Title:
The effect of audiovisual aids on perioperative stress response, pain and overall experience – a randomized controlled pilot study (AVA Pilot)

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The effect of audiovisual aids on perioperative stress response, pain and overall experience – a randomized controlled pilot study (AVA Pilot)

What is the condition or intervention to be studied?

The effect of personal audiovisual equipment (audio/video goggles) on perioperative stress, pain and overall experience in patients undergoing ambulatory meniscectomy under spinal anesthesia.

What is/are the research question(s)/specific aim(s)?
1) Evaluate the feasibility of the use of personal audiovisual equipment in patients undergoing meniscectomies under spinal anesthesia
2) Determine outcome estimates of the use of this equipment on stress levels using skin conductance measurement methodology, request for further sedation, postoperative pain levels and analgesic consumption, time to discharge readiness, and overall patient satisfaction
3) Collect thus far unavailable data on the stress response to perioperative stresses (such as IV insertion and spinal placement) in order to allow for power analyses for future studies

What is/are the hypothesis(es)?
1) The perioperative use of personal audio visual aids is feasible in the ambulatory surgical arena for meniscectomies under spinal anesthesia
2) The use of the audiovisual aid leads to a reduction in perioperative stress, less need for sedatives, lower postoperative pain levels and increased patient satisfaction comparable or superior to a more traditional sedation approach.

Primary outcome will be number of skin conductance responses per second (SCR/sec) and amplitude of skin conductance responses averaged over time in 5 minute intervals and at key time points such before, during and after insertion of an IV, discussion with surgeon, anesthesiologist, immediately before leaving the holding area, immediately after entering the OR, during application of monitors, before and after administration of sedatives, before, during and after spinal insertion, incision, immediately prior to leaving the OR, after arrival at PACU and monitors are placed, before discharge.

Identify and define the secondary outcome(s) and when they will be measured

- Heart rate, blood pressure and respiratory rate absolute and percent change
- Number of requests of additional sedation
- NRS levels in PACU until discharge and day after surgery

- narcotic consumption in PACU and cumulative over 24 h after PACU discharge pre (after consent) and postoperative (before discharge) anxiety level (State Trait Anxiety Inventory)
- patient satisfaction (Heidelberg Peri-Anaesthetic Questionnaire) in PACU upon spinal resolution
- patient feedback (CSQ8) in PACU upon spinal resolution provider feedback (form sent to providers at end of surgery day)
- Request for sedation/termination of AVA
- complications (headache, transient neurologic symptoms, nausea and vomiting, ...)

Explain why these research questions are being asked:
Little is known about perioperative stress responses and possible anxiety mitigating factors like audiovisual aids or even. IV sedation. Most studies use surrogate markers and retrospective questionnaires, not based on real time gathered data. With skin conductance measurements the sympathetic discharge can be evaluated down to fractions of a second and enables us therefore to continuously monitor stress responses as skin conductance responses/per second during the perioperative management.

What is the background of the topic that you believe is important for the reviewer to know in considering this protocol, including prior studies by this research team. Describe strengths and deficiencies of prior studies; explain how this study fits in. Include references.
Patients undergoing surgery are exposed to significant stress and anxiety that may negatively influence patient hemodynamics1, immune system2, perception of pain3, and overall experience and satisfactions. Traditionally, sedatives have been used to mitigate psychological distress even in situations where the surgery could potentially be performed purely under regional anesthesia. The addition of sedatives, however, can have significant side effects both short (respiratory depression/compromise, confusion, hemodynamic depression) and possibly long term in various patient populations where this device might also be applicable. e.g. cataract surgery.[4] Passive listening to prerecorded music has been shown to alleviate perioperative anxiety[5] and one recent study showed beneficial effects on hemodynamic stress response when using additional visual stimulation during neuraxial anesthesia.[1] Skin conductance measurement (facilitated by two leads similar (but smaller) to ECG leads preferably attached to the thenar/hypothenar region) picks up sympathetic discharges of neurons leading to the skin. This has been demonstrated to reflect stress, emotional arousal and mental activities (as can be felt by everyone with emotional sweating) and can be picked up as immediate response to a stimulus, but also over time with the frequency and amplitude these discharges occur. Skin conductance measurements have been used for many years in neuroscience and behavioral studies and been linked to stress responses, emotional arousal and mental activities) both in controlled environments and for example workplace studies.[6] In the last years a workgroup surrounding Dr. Storm has evaluated skin conductance measurements and its correlation to perioperative stress, both under general anesthesia[7], for different sedation levels[8] and spinal anesthesia[9] and found a correlation to specific stress markers. Still, data on more detailed markers

of perioperative stress, like skin conductance measurements, and the use of audiovisual stimulation to reduce perioperative stress is lacking.

REFERENCES:
1.Masoudifar M, Abrishamkar S, Rouhani F, Fard SA, Noorian A: Analyzing the effects of intraoperation videoclip display on hemodynamic and satisfaction of patients during lumbar discectomy under spinal anesthesia. Saudi J. Anaesth. 2013; 7:415–9
2. Bartal I, Melamed R, Greenfeld K, Atzil S, Glasner A, Domankevich V, Naor R, Beilin B, Yardeni IZ, BenEliyahu S:Immune perturbations in patients along the perioperative period: alterations in cell surface markers and leukocyte subtypes before and after surgery. Brain. Behav. Immun. 2010; 24:376–86
3. Kain ZN, Sevarino F, Pincus S, Alexander GM, Wang SM, Ayoub C, Kosarussavadi B: Attenuation of the preoperative stress response with midazolam: effects on postoperative outcomes. Anesthesiology 2000; 93:141–7
4. Sanders RD, Maze M: Contribution of sedativehypnotic agents to delirium via modulation of the sleep pathway. Can. J.Anaesth. 2011; 58:149–56
5. Bradt J, Dileo C, Shim M: Music interventions for preoperative anxiety. Cochrane database Syst. Rev. 2013; 6:CD006908
6. Boucsein W: Electrodermal Activity. Boston, MA, Springer US, 2012 doi:10.1007/9781461411260
7. Storm H, Myre K, Rostrup M, Stokland O, Lien MD, Raeder JC: Skin conductance correlates with perioperative stress. Acta Anaesthesiol. Scand. 2002; 46:887–95
8. Gjerstad AC, Storm H, Hagen R, Huiku M, Qvigstad E, Raeder J: Skin conductance or entropy for detection of nonnoxious stimulation during different clinical levels of sedation. Acta Anaesthesiol. Scand. 2007; 51:1–7
9. James J. Bae, MSc, Semih Gungor, MD, Valeria Buschiazzo1, Carey Ford, Karina Gritsenko, MD, Hanne Storm, MD, Paul J. Christos, DrPH M: The Effect of Acute Pain and Emotional Stressors on Skin Conductance Indices 2013 Reg Anesth Pain Med Spring meeting 2012;

Identify specific gaps in current knowledge that this study is intended to fill.
Most (of the few existing studies) on perioperative stress and interventions to reduce anxiety use subjective questionnaires or surrogate markers like hemodynamic changes. This study will be able to depict a profile of the stress response over time during meniscectomies and the influence of audiovisual aids and sedation on a stress specific marker. Even standard IV sedation has not been evaluated as such, with studies mostly focusing on VAS scores or satisfaction scores.

How will answering these questions change clinical practice, change concepts about the topic or confirm the work of other investigators?
Objective information on patients stress responses to perioperative procedures and settings will help us control for these situations better and enable the development of a setting that limits patients stress. Further we will collect data on current practices and possible improvements in the HSS and everyday sedation management.

Is this a pilot study that could lead to a more definitive protocol or different study?
Yes

Experimental:
Randomized
Controlled
Clinical Trial
This is the “gold standard” for clinical research. These prospective studies have at least two groups. Patients meeting strict inclusion/exclusion criteria are enrolled and randomly assigned to receive either an experimental intervention or to receive what is considered to be an acceptable alternative – usually the current standard of care or a placebo (e.g., study of hylauronic acid injection versus cortisone for arthritis).

Specify all devices used on this study:

Investigational
Device Not Yet Approved for use. This device is completely noninvasive.
The HappyMed System is connected to the Zeiss Cinemizer OLED Glasses to play the video content. This use of this device for the study is aligned with the manufacturer's instructions. This device does not pose a significant risk to study participants and therefore does not need an IDE number. Website:
http://happymed.org/

Participants will be asked to place sensors with adhesives on the palm of their hands so that measurements from the device can be recorded. This use of this device for the study is aligned with the manufacturer's instructions. This device does not pose a significant risk to study participants and therefore does not need an IDE number. In addition, this device has been used successfully at HSS for two previously conducted studies.
Participants will be asked to wear the glasses before, during, and after their surgery. Participants will have the option to remove the glasses at any time should they feel any discomfort from wearing the glasses. This use of this device for the study is aligned with the manufacturer's instructions. This device does not pose a significant risk to study participants and therefore does not need an IDE number.

Assess the level of risk these devices pose to study participants:
Non-Significant Risks

Justify your risk assessment above:
The devices used for the study do not pose a significant risk to participants due to their noninvasive nature. The devices are being utilized according to the manufacturers' instructions.

As with other audio devices, if the Cinemizer OLED glasses are worn for long periods of time at a very high volume setting hearing may be affected or participants may

experience feelings of claustrophobia. Similar to computers and video games, when used for prolonged periods of time there are some side effects that users may experience when wearing the video glasses. This includes headaches, dizziness, disorientation or eye twitching. Participants will be made aware of their option to remove the Cinemizer glasses should they experience any unwanted effects.

Per the FDA website: "Nonsignificant risk devices are devices that do not pose a significant risk to the human subjects. Examples include most daily wear contact lenses and lens solutions, ultrasonic dental scalers, and Foley catheters.

A nonsignificant risk device study requires only IRB approval prior to initiation of a clinical study. Sponsors of studies involving nonsignificant risk devices are not required to submit an IDE application to the FDA for approval."
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm046164.htm#non_sig_risk

Describe your plan for storage and control of experimental devices: The devices used for the study will be stored in a locked cabinet in the Anesthesiology research office. Only study team members will have access to the devices.

Inclusion Criteria:

- Patients scheduled for primary, ambulatory, arthroscopic meniscectomy under spinal anesthesia

Exclusion Criteria:

- Patients with psychiatric disease and those on antidepressants
- Contraindications to spinal anesthesia or allergy to study medication
- Age < 18 years
- Patients with audiovisual impairments prohibiting them from proper use of the study device
- Patients who are blind
- Patients who wear hearing aids
- Patients with inability to communicate in English or understand the study requirements
- Chronic pain patients +/opioid use
- Patients with (neuro)dermatoses encompassing the hand
- Patients with pacemakers
- Patients with diabetes or known neuropathic disease
- Patients with prior history of claustrophobia
- Patients with prior history of epilepsy or seizure disorder
- Patients undergoing a revision or open procedure

Age Range:
18 and above

Describe how you will identify and recruit potential subjects for participation in the study.
Patients matching the inclusion criteria for this study will be identified the day before surgery. Patients will be approached about the study in the holding area on the day of surgery. Written consent for all patients will be obtained by research staff or co-investigators.

Please select enrollment type from following drop down list:
Over Course of Study

Target Enrollment
What is the maximum number of subject you plan to enroll in this study?
30

How subjects will be identified

- Potential subjects will be identified after a review of medical records of patients under the care of one or more of the study investigators
- Medical records and/or other Institution sources (databases, registries, billing records, pathology reports, and admission logs) will be reviewed to identify potential participants. May involve access of records by individuals not involved in the patient's care.

We will enroll patients scheduled for primary, ambulatory, arthroscopic meniscectomy under spinal anesthesia, as complete surgical anesthesia can be provided to the surgical site and sedation is essentially optional.

After obtaining written informed consent in the holding area, the research staff will attach a skin conductance device to the patients to measure levels of sympathetic discharge (MedStorm Stress Detector). We will administer the State Trait Anxiety Inventory (STAI) immediately after obtaining consent in the holding area and in the PACU before discharge.
Patients will be randomly assigned to one of two groups, each composed of 15 patients:

1. Audiovisual equipment (Zeiss, Cinema ProMED; HappyMed System) in the holding area, OR and PACU + 2 mg midazolam upon arrival in OR
(Patients can choose audiovisual content from a preexisting library of nature programs)
2. Traditional sedation with 2 mg midazolam upon arrival in OR

Patients can change their mind anytime and ask for additional sedatives in 1 mg increments of midazolam. The spinal anesthetic administered will be up to 3.5 cc 1.5% mepivacaine or between 23 cc 2% chloroprocaine at the discretion of the anesthesiologist. There will be standard ASA monitoring with O2 administered via nasal cannula. 4 mg ondansetron and up to 30 mg ketorolac will be administered as per routine. Hemodynamic instability will be treated as per clinical judgment of the attending

anesthesiologist with ephedrine, beta blockers or other medications as indicated. Because intraoperative administration of ketorolac, dexamethasone, and periarticular prednisone and morphine could affect pain management, we will record information (dose, amount) about these medications.

Equipment will be removed in the PACU at the patient's request or upon spinal resolution. After spinal resolution, patients will complete the Heidelberg Perianaesthetic Questionnaire. If patients are randomized to the audiovisual equipment group, they will also provide feedback regarding their experience with the audiovisual equipment when they complete the CSQ8 questionnaire. Providers will also receive a survey about the audiovisual equipment at the end of the surgery day.

On POD 1, patients will report their opioid consumption and pain level since discharge.

Data will be collected:

Day of Surgery Preoperatively: from chart and patient interview
a. Patient demographics – date of birth, race, ethnicity, gender, education level, prior surgeries
b. StateTrait Anxiety Inventory (STAI) score
c. NRS pain scores at rest
d. Start time of Zeiss and HappyMed System audiovisual aids

PACU: from chart and patient interview.
a. Anxiolytic, hemodynamic and opioid medication consumption (Also recording intraop administration of ketorolac, dexamethasone, and periarticular prednisone and morphine)
b. End time of Zeiss and HappyMed system audiovisual aids (start and end times will be used to calculate total viewing time)
c. Type of movie/program viewed on Zeiss and HappyMed System audiovisual aids
d. NRS pain scores at rest
e. STAI score
f. Patient satisfaction (Heidelberg Perianaesthetic Questionnaire score)
g. Patient feedback regarding use of audiovisual equipment (if randomized to that group)
h. Provider feedback regarding use of audiovisual equipment (survey sent via email at end of surgery day)

Continuous Throughout Hospital Stay*: MedStorm Stress Detector
a. Skin Conductance responses per second
b. Amplitude of skin conductance responses
c. Heart rate
d. Blood pressure
e. Respiratory rate
f. Complications

Postoperative Day 1: patient interview
a. NRS pain scores at rest
b. Opioid medication consumption

**Certain time points will be flagged in the recordings: before, during and after insertion of an IV, discussion with surgeon, anesthesiologist, leaving holding area, entering OR, application of monitors, administration of sedatives, before, during and after spinal insertion, incision, leaving OR, entry to PACU, resolution of spinal*

NOTE: After conducting the interim analysis and plotting the skin conductance data, we have determined that the graphs are not consistent enough to draw any conclusions. Given the technical difficulties we have encountered with the MedStorm Stress Detector, as well as the labor intensity associated with it, we have decided that we will no longer use it from patient 14 on. We will not mark hand movements, as this data was used to understand the skin conductance data. We will continue to enroll patients to complete this pilot/exploratory study, as the other secondary outcomes in particular, the surveys could provide valuable information. Patient satisfaction questionnaires will be the priority in our data analysis the "new primary outcome."

When the data will be collected?
Data will be collected on the day of surgery in the holding area, during the procedure, in the PACU until discharge, and on post-operative day 1
The following source will be used:

- Medical Records
- Patient
- No Private Office Charts Please specify which private office:
- No Registries

Sample Size and Data Analysis

Patients will be randomly assigned to one of two groups each composed of 15 patients. A computer generated randomization table will be generated by a statistician. A concealed allocation randomization schema will be used with randomization to occur after the patient consents to be in the research study. This is an un-blinded study group assignment is not concealed from the patients and the treating physicians.

1. Audiovisual equipment (Zeiss Cinema ProMED; HappyMed System) in the holding area OR and PACU + 2 mg Midazolam upon arrival in OR
2. Traditional sedation with 2 mg midazolam upon arrival in OR (control)

Phone follow ups, survey administrations and the use of the audiovisual device are not standard of care. The Department of Anesthesiology Research and Education Fund will cover the associated costs.

Instruments and questionnaires to be used on this study:

- CSQ 8
- State-Trait Anxiety Inventory

Describe any risks to participants in the Placebo of No-Treatment Arm of the study:

There are no known risks at this time to participants in the no-treatment arm of the study.

Provide a scientific or ethical justification for using a Placebo or No-Treatment Arm:

This is considered a desirable characteristic of randomized controlled trials. Since the protocols for both groups are otherwise identical, any differences between the groups may be attributed to whether or not patients are using the audio visual aid.

Sample size and data analysis:

Is this is a case series based only on the patients available using descriptive statistics in lieu of a sample size calculation?

Yes

Data Analysis:

We will provide means/medians with SD or IQR as per distribution and differences with 95% CI for all outcomes.

We would like to undertake an interim analysis to assess the overall quality of the skin conductance data collected thus far by the MedStorm Stress Detector. Data will be considered of reasonable quality if there is limited variability in skin conductance values over very small periods of time (i.e., a few seconds or less) in the absence of disruptive stimuli, such as hand movements.

We may also compare the range of values found in our data to those reported in previously published studies that used the MedStorm Stress Detector. This is another way in which we can check the quality of our measurements.

Because this is a pilot study with a relatively small projected sample size, we believe it is important to perform this interim analysis to ensure that the instruments used to collect the skin conductance data a primary outcome for this pilot study are reliable.

Describe how, when, and where the consent process will be initiated:

Patients matching the inclusion criteria for this study will be identified the day before surgery. Patients will be approached about the study in the holding area on the day of surgery. Written consent for all patients will be obtained by research staff or co-investigators.