Single-channel electroencephalography and its associations with anxiety and pain during oral surgery: a preliminary report

Roberto de Oliveira Jabur1, Ramon Cesar Godoy Gonçalves2, Kethleen Wiechetek Faria2, Izabelle Millene Semczik4, Juliana Cama Ramacciato1, Marcelo Carlos Bortoluzzi2,3,5

1Dentistry Sciences Post-Graduate Program, São Leopoldo Mandic University, Campinas, Brazil
2Health Sciences Post-Graduate Program, State University of Ponta Grossa (UEPG), Ponta Grossa, Brazil
3Dentistry Post-Graduate Program, State University of Ponta Grossa (UEPG), Ponta Grossa, Brazil
4Science Initiation Program, School of Dentistry, State University of Ponta Grossa (UEPG), Ponta Grossa, Brazil
5Oral and Maxillofacial Surgery Residency Program at University Hospital of Campos Gerais (HUGC), Ponta Grossa, Brazil

Background: This study aimed to assess the course of anxiety and pain during lower third molar (LTMo) surgery and explore the role of mobile and single-channel electroencephalography under clinical and surgical conditions.

Methods: The State-Trait Anxiety Inventory (STAI), Corah’s Dental Anxiety Scale (DAS), and Interval Scale of Anxiety Response (ISAR) were used. The patient self-rated anxiety (PSA), the pain felt during and after surgery, EEG, heart rate (HR), and blood pressure (BP) were assessed.

Results: The Attention (ATT) and Meditation (MED) algorithms and indicators evaluated in this study showed several associations. ATT showed interactions and an association with STAI-S, pain during surgery, PSA level, HR, and surgical duration. MED showed an interaction and association with DAS, STAI-S, and pain due to anesthesia. Preclinical anxiety parameters may influence clinical perceptions and biological parameters during LTMo surgeries. High STAI-Trait and PSA scores were associated with postoperative pain, whereas high STAI-State scores were associated with more pain during anesthesia and surgery, as well as DAS, which was also associated with patient interference during surgery due to anxiety.

Conclusions: The findings suggest that single-channel EEG is promising for evaluating brain responses associated with systemic reactions related to anxiety, surgical stress, and pain during oral surgery.

Keywords: Anxiety; Electroencephalography; Oral Surgery; Pain; State-Trait Anxiety Inventory; Third Molar.

INTRODUCTION

Anxiety during dental treatment is common and has been defined as an organic response characterized by apprehension and increased surveillance in situations of uncertain danger or potential threats to the integrity of the organism [1]. It has been described that impacted lower third molar (LTMo) extraction may be significantly more difficult in anxious patients, given their increase in heart rate and blood pressure [2-4], and dental anxiety may be a significant predictor of pain during and after dental treatment [1,5-7]. Lin et al. (2016) [1] concluded that anxiety should be assessed as a critical step not only
for anxiety management, but also for better pain control during dental treatments, and understanding this emotional state is important for the comfort of both patients and dentists [8,9].

Electroencephalography (EEG) is one of the most commonly used techniques for neurological and psychological assessments, and it has been performed with highly sensitive time-consuming assembly and expensive electronic devices [10-12]. Advances in technology have facilitated the production of mobile and low-cost EEG apparatus and the development of brain-computer interfaces, which, in turn, enable EEG recordings in previously impossible situations [10-12], such as driving, cycling, and undergoing surgery under local anesthesia. Rieiro et al. (2019) [12] compared this form of EEG to medical-grade EEG and observed a substantial agreement between the equipment recordings, indicating that the metrics from both were significantly correlated. Rogers et al. (2016) [10] assessed the test-retest reliability of a single-channel EEG and concluded that the device may provide a viable alternative to conventional lab-based recording systems for assessing changes in electrophysiological brain signals and suggested that the new system is a potentially sensitive biological marker. They [10] concluded that the study of brain function using devices such as the aforementioned should be encouraged. More recently, Johnstone et al. (2020) [13] replicated the frontal findings of previously reported EEG activation effects in 185 children using a single-channel EEG and, according to the authors, their findings contribute to the validation of the single-channel, dry-sensor, and frontal EEG.

This study aimed to assess the course of anxiety and pain during LTMo surgery and explore the role of mobile and single-channel electroencephalography under clinical and surgical conditions. A second and additional objective was to verify whether increased parameters of anxiety may result in more pain during and after the surgical procedure.

### METHODS

This was a clinical observational and prospective study that aimed to investigate the role of a single-channel electroencephalogram device (Brainwave Starter Kit Mobile 2®, NeuroSky Inc., San Francisco, USA - BSK-eeg) for the evaluation of several parameters during oral surgery under local anesthesia. This study was submitted and approved by the University’s Ethical Committee for Human Research (number: 21592119.3.0000.0105), and informed consent was obtained from all study participants.

We included healthy patients (American Society of Anesthesiologists Classification - ASA I) who accepted the terms of the research, were aged 18-45 years old, were not using any medication, and needed a third molar removal under local anesthesia. The exclusion criteria were as follows: patients who needed anxiolytic premedication, pregnant patients or those under lactation, and those who failed to respond or give back the postoperative diary were excluded.

The sample for this preliminary and exploratory trial was obtained by convenience, and the patients were included consecutively in a non-probabilistic manner.

1. **Third molar surgery**

A single LTMo was removed using the procedure. All procedures were conducted by oral and maxillofacial residents with the same degree of experience, and the surgeries and outcomes were performed under the supervision of two oral and maxillofacial surgeons. The surgeries were performed during the same period of the day, with starting times ranging from 13:00 to 15:00 GMT, under the most rigorous control of microbiologic contaminants, including the use of a sterile surgical apron, sheets, and gloves. All patients received a similar prescription of analgesics, nonsteroidal anti-inflammatory drugs, and antibiotics; however, they were allowed to discontinue these drugs, except the antibiotics, if no symptoms were present but advised to take the analgesic tablet as soon as their pain started. A mouth rinse with
15 mL of 0.12% chlorhexidine solution was used before surgery for 1 min in all patients.

The LTMos were classified based on position (Pell and Gregory - P&G- classification system) and inclination (Winter classification system) using the Pederson scale. The presumed LTMo difficulty rating ranges from 3 to 10 (little difficulty, 3–4 points; moderate difficulty, 5–6 points; great difficulty, 7–10 points) [14,15].

The surgeon rated the surgery difficulty as follows: (0) Easy (only required elevators/forceps); (1) little difficulty (required flap and ostectomy, but the tooth came out easy); (2) medium difficulty (also required odontotectomy, but the tooth came out easy); (3) great Difficulty (also required odontotectomy, but the tooth did not come out easily, which necessitated an extension of ostectomy); (4) complex (also required root sectioning); (5) very complex (still required additional and large ostectomy to finish).

2. Brainwave Starter Kit Mobile 2®, NeuroSky Inc, San Francisco, USA (NBSK-eeg)

The NeuroSky Brainwave Starter Kit Mobile 2® (NBSKeeg) (http://neurosky.com/) is a single-channel electroencephalography (EEG) device (Fp1; Left-Frontal pole, International System 10-10) that allows the creation of a brain-computer interface for detecting brain waves of EEG. The device is mobile and ergonomic, and it has a dry electrode, is battery-operated, and takes approximately 1 min to complete the adjustment for the patient. NeuroSky offers software for computers or smartphone applications (apps), which enables the capturing of brain waves and their data or metrics that can be viewed and recorded. The company also provides algorithms that are used to measure specific brain functions. These applications have been made available by the company or partners on the webpage (http://neurosky.com/) or via the Google Play® app store. This study used two algorithms as follows. (1) Attention (ATT): the Attention algorithm indicates the intensity of mental “focus” or “attention.” The values range from 0 to 100. The attention level increases when a user focuses on a single thought or an external object and decreases when distracted. (2) Meditation (MED): The meditation algorithm indicates the level of mental “calmness” or “relaxation.” The value ranges from 0 to 100, and it increases when users relax their minds and decreases when they are uneasy or stressed.

3. Mobile app for data recording

Among several available apps that were tested, the eegID was selected. The eegID (Isomer Programming LLC, Hampton, VA; www.isomerprogramming.com) is free and allows connection over Bluetooth to the NBSKeeg for viewing and recording EEG data (.CSV), specifically for the following: signal quality, EEG raw value, EEG raw value voltages, attention level, meditation level, link strength, delta (1–3 Hz), theta (4–7 Hz), alpha low (8–9 Hz), alpha high (10–12 Hz), beta low (13–17 Hz), beta high (18–30 Hz), gamma low (31–40 Hz), and gamma mid (41–50 Hz). According to the manufacturer, the purpose of this application is to allow easy mobile EEG data capturing with simple immediate measurements and deep analysis or data storage (https://www.isomerprogramming.com/downloads/android-apps/eegid).

Five measurements of EEG, heart rate, and systolic and diastolic blood pressures were obtained at the following times: (1) pre-surgery in the waiting room; (2) pre-surgery in the dentist chair (before the wearing of sterile surgical sheets); (3) trans-surgery, during anesthesia; (4) trans-surgery during the middle of the procedure (Figure 1); (5) immediately at end of the surgery, just after the removal of the surgical sheets. The EEG recordings were obtained for 1 min during these times with a recording interval of one capture every 1 s, and the mean value was used. To reduce noise, the procedure was paused, and the patient was informed about the data collection and asked to remain silent with the eyes closed. The data were evaluated as pre-surgical (measurements 1 and 2), trans-surgical (measurements 3 and 4), and post-surgical (measurement 5).
4. Clinical anxiety evaluation

To rate anxiety, the patients were asked to complete two questionnaires immediately preoperatively: the State-Trait Anxiety Inventory (STAI) and the Corah’s Dental Anxiety Scale. The surgeon completed the Interval Scale of Anxiety Response (ISAR) questionnaire, and the anxiety during the surgery was self-rated by the patient immediately after the procedure.

5. State-trait anxiety inventory (STAI)

The STAI questionnaire consists of 40 questions, divided into two groups, for assessing anxiety as a transient state (state anxiety) and latent trait (trait anxiety). State anxiety is considered a transitory emotional state characterized by subjective feelings, apprehension, and autonomic nervous system hyperactivity. Trait anxiety is a relatively stable state of individuals with a tendency to perceive situations as threatening. Both the state and trait scales consist of 20 items, including direct and reverse-worded questions and punctuation. The scores range from 20 to 80, with higher scores indicating greater levels of anxiety[1,16-19]. The STAI final scores were obtained using an online calculator (https://www.nsrusa.org/score.php) to avoid confusion about the reverse-worded punctuation.

6. Dental anxiety scale (DAS)

Dental anxiety was measured using the Portuguese version of the DAS (Corah). The questionnaire is composed of four questions with the scores for the answers ranging from 1 (not anxious) to 5 (extremely anxious) and higher scores indicating higher levels of anxiety (4-20 points). The DAS explores the level of anxiety that the respondent feels due to dental treatment.[20].

7. Interval scale of anxiety response (ISAR)

The adapted ISAR was used to determine the transoperative anxiety as observed by the surgeon [2] as soon as the surgery was completed. This questionnaire comprises 10 questions for investigating the following: perspiration, muscle tension, respiration rate, trembling, facial signs, vocal signs, patient self-expression of fear or anxiety, patient questions about the necessity of the treatment or hurt, patient interruptions of the procedure, and the surgeon’s overall view of patient anxiety. Additional questions for the surgeon were related to the presentations of nausea or fainting and how much the patient interfered during the surgery due to anxiety.

8. Transoperative patient self-rated anxiety (PSA)

Transoperative anxiety was recorded as soon as the surgery ended. The patient was asked to rate the anxiety that he felt on a visual scale ranging from 0 (no anxiety) to 10 (very much anxious).

9. Pain evaluation

The patient received a diary of the postoperative records. Pain was self-rated using a visual analog scale (0-100) [21] for 11 times within 5 days, starting at 3 h after surgery (3h, 6h, and 12h) on day zero and at waking time and at the end of the day (standardized between 6 to 8 p.m.) on days 1 to 4. The patients recorded pain considering the worst experience during the period between the previous annotations. The means of the measurements were used for analysis (example: Day 0 = mean of 3 measurements; 3, 6, and 12 h after the surgery). To quantify the actual intensity of pain, the pain scores were added consecutively and divided by the
Table 1. Descriptive and inferential statistics (repeated measurements - Friedman test) for the instruments used to measure anxiety, the measurements for EEG, heart rate, blood pressure, and pain

|                          | Minimum | Maximum | Mean   | Std. Deviation | Statistics               |
|--------------------------|---------|---------|--------|----------------|-------------------------|
| DAS (4-20)               | 5       | 19      | 10.1   | 3.5            |                         |
| STAI-State (20-80)       | 30.00   | 65.00   | 42.0   | 8.0            |                         |
| STAI-Trait (20-80)       | 27.00   | 67.00   | 41.8   | 8.9            |                         |
| ISAR (sum; 10 items ranked from 0-10) | 4.00    | 72.00   | 29.7   | 17.7           |                         |
| Patient Self-Evaluation of Anxiety (PSA) (0-10) | 1.00    | 10.00   | 5.3    | 2.9            |                         |
| Attention (preop) (0-100)| 17.00   | 72.00   | 40.9   | 11.9           | More alert: 5 patients  |
| Attention (transop) (0-100)| 13.00   | 64.50   | 44.3   | 11.7           | More alert: 9 patients  |
| Attention (postop) (0-100)| 13.00   | 69.00   | 45.9   | 14.9           | More alert: 12 patients |
| Meditation (preop) (0-100)| 32.50   | 70.50   | 52.3   | 8.0            | More anxious: 7 patients|
| Meditation (transop) (0-100)| 25.00   | 70.50   | 51.1   | 10.5           | More anxious: 19 patients|
| Meditation (postop) (0-100)| 20.00   | 75.00   | 49.2   | 11.8           | More anxious: 15 patients|
| Heart Rate (mean; 5 measurements M1 to M5; b.p.m.) | M1 = 82 / M2 = 80 / M3 = 83 / M4 = 89 / M5 = 80 | Friedman Test P = 0.01 |
| Systolic Blood Pressure (mean; 5 measurements M1 to M5; mmHg) | M1 = 125 / M2 = 129 / M3 = 125 | Friedman Test P = 0.003 |
| Diastolic Blood Pressure (mean; 5 measurements M1 to M5; mmHg) | M1 = 76 / M2 = 77 / M3 = 75 / M4 = 79 / M5 = 78 | Friedman Test P = 0.05 |
| Pain (accumulated mean) | Day0 = 35 / Day1 = 32 / Day2 = 29 / Day3 = 27 / Day4 = 26 | Friedman Test P < 0.001 |
| Pain (daily mean)       | Day0 = 35 / Day1 = 27 / Day2 = 22 / Day3 = 22 / Day4 = 20 | Friedman Test P < 0.001 |

NS, not statistically significant; bpm, beats per minute; mmHg, millimeters of mercury; Day 0, surgery day; DAS, Dental Anxiety Scale; STAI, State-Trait Anxiety Inventory; ISAR, Interval Scale of Anxiety Response; PREOP, preoperative; TRANSOP, transoperative; POSOP, immediate postoperative.

The transoperative pain was recorded as soon as the surgery ended. The patient was asked to rate the pain that he felt during the following on a visual scale ranging from 0 (no pain) to 10 (the most severe possible) : (a) anesthesia, (b) the surgery, and (c) the suturing at the end of the surgery.

10. Statistical procedures

A statistical program (IBM® SPSS® 15.0; Chicago, IL, USA) was used to explore the data through descriptive and inferential analyses. Statistical significance was defined as a two-tailed probability of $P \leq 0.05$. The values were analyzed based on whether the variables were continuous, ordinal, or nominal. The statistical tests were applied as recommended, taking into consideration the distributions of the variables (normal: Gauss distribution; non-normal: Shapiro-Wilk test and Kolmogorov-Smirnov test). Continuous variables were analyzed using correlation tests and multiple linear regressions. The EEG was also analyzed dichotomously as follows. For the MED algorithm, the patients with mean scores lower than 50 points were classified as more anxious, and those with mean scores of 51 points or more were classified as more relaxed. For the ATT algorithm, the patients with mean scores of 51 or more were classified as more alert, while those with scores of 50 points or less were classified as less alert. The variations in the analysis are fully described in the main results for each of the applied tests.

RESULTS

The sample was composed of 28 patients (18 female, 10 male), with ages ranging from 18 to 45 years (mean, http://www.jdapm.org 159
Table 2. Sociodemographic characteristics and homogeneity of the sample with the measurements of anxiety and EEG attention and meditation (immediate preoperative, transoperative, and immediate postoperative)

| Variables          | DAS | STAI-STATE | STAI-TRAIT | ISAR | PSA | ATT PREOP | MED PREOP | ATT TRANSOP | MED TRANSOP | ATT POSOP | MED POSOP |
|--------------------|-----|------------|------------|------|-----|----------|-----------|-------------|-------------|------------|-----------|
| Gender             |     |            |            |      |     |          |           |             |             |            |           |
| Male               | 8.7 | 39.7       | 38.2       | 26.3 | 4.6 | 36.6     | 51        | 41.9        | 50.9        | 49.6       | 46.2      |
| Female             | 11  | 43.3       | 43.8       | 31.6 | 5.8 | 43.4     | 53        | 45.7        | 51.2        | 41.9       | 51        |
| Sig.               | NS  | NS         | NS         | NS   | NS  | NS       | NS        | NS          | NS          | NS         | NS        |
| Age                |     |            |            |      |     |          |           |             |             |            |           |
| up to 24 years    | 10  | 42.7       | 42.4       | 27.7 | 5.3 | 41.9     | 52.2      | 43.3        | 49.6        | 43         | 49.2      |
| 25 years or more  | 10.4| 40.5       | 40.5       | 33.8 | 5.5 | 39       | 52.4      | 46.6        | 54.1        | 52.1       | 49.3      |
| Sig.               | NS  | NS         | NS         | NS   | NS  | NS       | NS        | NS          | NS          | NS         | NS        |
| Body Mass Index    |     |            |            |      |     |          |           |             |             |            |           |
| Normal weight ≤ 24.9 | 10.1| 42         | 42.6       | 31.8 | 5.7 | 41.9     | 53        | 43.9        | 51.6        | 44.9       | 50.9      |
| Overweight to Obesity ≥ 25 | 10.1| 42.2     | 39.2       | 23.2 | 4.4 | 38.2     | 50.1      | 45.7        | 49.6        | 44.1       | 44.2      |
| Sig.               | NS  | NS         | NS         | NS   | NS  | NS       | NS        | NS          | NS          | NS         | NS        |
| Smoking            |     |            |            |      |     |          |           |             |             |            |           |
| No                 | 10  | 42.6       | 41.8       | 31.2 | 5.5 | 41.5     | 53        | 43.6        | 51.1        | 46.5       | 49.1      |
| Yes                | 10  | 37.6       | 41.3       | 16.6 | 4   | 36.5     | 46.3      | 50.6        | 51.1        | 41         | 50.3      |
| Sig.               | NS  | NS         | NS         | 0.01*| NS  | NS       | NS        | NS          | NS          | NS         | NS        |

*Statistically significant; NS, not significant; DAS, Dental Anxiety Scale; STAI, State-Trait Anxiety Inventory; ISAR, Interval Scale of Anxiety Response; PSA, Patient Self-Evaluation of Anxiety; ATT, EEG Attention; MED, EEG Meditation; PREOP, preoperative; TRANSOP, transoperative; POSOP, immediate postoperative.

Three of them were smokers (2 female; 1 male). The descriptive and inferential statistics for the instruments used to measure anxiety and the measurements for EEG, heart rate, blood pressure, and pain are shown in Table 1. Table 2 describes the sociodemographic characteristics and homogeneity of the sample, as well as the measurements of anxiety and EEG evaluations of attention, and meditation (immediate preoperative, transoperative, and immediate postoperative).

Table 3 shows the observed associations between the surgical variables and pain based on all the measurements of anxiety and EEG. Preclinical anxiety parameters may influence clinical perceptions and biological parameters during LTMo surgeries. High STAI-Trait scores and PSA were associated with postoperative pain, whereas high STAI-State scores were associated with more pain during anesthesia and more pain during the surgery, as well as DAS, which was also associated with patient interference during the surgery due to anxiety. High scores on DAS and STAI-Trait may also be good predictors of anxiety during oral surgery due to its correlation with ISAR and PSA. ISAR was correlated with the surgeon’s assessments of patient interference and PSA during the surgery. Table 4 shows the correlation between the anxiety questionnaire scores and EEG measurements.

The MED algorithm detected high anxiety in 7 patients (25%) preoperatively, 19 patients (68%) transoperatively, and 15 patients (53%) during the immediate postoperative period (Cochran Test, P = 0.008). For the ATT, focus increased during the surgery, and higher alertness was detected in 5 patients (18%) preoperatively, 9 patients (32%) transoperatively, and 12 patients (42%) during the immediate postoperative period (Cochran Test, P = 0.1). Regarding the transoperative anxiety parameters, higher MED scores for anxiety were associated with higher DAS (t-test, P = 0.001), STAI-S (t-test, P = 0.04), and STAI-T (t-test, P = 0.04) scores. Lower transoperative alertness, according to the ATT algorithm, was associated with lower DAS (t-test, P = 0.001), STAI-S (t-test, P = 0.04), and STAI-T (t-test, P = 0.04) scores.

A multiple linear regression (LR) model was used to analyze the transoperative MED scores (backward model P = 0.049; R square = .38; adjusted R square = .24), and it was based on five variables (DAS, P = 0.021; STAI-S, P = 0.013; pain on anesthesia, P = 0.035; pain during surgery, P = 0.083; PSA, P = 0.2). The same model was used for ATT (backward model, P = 0.006; R square...
Table 3. The observed associations of surgical variables and pain with measurements of anxiety and EEG attention and meditation (immediate preoperative, transoperative, and immediate postoperative)

| Variables                                      | DAS   | STAI-STATE | STAI-TRAIT | ISAR  | PSA   | ATT PREOP | MED PREOP | ATT TRANSOP | MED TRANSOP | ATT POSOP | MED POSOP |
|------------------------------------------------|-------|------------|------------|-------|-------|-----------|-----------|-------------|-------------|------------|-----------|
| Surgical time                                  | Minutes | N/A        | N/A        | NS    | NS    | NS        | NS        | rₚ = -0.57* | NS          | NS         | NS        |
| Amount of anesthesia                           | Tubes 1-3 | NS         | NS         | NS    | NS    | NS        | NS        | NS          | NS          | NS         | NS        |
| Surgery difficulty                             | By surgeon 0-5 | NS        | NS         | NS    | NS    | NS        | NS        | NS          | NS          | NS         | NS        |
| Surgery difficulty/Pederson                    | P6G and W Classification 0-10 | N/A      | N/A        | NS    | NS    | NS        | NS        | NS          | NS          | NS         | NS        |
| Patient Pain tolerance                         | Self rated 0-10 | NS        | NS         | NS    | NS    | rₛ = 0.53* P = 0.003 | NS        | NS          | NS          | NS         | NS        |
| Patient interfering with surgery               | By patient 0-10 | rₛ = 0.41* P = 0.02 | NS        | NS    | NS    | rₛ = 0.52* P = 0.005 | NS        | NS          | NS          | NS         | NS        |
| Pain due anesthesia                             | By patient 0-10 | NS        | rₛ = 0.48* P = 0.01 | NS    | NS    | NS        | NS        | rₛ = 0.42* P = 0.02 | NS          | NS         | NS        |
| Pain during the surgery                        | By patient 0-10 | NS        | rₛ = 0.37* P = 0.05 | NS    | NS    | NS        | NS        | NS          | NS          | NS         | NS        |
| Pain during sutures                            | By patient 0-10 | NS        | NS         | NS    | NS    | NS        | NS        | NS          | NS          | NS         | NS        |
| Systolic Blood Pressure (PRE)                  | Pre-operative M1 and M2 | NS        | NS         | NS    | NS    | NS        | NS        | rₛ = 0.44* P = 0.02 | NS          | NS         | NS        |
| Systolic Blood Pressure (TRANS)                | Trans-operative M3 and M4 | NS        | NS         | NS    | NS    | NS        | NS        | rₛ = 0.4* P = 0.03 | NS          | NS         | NS        |
| Systolic Blood Pressure (POS)                  | Pos-operative M5 | NS        | NS         | NS    | NS    | NS        | NS        | rₛ = 0.39* P = 0.03 | NS          | NS         | NS        |
| Diastolic Blood Pressure (PRE)                 | Pre-operative M1 and M2 | NS        | NS         | NS    | NS    | NS        | NS        | rₛ = 0.47* P = 0.01 | NS          | NS         | NS        |
| Diastolic Blood Pressure (TRANS)               | Trans-operative M3 and M4 | NS        | NS         | NS    | NS    | NS        | NS        | rₛ = 0.4* P = 0.03 | NS          | NS         | NS        |
| Diastolic Blood Pressure (POS)                 | Pos-operative M5 | NS        | NS         | NS    | NS    | NS        | NS        | rₛ = 0.45* P = 0.03 | NS          | NS         | NS        |
| Heart rate (PRE)                               | Pre-operative M1 and M2 | NS        | NS         | NS    | NS    | NS        | NS        | rₛ = 0.43* P = 0.02 | NS          | NS         | NS        |
| Heart rate (TRANS)                             | Trans-operative M3 and M4 | NS        | NS         | NS    | NS    | NS        | NS        | rₛ = 0.39* P = 0.03 | NS          | NS         | NS        |
| Heart rate (POS)                               | Pos-operative M5 | NS        | rₛ = 0.41* P = 0.03 | NS    | NS    | NS        | NS        | NS          | NS          | NS         | NS        |
| Pain day 0 (surgery day)                       | Mean of 3 measurements | NS        | NS         | NS    | NS    | NS        | NS        | NS          | NS          | NS         | NS        |
| Pain day 1                                     | Mean of 5 measurements | NS        | NS         | rₛ = 0.39* P = 0.03 | NS    | NS    | NS        | NS        | NS          | NS          | NS         | NS        |
| Pain day 2                                     | Mean of 7 measurements | NS        | rₛ = 0.37* P = 0.03 | NS    | NS    | NS        | NS        | NS          | NS          | NS         | NS        |
| Pain day 3                                     | Mean of 9 measurements | NS        | rₛ = 0.42* P = 0.03 | NS    | NS    | rₛ = 0.39* P = 0.03 | NS        | NS          | NS          | NS         | NS        |
| Pain day 4                                     | Mean of 11 measurements | NS        | rₛ = 0.45* P = 0.03 | rₛ = 0.37* P = 0.05 | NS    | NS    | NS        | NS        | NS          | NS          | NS         | NS        |

*rs: Spearman correlation test statistically significant (bold); NS, statistically not significant; N/A, not applicable; DAS, dental anxiety scale; STAI, State-Trait Anxiety Inventory; ISAR, Interval Scale of Anxiety Response; PSA, Patient Self-Evaluation of Anxiety; ATT, EEG Attention; MED, EEG Meditation; PREOP, preoperative; TRANSOP, transoperative; POSOP, immediate postoperative.

The approach used in this research aimed to explore...
Table 4. Correlation between anxiety questionnaire scores and EEG measurements at different times

|   | DAS PREOP | STAI-STATE PREOP | STAI-TRAIT PREOP | ISAR TRANSOP | PSA TRANSOP | ATT PREOP | MED PREOP | ATT TRANSOP | MED TRANSOP | ATT POSOP | MED POSOP |
|---|-----------|-----------------|-----------------|-------------|------------|----------|----------|------------|------------|----------|----------|
| 1 | rs        | .55**           | .34             | .29         | .45*       | .42*     | -.11     | -.27       | .13        | .07      | -.21     |
|   | Sig       | .002            | NS              | NS          | .015       | .02      | NS       | NS         | NS         | NS       | NS       |
| 2 | rs        | .6**            | .18             | .31         | -.13       | -.26     | -.23     | .46*       | -.04       | .12      |         |
|   | Sig       | .001            | NS              | NS          | NS         | NS       | .013     | NS         | NS         | NS       | NS       |
| 3 | rs        | .06             | .41*            | -.07        | -.14       | -.32     | .34      | .06        | -.08       |         |         |
|   | Sig       | .030            | NS              | NS          | NS         | NS       | NS       | NS         | NS         | NS       | NS       |
| 4 | rs        | .66**           | .01             | .12         | .02        | .09      | .17      | -.23       |           |         |         |
|   | Sig       | < .001          | NS              | NS          | NS         | NS       | NS       | NS         | NS         | NS       | NS       |
| 5 | rs        | .053            | .01             | -.09        | .23        | .21      | .31      |           |           |         |         |
|   | Sig       | NS              | NS              | NS          | NS         | NS       | NS       | NS         | NS         | NS       | NS       |
| 6 | rs        | .01             | -.02            | -.54**      | .14        | .07      |         |           |           |         |         |
|   | Sig       | NS              | NS              | NS          | .003       | NS       | NS       | NS         | NS         | NS       | NS       |
| 7 | rs        | -.13            | .01             | -.13        | .01        | -.01     | .09      |           |           |         |         |
|   | Sig       | NS              | NS              | NS          | NS         | NS       | NS       | NS         | NS         | NS       | NS       |
| 8 | rs        | -.16            | -.03            | .09         |           |         |         |           |           |         |         |
|   | Sig       | NS              | NS              | NS          | NS         | NS       | NS       | NS         | NS         | NS       | NS       |
| 9 | rs        | -.29            | -.05            |           |         |         |         |           |           |         |         |
|   | Sig       | NS              | NS              | NS          | NS         | NS       | NS       | NS         | NS         | NS       | NS       |
| 10| rs        | -.04            |                 |             |           |         |         |           |           |         |         |
|   | Sig       |                 |                 |             |           |         |         |           |           |         | NS       |

*rs: Spearman correlation test, statistically significant (bold); NS, not statistically significant; DAS, dental anxiety scale; STAI, State-Trait Anxiety Inventory; ISAR, Interval Scale of Anxiety Response; PSA, Patient Self-Evaluation of Anxiety; ATT, EEG Attention; MED, EEG Meditation; PREOP, preoperative; TRANSOP, transoperative; POSOP, immediate postoperative.

as much information as possible for third molar surgery and the variable interactions and implications for systemic behavior in patients undergoing oral surgeries under local anesthesia. In this study, we used several indicators of surgical stress (such as heart rate and blood pressure) [3,4], psychological fear- and anxiety-validated questionnaires (such as the DAS and STAI) [1,3,8,9,19], the ISAR for surgeon assessments of patient anxiety [2], and the self-reported patient anxiety (PSA) and pain during and after the procedure. The innovation of this study was the use of a single-channel and portable EEG device to explore brain activity. Possible associations between clinical perceptions and measurements were also investigated. An enormous amount of EEG data remains to be explored using informatics and advances in this field, such as machine learning and artificial intelligence [22]. With these, the brain activities of patients related to anxiety and alertness, as well as pain and other effects, after local anesthesia and the administration of anxiolytic drugs may be observed with more clarity. This may lead oral surgeons and dentists to better understand and treat dental patients more effectively.

This study also provided a different perspective on the interplay and interactions of the anxiety parameters described above with the variables of the surgical process. One of the findings of this study, which corroborates those of previous studies on hemodynamic variability during TMo surgeries, was the increase in the patient heart rate and blood pressure during surgery [3,4]. Interestingly, the mean transoperative increases in the pulse and systolic blood pressure were also associated with an increase in the transoperative ATT measurement by EEG. Trans-surgical ATT measurements were also inversely correlated with surgical duration, indicating that tiredness decreased alertness. The multivariable linear regression found an association between ATT scores and preoperative anxiety scales (DAS and STAI-S) and physiological parameters of surgical stress, such as prolonged surgical time, HR, and pain during anesthesia. EEG indicates the number of neurons that discharge at
the same time, which generates oscillatory activities that can be influenced by several factors and tasks, and this reflects the state of the mind, such as attention, concentration, calmness, and executive functions [23]. Interpreting the brain waves and oscillations is key to understanding each factor.

This study is also consistent with previous studies, which indicated that high anxiety levels are associated with pain during and after dental treatment [1,5]. Lin et al. (2016) [1] observed in a meta-analysis that dental anxiety is a significant predictor of expected pain and pain during treatment and post-treatment, whereas differences related to the state or trait of anxiety may arise. State anxiety has been shown to be associated with trans-surgical pain, and the trait of anxiety is considered more associated with postoperative pain [1,5,23]. The results obtained in this study are very similar to those obtained by previous studies. The EEG MED algorithm measurements were found to be associated with pain during anesthesia; however, it was a positive association, which, according to the software developers, should indicate calmness or a higher state of meditation. The MED algorithm was not designed for pain exploration, and this association may be a response to fear. Linear regression showed that the scores of MED were associated with those of the psychological parameters of anxiety, such as DAS and STAI-S scores, as well as pain during anesthesia.

To our knowledge, this is the first study to use a mobile single-channel EEG device to monitor TMo surgeries; for this reason, there is no comparative method. It should be viewed as an exploratory study with highly interesting points that may direct the development of a new device for identifying biological markers to explore surgical stress in oral surgery; NBSKeeg, used in this research, shows fair validity and reliability, and it has been employed by several clinical studies [10-13,23-26]. Clinical modifications of the initial protocol, such as expanding the EEG monitoring period to cover the full surgery and clinically time-controlling the events of the trans-surgical development, could also be an interesting approach. We used a large number of variables, which allowed us to have a better assessment of the associations between systemic and brain reactions using standard psychological instruments for evaluations for dental anxiety in a single study. The use of single-channel EEG in dentistry and oral surgery may soon become mainstream for clinical research and patient evaluation due to the rapid advances in this field and the possible development of specific software for specific purposes. This study highlights the need to explore the potential of emerging technologies of mobile EEG devices in oral surgery.

Within the limitations of this study, the findings suggest that the single-channel EEG (NBSKeeg) is a promising device for evaluating brain responses associated with systemic reactions related to anxiety, surgical stress, and pain during oral surgery.

Regarding ATT, the number of patients classified as more alert increased during the surgery from preoperative to postoperative. Univariate analysis showed that ATT was associated with blood pressure, heart rate, and surgical duration, as well as lower scores of anxiety (DAS, STAI-S, and STAI-T). Multivariate analysis showed an interaction and association between ATT and STAI-S scores, pain during surgery, PSA, HR, and surgical duration. Regarding MED, the number of patients classified as more anxious dramatically increased during the preoperative and transoperative courses of the surgery, and it showed a slight decrease within the immediate postoperative period. The univariate analysis showed that MED was associated with pain during anesthesia and the DAS, STAI-S, and STAI-T scores. The multivariate analysis showed an interaction and association between MED and DAS, STAI-S, and pain during anesthesia.

**AUTHOR ORCIDs**

Roberto de Oliveira Jabur: https://orcid.org/0000-0002-2026-1748
Ramon Cesar Godoy Gonçalves: https://orcid.org/0000-0002-7488-0771
Kethleen Wiechetek Faria: https://orcid.org/0000-0003-2235-2122
Juliana Cama Ramaccia: https://orcid.org/0000-0002-3081-1504
Izabelle Millene Semczik: https://orcid.org/0000-0002-6024-8345
Marcelo Carlos Bortoluzzi: https://orcid.org/0000-0003-2756-5047
AUTHOR CONTRIBUTIONS

Roberto de Oliveira Jabur: Conceptualization, Investigation, Writing - original draft, Writing - review & editing
Ramon Cesar Godoy Gonçalves: Investigation, Project administration
Kethleen Wiechetek Faria: Data curation, Investigation
Juliana Cama Ramacciato: Supervision, Writing - review & editing
Izabelle Millene Semczik: Investigation
Marcelo Carlos Bortolozzi: Conceptualization, Formal analysis, Writing - original draft, Writing - review & editing

FUNDING: None

COMPETING INTERESTS: The authors declare no conflicts of interest.

ETHICAL APPROVAL: This study was submitted to and approved by the University’s Ethical Committee for Human Research (number, 21592119.3.0000.0105), and informed consent was obtained from all study participants.

ACKNOWLEDGMENT: We wish to thank the Conselho Nacional de Desenvolvimento Científico e Tecnológico - CNPq (Ministério da Ciência, Tecnologia, Inovações e Comunicações, Brasil) for the scholarship granted to Izabelle Millene Semczik, an undergraduate student, as a research assistant.

REFERENCES

1. Lin CS, Wu SY, Yi CA. Association between anxiety and pain in dental treatment: a systematic review and meta-analysis. J Dent Res 2016; 96: 153-62.
2. Aznar-Arasa L, Figueiredo R, Valmaseda-Castellón E, Gay-Escoda C. Patient anxiety and surgical difficulty in impacted lower third molar extractions: a prospective cohort study. Int J Oral Maxillofac Surg 2014; 43: 1131-6.
3. Hollander MH, Schortinghuis J, Vissink A. Changes in heart rate during third molar surgery. Int J Oral Maxillofac Surg 2016; 45: 1652-7.
4. Le SH, Tonami K, Umemori S, Nguyen LT, Ngo LT, Mataka S. The potential of heart rate variability for exploring dental anxiety in mandibular third molar surgery. Int J Oral Maxillofac Surg 2018; 47: 809-15.
5. Heaton IJ. Self-reported dental anxiety is associated with both state anxiety and dental procedure-related pain. J Evid Based Dent Pract 2017; 17: 45-7.
6. Reyes-Gilabert E, Luque-Romero LG, Bejarano-Avila G, García-Palma A, Rollon-Mayordomo A, Infante-Cossio P. Assessment of pre and postoperative anxiety in patients undergoing ambulatory oral surgery in primary care. Med Oral Patol Oral Cir Bucal 2017; 22: e716-e22.
7. Lago-Méndez L, Diniz-Freitas M, Senra-Rivera C, Seoane-Pesquera G, Gándara-Rey JM, García-García A. Postoperative recovery after removal of a lower third molar: role of trait and dental anxiety. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2009; 108: 855-60.
8. Astramskaite I, Poškevičius L, Juodžbalys G. Factors determining tooth extraction anxiety and fear in adult dental patients: a systematic review. Int J Oral Maxillofac Surg 2016; 45: 1630-43.
9. Astramskaite I, Juodžbalys G. Scales used to rate adult patients' psycho-emotional status in tooth extraction procedures: a systematic review. Int J Oral Maxillofac Surg 2017; 46: 886-98.
10. Rogers JM, Johnstone SJ, Aminov A, Donnelly J, Wilson PH. Test-retest reliability of a single-channel, wireless EEG system. Int J Psychophysiol 2016; 106: 87-96.
11. So WKY, Wong SWH, Mak JN, Chan RH M. An evaluation of mental workload with frontal EEG. PLoS One 2017; 12: e0174949.
12. Rieiro H, Diaz-Piedra C, Morales JM, Catena A, Romero S, Roca-Gonzalez J, et al. Validation of electroencephalographic recordings obtained with a consumer-grade, single dry electrode, low-cost device: a comparative study. Sensors (Basel) 2019; 19: 2808.
13. Johnstone SJ, Jiang H, Sun L, Rogers JM, Valderrama J, Zhang D. Development of frontal EEG differences between eyes-closed and eyes-open resting conditions in children: data from a single-channel dry-sensor portable device. Clin EEG Neurosci 2020; 31: 1550059420946648.
14. Diniz-Freitas M, Lago-Méndez L, Guade-Sampedro F, Somoza-Martin JM, Gándara-Rey JM, García-García A. Pederson scale fails to predict how difficult it will be to extract lower third molars. Br J Oral Maxillofac Surg 2007;
15. Almendros-Marqués N, Berini-Aytés I, Gay-Escoda C. Evaluation of intraexaminer and interexaminer agreement on classifying lower third molars according to the systems of Pell and Gregory and of Winter. J Oral Maxillofac Surg 2008; 66: 893-9.

16. Spielberger CD, Gorsuch RL, Lushene, R, Vagg, PR, & Jacobs, GA. Manual for the state-trait anxiety inventory. Palo Alto, CA, Consulting Psychologists Press. 1983.

17. Doganer YC, Aydogan U, Yesil HU, Rohrer JE, Williams MD, Agerter DC. Does the trait anxiety affect the dental fear? Braz Oral Res 2017; 31: e36.

18. Koga S, Seto M, Moriyaama S, Kiluta T. Anxiety before dental surgery under local anesthesia: reducing the items on state anxiety in the state-trait anxiety inventory-form x. J Dent Anesth Pain Med 2017; 17: 183-90.

19. Sirin Y, Yildirimturk S, Ay N. Do state-trait anxiety and previous unpleasant dental experiences predict the need for sedation in women having third molar surgery? Br J Oral Maxillofac Surg 2020; 58: 530-4.

20. Bonafé FS, Campos JA. Validation and invariance of the dental anxiety scale in a brazilian sample. Braz Oral Res 2016; 30: e138.

21. Bortoluzzi MC, Capella DL, Barbieri T, Pagliarini M, Cavaliert T, Manfro R. A single dose of amoxicillin and dexamethasone for prevention of postoperative complications in third molar surgery: a randomized, double-blind, placebo controlled clinical trial. J Clin Med Res 2013; 5: 26-33.

22. Rajpurkar P, Yang J, Dass N, Vale V, Keller AS, Irvin J, et. al. Evaluation of a machine learning model based on pretreatment symptoms and electroencephalographic features to predict outcomes of antidepressant treatment in adults with depression: a prespecified secondary analysis of a randomized clinical trial. JAMA Netw Open 2020; 3: e206653.

23. Morales JM, Ruiz-Rabelo JF, Diaz-Piedra C, Di Stasi LL. Detecting mental workload in surgical teams using a wearable single-channel electroencephalographic device. J Surg Educ 2019; 76: 1107-15.

24. Hemington KS, Reynolds JN. Electroencephalographic correlates of working memory deficits in children with fetal alcohol spectrum disorder using a single-electrode pair recording device. Clin Neurophysiol 2014; 125: 2364-71.

25. Fong SS, Chung JW, Cheng YT, Yam TT, Chiu HC, Fong DY, et. al. Attention during functional tasks is associated with motor performance in children with developmental coordination disorder: a cross-sectional study. Medicine (Baltimore) 2016; 95: e4935.

26. Wong SW, Chan RH, Mak JN. Spectral modulation of frontal EEG during motor skill acquisition: a mobile EEG study. Int J Psychophysiol 2014; 91: 16-21.