other category. Examples include the biophilia hypothesis (e.g., Antonioli and Reveley, 2005; Gee et al., 2019) or the hypothesis that the sound of insects can create nostalgic feelings (Park et al., 2019). In total, we identified 15 studies with other factor hypotheses, which accounted for 8.72% of the analyzed studies.

**Presence of animal.** In this category we included all studies that considered the presence of an animal as a possible mechanism of AAIs. For example, some claimed that the presence of an animal (in contrast to interacting with an animal) has a calming effect (Allen et al., 2021) or can distract from stressful situations (Hansen et al., 1999). We found that 6.98% ($n$ = 12) of the studies mentioned the presence of an animal as a possible mechanism.

**Physical contact.** This category encompassed hypotheses addressing physical contact with the animal as a possible mechanism of AAIs. For example, some authors suggested that petting an animal increases autonomic arousal (Vandagriff et al., 2021). We found that 10 studies mentioned physical contact as a possible mechanism of AAIs, which accounted for 5.81% of the analyzed studies.

**Social or emotional support.** In this category, we included hypotheses that animals can provide either social or emotional support to humans. An example is the suggestion that an animal can provide social support comparable to that of a human (Lass-Hennemann et al., 2014). Authors of six studies mentioned animals as social or emotional support as a hypothesis for the effects of AAIs. This accounted for 3.49% of the analyzed studies.

**Taking care of an animal.** In this category, we included studies where the authors hypothesized that the opportunity to take care of an animal can enhance the effects of AAIs (e.g., Murry and Allen, 2012; Eckes et al., 2020). We found five studies where authors mentioned this as a potential mechanism of AAIs. This accounted for 2.91% of the analyzed studies.

**Physical activity.** We subsumed hypotheses about the importance of physical activity for the effects of AAIs in this category. For example, some authors suggested that exercising with animals (e.g., walking with an animal) leads to an effect (Aranda-Garcia et al., 2015). In total, 2.91% (*n* = 5) of the analyzed studies mentioned physical activity as a possible mechanism of AAIs.

### 3.4 Specific factors of AAIs

We identified nine categories of specific factors of AAIs that were reflected in the control conditions of published AAI studies. Ordered by frequency, these categories were: (1) animal, (2) interaction with an animal, (3) movement by the animal, (4) physical contact, (5) taking care of an animal, (6) training an animal, (7) other, (8) social interaction, (9) relationship with an animal (see Table 2 and Figure 3). A detailed description of all the categories of specific factors can be found in the Supplement, S3.

**Animal.** In the category “animal,” we included studies that had an experimental condition with a live animal and that compared that condition to a control condition with no animal present (e.g., Julius et al., 2013; Kim et al., 2016; Branson et al., 2017; Hartfiel et al., 2017; Levinson et al., 2017; Schuck et al., 2018; Wolynczyk-Gmaj et al., 2021; Abdel-Aziem et al., 2022). We found that 88.37% (*n* = 152) of the studies controlled for an animal as a specific factor.

**Interaction with an animal.** Here we included studies with experimental conditions that contained a specific form of interaction with an animal, such as playing with an animal or free interaction (e.g., Hansen et al., 1999; Machova et al., 2019; Gebhart et al., 2020). We also included petting in this category if it was only mentioned as one of many ways that subjects could interact with an animal (e.g., Crump and Derting, 2015; Gocheva et al., 2018). If physical contact was part of the intervention—for example, if participants had to pet an animal—we categorized the factor under "physical contact" (e.g., Charnetski et al., 2004; Binfet et al., 2021). Further, in this category, we included studies that defined the reaction of the animal—such as sounds or other responses—as important for the interaction. Analyses revealed that 46.51% (*n* = 80) of the studies controlled for the interaction with an animal as a specific factor.

**Movement by the animal.** In this category, we included studies with experimental conditions that incorporated movement by an animal as part of the intervention, such as while horseback riding (e.g., Lechner et al., 2007; Kim et al., 2014; Alemdaroğlu et al., 2016; Abdel-Aziem et al., 2022). We determined that 17.44% (*n* = 30) of the studies controlled for movement as a specific factor.

**Physical contact.** In this category, we included studies with experimental conditions that specified physical contact with an animal, such as petting, as the factor in their intervention (e.g., Crump and Derting, 2015; Holman et al., 2020; Binfet et al., 2021). We found that 12.79% (*n* = 22) of the studies controlled for physical contact as a specific factor.

**Taking care of an animal.** Here, we included studies with experimental conditions where participants took care of an animal, for example, by grooming, feeding, or milking it (e.g., Berget and Braastad, 2008; Ko et al., 2016; Gocheva et al., 2018). Of the analyzed studies, 12.21% (*n* = 21) defined taking care of an animal as a specific factor.

**Training an animal.** In this category, we included studies with experimental conditions where subjects could teach or train animals, for example, by giving animal commands (e.g., Rawleigh and Purc-Stephenson, 2021). We found that 11 studies included training animals as a specific factor, which accounted for 6.39% of the analyzed studies.

**Other.** Here we included studies with characteristics in their experimental conditions that did not match any other category and that were not mentioned more than twice. Examples in this category are mounting material (Bravo Gonçalves Junior et al., 2020), the familiarity of the animal (Odendaal, 2001), or the frequency of the intervention (Vidal Prieto et al., 2021). We found 11 studies that controlled for other specific factors. This accounted for 6.39% of the included studies.

**Social interaction.** In this category, we included studies with experimental conditions where subjects engaged with other human beings, for example, in group activities or by talking to another person (e.g., Palsdottir et al., 2020; Asqarova, 2021). Analyses showed that 5.81% (*n* = 10) of the studies controlled for social interaction as a specific factor.

**Relationship with an animal.** In this category, we included studies with experimental conditions where relationship-building between subjects and an animal was promoted, for example, when subjects could work for a longer time with one animal in order to build a relationship with the animal (e.g., Seivert, 2014). We found that 2.32% (*n* = 4) of the studies controlled for the relationship with the animal as a specific factor.

### 3.5 Nonspecific factors of AAIs

Comparing the control and the experimental condition in previously published studies, we identified the following 14 categories of nonspecific factors, ordered by frequency: (1) therapeutic aspects, (2) social interaction, (3) physical activity, (4) activity, distraction, or absorption, (5) education or training, (6) plush or toy animal, (7) animal, (8) environment, (9) interaction with something like an animal, (10) movement or rhythm, 11) relaxation, (12) watching or seeing an animal, (13) other, and (14) novelty (see Table 2 and Figure 4). Detailed information about the nonspecific categories can be found in the Supplement, S4.

**Therapeutic aspects.** In this category, we included studies with control conditions that had a therapeutic component, such as trauma-focused therapy (e.g., Allen et al., 2021), psychological treatment (e.g., Muela et al., 2017; Holman et al., 2020), or physiotherapeutic treatment (e.g., Beinotti et al., 2013; Rodrigo-Claverol et al., 2020). In total, 37.21% (*n* = 64) of the analyzed studies controlled for therapeutic aspects as a nonspecific factor.

**Social interaction.** Here we included studies with control conditions that contained contact or interaction with other humans, such as speaking to another human or playing group sports (e.g., Crump and Derting, 2015; Grubbs et al., 2016; Foerder and Royer, 2021). Analyses showed that 57 studies controlled for social contact or interaction as a nonspecific factor. This accounted for 33.14% of the included studies.

**Physical activity.** In this category, we included studies with control conditions that controlled for physical activity, such as rehabilitation exercises (e.g., Alemdaroğlu et al., 2016), group sports (e.g., Calvo et al., 2016), or dance classes (e.g., Souza-Santos et al., 2018). We found that 51 studies controlled for physical activity as a nonspecific factor. This accounted for 29.65% of the included studies.

**Activity, distraction, or absorption.** In this category, we subsumed studies with control conditions that offered an activity or that distracted or occupied participants or demanded their attention by, for example, having them read (e.g., Heyer and Beetz, 2014; Barker et al., 2020), color (e.g., Kline et al., 2020), or write (e.g., Hunt and Chizkov, 2014). Of the analyzed studies, 27.91% ($n$ = 48) controlled for activity, distraction, or absorption as a nonspecific factor.

**Education or training.** Here we included studies with control conditions that contained educational aspects, such as social-skills training (e.g., Becker et al., 2017) or empathy training (e.g., Julius et al., 2013; Dunlap, 2020). We found that 15.17% ($n$ = 26) of the studies controlled for education or training as a nonspecific factor.

**Plush or toy animal.** In this category, we included all studies with control interventions that incorporated a plush or toy animal, such as a plush dog (e.g., Branson et al., 2017), toy dog (e.g., Martos-Montes et al., 2020), or stuffed plush horse (e.g., Gabriels et al., 2018). We found that 20 studies controlled for interacting with a plush or toy animal as a nonspecific factor. This accounted for 11.63% of the included studies.

**Animal.** In this category, we included studies with control conditions where subjects had contact with a live animal but where the degree of contact and interaction varied. For example, in one study, the animal in the control condition was only present (compared to training with the animal in the experimental condition) (Tepper et al., 2021), or some studies compared control conditions in which subjects interacted with an animal, such as by walking with a dog, to working with an animal in the experimental condition (Seivert, 2014). We found that 15 studies controlled for the presence, contact, or interaction with the animal as a nonspecific factor. This accounted for 8.72% of the included studies.

**Environment.** In this category, we included studies that controlled for environmental factors, such as being in water (e.g., Antonioli and Reveley, 2005; Hernandez-Espeso et al., 2021), being outdoors (e.g., Urban et al., 2015), or being on a farm (e.g., Breitenbach et al., 2009) in the control condition. We found that 14 studies controlled for the environment as a nonspecific factor. This accounted for 8.14% of the included studies.

**Interaction with something like an animal.** In this category, we included studies with control conditions that simulated human–animal interaction or contact with another object by, for example, grooming a plush cat (e.g., Boyer and Mundschenk, 2014) or riding a mechanical horse (e.g., Kim et al., 2016; Funakoshi et al., 2018). We found that 11 studies controlled for interaction with something like an animal as a nonspecific factor. This accounted for 6.35% of the included studies.

**Movement or rhythm.** All studies with conditions that controlled for movement or rhythm were included in this category. They included rhythm and music-based therapy (e.g., Bunketorp Kall et al., 2012) or the vibrations or movements of a mechanic horse (Cho, 2017; Funakoshi et al., 2018; Kim et al., 2018). We found that 5.81% ($n$ = 10) of the studies controlled for rhythm or movement as a nonspecific factor.

**Relaxation.** In this category, we included studies with control conditions where subjects were asked to sit and relax for a certain amount of time (Fiocco and Hunse, 2017; Machová et al., 2020; Machova et al., 2020). We found that nine studies controlled for relaxation as a nonspecific factor. This accounted for 5.23% of the included studies.

**Watching or seeing animal.** Here we included studies with control conditions that exposed subjects to visual stimuli of animals, such as through videos or pictures (e.g., Hession et al., 2019; Thelwell, 2019; Vandagriff et al., 2021). We found eight studies that controlled for watching or seeing an animal as a nonspecific factor. This accounted for 4.65% of the included studies.

**Other.** In this category, we included studies with characteristics of the control condition that did not match any other category, such as the sound of an animal (Park et al., 2019) or a proximity effect (Vandagriff et al., 2021). We found that 4.65% ($n$ = 8) of the studies controlled for other factors as nonspecific factors.

**Novelty.** In this category, we included studies that controlled for a novelty effect by including control conditions with novel toys or plush animals (Branson et al., 2017; Germone et al., 2019; Mueller et al., 2021). We found three studies that controlled for a novelty effect as nonspecific factor. This accounted for 1.74% of the included studies.

## 4. DISCUSSION

The aim of this systematic review was to present an overview of explicit factor hypotheses that researchers have presented in previous AAI studies and to identify factors that have been implicitly considered as specific factors or nonspecific factors in AAI research.

### 4.1. Factor hypotheses of AAIs

We found that the majority of the studies (84%) mentioned a hypothesis. However, a substantial portion (16%) of the analyzed studies did not specify any factor hypotheses referring to concrete working mechanisms of AAIs in their introductions. The most frequently mentioned factor hypothesis was that human–animal interaction leads to the effects of AAIs, followed by movement by the animals, animals as social facilitators or catalysts, and the presence of an animal. These extracted factor hypotheses all represent hypothesized working mechanisms by the authors, but most of them are not sufficiently specific for authors to avoid making assumptions about how different specific components of AAIs contribute to its effects. While human–animal interaction was mentioned by several authors as a specific factor, human–animal interaction comprises a multitude of components. For example, several studies hypothesized that human–animal interaction can reduce stress (Fiocco and Hunse, 2017; Pan et al., 2019; Machova et al., 2020), but they did not specify how human–animal interaction leads to this possible stress-reducing effect. These rather vague factor hypotheses about human–animal interaction and AAIs reflect the current problem in the AAI research where the question of *how* AAIs work is still neglected (López-Cepero, 2020).

Nevertheless, our review also revealed that some studies defined factor hypotheses that are quite specific, such as the movement of the involved animals. For example, the tridimensional (Cho, 2017; Vidal Prieto et al., 2021), repetitive (Funakoshi et al., 2018; Vidal Prieto et al., 2021), and rhythmic movements of a horse (Vidal Prieto et al., 2021) have been defined as specific factors of horseback riding that are assumed to have positive effects on the humans riding the horse. But given the strong and decade-old recommendations in the literature to specify what characteristics of AAIs are important for the effects (Marino, 2012; López-Cepero, 2020), we were surprised not to find more specific factor hypotheses. We strongly suggest that authors explicitly state their hypotheses about how the presence of an animal may enhance interventions.

### 4.2. Specific factors of AAIs

Based on the approach of component studies, which provide a method for examining the active components of a treatment, we compared the control conditions with the experimental conditions of each study. We defined a factor as specific if it was present in the experimental condition but not in the control condition. We identified that “animal” and “interaction with an animal” were the most frequent categories that previously published AAI studies have implicitly considered a specific and active component of AAIs. By using different control conditions, the studies also controlled for specific factors such as “movement by the animal,” “physical contact,” and “taking care of an animal.” For example, “movement by the animal” was controlled for by comparing horseback riding with physiotherapy (e.g., Abdel-Aziem et al., 2022), “physical contact” by comparing being interviewed while petting a dog to being interviewed without a dog (Krause-Parello and Gulick, 2015), and “taking care of an animal” by comparing participants attending lectures about healthy lifestyle choices with participants taking care of crickets (Ko et al., 2016).

The results indicate that the authors of the majority of studies implicitly considered the animal as a specific factor of the AAI. This reflects the common assumption in the AAI literature that the animal is crucial for the effects of AAIs (Marino, 2012). However, since the animal is itself a complex stimulus (Marino, 2012; Rodriguez et al., 2021) and since interaction with an animal has many different components, the animal might not be suitable as a specific factor. But the results make clear what steps are needed in AAI research. First, studies need to investigate if the animal is a specific factor and if it is needed for the effects of AAIs. And then the effects of different characteristics of animals need to be disentangled.

One characteristic of an animal that we found defined as a specific factor in several on studies equine-assisted interventions (17%) was the movement of a horse during riding. Especially in hippotherapy, research is already investigating highly specific mechanisms. If the movement of a horse is considered a specific factor in equine-assisted interventions, the question arises if this movement needs to be performed by a live horse or if it can be substituted. Similar questions are increasingly being addressed, for example, in this specific case by comparing the effects of riding on a real horse with riding on a horse stimulator (Temcharoensuk et al., 2015; Kim et al., 2016; Cho, 2017; Kim et al., 2018).

Although rarely mentioned, we also identified factors that were considered as specific but were independent of the animal, such as mounting material (Bravo Gonçalves Junior et al., 2020), distraction by the presence of an animal (Gee et al., 2019), frequency of the intervention (Matusiak-Wieczorek et al., 2020), familiarity with the animal (Odendaal, 2001), recreational aspects (Breitenbach et al., 2009), and therapeutic aspects (Scheidhacker et al., 2002; Breitenbach et al., 2009). This indicates that researchers are beginning to investigate and to understand what factors in AAIs can be separated from the animal.

### 4.3 Nonspecific factors of AAIs

We found that previous AAI studies have already controlled for several different nonspecific factors. We considered a factor to be implicitly defined as nonspecific if it was present in both the experimental and the control intervention. Most frequently, therapeutic aspects and social interactions were identified as nonspecific factors. For example, some studies compared a control condition consisting of standard physiotherapy while the experimental condition consisted of standard physiotherapy with the addition of an animal (Berry et al., 2012; Machova et al., 2019; Rodrigo-Claverol et al., 2020). We thus interpreted the authors of these studies to be attempting to control for nonspecific effects of the therapeutic context present in both interventions.

Some of the studies also controlled for specific elements of the interaction with the animal or the animal itself, for example, by defining the presence of an animal (Tepper et al., 2021) or simply walking with a dog (Syzmanski et al., 2018) as nonspecific factors. One such study had a control group with an animal present during classroom activities and an experimental group where participants interacted with an animal to complete different tasks (Tepper et al., 2021). Another study defined walking with a dog as the control intervention, while the experimental intervention had participants train dogs to be more suitable for adoption (Syzmanski et al., 2018). Other examples of such specific factors of an animal were the sound of an animal (Park et al., 2019), proximity to an animal (Pendry and Vandagriff, 2019; Pendry et al., 2019; Vandagriff et al., 2021), or taking care of another living being (Colombo et al., 2006). We also found that a minority of studies defined novelty as a nonspecific factor. While only Mueller et al. (2021) explicitly mentioned having a stuffed toy present in the control group to control for the novelty effect of the animal in the intervention group, we interpreted two other studies also to be controlling for novelty when they included “novel” toys in the control condition (Branson et al., 2017; Germone et al., 2019). It has already been suggested that AAIs might be prone to novelty effects, which is thus a threat to construct validity (Marino, 2012), so it is rather surprising that we only identified one study that specifically controlled for novelty as a nonspecific effect. This also makes clear how important it is for authors to explicitly mention their hypotheses about working mechanisms and what they considered in designing the control and the experimental conditions. Having a stuffed toy present can function as a control for different components such as feeling fur, being confronted with a novel stimulus, or receiving support.

Moreover, AAIs are thought to be vulnerable to placebo effects because the nature of the treatment is usually evident to the subjects (Marino, 2012). Studies on placebo effects have demonstrated that psychosocial and contextual factors related to patient perceptions of the intervention—including information about the treatment, expectations, and the treatment environment—can contribute to the overall effect of the intervention (Wager and Atlas, 2015). Moreover, research has shown that a significant part of our responses to various interventions can be explained by these contextual factors and thus by mechanisms that elicit placebo effects rather than by the specific intervention itself (Wager and Atlas, 2015). In randomized controlled trials, such contextual factors are usually controlled for with a placebo control (Colloca and Benedetti, 2005). The results from our systematic review show, however, that none of the included studies explicitly controlled for placebo effects. Dietz et al. (2012) investigated the effects of animal-assisted therapy on trauma symptoms and compared animal-assisted therapy not only to a control group but also had an intervention group that was provided narratives about the therapy dog while the other intervention group received no such narratives about the dog. Such stories might have influenced the expectations of the participants, but the authors did not mention that these conditions were intended to control for participants’ expectations as a part of a placebo effect. The lack of a control for placebo effects in previous AAI research may have led to false attributions: it might not be the animal that produces the effects of AAIs but rather participants’ expectations regarding the animal or a combination of both. Considering that a large part of treatment responses in other interventions such as psychotherapy or physiotherapy (Wampold, 2015; Testa and Rossettini, 2016) can be explained by contextual factors rather than by their specific factors, it seems likely that these factors also explain a large portion of the effects in AAIs.

### 4.3. Limitations, strengths, and future research

Several studies we analyzed lacked detailed information regarding the study design and the experimental and the control conditions. Since we identified factors by looking at the study design and by comparing the control and experimental conditions, the information about the way the animal was integrated in the intervention was crucial for our results. For example, it was sometimes not clear if the animal was just present or embedded in a therapeutic narrative, what role the animal had, what amount of physical contact occurred, or even if participants rode the horses they were working with. This lack of information could have affected our categories and whether they correctly reflect the studies. For example, we might have missed specific or nonspecific factors that were taken into account. We also included only English and German publications and were not able to obtain several manuscripts. Moreover, our categories reflect a subjective classification. Finally, we only analyzed studies with active control conditions. Authors of studies without a control group might have proposed hypotheses about working mechanisms that we thus missed. A strength of this review is that we included previously published controlled studies with different types of AAIs. We thus ensured that the results are representative of different fields ranging from dog-assisted interventions to hippotherapy to educational programs including animals. In order to minimize publication bias, we also included non-peer-reviewed manuscripts, though the study quality was sometimes low. Our review presents a representative overview of the current status of hypotheses about specific and nonspecific factors in AAI research based both on explicit statements by authors and on implicit measures. This is a significant step in addressing a crucial knowledge gap and provides a basis for recommendations for future research.

In future studies, authors should clearly state their hypotheses about the working mechanisms. As López-Cepero (2020) suggested, integrating an animal in human services should be justified through mechanisms that we can hypothesize and that then can be verified through a scientific methodology.

Similar to other treatments like psychotherapy, AAIs are faced with the challenge of identifying how and why AAIs lead to changes (Kazdin, 2007; 2009). In order to understand how AAIs work, identifying specific factors in AAIs is crucial. We propose using component studies to examine the active components of AAIs. This means that future studies need to carefully plan their control conditions. The results of this review provide some indications of how the familiarity of the animal (Odendaal,

2001) or the relationship to the animal (Seivert, 2014; Machova, 2019) could be considered as specific factors to be controlled for, but further specific factors should be identified. Moreover, future research should try to disentangle the specific effects by treating the animal as a complex stimulus. Authors should try to define and examine exactly what characteristics are specific to the animal and what characteristics can be substituted by a human or a nonliving animal. By using robotic dogs, for example, certain confounding components such as novelty, demand characteristics, expectations, caring for someone, and physical activity can be controlled for. To design good component studies on AAIs, we hypothesize that future studies need more specific and innovative control interventions. We recommend that future studies not only examine more specifically which components of the animal or of the interaction with the animal may have effects but also start to acknowledge and implement knowledge from placebo research to examine the impact of contextual factors in AAIs. We believe that this will help us better understand the mechanisms of AAIs and also determine how important the animal is for the effects of AAIs. The results of this review show that some nonspecific factors such as therapeutic aspects and social interaction have already been controlled for in past studies, which suggests that the field is moving in the right direction. However, we suggest that future research pay attention to patients' perceptions of the intervention such as information and expectations about the treatment, the treatment environment, and the therapeutic alliance. It could even be argued that the animal in AAIs may not need to be a specific factor but could rather be seen as a contextual factor. We hope to stimulate this debate in future research with this paper.

## 5. CONCLUSION

A substantial portion of previously published controlled AAI studies did not define specific hypotheses about working mechanisms. By analyzing their control conditions, we assumed that in most controlled studies, the animal or the interaction with an animal were implicitly considered a specific factor for the effects of AAIs. Nonspecific factors such as therapeutic aspects, social interaction, or novelty have also been controlled for. We conclude that AAI research still cannot answer the question of how and why AAIs work. The hypotheses and results about the specific and nonspecific factors in the literature on AAIs are insufficient. This poses a major knowledge gap and challenge for the future. With this paper, we have presented the first overview of what AAI research has considered as possible specific and nonspecific factors. These can be used in future research to address the question of the mechanisms of AAIs. To disentangle the mechanisms of AAIs, future research should employ component studies with innovative control conditions and draw on knowledge from placebo research.

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## 7. CONTRIBUTION TO THE FIELD STATEMENT

Research on animal-assisted interventions (AAIs) has increased massively in the last few years. But it is still not clear how AAIs work and how important the animal is in such interventions. The aim of this systematic review was to compile the existing state of knowledge about the working mechanisms of AAIs.

In this review, we collected previously published hypotheses about the working mechanisms of AAIs and extracted factors that have been implicitly considered as specific or nonspecific in AAI research by categorizing the control conditions of previous controlled studies. While we conclude that AAI research still cannot answer the question of how and why AAIs work, we offer concrete recommendations for future studies about what they should control for based on our findings. This will help the field address this major research gap. To disentangle the mechanisms of AAIs, we suggest that it is important to use component studies using innovative control conditions and knowledge from placebo research to address both specific and nonspecific, or contextual, factors.

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## 9. FIGURE LEGENDS

**(A)**
**Figure 1.** Flow chart

**(B)**
**Figure 2.** Number of identified factor hypotheses

**(C)**
**Figure 3.** Number of identified specific factors

**(D)**
**Figure 4.** Number of identified nonspecific factors

**Table 1.** *Study Characteristics*

| First author | Year | Country | Type of publication | Animals | Control condition | Intervention |
|---|---|---|---|---|---|---|
| Abdel-Aziem | 2022 | Saudi Arabia | Journal article | Horse | Physiotherapy (Schroth exercises) | Hippotherapy plus home workouts exercises |
| Alemdaroğlu | 2016 | Turkey | Journal article | Horse | Conventional rehabilitation | Horseback riding plus therapist-directed exercises |
| Allen | 2021 | USA | Journal article | Dog | Trauma-Focused Cognitive-Behavioral Therapy (TF-CBT) | TF-CBT with AAT as adjunctive therapy |
| Ambrozy | 2017 | Poland | Journal article | Horse | Physical education classes | Horse's walk and horse's trot |
| An | 2021 | South Korea | Journal article | Dog | Gait traininig | Gait training with dog |
| Antonioli | 2005 | Honduras | Journal article | Dolphin | Outdoor nature program (water activities) | Play, swim, and take care of the animals |
| Aranda-Garcia | 2015 | Spain | Journal article | Horse | Two control condition: a) traditional exercise program or b) CG: none | Fun-oriented exercise and body workouts involving the horse |
| Ashtari | 2018 | Iran | Journal article | Dolphins | Training and playing in water | Interaction and swimming with dolphins |
| Asqarova | 2021 | USA | Dissertation | Guinea pig | Reading session | Guinea pig therapy |
| Bachi | 2014 | USA | Dissertation | Horse | Correctional & vocational programs | Equine-assisted intervetion |
| Bailey | 1987 | USA | Dissertation | Dog | Two control conditions: a) structured curriculum about pets and pet care; b) small group activities unrelated to the pet curriculum | A humane education curriculum guide and interaction with puppy |
| Banks | 2008 | USA | Journal article | Dog | Two control conditions: a) visit of the robot dog AIBO or b) no intervention | Sitting in chair or upright in bed with the dog next to the resident |
| Barak | 2001 | Israel | Journal article | Dog & cat | Reading and discussing news in group | Taking care of dog or cat |
| Barker | 2020 | USA | Journal article | Dog | Waiting room without animal | AAI with dog |
| Barker | 2016 | USA | Journal article | Dog | Attention-control condition (completing the Family Life-Space Diagram) | Free interaction with dog |
| Barker | 2003 | USA | Journal article | Dog | Reading magazines for 15 minutes | Conversation with dog handler, interaction with dog |

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|---|---|---|---|---|---|---|
| Beck | 2012 | USA | Journal article | Dog | Occupational therapy life skills classes | Interaction with dog and obedience |
| Becker | 2017 | USA | Journal article | Dog | Social skills training | Animal-assisted Social Skills Training group activity with dog |
| Beetz | 2012 | Germany | Journal article | Dog | Two control conditions: trier social stress test with a) toy-dog or b) friendly female student | Trier social stress test in the presence of a dog |
| Beetz | 2015 | Germany | Journal article | Horse | Conventional play-based early intervention (PBI) | Riding and different activities on the horse |
| Beinotti | 2013 | Brazil | Journal article | Horse | Physiotherapy | Touching animal or reaching for an object |
| Beinotti | 2010 | Brazil | Journal article | Horse | Physiotherapy | Hippotherapy |
| Benda | 2003 | USA | Journal article | Horse | Sitting astride the barrel and watched a horse video | Horseback riding |
| Berget | 2008 | Norway | Journal article | Farm animals | Ordinary psychiatric treatment | Working with farm animals |
| Berry | 2012 | Italy | Journal article | Dog | Physical therapy/socialization group | Physical therapy session or social session with a dog |
| Bialoszewski | 2011 | Poland | Journal article | Horse | Home-based rehabilitation | Exercises with the horse at walk, trot, or while standing in place |
| Binfet | 2021 | USA | Journal article | Dog | Handler-only interaction | Canine assisted intervention with or without physical contact |
| Bowin | 2020 | USA | Dissertation | Dog | Cold pressor test without dog present | Cold pressor test with physical contact to dog afterwards |
| Boyer | 2014 | USA | Journal article | Cat | Toy cat activity | Interaction and taking care of cat |
| Branson | 2017 | USA | Journal article | Dog | Plush stuffed dog | Interaction with therapy dog |
| Bravo Gonçalves | 2020 | Brazil | Journal article | Horse | Walking alongside a horse | Hippotherapy with blanket or saddle mount |
| Breitenbach | 2009 | Germany | Journal article | Dolphins/ (farm animals) | Three control conditions: a) interaction with dolphins, b) farm animals or c) no treatment | Dolphin assisted-therapy sessions (different stages: introduction, interaction, play, direct contact, swim) |
| Bunketorp | 2012 | Sweden | Journal article | Horse | Rhythm and music-based therapy | Therapeutic riding |
| Bunketorp | 2019 | Sweden | Journal article | Horse | Music-based therapy | Hippotherapy |
| Calvo | 2016 | Spain | Journal article | Dog | Choosing a single activity (art therapy, group sports, dynamic | Interaction with therapy dog |

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|---|---|---|---|---|---|---|
| | | | | | psycho-stimulation or gymnastics) | |
| Capparelli | 2020 | USA | Journal article | Dog | Interview | Interview with a dog in the room |
| Charnetski | 2004 | USA | Journal article | Dog | Two control conditions: a) petting stuffed animal or b) sitting comfortable on couch | Petting a real-life dog |
| Chen | 2021 | Taiwan | Journal article | Dog | Non-animal related intervention | AAT group with dog |
| Cho | 2017 | South Korea | Journal article | Horses | Mechanical horseback riding | Horseback riding |
| Clark | 2020 | USA | Journal article | Dog | Visit handler only | Visit of dog and handler |
| Cole | 2007 | USA | Journal article | Dog | Two control condition: a) visit volunteer or b) usual care | Patients may pet the dog and talk to the dog and volunteer |
| Colombo | 2006 | Italy | Journal article | Canary | Two control condition: a) receiving plant or b) receiving nothing | Look after canary |
| Costa | 2019 | Brazil | Journal article | Dog | Speech Therapy | Speech Therapy Program with Dog |
| Crossman | 2015 | USA | Journal article | Dog | Two control conditions: a) viewing images of dog or b) no treatment control | Free interaction with dog (petting, playing etc.) |
| Crump | 2015 | USA | Journal article | Dog | Study 1: non-stressful activities // Study 2: drawing activities. | Animal-assisted activity with a dog |
| Dietz | 2012 | USA | Journal article | Dog | Two control conditions: a) no dog, b) no story, dog present | Group therapies with dogs integrated in stories |
| Dunalp | 2020 | USA | Dissertation | Fish | Empathy-based mini lessons in classroom | Empathy-based lessons with pet fish |
| Eckes | 2020 | Germany | Journal article | Mice | Biology lessons | Care treatment and lesson with mice |
| El-Maniawy | 2012 | Egypt | Journal article | Horse | Designed excercise programm | Horseback riding |
| Fiocco | 2017 | Canada | Journal article | Dog | Relax in a seated position for 10 minutes | Free interaction with therapy dog |
| Flynn | 2019 | USA | Journal article | Dog | Intensive family preservation services | AAT as adjunctive to IFPS |
| Foerder | 2021 | USA | Journal article | Dog | Waiting with stuffed dog / Waiting with research assistant | Waiting room with dog |
| Friedmann | 2015 | USA | Journal article | Dog | Attentional control intervention | Skills taught/reinforced with different components of the dog visit program include: feeding, brushing etc. |
| Funakoshi | 2018 | Japan | Journal article | Horse | Exercise using the horseback riding simulator | Horseback riding |

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|---|---|---|---|---|---|---|
| Fung | 2014 | Hong Kong | Journal article | Dog | Identical play therapy procedure using a doll | Play therapy with a dog |
| Gabriels | 2015 | USA | Journal article | Horse | Barn activity | Therapeutic horseback riding |
| Gabriels | 2018 | USA | Journal article | Horse | Barn activity | Therapeutic horseback riding |
| Germone | 2019 | USA | Journal article | Dog | Novel toy and handler control | Animal-assisted activities in small groups |
| Gocheva | 2018 | Switzerland | Journal article | Suitable animal | Standard therapy session | AAT |
| Gee | 2019 | USA | Journal article | Fish | Two control conditions: a) viewing plants and water; b) viewing empty tank | Viewing fish tank |
| Grajforner | 2017 | UK | Journal article | Dog | Two control conditions: a) interaction with the dog or b) interaction with the handlers only | Interaction with dog and handler |
| Grubbs | 2016 | USA | Journal article | Dog | Exercise group | Exercise group with dogs and animal-assisted team |
| Gebhart | 2020 | Austria | Journal article | Dog | Distraction-focused interventions | Animal-assisted intervention with therapy dogs |
| Hansen | 1999 | USA | Journal article | Dog | Usual pediatric exam without a dog present | Pediatric examination in the presence of a dog |
| Hartfiel | 2017 | Germany | Journal article | Dog | Group therapy | Therapy session with animal |
| Hartwig | 2017 | USA | Journal article | Dog | Interactive and activity-based curriculum | Canine-assisted therapy based curriculum in HART intervention |
| Havener | 2001 | USA | Journal article | Dog | Dental procedure | Contact/interaction with a dog during dental procedure |
| Hediger | 2019 | Switzerland | Journal article | Horses, donkeys, sheep, goats, miniature pigs, cats, chickens, rabbits and guinea pigs | Conventional therapy session | Different therapies including an animal |
| Heidger | 2019 | Switzerland | Journal article | Dog, rabbits, guinea pigs | Occupational therapy | Animal-assisted therapy Affolter Concept |
| Henry | 2015 | USA | Journal article | Dog | Exercises involving focus on the body and physical movement | Intervention with dog |
| Hernandez-Espeso | 2021 | Spain | Journal article | Dolphin | Therapy without dolphins | Dolphin-assisted therapy and |

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|---|---|---|---|---|---|---|
| | | | | | | interaction with the therapist and the dolphin trainer |
| Hession | 2019 | Ireland | Journal article | Horses | Two control conditions: a) audiovisual intervention or b) waitlist | Horseback riding intervention |
| Heyer | 2014 | Germany | Journal article | Dog | Reading with plush dog | Reading with dog (active involvement of the dog) |
| Hinic | 2019 | USA | Journal article | Dog | Completed a jigsaw puzzle depicting an underwater scene with a research assistant and parent | Pet therapy with handler and dog, interaction with dog |
| Holman | 2020 | USA | Journal article | Dog | CBT manualized psychoeducational intervention | Canine-assisted therapy |
| Hunt | 2014 | USA | Journal article | Dog | Two control conditions: a) write about a negative or traumatic event or b) described in detail the dimensions and furnishings of three different rooms in three writing sessions | Writing in the presence of a dog |
| Hyeon Su | 2014 | South Korea | Journal article | Horse | Trunk stability exercise | Horseback riding |
| Janura | 2015 | Czech Republic | Journal article | Horse | Physiotherapy | Hippotherapy in addition to standard physiotherapy |
| Jasperson | 2013 | USA | Journal article | Dog | Group therapy | Intervention with dog |
| Johnson | 2008 | USA | Journal article | Dog | Two control conditions: a) friendly human visit or b) quiet reading group | Dog visit |
| Julius | 2013 | Germany | Journal article | Guinea pig | Empathy-training | Empathy-training with guinea pig |
| Kemeny | 2021 | USA | Journal article | Horse | HeartMath (HM) mindfulness-based intervention | Therapeutic horseback riding |
| Kim | 2016 | South Korea | Journal article | Horse | Horse riding simulator (HRS) | Horseback riding |
| Kim | 2018 | South Korea | Journal article | Horse | Simulated horseback riding | Horseback riding |
| Kim | 2014 | South Korea | Journal article | Horse | Treadmill Training | Horseback riding |
| Kline | 2020 | USA | Journal article | Dog | Coloring a mandala | Interaction with therapy dog |
| Ko | 2016 | South Korea | Journal article | Insects (crickets) | Lectures that focused on healthy lifestyle choices | Taking care of crickets |
| Kraft | 2019 | USA | Journal article | Horse | Standard outpatient physical therapy (PT) | Hippotherapy |
| Krause-Parello | 2015 | USA | Journal article | Dog | Standard forensic interview | AAI-canine in forensic interview |

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| Krause-Parello | 2019 | USA | Journal article | Dog | Informational session about assistance dogs | Intervention with handler and therapy dog |
| Kwangmin Ryu | 2016 | South Korea | Journal article | Horse | Two control conditions: a) aquatic movement therapy or b) watching a movie | Horseback riding |
| Kwon | 2015 | South Korea | Journal article | Horse | Home-based aerobic exercise | Hippotherapy and active exercises |
| Lahav | 2019 | Israel | Journal article | Dog | Group intervention (solving problems and group sport) | Intervention with dog (educational topics about dog, getting to know the dog, interaction, practical training) |
| Lanning | 2014 | USA | Journal article | Horse | Educational and recreational activities | Equine-assisted activity to improve riding and horsemanship skills |
| Lang | 2010 | Germany | Journal article | Dog | A 30 min talk with the same research assistant | Dog-assisted interview |
| Lass-Hennemann | 2018 | Germany | Journal article | Dog | Two control conditions: a) watching a 15-min film of a person interacting with one of the therapy dogs or b) relaxing | Interaction with dog after traumatic film clip (physical contact was encouraged) |
| Lass-Hennemann | 2014 | Germany | Journal article | Dog | Three control conditions: a) watching clip with friendly human, b) watching clip with toy-animal or c) watching clip alone | Interaction/ physical contact with dog during trauma film |
| LeRoux | 2014 | South Africa | Journal article | Dog | Tree control conditions: a) reading to an adult, b) reading to a teddy bear or c) no intervention | Interacting with and reading out loud to dog |
| Lechner | 2007 | Switzerland | Journal article | Horse | Three control conditions: a) sitting astride on Bobath Roll, b) sitting on a rocker board (inside of a wooden stool) or c) received no intervention | Horseback riding |
| Lee | 2014 | South Korea | Journal article | Horse | Treadmill | Hippotherapy |
| Lenihan | 2016 | USA | Journal article | Dog | Reading to adult volunteer | Weekly reading to same dog |
| Levinson | 2017 | USA | Journal article | Dog | Reading to peers | Reading to dog |
| Machova | 2019 | Czech Republic | Journal article | Dog | Standard physiotherapy and occupational therapy | Supplement of AAT |
| Machova | 2018 | Czech Republic | Journal article | Dog | Conventional speech therapy | Speech therapy with a dog |

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| Machova | 2020 | Czech Republic | Journal article | Dog | Relaxation technique | AAA with a dog |
| Machova | 2019 | Czech Republic | Journal article | Dog | Two control conditions: a) normal working process without a break or b) normal working process with a break of choice | Work break in the presence of a dog |
| Marr | 2000 | USA | Journal article | Dogs, rabbits, ferrets, and guinea pigs | Substance abuse education group | Animal visit, free interaction with animal |
| Martos-Montes | 2020 | Spain | Journal article | Dog | Toy dog | Human-dog interaction |
| Matsuura | 2020 | Japan | Journal article | Horse | Stuffed toy horse | AAT with horse |
| Matusiak-Wieczorek | 2020 | Poland | Journal article | Horse | Less sessions of hippotherapy | Hippotherapy |
| Menna | 2016 | Italy | Journal article | Dog | Two control conditions: a) activities based on the formal reality orientation (ROT) group or b) no activities | AAT intervention with dog |
| Menna | 2019 | Italy | Journal article | Dog | Formal reality orientation (ROT) intervention without the dog | AAT with dog |
| Mossello | 2011 | Italy | Journal article | Dog | Control activity with plush dogs | Interaction with dog |
| Muela | 2017 | Spain | Journal article | Dog, horses; cats and farm animals (such as sheep, goats, chickens, and pigs) | Standard daily routine & psychotherapy | Treatment including animal (guided interactions with animals) |
| Mueller | 2021 | USA | Journal article | Dog | Two control conditions: a) stuffed toy dog or b) social interaction with animal | Social interaction and physical contact with a therapy dog |
| Munoz-Lasa | 2011 | Spain | Journal article | Horse | Physiotherapy | Horseback riding |
| Murry | 2012 | USA | Journal article | Reptile | The control group discussed death and grief without reference to, or interactions with, reptiles. | Reptile-assisted support group discussed death and grief along with training in animal care |
| Mutoh | 2019 | Japan | Journal article | Horse | Outdoor recreation program | Hippotherapy |

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| Nathans-Barel | 2005 | Israel | Journal article | Dog | General discussions, learning about caring for animals, particularly dogs, and walks on hospital grounds with the therapist for similar periods as in the active group. | AAT with dog (interaction and activites) |
| Ngai | 2021 | Hong kong | Journal article | Dog | School program | Competence in Active Resilience for Kids (CARing Kids) humane education with animal- assisted SEL |
| Nilsson | 2015 | Sweden | Journal article | Dog | Visits only by researchers | Visits by researchers with an additional visit by a therapy dog and its handler. |
| Nurenberg | 2015 | USA | Journal article | Horses, dogs | Two control conditions: a) environmentally enhanced social skills group psychotherapy (SSP) or b) regular hospital care (standard control) | Equine-assisted-therapy |
| Odendaal | 2001 | USA | Disseration | dog | Read a book | Contact to dog (stroking) |
| O'Haire | 2015 | Australia | Journal article | Guinea pigs | Three control conditions: a) playing with toys, b) reading aloud or c) reading silently | Freeplay with peers and animals |
| Oh | 2018 | South Korea | Journal article | Horse | Pharmacotherapy | Hippotherapy |
| Palsdottir | 2020 | Sweden | Journal article | Horse | Physical activity | Equine-assisted intervention |
| Pan | 2019 | USA | Journal article | Horse | Pony-sized stuffed horse, to practice activities (e.g., grooming and tacking) | Therapeutic horseback riding |
| Park | 2019 | South Korea | Journal article | Cricket | Auditory effects of pet crickets and telephone counseling | Insect-rearing |
| Pendry | 2019 | USA | Journal article | Dog | Academic Stress Management (ASM) | Interaction with therapy dog and handler or anti-stress management with dog |
| Pendry a) | 2019 | USA | Journal article | Dog or cat | Two control conditions: a) Watching others pet animal or b) Viewing visuals of animals | Animal visitation program with dog or cat |
| Pendry b) | 2020 | USA | Journal article | Dog | Academic stress management (ASM) | Interaction with therapy dog and |

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|---|---|---|---|---|---|---|
| | | | | | | handler or ASM with dog |
| Pendry b) | 2021 | USA | Journal article | Dog | Academic stress management (ASM) | Interaction with therapy dog and handler or anti-stress management with dog |
| Pendry | 2020 | USA | Journal article | Dog | Academic stress management (ASM) | Interaction with therapy dog and handler or ASM with Dog |
| Pendry a) | 2019 | USA | Journal article | Dog or cat | Two control conditions: a) watching others pet animals or b) viewing slideshow with animals | Animal visitation program with dog or cat |
| Peters c) | 2021 | USA | Journal article | Horse | Occupational therapy in a garden | Equine-assisted therapy |
| Peters c) | 2021 | USA | Journal article | Horse | Occupational therapy in a garden | Equine-assisted therapy |
| Petty | 2017 | USA | Journal article | Horse | Learning about horses | Horseback riding |
| Polheber | 2014 | USA | Journal article | Dog | Two control conditions: a) speaking with their good friend or b) sit quietly and wait | Interaction with dog |
| Rawleigh | 2021 | Canada | Journal article | Dog | Two control conditions: a) a dog visitation program or b) counseling | Dog training and vocational program |
| Richeson | 2003 | USA | Journal article | Dog | Two control conditions: a) human visitor or b) no visitors | Intervention with dog and handler |
| Rodrigo-Claverol | 2019 | Spain | Journal article | Dog | Kinesitherapy | Therapeutic exercises with animal |
| Rodrigo-Claverol | 2020 | Spain | Journal article | Dog | Physiotherapy | Physiotherapy + supplement of AAT |
| Ruzic | 2011 | Croatia | Journal article | Dog | Daily walk | Dog-walking |
| Santaniello | 2020 | Italy | Journal article | Dog | Formal reality orientation therapy (ROT) | AAT interventions adapted to the formal ROT |
| Scheidhacker | 2002 | Germany | Journal article | Horse | Horseback riding lesson | Therapeutic horseback riding |
| Schneider | 2016 | Canada | Journal article | Horse | Therapeutic skiing | Riding lessons |
| Schuck | 2015 | USA | Journal article | Dog | Two control conditions: a) cognitive-behavioral intervention or b) waitlist | Intervention with therapy dog and handler |
| Schuck | 2018 | USA | Journal article | Dog | Two control conditions: a) cognitive-behavioral intervention with toy dog or b) waitlist | Animal-assisted intervention with therapy dog and handler |

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| Scorzato | 2017 | Italy | Journal article | Dog | Activity (substitution by an unanimated object) | Dog-assisted treatment intervention |
| Seivert | 2014 | USA | Journal article | Dog | Dog-walking | Dog training and education component |
| Smith | 2010 | USA | Dissertation | Dog | Read aloud independently in an assigned area of the public library | Reading sessions with therapy dog |
| Souza-Santos | 2018 | Brazil | Journal article | Horse | Dance | Horseback riding |
| Syzmanski | 2018 | USA | Journal article | Dog | Dog-walking | Training of undersocialized dogs |
| Temcharoensuk | 2015 | Thailand | Journal article | Horse | Two control conditions: a) mechanical horse-riding simulator while watching an animated movie or b) horse riding simulator was powered off | Horseback riding |
| Tepper | 2021 | Australia | Journal article | Dog | Two control conditions: a) Dog present, b) reading out lout to dog | Training with dog |
| Thakkar | 2021 | India | Journal article | Dog | Dental treatment | Dental treatment in the presence of a dog |
| Thelwell | 2019 | England | Journal article | Dog | Watching videos of dogs | 10 min free interaction with dog |
| Thodberg | 2016 | Denmark | Journal article | Dog | Two control conditions: a) interacting with a robot seal (PARO) or b) interacting with a soft toy cat | Intervention with real life dog |
| Thodberg | 2021 | Denmark | Journal article | Dog | Two control conditions:a) Visits with a dog, no activity (D) or b) Visits without dog, with an activity (A). | Dog visit with activity |
| Travers | 2013 | Australia | Journal article | Dog | Human-therapist-only intervention with an article to stimulate discussion | Intervention with dog |
| Trujillo | 2020 | USA | Journal article | Dog | Manual-standardized motivational interviewing and acceptance and commitment therapy, called impACT | AAT + impACT |
| Urban | 2015 | Germany | Journal article | Dog | Walking with nurse | Dog walking |
| Vagnoli | 2015 | Italy | Journal article | Dog | Venipuncture without dog present | Venipuncture with dog present |

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| Vandagriff | 2021 | USA | Journal article | Cats and dogs | Three control conditions: a) animal visit program proximit,; b) animal visit program imaginary or c) waitlist | Free interaction with dog and cats, engaging in petting and stroking (for 10min) |
| Spruin | 2021 | UK | Journal article | Cog | Mindfulness condition | Pets As Therapy (PAT) dog |
| Vidal Prieto | 2021 | Brasil | Journal article | Horse | Hippotherapy once a week | Hippotherapy twice a week |
| Villalta-Gil | 2009 | Spain | Journal article | Dog | Integrated psychological treatment | Intervention with dog |
| Voznesenskiy | 2016 | Ecuador | Journal article | Horses | Regular adapted physical education activities | Adaptive horseback riding |
| Wanser | 2020 | USA | Journal article | Dog | Dog walking intervention | "Do As I Do" dog training intervention |
| Wesenberg | 2019 | Germany | Journal article | Dog | Psychosocial group excercise sessions | Animal-assisted intervention |
| Wesley | 2009 | USA | Journal article | Dog | Group therapy session | Group therapy sessions with a therapy dog |
| White-Lewis d) | 2019 | USA | Journal article | Horses | Evidence based exercise education | Equine-assisted therapy (grooming, saddling, riding) |
| White-Lewis d) | 2018 | USA | Dissertation | Horses | Attention control exercise education group | Horseback riding |
| Wolynczyk-Gmaj | 2021 | Poland | Journal article | Dog | Walk with a researcher | Walk with dog and handler |
| Woolley | 2004 | USA | Dissertation | Dogs, cats, lamas, farm animals | Conventional psychotherapy only | Conventional psychotherapy and an AAT program |
| Zisselman | 1996 | USA | Journal article | Dog | Exercise control group | Dog visit |

AAT = animal-assisted activity; AAI= anima-assisted intervention; AAT = animal-assisted therapy

**Table 2.** *Identified factor hypotheses, specific and non-specific factors of each study*

| Author | Year | Factor hypotheses | Specific factors | Non-specific factors |
|---|---|---|---|---|
| Abdel-Aziem | 2022 | Movement by the animal | Animal; movement by the animal | Physical activity; therapeutic aspects |
| Alemdaroğlu | 2016 | Not specified | Animal; movement by the animal | Physical activity |
| Allen | 2021 | Presence of animal | Animal | Therapeutic aspects; plush or toy animal |
| Ambrozy | 2017 | Movement by the animal | Animal, movement by the animal | Physical activity; environment |
| An | 2021 | Not specified | Animal; interaction with an animal | Physical activity; therapeutic aspects |
| Antonioli | 2005 | Other | Animal; interaction with an animal, taking care of an animal | Physical activity; environment; social contact |
| Aranda-Garcia | 2015 | Physical activity | Animal | Physical activity |
| Ashtari | 2018 | Relationship with an animal | Animal; interaction with an animal | Physical activity; environment; playing |
| Asqarova | 2021 | Not specified | Animal; interaction with an animal, social interaction | Activity, distraction, or absorption; education/ training |
| Bachi | 2014 | Relationship | Animal | Education / training |
| Bailey | 1987 | Taking care of an animal | Animal; interaction with an animal | Social interaction; education or training |
| Banks | 2008 | Relationship with an animal | Animal | Social interaction; plush or toy animal |
| Barak | 2001 | Social facilitator/ or catalyst; relationship with an animal | Anima; taking care of an animal | Social interaction; activity, distraction, or absorption |
| Barker | 2020 | Not specified | Animal; interaction with an animal; social interaction | Activity, distraction, or absorption |
| Barker | 2016 | Human-animal interaction | Animal; interaction with an animal | Activity, distraction, or absorption |
| Barker | 2003 | Human-animal interaction | Animal; social interaction; interaction with an animal | Activity, distraction, or absorption |
| Beck | 2012 | Human-animal interaction | Animal; training an animal; physical contact; interaction with an animal | Therapeutic aspects |
| Becker | 2017 | Social facilitator or catalyst; human-animal interaction | Animal; physical contact; training an animal; taking care of an animal; social interaction | Social interaction; education or training |
| Beetz | 2012 | Social or emotional support | Animal; interaction with an animal; physical contact | Social interaction |
| Beetz | 2015 | Social facilitator or catalyst; physical contact | Animal; interaction with animal, movement by the animal | Therapeutic aspects; social interaction; activity, distraction, or absorption |
| Beinotti | 2013 | Movement by the animal; taking care of an animal; social facilitator or catalyst | Animal; physical contact | Physical activity |

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|---|---|---|---|---|
| Beinotti | 2010 | Movement by the animal | Animal; movement by the animal | Physical activity |
| Benda | 2003 | Movement by the animal | Animal; movement by the animal | Activity, distraction, or absorption; interaction with something like an animal; relaxation; watching or seeing animal |
| Berget | 2008 | Taking care of an animal; human-animal interaction | Animal; physical contact; taking care of an animal | Therapeutic aspects |
| Berry | 2012 | Social facilitator or catalyst | Animal; interaction with an animal | Physical activity; therapeutic aspects; social interaction |
| Bialoszewski | 2011 | Human-animal interaction | Animal; movement by the animal | Physical activity; therapeutic aspects |
| Binfet | 2021 | Physical contact | Physical contact | Social interaction; animal |
| Bowin | 2020 | Human-animal interaction | Animal; interaction with an animal | Activity, distraction, or absorption |
| Boyer | 2014 | Social facilitator or catalyst | Animal | Plush or toy animal; interaction with something like an animal |
| Branson | 2017 | Human-animal interaction | Animal | Plush or toy animal; interaction with something like an animal; novelty |
| Bravo Gonçalves | 2020 | Other (mount material) | Other (mount material) | Animal; interaction with something like an animal; physical activity |
| Breitenbach | 2009 | Other (parental involvement) | Other (recreational/vacation atmosphere, therapeutic aspects) | Environment; animal; interaction with something like an animal |
| Bunketorp | 2012 | Movement by the animal | Animal; movement by the animal, taking care of an animal | Therapeutic aspects; movement or rhythm |
| Bunketorp | 2019 | Not specified | Animal; interaction with animal | Therapeutic aspects; social interaction; movement or rhythm |
| Calvo | 2016 | Social facilitator or catalyst; human-animal interaction | Animal; interaction with an animal; training an animal; taking care of an animal | Physical activity; therapeutic aspects; social interaction; activity, distraction, or absorption |
| Capparelli | 2020 | Social facilitator or catalyst; social or emotional support | Animal; interaction with an animal; physical contact | Activity, distraction, or absorption |
| Charnetski | 2004 | Physical contact; presence of animal | Animal; physical contact | Plush or toy animal; interaction with something like an animal; relaxation |
| Chen | 2021 | Human-animal interaction; social or emotional support | Animal; interaction with an animal | Therapeutic aspects; social interaction |
| Cho | 2017 | Movement by the animal | Animal | Physical activity; interaction with something like an animal; movement or rhythm |

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|---|---|---|---|---|
| Clark | 2020 | Human-animal interaction | Animal; interaction withan animal | Social interaction |
| Cole | 2007 | Human-animal interaction; relationship with an animal | Animal; physical contact, interaction with an animal | Social interaction |
| Colombo | 2006 | Relationship with an animal | Animal | Other (taking care / responsibility) |
| Costa | 2019 | Human-animal interaction | Animal; interaction with an animal | Therapeutic aspects |
| Crossman | 2015 | Human-animal interaction | Animal; interaction with an animal | Watching or seeing animal |
| Crump | 2015 | Human-animal interaction; physical contact; relationship with an animal | Animal; interaction with an animal; physical contact | Activity, distraction, or absorption; social interaction |
| Dietz | 2012 | Not specified | Other (integrating dog in story) | Animal; social interaction; therapeutic aspects |
| Dunalp | 2020 | Presence of animal | Animal | Social interaction; education or training |
| Eckes | 2020 | Taking care of an animal | Animal; taking care of an animal | Social interaction; education or training |
| El-Maniawy | 2012 | Movement by the animal | Animal; movement by the animal | Physical activity |
| Fiocco | 2017 | Human-animal interaction | Animal; interaction with an animal | Relaxation |
| Flynn | 2019 | Social facilitator or catalyst | Animal; interaction with an animal; taking care of an animal | Education or training |
| Foerder | 2021 | Human-animal interaction | Animal, interaction with an animal | Plush or toy animal; social interaction |
| Friedmann | 2015 | Social facilitator or catalyst; social or emotional support | Animal | Therapeutic aspects; social interaction; activity, distraction, or absorption |
| Funakoshi | 2018 | Movement by the animal | Animal | Physical activity, movement or rhythm, interaction with something like an animal |
| Fung | 2014 | Social facilitator or catalyst | Animal | Therapeutic aspects; social interaction; activity, distraction, or absorption |
| Gabriels | 2015 | Human-animal interaction; relationship with an animal | Animal; movement by the animal; taking care of an animal, interaction with an animal | Plush ortoy animal; education or training; therapeutic aspects; environment |
| Gabriels | 2018 | Human-animal interaction; relationship with an animal | Animal; movement by the animal; taking care ofan animal; interaction with an animal | Plush or toy animal; education or training; therapeutic aspects; environment |
| Germone | 2019 | Social facilitator or catalyst | Animal; interaction with an animal | Social interaction; activity, distraction, or absorption; novelty |
| Gocheva | 2018 | Not specified | Animal; interaction with an animal; taking care of an animal | Therapeutic aspects; physical activity; activity, distraction, or absorption |

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| Gee | 2019 | Other (biophilia) | Animal; other (distraction presence of animal) | Enviroment; activity, distraction, or absorption |
| Grajforner | 2017 | Human-animal interaction | Interaction with an animal; social interaction | Social interaction; animal |
| Grubbs | 2016 | Social facilitator or catalyst | Animal; interaction with an animal; social interaction | Physical activity; social interaction |
| Gebhart | 2020 | Not specified | Animal; interaction with an animal | Movement or rhythm; activity, distraction, or absorption; social interaction; other (distraction) |
| Hansen | 1999 | Presence of animal; other (distraction) | Animal; interaction with an animal | Therapeutic aspects |
| Hartfiel | 2017 | Social facilitator or catalyst | Animal | Social interaction |
| Hartwig | 2017 | Not specified | Animal | Therapeutic aspects; social interaction |
| Havener | 2001 | Relationship with an animal; other (distraction) | Animal; interaction with an animal | Therapeutic aspects |
| Hediger | 2019 | Animal as social facilitator or catalyst | Animal | Therapeutic aspects |
| Heidger | 2019 | Not specified | Animal | Therapeutic aspects |
| Henry | 2015 | Human-animal interaction | Animal; interaction with an animal | Physical activity; therapeutic aspects; activity, distraction, or absorption |
| Hernandez-Espeso | 2021 | Human-animal interaction | Animal; interaction with an animal | Environment; therapeutic aspects; social interaction |
| Hession | 2019 | Movement by the animal | Animal; movement by the animal | Therapeutic aspects; movement or rhythm; watching or seeing animal |
| Heyer | 2014 | Other (integrating real-life animal) | Animal; interaction with an animal | Plush or toy animal; activity, distraction, or absorption |
| Hinic | 2019 | Not specified | Animal; interaction with an animal | Social interaction; activity, distraction, or absorption; education or training |
| Holman | 2020 | Human-animal interaction | Animal, interaction with an animal; physical contact; social interaction | Therapeutic aspects |
| Hunt | 2014 | Social facilitator or catalyst | Animal | Activity, distraction, or absorption |
| Hyeon Su | 2014 | Movement by the animal | Animal; movement by the animal | Physical activity |
| Janura | 2015 | Movement by the animal | Animal; movement by the animal | Therapeutic aspects; physical activity |
| Jasperson | 2013 | Human-animal interaction | Animal; interaction with an animal; physical contact | Therapeutic aspects; social interaction; education |
| Johnson | 2008 | Not specified | Animal; interaction with an animal; taking care of an animal; physical contact | Social interaction; activity, distraction, or absorption |
| Julius | 2013 | Human-animal interaction | Animal | Therapeutic aspects; education or training |

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| Kemeny | 2021 | Human-animal interaction; other (large animal) | Animal; interaction with an animal; movement by the animal; relationship with an animal | Therapeutic aspects; relaxation |
| Kim | 2016 | Not specified | Animal | Physical activity; movement or rhythm; interaction with something like an animal |
| Kim | 2018 | Physical activity | Animal | Physical activity; movement or rhythm; interaction with something like an animal |
| Kim | 2014 | Movement by the animal | Animal; movement by the animal | Physical activity |
| Kline | 2020 | Human-animal interaction | Animal; interaction with an animal | Activity, distraction, or absorption |
| Ko | 2016 | Human-animal interaction | Animal; taking care of an animal | Social interaction; education or training |
| Kraft | 2019 | Movement by the animal | Animal; movement by the animal | Therapeutic aspects; physical activity |
| Krause-Parello | 2015 | Not specified | Animal; physical contact | Activity, distraction, or absorption |
| Krause-Parello | 2019 | Not specified | Animal; interaction with an animal | Education or training |
| Kwangmin Ryu | 2016 | Movement by the animal | Animal; movement by the animal | Physical activity; environment; activity, distraction, or absorption |
| Kwon | 2015 | Movement by the animal | Animal; movement by the animal | Physical activity; therapeutic aspects |
| Lahav | 2019 | Social facilitator or catalyst; presence of animal | Animal; training an animal; interaction with an animal; other (educational topics of animal); | Physical activity; social interaction, activity, distraction, or absorption |
| Lanning | 2014 | Movement by the animal; relationship with an animal | Animal; movement by the animal; taking care of an animal | Social interaction; activity, distraction, or absorption; education or training |
| Lang | 2010 | Not specified | Animal; interaction with an animal | Social interaction; other (talking about pet/animals) |
| Lass-Hennemann | 2018 | Human-animal interaction | Animal; interaction with an animal; physical contact | Watching or seeing animal; animal; interaction with something like an animal |
| Lass-Hennemann | 2014 | Social or emotional support; presence of animal | Animal; interaction with an animal; physical contact | Plush or toy animal; social interaction; activity, distraction, or absorption |
| LeRoux | 2014 | Not specified | Animal | Plush or toy animal; social interaction; activity, distraction, or absorption |
| Lechner | 2007 | Movement by the animal | Animal; movement by the animal | Physical activity |
| Lee | 2014 | Movement by the animal | Animal; movement by the animal | Physical activity |

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|---|---|---|---|---|
| Lenihan | 2016 | Human-animal interaction | Animal; relationship with the animal | Social interaction; activity, distraction, or absorption |
| Levinson | 2017 | Not specified | Animal | Social interaction; activity, distraction, or absorption |
| Machova | 2019 | Presence of animal | Animal; interaction with an animal; relationship with an animal | Therapeutic aspects; physical activity |
| Machova | 2018 | Presence of animal | Animal; interaction with an animal; physical contact | Therapeutic aspects |
| Machova | 2020 | Human-animal interaction | Animal; interaction with an animal | Relaxation |
| Machova | 2019 | Presence of animal | Animal; interaction with an animal | Relaxation |
| Marr | 2000 | Social facilitator or catalyst | Animal; interaction with an animal | Social interaction; education or training |
| Martos-Montes | 2020 | Human-animal interaction | Animal; interaction with an animal | Plush or toy animal |
| Matsuura | 2020 | Physical contact | Physical contact | Plush or toy animal; interaction with something like an animal; watching or seeing animal |
| Matusiak-Wieczorek | 2020 | Not specified | Other (frequency) | Animal; movement or rhythm |
| Menna | 2016 | Relationship with an animal | Animal; interaction with an animal | Therapeutic aspects |
| Menna | 2019 | Human-animal interaction; physical contact | Animal; interaction with an animal | Therapeutic aspects |
| Mossello | 2011 | Physical contact | Animal | Plush or toy animal; interaction with something like an animal |
| Muela | 2017 | Not specified | Animal | Therapeutic aspects |
| Mueller | 2021 | Human-animal interaction;physical contact | Physical contact; interaction with an animal | Plush or toy animal; novelty |
| Munoz-Lasa | 2011 | Movement by the animal | Animal; movement by the animal | Physical activity; therapeutic aspects |
| Murry | 2012 | Taking care of an animal | Animal; taking care of an animal; other (education about animal) | Social interaction; education or training |
| Mutoh | 2019 | Movement by the animal | Animal; movement by the animal | Environment; activity, distraction, or absorption |
| Nathans-Barel | 2005 | Human-animal interaction | Animal; interaction with an animal | Physical activity; social interaction, education or training |
| Ngai | 2021 | Not specified | Animal; interaction with an animal | Education or training |
| Nilsson | 2015 | Human-animal interaction | Animal; interaction with an animal; physical contact | Social interaction |
| Nurenberg | 2015 | Not specified | Animal; interaction with an animal; training animal | Therapeutic aspects; environment; social interaction |
| Odendaal | 2001 | Human-animal interaction | Other (familiarity) | Activity, distraction, or absorption |

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| O'Haire | 2015 | Social facilitator or catalyst | Animal; interaction with an animal | Social interaction; activity, distraction, or absorption |
| Oh | 2018 | Human-animal interaction | Animal; movement by the animal | Therapeutic aspects |
| Palsdottir | 2020 | Not specified | Animal; movement by the animal; social interaction | Physical activity |
| Pan | 2019 | Human-animal interaction | Animal; movement by the animal | Plush or toy animal; activity, distraction, or absorption; interaction with something like an animal |
| Park | 2019 | Other (animal can create nostalgia feeling) | Animal; taking care of an animal | Other (sound of animal); therapeutic aspects |
| Pendry | 2019 | Human-animal interaction | Animal; interaction with an animal | Therapeutic aspects; physical activity, education or training |
| Pendry a) | 2019 | Human-animal interaction | Interaction with an animal; social interaction | Activity, distraction, or absorption; watching or seeing animal; other (proximity) |
| Pendry b) | 2020 | Human-animal interaction | Animal; interaction with an animal | Therapeutic aspects; activity, distraction, or absorption; education or training |
| Pendry b) | 2021 | Human-animal interaction | Animal; interaction with an animal | Therapeutic aspects; activity, distraction, or absorption; education or training |
| Pendry | 2020 | Human-animal interaction | Animal; interaction with an animal | Therapeutic aspects; activity, distraction, or absorption; education or training |
| Pendry a) | 2019 | Human-animal interaction | Interaction with an animal; social interaction | Activity, distraction, or absorption; watching or seeing animal; other (proximity) |
| Peters c) | 2021 | Not specified | Animal; interaction with an animal | Therapeutic aspects; environment, social interaction; education or training; activity, distraction, or absorption |
| Peters c) | 2021 | Human-animal interaction, social facilitator or catalyst | Animal; interaction with an animal | Therapeutic aspects; environment; social interaction, education or training; activity, distraction, or absorption |
| Petty | 2017 | Human-animal interaction; relationship with an animal | Animal; movement by the animal; taking care of an animal | Education or training; environment; plush ortoy animal |
| Polheber | 2014 | Social or emotional support | Animal; interaction with an animal | Social interaction; relaxation |
| Rawleigh | 2021 | Human-animal interaction | Training an animal | Animal; therapeutic aspects |
| Richeson | 2003 | Relationship with an animal | Animal; interaction with an animal | Social interaction; activity, distraction, or absorption |

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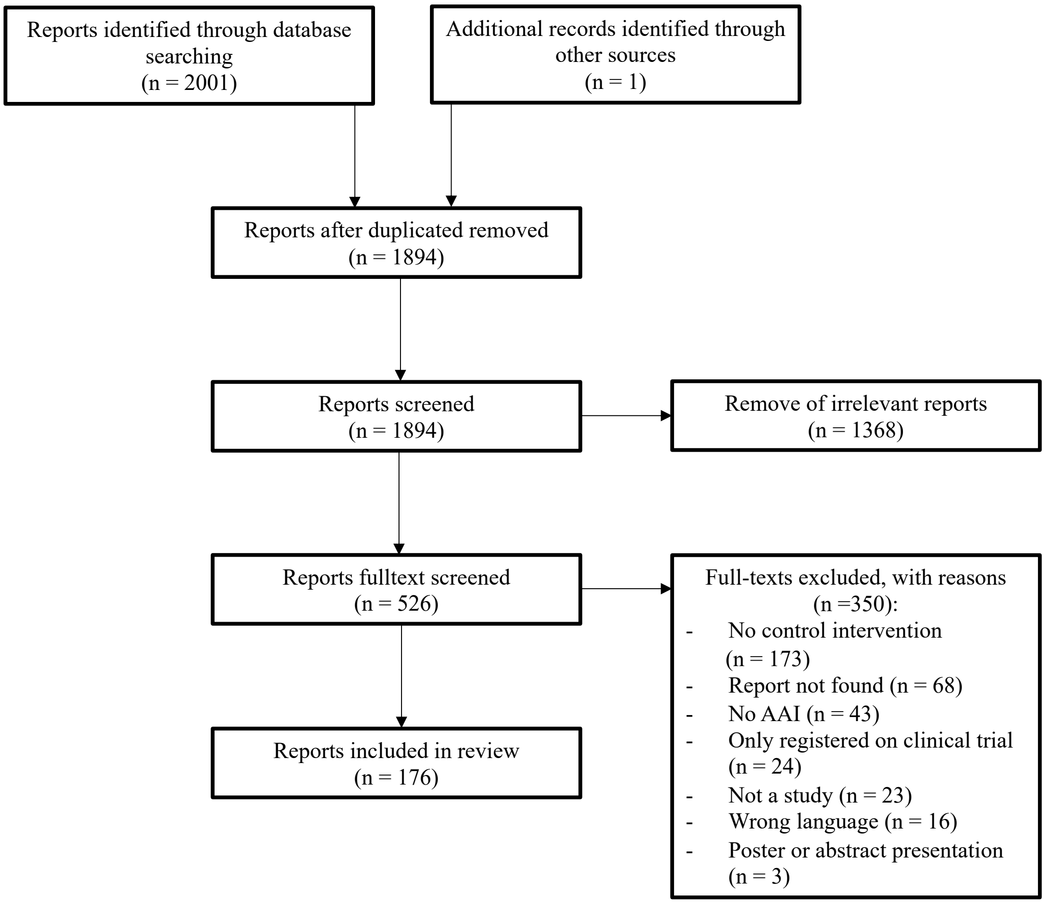
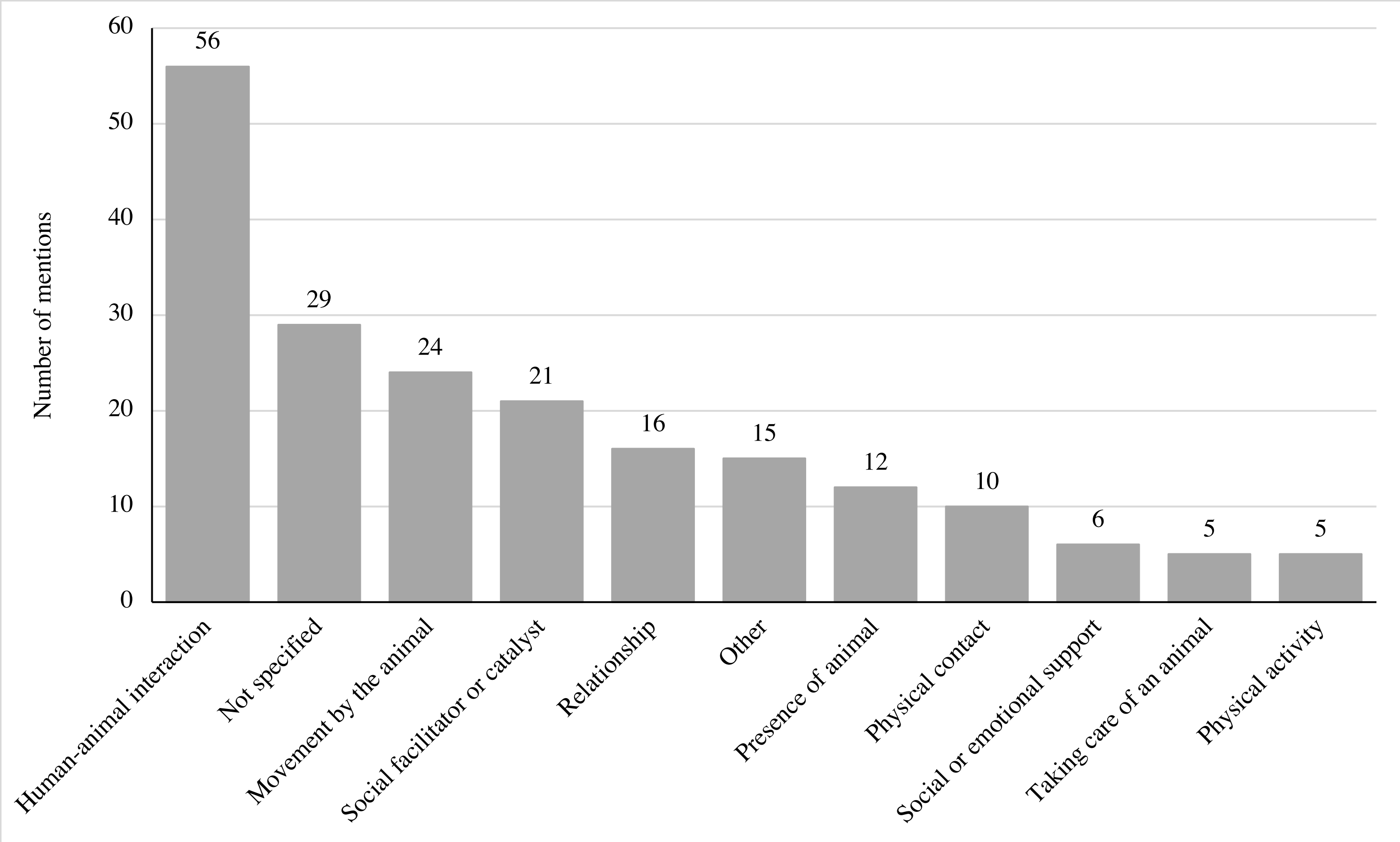
| Rodrigo-Claverol | 2019 | Human-animal interaction | Animal | Physical activity; therapeutic aspects |
| Rodrigo-Claverol | 2020 | Not specified | Animal; interaction with an animal; physical contact | Therapeutic aspects; physical activity; social interaction |
| Ruzic | 2011 | Physical activity | Animal; taking care of an animal | Physical activity |
| Santaniello | 2020 | Human-animal interaction | Animal; interaction with an animal | Therapeutic aspects |
| Scheidhacker | 2002 | Not specified | Other (therapeutic aspects) | Animal; other (horseback riding) |
| Schneider | 2016 | Human-animal interaction | Animal; movement by the animal | Physical activity; therapeutic aspects |
| Schuck | 2015 | Social facilitator or catalyst; human-animal interaction | Animal | Therapeutic aspects; plush or toy animal |
| Schuck | 2018 | Human-animal interaction | Animal | Therapeutic aspects; plush or toy animal |
| Scorzato | 2017 | Not specified | Animal; interaction with an animal | Activity, distraction, or absorption |
| Seivert | 2014 | Human-animal interaction | Training an animal; relationship with an animal | Animal; physical activity |
| Smith | 2010 | Not specified | Animal | Activity, distraction, or absorption; environment |
| Souza-Santos | 2018 | Physical activity | Animal; physical contact; movement by the animal | Physical activity; social interaction |
| Syzmanski | 2018 | Human-animal interaction | Training an animal | Animal; physical activity |
| Temcharoensuk | 2015 | Movement by the animal | Animal | Physical activity; activity, distraction, or absorption; interaction with something like an animal |
| Tepper | 2021 | Human-animal interaction | Training an animal | Animal |
| Thakkar | 2021 | Physical contact | Animal | Therapeutic aspects |
| Thelwell | 2019 | Human-animal interaction | Animal, interaction with an animal | Watching or seeing animal |
| Thodberg | 2016 | Human-animal interaction | Animal | Plush or toy animal; interaction with something like an animal |
| Thodberg | 2021 | Presence of animal | Other (combination of activity with dog) | Animal; physical contact; activity, distraction, or absorption |
| Travers | 2013 | Social facilitator or catalyst; physical contact | Animal; interaction with an animal | Social interaction; other (bringing article to stimulate discussion) |
| Trujillo | 2020 | Social facilitator or catalyst | Animal | Therapeutic aspects |
| Urban | 2015 | Not specified | Animal | Physical activity; social interaction; environment |
| Vagnoli | 2015 | Not specified | Animal | Therapeutic aspects |
| Vandagriff | 2021 | Physical contact | Physical contact; interaction with an animal | Animal; watching or seeing animal; other (proximity) |
| Spruin | 2021 | Not specified | Animal; interaction with an animal | Activity, distraction, or absorption; relaxation |

| | | | | |
|---|---|---|---|---|
| Vidal Prieto | 2021 | Movement by the animal | Other (frequency) | Animal; movement or rhythm |
| Villalta-Gil | 2009 | Not specified | Animal; interaction with an animal | Therapeutic aspects; social interaction |
| Voznesenskiy | 2016 | Physical activity | Animal; movement by the animal | Physical activity |
| Wanser | 2020 | Relationship with an animal | Training an animal | Animal; physical activity |
| Wesenberg | 2019 | Presence of animal | Animal; physical contact; taking care of an animal; training of an animal | Physical activity; social interaction |
| Wesley | 2009 | Social facilitator or catalyst | Animal | Therapeutic aspects; social interaction |
| White-Lewis d) | 2019 | Movement by the animal | Animal; movement by the animal | Physical activity; education or training |
| White-Lewis d) | 2018 | Movement by the animal | Animal; movement by the animal, taking care of an animal; training an animal | Physical activity; education or training |
| Wolynczyk-Gmaj | 2021 | Presence of animal | Animal | Physical activity; social interaction |
| Woolley | 2004 | Not specified | Animal, interaction with an animal; taking care of an animal | Therapeutic aspects; social interaction |
| Zisselman | 1996 | Relationship with an animal | Animal; interaction with an animal; social interaction | Physical activity |



Reports identified through database searching (n = 2001)
Additional records identified through other sources (n = 1)
Reports after duplicated removed (n = 1894)
Reports screened (n = 1894)
Remove of irrelevant reports (n = 1368)
Reports fulltext screened (n = 526)
Full-texts excluded, with reasons (n =350):
- No control intervention (n = 173)
- Report not found (n = 68)
- No AAI (n = 43)
- Only registered on clinical trial (n = 24)
- Not a study (n = 23)
- Wrong language (n = 16)
- Poster or abstract presentation (n = 3)
Reports included in review (n = 176)


**Figure 1.**



Number of mentions
60
50
40
30
20
10
0
56
29
24
21
16
15
12
10
6
5
5
Human-animal interaction
Not specified
Movement by the animal
Social facilitator or catalyst
Relationship
Other
Presence of animal
Physical contact
Social or emotional support
Taking care of an animal
Physical activity


**Figure 2.**

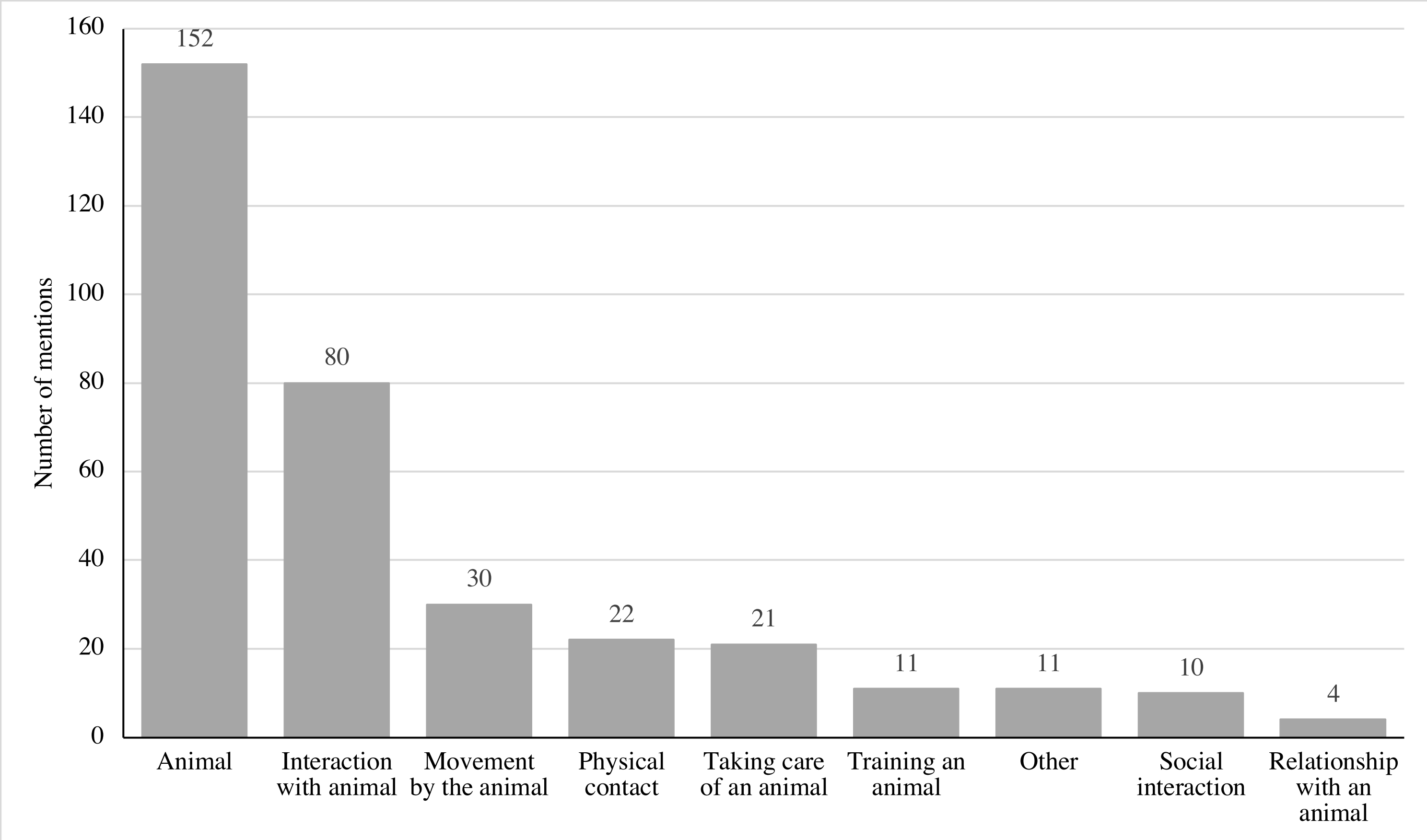

Number of mentions
160
140
120
100
80
60
40
20
0
152
80
30
22
21
11
11
10
4
Animal
Interaction with animal
Movement by the animal
Physical contact
Taking care of an animal
Training an animal
Other
Social interaction
Relationship with an animal

**Figure 3.**

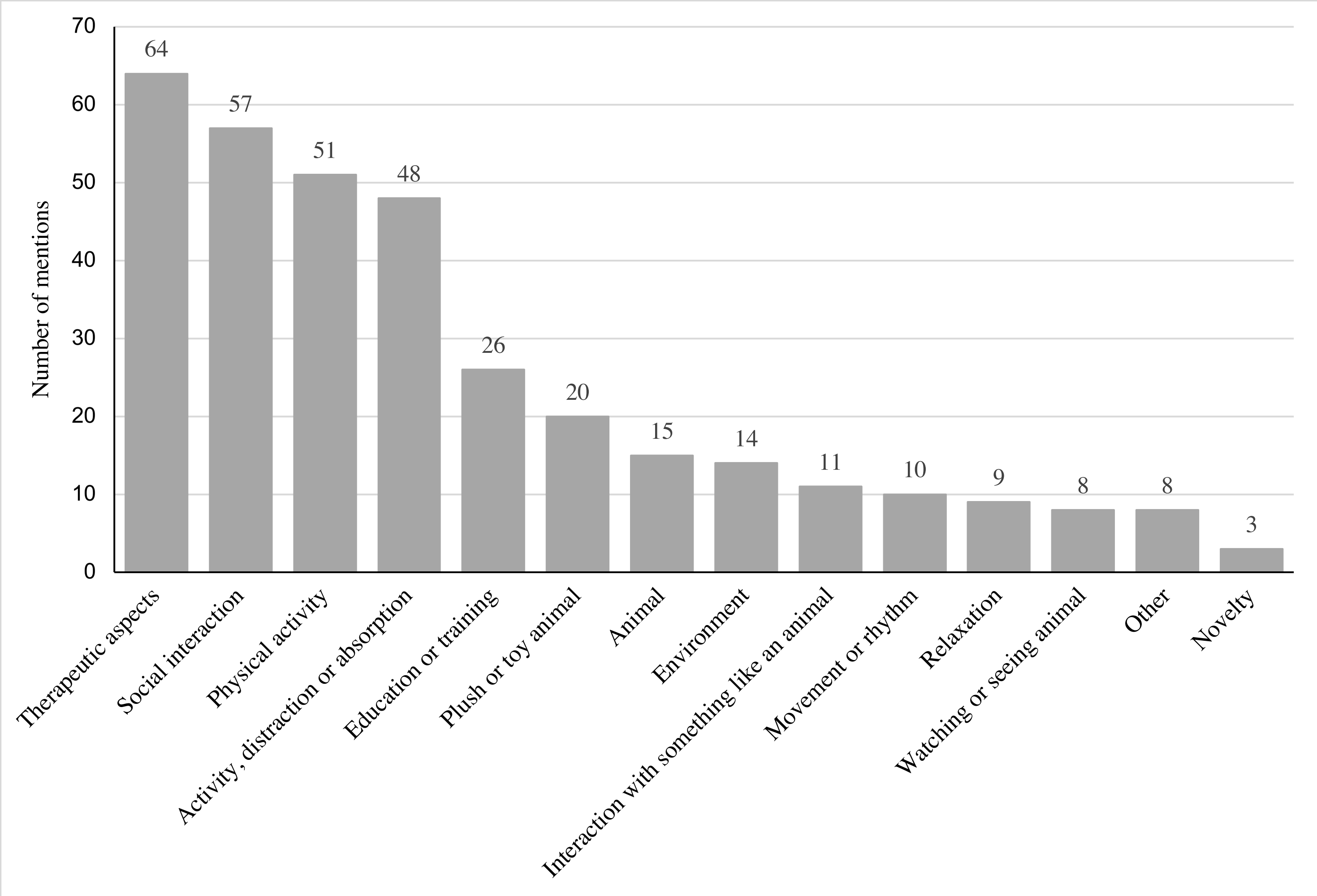

Number of mentions
70
60
50
40
30
20
10
0
64
57
51
48
26
20
15
14
11
10
9
8
8
3
Therapeutic aspects
Social interaction
Physical activity
Activity, distraction or absorption
Education or training
Plush or toy animal
Animal
Environment
Interaction with something like an animal
Movement or rhythm
Relaxation
Watching or seeing animal
Other
Novelty

**Figure 4.**

**SUPPLEMENTARY MATERIALS**

**Table of Contents**



**SI: Methods: Search strings**

**PsycINFO (Ovid)**

(("Animal intervention*" or "Animal therap*" or "Animal assisted" or "Animal facilitated" or Anthrozoology or "Assistance animal*" or
"Assistance dog*" or "Assistance horse*" or "Canine therap*" or "Canine assisted" or "Canine facilitated" or "Companion animal*" or
"Dog therap*" or "Dog assisted" or "Dog facilitated" or "Dolphin therap*" or "Dolphin assisted" or "Dolphin facilitated" or "Equine therap*" or "Equine assisted" or "Equine facilitated" or Hippotherapy or "Horseback riding" or "Human animal bond*" or "Human animal interaction*" or "Pet therap*" or "Pet assisted" or "Pet facilitated" or "Service animal*" or "Service dog*" or
"Service horse*" or "Therapeutic animal*" or "Therapeutic dog*" or "Therapeutic horse*" or "Therapeutic pet*" or "Therapeutic riding" or
"Therapy with animal*").ti,ab,id OR ("Animal Assisted Therapy" OR "Service animals").sh or ("Animal Assisted Therapy" or "Bonding, Human-Pet"
or "Equine-Assisted Therapy").mh) and ((Interspecies or animal* or pet* or "human animal*" or dog* or canine* or equine* or horse* or dolphin* or mammal* or goat* or cat* or pig*
or rabbit* or bird* or sheep or chicken* or turtle* or fish or aquarium or farm*).ti,ab,id. OR (Mammals OR "Interspecies Interaction" OR Dogs OR
Animals OR Pets OR Horses OR Dolphins OR Goats OR Cats OR "Guinea Pigs" OR Pigs OR Rabbits OR Birds OR Sheep OR Chickens OR Turtles OR Fishes).sh
or (Animals or "Animals, Domestic" or Pets or Dogs or Cats or Sheep or Horses or Dolphins or Mammals or Goats or "Guinea Pigs" or Swine or Rabbits
or Birds or Chickens or Turtles or Fishes or Farms).mh) and (("Controlled trial*" or "Control group*").ti,ab,id. or ("Randomized Controlled Trials").sh
or ("Randomized Controlled Trial").mh)

**PSYNDEX (OVID)**

(("Animal intervention*" or "Animal therap*" or "Animal assisted" or "Animal facilitated" or Anthrozoology or "Assistance animal*" or
"Assistance dog*" or "Assistance horse*" or "Canine therap*" or "Canine assisted" or "Canine facilitated" or "Companion animal*" or
"Dog therap*" or "Dog assisted" or "Dog facilitated" or "Dolphin therap*" or "Dolphin assisted" or "Dolphin facilitated" or
"Equine therap*" or "Equine assisted" or "Equine facilitated" or Hippotherapy or "Horseback riding" or "Human animal bond*" or
"Human animal interaction*" or "Pet therap*" or "Pet assisted" or "Pet facilitated" or "Service animal*" or "Service dog*" or
"Service horse*" or "Therapeutic animal*" or "Therapeutic dog*" or "Therapeutic horse*" or "Therapeutic pet*" or "Therapeutic riding" or
"Therapy with animal*").ti,ab,id OR ("Animal Assisted Therapy" OR "Service animals").sh) and ((Interspecies or animal* or pet* or "human animal*" or dog* or canine* or equine* or horse* or dolphin* or mammal* or goat* or cat* or pig* or rabbit* or bird* or sheep or chicken* or turtle* or fish or aquarium or farm*).ti,ab,id. OR (Mammals OR "Interspecies Interaction" OR Dogs OR Animals OR Pets OR Horses OR Dolphins OR Goats OR Cats OR "Guinea Pigs" OR Pigs OR Rabbits OR Birds OR Sheep OR Chickens OR Turtles OR Fishes).sh) and
(("Controlled trial*" or "Control group*").ti,ab,id. or ("Randomized Controlled Trials").sh)

**ERIC (Ovid)**

(("Animal intervention*" or "Animal therap*" or "Animal assisted" or "Animal facilitated" or Anthrozoology or "Assistance animal*" or
"Assistance dog*" or "Assistance horse*" or "Canine therap*" or "Canine assisted" or "Canine facilitated" or "Companion animal*" or
"Dog therap*" or "Dog assisted" or "Dog facilitated" or "Dolphin therap*" or "Dolphin assisted" or "Dolphin facilitated" or
"Equine therap*" or "Equine assisted" or "Equine facilitated" or Hippotherapy or "Horseback riding" or "Human animal bond*" or
"Human animal interaction*" or "Pet therap*" or "Pet assisted" or "Pet facilitated" or "Service animal*" or "Service dog*" or
"Service horse*" or "Therapeutic animal*" or "Therapeutic dog*" or "Therapeutic horse*" or "Therapeutic pet*" or "Therapeutic riding" or
"Therapy with animal*").ti,ab,id or (Animals and Therapy).sh) and ((Interspecies or animal* or pet* or "human animal*" or dog* or canine* or equine* or horse* or dolphin* or mammal* or goat* or cat* or pig*
or rabbit* or bird* or sheep or chicken* or turtle* or fish or aquarium or farm*).ti,ab,id. OR (Animals).sh) and (("Controlled trial*" or "Control group*").ti,ab,id. or ("Randomized Controlled Trials").sh)

**MEDLINE (Ovid)**

(("Animal intervention*" or "Animal therap*" or "Animal assisted" or "Animal facilitated" or Anthrozoology or "Assistance animal*" or
"Assistance dog*" or "Assistance horse*" or "Canine therap*" or "Canine assisted" or "Canine facilitated" or "Companion animal*" or

"Dog therap*" or "Dog assisted" or "Dog facilitated" or "Dolphin therap*" or "Dolphin assisted" or "Dolphin facilitated" or
"Equine therap*" or "Equine assisted" or "Equine facilitated" or Hippotherapy or "Horseback riding" or "Human animal bond*" or
"Human animal interaction*" or "Pet therap*" or "Pet assisted" or "Pet facilitated" or "Service animal*" or "Service dog*" or
"Service horse*" or "Therapeutic animal*" or "Therapeutic dog*" or "Therapeutic horse*" or "Therapeutic pet*" or "Therapeutic riding" or
"Therapy with animal*").ti,ab,id or ("Animal Assisted Therapy" or "Bonding, Human-Pet"
or "Equine-Assisted Therapy").sh) and ((Interspecies or animal* or pet* or "human animal*" or dog* or canine* or equine* or horse* or dolphin* or mammal* or goat* or cat* or pig*
or rabbit* or bird* or sheep or chicken* or turtle* or fish or aquarium or farm*).ti,ab,id. OR (Animals or "Animals, Domestic" or Pets or Dogs
or Cats or Sheep or Horses or Dolphins or Mammals or Goats or "Guinea Pigs" or Swine or Rabbits or Birds or Chickens or Turtles or Fishes or Farms).sh) and
(("Controlled trial*" or "Control group*").ti,ab,id. or ("Randomized Controlled Trial").sh)

**Embase (Ovid)**

(("Animal intervention*" or "Animal therap*" or "Animal assisted" or "Animal facilitated" or Anthrozoology or "Assistance animal*" or
"Assistance dog*" or "Assistance horse*" or "Canine therap*" or "Canine assisted" or "Canine facilitated" or
"Dog therap*" or "Dog assisted" or "Dog facilitated" or "Dolphin therap*" or "Dolphin assisted" or "Dolphin facilitated" or
"Equine therap*" or "Equine assisted" or "Equine facilitated" or Hippotherapy or "Horseback riding" or "Human animal bond*" or
"Human animal interaction*" or "Pet therap*" or "Pet assisted" or "Pet facilitated" or "Service animal*" or "Service dog*" or
"Service horse*" or "Therapeutic animal*" or "Therapeutic dog*" or "Therapeutic horse*" or "Therapeutic pet*" or "Therapeutic riding" or
"Therapy with animal*").ti,ab,kw or ("animal assisted therapy" or "human-animal bond" or "service dog" or hippotherapy).sh) and ((Interspecies or animal* or pet* or "human animal*" or dog* or canine* or equine* or horse* or dolphin* or mammal* or goat* or cat* or pig* or rabbit* or bird* or sheep or chicken* or turtle* or fish or aquarium or farm*).ti,ab,kw. or (animal or "PET ANIMAL" or DOG or CANIDAE
or HORSE or "toothed whale" or MAMMAL or GOAT or CAT or "GUINEA PIG" or PIG or Leporidae or BIRD or SHEEP or CHICKEN or TURTLE or FISH or rabbit or "agricultural land" or "domestic pig" or "domestic animal").sh) and
(("Controlled trial*" or "Control group*").ti,ab,kw. or ("controlled study").sh) and (psychiatry).ec

**PubMed**

("Animal intervention"[Title/Abstract] or "Animal therapy"[Title/Abstract] or "Animal assisted"[Title/Abstract] or "Animal facilitated"[Title/Abstract]
or Anthrozoology[Title/Abstract] or "Assistance animal"[Title/Abstract] or "Assistance dog"[Title/Abstract] or "Assistance horse"[Title/Abstract]

or "Canine therapy"[Title/Abstract] or "Canine assisted"[Title/Abstract] or "Canine facilitated"[Title/Abstract] or "Companion animal"[Title/Abstract] or "Dog therapy"[Title/Abstract] or "Dog assisted"[Title/Abstract] or "Dog facilitated"[Title/Abstract] or "Dolphin therapy"[Title/Abstract] or "Dolphin assisted"[Title/Abstract] or "Dolphin facilitated"[Title/Abstract] or "Equine therapy"[Title/Abstract] or "Equine assisted"[Title/Abstract] or "Equine facilitated"[Title/Abstract] or Hippotherapy[Title/Abstract] or "Horseback riding"[Title/Abstract] or "Human animal bond"[Title/Abstract] or "Human animal interaction"[Title/Abstract] or "Pet therapy"[Title/Abstract] or "Pet assisted"[Title/Abstract] or "Pet facilitated"[Title/Abstract] or "Service animal"[Title/Abstract] or "Service dog"[Title/Abstract] or "Service horse"[Title/Abstract] or "Therapeutic animal"[Title/Abstract] or "Therapeutic dog"[Title/Abstract] or "Therapeutic horse"[Title/Abstract] or "Therapeutic pet*"[Title/Abstract] or "Therapeutic riding"[Title/Abstract] or "Therapy with animals" [Title/Abstract] or "Animal Assisted Therapy"[MeSH Terms] or "Bonding, Human-Pet"[MeSH Terms] or "Equine-Assisted Therapy"[MeSH Terms]) and (Interspecies[Title/Abstract] or animal[Title/Abstract] or pet[Title/Abstract] or "human animal"[Title/Abstract] or dog[Title/Abstract] or canine[Title/Abstract] or equine[Title/Abstract] or horse[Title/Abstract] or dolphin[Title/Abstract] or mammal[Title/Abstract] or goat[Title/Abstract] or cat[Title/Abstract] or pig[Title/Abstract] or rabbit[Title/Abstract] or bird[Title/Abstract] or sheep[Title/Abstract] or chicken[Title/Abstract] or turtle[Title/Abstract] or fish[Title/Abstract] or aquarium[Title/Abstract] or farm[Title/Abstract] or Animals[MeSH Terms] or "Animals, Domestic"[MeSH Terms] or Pets[MeSH Terms] or Dogs[MeSH Terms] or Cats[MeSH Terms] or Sheep[MeSH Terms] or Horses[MeSH Terms] or Dolphins[MeSH Terms] or Mammals[MeSH Terms] or Goats[MeSH Terms] or "Guinea Pigs"[MeSH Terms] or Swine[MeSH Terms] or Rabbits[MeSH Terms] or Birds[MeSH Terms] or Chickens[MeSH Terms] or Turtles[MeSH Terms] or Fishes[MeSH Terms] or Farms[MeSH Terms]) and ("Controlled trial"[Title/Abstract] or "Control group"[Title/Abstract] or "Randomized Controlled Trial"[MeSH Terms])

**Cochrane Library**

("Animal intervention*" or "Animal therap*" or "Animal assisted" or "Animal facilitated" or Anthrozoology or "Assistance animal*" or "Assistance dog*" or "Assistance horse*" or "Canine therap*" or "Canine assisted" or "Canine facilitated" or "Companion animal*" or "Dog therap*" or "Dog assisted" or "Dog facilitated" or "Dolphin therap*" or "Dolphin assisted" or "Dolphin facilitated" or "Equine therap*" or "Equine assisted" or "Equine facilitated" or Hippotherapy or "Horseback riding" or "Human animal bond*" or "Human animal interaction*" or "Pet therap*" or "Pet assisted" or "Pet facilitated" or "Service animal*" or "Service dog*" or "Service horse*" or "Therapeutic animal*" or "Therapeutic dog*" or "Therapeutic horse*" or "Therapeutic pet*" or "Therapeutic riding" or "Therapy with animal*") AND (Interspecies or animal* or pet* or "human animal*" or dog* or canine* or equine* or horse* or dolphin* or mammal* or goat* or cat* or pig* or rabbit* or bird* or sheep or chicken* or turtle* or fish or aquarium or farm*) AND ("Controlled trial*" or "Control group*")

**Web of Science**

(("Animal intervention*" or "Animal therap*" or "Animal assisted" or "Animal facilitated" or Anthrozoology or "Assistance animal*" or
"Assistance dog*" or "Assistance horse*" or "Canine therap*" or "Canine assisted" or "Canine facilitated" or "Companion animal*" or
"Dog therap*" or "Dog assisted" or "Dog facilitated" or "Dolphin therap*" or "Dolphin assisted" or "Dolphin facilitated" or
"Equine therap*" or "Equine assisted" or "Equine facilitated" or Hippotherapy or "Horseback riding" or "Human animal bond*" or
"Human animal interaction*" or "Pet therap*" or "Pet assisted" or "Pet facilitated" or "Service animal*" or "Service dog*" or
"Service horse*" or "Therapeutic animal*" or "Therapeutic dog*" or "Therapeutic horse*" or "Therapeutic pet*" or "Therapeutic riding" or
"Therapy with animal*") and (Interspecies or animal* or pet* or "human animal*" or dog* or canine* or equine* or horse* or dolphin* or mammal* or goat* or cat* or pig* or rabbit* or bird* or sheep or chicken* or turtle* or fish or aquarium or farm*) and ("Controlled trial*" or "Control group*"))

**Scopus**

(TITLE-ABS-KEY ( "Animal intervention*" or "Animal assisted" or "Animal facilitated" or Anthrozoology or "Assistance animal*" or
"Assistance dog*" or "Assistance horse*" or "Canine therap*" or "Canine assisted" or "Canine facilitated" or "Dog therap*" or "Dog assisted" or
"Dog facilitated" or "Dolphin therap*" or "Dolphin assisted" or "Dolphin facilitated" or "Equine therap*" or "Equine assisted" or "Equine facilitated"
or Hippotherapy or "Horseback riding" or "Human animal bond*" or "Human animal interaction*" or "Pet therap*" or "Pet assisted" or "Pet facilitated"
or "Service animal*" or "Service dog*" or "Service horse*" or "Therapeutic animal*" or "Therapeutic dog*" or "Therapeutic horse*" or "Therapeutic pet*"
or "Therapeutic riding" or "Therapy with animal*" ) AND ( "Controlled trial*" or "Control group*" ) )

**CINAHL (EBSCO)**

(TI ("Animal intervention*" or "Animal therap*" or "Animal assisted" or "Animal facilitated" or Anthrozoology or "Assistance animal*" or
"Assistance dog*" or "Assistance horse*" or "Canine therap*" or "Canine assisted" or "Canine facilitated" or "Companion animal*" or
"Dog therap*" or "Dog assisted" or "Dog facilitated" or "Dolphin therap*" or "Dolphin assisted" or "Dolphin facilitated" or
"Equine therap*" or "Equine assisted" or "Equine facilitated" or Hippotherapy or "Horseback riding" or "Human animal bond*" or
"Human animal interaction*" or "Pet therap*" or "Pet assisted" or "Pet facilitated" or "Service animal*" or "Service dog*" or
"Service horse*" or "Therapeutic animal*" or "Therapeutic dog*" or "Therapeutic horse*" or "Therapeutic pet*" or "Therapeutic riding" or
"Therapy with animal*") OR AB ("Animal intervention*" or "Animal therap*" or "Animal assisted" or "Animal facilitated" or Anthrozoology or "Assistance animal*" or
"Assistance dog*" or "Assistance horse*" or "Canine therap*" or "Canine assisted" or "Canine facilitated" or "Companion animal*" or

"Dog therap*" or "Dog assisted" or "Dog facilitated" or "Dolphin therap*" or "Dolphin assisted" or "Dolphin facilitated" or
"Equine therap*" or "Equine assisted" or "Equine facilitated" or Hippotherapy or "Horseback riding" or "Human animal bond*" or
"Human animal interaction*" or "Pet therap*" or "Pet assisted" or "Pet facilitated" or "Service animal*" or "Service dog*" or
"Service horse*" or "Therapeutic animal*" or "Therapeutic dog*" or "Therapeutic horse*" or "Therapeutic pet*" or "Therapeutic riding" or
"Therapy with animal*") OR SU ("Animal Assisted Therapy (Iowa NIC)" or "Service Animals" or "Equine-Assisted Therapy" or "Human-Pet Bonding" or "Pet Therapy"))
AND (TI (Interspecies or animal* or pet* or "human animal*" or dog* or canine* or equine* or horse* or dolphin* or mammal* or goat* or cat* or pig*
or rabbit* or bird* or sheep or chicken* or turtle* or fish or aquarium or farm*) OR AB (Interspecies or animal* or pet* or "human animal*" or dog* or canine*
or equine* or horse* or dolphin* or mammal* or goat* or cat* or pig* or rabbit* or bird* or sheep or chicken* or turtle* or fish or aquarium or farm*)
OR SU (animals OR pets OR dogs OR horses OR DOLPHINS OR mammals OR goats OR cats OR "guinea pigs" OR swine OR rabbits OR birds OR sheep OR turtles OR fish))
AND (TI ("Controlled trial*" or "Control group*") OR AB ("Controlled trial*" or "Control group*") OR SU ("Randomized Controlled Trials"))

**PTSDpubs (ProQuest)**

[STRICT](TI( "Animal intervention*" or "Animal therap*" or "Animal assisted" or "Animal facilitated" or Anthrozoology or "Assistance animal*" or "Assistance dog*" or "Assistance horse*" or "Canine therap*" or "Canine assisted" or "Canine facilitated" or "Companion animal*" or "Dog therap*" or "Dog assisted" or "Dog facilitated" or "Dolphin therap*" or "Dolphin assisted" or "Dolphin facilitated" or "Equine therap*" or "Equine assisted" or "Equine facilitated" or Hippotherapy or "Horseback riding" or "Human animal bond*" or "Human animal interaction*" or "Pet therap*" or "Pet assisted" or "Pet facilitated" or "Service animal*" or "Service dog*" or "Service horse*" or "Therapeutic animal*" or "Therapeutic dog*" or "Therapeutic horse*" or "Therapeutic pet*" or "Therapeutic riding" or "Therapy with animal*" ) OR AB ( "Animal intervention*"
or "Animal therap*" or "Animal assisted" or "Animal facilitated" or Anthrozoology or "Assistance animal*" or "Assistance dog*" or "Assistance horse*" or "Canine therap*" or
"Canine assisted" or "Canine facilitated" or "Companion animal*" or "Dog therap*" or "Dog assisted" or "Dog facilitated" or "Dolphin therap*" or "Dolphin assisted" or "Dolphin facilitated" or "Equine therap*" or "Equine assisted" or "Equine facilitated" or Hippotherapy or "Horseback riding" or "Human animal bond*" or "Human animal interaction*"
or "Pet therap*" or "Pet assisted" or "Pet facilitated" or "Service animal*" or "Service dog*" or "Service horse*" or "Therapeutic animal*" or "Therapeutic dog*"
or "Therapeutic horse*" or "Therapeutic pet*" or "Therapeutic riding" or "Therapy with animal*" ) OR SU( "Animal Assisted Therapy" )) AND (TI( Interspecies or animal* or pet* or "human animal*" or dog* or canine* or equine* or horse* or dolphin* or mammal* or goat* or cat* or pig*
or rabbit* or bird* or sheep or chicken* or turtle* or fish or aquarium or farm* ) OR AB ( Interspecies or animal* or pet* or "human animal*" or dog* or canine*
or equine* or horse* or dolphin* or mammal* or goat* or cat* or pig* or rabbit* or bird* or sheep or chicken* or turtle* or fish or aquarium or farm* ) OR

SU ( pets OR animals OR dogs OR horses OR "dolphins & porpoises" OR mammals OR "marine mammals" OR cats OR rabbits OR birds OR sheep OR fish OR aquariums OR farms )) AND (TI( "Controlled trial*" or "Control group*" ) OR AB( "Controlled trial*" or "Control group*" ) OR SU( "Randomized Clinical Trial" ))

**Dissertations & Theses (ProQuest)**

[STRICT](TI( "Animal intervention*" or "Animal therap*" or "Animal assisted" or "Animal facilitated" or Anthrozoology or "Assistance animal*" or "Assistance dog*" or "Assistance horse*" or "Canine therap*" or "Canine assisted" or "Canine facilitated" or "Companion animal*" or "Dog therap*" or "Dog assisted" or "Dog facilitated" or "Dolphin therap*" or "Dolphin assisted" or "Dolphin facilitated" or "Equine therap*" or "Equine assisted" or "Equine facilitated" or Hippotherapy or "Horseback riding" or "Human animal bond*" or "Human animal interaction*" or "Pet therap*" or "Pet assisted" or "Pet facilitated" or "Service animal*" or "Service dog*" or "Service horse*" or "Therapeutic animal*" or "Therapeutic dog*" or "Therapeutic horse*" or "Therapeutic pet*" or "Therapeutic riding" or "Therapy with animal*" ) OR AB ( "Animal intervention*"
or "Animal therap*" or "Animal assisted" or "Animal facilitated" or Anthrozoology or "Assistance animal*" or "Assistance dog*" or "Assistance horse*" or "Canine therap*" or
"Canine assisted" or "Canine facilitated" or "Companion animal*" or "Dog therap*" or "Dog assisted" or "Dog facilitated" or "Dolphin therap*" or "Dolphin assisted" or "Dolphin facilitated" or "Equine therap*" or "Equine assisted" or "Equine facilitated" or Hippotherapy or "Horseback riding" or "Human animal bond*" or "Human animal interaction*"
or "Pet therap*" or "Pet assisted" or "Pet facilitated" or "Service animal*" or "Service dog*" or "Service horse*" or "Therapeutic animal*" or "Therapeutic dog*"
or "Therapeutic horse*" or "Therapeutic pet*" or "Therapeutic riding" or "Therapy with animal*" ) OR SU( "animal assisted therapy" )) AND (TI( Interspecies or animal* or pet* or "human animal*" or dog* or canine* or equine* or horse* or dolphin* or mammal* or goat* or cat* or pig*
or rabbit* or bird* or sheep or chicken* or turtle* or fish or aquarium or farm* ) OR AB ( Interspecies or animal* or pet* or "human animal*" or dog* or canine*
or equine* or horse* or dolphin* or mammal* or goat* or cat* or pig* or rabbit* or bird* or sheep or chicken* or turtle* or fish or aquarium or farm* ) OR
SU ( pets OR animals OR dogs OR horses OR "dolphins & porpoises" OR mammals OR "marine mammals" OR cats OR rabbits OR birds OR sheep OR fish OR aquariums OR farms )) AND (TI("Controlled trial*" or "Control group*") OR AB( "Controlled trial*" or "Control group*" )

**S2: Categories of the factor hypothesis and the corresponding content**

| Category | Content |
|---|---|
| Human-animal interaction | Human-animal interaction has positive effects, e.g., reduce psychological distress and anxiety, calming effect, enhances self-esteem, affect biobehavioral stress response, activate oxytocin system, activation of secure relationship strategies, increases levels of neurochemicals, can result in learning process being more comfortable and enjoyable, greater increase in observed appropriate social behaviors, promotion of social competence etc. |
| Not specified | Not specified effects of different animal-assisted interventions, e.g., pet therapy, animal-assisted activities, horseback riding, animal-assisted interventions, animal-assisted reading program, animal-assisted psychotherapies etc. |
| Movement by the animal | Natural movement of a horse, rhythm/movement of horse |
| Social facilitator or catalyst | Animals as social catalyst, as social facilitator; animals can facilitate trust and bonding; companion animals facilitate social behavior; foster social communication and interaction skills; animal as catalysator for social learning |
| Relationship with an animal | Bond between human and animals; pet ownership; positive effects of human-animal bond; positive effects of relationship to animal; positive effects of attachment between human and animal |
| Other | Real life animal (1x); water (environment) (1x); biophilia (2x); non-verbal communication (1x); parental involvement (1x); influence of mount materials on the neuromuscular activation (1x); large animal (1x); insects can create nostalgic feelings (1x); concrete natural reinforcement for communication (1x); novel intervention (1x) |
| Presence of animal | Positive effects of presence of animal, e.g., ameliorating heart/respiratory/pulse rates, calming effect, distraction |
| Physical contact | Activation of oxytocin system through interaction (physically); physical contact (petting) ameliorates heart/respiratory/pulse rates; tactile stimulation |
| Social or emotional support | Animal as an emotional social supporter; comparable to social support by a friendly person; social support from the presence of an animal |
| Taking care of an animal | Animal enhances the role-taking abilities; focusing on giving care to animals |
| Physical activity | Exercise with animals (e.g., walking a pet, exercise intervention with horses); horse riding exercise |

**S3: Detailed information on the categories of the specific factors and the corresponding content**

| Category | Content | Multiple categories applicable |
|---|---|---|
| Animal | Real-life animal, animal as factor; presence of animal | |
| Interaction with animal | Playing with animal; response of animal; sound of animal; free interaction with dog (petting, playing etc.); individual chose of activity (grooming, petting, playing, teaching, walking on leash); exercise with animal (jumping over dog, crawling under dog etc.) | |
| Movement by the animal | Riding; horseback riding; three-dimensional movement of horse | |
| Physical contact | Petting | |
| Taking care of an animal | Responsibility for animal; grooming an animal; training in animal care; feeding animal; brushing animal; working with farm animals; taking dog for a walk; rearing insects | training in animal care |
| Training an animal | Giving animal commandos; teaching tricks and commandos; training in animal care | training in animal care |
| Social interaction | Group activity; talking to another person (dog owner, researcher or trainer) | |
| Other | Mount material (1x); Recreational/vacation atmosphere and therapeutic aspects (1x); distraction (1x); education about animal (2x); frequency (2x); familiarity (1x); therapeutic riding (1x); combination of activity and animal (1x) | |
| Relationship with an animal | Bonding with animal; companionship; facilitate relationship between subject and animal | |

**S4: Detailed information on the categories of the nonspecific factors and the corresponding content**

| Category | Content | Multiple categories applicable |
|---|---|---|
| Therapeutic aspects | Occupational therapy; psychiatric treatment; physiotherapy; pharmacotherapy; kinesitherapy; therapeutic skiing; integrated psychological treatment; cognitive-behavioral intervention; psychotherapeutic treatment program; counseling; solution-focused therapy; aquatic-movement therapy; conventional play-based early intervention (PBI); attentional control intervention; empathy training; reality orientation therapy; social skills group psychotherapy; therapeutic skiing; pediatric examination; mindfulness-based intervention; medical treatment (e.g., dentist, venipuncture) | Physiotherapy; aquatic-movement therapy; exercises involving focus on the body and physical movement; psychoeducation; empathy training; academic-stress-management condition; kinesitherapy; therapeutic skiing |
| Social interaction | Group activity; talking to another person (e.g., dog owner, researcher or trainer) | Group sports; group training of social skills; being interviewed |
| Physical activity | Rehabilitation exercises; physical classes; physical activity; physiotherapy; home-based rehabilitation; group sports; movement of horse; riding; exercise group program; body and physical movements; stability exercises; treadmill; walking; therapeutic skiing; dance classes; aquatic-movement therapy; exercises involving focus on the body and physical movement; kinesitherapy | Group sports; physiotherapy; aquatic-movement therapy; physical-education classes; rhythm and music-based therapy; exercises involving focus on the body and physical movement; kinesitherapy; therapeutic skiing |
| Activity, distraction or absorption | Writing, reading alone; reading out loud to peers/ animal/ plush; recreation and occupation program; playing with toys/ peers; engaging in activities; watching movie; puzzle activity; recreational activities; playing; watching film of animal; focus view on living being (plant) or empty tank; exercises involving focus on the body and physical movement; educational and recreational activities; access to phone or tablet; drawing; being interviewed; distraction; cold pressor test | Exercises involving focus on the body and physical movement; educational and recreational activities; academic-stress-management condition; being interviewed |
| Education or training | Physical education classes; curriculum about pets and pet care; social skill training; horsemanship skills; coping skills education; lectures on healthy lifestyle choices; information about assistance dog; educational activities/ program; learning about caring for animals; content presentations and guided activities focused on enhancing self-regulation; learning about horses, attention exercise education; correctional & vocational programs; empathy training; educational and recreational activities; school lessons | Physical-education classes; psychoeducation; empathy training; group training of social skills; educational and recreational activities; academic-stress-management condition |
| Plush or toy animal | Plush animal; toy animal; robot | Condition with novel plush animal |

| | | |
|---|---|---|
| Environment | Outdoor; water; aquatic movement; view on living being (plant) or empty tank; new setting/ environment; aquatic-movement therapy; farm, barn | Aquatic-movement therapy; focus gaze on living being (plant) or empty tank |
| Animal | Animal present; walking dog etc. | |
| Interaction with something like an animal | Petting (plush animal); grooming and tacking stuffed toy horse; interaction with plush animal; grooming plush cat; horse riding simulator (HRS); simulated horseback riding; symmetrical sitting on stationary barrel | Horse-riding simulator (HRS); simulated horseback riding |
| Movement or rhythm | Rhythm and music-based therapy; movement on mechanic horse; vibration; auditory perception of beat based rhythms; audio consisted of the rhythmical beat-based sounds of horses | Rhythm and music-based therapy |
| Watching or seeing animal | Exposure to pictures of the dog; visual of the animal; observation of dog-human interaction; watching film of animal | Watching film of an animal |
| Other | Bringing article to stimulate discussion (1x); sound of animal (1x); proximity effect (2x); talking about animals/pet (1x); horseback riding (not in a therapeutic context) (1x); taking care of something (1x); distraction (1x) | |