TITLE: Evaluating effects of animal assisted therapy on anxious pediatric dental patients using objective physiologic measures and self-reports of stress

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ABSTRACT:

A striking 50-80% of adults and 6-22% of children suffer from dental anxiety which leads to disruptive behavior during appointments and avoidance of regular dental care. Though routinely used, common pharmacological interventions (i.e. oral sedation, general anesthesia) for anxiety management carry risks of adverse effects including stress on the respiratory and cardiovascular systems, neurologic injury, and even death. Data from various healthcare settings show reductions in pain and stress indicators in patients after implementation of a therapy dog for appointments. However, few studies have explored the physiologic and subjective effects of AAT on pediatric dental patients undergoing invasive procedures. To address this gap in knowledge and explore the effectiveness of animal-assisted therapy (AAT) in pediatric dentistry, we will study the subjective and objective responses of patients undergoing operative dental procedures that include an injection.

Our central hypothesis is that children who interact with a therapy dog before their dental procedure will have significantly lower physiologic and subjective, self-reported responses to anxiety. We will test this hypothesis with the following aims: **We will measure the physiologic effects of animal assisted therapy on pediatric patients' stress levels** by analyzing salivary stress hormones (i.e. alpha-amylase and cortisol) during invasive dental procedures (primary aim). For supplemental aims, **we will measure participants' heart rate throughout the dental visit, will evaluate the patients' self-perceptions of pain and anxiety** using pre-, intra- and post-procedural validated scales to assess responses to AAT and **will analyze participants' behaviors using observational coding**. **Data will guide the implementation of AAT as a non-pharmacological anxiety management tool in dentistry, with the goal of improving access to care and patient safety among anxious pediatric patients.**

SPECIFIC AIMS:

Dental anxiety is linked to avoidance behavior and an increased pain response during dental procedures.[1,2] At this time, limited methods for non-pharmacological anxiety control exist. The burden of sedation dentistry comes with many risks and financial costs. Some serious unwanted side effects include compromise to the patient's respiratory drive, airway reflexes and airway patency, as well as the cardiovascular system.[3] Sedation for anxiety control is also costly for the patient and healthcare system, with deleterious effects on access to care. **Dentistry is in need of anxiety control measures other than pharmacological sedation** to reduce the risk to patients, lower the cost of treatment and thus increase access to dental care. One promising approach is animal-assisted therapy (AAT) using a well-trained therapy dog. In medical settings, AAT has been implemented in various clinical situations and has been shown to help reduce pain and stress indicators in patients.[4] Research into AAT as a non-pharmacological behavior management and anxiety reduction techniques in dentistry is limited as many publications are surveys[5] with a low sample size and are not conducted in the pediatric and/or dental patient population.[2]

To explore the effectiveness of non-pharmacological anxiety-reduction approaches, we will study the effects of animal-assisted therapy (AAT) on pediatric patients undergoing invasive dental procedures that include an injection. The University of North Carolina has a unique opportunity to explore animal-assisted therapy because the dental school has a certified therapy dog. **Our central hypothesis is** that children who interact with a therapy dog before their dental procedure will have significantly lower physiologic and subjective responses to stress. We will test this hypothesis by following aims:

Primary Aim: **We will measure the effects of animal assisted therapy on pediatric patients' stress levels** by analyzing objective physiologic measures (salivary amylase and cortisol) during invasive dental procedures.
Supplemental Aims: **We will measure participants' heart rate throughout dental visit, will evaluate patients' perceptions of pain and anxiety using pre-, intra-, and post-procedural surveys** to assess the patients' subjective responses to animal-assisted therapy and **will analyze participants' behaviors using observational coding**.

The proposed study will examine the effectiveness of animal-assisted therapy on pediatric dental patients from a subjective and objective perspective to guide implementation of AAT in pediatric dental settings for anxious patients**.**

BACKGROUND AND SIGNIFICANCE:

Dental anxiety (DA) negatively impacts oral health worldwide. A meta-analysis reviewing DA in patients ages 3-18 years-old found a prevalence of 23.9%.[6] Many adults attribute their dental anxiety to an earlier, traumatic dental experience.[3] In a survey of 1,420 subjects, 16.4% adults had dental anxiety with 50.9% reporting dental anxiety onset in childhood.[7] Dental anxiety is linked to avoidance behavior and an increased pain response during dental procedures.[1,2,8] Avoidance behavior can lead to increased complexity of dental treatments, increased costs and often tooth loss with more emergency visits, increased probability of infection, and in severe cases, even death. [9] A parent's own dental anxiety can also present a barrier to their child's access to dental care.[10]

Behavioral management and anxiety control techniques are essential to improving a child's experience and to avoid a lifelong fear of dental procedures.[11] The American Association of Pediatric Dentists (AAPD) recommends the use of pharmacological and non-pharmacological techniques to provide dental care for children with DA.[12] Even when regularly and safely used, moderate and deep sedation as well as general anesthesia pose patient risks including compromise to respiratory drive, airway reflexes and airway patency, and the cardiovascular system.[3,13] For this reason, pharmacological behavioral management is often met with resistance from parents.[14] Moderate to deep sedation and general anesthesia for anxiety control is also costly for the patient and the healthcare system. In a review of Medicaid claims in North Carolina from 2011-2015, general anesthesia was used in 15.8 out of 1,000 cases and cost approximately $16.7 million per year. Expenditures on general anesthesia for dental procedures continue to increase.[15] At this time, limited methods for non-pharmacological anxiety control exist. A low cost, low risk alternative to sedation is needed for anxious pediatric dental patients.

Animal assisted therapy (AAT) is a promising option for treating children with DA. AAT is an intervention that involves a well-trained therapy dog to reduce anxiety. Dogs can sense elevated stress hormones like glucocorticoids and catecholamines and respond accordingly.[4] Data regarding AAT's positive effects are encouraging and abundant in medicine. Brief interactions with therapy dogs have been shown to decrease stress hormones and increase endorphins in adult patients.[9] The positive effects can even be seen in healthcare workers. In one study, healthcare workers who had an interaction with a therapy dog were shown to have reduced serum cortisol.[16]

The use of AAT in dentistry is just beginning, though initial data is promising. [4,17–26] In a study of children who verbalized distress, the presence of the dog decreased their physiological arousal while waiting for their dental provider.[18] In a randomized clinical trial in India, children's 15-minute interactions with a therapy dog at a pediatric dental office in the waiting area reduced subjective stress levels.[26] The acceptability of AAT by caregivers has been explored in a survey performed at Case Western Reserve where their research team found that 90% of caregivers expressed acceptability of a therapy dog in the pediatric dental setting while 68% expressed a demand for a

therapy dog to be included in part of the child's treatment.[5] Existing dental AAT studies have used skin temperature, heart rate and blood pressure to quantify effects.[18,27] Separately, validated scales have also been used to assess anxiety level. [28,29] Interventional studies focused on pediatric dental patients receiving AAT involved non-invasive dental procedures such as sealants and suction placement (Isodry®).[28] Though valuable, the literature is missing a comprehensive, larger study that evaluates the physiological and emotional impacts of AAT in dentistry.

Currently there are no studies that use observational coding, galvanic skin (sweat) response, and cortisol and salivary amylase samples to measure the effects of AAT in dental contexts. At this time, there are no large-scale randomized controlled trials evaluating efficacy of AAT during invasive dental procedures in pediatric patients. The University of North Carolina at Chapel Hill (UNC-CH) has a distinctive opportunity to conduct such a study and explore AAT because the dental school has a trained therapy dog for its graduate pediatric department.

Dentistry is in need of anxiety control measures other than sedation in order to reduce risk to patients, lower the cost of treatment and increase access to dental care. The pediatric dental experience may be improved by the implementation of a therapy dog for anxiety, pain and behavior management. Our investigation will be the first to comprehensively assess physiological and psychological effects of AAT using a randomized controlled trial with a therapy dog intervention. If efficacious at anxiety, pain and behavior management, AAT will offer dental providers a non-invasive, low-risk approach to provide positive dental experiences, with the translational goal of reducing dental avoidance and its significant negative health sequelae.

EXPERIMENTAL DESIGN AND METHODS:

We have designed a cross-sectional prospective controlled trial assessing whether AAT (intervention with a therapy dog) impacts physiologic biometrics and perceptions of anxiety, pain and future expectations during a dental procedure in pediatric patients.

Screening for research participants includes searching the dental school graduate pediatric clinic schedule for potentially qualifying participants scheduled for operative or restorative dental treatment. Inclusion and exclusion criteria can be found in **Table 1**.

Table 1: Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
Ages 7-17, male or female	Fear or allergy to dogs
Patient receiving treatment at UNC Pediatric Dental Clinic	Non-English and non-Spanish speakers
Parent and participant speak English or Spanish	Learning disability or a developmental delay
Able to comprehend and follow the requirement of the study	Medical history that complicates dental treatment
Frankl Behavioral Scale II, III, or IV	Xerostomia (dry-mouth)

This study has been approved by the UNC IRB (IRB Number: 19-1911; Title: Animal Assisted Therapy's Effects on Dental Patients)

The research team calls to interview parents/caregivers of patients for enrollment criteria (**Table 1**). If a participant enrolls, he or she is assigned to a random weekday which determines the therapy animal's availability and will be either the active control group or the experimental AAT (dog intervention) group. The research team sets up a Go-Pro camera to film the visit and places the heart rate monitor (Shimmer or Polar device) on the patient's wrist in the pediatric clinic's consultation room. The participant is asked a standardized set of anxiety scale questionnaires: the Modified Child

Dental Anxiety Survey (MCDAS) and the Children's Fear Survey Schedule, Dental Subset (CFSS-SD). The child also rates their current pain level using Wong-Baker FACES (WBS), a numeric scale, and the visual analog scale (VAS). After the interview, the AAT intervention or control (i.e. coloring or sitting in silence) takes place for 3 minutes. The intervention group will interact with the therapy dog using a reproducible, standardized method. The handler will introduce the dog, and the participant pets the therapy dog, shakes her paw, gives her a treat, and then says goodbye in the clinic's consultation room. The control group will color a picture of a dog (active) or sit in silence (passive) for 3 minutes. C-DART database software will be used to record patient responses and guide the research visit in a structured manner. Following the intervention, the child is taken into the treatment room with the heart rate device still on his or her wrist, collecting objective physiological data. The GoPro camera will be taken into the treatment room, to provide for simultaneous video and physiological data collection. Salivary samples using salivettes will be collected at 4 timepoints during the visit, as described in **Table 1**. See **Figure 1** for treatment visit protocol.

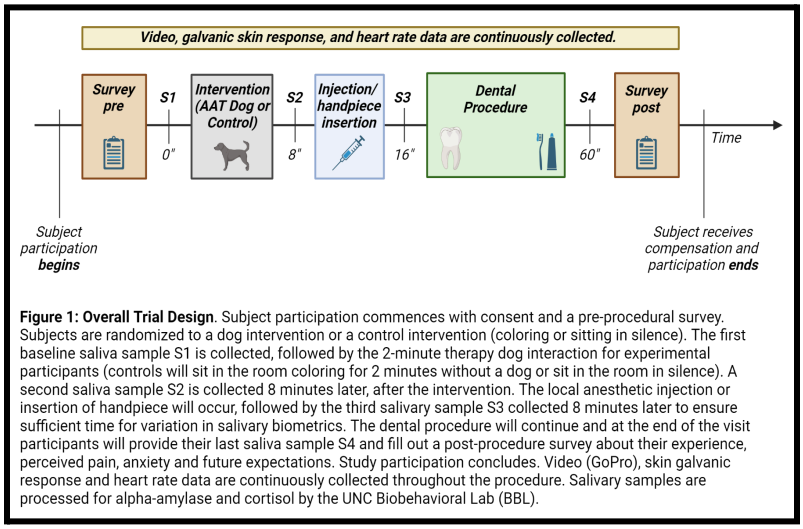

Figure 1: Overall Trial Design. Subject participation commences with consent and a pre-procedural survey. Subjects are randomized to a dog intervention or a control intervention (coloring or sitting in silence). The first baseline saliva sample S1 is collected, followed by the 2-minute therapy dog interaction for experimental participants (controls will sit in the room coloring for 2 minutes without a dog or sit in the room in silence). A second saliva sample S2 is collected 8 minutes later, after the intervention. The local anesthetic injection or insertion of handpiece will occur, followed by the third salivary sample S3 collected 8 minutes later to ensure sufficient time for variation in salivary biometrics. The dental procedure will continue and at the end of the visit participants will provide their last saliva sample S4 and fill out a post-procedure survey about their experience, perceived pain, anxiety and future expectations. Study participation concludes. Video (GoPro), skin galvanic response and heart rate data are continuously collected throughout the procedure. Salivary samples are processed for alpha-amylase and cortisol by the UNC Biobehavioral Lab (BBL).

Primary Aim: **We will measure the physiologic effects of animal assisted therapy on pediatric patients' stress levels**. Salivary alpha-amylase (sAA) functions as a digestive enzyme involved in the breakdown of glycogen and starch as well as part of the immune system by protecting the oral cavity from harmful microorganisms.[30] Salivary alpha-amylase increases in response to stress.[31] In a study of 99 patients undergoing an invasive dental procedure, Jafari et. al presented evidence to support the dependability and objectivity of using sAA to measure the acute stress response in patients with dental anxiety.[32]

Another physiological indicator of stress response that can be measured in the dental setting is salivary cortisol. The hypothalamic-pituitary-adrenal axis (HPA) is an important aspect of the endocrine system which leads to release of cortisol from the adrenal glands when the body is subject to physical or emotional stress.[33] As supported by the 2007 meta-analysis by Miller et. al exploring cortisol levels and stress, the use of salivary cortisol levels is well cited in the scientific literature to be a validated biomarker for stress.[34]

To collect a saliva sample, the research team places a salivette in the mandibular vestibule for 5 minutes at the following timepoints:

Table 2: Timepoints for salivary data collection

Timepoint	Description
S1	Baseline (pre-intervention, in consultation room)
S2	Post-intervention (8 minutes after intervention)
S3	8 minutes into the dental procedure
S4	8 minutes after completion of the procedure at the end of the study visit

<u>Supplemental Aims:</u> We will measure participants' heart rate throughout dental visit, will evaluate patients' perceptions of pain and anxiety using pre-, intra-, and post-procedural surveys and will analyze participants' behaviors using observational coding.
The Shimmer 3 GSR+ and Polar are small wearable wrist devices that measure heart rate through the wrist, with Shimmer 3 GSR+ also measuring sweat response through sensors that are fastened to the fingers. The Shimmer/Polar device will be connected to the patient during the pre-procedural interview, dog or control intervention, and procedure, continuously collecting heart rate and/or galvanic skin response (GSR) data.

Because heart rate is known to reliably increase under acute mental stress, it is widely used in medical research to evaluate stress response.[35] The Galvanic Skin Response (GSR) is a biomarker that quantifies the small electrical current induced by sweat which is released when the body is under stress.[36] The most significant psycho-activity and concentration of the epidermal sweat glands is on the sole of foot and the palm of the hand, particularly on the volar surface of the finger tips.[36] In a study completed by Caprara et. al in 2003, GSR was linked to increased dental anxiety in patients before undergoing a root canal treatment.[37]

The video of the procedure as well as the heart rate data and GSR from the Shimmer device is loaded on to an external hard drive. The video will be coded with established behavioral codes using the Noldus software. The HR and GSR data are reviewed for inconsistencies using MindWare software. Both software are on a computer located in the bio-behavioral lab (BBL). The salivettes are transferred in a temperature-controlled container to the BBL where they are analyzed by ELISA for salivary alpha-amylase and salivary cortisol.

Pre-intervention and post-intervention interviews will include the Child Fear Survey Schedule-Subset Dental (CFSS-SD), and the Modified Child Dental Anxiety Scale (MCDAS) to rate anxiety. To rate pain, the Wong-Baker FACES Scale (WBS), a numeric scale, and Visual Analog Scale (VAS) will also be used. The three pain rating scales will be repeated immediately after the injection. At the end of the procedures, the research team will repeat the CFSS-SD and the MCDAS for anxiety. They will also ask the child to rate his or her pain level again using the WBS, numeric scale, and VAS.

Pictorial representation of pain response, like The Wong-Baker FACES Scale (WBS), are preferred by children to express their level of pain regardless of age.[38] The Modified Child Dental Anxiety Survey (MCDAS) and the Children's Fear Survey Schedule, Dental Subset (CFSS-SD) are valid and reliable questionnaires in rating a child's anxiety in the dental setting.[39]

<u>STATISTICAL ANALYSIS PLAN:</u>

To evaluate the values obtained on the various surveys, a RH Row Mean test will be utilized to compare questions that have Likert scale / ordinal responses and a chi square test will be used for categorical data. A bivariate analysis will be performed to compare the treatment outcome relative to the main exposure, which is the presence of the animal assisted therapy. The significance level will be $P < 0.05$.

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