

Pain Management

Evaluation of Facial Electromyographic Pain Responses in Healthy Participants

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4 Summary points:
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- 7 • Facial expression is one of the most common diagnostic predictors of pain, alongside
8 pain reports
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 - 11 • While pain report is regarded as consistent among gender, age or cognitive states,
12 reliance is diminished in patients who are sedated or unable to provide verbal
13 reports, such as very young children
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 - 16 • The emergence of electromyography provides the means of recording muscle
17 activity in an objective manner, which particularly suits research investigations
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 - 20 • An exploration of functional electromyography on facial muscles opens the
21 opportunity of recording pain response to experimental pain
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 - 24 • The recording of painful expressions is still in its infancy and its use has not been
25 tested in the clinical setting
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 - 28 • This pilot study aims to validate the perception of pain via the recording of facial
29 muscle activity that serves to diagnose this symptom in patients unable to provide a
30 verbal report
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3 Abstract:
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6 **Objective:** To conduct a pilot study to test the feasibility of using facial electromyography
7 (fEMG) to assess pain in patients undergoing a painful surgical intervention.
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10 **Methods:** fEMG activity of 4 facial muscles was recorded from 24 healthy volunteers
11 experiencing a standardised painful stimulus - the cold pressor test (CPT). Self-reported pain
12 scores were simultaneously recorded, alongside the physiological variables: respiratory rate,
13 heart rate and skin conductance.
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20 **Results:** The CPT provided a robust response, with the majority of participants reporting mid
21 to high intensity pain scores, that correlated inversely with the extent of time to reach peak
22 pain perception. This model of experimental pain elicited significant changes in activity on
23 all four facial muscles investigated using fEMG. Moreover, three of these muscles –
24 mentalis, corrugator supercilii and orbicularis oculis – showed a statistically significant
25 correlation against the calculated ratio of pain intensity versus length of time to reach peak
26 pain. Finally, CPT did not induce significant changes to skin conductance or respiratory rate
27 but did increase heart rate, which correlated positively with changes in activity of all four
28 facial muscles of interest.
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44 **Conclusions:** This pilot represents a proof of concept for an objective method for assessing
45 pain based on fEMG output. These techniques may allow the evaluation of pain in clinical
46 populations who cannot communicate verbally such as patients with temporary or
47 permanent cognitive impairment due to sedation, learning difficulties or dementia, as well
48 as very young children.
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59 Keywords: Pain; fEMG; facial muscles; hand surgery
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Introduction:

The backdrop for this study was the need to conduct a pilot study to test a clinically-relevant paradigm that assesses facial pain expression on patients undergoing surgery. Facial pain, as characterized by Williams [1 *of considerable interest*], is an integral element of the affective component of pain [2] yet arguably one of the most difficult diagnostic predictors for healthcare professionals [3 *of interest*]. Our particular interest, therefore, is to gauge its suitability in assessing pain during the operative or immediate postoperative periods in place of the more traditional oral self-reports. The latter, despite being the standard quantifier at both the clinical and research settings, may not be carried out adequately during the two delicate periods stated above. In addition, the need for more objective pain measures is also driven by a requirement to help patients with conditions that prevents the ability to communicate self-reports. Examples of such cases include sedated patients on ITU or patients with dementia [4,5].

Research into facial expression has led to the development methodologies that allowed a more objective analysis of muscle activity at a functional level, leading to the concept of Facial Action Coding System (FACS) [6 *of interest*]. In addition, evaluating expressions using this technique brought about the discovery and definition of a specific pattern of muscle activity characterising facial pain expressions: lowering of the brow, eyelid and orbit tightening (via cheek-raising), wrinkling of the nose and raising the upper-lip raising [7 *of considerable interest*]. Moreover, similar expressions were observed in neonates, children, adults and the elderly, suggesting that there is a core expression of pain drawing on the activity from these four key facial areas [8,9,10].

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3 However, while the broader consensus is that the monitoring of pain expression is
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5 demonstrably reliable and consistent [11], questions soon surfaced over its relationship
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7 towards other signs of pain, in particular the self-reports. In addition, the FACS technique
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9 has some drawbacks such as necessitating initial training by human coders, or that it is
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11 modelled on a categorical approach – an expression is either present or absent. As visual
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13 methods are indirectly assessing muscle actions based on what is happening at the skin
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15 surface, here is no ability to measure changes in muscle tone in a continuous way. Thus, in
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17 developing a pain-assessment model, we opted in the first instance to test muscular activity
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19 by measuring its electrical output by using facial electromyography (fEMG) electrodes and
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21 standardised methodologies [12 *of interest*]. Also, to standardise the study of behavioural
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23 responses we opted initially to apply this technique on healthy participants undergoing an
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25 acute model of experimental pain and to monitor self-reports, thus providing the means to
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27 compare both variables. To date only a single pilot study has used EMG purposely to
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29 investigate facial pain in the form of muscle reactions, but this investigation did not
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31 consider the added component of monitoring self-reported pain [13]. The present study
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33 sought to answer the question: can our model of using fEMG replace self-reports as a
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35 reliable and objective measure of assessing pain on our follow-on study using patients?
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Methods:

Study outline

The objective of this study opted to explore the technique of fEMG to investigate pain expressions on healthy volunteers subjected to the cold pressor test (CPT), an experimental model of short-term cutaneous pain. Experiments were conducted at the

[REDACTED]

[REDACTED] All aspects of the study, such as experimental procedures outlined below, were carried out in accordance with the recommended guidelines outlined by the

[REDACTED]

Participants

Twenty four healthy volunteers from the American School of Anaesthesiology (ASA) grade I and II were recruited. All participants gave written consent, screened prior to the study for any of the study exclusion criteria and again on the study day. All procedures were conducted in the presence of a male anaesthetist.

The CPT and study paradigm

The CPT is an experimental procedure originally conceived to induce systemic stress, a procedure that particularly suited investigations into autonomic responses to stress, such as cardiovascular changes [14]. However, since the test can be attuned to deliver a noxious stimulus of sufficient magnitude to elicit a painful response it has since become a regular

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3 tool in many pain studies, as exemplified by Stening's work [15]. Our study replicated this
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5 described setup, save for setting the water bath to 7°C and of sufficient depth for the
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7 participant to completely immerse their non-dominant arm. The water temperature was
8
9 then kept constant throughout the procedure.
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18 The experimental setup consisted of first placing the fEMG transducers on the relevant
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20 locations traditionally used to monitor facial muscle activity, as detailed below. This was
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22 followed by connecting other monitoring equipment to record heart rate, respiratory rate,
23
24 blood pressure and skin conductivity (also detailed below). The participant was then sat in
25
26 front of video recording equipment and a computer screen. The latter was used to display
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28 the visual analogue scale (VAS), a measurement instrument used universally to rate the
29
30 experience of pain, ranging from 0 (no pain) to 10 (maximum tolerable pain).
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35 Video recordings, in turn, were included in order to assess artefacts in biometric sensor data
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37 caused by head movement or blinking and managed in the data analysis. Participants were
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39 unaware of these recordings until the procedure was completed, to prevent knowledge of
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41 the recording leading to conscious or unconscious changes in facial expression. A cover story
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43 (measuring skin temperature) was used to explain the use of contact sensors.
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52 The procedure itself comprised of three main phases: baseline (BSL), CPT and post-CPT. BSL
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54 applies to the phase prior to CPT, where the participant was required to remain as still as
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56 possible over a two minute period while baseline data for all EMG and physiological
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58 variables outlined above was recorded. This was followed by the CPT phase of the
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3 procedure whereupon the participant was instructed to insert the left forearm into the bath
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5 up to a cut-off period of five minutes or until such time that pain became intolerable. During
6
7 this period, participants were asked to rate pain perception continuously using the VAS.
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10 Finally, the post-CPT phase refers to the five minute time interval counting from the
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12 moment that the arm is removed from the bath or once the cut-off period is reached.
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20 **EMG and physiological setup**

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22 We used Biopac sensors (Bionomadix Wireless EMG) along with, 11mm electrode diameter
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24 electrodes (Biopac EL-500) to acquire the fEMG data. Prior to sensor application, the skin
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26 was cleaned with 70% alcohol / 2% chlorhexidine swabs and then lightly abraded with a
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28 scouring pad as per standard protocols. The fEMG electrodes were then placed according to
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30 an adapted version of a protocol described by van Boxtel [12], as shown in Figure 1 below,
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32 with only minor modifications according to recommendations by Dr Charles Nduka, the
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34 supervising consultant plastic surgeon, to ensure accuracy of technique.
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40 Raw data from each physiological output channel was recorded with a frequency of 2kHz.
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42 fEMG data was filtered using a bandpass filter (20-500Hz), to reduce the influence of
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44 artefact caused by swallowing, blinking, respiration etc. Additional notch filtering at 50Hz
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46 was carried out to reduce interference from power lines.
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55 Additional physiological variables were recorded, to assess the impact of CPT-induced stress
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57 on the autonomic system:
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- Heart rate transmitter attached to the middle and ring fingers of the participant's right hand (Biopac Bionomadix Wireless Photoplethysmogram)
- Respiratory rate, with the wireless transducer placed in the standard position around the participant's thorax (Biopac Bionomadix Wireless Respiration Transducer)
- Electrodermal activity (sometimes known as galvanic skin response), with the wireless sensor attached to the middle and ring fingers of the participant's right hand (Biopac Bionomadix Electrodermal activity)

Data processing and statistical analyses

Processing of both the fEMG and physiological data was performed using Matlab (MathWorks, Version 8.6 R2015b) or Excel (Microsoft, Version 16.26) or AcqKnowledge (Bopac Systems, Version 4.4), while all statistical analysis plus graphic imaging was done using Prism (GraphPad Software, Version 8.12). Raw data was handled initially at single-subject level by first conducting a signal rectification followed by averaging every 200 data points, so that each procedure yielded 600-700 figures whereby each corresponded to a duration of 0.1 sec. Of these, a sample of 120 sec of data was extracted from each phase, equating to the whole BSL, the first two minutes after start of CPT and the first two minutes post-CPT.

These 120 sec blocks of waveform data was then used to calculate the generalized mean for each of the three phases using the integrated (RMS) tool of Acqknowledge. Change in muscle activity from CPT or during post-CPT, in microvolts, was then calculated by applying the following formulas to subtract baseline effects, using Excel:

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3 CPT – BSL
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12 Post-CPT – BSL
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16 These definitive figures for each participant were then pooled to conduct a second-level
17 analysis, to investigate CPT effects at population level using one-way repeated measures
18 ANOVA with Dunnett’s multiple comparisons post-test.
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29 All raw data pertaining to pain perception in the form of continuous VAS scores was equally
30 averaged into 0.1 sec periods, as described above. We then analysed each time course at
31 subject-level to record both the ‘peak’ pain score, representing the highest score recorded
32 during CPT, as well as the interval of time to reach said peak. These were extracted from all
33 participants and plotted in order to carry out a correlation analysis – defined as ‘Gradient’.
34 Each Gradient number was in turn used in the correlation analysis against changes in muscle
35 activity obtained using the above formulae, as well as against the physiological parameters
36 recorded.
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Results:

Participants

A total of 24 datasets were obtained from a cohort of healthy volunteers (12 female; aged 18-40). All underwent the procedure without reporting any adverse side effects, required special attention or to be withdrawn from the study.

The cold pressor test

Analysis of the VAS ratings acquired continuously throughout exposure to the cold water revealed that this stimulus was clearly robust, with 23 of the 24 participants reporting experiencing pain – commonly defined as VAS above 1 – that averaged (std dev) 6.24 (2.1), with no significant difference between genders ($p = 0.286$, 2-sided T-test). In addition, despite some participants showing some degree of acclimatization, an under the curve analysis of each participant's timeline revealed that the overwhelming majority perceived pain during CPT that extended into the post-CPT phase, where the group average (SD) shows a VAS score over 1 for 72.5% (22) of the combined periods (data not shown).

Analysis of the VAS scores revealed a differing range of peak VAS scores across the participant cohort, reinforcing the generally accepted notion of pain perception is subjective in nature. In addition, the time interval – in seconds – to reach said peak also differed between participants. Thus, it was decided to investigate for any pattern linking these two variables, by plotting peak VAS against time to peak, as shown in Figure 2. Subsequent

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3 analysis revealed that these parameters were inversely related ($r = -0.56$, $p < 0.01$ Pearson
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6 r), whereby participants who perceived higher pain intensity did so quicker while those
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8 scoring lower pain took longer.
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16 **Facial muscle integrated (RMS) analysis**

19 Table 1 summarises the outcome of the one-way repeated measures ANOVA analysis
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21 (column A) and Dunnett's post-test between CPT and baseline (column B) or post-CPT
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23 versus baseline (column C) for each of the facial muscles of interest. Results showed that
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25 activity from all muscles except the corrugator supercilii changed significantly across all
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27 phases of the procedure. A deeper analysis comparing the BSL phase versus the other two,
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29 in turn showed that CPT caused a significant change in activity by all four muscles, which
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31 remained for both the Mentalis/Zygomatic and levator labii during post-CPT.
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43 **Gradient versus facial muscle RMS correlation analysis**

45 Consistent with our prediction that CPT induced significant changes in activity from all the
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47 facial muscles of interest, we conducted a further correlation analysis by plotting the RMS
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49 changes versus the gradient scores, calculated as VAS/time, shown in Figure 3. Table 2, in
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51 turn summarises the linear regression analysis in terms of deviation from zero.
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55 An equivalent analysis for the post-CPT phase versus BSL in turn revealed that the only two
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57 muscles that showed a significant ($p < 0.05$) positive correlation were the zygomatic and
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3 orbicularis muscles. The remainder showed no significant difference, suggesting a return to
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5 baseline status.
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13 **Facial muscle RMS versus biophysical parameters**

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16 The final element of the study was to investigate muscle activity versus the physiological
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18 parameters: heart rate (HR, Figure 4), skin conductance or respiratory rate. For most
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20 variables the outcome came out as not incurring significant changes except for HR, shown in
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22 Figure 4, which indicated that only this particular parameter increased markedly in response
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24 to the CPT.
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Discussion:

This study proposed to expand on the growing number of investigations promoting the use of EMG in clinical research, in particular to develop models of facial pain expression that are directly relevant to the experience of acute or chronic pain. The pursuit of objectively measuring pain experience allows the opportunity to exploit new avenues of research, diagnosis or potential treatments. This is, however, a challenging undertaking given the well-known complexity of factors that affect an individual's interpretation of this particular symptom. Imaging studies, for instance, have identified numerous brain regions encoding emotional, cognitive or pathological processes and the interplay of which alter the resulting pain experience, as reviewed by Tracey [16], but at the same time can provide useful targets for pain-relieving compounds [17].

EMG studies, in combination with MRI or alone, have contributed to this field by correlating individual pain experience with activity in motor regions encoding facial expression [18] as well as naming specific muscles within those involved in facial expressions that are regarded as pain-specific [13 *of interest*]. These advances towards recognizing the multiple facets of pain experience represent a considerable step forward from the traditional pain report or similar psychophysical analysis. However, some of these study paradigms may not necessarily be ideal or suitable to conduct in patients suffering from acute or chronic pain. Any such investigation presents considerable ethical and technical challenges such as the need to simplify procedures or minimize suffering yet still requiring participation to provide sufficient data, as well as consider the many elements that not only affect the definite pain experience, as stated above, but foremost to include the anticipation of pain [19]

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3 In this study our group used fEMG to investigate facial muscle activity in response to a
4 commonly employed model of experimental cutaneous pain. The purpose was two-fold: to
5 further validate the utility of fEMG as an effective tool in describing the facial signature of
6 pain, through the activity of key muscles involved in this behavioural response, as previously
7 investigated by Wolf's group [13] and, more importantly, to develop a study paradigm that
8 can be reliably employed in the clinical setting to quickly and objectively assess facial pain
9 expression on patients scheduled to undergo surgical procedures.
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25 During the preliminary stages of this pilot study, the developing paradigm presented us with
26 two main technical challenges, namely (i) interpersonal (i.e. participant) variability and (ii)
27 potential compounding factors such as boredom or anxiety that can impact of the fEMG
28 recording. Addressing the latter issue first, there are to date no studies that specifically
29 investigated differences in pain expression across multiple sessions. However, Gaudet and
30 colleagues recently examined the issue of intra- and intersession variability using surface
31 EMG on forearm muscles, reporting that differences obtained between sessions actually
32 have an insignificant impact, in comparison with the choice of arm-movement task that
33 accounted for the greatest within-session change [20]. This and similar work provide
34 evidence that EMG provides a reliable output irrespective of when the recordings are done,
35 which supports the view that anxiety experienced when undertaking a novel test, or indeed
36 boredom after repeated tests, does not appear to have a significant effect. In support of
37 this, we also obtained precise recordings from a range of physiological parameters, namely
38 pulse rate, skin conductance and respiratory rate. This supplementary comparative analysis
39 performed revealed that these physiological parameters did not change to any great degree
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3 between the three main study periods. It should be recognized that this does not suggest
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6 equivalency between the participants with regards to mental status, since we did not
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8 employ any of the questionnaires commonly employed to assess state or trait [21]. These
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10 would certainly be compulsory if the same study were to be conducted on any patients
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12 suffering chronic pain, since these demonstrate a clearly altered emotional status that is
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14 generally attributed to maladaptive changes taking place at the central nervous system (for
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16 review see May [22]), and the elements of which exacerbate the pain response, as discussed
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18 in the previous paragraph. Given that this study recruited healthy individuals with no pre-
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20 existing conditions, however, we are confident that the EMG data most likely reflects the
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22 nociceptive effect by the CPT alone and was not shaped by higher centre processes such as
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24 mood or even anticipation.
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35 Turning to the first technical challenge, we opted to use the CPT as the stimulus of interest
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37 given its frequent use in pain studies (for example the work by Stening [15]) and due to the
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39 fact that it requires very little or no medical supervision or equipment, so is generally
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41 regarded as safe. We consider that the type and magnitude of nociceptive input this pain
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43 model provides was sufficiently robust but, more importantly, that the participant response
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45 would be akin to what is expected in any follow-on study using patients suffering from acute
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47 pain and need to undergo a 10-minute procedure.
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57 Data acquisition was carried out in a manner that included the continuous recording of pain
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59 report – in the form of timelines of pain intensity – alongside the EMG. Its purpose was to
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3 serve as a control when analyzing the timeline of facial muscle activity, which would allow
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5 us to relate the latter with the magnitude of pain being experienced. When plotting pain
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7 intensity and duration to reach peak pain we observed a wide pattern of differing scores.
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10 While it was not this study's intent to investigate the reasons behind this outcome, it should
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12 be mentioned at this point that published evidence suggests that genetic variation,
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14 specifically those affecting transient receptor potential (TRP) channels [23,24] could account
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16 for this broad range of subjective experiences. Nonetheless, a correlation analysis by these
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18 two variables demonstrated a significant negative trend, which we predict would be similar
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20 on patients suffering acute pain. Accordingly, we applied these figures in the subsequent
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22 analysis against EMG activity. The latter data revealed that CPT induced significant increase
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24 of activity on all facial muscles of interest: mentalis/zygomatic, corrugator supercilii, levator
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26 labii and orbicularis oculis. This was not only consistent across virtually all participants but
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28 also validating Wolf's list of facial muscles identified as responding to noxious stimuli [13].
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30 Thus, this pilot work, as well as prior efforts from our group [25] and other published
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32 evidence [12,26,27], continue to endorse EMG as an essential tool capable of providing an
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34 objective evaluation of facial expressions that portray emotion, including pain. Of interest to
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36 our group now, is the application of this model to a patient cohort during the operative and
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38 post-operative periods, i.e. while sedated and therefore unable of self-reporting pain, as
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40 recently reviewed [4].
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55 In conclusion, we believe that our experimental model will provide in the long term an
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57 effective and clinically-relevant method of assessing pain in patients suffering acute pain
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59 from injuries while undergoing surgical repair. This is validated by our protocol successfully
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3 recording noxious-related changes in activity on a group of muscles commonly identified as
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6 expressing pain.
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For Review Only

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5 EDITORIAL NOTE: FIGURE 1 HAS BEEN REDACTED FOR BLINDED PURPOSES.
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8 However, it has been assessed by the in house Editorial Team.
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15 Figure 1: fEMG sensor placements for the study. Corrugator supercilii (above eyebrow),
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17 levator labii (on side of nose), orbicularis oculi (lower side of eye) and mentalis (chin).
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19 Reference electrodes (upper forehead) are also present. Eight participants had facial hair
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21 preventing good contact of the mentalis sensor, so the zygomaticus was recorded instead.
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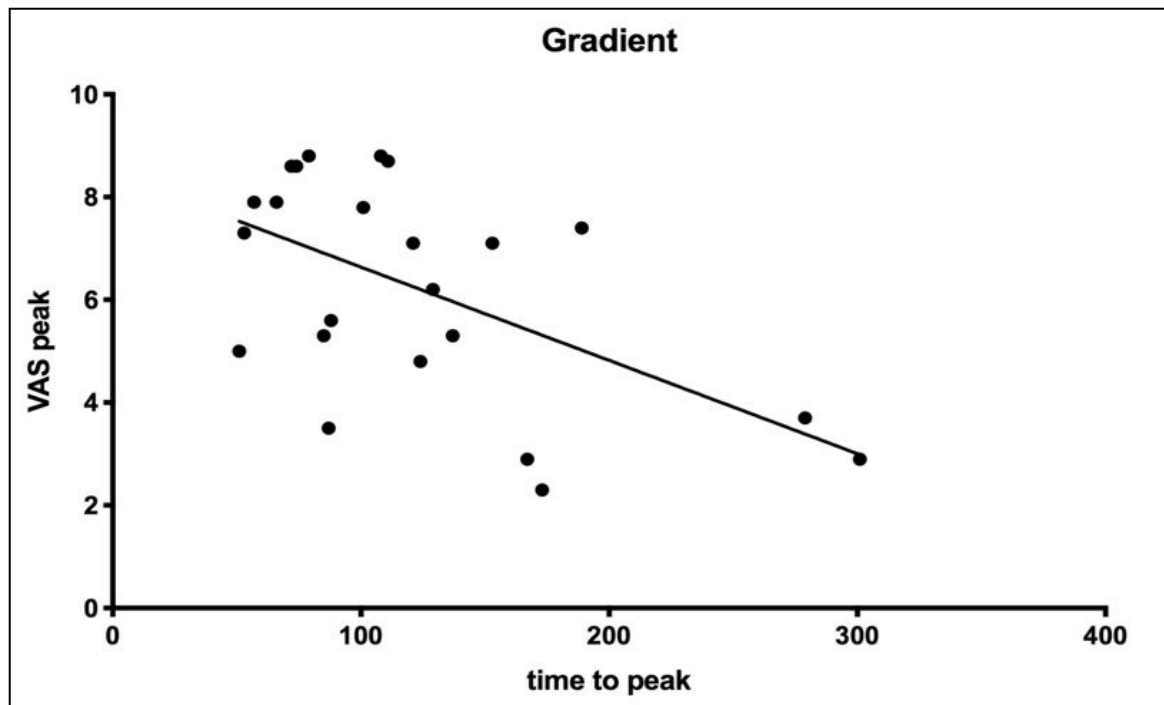


Figure 2: Correlation analysis of pain perception, expressed in terms of recording pain intensity (Y axis) versus length of time, in seconds, to reach peak pain perception (X axis).

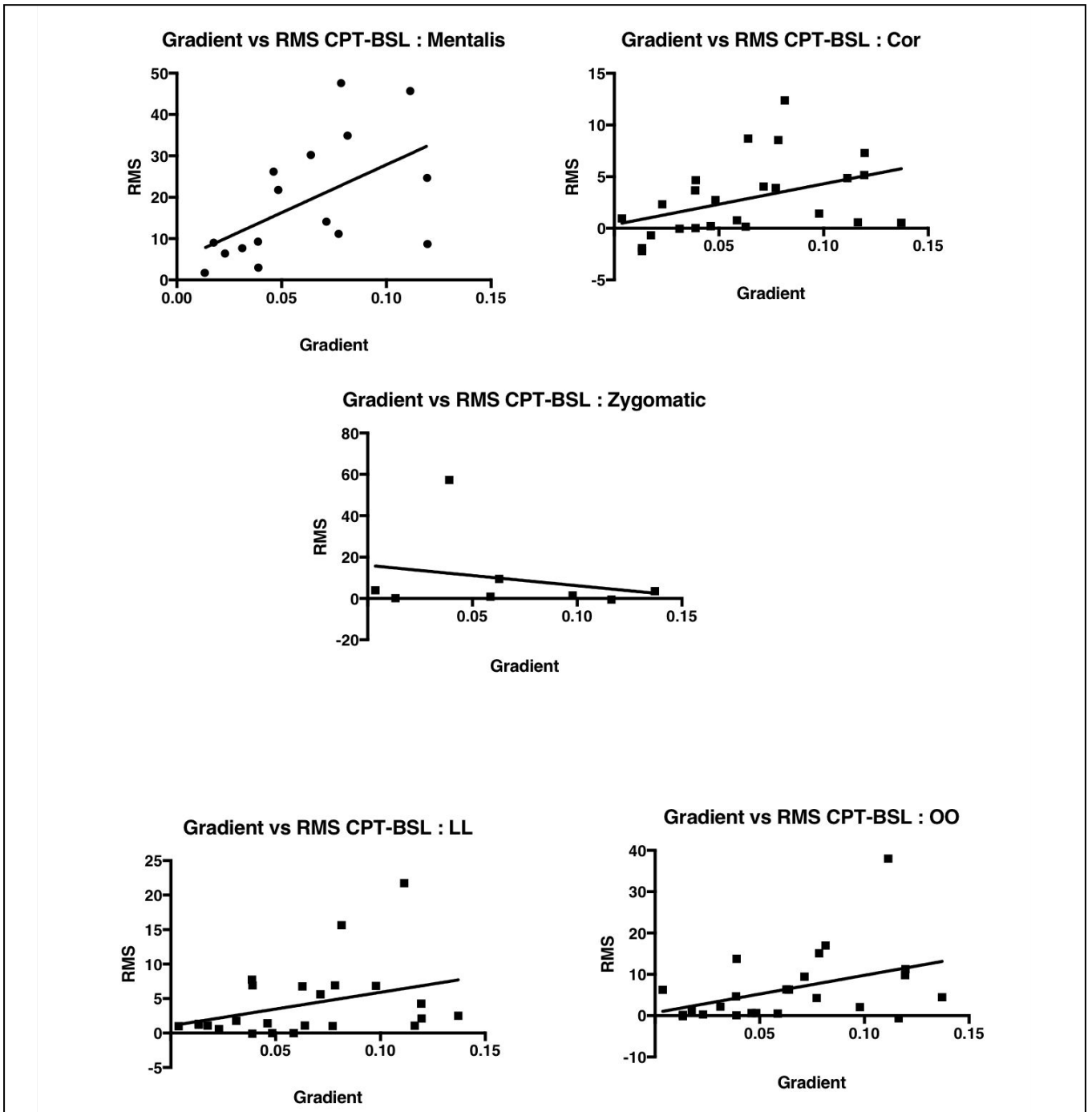


Figure 3: linear regression analysis of facial muscle activity (RMS, in microvolts) against gradient. Incidences of slope significantly deviating from zero is summarized in Table 2. Cor, Corrugator supercillii; LL, levator labii; OO, orbicularis oculi.

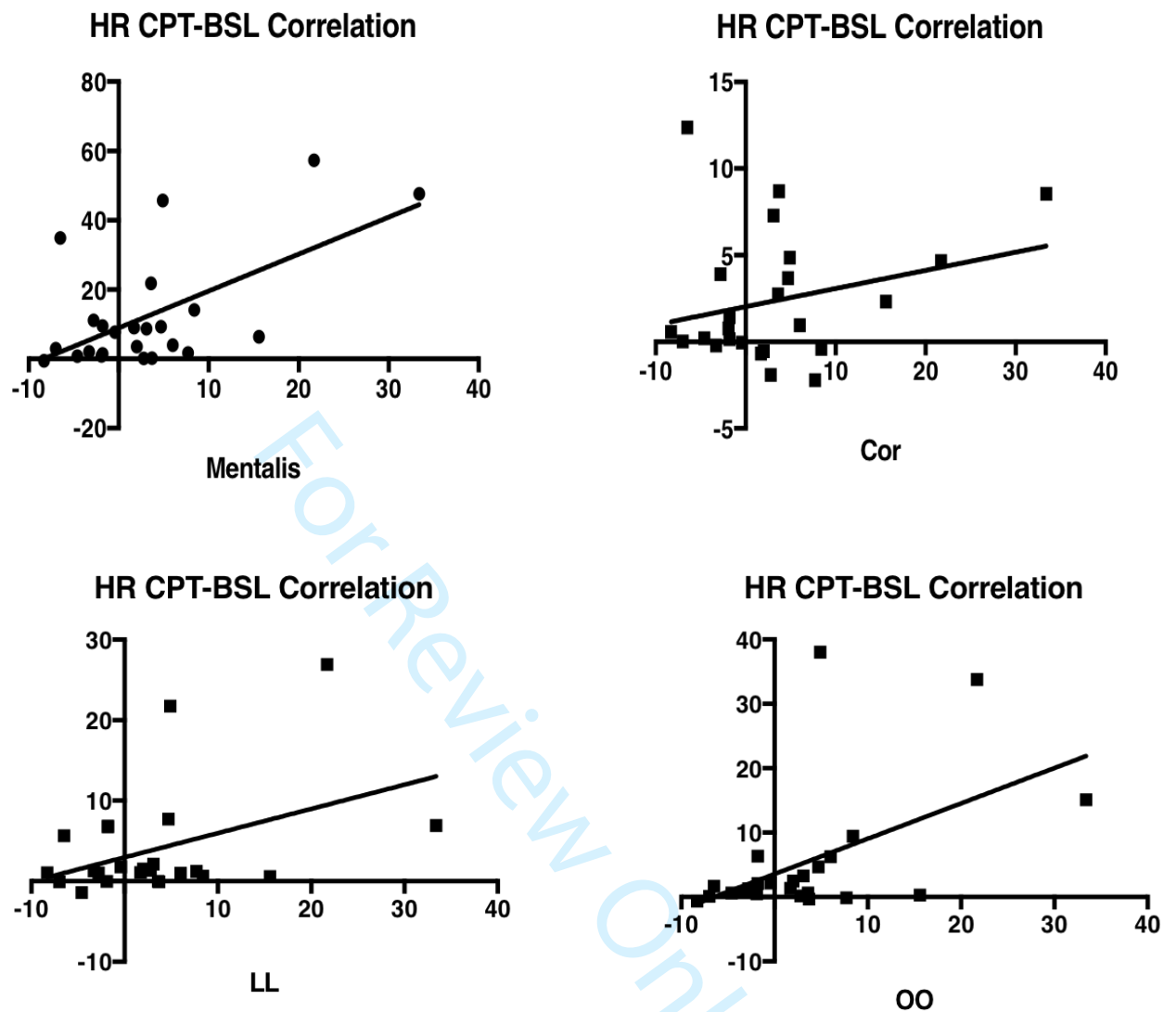


Figure 4. Correlation analysis of changes in heart rate (HR) versus changes in muscle activity during the CPT period versus baseline (BSL). Cor, Corrugator supercillii; LL, levator labii; OO, orbicularis oculi.

Muscle	A: 1-way ANOVA	B: CPT vs BSL	C: Post-CPT vs BSL
Mentalis & zygomatic	$F_{(2,24)} = 15.62$ ($p < 0.001$)	$p < 0.001$	$p < 0.05$
Corrugator supercilii	$F_{(2,24)} = 3.06$ ($p > 0.05$)	$p < 0.01$	ns
Levator labii	$F_{(2,24)} = 7.7$ ($p < 0.01$)	$p < 0.05$	$p < 0.01$
Orbicularis oculis	$F_{(2,24)} = 6.34$ ($p < 0.05$)	$p < 0.05$	ns

Table 1. Incidences of significance from the one-way repeated measures ANOVA (column A) and Dunnett's (columns B and C) analysis for each of the four facial muscles of interest. ns, non-significant.

Muscle	Pearson
Mentalis *	$r^2 = 0.3$ (F = 6.16, p < 0.05)
Zygomatic *	$r^2 = 0.058$ (F = 0.37, p > 0.05)
Corrugator supercilii	$r^2 = 0.18$ (F = 4.73, p < 0.05)
Levator labii	$r^2 = 0.13$ (F = 3.12, p > 0.05)
Orbicularis oculis	$r^2 = 0.17$ (F = 4.50, p < 0.05)

Table 2. Tabular results of the linear regression analysis for each of the facial muscles of interest. * For this particular analysis the data from mentalis and zygomatic muscles were analysed separately given the outcome from Figure 3 which showed a clear difference in slope.