

The Science Behind Animal-Assisted Therapy

Dawn A. Marcus

Published online: 22 February 2013
© Springer Science+Business Media New York 2013

Abstract Animal-assisted therapy is a complementary medicine intervention, typically utilizing dogs trained to be obedient, calm, and comforting. Several studies have reported significant pain relief after participating in therapy dog visits. Objective reports of reduced pain and pain-related symptoms are supported by studies measuring decreased catecholamines and increased endorphins in humans receiving friendly dog visits. Mirror neuron activity and disease-perception through olfactory ability in dogs may also play important roles in helping dogs connect with humans during therapeutic encounters. This review will explore a variety of possible theories that may explain the therapeutic benefits that occur during therapy dog visits.

Keywords Catecholamines · Electronic nose · Empathy · Endorphin · Mirror neurons · Therapy dog

Introduction

Animal-assisted therapy is a complementary intervention using animals, usually dogs trained to be obedient, calm, and comforting, for therapeutic benefit across a broad range of medical conditions [1, 2]. Pet dogs and their owners (called handlers) undergo general obedience and specialized therapy dog training, testing, and certification prior to making visits to insure interactions will be positive, safe, and not disruptive. The typical therapy dog visit involves a patient

spending about 10–15 min petting or playing with a trained and certified dog while the handler monitors the dog, tends to the dog's needs, and answers questions about the dog. The dog's handler also ensures that infection control protocols are followed to avoid spread of infection [3]. In medical settings, therapy dog visits, typically provided through volunteer services, are targeted to patients, visitors, and healthcare workers to help reduce stress and enhance mood [4].

Published data are available investigating the impact of therapeutic animal visits for patients with diverse conditions, including pervasive developmental disorders, cardiovascular disease, psychiatric disorders, Alzheimer's disease, and cancer [1, 2]. A literature review provided Class IIa-IIb evidence (shown to be acceptable and useful) for recommending animal-assisted therapy to optimize healing environments [5]. Animal-assisted therapy with dogs has been documented to produce objective health changes, with reductions in measures of cardiovascular stress markers [6, 7] and enhancement of immune factors [8]. Interestingly, one study testing pre-study attitude toward pets found physiological benefit was independent of baseline Pet Attitude Scale score [8], supporting biological in addition to potential psychological benefits.

This review will briefly catalogue studies showing subjective pain reduction following animal-assisted interventions with therapy dogs, and provide theories for possible biological explanations for these positive interactions. Physiological changes have been identified in both humans and the dogs visiting them that support subjective impressions of reduced distress, decreased pain, and mood enhancement. In addition, new research on mirror neurons has been used to support imitated empathic behavior. For example, observing a happy person may also make the observer feel happier, with this empathic link explained, at least in part, by activation of mirror neurons [9]. Finally, the ability of dogs to identify and provide attention to individuals most in need of a therapeutic interaction might be explained by chemical changes

This article is part of the Topical Collection on *Cancer Pain*

D. A. Marcus
Department of Anesthesiology, University of Pittsburgh School
of Medicine, Pittsburgh, PA, USA

D. A. Marcus (✉)
Pain Medicine, Suite 400, Centre Commons Building, 5750 Centre
Avenue, Pittsburgh, PA 15206, USA
e-mail: marcusd@upmc.edu

occurring as part of the human stress response and the olfactory perceptive power of dogs.

Animal-Assisted Therapy for Pain Relief

Several studies have investigated pain-relieving effects of therapy dog interactions for pediatric and adult patients, with studies conducted in both inpatient and outpatient settings (Table 1) [4, 10–14]. Significant pain reduction has been reported for acute and chronic pain after visits typically lasting about 10–20 min. In addition to pain reduction, therapy dog visits in these studies were also associated with significant decreases in stress, mood disturbance, and fatigue [4, 12, 14]. Because psychological and somatic symptoms may also influence the pain experience [15–18], these studies measuring subjective pain severity cannot determine if the therapy dog visit directly reduced pain perception or if pain impact may have been diminished secondarily because of other improvements. Several studies, described below, help to show that the subjective improvements in pain and related symptoms (e.g., stress and mood disturbance) are supported by experiments showing objective changes in chemicals important for these symptoms.

Physiology Behind Therapy Dog Encounters

Immediate benefits from therapy dog visits might be anticipated due to simple distraction during the time of the visit. Two small studies have shown enduring effects between visits in nursing home residents receiving weekly therapy dog visits for decreasing loneliness ($N=45$) [19] and twice monthly therapy dog visits for improving mental functions ($N=10$) [20]. These studies support that benefits may represent more than short-term entertainment value. Indeed, research studies support that changes observed with therapy dog visits may be rooted in physiological changes important for improving health.

Physiological Changes in Humans Receiving Therapy Dog Visits

Brief therapy dog visits result in reductions in stress hormones, such as epinephrine and norepinephrine, as well as increases in endorphin levels [21, 22]. Oxytocin also offers anti-stress effects and increases pain threshold [23], with levels shown to increase following dog interactions [21, 24, 25]. For example, Odendaal and Meintjes measured blood pressure and serum neurochemical levels in 18 healthy adults before and after quiet reading or a positive dog interaction [21]. Blood pressure was significantly reduced after the dog visit, with changes occurring over a range of 5–24 min

(average time=15 min). Average mean arterial pressure decreased from 87.6 mmHg before the dog visit to 84.4 mmHg after the visit ($P<0.01$). Blood pressure was not reported for quiet reading. Significant changes in neurochemical levels occurred after quiet reading or the dog visit, although greater improvements occurred with the dog visit (Table 2). Changes occurred in a broad range of chemicals, supporting subjective reports for reduced stress, improved mood, social bonding, and pain reduction with therapy dog visits.

Healthcare workers receiving therapy dog visits may also experience measurable reductions in stress markers that persist after the worker is no longer in contact with the dog. In one study, cortisol was measured over one hour in healthcare workers completing one of three interventions: (1) a brief 5-min therapy dog visit, (2) a 20-min therapy dog visit, or (3) 20 min of quiet rest [22]. Significant reductions in serum cortisol occurred with each intervention, including the very brief dog encounter (Fig. 1).

Longer-term physiological changes were demonstrated in a study measuring salivary chromogranin A in seniors with dementia attending adult day care [26]. Chromogranin A is a protein produced by the adrenal glands and released when the nervous system is stressed. In this study, therapy dog visits occurred every other week. Chromogranin A levels were measured at the beginning of the study and after the dog had been visiting for 3 months. Therapy dog sessions were provided at the same time, with chromogranin A measured at fixed times to avoid circadian variability. Changes in chromogranin A were compared for seniors receiving and seniors not receiving therapy dog visits. After the final visit, chromogranin A levels had dropped by 57 % in seniors who visited with the therapy dog over the 3 months, compared with a 19 % increase in residents who did not receive visits.

Physiological Changes in Therapy Dogs

In the study above from Odendaal and Meintjes, neurophysiological markers were also measured in the dogs participating in the study [21]. Similar to the response detected in humans, the visits likewise resulted in significant positive changes ($P\leq 0.01$) in endorphin, oxytocin, prolactin, phenyl acetic acid, and dopamine levels in the dogs. These changes support that the experience is similarly positive and associated with positive bonding experiences for the dogs. Unlike the response in humans, however, serum cortisol levels rose in the dogs from 366.5 to 416.0 mmol/L, although this difference did not achieve statistical significance ($P=0.30$). Failure of dogs to experience a significant decrease in cortisol suggests that visits are not a stress reliever for dogs. The numerical increase in cortisol in the dogs supports that dogs experience therapy dog visits as a work experience. These data support that sitting or standing quietly, maintaining a high level of obedience and

Table 1 Therapy dog interventions targeting pain relief

Reference	Setting/design	Interaction	Pain assessment	Outcome
Sobo 2006 [10]	Children (5–18 years old) with acute postoperative pain (N=25)	Therapy dog visit lasting ≤10 min for 24 % of participants, 11–20 min for 60 %, and >20 min for 16 % Therapy dog added to facility	1–10 mm scales with faces for physical pain (hurting) and emotional pain (scared, nervous, worried) Average number of as-needed analgesic medications used was compared during the 3 months prior to the therapy dog and for 6 months after addition of therapy dog	Physical pain decreased from 3.8 to 1.6 (P=0.001). Emotional pain decreased from 3.9 to 1.2 (P<0.001) Average number of as-needed analgesics decreased from 6.7 to 3.5 (P=0.017)
Lust 2007 [11]	Adults at rehabilitation facility with brain or spinal cord injuries, degenerative diseases, or severe physical disabilities (N=58)	10-minute therapy dog visit	11-point numeric scale FACES pain scale (0 = smiling, no pain, 5 = crying, worst pain)	Pain decreased from 3.2 to 2.5 (P=0.001) Pain decreased significantly more after the therapy dog visit (-1.6 vs. -0.3, P=0.006)
Coakley 2009 [12]	Medical and surgical adult inpatients (N=59)	15–20 min visit from a therapy dog (N=18; pre-treatment pain using an 11-point scale=4.7) or sitting quietly alone for 15 min (N=39; pre-treatment pain=5.2)	11-point numeric scale	Mean pain scores decreased significantly from 6.7 to 5.7 with dog (P<0.001) and were unchanged (from 6.3 to 6.4) in the waiting room. Among patients with pain ≥5, clinically meaningful pain relief ^a occurred for 26 % visiting the therapy dog and 3 % in the waiting room control
Braun 2009 [13]	Pediatric inpatients (3–17 years old) with pain	Waiting before/between appointments with therapy dog (mean 11 min) vs. traditional waiting room with television and magazines (mean 16 min)	11-point numeric scale	Mean pain scores decreased significantly from 7.1 to 6.0 with dog (P<0.001) and were unchanged (from 7.0 to 7.3) in the waiting room. Among patients with pain ≥5, clinically meaningful pain relief ^a occurred for 34 % visiting the therapy dog and 4 % in the waiting room control
Marcus 2012 [4•]	Adult outpatients with chronic pain (N=230 therapy dog visits vs. N=83 waiting room controls)	Waiting before/between appointments with therapy dog (mean 12 min) vs. traditional waiting room with television and magazines (mean 17 min)	11-point numeric scale	Mean pain scores decreased significantly from 7.1 to 6.0 with dog (P<0.001) and were unchanged (from 7.0 to 7.3) in the waiting room. Among patients with pain ≥5, clinically meaningful pain relief ^a occurred for 34 % visiting the therapy dog and 4 % in the waiting room control
Marcus 2013 [14]	Adult outpatients with fibromyalgia (N=106 therapy dog visits vs. N=49 waiting room controls)	Waiting before/between appointments with therapy dog (mean 12 min) vs. traditional waiting room with television and magazines (mean 17 min)	11-point numeric scale	Mean pain scores decreased significantly from 7.1 to 6.0 with dog (P<0.001) and were unchanged (from 7.0 to 7.3) in the waiting room. Among patients with pain ≥5, clinically meaningful pain relief ^a occurred for 34 % visiting the therapy dog and 4 % in the waiting room control

^a Clinically meaningful pain relief was defined as a reduction on an 11-point severity scale of ≥2

Table 2 Median values (interquartile range) for physiological markers experiencing a significant change after a positive dog encounter or quiet reading. (Based on Odendaal 2003 [21]; Reprinted withpermission from Marcus DA: *Therapy Dogs in Cancer Care*. New York: Springer; 2012. Approved with permission of Springer, 2013)

Serum marker	Interpretation of change	Significant change reported with dog visit*		Significant change reported with quiet reading*	
		Baseline	Post-visit	Baseline	Post-reading
B-endorphin (pmol/L)	Increase linked to pain reduction	3.1 (5.4)	8.0 (6.5)	3.5 (6.7)	5.1 (6.4)
Oxytocin (ng/L)	Increase linked to positive social bonding	2.1 (2.5)	4.0 (1.0)	2.5 (2.0)	2.9 (2.0)
Prolactin (ng/L)	Increase linked to positive social bonding	9.2 (9.1)	11.6 (10.1)	10.2 (7.1)	10.4 (6.2)
Phenyl acetic acid (pg/L)	Increase linked to positive social attachment	123.5 (4.0)	143.0 (8.0)	NR	NR
Dopamine (pg/L)	Increase linked to pleasurable sensations	86.5 (7.0)	107.0 (9.0)	NR	NR
Cortisol (mmol/L)	Decrease linked to positive social bonding and stress relief	317.0 (224.0)	309.0 (222.0)	NR	NR

Only significant changes were reported in this publication, with values representing nonsignificant changes for quiet reading not provided
NR not reported as significant

* Significant pre-intervention to post-intervention change, $P < 0.01$

calm instead of engaging in play, and accepting handling from strangers require work and effort by the therapy dog.

Researchers from the Institute for Anthropology in Austria likewise evaluated cortisol levels in 18 therapy dogs as a marker of stress [27]. Over a 3-month period, saliva samples were obtained from dogs on days when they were not making visits ($N=165$ samples) and visit days ($N=347$ samples), making comparisons based on time of day when the sample was collected. Average cortisol levels were significantly higher on visit days vs. non-visit days (2.2 vs. 1.7 nmol/L, $P \leq 0.001$), supporting physiological arousal or stress response occurred when making visits. Cortisol was additionally increased relative to the number of visits performed during the sample period ($P \leq 0.001$), further supporting the stressful nature of therapy work for dogs and the need to limit visit frequency.

Despite these data demonstrating a mild stress response performing therapy dog visits, ethicists have concluded that, on balance, the benefits to dogs from serving as therapy dogs support utilizing animal-assisted therapy [28]. Specifically, the social nature of dogs and the positive aspects of bonding that occur through the dog-handler training are believed to offset potential negatives of therapy dog work.

Mirror Neurons

Mirror neurons were first described in primate studies, in which visuomotor neurons would fire in response to a monkey performing a task or observing a task being performed by another primate [29, 30]. Human studies also support mirror activity for observing both physical actions and emotional/affective stimuli [31]. A meta-analysis of 125 studies exploring mirror neurons in humans identified consistent activation in a broad range of brain regions, including the inferior frontal gyrus, ventral premotor cortex, inferior and superior parietal

lobules, the dorsal premotor cortex, the insula, and the temporal gyri [31].

The presence of mirror neurons in humans can help explain how one can “learn” to complete a skill by watching someone else perform the task, with mirror neuron activation helping to train the brain [29]. Humans have also been shown to mirror emotional expressions of others. For example, the amygdala and insula are activated when exposed to disgusting odors or tastes [29]. Studies have also shown that observing the faces of others showing disgust activates these same regions in the amygdala and insula [29]. Furthermore, experiments evaluating human brain activation through functional magnetic resonance imaging (fMRI) show that similar brain regions are activated when subjects actually smile or when they observe others smiling [32]. Other studies showed similar activation of the anterior insula and the anterior cingulate cortex when a subject received a painful electric shock or was asked to watch a loved one receiving the same shock [29].

While studies specifically investigating the effect of viewing therapy dogs have not been conducted, researchers at the University of Parma found similar activation in humans observing food biting behavior performed by another human or a monkey or dog [33]. This study supports the hypothesis that humans witnessing “cheerful” behavior in a friendly dog (such as attentiveness to the subject, mouth slightly open and ‘smiling,’ and tail wagging) might result in empathic imitation of cheerful behavior, possibly mediated by activation of mirror neurons.

Sniffing Out Disease and Distress

Controlled research studies and anecdotal reports demonstrate a dog’s ability to detect a variety of diseases, including cancer,

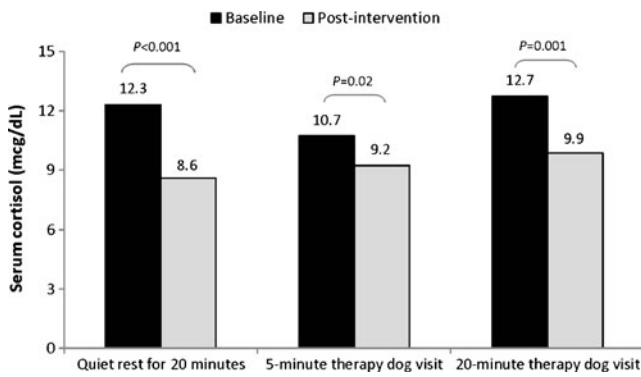


Fig. 1 Serum cortisol in healthcare workers at baseline and 1 h after a brief therapy dog visit or quiet rest (adapted from Barker 2005 [22])

seizures, and hypoglycemia [34]. Medical detection dogs are service dogs that have been trained to alert their human partners to impending medical symptoms, like seizures for people with epilepsy or hypoglycemia for people with diabetes. Some companion or pet dogs have also been found to be able to consistently alert their owners with diabetes to early hypoglycemia, allowing for early identification and treatment of low glucose before the person becomes symptomatic [35]. A recent survey of migraineurs living with a dog likewise found that about half noted a consistent change in their dog's behavior before or during the early stages of a migraine attack [36]. Among these, 57 % were able to identify dog-alerting behavior before symptoms of a migraine attack would typically begin, usually within 2 h before the onset of initial migraine symptoms. While therapy dogs are not trained to identify disease, anecdotal reports from therapy dog handlers suggest that, when therapy dogs are placed in a room with a number of people, the dogs tend to seek out for their attention those individuals who are ill or in distress [37].

Dogs' ability to identify people with illness has been postulated to result from their superior olfactory ability. For example, the olfactory epithelium surface area in the dog measures about 170 cm², compared with 10 cm² in humans [38]. Also in dogs, a pocket created by a bony subethmoidal shelf during exhalation permits odor accumulation that can allow dogs to retain and concentrate weak odors to improve odor exploration [39]. Biomedical engineers have developed electronic noses designed to sample and analyze volatile gases, with applications shown for the detection of metabolic diseases, infections, respiratory disease, and cancers [40].

Therapy dogs may also correctly identify people experiencing emotional distress due to chemical changes. The stress response includes increases in glucocorticoids and catecholamines through activation of the hypothalamic-pituitary-adrenal axis and the sympathetic nervous system [41]. Increases in a variety of biomarkers, including cytokines and growth factors, have been linked with illness, depression, and stress [42]. Researchers from Karolinska Institute measured

cytokines, cell growth factors, and hormones in three groups of women: healthy control workers, healthcare personnel reporting significant occupational stress/burnout, and workers on sick leave for at least 3 months for affective or stress-related disorders [43]. After adjusting for differences in age, the cytokine and inflammatory marker monocyte chemoattractant protein-1 (MCP-1) and growth factors [epidermal growth factor (EGF) and vascular endothelial growth factor (VEGF)] were found to be significantly elevated with increased stress. Stress marker levels for controls vs. high-stress workers vs. workers on long-term leave, respectively, were: 160.2 vs. 217.8 vs. 348.4 pg/mL for MCP-1; 29.4 vs. 70.6 vs. 117.0 pg/mL for EGF; and 10.3 vs. 18.4 vs. 30.9 pg/mL for VEGF. Differences in levels between controls vs. high-stress workers and controls vs. workers on leave were significant for each marker ($P < 0.001$). Differences between high-stress workers and workers on leave were significant for MCP-1 and EGF. Although studies are not available to determine a dog's response to these chemical changes, it is possible that these changes or alterations in other chemicals related to the stress response or illness might be detected and identified as abnormal by dogs using olfactory detection.

Benefit From Dog Vs. Friendly Volunteer

Because animal-assisted therapy involves both the animal and its human handler, benefits achieved may result from the human:human interaction rather than the human:dog encounter. Mirror neurons evoking empathy, for example, may be activated because the patient sees the friendly volunteer smile rather than in response to witnessing the dog's playful behavior. Several studies have investigated the additive benefit of including a dog in a friendly encounter with patients. For example, in one study, 30 inpatients receiving non-palliative cancer treatment were randomly assigned to one of three 15-min treatment conditions: (1) a therapy dog visit during which the dog's handler was advised not to interact with the patient, (2) a visit from a friendly volunteer, (3) or quiet time for reading magazines [44]. Interventions were rated from 1 (negative experience) to 5 (positive experience). Scores were significantly higher compared with quiet reading (2.7) for both the friendly volunteer (3.8, $P = 0.011$) and the dog (4.2, $P < 0.001$). Overall, impressions were most positive for the dog visit. For example, the patient's therapy was perceived as becoming easier after the intervention for 70 % after the dog visit, 50 % after the friendly volunteer, and 20 % after quiet reading. Patients were more likely to look forward to receiving a dog visit (70 %) compared with the friendly volunteer visit (30 %) or quiet reading (40 %). People were also more likely to feel attached to the dog (90 %) than the human volunteer (20 %).

Researchers at the University of California in Los Angeles helped to quantify effects from the dog vs. the dog's handler in an experiment in which 76 adults with heart failure were

randomized to one of three groups: (1) 12-min visit with a therapy dog with a volunteer, (2) 12-min visit with a volunteer with no dog, or (3) a control group [45]. Hemodynamic measures, neurohormone levels, and anxiety were recorded. Hemodynamic improvements compared with control were seen for both 12-min interventions. Compared with the volunteer-only group, the volunteer-dog group experienced significantly greater decreases in mean systolic pulmonary arterial pressure (-5.48 mmHg; $P=0.01$) and mean pulmonary capillary wedge pressure (-3.30 mmHg; $P=0.003$). Epinephrine ($P=0.04$) and norepinephrine ($P=0.02$) levels likewise experienced significantly greater reductions with the volunteer-dog visit compared with the volunteer-only group. Anxiety levels were 9 points lower after the dog visit compared with the control ($P<0.001$) and 7 points lower after the dog visit compared with the volunteer-only intervention ($P=0.002$). Their data support the subjective reports of enhanced benefit by including a therapy dog during a volunteer visit.

Conclusion

Therapy dogs offer a novel and useful complementary therapy for patients with pain complaints in a variety of settings. Therapy dog visits have been linked with both objective and subjective benefits for reducing pain and related symptoms. Studies support that benefits from therapy dog visits exceed those from simply spending time with a friendly volunteer and that benefits endure beyond the time of the human:dog encounter. As a volunteer service, therapy dog visits can provide an effective and cost-free option for enhancing pain management, with validity of symptomatic benefits supported by identified physiological changes.

Disclosure Dr. Dawn Marcus reported no potential conflicts of interest relevant to this article.

References

Papers of particular interest, published recently, have been highlighted as:

- Of importance
- Of major importance

1. Muñoz Lasa G, Ferriero G, Brigatti E, Valero R, Franchignoni F. Animal-assisted interventions in internal and rehabilitation medicine: a review of the recent literature. *Panminerva Med.* 2011;53:129–36.
2. Kniseley JS, Barker SB, Barker RT. Research on benefits of canine-assisted therapy for adults in nonmilitary settings. *US Army Med Dep J.* 2012, Apr–Jun:30–37.
3. Lefebvre SL, Golab GC, Christensen E, et al. Guidelines for animal-assisted interventions in health care facilities. *Am J Infect Control.* 2008;36:78–85.

4. • Marcus DA, Bernstein CD, Constantin JM, et al. Animal-assisted therapy at an outpatient pain management clinic. *Pain Med.* 2012;13:45–57. *Prospective, controlled study investigating impact of a therapy dog on patients, visitors, and staff in an outpatient pain clinic.*
5. Halm MA. The healing power of the human–animal connection. *Am J Crit Care.* 2008;17:373–6.
6. Allen K, Shykoff BE, Izzo JL. Pet ownership, but not ACE inhibitor therapy, blunts home blood pressure responses to mental stress. *Hypertension.* 2001;38:815–20.
7. Allen K, Blascovich J, Mendes WB. Cardiovascular reactivity and the presence of pets, friends, and spouses: the truth about cats and dogs. *Psychosom Med.* 2002;64:727–39.
8. Charnetski CJ, Riggers S, Brennan FX. Effect of petting a dog on immune system function. *Psychol Rep.* 2004;95:1087–91.
9. Baird AD, Scheffer IE, Wilson SJ. Mirror neuron system involvement in empathy: a critical look at the evidence. *Soc Neurosci.* 2011;6:327–35.
10. Sobo EJ, Eng B, Kassity-Krich N. Canine visitation (pet) therapy: pilot data on decreases in child pain perception. *J Holist Nurs.* 2006;24:51–7.
11. Lust E, Ryan-Haddad A, Coover K, Snell J. Measuring clinical outcomes of animal-assisted therapy: impact on resident medication usage. *Consult Pharm.* 2007;22:580–5.
12. Coakley AB, Mahoney EK. Creating a therapeutic and healing environment with a pet therapy program. *Complement Ther Clin Pract.* 2009;15:141–6.
13. Braun C, Stangler T, Narveson J, Pettingell S. Animal-assisted therapy as a pain relief intervention for children. *Complement Ther Clin Pract.* 2009;15:105–9.
14. Marcus DA, Bernstein CD, Constantin JM, et al. Impact of animal-assisted therapy for outpatients with fibromyalgia. *Pain Med.* 2013;14:43–51.
15. Celiker R, Borman P, Oktem F, Gökçe-Kutsal Y, Başgöze O. Psychological disturbance in fibromyalgia: relation to pain severity. *Clin Rheumatol.* 1997;16:179–84.
16. Bair MJ, Robinson RL, Katon W, Kroenke K. Depression and pain comorbidity: a literature review. *Arch Intern Med.* 2003;163:2433–45.
17. Kroenke K, Wu J, Bair MJ, et al. Reciprocal relationship between pain and depression: a 12-month longitudinal analysis in primary care. *J Pain.* 2011;12:964–73.
18. Consoli G, Marazziti D, Ciapparelli A, et al. The impact of mood, anxiety, and sleep disorders on fibromyalgia. *Compr Psychiatry.* 2012;53:962–7.
19. Banks MR, Banks WA. The effects of animal-assisted therapy on loneliness in an elderly population in long-term care facilities. *J Gerontol A Biol Sci Med Sci.* 2002;57:M428–32.
20. Kawamura N, Niiyama M, Niiyama H. Long-term evaluation of animal-assisted therapy for institutionalized elderly people: a preliminary result. *Psychogeriatrics.* 2007;7:8–13.
21. Odendaal JJ, Meintjes RA. Neurophysiological correlates of affiliative behaviour between humans and dogs. *Vet J.* 2003;165:296–301.
22. Barker SB, Knisely JS, McCain NL, Best AM. Measuring stress and immune response in healthcare professionals following interaction with a therapy dog: a pilot study. *Psychol Rep.* 2005;96:713–29.
23. Beetz A, Uvnäs-Moberg K, Julius H, Kotrschal K. Psychosocial and psychophysiological effects of human-animal interactions: the possible role of oxytocin. *Front Psychol.* 2012;3:234.
24. Miller SC, Kennedy C, Devoe D, et al. An examination of changes in oxytocin levels in men and women before and after interaction with a bonded dog. *Anthrozoös.* 2009;22:31–42.
25. Handlin L, Hydbring-Sandberg E, Nilsson A, et al. Short-term interaction between dogs and their owners—effects on oxytocin, cortisol, insulin and heart rate—an exploratory study. *Anthrozoös.* 2011;24:301–16.
26. Kanamori M, Suzuki M, Yamamoto K, Kanda M, et al. A day care program and evaluation of animal-assisted therapy (AAT)

- for the elderly with senile dementia. *Am J Alzheimers Dis Other Dement.* 2001;16:234–9.
27. Haubenhofer DK, Kirchengast S. Physiological arousal for companion dogs working with their owners in animal-assisted activities and animal-assisted therapy. *J Appl Anim Welf Sci.* 2006;9:165–72.
 28. Zamir T. The moral basis of animal-assisted therapy. *Soc Anim.* 2006;14:179–99.
 29. Fabbri-Destro M, Rizzolatti G. Mirror neurons and mirror systems in monkeys and human. *Physiology.* 2008;23:171–9.
 30. • Oztop E, Kawato M, Arbib MA. Mirror neurons: functions, mechanism and models. *Neurosci Lett.* In press. *Recent review describing mirror neurons and the models that may utilize them.*
 31. •• Molenberghs P, Cunnington R, Mattingley JB. Brain regions with mirror properties: a meta-analysis of 125 human fMRI studies. *Neurosci Biobehav Rev.* 2012;36:341–9. *Meta-analysis of human fMRI studies investigating mirror neurons for motor and non-motor stimuli.*
 32. Hennenlotter A, Schroeder U, Erhard P, et al. A common neural basis for receptive and expressive communication of pleasant facial affect. *NeuroImage.* 2005;26:581–91.
 33. Buccino G, Lui F, Canessa N, et al. Neural circuits involved in the recognition of actions performed by nonconspecifics: an fMRI study. *J Cogn Neurosci.* 2004;16:114–26.
 34. Wells DL. Dogs as a diagnostic tool for ill health in humans. *Altern Ther Health Med.* 2012;18:12–7.
 35. Wells DL, Lawson SW, Siriwardena AN. Canine responses to hypoglycemia in patients with type 1 diabetes. *J Altern Complement Med.* 2008;14:1235–41.
 36. Marcus DA, Bhowmick A. Survey of migraine sufferers with dogs to evaluate for canine migraine-alerting behaviors. *J Altern Complement Med.* In press.
 37. Marcus DA. The power of wagging tails: a doctor's guide to dog therapy and healing. New York: Demos Health; 2011.
 38. Lippi G, Cervellin G. Canine olfactory detection of cancer versus laboratory testing: myth or opportunity? *Clin Chem Lab Med.* 2012;50:435–9.
 39. Alabama A&M and Auburn Universities. The dog's sense of smell. Available at www.aces.edu/pubs/docs/U/UNP-0066/UNP-0066.pdf. Accessed January 2013.
 40. • Wilson AD, Baietto M. Advances in electronic-nose technologies developed for biomedical applications. 2011;11:1105–76. *Comprehensive review of the development and application of electronic nose technology toward detecting and analyzing a broad range of medical conditions.*
 41. Miller DB, O'Callaghan JP. Neuroendocrine aspects of the response to stress. *Metabolism.* 2002;6 suppl 1:5–10.
 42. Anisman H, Hayley S. Inflammatory factors contribute to depression and its comorbid conditions. *Sci Signal.* 2012;5:pe45.
 43. Åsberg M, Nugren A, Leopardi R, et al. Novel biomarkers of psychosocial stress in women. *PLoS One.* 2009;4:e3590.
 44. Johnson RA, Meadows RL, Haubner JS, Sevedge K. Human-animal interaction: a complementary/alternative medical (CAM) intervention for cancer patients. *Am Behav Sci.* 2003;47:55–69.
 45. Cole KM, Gawlinski A, Steers N, Kotlerman J. Animal-assisted therapy in patients hospitalized with heart failure. *Am J Crit Care.* 2007;16:575–85.