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Evaluating a sensor of skin conductance to assess dental anxiety

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Finding new ways to help anxious patients in dental offices

Abstract

The anxiety related problems that adult population experience, are a common issue in Dental Practice. To overcome these problems it would be helpful to have an objective measure of the current anxiety of the patient. With this information, it should be possible to link the measured anxiety to an automated system that could distract the patient by altering the surrounding environment, i.e. Ambient Intelligence.

This project consisted in measuring the skin conductance signal and correlating the responses related with documented dental stressful procedures. This was executed in a real clinical environment. Dental anxiety was assessed in over 70 patients with a 3 question survey using the Likert scale. Each answer was registered together with the level of skin conductance measured with a sensor placed in the patient fingers. The results showed a significant association between the dental anxiety score on two of the questions and the quantified skin electrodermal response. These findings aim to help design a future system based on ambient intelligence to distract and reduce dental anxiety during treatment.

Keywords: Skin Conductance Level, Electrodermal Response, Dental Anxiety, Dental Phobia, Ambient Intelligence

Resumo

Uma parte significativa da população adulta tem problemas provocados pela ansiedade originada com a ida à consulta de Medicina Dentária. Seria vantajoso existir uma avaliação objetiva do nível de ansiedade do paciente durante a consulta para se ultrapassar estes problemas. Com esta informação seria possível alterar o ambiente envolvente através da ligação a um sistema automatizado inteligente para a distração do paciente durante a consulta.

Este projeto consistiu na medição do sinal de condutividade da pele e correlação desta com as respostas a um questionário relacionado com atos dentários reconhecidos como causadores de grande ansiedade dentária. A ansiedade dentária foi avaliada em cerca de setenta pacientes por um questionário de três perguntas utilizando uma escala de Likert. Simultaneamente foi medida a condutividade da pele por um sensor colocado nos dedos da mão. Os resultados mostram uma associação significativa entre o nível de ansiedade obtido em duas das questões e a alteração da condutividade da pele. Estes resultados visam fornecer uma base para desenhar um futuro sistema de Ambiente Inteligente para distração da ansiedade dentária.

Palavras chave: Nível de Condutividade da Pele, Resposta Electrodermica, Ansiedade Dentária, Fobia Dentária, Ambientes Inteligentes.

Resumo alargado¹

Uma parte significativa da população adulta tem problemas provocados pela ansiedade originada com a sua ida à consulta de Medicina Dentária. Os estudos calcularam percentagens variáveis desde 11 % na Alemanha e nos Estados Unidos, a cerca de 15% no Reino Unido [1][2] e a 28.7% em Portugal.

A “qualidade de vida relacionada com a saúde oral” pode ser avaliada pela forma como a saúde oral afeta a mesma. Esta qualidade de vida diminui com dificuldades decorrentes da completa ausência de visitas ao dentista, ou a pouca cooperação quando o paciente está no dentista. A fobia dentária pode ser associada à família ou ao ambiente social em que se está inserido. Os pacientes com grande ansiedade dentária também relatam experiências traumáticas de dor que se traduzem em medo e em abstenção em se dirigir ao médico dentista.

Os pacientes ansiosos sofrem de um ciclo vicioso que por não ir ao dentista, pioram o estado oral. Desse modo tornam-se emocionalmente desgastados com sinais de vergonha e inferioridade [3]. Deveremos dialogar com estes pacientes no intuito de baixar as barreiras psicológicas que fazem evitar os cuidados de saúde oral. Não se deverá enfatizar os benefícios de uma boa higiene oral, porque desse modo, ao sublinhar os benefícios apenas estaremos a criar mais embaraço ao paciente [4].

Existem várias metodologias para aferir a ansiedade dentária. As mais comuns são feitas com o uso de questionários como o *Modified Dental Anxiety Scale*. A fiabilidade destas escalas é muito variável e portanto seria vantajoso usar uma avaliação objetiva do nível de ansiedade do paciente durante a consulta.

A bio impedância descreve as propriedades elétricas passivas dos materiais biológicos. Esta propriedade dos tecidos traduz-se no uso de técnicas simples para transdução indireta dos eventos fisiológicos. O tecido é composto de células que têm capacidades capacitivas, o que se traduz em baixa impedância. A impedância é a qualidade de um material se opor ao fluxo elétrico. A condutividade do corpo é do tipo eletrolítico, devido à presença de iões , i.e. Na, CL, nos fluídos corporais.

O suor pode ser criado em resposta à temperatura ambiente quente, ao exercício físico e ao nível de ansiedade. O aumento da sudação altera o nível de potencial da pele e o nível de condutância da pele. Os canais excretores das glândulas sudoríparas são principalmente resistivos e estão dispostos em paralelo na zona córnea da pele. As atividades emocionais têm um efeito direto na glândula sudorípara através do nervo simpático. Assim é possível uma medição da atividade do sistema nervoso autónomo

¹ Em cumprimento do disposto no artigo 27º. nº3. da deliberação nº 1506/2006 (regulamento de estudos pós graduados da universidade de lisboa), de 30 de Outubro

através de sensores de condutividade dérmica. Os estímulos emocionais traduzem-se num rápido aumento da condutância pelo preenchimento dos canais excretores.

O Ambient Intelligence (AmI) é um conceito que tem como objetivo o aumento da interação entre os humanos e a informação digital através do uso de dispositivos computacionais ubíquos. Um ambiente inteligente é visto como um processo piramidal em que a base é representada pela parte física do sistema com sensores multimodais, atuadores, e interfaces de hardware e o topo é formado pela parte lógica. Os sensores darão a informação ao sistema operativo (OS) do AmI. O OS irá alojar o algoritmo de decisão e a base de dados preditiva para interagir com o meio envolvente. O ciclo de ação será da parte lógica (topo) para os atuadores (base). O ciclo de perceção do que está a acontecer trata a informação consoante os objetivos da tarefa e julga os resultados e as ações possíveis para transformar o ambiente no estado pretendido.

É possível medir a ansiedade através de dados bioquímicos como seja o nível de catecolaminas [5] e também estimar o nível de ansiedade dos pacientes através da frequência cardíaca, electromiografia e condutividade dérmica.

É importante ter uma relação entre o sinal de condutividade dérmica e a estimativa de ansiedade do paciente. Um sensor da condutividade dérmica poderá ser usado no sistema de ambiente inteligente. Este sistema automatizado processará o sinal medido e poderá intervir no ambiente envolvente para a distração do paciente. Como os pacientes podem manifestar um maior grau de dor quanto mais ansiosos estiverem, se for possível controlar a ansiedade ter-se-á ajudado a ultrapassar uma das principais barreiras do regresso a uma próxima consulta dentária.

Este projeto consistiu na medição do sinal de condutividade da pele e associação desta com as respostas a um questionário com uma escala de ansiedade sobre procedimentos desencadeantes de stress num ambiente dentário. A ansiedade dentária foi avaliada em cerca de setenta pacientes escolhidos ao acaso, através de um questionário de três perguntas numa escala de Likert. Ao mesmo tempo foi medida a condutividade da pele com um sensor colocado nos dedos da mão. Os resultados mostram uma associação significativa entre as respostas a duas das perguntas e a variação da condutividade da pele.

Estes resultados podem servir de base ao desenvolvimento de um sistema automatizado de AmI para ser usado num espaço de cuidados de saúde orais. Um futuro sistema deste género poderá ajudar a decidir se um ambiente inteligente (AmI) poderá ser usado para reduzir o nível de ansiedade durante o tratamento dentário?

Existem várias técnicas psicológicas eficazes para reduzir a ansiedade, incluindo as técnicas cognitivas-comportamentais. De entre estas técnicas a distração é um dos métodos que mostraram uma eficácia considerável. Como a mente humana tem recursos

limitados de atenção, uma distração irá absorver uma porção desses recursos e acredita-se que limita igualmente a capacidade cognitiva para processar a dor.

A investigação nesta área revelou que os jogos eletrônicos, a televisão e instruções de relaxamento gravadas podem controlar altos níveis de medo nos pacientes que se dirijam a consultas médicas e dentárias. Outras técnicas de distração incluem: música ambiente, intensidade e tonalidade da luz, a projeção de imagens personalizadas nas paredes e teto, a utilização de realidade virtual ou mesmo o uso de fragâncias. Apesar da consulta dentária ser uma situação ideal para o uso de técnicas hipnóticas, este método é raramente usado por falta de formação e mitos associados ao seu uso.

Um sistema de distração pode, ao personalizar o ambiente, ter a capacidade de criar conforto no paciente e assim ajustar-se ao seu nível de ansiedade. Isto terá efeitos na redução do stress e poderá permitir ao paciente uma sensação de controlo.

A deteção do nível de ansiedade do paciente é vista como uma mais-valia no tratamento de pacientes ansiosos. Um sistema de ambiente inteligente low cost poderá ler o nível de ansiedade através de biossensores economicamente acessíveis e assim utilizar usar num futuro próximo métodos de relaxamento e desvio de atenção.

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Abbreviations and Acronyms

LIST ORDERED BY NAME:

DFA	Dental Fear and Anxiety
EDA	Electrodermal Activity
EDL	Electrodermal Level
EDR	Electrodermal Response
FCUL	Faculdade de Ciências da Universidade de Lisboa
FMDUL	Faculdade de Medicina Dentária da Universidade de Lisboa
GSC	Galvanic skin conductance
GSR	Galvanic skin response
ISTAG	European Commission's Information Society Technologies programme Advisory Group
MDAS	Modified Dental Anxiety Scale
SCL	Skin Conductance Level
SCR	Skin Conductance Response
SPL	Skin Potential Level
SPR	Skin Potential Response
SRR	Skin Resistance Response

Chapter 1 Introduction:

Dental treatment is related to pain and anxiety. This is true, even since the adoption of modern techniques and anesthetics. It is one of the most frequent fears in Western World [6]. It can go from 11 to 20 % in the adult population of the United States of America (USA) [2], and about 11.6% in the United Kingdom (UK). In other countries around the world, it can vary from 4% in Denmark to 30% in Hong Kong Chinese [7] (Table 1).

Table 1 Reported prevalence of Dental Anxiety internationally (adapted [7][8])

Country	Level of High Dental/Anxiety
Australia	13.70%
Canada	4.4%-16.4%
China (Hong Kong)	30%
Denmark	4.20%
Iceland	4.80%
Japan	20.90%
Netherlands	3.9%-10.8%
New Zealand	12.5%-21.1%
Portugal	14.7%-28.7%
Singapore	7.8%-20.8%
United States	10%-19%

The inconsistent findings across studies are the result of using different measures to assess the construct of dental anxiety [9]. Patients with dental fear and anxiety (DFA) suffer from negative experiences, fears, sleep disturbances and often avoid dental treatment.

1.1 Dental pain

Public awareness of dental care is more or less equal to dental pain. Nevertheless dental pain act as a warning signal to indicate potential injury, illness or danger and can force individuals to seek treatment when it is intense. Dental pain is unique in nature. It comes from activated unmyelinated C-fibers in tooth pulp which send signals to the brain.

Dental pain is subject to environmental, emotional and cognitive determinants. Environmental factors like ambiance of the dental office and the social interactions with dental staff modify reported pain. This reflects one important aspect of the social interaction: the provider-patient communication. The environmental determinants can be modified with distraction, predictability and controllability. Distraction is a way to successfully reduce the pain experienced by the patient. Predictability happens when the

patient is informed of what will occur during the treatment procedures and instruments used. Controllability is the ability of a patient to influence what happens during treatment.

Several models exist for emotional determinants: Mowrer's, Davey's, Fear-Avoidance, Expectancy, Acceptance-based. The models conceptualize the affective states like anxiety, fear, panic or depression, and help professionals focus the patients attention away from the pain.

The cognitive processes related to memory are critically important to patient's perceptions of dental pain. High anxiety patients recall greater pain experiences, and others can have a catastrophizing tendency to focus and excessively worry on predicted pain. Pain is associated to individual characteristics like age, gender, socio economic status and culture, and both the patient and the dental personnel can influence a patient's response [10].

1.2 Quality of life

The Oral health-related quality of life is a recent patient-centered approach to the evaluation of how oral health affects quality of life. The oral health can affect masticatory functioning like chew, bite or swallow and the function of speech. Patients can also be psychological affected due to dissatisfaction of the teeth and smile, and of low self-esteem. Social interactions can be difficult in terms of communication and intimacy. The pain and discomfort of low oral health quality of life are present in acute or chronic episodes, i.e. when patients use removable prosthesis [11].

1.3 Dental anxiety

Dental anxiety can be formally defined in a dental context as an unpleasant psychological reaction to a poorly-defined or not straightaway present dental stimulus, seen as potentially harmful or dangerous [12].

In spite of the terms 'fear', 'anxiety' and 'phobia' are often used synonymously certain distinctions should be made. Dental fear is a normal emotion generally observed in small children, and dental anxiety and phobia is a disorder-like characteristic of more mature children and adults. Treatment should be different [13]. Fear is a natural response to situations recognized as truly threatening. The reaction is based on the activation of the sympathetic branch of the autonomic nervous system that triggers the fight or flight responses. Fear is by definition a normal rational preventive response.

Anxiety is like fear but has one fundamental difference: it appears without a stimulus. The main reason for anxiety is anticipating future events connected with previous bad

experiences. Anxiety is an irrational disorder because there is no imminent threat but there is a powerful and unreasonable reaction.

Dental phobia is defined with a clinical diagnosis in correspondence with the diagnostic criteria used (DSM-5 [14] or ICD-10 - F40.2 [15]). It is assumed as a clinical mental disorder in which the patient's marked and persisting fear or anxiety is out of proportion to the actual danger posed by the specific object or situation and to the sociocultural context. It also causes clinically significant distress or impairment in daily life.

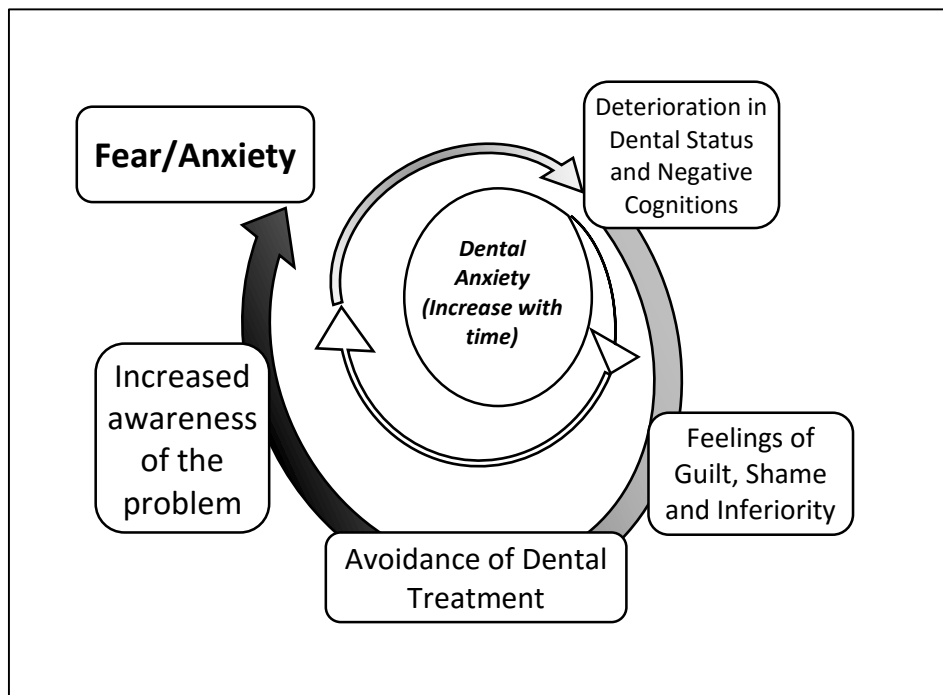


Figure 1 Vicious spiral of Dental Anxiety (adapted [16])

The phobic patient shows avoidance behaviour and, if it comes to a treatment, the dentist is endured with intense fear or anxiety of the patient. He can have secondary fears of dying, losing control or going mad, which may take the form of a panic attack. Phobic anxiety and depression often coexist. Dental phobic patients tend to avoid seeking the dentist, and only go to the clinic when severe pain is experienced. This stresses the procedures and interferes with the dentist's ability to give proper treatment. In addition, the anxious patient have more dental problems in contrast with control groups. This type of patients have more missing teeth, tooth decay and bone loss. It seems that phobic patients are caught in a cycle (Figure 1), where fear, pain, and guilt may prevent oral hygiene and treatment [17]. Equally, dentists in general, lack sufficient knowledge to address anxiety-related issues and compromise the quality of care given [18]. If dentists can lower patient's anxiety, the patients will be more encouraged to obtain dental care.

Dental phobia is a multi-factorial disorder with an interaction between dental factors and vulnerability factors. The vulnerability factors include personal qualities like sex, age and maturity, and external or social circumstances. For example hearing dental anxiety situations from parents or friends or being in groups with lower socioeconomic status.

Anxious patients are more difficult to treat because of a lower pain threshold. This problem results in internal and interpersonal vicious cycles (Figure 2). When dental problems are not treated in regular appointments, they trigger the use of emergency dental services intrinsically invasive and painful. These emotions make part of non cooperative behaviour of patients [19].

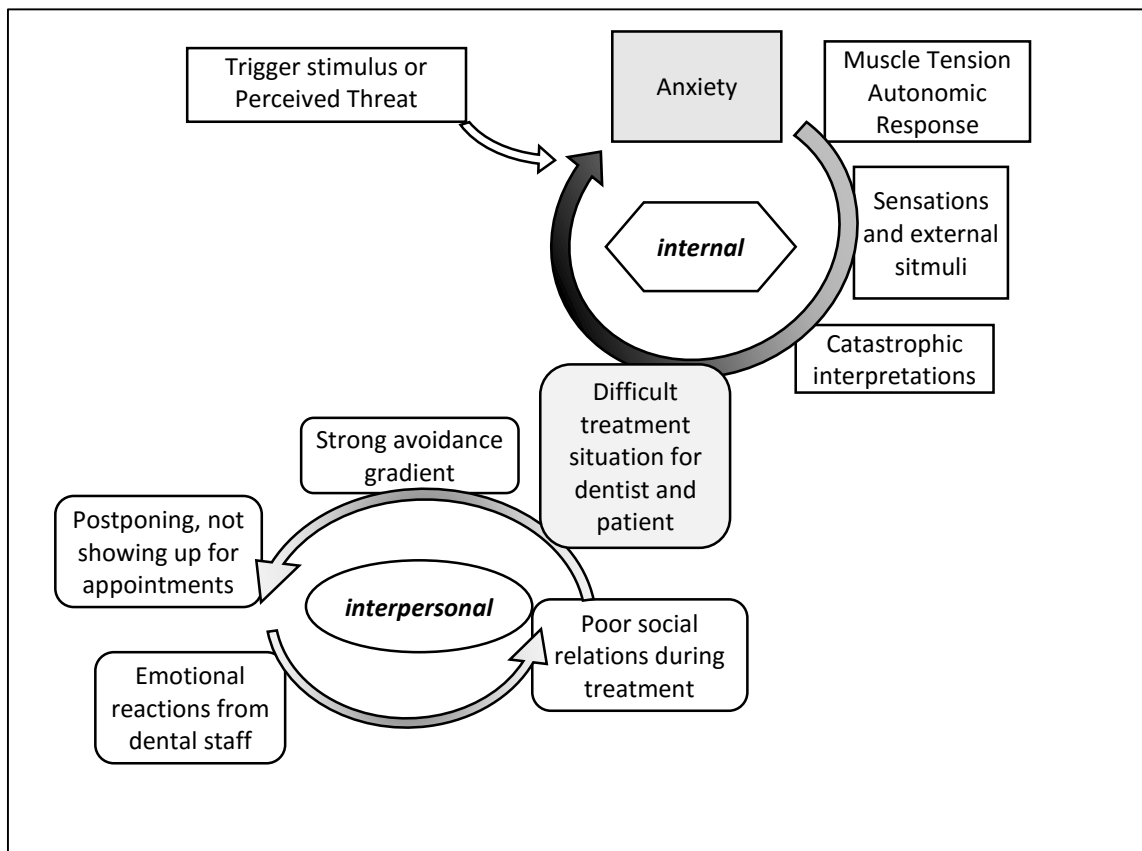


Figure 2 Dental fear relations: internal and interpersonal vicious cycles (adapted [20])

Higher levels of preoperative dental anxiety is the strongest predictor of reported pain experience during dental procedures [21]. Other results shows that anxious dental patients experience pain of higher intensity and of longer duration [22]. In child dentistry, dental behaviour management problems (DBMP) are common. DBMP are uncooperative and disruptive behaviours that result in delay or complete impossibility of treatment of patients. It is directly a view of the dentist and does not correspond to the child's point of view or the child level of dental fear and anxiety[23].

Psychological services for dentally anxious patients are not easy to find. So they prefer to avoid dentistry, while others only agree to referral for dental treatment under sedation or general anaesthesia which is more difficult to get and expensive. Access to dental services would improve if there was an increase in a united treatment with other psychological management of proven efficacy [24]. Stress is a response state where an environmental demand exceeds the natural regulatory homeostasis of an organism in unpredictable and uncontrollable situations. Patients with dental stress are at higher risk of oral problems. [25].

The Dental Fear and Anxiety (DFA) is both a barrier to oral health, and a challenge to find ways of controlling anxious patients. As a German study evokes even the most cruel human being can have fear of his personal dentist, as did Hitler[26]. In dental practice, anxious patients seldom go to the dentist. They only go when the pain is strong and does not disappear with medication. The benefits of helping these patients are equally good for all, patients and doctors.

In the concept of approach-avoidance conflict, a person may have two competing tendencies. One is that the patient knows the need for dental care and is motivated to approach a dentist. The other is the patient is fearful of going to the dentist and is avoiding the experience. It is an equilibrium: the farther away from the appointment, the more motivated the patient is. On the other hand, the nearer the appointment is scheduled, the stronger the feel of avoidance. This concept can help explain patients cancelling or not appearing for appointments. In this concept the solution should focus on lowering the avoidance barriers [4].

Patients have three major factors to develop fear and uncooperative behaviour: the pain stimulus, the dental vulnerability and a poor dentist performance. The dentist can adapt his performance during treatment to the patient needs, lowering the pain and uncooperative behaviour.

The pain is a complex phenomenon related to dental treatment. It emerges as the disease bypasses the sensory threshold and causes an anxiety indistinguishable from pain in acute situations. This state is influenced by previous experiences that occurred in the past. The interpretation of these conditions helps the construction of cognitive response factors like expectancy and predictability, as a strategy to overcome the experience of pain. The patient can react with verbal, physiological and behavioural responses. This has several consequences in the future when coping with new pain situations. Dental phobia is estimated to develop around 12 years old, so this disorder should be prevented when treating children and adolescents [27].

1.4 Emotions

Emotions are one of the least developed fields in human-computer interaction. This can be an implication of the rational logic intrinsic to computers, which contrast with the irrational logic nature of emotions. Even humans cannot fully agree what is the best definition of emotions. To be able to characterize emotion and distinguish from other states is a difficult problem. There is no consensus in modelling emotions. The concept of emotion and the analysis of emotions is an insoluble problem. An affective computing system, is concerned with recognizing , representing, giving feedback, and expressing emotion [28]. Emotions are part of an adaptive motivational system involved in establishing the behavioural reaction to environmental and internal events for the needs and goals of an animal [29].

Fear is an emotion that can be described in three components. One component is a distinct form of facial expression (raised eyebrows and tensed lips). Another component is the distinct physiological changes which includes an increase in the heart rate and in the skin conductance. The third component is the subjective feeling state of the individual. Fear is experienced as being frightened, nervous and apprehensive. Emotions are a different part of an integrated psychophysiological response system [30].

1.5 Ambient intelligence

As the hardware is becoming less expensive and getting smaller over time, there is a concept called Ambient Intelligence (AmI). AmI, developed by the Advisory Group of the European Commission's Information Society Technologies programme (ISTAG). ISTAG published in 2001 an holistic view of AmI, focusing in the science chain from research to the end user. AmI environments are automated aware environments applied in several places like homes, offices, hospitals, transports, and at some point, in private health environments like dental clinics. AmI theorizes a computing environment that allows human and computer interaction in a non-obtrusive way. AmI uses several types of artificial intelligence (AI) systems, like automation, computer graphics, ubiquitous computing and communication. The sensors, part of the automation systems, are used to measure the environment qualities. Biosensors can tap the human vital signs directly (invasive) as the standard sensors of heart rate, electrocardiogram or skin conductivity. Indirect (non contact or passive) biosensors work with non-invasive devices like charge-coupled device cameras (CCD)[31]. AmI environments are made of computers that autonomously setup their functionality determining their context from sensors input data. AmI design allows a better support interaction between humans and the environment.

As AmI can have several domains, the international conferences on AmI focus on certain promising tracks that include ambient assisted living, internet of things, ambient play and learning, smart buildings and learning, intelligent driving and data science

In human computer interaction (HCI) it is difficult to measure the “valence” of a state as compared to the “arousal” which may be gauged using biosensors. Most research focus on affective states that exist in a relatively short period of time and are related to a particular event, an object or action. Mood is different from emotion, and is viewed as a transient episode of feeling or affect. Moods are much longer and may last for some hours or even several days. Expressions like a smile or a frown can give more context information than physiological measurements. However, facial expression recognition is a computational method less developed than eye-gaze tracking, facial recognition and conversational characters [32]. Emotions are multi-modal aspects of human behaviour. There are a number of potential recognition methods such as speech, facial expression, gestures and physiological signs. An HCI system should also take in account the effectiveness of the system, the computational complexity, the degree of intrusion and the quality of the customization to the users. Bio sensors have advantages over cameras or microphones. The hardware size is getting smaller and can be incorporated in jewellery and wrist watches. Low light levels, or the user moving can make it difficult to do a proper facial expression recognition. Recognizing speech has also the drawback of the background noise interference.

There are two base models of labelling emotions: by subjective chosen words as with joy, fear, etc (discrete classification), or by having scales to classify emotions (multidimensional scales). The problem with discrete categories is the limited (mixed emotions) and culturally dependent choice of words. Alternatively, two common scales to categorize emotions are valence and arousal. Valence is the scale of the pleasantness of a stimulus and runs from the most negative emotion (unpleasant) to the most positive or pleasant affective state. Arousal or activation level operates from low to high arousal and refers to the intensity of an emotional response. This two-dimension model intersect and separate four quadrants. Two quadrants are in the negative valence side, one with low arousal (sadness) and one with high valence (anger), and the other two quadrants have positive valence, one with positive valence and low arousal (pleasure) and one with positive valence and high arousal (joy). Positive emotions are characterized by a lack of autonomic activation and this can be a reason for more research being done in negative emotions [33]. In this two dimensional model, fear and anxiety (distress) are in the quadrant with negative valence (misery) and high arousal or activity [34].

The body signs are monitored and measured with biosensors. In an emotional response, the equilibrium of the autonomic nervous system is unbalanced. This visceral

system mainly controls heart muscle, smooth muscle and exocrine glands. The involuntary nervous system is subdivided in a sympathetic branch responsible for the “fight or flight” response, the parasympathetic branch in charge for the “rest and digest” or “feed and breed” state, and the gastrointestinal branch.

Gathering good affective data is difficult with one dimensional waveforms. Even though microphones and cameras and digitizers are reliable and easy to use, on the other hand, it takes a good amount of effort to understand the technical factors that can influence a reliable and accurate good physiological signal from a sensor. The aspects of the data capture systems are not as reliable and are influenced by determinants like the subject washing the hands, how much gel is applied under an electrode (has to be isotonic), motion artifacts and the location where the sensor was placed [35].

The techniques used in evaluating bio signals include electromyography (EMG), skin conductance (SC), skin temperature, blood volume pulse (BVP), electrocardiogram (ECG) and respiration activity. EMG measures muscle tension related to activity and frequency under stress. SC measures the conductivity of the skin, which increases in stress stimulus, and help to differentiate between conflict, or anger and fear situations. This signal is influenced by external factors such as temperature and movement of the limb attached to the sensor, thus the need for reference measures and calibration. Skin temperature detects muscle tension as the tension makes vasoconstriction and lower surface skin temperature. It also depends on external factors and is a slow indicator of emotional status. BVP functions by measuring the flow of blood in the vessels by a photo sensor that assess the amount of reflected light (photoplethysmography). It can read vasoconstriction and heart rate. ECG gage the electrical conduction system and contractile activity of the heart. The sensors are normally put on the chest or on the arms and legs. It can evaluate the heart rate and the inter-beat intervals that determine the heart rate variability (HRV). A relaxes state has a low HRV, while a state of mental stress or frustration shows an increased HRV. Respiration sensors measure by a rubber band around the chest, the intensity and rate of breathing. Excitement like in anger/fear/joy has fast and deep breathing. Instead, if the breathing is rapid and shallow, indicates tension as in panic, fear or concentration. A relaxed state has a slow and deep breathing. However, in feelings of withdrawal, peaceful happiness or calm depression the person has a slow and superficial breathing. All these signals have features that can be used to train a neural network classifier. It can be applied to automatically assess the emotional state of a subject in terms of arousal and valence values, based on the classification of the monitored sensor data sets [36].

1.6 Stress management

Stress management is an important area of research in medical environments. The passive detection of the anxiety level of a patient during a medical procedure is helpful for the doctor to address and control the patient. The patient's fear if controllable can lessen the avoidance of the dental appointment and diminish the reported dental pain during the treatment.

Distraction is a technique to direct the patient attention away from the sensations or emotional reactions produced by a noxious stimulus. A distraction strategy technique has the intention to block awareness of the painful stimulus or its effects [37]. Fear is a learned behaviour, and for that reason it can be prevented and replaced with another conduct [38]. Distraction techniques will be more effective for mild dental anxieties. They are not as effective with serious anxious patients. The more common techniques use music (ambient or headphones), watching television and playing video games (on the ceiling). Virtual reality research yields good results using virtual reality. However these approaches could potentially disrupt or distract the doctor because it needs control and access to the distractors during treatment [39]. The stimulus intensity determines whether and when a distraction will occur. To evaluate the pain rating after a distraction, the rating should assess the cognitive component (thinking about the pain), the affective (distressing) component and the sensory (intensity, quality, duration and locus) component. This scale should have reliability, that is, similarity or consistency of descriptors between and within patients, and objectivity, referring to the degree of giving similar answers for the same descriptors [40]. Pain needs attention and, for instance, interacting with virtual reality devices, spends a substantial part of the finite attentional capacity [41]. The use of more sophisticated and immersive virtual reality technology is associated with a greater pain relief, due to the less available cognitive resources for processing pain [42].

1.7 Project's Goal

The project main goal is to determine the use of a skin conductance biosensor as a dental stress gauge. The objective is to validate the sensor to detect the arousal of the patient, in the context of dental anxiety.

A valid sensor can be used as an input for a future AI system. This system would collect the anxiety level of the patient during the dental procedure and, based on the readings of the sensor, try to lower patient anxiety by altering the surrounding environment. The clinical sampling will try to measure the sensors accuracy, precision and reliability in a dental setting. The Clinical Protocol will be processed in a dental environment to be executed as a real life situation.

The ideal expected result would be a robust sensor with significant correlation between the signal variation and the anxiety level of the patient. This result will be important to develop affective system based on sensors that gather biological data during dental treatments.

1.8 Motivation

A common source of stress for most dentists are dentally anxious patients. A dentist would be more confident and would take less time to treat a dental stressed patient if it had more control on patient anxiety. There are a great number of potential anxious patients not presently receiving care.

Being a dentist is in itself a challenging and stressful job. A less anxious patient decreases the stress for the doctor and staff. If a dentist can help the patient overcome this fear barrier, he would diminish the tension of dental practice and the risk of professional burnout.

A Dentist can feel incompetent and unsuccessful because he do not know how to treat very anxious patients. In these cases, Doctors do less quality dental work because of the circumstances and ultimately losing patience. After that, even if the patient is trying to cooperate he inevitably gives up, or is sent away.

In dental practice a good dentist is able to help people with dental anxiety or phobia and this can take his career to a new dimension. This equally will prevent occupational stress and improve the auxiliary staff performance. Therefore, instead of a drill, fill and bill situation, it could change to drill, smile and bill treatment.

A system that measures dental anxiety will eventually prevent iatrogenic dental phobia. All the dimensions and complex dynamics that occur in a dental treatment: acceptance, distraction, relaxation, acquired skill for pain tolerance and discomfort; are affected in a the future dental ambient intelligence office.

1.9 Overview of Dissertation

The project was executed with the collaboration of the Faculdade de Medicina Dentária of Universidade de Lisboa (FMDUL). The sensor applied in the clinical trial was owned by Lasige Laboratory from Faculdade de Ciências da Universidade de Lisboa (FCUL). The document has five chapters:

- The first chapter is the introduction. It focus on several aspects of dental anxiety. It includes an overview of dental pain in general, and the theoretical concepts associated. Focus in a new dilemma in quality of life linked with

Oral Health. Then it makes a clear definition of different terms used like fear, anxiety and phobia. Next it describes what is the relation of phobic patients and dental care. It continues with the informatics part introduction where Ambient Intelligence, emotions and human computer interaction are described in detail. It talks about the biological sensors currently used in affective computing. The first chapter ends with a section about stress management in dental care. It has also the project goal, the motivation for doing this type of work and this overview.

- The second chapter focus the related work and state of the art research in solving the detection and management of dental anxiety in dental office. It starts with dental anxiety scales used for measuring dental anxiety and fear. The next section emphasizes biosensor detection of anxiety with the research made using Skin Conductance. Then studies in ambient intelligence and emotional detection are described and evaluated. The last research concentrate in several ways of using distraction for effectively lower anxiety.
- The third chapter describes in detail the clinical sample protocol that follows the Guidelines for Good Clinical Practice of the International Conference on Harmonisation [43]. It starts with the general information that has the title and protocol standard information required. Next it explains the objectives and purpose of the clinical sample. The protocol continues with the methodological approach for the selection of subjects.
- The fourth chapter describes the results. It summarizes the statistical procedure and review of the data taken with the skin conductance sensor. Ends with the discussion of the results.
- The fifth chapter have the conclusions taken from this project. Afterward it refers to the possibilities of a system made with standard low cost technologies.

The references presents the bibliography used in this project.

The appendices enclose figures and tables for added reference for the dissertation chapters.

1.10 Disclaimer statements

Contributors: none; Funding: none; Conflicts of interest: none, Ethics approval: yes.

Chapter 2 **Related Work**

The variability in the response of the autonomic nervous system to an equal stimulus is called by psychologists autonomic as response stereotypy. However, this response has no unique pattern to fear. The individual response is extremely variable and non-context specific (e.g. anger and fear) [44]. This problem appears in the polygraph, a machine that uses the bio signals to detect deception or lies, in a mix of pseudoscience with interrogation techniques by a structured but unstandardized series of questions. Currently the polygraphs are used, mostly, in the United States Government and Police departments, to interrogate suspects and screen new employees. The instrumentation and recording of a polygraph includes sensors for respiration (thoracic and abdominal patterns), electrodermal activity (EDA), cardiovascular activity (blood pressure, pulse rate and amplitude) and motion. Bi-annually the instrument needs a manufacturer recommended calibration test [45]. The polygraph tries to infer deception through the analysis of physiological reactions to questions, and it is necessary that during each test the signals recordings be continuous and of sufficient amplitude to be readable by the examiner. So the polygraph is an instrument that proves that the task of measuring emotions is complex, and especially the measure of anxiety. Scientifically is not technically feasible yet. Therefore, the state of the art related research focus in reducing this difficult problem and considers parts of it, that nevertheless, are still interesting challenges.

Ambient Intelligence (AmI) is a concept developed by ISTAG (2001) for the use of artificial intelligence environments in a pervasive and unobtrusive way for supporting the activities and interactions of the users [46].

A future system of Ambient Intelligence that measures dental anxiety and (re)acts upon the environment should concentrate on two parts: dental stress management, and informatics. The related work of this project is centered on dental fear and anxiety, skin conductance, ambient intelligence and distraction.

2.1 Dental Fear and Anxiety

A general assessment of dental fear and anxiety is usually seen in the patient's body language. Anxious patients will not be still, they will have a higher respiration rate and present diaphoresis. It is important to ask for previous dental experiences. That will help to discover the comfort level of the patient and improve the doctor patient relationship [38]. Studies show that high anxiety during dental procedures tend to require longer treatment times and have longer discomfort in postoperative recovery[47].

Fear in dentistry can be divided in objective and subjective fear. Objective anxiety comes from experiences directly experienced by the patient. Objective fear originates from previous dental treatment (direct objective fear) or from other previous experiences

that occurred on other health environments as in different doctors or a pharmacy (indirect objective fear). When dental anxiety occurs by suggestion of bad experiences told by the patient parents, relatives or friends, the patient undergoes subjective anxiety. Subjective anxiety is encouraged not only by words, but also by facial expressions related to frightening stories told to the patient. This type of fear is more difficult to overcome because the dentist does not know what causes this anxiety. There are also other situations that condition a fear response, like family problems as divorces, born of a brother or sister (children) or deaths of relatives [48].

A high number of indices exist to measure dental anxiety since there is no agreement on the concepts of dental fear and anxiety and the best technique how they should be measured (Table 2) [49].

Table 2 Dental anxiety scales (adapted [49][50])

Dental anxiety scales	Origin	Scale items
Adult Scales		
Corah's Dental Anxiety Scale (DAS)	Corah and Pantera, 1968	4
Modified Dental Anxiety Scale (MDAS)	Humphris et al, 1995	5
Kleinknecht's Dental Fear Scale (DFS)	Kleinknecht et al, 1973	20
Dental Fear Assessment Scale (DFAS)	Rowe and Moore, 1997	31
Gatchel's 10-Point Fear Scale (FS)	Gatchel et al, 1983	1
Stouthard's Dental Anxiety Inventory (DAI)	Stouthard et al, 1993	36
Dental Anxiety Inventory Short Version (DAI-S)	Stouthard et al, 1994	9
Gale's Ranking Questionnaire (RQ)	Gale, 1972	25
Photo Anxiety Questionnaire (PAQ/FAV ²)	Stouthard et al, 1991	10
Hierarchical Anxiety Questionnaire (HAQ/HAF ³)	Jöhren, 1999	11
Fear of Dental Pain (FDP) questionnaire	McNeil and Rainwater, 1998	18
Hospital Scales		
Spielberger's State-Trait Anxiety inventory (STAI-S)	Spielberger et al, 1983	10
Hospital Anxiety and Depression Scale-Anxiety subscale (HADS)	Zigmond and Snaith, 1983	7
Child-specific		
Children's Fear Survey Schedule-Dental Subscale (CFSS-DS)	Cuthbert and Melamed, 1982	15
Modified Child Dental Anxiety Scale (MCDAS)	Wong et al, 1998	8
Frankl Behaviour Rating Scale (FBRS)	Frankl et al, 1962	1
Venham Picture Scale (VPS)	Venham, 1979	8
Facial Image Scale (FIS)	Buchanan, 2002	4
Morin's Adolescent's Fear of Dental Treatment Cognitive Inventory (AFDTCI)	Gauthier et al, 1991	23

² Foto Angst Vragenlijst in the original language (Dutch)

³ Hierarchischer Angstfragebogen in the original language (German)

There are several questionnaires to evaluate the Dental Fear. The Modified Dental Anxiety Scale (MDAS) has been selected in UK because it is simple and consists of only five questions on a Likert scale from “not anxious” to “extremely anxious”. The total score is a sum of all five items, ranging 5 to 25. When the sum is 19 or greater, it indicates a highly dentally anxious patient and possibly dentally phobic (Table 3)[51].

MDAS is quick to complete and widely used in United Kingdom surveys and clinical studies. It has evidence for validity and relates to other measures like Corah’s Dental Anxiety and is officially translated in several languages: www.st-andrews.ac.uk/dentalanxiety/scaletranslations/. MDAS works as a comparable screening tool due to a good acceptability in respondents and prevents raising anxiety in patients prior to the treatment.

Table 3 Interpretation of MDAS scale (adapted [52])

Score	Level of Anxiety
<11	Not anxious
≥11	Anxious
11-14	Moderately Anxious
15-18	Highly anxious
≥19	Extremely anxious

2.2 Electrodermal activity

Historically electrodermal responses (EDR) measurements started right from the animal studies of Luigi Galvani in 1791. Then a century after Féré in 1870s studied the skin resistance and the psychological state. Around a decade after Féré, a Russian physiologist Tarchanoff studied independently the correlation between electricity and emotion. Near the beginning of the 20th century Wilhelm Wundt a german physician and then Carl Jung a swiss psychiatrist, also developed protocols in this area. In the United States the Chicago police department began using in 1930s polygraphs as lie detectors that employed skin resistance and therefore was critical to defend its validity of the evidence presented in court [53].

EDR was referred in older literature as Galvanic Skin Response/Reaction/Reflex before the 70’s. EDR is controlled by the sympathetic division of the autonomic nervous system that activates the eccrine sweat glands. The sudomotor nerve activity causes sweat secretion and changes skin conductivity. Mathematically the sudomotor nerve activity can be considered as a driver, formed of a sequence of distinct impulses, which trigger a specific impulse responses.

EDR is stimulated by novel experiences, unexpected, intense, complex, emotionally arousing or personally significant. It is also triggered by the anticipation of significant stimuli. Electrodermal activity (EDA) varies with gender, age and race.

Impedance (ohm), or the ability to oppose electric flow, is the inverse of admittance. So, the admittance is a measure of how easily a material will allow a current to flow.

The bioimpedance describes the passive electrical properties of biological materials. This property of tissues translates in the use of simple techniques. These techniques require only the application of two or more electrodes for indirect transducing the physiological events. Tissue is composed of non-conducting cells with capacitive properties. Because of this, tissue cells have lower impedance with higher frequency electric currents. A capacitive tissue can store electrical charges. The impedance is the quality of opposing electric flow. The skin impedance is due to the presence of a stratum corneum. The impedance of the stratum corneum depends on its water content. The stratum corneum has a thick level of keratinized cells that form a barrier through which the current must pass[54] (Figure 3).

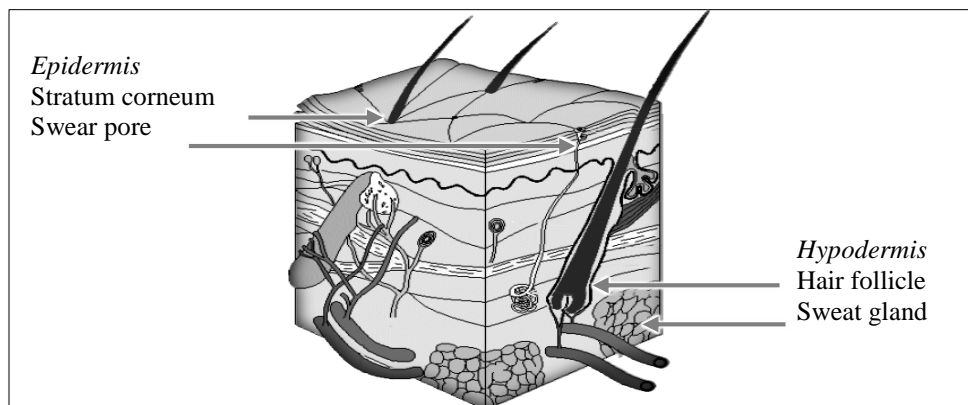


Figure 3 Skin anatomy involved in electrodermal activity (adapted [55])

The type of conductivity in the body is electrolytic for the presence of ions, i.e. Na^+ and Cl^- , in body fluids. The ionic flow differs from the electronic conduction of other materials such as metals, because it is combined with substance flow. This will make changes in the concentrations of the fluids near the electrodes. The electrode will start to suffer a process of polarization, which is a common source of error. With two electrodes the current carrying and signal pick-up are the same. At low frequencies (less than 1kHz) the result is dominated by the high impedance of the human skin. At high frequencies ($>100\text{kHz}$) the results are governed by deeper layer tissues [56].

The study of the electrical activity of the skin or electrodermal activity (EDA) is an old generic designation (1966) and broadly refers to passive and active electrical activity. EDA recordings that do not use an external current are *endosomatic* and the ones that use

an external recording are named *exosomatic*. Endosomatic recordings only use potential differences that originate in the skin itself (Figure 4).

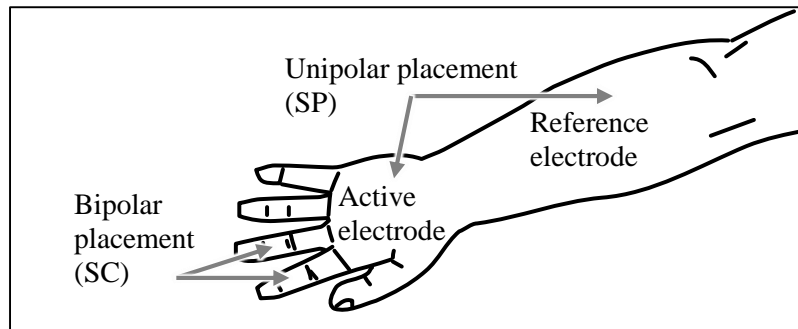


Figure 4 Measurement electrode sites of skin conductance (SC) and skin potentials (SP) (adapted [57])

The endogenous measurements highly correlate with exosomatic recordings. There is a high degree of correlation between skin impedance and skin potential, maybe because endosomatic EDA potential is produced by direct current streaming potentials in the sweat ducts. The skin impedance however could be due to the shunting effect of the filled sweat ducts and therefore only could return to tonic level when the ducts emptied [58].

When there is no sweat gland activity there is an absence of EDR signals. Skin conductance response (SCR) has a simpler curve form and has an initial rapid increase and a slower recovery [55].

Exosomatic readings can use a direct current (DC) or an alternating current (AC). If DC recordings keep the voltage constant are called skin *conductance*, whereas, if DC measurement keeps the current constant is called skin *resistance*. Skin conductance reflects the flow of the electrical current in the skin, whereas skin resistance replicates the electrical resistance of the skin. In the case of AC recordings, keeping the effective voltage constant is termed skin *admittance*, and maintaining the effective current constant is named skin *impedance* (Table 4).

Table 4 Electrodermal Reading Methods (adapted [57])

Electrodermal Response (EDR) Reading Methods	Abbreviations
<u>Endosomatic</u> (internal potential)	
Skin Potencial Level (Tonic or baseline)	SPL
Skin Potencial Phasic (Response or event)	SPR
<u>Exosomatic</u> (external current)	
<i>Direct Current</i>	
Skin Resistance Level (Tonic or baseline)	SRL
Skin Resistance Phasic (Response or event)	SRR
Skin Conductance Level (Tonic or baseline)	SCL
Skin Conductance Phasic (Response or event)	SCR

Alternating Current

Skin Impedance Level (Tonic or baseline)	SZL
Skin Impedance Phasic (Response or event)	SZR
Skin Admittance Level (Tonic or baseline)	SYL
Skin Admittance Phasic (Response or event)	SYR

The properties of the electrodermal system can be modelled as a system of resistive pathways through the skin. These pathways contain a set of serial and parallel resistors and capacitors (Figure 5). This circuit is formed by a variable resistor and capacitor in the stratum corneum, a fixed resistor in the epidermal barrier, a fixed low resistance of the dermis and also other horizontal resistances across the lower layers of the skin.

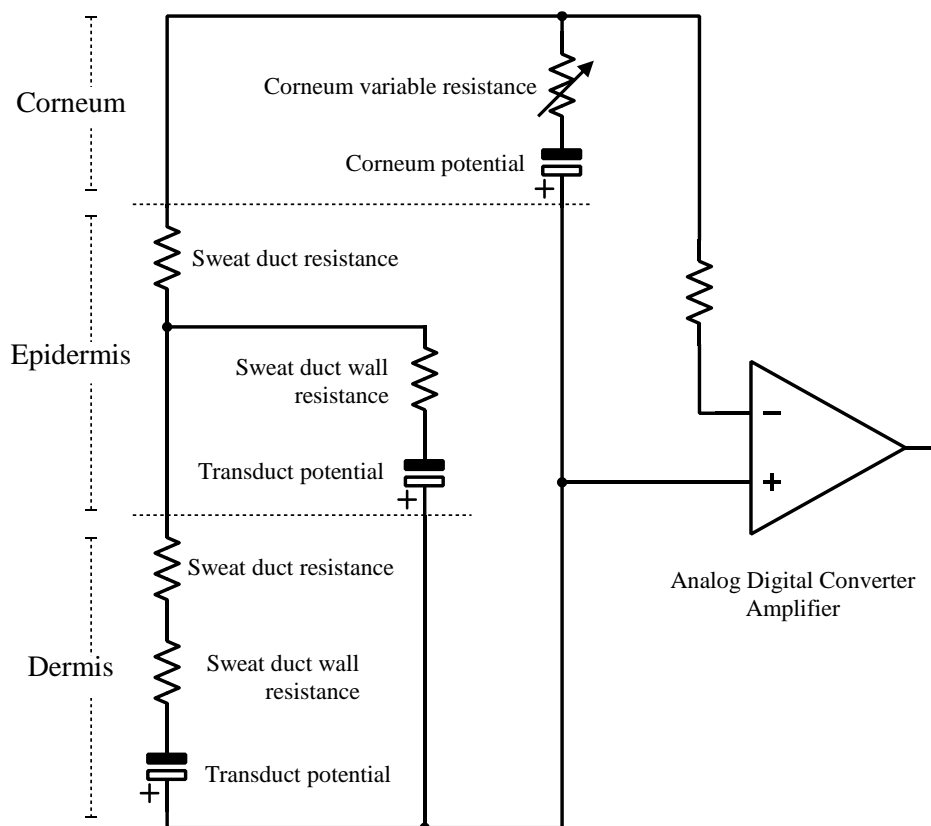


Figure 5 Simplified equivalent circuit of the resistive pathways of the electrodermal system (adapted from [53])

The basic circuit for measuring skin resistance is based on a constant current that goes through a series resistor and the skin producing a voltage drop. This change is then amplified. The series resistor is 10 to 50 times larger than skin resistance (SR). According to Ohm's Law, skin resistance (SR) equals the voltage (V) applied between the electrodes divided by the current (I) passed through the skin ($SR=V/I$). Skin resistance will be directly proportional to the voltage difference with I constant (see Figure 6 - A).

The reading of skin conductance (SC) is based on the same equation ($I=U \times SC$) in which there is a known constant voltage (U) applied to the skin and then the current is measured. The battery resistance R_e and the signal resistor R_x are smaller than skin resistance, so the output voltage drop across the electrodes change proportionally to the current I (see Figure 6 - B).

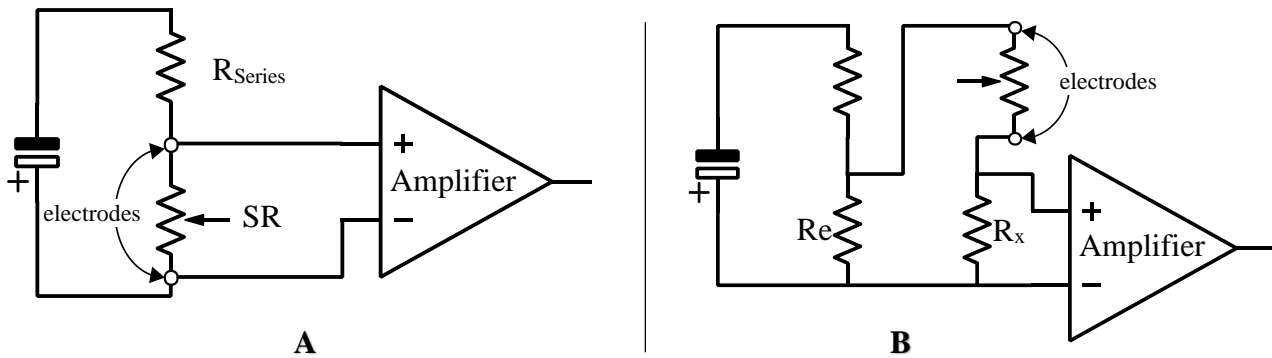


Figure 6 Basic circuits to measure exosomatic electrodermal response. A – circuit to measure skin resistance (SR), B – circuit to determine skin conductance (adapted from [59])

The exosomatic readings are monophasic, and react to a after a period known as latency. The stimulus will trigger a deflection correlating with an increase in SC or a decrease in SR (determined by the recording technique). SCR is measured in micro Siemens (μS), the unit of electrical conductance, and SRR is evaluated in kilo Ohm ($k\Omega$). Micromho is an old unit of conductance not currently used longer that spelled ohm backwards as mathematically conductance is the inverse of resistance.

SCL has a latency response that can go up to 5 seconds, i.e. it is a relatively slow-moving response compared with other responses like cortical potentials. The delay between the onset of the eliciting stimulus and onset of the response may vary from one to three seconds (rise time). The reason for the time delay is the addition of a chemical reaction with the electrical reaction. The chemical reaction usually is slower than the electrical response. When designing a study and to avoid the merging of the responses, it is important to consider sufficient time to recover. The evaluation of EDR amplitudes should be carefully executed. In Figure 7 there are two types of overlapping. When there are independent peaks there is method 1 and 2. When the curve has no distinct peaks it can be applied method 3 and method 4 (analogous of method 2). The important aspect to avoid bias is to fix only one criteria before the electrodermal analysis.

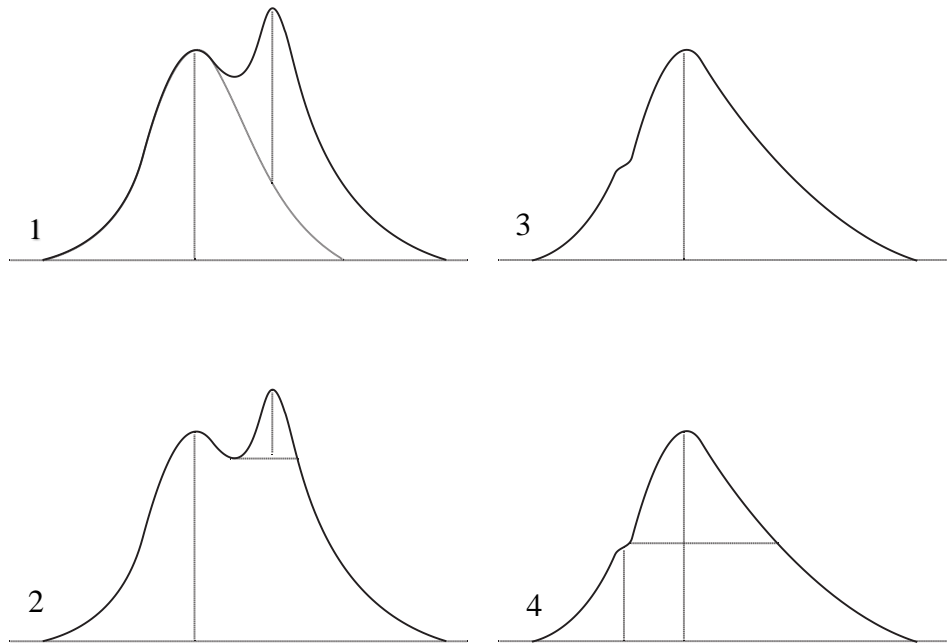


Figure 7 Evaluation methods for the overlapping of electrodermal responses (adapted [57])

The skin conductance signal is described with a slowly varying SC level which is superposed by bursts of phasic SCRs. The general interest is measure the amplitude of the phasic response to a known stimulus. Minima values are the onset and maxima is a peak. SCR latency is the time from stimulus onset to SCR onset. The amplitude is the difference of the SC values for onset and peak. The SCL can be estimated for intervals free of SCRs by average of SC scores in that interval. Non specific SCRs (NS.SCR.freq) can be assumed to be non specific tonic electrodermal electric currents.

In resting conditions there are phasic variations that cannot relate to an identifiable eliciting stimuli. These non specific electrodermal responses are associated with the participants arousal and belong to his EDA tonic level. To record the frequency of this non specific responses, there should be a baseline measure of EDA from two to five minutes. This permit to define a median threshold for NS.SCR.freq not lower than 4 times the sensor highest resolution. It is recommended that this will be around $0.05 \mu\text{S}$. This can detect people with high NS.SCR.freq. High NS.SCR.freq persons are called *labile* and people with low frequency are called *stabile* [60]. Labile persons are better at vigilance tasks and have a lower vigilance reduction over time than stabile persons. Skin hydration vary the skin resistance from 300-500 ohm in wet skin to 400 kohm in dry skin [61]. An ideal skin conductance response to a specific eliciting stimuli is depicted in Figure 8.

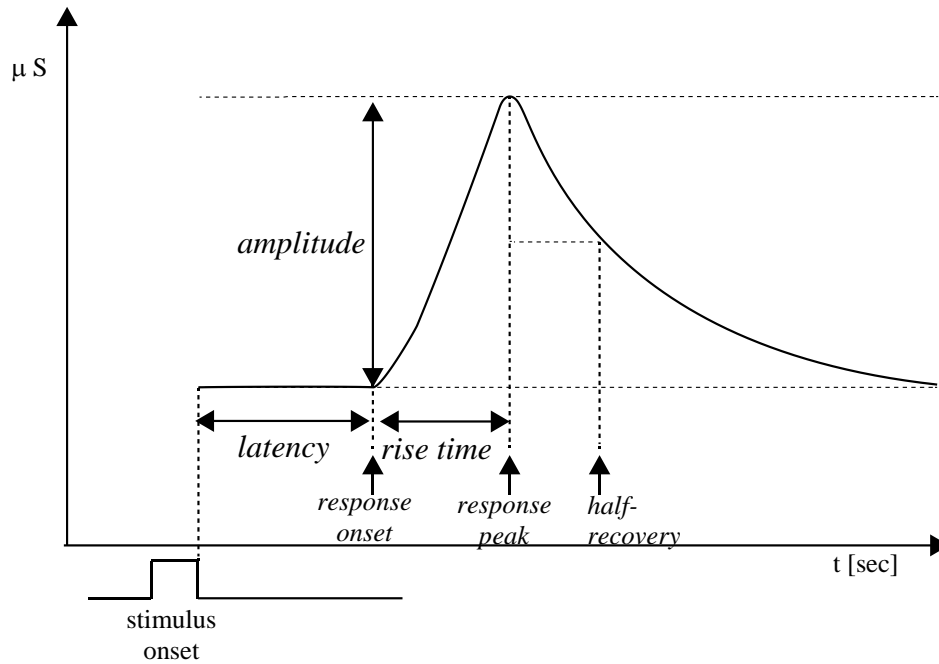


Figure 8 Ideal reading of a skin conductance response (phasic) (adapted [57])

The parameters of SCR measured are *amplitude*, *latency*, *rise time* and *half-recovery time*. The amplitude is the difference between baseline skin conductance at the time the response starts and the skin conductance at the peak of the reaction. Latency is the time between the stimulus and the start of the SC response. Rise time is the period between the response onset and the peak of the response. Half recovery time is the time between the top of the response and half of the amplitude to the peak (Table 5).

Table 5 Typical values of parameters measured in SC

Parameters	Typical Values
Skin Conductance Level Baseline (μS)	2-50 μS
Latency (s)	<4 s
Amplitude (μS)	variable
Rise time of the skin conductance response (s)	1-3 s
Half-recovery time (s)	2-10 s

Validity of SCR has several limitations. Skin electrical responses have habituation in that the responses decrease with continuous presentation. This may interfere with the testing of skin reactions. Skin conductance has also large individual differences as exist in labile and stabile persons [62].

Some artifacts can alter the reading of good event related responses. Sweat can be created in response to hot ambient temperature and can alter readings. Is difficult to isolate specific psychological responses since skin conductance can change by so many stimuli. For instance variations in respiration can alter heart rate and EDA [63]. Skin conductance response is also movement sensitive. The electrodermal response has little data differentiation among users in biometric tests [64]. To overcome this researchers can use a time frame window of response of 1 to 5 seconds, decreasing confounding spontaneous SCR in 50% from a spontaneous SCR rate of 7.5 per minute [55].

Skin potential is not affected on electrode area whereas skin conductance recording depend on electrode size [58]. The electrodes used in sensors should have minimal bias potential minimizing drift, must not polarize with the flow of current. Reversible Ag/AgCl (silver/silver chloride) disk electrodes are the most common used sensors with the standard diameter size of 8 to 10 mm used by approximately 70% of researchers [60].

In spite of more developed methods of tapping on neural activity as magnetic resonance imaging (MRI) and positron emission tomography (PET) skin EDA is still used because is easy to use discretely, reliably and also is reasonably cheap [65].

The eccrine sweat glands aid in the maintenance of body temperature and are ten times more dense on palmar skin of hands and feet. They act as a survival neural response system controlled via the autonomic nervous system. The three pathways controlling sweat gland activation are the premotor cortex descending through the pyramidal tracts, the hypothalamus of the limbic system and the reticular formation (cholinergic). The neurotransmitters to the sweat glands are acetylcholine instead of the normal sympathetic norepinephrine.

In general each sensor comes with its proprietary software, like, AcqKnowledge software in Biopac hardware (USA), Biotrace in Nexus Mind Meedia (Netherlands), LabScribe in iWorkx Systems (USA), Biograph infiniti in Procom (Canada), ProRelax from Mindlife (Israel) and Med-Storm from Med-Storm Innovation (Norway). To help analyze EDR data in psychophysiology the sensor data can be exported to Matlab. There are two main open source Matlab scripts for the automatic analysis of SC. Ledalab is a script to perform event-related analysis and report various parameters of phasic and tonic activity. It has two EDA analysis methods: the Continuous Decomposition Analysis (CDA) and the Discrete Decomposition Analysis (DDA). CDA performs a decomposition of SC data into continuous signals of phasic and tonic activity, by retrieving the signal characteristics of the underlying SNA. It is valuable for scoring of phasic and tonic activity. DDA does the decomposition of SC data into distinct phasic components and a tonic component by nonnegative deconvolution. This analysis is advantageous for the study of the SCR shape[66][67]. SCRalyse implements two causal models for analysis of

SC data: the General Linear Convolution Model for evoked SCR and the Dynamic Causal Modelling for non-linear models of SCR signals, like spontaneous fluctuations or anticipatory responses. The inference is made in a hierarchical statistic approach [68]. EDA has a wide number of applications focusing areas of attention, habituation, arousal, cognitive work and others [65]. The skin conductance sensors are well known in the psychological field, for the simple use and evaluation of emotional stress. It was discovered more than a century ago and it has several guidelines published [69]

2.3 Ambient Intelligence

The ambient intelligence AmI has gone several iterations from the first system proposed, and today has several synonyms like Ubiquitous Computing, Pervasive Computing, Embedded Systems, Context Awareness and Smart Environments [70]. At the Department of Radiology of the Advocate Lutheran General Hospital in Chicago, there is an AmI system that tries to relax children when taking a CT Scan [71]. In Mälardalen University of Sweden there was also a study of measuring the stress level of car drivers using the skin conductance level with the sensor attached to the user's clock watch [72]. In machine learning emotions are defined as short duration psychological and physiological state triggered by a affective stimulus.

In the field of affective computing there is a Portuguese project called Himotion [73]. This is a multimodal database system that does acquisition and processing of several type of human biometric data not only in the lab but also in natural setting. It includes electroencephalography (EEG 4-Ch), electromyography (EMG 2-Ch), electrodermal activity (EDA), electrocardiogram (ECG), blood volume pulse (BVP), skin temperature (TEMP) and respiration (RESP). These datasets and other support tools can be used in several areas like behavioral biometrics, cognition/attention detection and emotion analysis and are available to researchers upon request. Himotion project has detected an equal error rate in EDA signals between 10 to 35%. The authors acknowledge that the cognitive component is less researched in the field of human computer interaction and note that no state-of-the-art exist for computer based affective protocols.

Research in Japan report an exploratory study to develop a user affective interface with physiological data (skin conductance and electromyography) in real-time. The system use a Bayesian network and combine muscle activity with skin conductance. It compares the current mean signal values with baseline value. After a relaxation period the mean is calculated in five seconds segment. When SC is over 15-30% is classified as high and more than 30% as very high. The SC is reduced when the interface character gives empathy for a deliberately frustrated user. When the character interface does not have empathy for the user skin conductance is higher. This system's goal is to provide a

more natural, enjoyable and productive human computer interaction allowing user's emotions to be recognized by a computer [74].

Sensory adapted dental environment (SDE) is used to potentially reduce dental anxiety and maladaptive children behavior in dental clinic. In Israel a pilot study of a new therapeutic behavioral method to treat pediatric dental patients used SDE. SDE is based on Snoezelen multisensory adapted environment. This environment has a combination of light effects, relaxing music, vibration and aromas. Snoezelen settings are tested to calm individuals with developmental disability, Alzheimer's disease, traumatic brain injury and people suffering from anxiety, pain and unrest such as hyperactive children. The measured physiological and psychophysiological parameters on SDE improved significantly in a sample of 19 children between 6-11 years old. There was a mean difference of EDA in arousal and relaxation states of approximately 157 kOhms between regular and sensory adapted dental environment during dental hygiene care [75].

In general low cost sensors have low signal quality. Bitalino is a Lego type Arduino based Portuguese low cost multimodal hardware bio signals acquisition platform that is designed to have a good quality analog to digital signal conversion. It was tested in several parameters: SNR (signal to noise ratio), ENOB (effective number of bits, SINAD (signal to noise ratio plus distortion) and THD (total harmonic distortion). Bitalino connects via Bluetooth and has several sensors available including EDA [76]. Bitalino EDA default sampling rate is 1000Hz, has a cut-off filter of 3Hz and a sensibility of $[1-\infty]$ μ S.

Sensors are used as interfaces in smart space interaction. Smart space interaction is based on knowledge processing, interfaces and infrastructure. Infrastructure is the glue providing the hardware, the connectivity and the software. Interfaces such as I/O devices, sensors and actuators and software interfaces allow users to interact with resources. Knowledge processing specifies the semantics to the interaction. It has two integrated services: context modelling to form common concepts and context reasoning to understand the information captured via interfaces and build the rules and logic for making decisions [77].

In a study to aid the prevention of stress and burnout syndromes, the sensor data was mashed up in a star plot visualization [78]. The star plot diagram of physiological data gave a clear and objective insight on the subject state. The plot is a n dimensional representation of multivariate data. This type of representation is suitable for mobile and touch computers. The setup used sensors of EDA and BVP. BVP sensor was used to do power spectrum analysis, calculate heart rate variability and measure the fraction of consecutive normal sinus (NN) intervals that differ by more than 50 ms (pNN50) and the root mean square successive difference (RMSSD) for parasympathetic activity. In a

stressful state, the spider net alike plot gave a substantial graphic difference in EDA features (sum of energy, rising time and number of responses).

2.4 Distraction

Distraction can be done in several ways and is more effective when more human sensory organs are involved. The shift of the patient attention from the dental environment or dental pain is successful in reducing pain perception. Virtual reality, movies, video games can lessen more the patient discomfort than music. Virtual reality can be adapted and used when the patient is under treatment [79].

Hypnosis also distract by way of states of relaxation, suggestibility and trance [10]. Distraction is harder to maintain in longer dental procedures as it needs more focus on the distracter. Distraction is often used to reduce child's anxiety to make it possible to execute the dental treatment. This facilitates the control of behavior management problems boosting predictability and satisfaction both of the doctor and the patient [80].

Music is known to reduce anxiety, lower the heart rate and blood pressure, reduce pain perception and decrease chronic anxiety [81]. A study has demonstrated that distraction in the form of listening to tape-recorded instructions for relaxation with a soft-tone, slow and repetitive voice was effective in psychological stress reduction during dental treatment [82].

Study in the music field correlates frisson, with increases in skin conductance. Frissons are chills or thrills accompanied with piloerection and sensations of coldness and pleasure. Frissons theoretical explanation is that it can originate as negative natural subcortical valence effects transformed by cortical appraisal into positive experiences. This effects are resistant to habituation much like defensive responses [83]. Skin EDR is used in the "mood organ". The *mood organ* is a theory based on various signals collected to measure musical emotion [84]. It generates music that match the emotional state of the performer. Tests with emotionally powerful pieces of music revealed significant increases in skin conductance offering some support that emotional responses to music are equal do non aesthetic stimuli and music can be used to modify emotions [85].

Chapter 3 **Clinical Research Protocol**

The plan of the Clinical Research Sample is based on the Guidelines for Good Clinical Practice of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)[43]. The protocol also includes guidance from the templates of the Human Subjects Protection Office of University of Connecticut Health Center [86]. The research protocol is clearly enumerated and helps to focus on key ideas. It offers guidance through all phases of the study execution in a consistent outlook.

3.1 Title of the research

Evaluating a sensor of skin conductance to assess dental anxiety

3.2 Background

The problem of dental anxiety and treatment of dental anxious patients is not new. Nevertheless is still an actual and future problem. Patients suffer from previous devastating dental experiences and have natural fear of the unknown like children. In the extreme they show irrational phobias and emotional dental stress incapacitating going and being dentally treated. Dental anxiety is prevalent worldwide. Various scales and studies try to quantify this problem. The state of the art research show that 5-30% of the population has a high dental stress.

There is continuous need to design and help lighten this problem in everyday practice. Higher anxiety demands novelty ways of objectively quantify the dental anxiety of a patient. If it be used an inexpensive sensor to measure dental anxiety during treatment, is a good option to help detect and control the dental anxiety itself. There are pharmacological drugs that reduce this problem but ideally the best option should be in a non-pharmacological way.

There are several subjective scales but few or none mechanisms of imputing bio signals of the dental anxiety in dental setting. There is one experience with a multi sensorial distracting environment that use skin conductance as an assessment of physiological arousal states correlated with children anxiety [75]. If this input could be made active as an input to the environment that would be one crucial innovation.

3.2.1 Hypotheses

Dental anxiety in the general population can be successfully assessed with a quality skin conductance sensor while attending in-office dental treatment.

3.3 Research Question

Can this type of skin conductance sensor assess dental anxiety in dental patients attending dental treatment?

This is a PICOT research question with the objective of optimizing the chances of obtaining clinically helpful answers (Table 6).

Table 6 PICOT research question

Population	dentally anxious patients
Intervention (variable of interest)	anxiety level
Comparison	non anxious patientes
Outcome	dental anxiety
Time	duration of dental treatment

3.3.1 Goal

The goal of this study is to verify if this type of sensor is statistically valid to assess dental anxiety. By using this sensor in dental setting the doctor can assess noninvasively the dental anxiety state of the patient in specific stressful dental procedures.

3.3.2 Specific Objectives

The first objective is to make a meta analysis of bibliography of prevalence of dental anxiety in the population. The second objective will be the selection and test of the sensor. The third objective will be the completion of a MDAS survey. The fourth objective will be collecting the data of an EDR survey. The fifth objective will be the statistical analysis of the EDR data survey. The last objective will be writing the final complete report of the project.

3.3.3 Study Design and Procedures

The study will have two surveys. The first is the modified dental anxiety scale (MDAS) survey. The second is the EDA survey. Both the surveys will be conducted by the principal investigator. The milestone will be data analysis and statistics. The last milestone of the study with be writing the final report.

I. Step by step MDAS Survey

- i. Patient invited in the waiting room;
- ii. Patient accepts the informed consent;
- iii. Question 1 + answer Q1
- iv. Question 2 + answer Q2

- v. Question 3 + answer Q3
- vi. Question 4 + answer Q4
 - i. Question 5 + answer Q5
 - ii. Evaluator thanks the patient.

II. Step by step EDR Survey (Figure 9):

This survey should take place with 22-24°C ambient temperature. The temperature must not vary greatly during the experience.

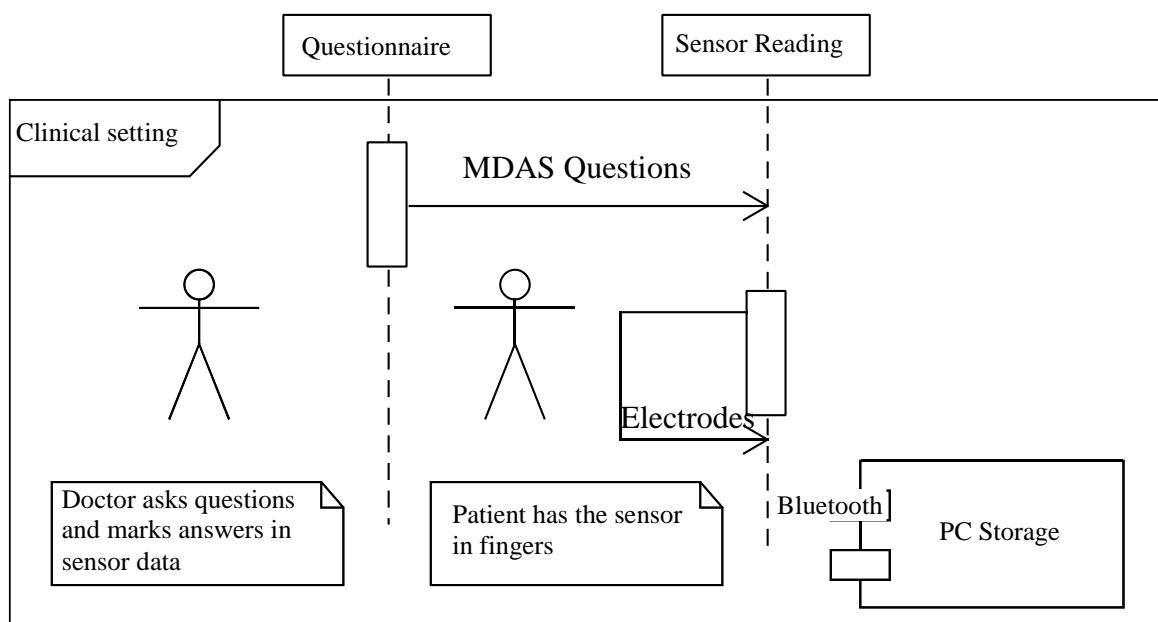


Figure 9 User case diagram of clinical sample trial

- i. Patient invited in the waiting room;
- ii. Patient accepts the informed consent;
- iii. Patient sits in dental chair;
- iv. Patient fingers are examined for skin problems or lesions;
- v. The EDA electrodes are carefully adapted to middle and index finger of the patient (avoiding too tight to not impair blood flow). It is indifferent which electrode is placed on which finger as polarity is not important;
- vi. Nexus 4 Bluetooth unit is turned on (green light);
- vii. EDA level is checked in the display software;
- viii. Recording of EDA started;
- ix. Question 1 + answer Q1 + marker Q1;
- x. Question 2 + answer Q2 + marker Q2;
- xi. Question 3 + answer Q3 + marker Q3;

- xii. Recording of EDA stopped;
- xiii. Recording is saved;
- xiv. Patient signed the informed consent;
- xv. Evaluator thanks the patient;
- xvi. Electrodes are disinfected;

EDA recording should follow some practical recommendations to minimize noise level and artifacts:

- i. The patient should stay still during recording;
- ii. He should keep the limbs relaxed;
- iii. He must not see the data until the experiment is over;
- iv. Should be done in a quiet setting;
- v. Should not be used alcohol to clean the fingers because it dehydrates the skin;
- vi. Check for electromagnetic fields (mobile phones);
- vii. Make a field test of the complete system before the trial.

III. MDAS survey step by step data analysis:

- i. Data screening;
- ii. Dataset aggregation;
- iii. Descriptive statistics in SPSS;
- iv. Inferential statistics in SPSS (optional);
- v. Statistical tests (optional).

IV. EDR survey step by step data analysis (Figure 10):

- i. Data screening with artifact cases cleaning;
- ii. Feature extraction and visual analysis: tonic level (mean), phasic responses or burts (amplitude), number of skin resistance responses
- iii. Dataset aggregation;
- iv. Dataset descriptive statistics in SPSS;
- v. Descriptive statistics in SPSS;
- vi. Inferential statistics in SPSS;
- vii. Statistical tests.

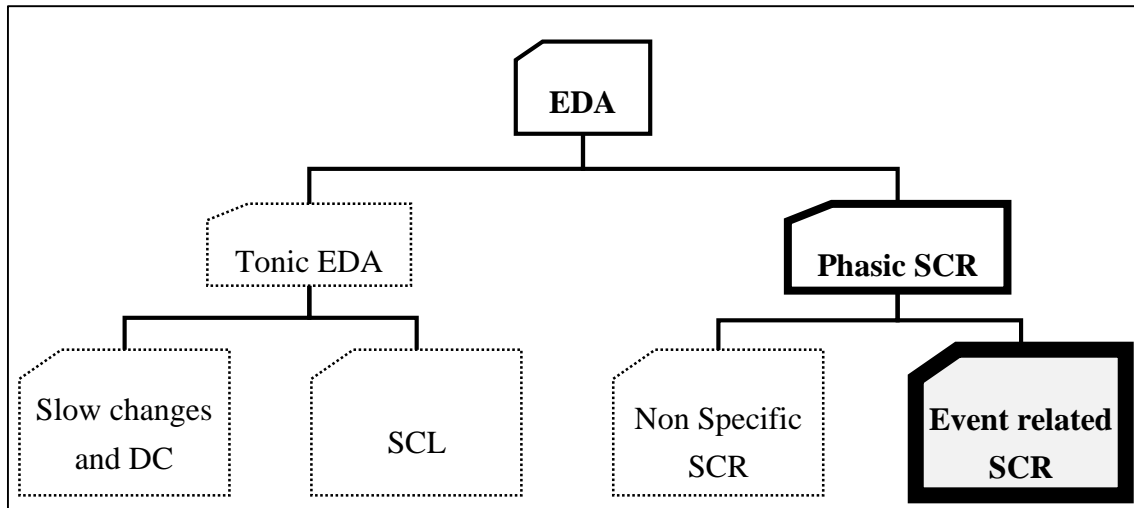


Figure 10 Signal decomposition feature extraction (adapted from [87])

Analyzing EDR data follows some theoretical recommendations:

- i. Each sweat gland is innervated by many fibers and vice versa;
- ii. Each sudomotor unit innervates a skin area of about 1.28 cm²;
- iii. Sweat glands vary in their activity and differ on activation thresholds;
- iv. Post ganglionic sudomotor fibers fire in bursts with a mean duration of 638 ms;
- v. A burst corresponds to a single skin SCR;
- vi. The SCR amplitude is linear related to the activity of the sudomotor nerver reflecting the frequency of actions potentials
- vii. The SCR amplitude is related to the number of active sweat glands;
- viii. Sudomotor activity is known to be modulated by respiration and cardiac cycle;
- ix. Only SCRs within 1 to 5 seconds after stimulu and within an interval minimum of 0.01 to 0.05μS should be accepted;
- x. If the recovery slope cannot be subtracted, the peak latency and the amplitude of the next SCR will be underestimated;
- xi. Independent of which pretreatment is chosen always use the same procedute within the experience.

3.3.4 Methods

Subjects

The population studied will be attending regular or first time appointments in Dental Clinic. The expected sample size calculated to get statistical significance is about 90 patients for $\alpha=0.05$ (see 3.3.6). This number has been drawn from the expected anxiety level in Portuguese population of about 20% [88] and the *a priori* power analysis. The

total expected duration of the subject’s participation is 10 minutes. The main inclusion and exclusion criteria is accepting the informed consent form. Other exclusion criteria in the second survey will be some physical impairment that forbids the use of the sensor. This study will accept any age, gender, ethnicity, social or health status.

Recruitment

The potential patients will be randomly selected in the waiting room. The study coordinator will approach the potential patients and ask them if they have interest in participating in a study. The coordinator or principal investigator will not use other relatives or colleagues to enroll the study. As the study will be made in urban areas there will be no neighbors/friends/parents pressure. It is not planned any kind of incentive, free treatment or remuneration, in any form. The patients cannot expect to pay for or get any payment for enrolling in the study.

Survey Instrument

The Modified Dental Anxiety Scale (MDAS) survey will be hard copy. The electrodermal response (EDR) survey will be a computer based test. The study will collect age, gender and reported anxiety level. Both the surveys are built on a Likert type rating scale. The surveys are validated and referenced in the literature [51], [89]. The MDAS will be completed in around 5 minutes. The EDR will take 10 minutes. There will be no identifiers or codes in the survey, i.e. data will be anonymous. Both surveys are done in person, i.e. not written by the patient but by the investigator. If the data is collected outside the main research location there will be probably some adjusting to address cultural sensitivities for the local context, i.e. outside the college / rural area.

The system hardware used for recording electrical skin activity is in Table 7.

Table 7 Sensor system package

Nexus 4*	Two dry disc electrodes (10 mm)
	SC/GSR Sensor unit
Notebook (PC)	Bluetooth Dongle
	Biotrace+ Software
* Photos of the hardware are in Appendix 5 - EDR Hardware	

The Nexus 4 is a four channel bio amplifier (Nexus-4; Mind Media, Netherlands) and has 24 bit A/D conversion with a resolution from 1/10 to 1/1000 μ S. In order to preserve the natural skin, no isotonic electrode paste was used in this experiment. SC data was sampled at 32Hz. It has built in a Bluetooth radio ver. 1.1 with 10 meter range. It features also an internal flash memory of 64 Mbytes. The system is made with carbon cables with active shielding to lower the environment and movement noise levels.

The SC/GSR Sensor uses two electrodes of 1 cm of diameter each with Ag/AgCl embedded in Velcro straps. The polarity of the finger electrodes is not important. The sensor is designed to measure minute relative changes in skin conductance. To detect the skin resistance it injects a very small DC electrical current through the electrodes and measures the electrical voltage difference.

There are some cautions with the unit. It cannot operate at a greater range than 10 meter and it should not be used with a cellular mobile phone within 30 cm of the unit to avoid excessive noise on the signal. The electrodes present a potential risk of cross infection on damaged skin. They should be single use, nevertheless, if not, they should be disinfected or gas sterilized.

The official equation is $U_{gsr} = U_{aux} * R_{skin} / (R_{int} + R_{skin})$. The stabilized voltage from power source of encoder (U_{aux}) is approximately 5V and the internal resistance of the sensor (R_{int}) is 6.6Mohms (1%). This linear function is not optimal because the baseline of skin resistance is approximately 200kohms to 1Mohms (1-5 μ S). The quantitative determination of skin conductance is influenced by other electrical noise that can also be measured. Nexus sensor has an offset feature to check for the high limit offset from poor electrodes reading, flat lining the signal. All the electrodes have active shielding that protects them from movement artefact. Since it works with batteries the electric power line low frequencies produced noise is avoided. There are no high or low pass filters that can could cause signal phase shifts or filter overflow because the signals go directly from the first amplifier to the analog digital converter (ADC).

3.3.5 Procedure

Research Location

The main research location for the survey is Faculdade de Medicina Dentária da Universidade de Lisboa. The permission letter signed by the college board Director is in Appendix 6 - Sample Clinical Trial Permission Letter.

Consent process

The patient consent will be signed in the end of the procedure. The consent will take place in the private room where the survey will occur. Only the principal investigator will be authorized to obtain consent from patients. The step by step process is: patient is asked if he has interest to enroll in a study. If he accepts the consent is read to the patient. Should questions arise they are promptly explained. Then the patient is asked to summarize what he understood, if it does not understand after three times the patient does not enter the survey. To enroll in the survey the consent must be accepted at the same time of the appointment, but there will be a time frame of 10 minutes for allowing the patient to think

it over and not being forced to accept or refuse the enrollment. The patient is voluntary and, if he wants, can quit anytime during the survey, with no penalization. The consent form is written in Portuguese because it will be used in a Portuguese language population.

Procedures

The eligibility for taking the surveys is based on accepting the formal consent to participate. All patients are randomly chosen for the surveys. The principal investigator will personally conduct the survey. The privacy concern of patients in the aspect of controlling others from accessing their personal data, does not exist since the surveys are anonymous.

Risks

The study poses no sociological, economical or psychological risks. However, one possible risk is the cross infection with the reusable electrodes. This is minimized and avoided with disinfection of the sensors. There will be also screening of the skin area where the electrodes are going to be placed prior to the test.

Confidentiality

As data acquired from this project does not have personally identifiable information, it will not arise any privacy problems. It is an anonymous study so the data will be kept private and in the most part manner safely guarded in a hard disk. However one cannot guarantee the risks of data steal, or data destruction by natural disasters.

3.3.6 Data Analysis

The statistical methods chosen to analyze the data will use the appropriate descriptive statistics for both the surveys. The population selected for the first survey will be randomly chosen from the clinic waiting room. The sample size will be around 50 patients with arbitrary clinical characteristics of age, gender and anxiety. This first preliminary survey is being oriented to give a general view of anxiety in this geographical area. The EDR survey will use inferential statistics to check if anxiety is significantly detected by the sensor chosen.

Several software packages will be used for data analysis. Sensor data will be obtained with Biotrace 4 (Mind Media). General numeric data organization will use Microsoft Excel and for exploratory and inferential statistical data analysis the investigator will use SPSS for Windows (IBM, Armonk, New York).and R (R Core Team).

The expected primary variables to be measured are age, gender, Likert type questionnaire score responses and EDR data (Table 11). EDR data will be, if needed post processed to normalize the expected variability inter and intra individuals[66]. One

should avoid some potential confounding variables such as body temperature and movement.

Table 8 EDR variables

Variables	Measure	SPSS (measure)
Age	Continuous Quantitative	Scale
Gender	Nominal Qualitative	Nominal
Likert Score	Ordinal Qualitative	Ordinal
EDR data	Continuous Quantitative	Scale

The calculated sample size and tests were executed with G*Power [90]. If the sample data fit statistical normality, Table 9 has the needed values and estimated sample size. If the assumption of normality in data fails the non parametric test used is described in Table 10. In statistical sample data normality the a priori power analysis result for α of 0.05 and a test power of 0.9 is an estimated sample size of 88 patients divided in two groups of 44 patients each.

Table 9 A priori power analysis for EDR (parametric)

t tests - Means: Difference between two independent means (two groups)		
Analysis:	<i>A priori: Compute required sample size</i>	
Input:	Tail(s)	Two
	Effect size d	0.7
	α err prob	0.05
	Power (1- β err prob)	0.9
	Allocation ratio N2/N1	1
Output:	Noncentrality parameter δ	3.283
	Critical t	1.988
	Df	86
	Sample size group 1	44
	Sample size group 2	44
	Total sample size	88
	Actual power	0.901

The calculated sample size for non parametric data is 92 with $\alpha=0.05$ and $1-\beta=0.9$ with the sample split in two groups of 46 patients each.

Table 10 A priori power analysis for EDR (non parametric)

t tests - Means: Wilcoxon-Mann-Whitney test (two groups)		
Options:	<i>A.R.E. method</i>	
Analysis:	<i>A priori: Compute required sample size</i>	
Input:	Tail(s)	Two
	Parent distribution	Normal
	Effect size d	0.7
	α err prob	0.05
	Power (1- β err prob)	0.90

	Allocation ratio N2/N1	1
Output:	Noncentrality parameter δ	3.280
	Critical t	1.988
	Df	85.854
	Sample size group 1	46
	Sample size group 2	46
	Total sample size	92
	Actual power	0.900

The plot for the power analysis has a critical statistic t of 1.99 (Figure 11).

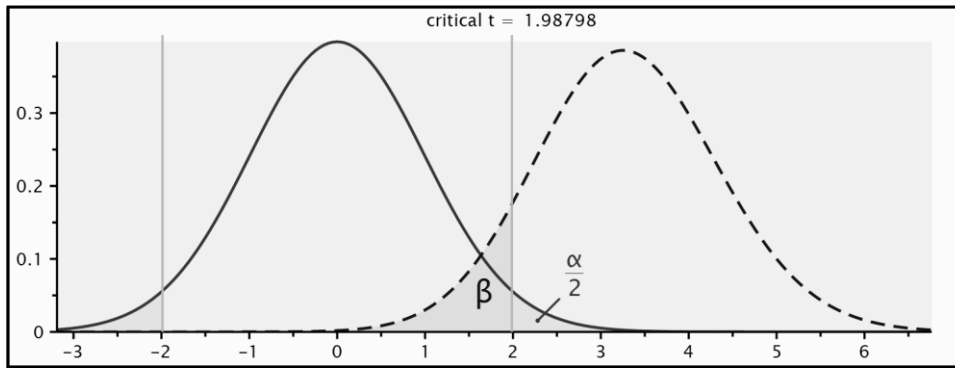


Figure 11 A priori power analyses expected plot for EDR survey

The Portuguese population has around 20% of highly anxious people so it is expected to use the non parametric test since there is a severe inequality expected between sample groups [88].

3.3.1 Timetable

The work plan and timetable for the project is in Table 11.

Table 11 Major Research Activities

Task	Subtask	Expected Time Duration
Bibliographical Research	Dental Anxiety	20h
=	Biosensors	10h
Protocol 1	Selection of Questionnaire 1	5h
Survey 1	Questionnaire 1	20h
Protocol 2	Selection of Questionnaire 2	5h
=	Selection of biosensor	10h
=	Test of biosensor	10h
Survey 2	Clinical Field Test	80h
Data analysis	Data Screening	10h
=	Statistical data analysis	50h
Report Preparation	Writing of dissertation	100h
Project Presentation	Thesis Defense	5h

3.3.2 Budget/Resources

The materials (hardware and software) needed for this research exist already in the Informatics Lab of the Faculty. The College will allow free use of the dental clinic space for the survey tests.

3.3.3 Dissemination

This project is part of the principal investigator dissertation on bioinformatics. Eventually it will be published online.

3.3.4 References

See References in .

3.3.5 Annexes

See questionnaire for MDAS in Appendix 1 - MDAS Questionnaire.

See consent form in Appendix 3 - EDR Informed Consent.

See questionnaire for EDR in Appendix 4 - EDR Questionnaire.

Chapter 4 Clinical Sampling

The study was done in two independent phases. The first stage was a Modified Dental Scale Anxiety (MDAS) survey, with 40 patients randomly selected in the waiting room of the Dentistry College clinics (FMDUL) that agreed to answer truthfully the MDAS questionnaire (Appendix 1 - MDAS Questionnaire).

The five questions of the MDAS Likert test were adapted from Portuguese modified dental anxiety scale [91] (Table 12). Table 13 lists the possible answers.

Table 12 MDAS Questionnaire

Order	Questions	Language: Portuguese (PT) / English (EN)
Q1	Sabendo que hoje tinha consulta no dentista como se sentiu ONTEM?	PT
1	If you went to your Dentist for TREATMENT TOMORROW, how would you feel?	EN
Q2	Hoje está aqui sentado na SALA DE ESPERA (à espera de tratamento), como se sente?	PT
2	If you were sitting in the WAITING ROOM (waiting for treatment), how would you feel?	EN
Q3	Se lhe estivessem prestes a BROCAR UM DENTE, como se sentiria?	PT
3	If you were about to have a TOOTH DRILLED, how would you feel?	EN
Q4	Se lhe estivessem prestes a fazer uma DESTARTARIZAÇÃO E POLIMENTO (limpeza), como se sentiria?	PT
4	If you were about to have your TEETH SCALED AND POLISHED, how would you feel?	EN
Q5	Se estivesse prestes a receber uma INJEÇÃO DE ANESTESIA LOCAL na sua gengiva, como se sentiria?	PT
5	If you were about to have a LOCAL ANAESTHETIC INJECTION in your gum, above an upper back tooth, how would you feel?	EN

Table 13 Possible answers of MDAS questionnaire

Answer	Likert Scale (English)	Likert Scale (Portuguese)	Score
A	Not anxious	Nada ansioso	1
B	Slightly anxious	Um pouco ansioso	2
C	Fairly anxious	Moderadamente ansioso	3
D	Very anxious	Muito ansioso	4
E	Extremely anxious	Extremamente Ansioso	5

The second stage was conducted with a different sample population. The data was obtained from an electrodermal response (EDR) survey performed in Faculdade de Medicina Dentária da Universidade de Lisboa (FMDUL), between January and April of 2011, and in a rural area dental clinic between October and November of 2013.

74 patients completed the EDR survey: 43 patients in the waiting room of FMDUL and 31 patients selected in the Dental Clinic. All the randomly selected patients agreed and signed the informed consent (see Appendix 7 - EDR Informed Consent).

The EDR survey was approved with some minor amendments by college Director, meaning that all ethical considerations for the research with human patients were fulfilled.

The sensor for EDR survey was based on several criteria. The sensor should:

- i. not disrupt the general dentistry procedures;
- ii. be robust with patients regardless of gender and age;
- iii. be reliable;
- iv. not require any calibration;
- v. be wireless;
- vi. be cost-effective;
- vii. be easy to clean and disinfect;
- viii. have an open interface to acquire the raw data in realtime.

After the sensor was selected, there was a field test. A sample measure was taken to verify that the system worked. The sensor passed.

The EDR questionnaire chosen was adapted from a previous similar study [89] (Table 14). Table 15 lists the possible answers.

Table 14 EDR Questionnaire

Order	Questions	Language: Portuguese (PT) / English (EN)
P1	Como se sente em relação à injeção de anestesia durante a consulta?	PT
Q1	How do you feel when you are receiving a local anaesthetic injection during treatment?	EN
P2	Como se sente em relação ao tratamento de desvitalização?	PT
Q2	How do you feel of doing root canal treatment?	EN
P3	Como se sente em relação ao barulho de brocar um dente durante a consulta?	PT
Q3	How do you feel when you hear the drill noise?	EN

Table 15 Possible answers of EDR questionnaire

Answer	Likert Scale (English)	Likert Scale (Portuguese)	Score
0	Don't Know	Não sei	1
1	Not anxious	Nada ansioso	2
2	Slightly anxious	Um pouco ansioso	3
3	Fairly anxious	Moderadamente ansioso	4
4	Very anxious	Muito ansioso	5

As the patient was at rest and did not need the dominant hand for any activity during the EDR survey the placement of the electrodes was indifferent. Nevertheless if the dominant hand had more calluses, thicker outer skin levels or other barriers that could

disrupt the fingerplates connection, the non-dominant hand was chosen. Also, poor EDR reading could happen if a patient had oily skin or had put hand cream and the electrodes could not stick to the skin.

4.1 Results MDAS

The Modified Dental Anxiety Scale sums all the responses to get a score. However the scoring procedure for MDAS is controversial. MDAS authors current cut-off for very dentally anxious is 19 or above. However for this study it was used a cut-off of 17 or above for grouping anxious patients. The MDAS authors acknowledge that 19 was previously selected on empirical grounds to provide greater confidence in interpretation of the score. Other scale measures like Corah's scale cut-offs may vary between 13 and 15. Nonetheless MDAS was tested on a large English community sample. However as the concept of dental anxiety is a continuum and the choice to score above a certain level is a clinical decision MDAS authors advert that the measure is an approximation and should not be a hard and fast judgement. Also, it may be that true phobic patients do not answer truthfully to the anxiety questionnaire, thus making it difficult to determine real dental phobia. For all these factors the cut-off level chosen for anxiety in this survey was equal or above 17.

Figure 12 has the percentage bar diagram of MDAS partial question scores percentages related to anxious and not anxious groups.

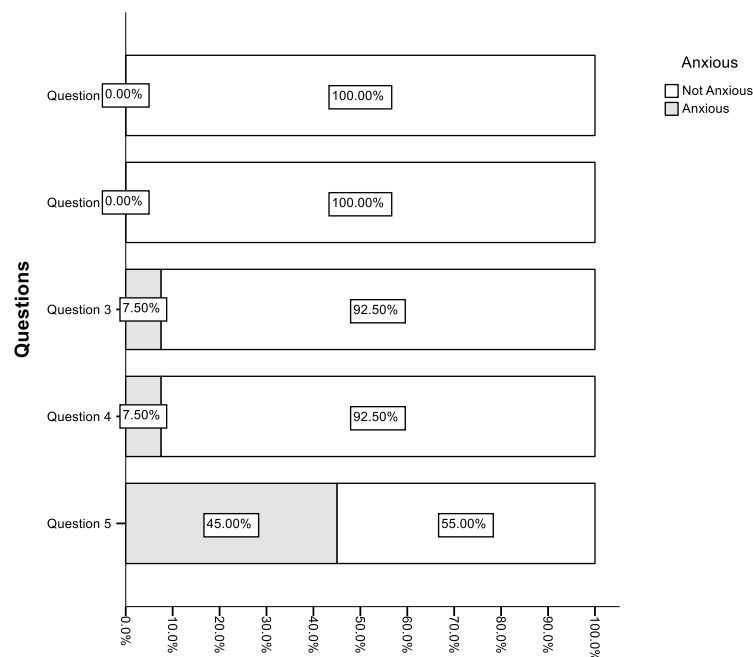


Figure 12 Results from the MDAS questionnaire

Table 16 has the total 40 patients MDAS scores percentages.

Table 16 MDAS scores

	Frequency	Percent
<i>Not Anxious</i>	36	90%
<i>Anxious</i>	4	10%
Total	40	100%

Table 17 has the MDAS scores descriptive statistics with mean, median, mode, variance and limits.

Table 17 MDAS Descriptive Statistics

N	Mean	Median	Mode	Std. Deviation	Variance	Range	Minimum	Maximum
Valid 40	12.3	12	12	2.82	7.96	11	8	19

The frequency score plot of all the MDAS questionnaire answers is in Figure 13

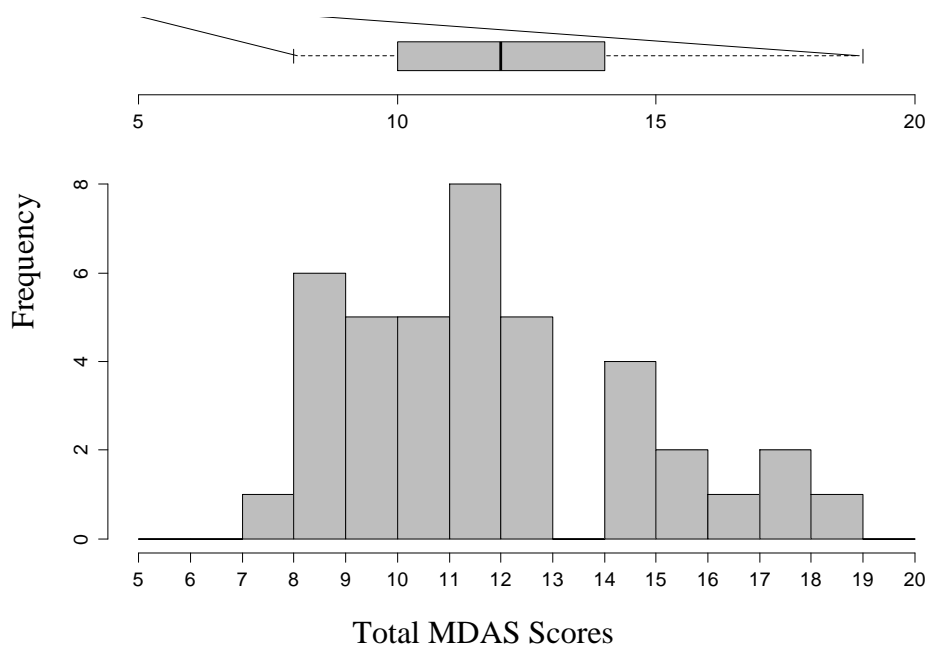


Figure 13 Frequency of scores in the answers of MDAS questionnaire

Table 18 lists the results of anxiety divided by gender.

Table 18 MDAS Crosstabs

Gender * Anxious Crosstabulation					
		Anxious			Total
		Not Anxious	Anxious		
Gender	Female	Count	20	1	21
		% within Anxious	55.6%	25.0%	52.5%
	Male	Count	16	3	19
		% within Anxious	44.4%	75.0%	47.5%
Total		Count	36	4	40
		% within Anxious	100.0%	100.0%	100.0%

Figure 14 has the box plot for MDAS scores vs gender. The median value is equal between genders. Males have more variability in the data

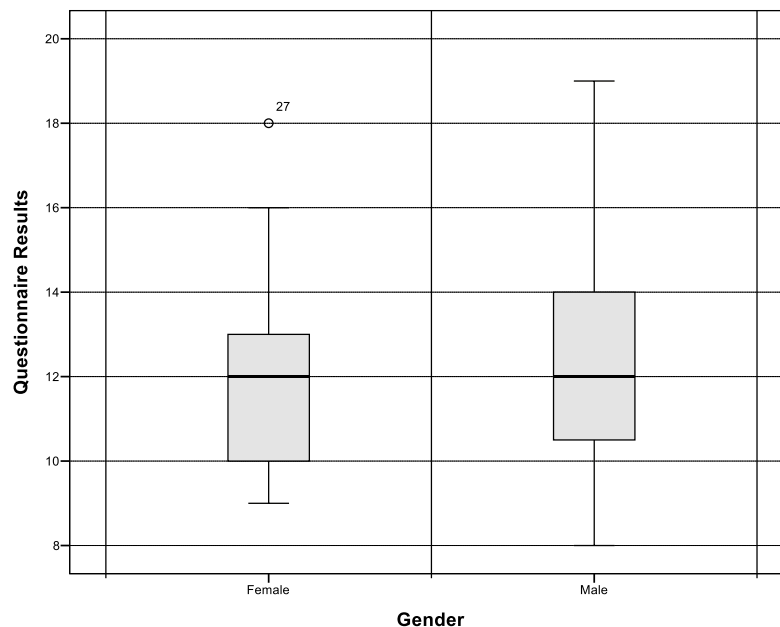


Figure 14 Boxplot of MDAS Scores vs Gender

The table of results of MDAS questionnaire is in Appendix 2 - MDAS Dataset.

4.2 MDAS Statistical analysis

The software used for statistical analysis was SPSS Statistics for Windows version 22 (Armonk, NY, IBM Corp). Some plots were made with R (R Core Team).

The hypothesis was: Does anxiety mean scores differ between genders?

The test of normality chosen for the distribution of MDAS scores was Shapiro-Wilk (S-W). The sample population had in each group $n < 30$. Shapiro-Wilk test has $p = 0.131$ for female and $p = 0.117$ for male genders, indicating that MDAS scores have normal

distribution (Table 19). As p value is over 0.05, the null hypothesis of both samples having a normal distribution is not rejected.

Table 19 MDAS Total score - Test of Normality

Gender		Shapiro-Wilk		
		Statistic	df	Sig.
Questionnaire Results	Female	0.929	21	0.131
	Male	0.921	19	0.117

As MDAS score is ordinal quantitative variable, the chosen statistical test was Mann-Whitney U (Table 21 and Table 21).

Table 20 Mann-Whitney U Test Ranks for MDAS answers

Ranks				
	Gender	N	Mean Rank	Sum of Ranks
Questionnaire Results	Female	21	20.55	431.50
	Male	19	20.45	388.50
	Total	40		

Table 21 Mann-Whitney U Test Results for MDAS answers

Test Statistics ^a	
	Questionnaire Results
Mann-Whitney U	198.500
Wilcoxon W	388.500
Z	-.027
Asymp. Sig. (2-tailed)	.978
Exact Sig. [2*(1-tailed Sig.)]	.979 ^b
Exact Sig. (2-tailed)	.984
Exact Sig. (1-tailed)	.492
Point Probability	.005
a. Grouping Variable: Gender	
b. Not corrected for ties.	

The test output is $p > 0.05$. There is no sufficient statistical evidence to reject the null hypothesis. Mean anxiety scores between genders are not statistically different.

4.3 Results EDR

The scoring procedure for the EDR questionnaire was calculated after splitting the group for each question. The anxious patients were selected with scores equal or above score 4. Figure 15 has the percentage bar diagram of EDR partial question scores percentages related to anxious and not anxious groups based solely on questionnaire answers.

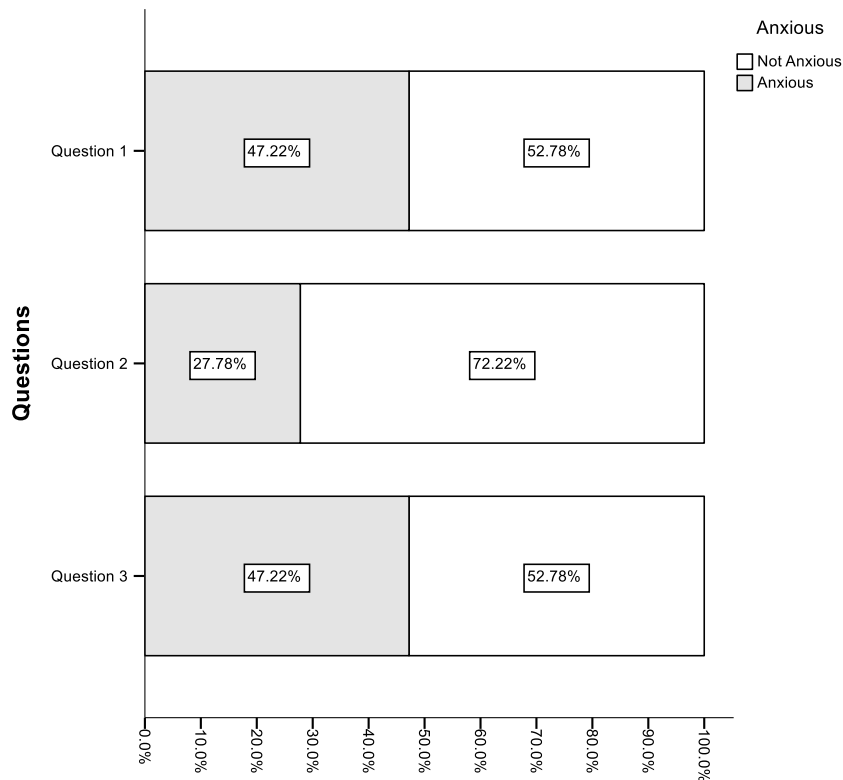


Figure 15 Percentages of Anxious vs not anxious in EDR questionnaire scores

Table 22 has the descriptive statistics for the raw skin resistance values taken in the study with Biotrace. These values aggregate all the dataset and are in kOhm.

Table 22 Sensor raw values statistics of skin resistance in EDR survey

<i>kOhms*</i>	Total	Q1 SRR	Q2 SRR	Q3SRR
average	794.872	792.325	765.64	757.3929
median	595.11	594.105	618.41	613.535
variance	11577.6	810.977	198.241	829.0503
minimum	103.27	103.27	121.66	116.55
maximum	2563.21	2393.1	2376.75	2401.92
range	2459.94	2289.83	2255.09	2285.37
1 kOhm = (1/kOhm * 1000) μS				

The process of normalizing the values for all the patients is in Table 23. The numeric values used from the dataset were: SRR (skin resistance response), mean of the SRR and standard deviation of SRR.

Table 23 Sensor normalized values calculation

Amplitude*	SRR – Mean (SRR)
SRR normalized*	Amplitude / Standard deviation (SRR)
*Values calculated for each row of the dataset (each patient)	

Table 24 provides the descriptive statistics of skin resistance normalized values of patients grouped by question.

Table 24 Sensor normalized values of skin resistance from EDR survey

		Question Q1	Question Q2	Question Q3
ANXIOUS	n	21	20	34
	mean	-0.967	-0.291	-0.987
	min	-2.139	-2.092	-3.264
	max	1.957	1.496	2.000
	SD	1.037	1.279	1.090
NON ANXIOUS	n	51	52	38
	mean	-0.467	-0.506	-0.536
	min	-3.498	-9.073	-6.338
	max	1.631	1.959	1.820
	SD	1.236	1.813	1.536

Table 25 contains question 1 descriptive statistics.

Table 25 Question 1 descriptive statistics

Q1 Skin Resistance Normalized	Non Anxious	Mean	-0.467
		Median	-0.725
		Variance	1.527
		Std. Deviation	1.236
		Minimum	-3.498
		Maximum	1.631
		Range	5.129
	Anxious	Mean	-0.967
		Median	-1.286
		Variance	1.075
		Std. Deviation	1.037
		Minimum	-2.139
		Maximum	1.957
		Range	4.095
Skewness	1.904		
Kurtosis	3.147		

Figure 16 has the boxplot for question 1. Median value and variability is higher in non anxious group.

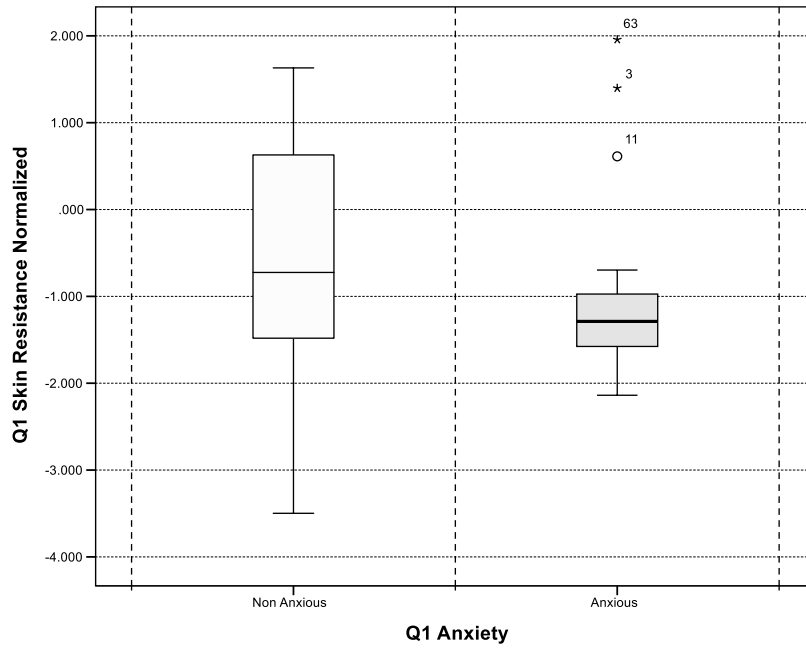


Figure 16 Question 1 – Boxplot

Table 26 lists question 2 descriptive statistics.

Table 26 Question 2 descriptive statistics

Q2 Skin Resistance Normalized	Non Anxious	Mean	-.506
		Median	-.680
Variance	3.285		
Std. Deviation	1.813		
Minimum	-9.073		
Maximum	1.959		
Range	11.032		
Skewness	-1.939		
Kurtosis	8.527		
	Anxious	Mean	-.291
	Median	-.425	
	Variance	1.636	
	Std. Deviation	1.279	
	Minimum	-2.092	
	Maximum	1.496	
	Range	3.588	
	Skewness	.080	
	Kurtosis	-1.762	

Figure 17 shows the boxplot for question 2. The median value is higher in anxious group and the variability is very similar.

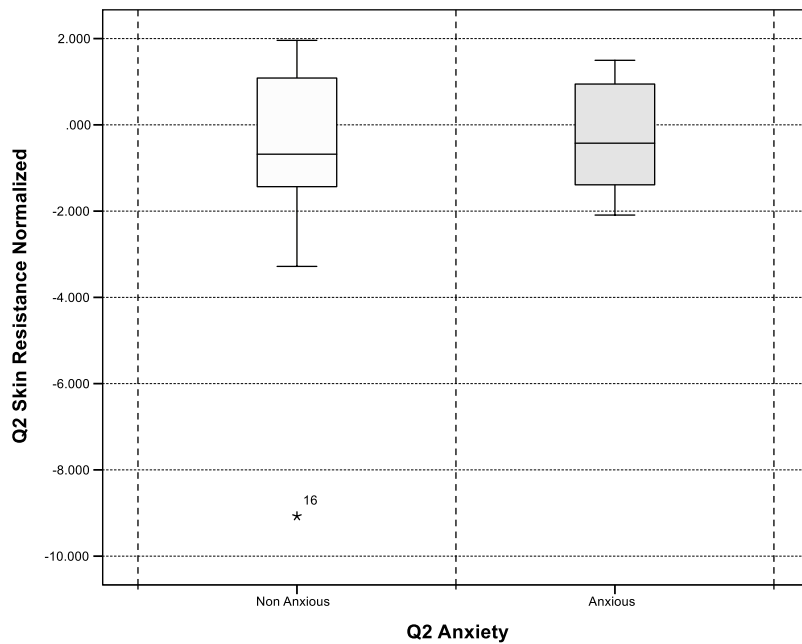


Figure 17 Question 2 – Boxplot

Table 27 enumerates question 3 descriptive statistics.

Table 27 Question 3 descriptive statistics

Q3 Skin Resistance Normalized	Non Anxious	Mean	-.536
		Median	-.869
Variance		2.358	
Std. Deviation		1.536	
Minimum		-6.338	
Maximum		1.820	
Range		8.158	
Skewness		-1.193	
Kurtosis		4.212	
Anxious	Mean	-.987	
	Median	-1.131	
	Variance	1.189	
	Std. Deviation	1.090	
	Minimum	-3.264	
	Maximum	2.000	
	Range	5.264	
	Skewness	.983	
Kurtosis	1.721		

Figure 18 contains the boxplot for question3. Median values of measured SRR are similar. Anxious population has less variability.

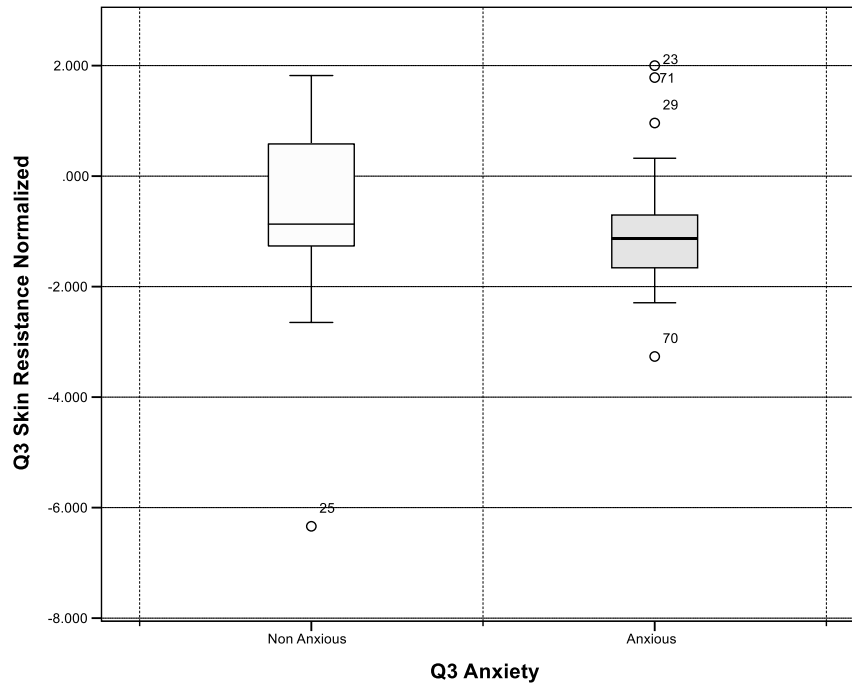


Figure 18 Question 3 – Boxplot

The table of results of EDR field clinical sampling are in Appendix 8 - EDR Data.

4.4 EDR Statistical analysis

The hypothesis tested was: is there a significant difference between anxiety level measured with the questionnaire scale and the anxiety level determined by the sensor skin resistance response? After testing for questionnaire scores distribution normality, the statistical non-parametric test chosen was the Mann-Whitney U test with $\alpha < 0.05$. MDAS scores and SRR values are independent variables.

During the exploratory data analysis some very extreme values were found. This values (SRR) can be artifacts related either to the sensor or to the patient. It was used a known rule of outlier labelling. The outlier was found by making the difference between third quantil and first quantil plus a constant of 2.2 (Table 28) [92].

Table 28 Statistics after Outlier Labelling

	N	Mean	Std. Deviation	Minimum	Maximum	Percentiles		
						25th	50th (Median)	75th
Q1 Skin Resistance Normalized	70	-0.679	1.146	-3.498	1.631	-1.520	-1.095	0.199
Q2 Skin Resistance Normalized	71	-0.325	1.330	-3.282	1.959	-1.425	-0.678	1.081
Q3 Skin Resistance Normalized	69	-0.745	1.118	-3.264	1.820	-1.460	-0.966	0.047

After the outlier labelling rule applied, the resulting dataset was tested for distribution normality. As every anxious group had $n < 30$, the chosen test was Shapiro-Wilk (Table 29, Table 30 and Table 31).

Table 29 Question 1 - Test of Normality

	Q1 Anxiety	Shapiro-Wilk		
		Statistic	df	Sig.
Q1 Skin Resistance Normalized	<i>Non Anxious</i>	.951	51.000	.035
	<i>Anxious</i>	.753	21.000	.000

Table 30 Question 2 - Test of Normality

	Q2 Anxiety	Shapiro-Wilk		
		Statistic	df	Sig.
Q2 Skin Resistance Normalized	<i>Non Anxious</i>	.821	52.000	.000
	<i>Anxious</i>	.877	20.000	.016

Table 31 Question 3 - Test of Normality

	Q3 Anxiety	Shapiro-Wilk		
		Statistic	df	Sig.
Q3 Skin Resistance Normalized	<i>Non Anxious</i>	.889	38.000	.001
	<i>Anxious</i>	.923	34.000	.019

Question 1, question 2 and question 3 anxiety scores have Shapiro-Wilk tests with $p\text{-values} < 0.05$, so the null hypothesis of question scores following a normal distribution is rejected. There is statistical evidence that question 1, 2 and 3 scores do not have normal distributions.

Table 32 and Table 33 have question 1 scores Mann-Whitney test results.

Table 32 Question 1 scores - Mann-Whitney U Test (Ranks)

	Q1 Anxiety	N	Mean Rank	Sum of Ranks
Q1 Skin Resistance Normalized	<i>Non Anxious</i>	51	39.098	1994
	<i>Anxious</i>	19	25.842	491
	Total	70		

Table 33 Question 1 scores - Mann-Whitney U Test (Statistics)

	Q1 Skin Resistance Normalized
Mann-Whitney U	301.000
Wilcoxon W	491.000
Z	-2.423
Asymp. Sig. (2-tailed)	.015
Exact Sig. (2-tailed)	.015

For question 1 there is statistical evidence to reject the null hypothesis with $\alpha < 0.05$. P value is .015. Group distribution in question 1 are significantly different. There is statistical evidence to assume the sensor can correctly assess dental anxiety in question 1.

Table 34 and Table 35 contain the results for Mann-Whitney U test for Question 2.

Table 34 Question 2 scores - Mann-Whitney U Test (Ranks)

	Q2 Anxiety	N	Mean Rank	Sum of Ranks
Q2 Skin Resistance Normalized	<i>Non Anxious</i>	51	36.235	1848
	<i>Anxious</i>	20	35.400	708
	Total	71		

Table 35 Question 2 scores - Mann-Whitney U Test (Statistics)

	Q2 Skin Resistance Normalized
Mann-Whitney U	498
Wilcoxon W	708
Z	-.153
Asymp. Sig. (2-tailed)	.878
Exact Sig. (2-tailed)	.884

For question 2, $p > 0.05$ so there is no statistical evidence to reject the null hypothesis with $\alpha < 0.05$. P value is 0.884. The groups in question 2 are not significantly different. There is no statistical significance to say that the sensor can properly assess dental anxiety in question 2.

Table 36 and Table 37 have the Mann-Whitney U test results for question 3.

Table 36 Question 3 scores - Mann-Whitney U Test (Ranks)

	Q3 Anxiety	N	Mean Rank	Sum of Ranks
Q3 Skin Resistance Normalized	<i>Non Anxious</i>	37	40.838	1511
	<i>Anxious</i>	32	28.250	904
	Total	69		

Table 37 Question 3 scores - Mann-Whitney U Test (Statistics)

	Q3 Skin Resistance Normalized
Mann-Whitney U	376
Wilcoxon W	904
Z	-2.599
Asymp. Sig. (2-tailed)	.009
Exact Sig. (2-tailed)	.009

For question 3 there is statistical evidence, p value is 0.09, to reject the null hypothesis with $\alpha < 0.05$. The groups in question 3 are significantly different. There is statistical evidence to assume the sensor can assess dental anxiety.

The devices used in clinical environments must be comparable to other measures. It was calculated sensitivity and specificity of this sensor. Looking at the data a natural breakpoint of -0.1 (skin resistance normalized) was selected to group patient anxiety in anxious and non anxious. The calculated contingency tables using the MDAS as gold standard are Table 38, Table 39, Table 40 and Table 41.

Table 38 Contingency Table for all the questions

Q1+Q2+Q3		Questionnaire		
SRR Normalized		Anxious	Non Anxious	Total
< -0.1	Anxious	56	19	75
\geq -0.11	Non Anxious	85	56	141
	Total	141	75	216

Table 39 Contingency Table for Question 1

Q1		Questionnaire		
SRR Normalized		Anxious	Non Anxious	Total
< -0.1	Anxious	18	3	21
\geq -0.1	Non Anxious	30	21	51
	Total	48	24	72

Table 40 Contingency Table for Question 2

Q2		Questionnaire		
SRR Normalized		Anxious	Non Anxious	Total
< -0.1	Anxious	10	10	20
\geq -.11	Non Anxious	31	21	52
	Total	41	31	72

Table 41 Contingency Table for Question 3

Q3	SRR Normalized	Questionnaire		
		Anxious	Non Anxious	Total
< 1	Anxious	28	6	34
≥ 1	Non Anxious	24	14	38
	Total	52	20	72

Table 42 list the calculated sensitivity and specificity of the sensor anxiety assessment:

Table 42 Statistical measures of sensor performance vs anxiety

Measure	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	False Negative Rate	Accuracy
Q1	37.50%	87.50%	85.71%	41.18%	16.67%	54.17%
Q2	24.39%	67.74%	50.00%	40.38%	100.00%	43.06%
Q3	53.85%	70.00%	82.35%	36.84%	21.43%	58.33%
Total quest. score	39.72%	74.67%	74.67%	39.72%	33.93%	51.85%

Generally the sensor has around 39% of sensitivity and 74% of specificity. Positive predictive vales are over 80% and negative predictive values over 36%. The accuracy or binary classification test is about 50%.

The last hypothesis tested was: is there correlation between questionnaire scores and the measured skin resistance?

Figure 19, Figure 20 and Figure 21 have the scatterplots of Questions Scores and the respective measured SRR.

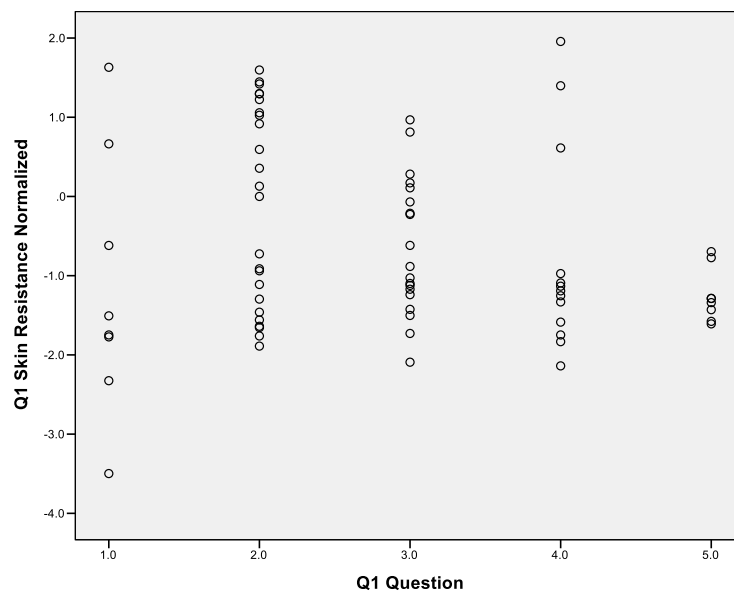


Figure 19 Question 1 – Scatterplot

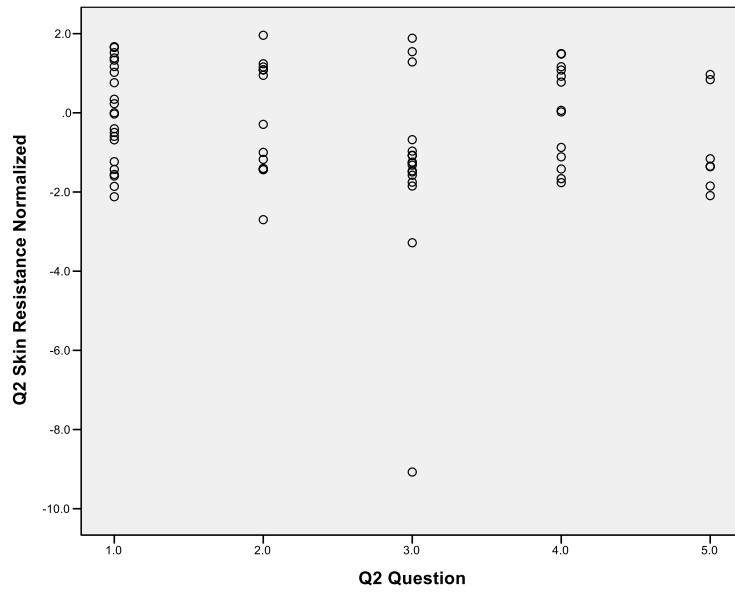


Figure 20 Question 2 – Scatterplot

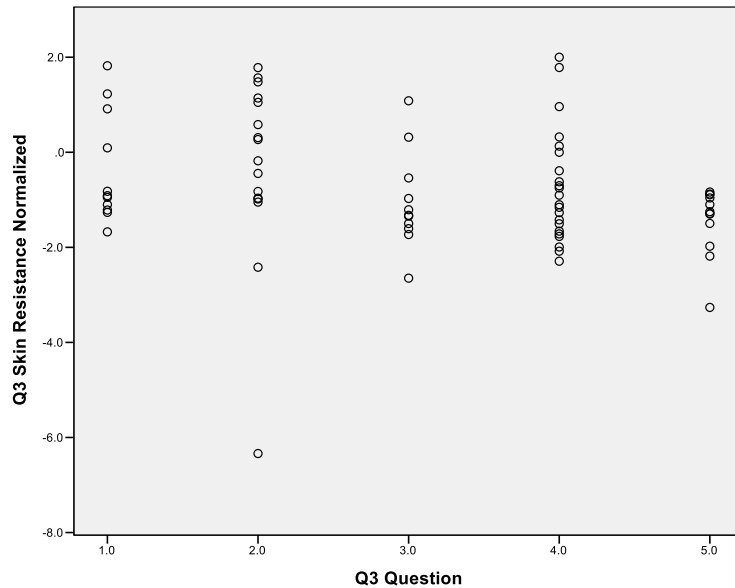


Figure 21 Question 3 – Scatterplot

As there is no assumed normality and questions are qualitative variables, the Spearman Correlation was calculated (Table 43, Table 44 and Table 45).

Table 43 Spearman Correlation of Question 1

		Q1 Skin Resistance Normalized	
Spearman's rho	Q1 Question	Correlation Coefficient	-.129
		Sig. (2-tailed)	.280
		N	72

Table 44 Spearman Correlation of Question 2

		Q2 Question	Q2 Skin Resistance Normalized
Spearman's rho	Q2 Question	Correlation Coefficient	1.000
		Sig. (2-tailed)	.190
		N	72

Table 45 Spearman Correlation of Question 3

		Q3 Question	Q3 Skin Resistance Normalized
Spearman's rho	Q3 Question	Correlation Coefficient	1.000
		Sig. (2-tailed)	.009
		N	72

** . Correlation is significant at the 0.01 level (2-tailed).

Question 1 and question 2 have $p > 0.05$, so there is no significance to reject the null hypothesis. Question 3 has $p < 0.05$ so there is evidence to reject the null hypothesis. The Spearman correlation in question 3 is different from zero and has a coefficient of -0.305.

4.1 Discussion

MDAS partials scores show no anxiety level in question 1 and question 2. In question 3 and 4 there is low anxiety score. In question 5 there is a substantial higher level of anxiety (Figure 12). The total scores of MDAS shows 10% of anxious patients (Table 16). This is probably a fact because of the nature of the patients that attend a dentistry College are less anxious than normal population.

The measure of central tendency for MDAS scores is 12, indicating that the data collected shows a low level of anxiety in the sum of the scores of all the questions (Figure 13). The boxplot in Figure 14 shows an equal median but a higher variation of males. However both gender groups do not have statistically significant differences in mean anxiety scores (**Error! Reference source not found.**).

The EDR survey data was very complex to analyze. It had several trial and errors with empirical data analysis, automated procedures and normalizing numeric values. EDR data was first screened and epochs with large incorrect readings and artifacts were excluded resulting in 72 of 74 patient sessions accepted (Figure 22).

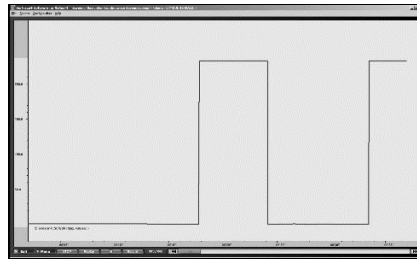


Figure 22 Sensor incorrect reading

The first data analysis iteration was done with Excel. The EDA data in each patient was exported in micro Siemens units to csv⁴ along with the markers. A complicated formula was designed to automate the average and amplitude values in the marker of SCR (Table 46). The results were difficult to compare and so data could not be statistically analyzed.

Table 46 EDR analysis Excel Automated Formulas

Mean Excel formula step by step		Amplitude Excel formula step by step	
Mean Time Value		Time range	
F1	=AVERAGEIFS (B15:B23,A15:A23,"00:09:01")	F1	= (INDEX (A15:A31,MATCH ("p1m",D15:D31,0))) +TIME (0,0,M5)
Find the marker		F2	
F2	=MATCH ("p1m",D15:D23,0)	= (INDEX (A15:A31,MATCH ("p1m",D15:D31,0))) -TIME (0,0,M5)	
Find the time		Amplitude	
F3	=INDEX (A15:A23,F20)	F3	=AVERAGEIFS (\$B\$15:\$B\$31,\$A\$15:\$A\$31,U19) -AVERAGEIFS (\$B\$15:\$B\$31,\$A\$15:\$A\$31,U20)
Aggregate		Dynamic Range	
F4	=AVERAGEIFS (B15:B23,A15:A23,INDEX (A15:A23,MATCH ("p1m",D15:D23,0)))	F4	=AVERAGEIFS (\$B\$15:INDIRECT ("&\$b"&\$I\$5),\$A\$15:INDIRECT ("&\$A"&\$I\$5),U19) -AVERAGEIFS (\$B\$15:INDIRECT ("&\$b"&\$I\$5),\$A\$15:INDIRECT ("&\$A"&\$I\$5),U20)
Dynamic marker		Dynamic Time Range	
F5	=AVERAGEIFS (\$B\$15:\$B\$28,\$A\$15:\$A\$28,INDEX (\$A\$15:\$A\$28,MATCH (J4,\$D\$15:\$D\$28,0)))	F5	=INDEX (\$A\$15:INDIRECT ("&\$A"&\$I\$5),MATCH (J4,\$D\$15:INDIRECT ("&\$D"&\$I\$5),0)) +TIME (0,0,M5)
Dynamic Range with match		Dynamic Amplitude	
F6	=MATCH (9.999999999999999E+307,\$A:\$A)	F6	=AVERAGEIFS (\$B\$15:INDIRECT ("&\$b"&\$I\$5),\$A\$15:INDIRECT ("&\$A"&\$I\$5),INDEX (\$A\$15:INDIRECT ("&\$A"&\$I\$5),MATCH (J4,\$D\$15:INDIRECT ("&\$D"&\$I\$5),0)) +TIME (0,0,\$M\$5)) -AVERAGEIFS (\$B\$15:INDIRECT ("&\$b"&\$I\$5),\$A\$15:INDIRECT ("&\$A"&\$I\$5),INDEX (\$A\$15:INDIRECT ("&\$A"&\$I\$5),MATCH (J4,\$D\$15:INDIRECT ("&\$D"&\$I\$5),0)) -TIME (0,0,\$M\$5))
Indirect Values		Amplitude label	
F6	=AVERAGEIFS (\$b\$15:INDIRECT ("&\$b"&\$F\$47),\$A\$15:INDIRECT ("&\$A"&\$F\$47),INDEX (\$A\$15:INDIRECT ("&\$A"&\$F\$47),MATCH (I4,\$D\$15:INDIRECT ("&\$D"&\$F\$47),0)))	F7	=MATCH (LEFT (N4,3),\$D\$15:INDIRECT ("&\$D"&\$I\$5),0)
IF marker not found		IF marker not found	
F7	=IFERROR (AVERAGEIFS (\$B\$15:INDIRECT ("&\$b"&\$I\$5),\$A\$15:INDIRECT ("&\$A"&\$I\$5),INDEX (\$A\$15:INDIRECT ("&\$A"&\$I\$5),MATCH (J4,\$D\$15:INDIRECT ("&\$D"&\$I\$5),0))), "NO "&J4)	F8	=IFERROR (AVERAGEIFS (\$B\$15:INDIRECT ("&\$b"&\$I\$5),\$A\$15:INDIRECT ("&\$A"&\$I\$5),INDEX (\$A\$15:INDIRECT ("&\$A"&\$I\$5),MATCH (LEFT (N4,3),\$D\$15:INDIRECT ("&\$D"&\$I\$5),0)) +TIME (0,0,\$M\$5)) -AVERAGEIFS (\$B\$15:INDIRECT ("&\$b"&\$I\$5),\$A\$15:INDIRECT ("&\$A"&\$I\$5),INDEX (\$A\$15:INDIRECT ("&\$A"&\$I\$5),MATCH (LEFT (N4,3),\$D\$15:INDIRECT ("&\$D"&\$I\$5),0)) -TIME (0,0,\$M\$5)), "NO "&J4)

⁴ csv stands for comma separated values file text format that is compatible with most spreadsheets applications

The second data analysis iteration employed an automated method of signal analysis with Ledalab [66] script. This script runs in MatLab and calculates skin conductance response with a graphic display using the Discrete Decomposition Analysis (DDA) model. In spite of having good potential to study SC signals, the data tested did not yield workable results. Ledalab was tested with Biotrace exported session data. Nevertheless Ledalab did not import it. After emailing the authors it was discovered an incompatibility in the filter because of the language of the software. Biotrace UK had a different export language than Biotrace DE. As a workaround it could work if all the headers were deleted. Three files of the source code of Ledalab: *getBiotraceData.m*, *import_data.m* and *ledagui.m* were adjusted and a new menu was added for importing directly from UK version. It was also discovered that the filter would not accept alphanumeric event markers. The new workaround was to change alphanumeric to numeric markers. In Ledalab all the features like down sampling and normalization were experimented. Yet results were not useful. Plus the fact that the answer markers were difficult to see in the graphic window. After analysis there were mostly no detected skin conductance responses.

Before the last iteration the sensor hardware electrical system was examined. The manufacturers were emailed. In searching for the model of the skin conductance sensor, the quest was to find out what were the raw unit measured. If it measured conductance or resistance. When the sensor connects with the PC by Bluetooth, the data is taken exclusively with Biotrace4. It is not an open source software so there is no easy way of capturing the real raw data from the sensor. Then, by chance, in Biotrace installation directory, it was discovered two executables "Nexus Analyse Tool.exe" (NXTool) and "regdll.exe". After registering the Bluetooth COM port with regdll.exe, NxTool found the Nexus unit. NxTool gives the raw signal data that arrives from the bluetooth serial COM port (Figure 23).

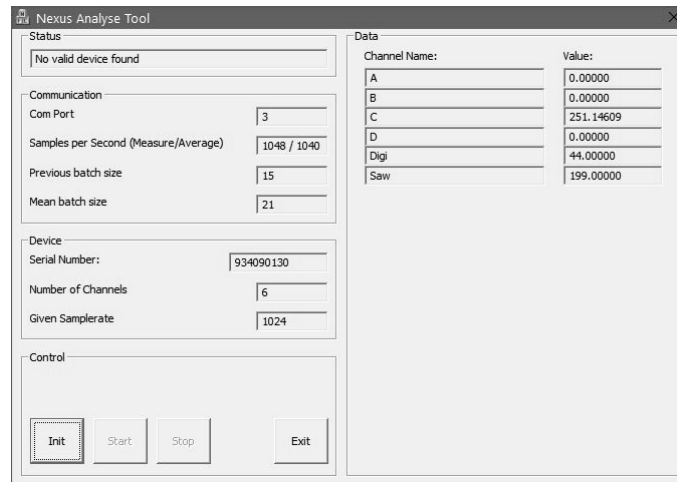


Figure 23 Nexus Analyse Tool

After some experimental detection tests it was found the operational raw limits:

- Maximum electrodermal resistance detected is 2 MOhm or 0.5 microS
- Minimum electrodermal resistance detected is 0.08 kOhm or 12500 microS

As the raw sensor data is in kOhms (resistance) whereas Biotrace was showing the inverse, it was calculated the rounding error software did when exporting in micro Siemens that was impairing any consistent results (Table 47).

Table 47 Biotrace Rounding Errors

	Min.	Max.	Mean
Sensor Raw data (kOhm)	198.38	281.40	235.47
Biotrace4 (microS)	3.55	5.04	4.28
1/Sensor Raw data (microS)	5.04	3.55	4.25
Biotrace4 Difference (microS)	-1.49	1.49	0.03
Biotrace4 Difference (kOhm)	-670.77	672.79	30143.63

As calculated the error can be exponential and as high as 30 megaOhm. In Nexus manual it is stated that all the raw data is saved. But it was not straight forward how to recalculate each session overview with the raw data in kOhm. After editing the channel settings a menu appears with right click that can recalculate the data (Figure 24).

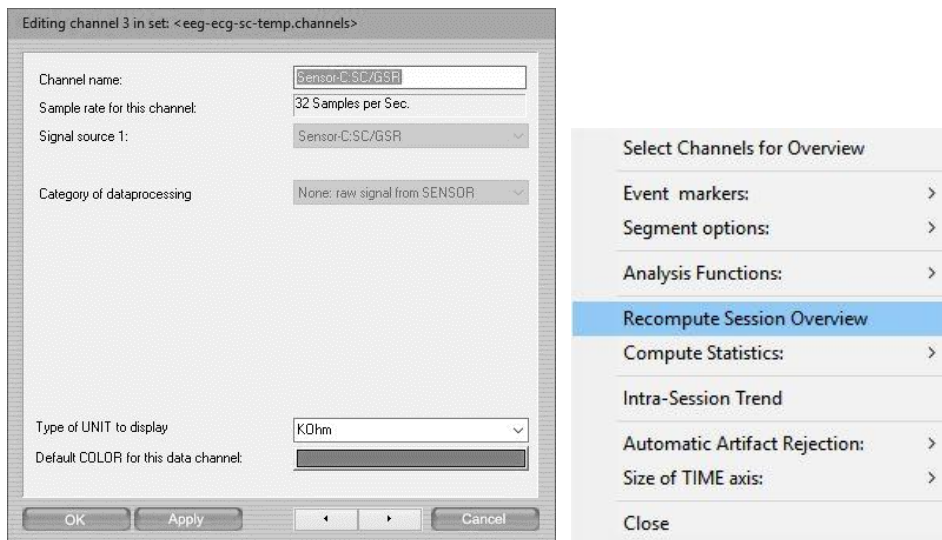


Figure 24 Recompute the data in Biotrace from μS to kOhm

Third and final data analysis iteration was done manually with each patient assessed visually in Biotrace graphic data display recalculated in kOhm units. The selection of the data was visually executed with the mouse and the mean, variance, maximum and minimum data was collected to Excel. Manual selection of the data followed specific criteria as latency, onset, rising slope, half recovery slope and magnitude.

The results of the sensor signal showed effectively that EDA signal require transformation to do a proper analysis. All data sets should be viewed for measures of skew, kurtosis and variance. There are three common ways of achieving comparable results to improve the validity and reliability of the data set. Range corrected scores where all SCR are a proportion of the maximum and minimum reading. Proportion of maximal response where values are corrected only with the maximal response like with a startle response (hand clap). Transformations into standard values in each raw SCR, mean SCR and standard deviation (SD) are used to calculate a Z score. Also Z-scores can also be transformed further in T-scores with a mean of 50 and a SD of 10.

Signal drift upward or downward was an important artifact encountered during the experiment. It should be controlled with the use of separate baseline screening sessions, or with the application of periodic rests and baseline calibration within experiments [87]. Each time an artifact or other technical problem exist and causes missing data reduces the correspondent statistical degrees of freedom.

The short duration of each patient EDA reading was a limitation of this experience but it worked as a test to a real life situation. Analysis was difficult because no real baseline signal level was properly detected. The literature advises to use 60 seconds minimum of baseline reading. Maybe if the questions were more separated in time the final data set was easier to analyze, however the sensor data should be able to classify

anxiety in real time because in dental settings treatments are uninterrupted. There is a polygraph technique that can help calibrate the recorded data. During a part of the session the patient sits quietly and without movement and a neutral question is asked like “Is your name X?”. The answer should be yes. After the EDR and level is back to normal it is asked the same question. This will continue until the patient has no EDR for three consecutive trials. This calibrated procedure could help to determine if the patient is hyper or hypo electrodermal responder. This ensures reading of NS.SCR.freq and reference tonic level.

In this experiment the primary objective was testing the skin conductance sensor to assess dental anxiety. The experiment partially succeeded. It can detect anxiety in patients. At the same time is not sensitive. A natural breakpoint of 1.0 normalized SRR permitted the construction of Table 42. This table shows that the specificity or true negative rate of the sensor is good but has a low sensitivity/precision or true positive rate. This means that non anxious patients were better identified, and anxious people are not. The sensor test gave low power in this contingency table calculation. This probably indicates that arousal is not always a form of dental anxiety. The sensor succeeded in correctly classifying the anxious population in two questions contrasting with the result of a similar earlier study [89]. This is probably a reflex of the geographical area of the study. Portuguese and North American population have equal fear of the injection, but Portuguese have equally fear of the drill noise. To test for reliability more tests should be performed with other clinical settings. The calculated binary test accuracy was about 43%. It is a low value maybe because the sensor breakpoint is hard to set. The magnitude of the values vary greatly between individuals. Also each individual has a variable tonic level.

Using the questionnaire as the gold standard the test of the sensor shows a strong positive predictive value and a low negative predictive value. If the patient is detected by the sensor as anxious there is a 70% probability it is really anxious. Question 1 and question 2 show no correlation between the questionnaire responses and the measured SRR. Question 3 has a low correlation negative coefficient between the responses and SRR. Patients feel of drill noise is significantly weakly related to SRR.

The good practice in a study of this nature is to check electrode contact, regulate ambient temperature, refrain the patient from doing movement artifacts, avoid coughing, sneezes, deep sighs and do the checking for responsiveness of the patient (hyper/hypo).

Chapter 5 Conclusion

The purpose of this project was to test a sensor of skin conductance (SC) to assess dental anxiety in dental clinic environments. The goal of the project was reached. The sensor has low sensitivity but high specificity. It is not precise but does have a good positive predictive value.

The main contributions of this work were the successful test of the sensor and a clinical protocol design that can be used for a large clinical trial. This experiment gave new data to use this physiological sensor to assess emotional stressful state.

Dental professionals need help in reducing dental anxiety. A starting point is to identify the level of dental stress when the patient is making a procedure and impeded to talk. A stressed patient can be managed more easily if a distraction is applied in certain moments when their anxiety climbs. This may contribute to reduce odontophobia and clinical appointment drop out.

Still there are several limitations in the sensor. Poor readings are common. The patient can have sudoresis. Every patient has a different skin conductance response level in dental stress conditions. Patients also avoid dental treatment because of perceiving lack of need for treatment, forgetting the appointment, or additionally, having poor cooperation (like young people). In this case, a new type of treatment is attractive. The link between dental fear in children and adolescents, that could go on as adults with odontophobia [93] could be broken. Current working methods to reduce dental anxiety are education of health care professionals on anxiety management and use of different anxiolytic drugs. Some anxious patients could also seek alternative medicines like acupuncture, hydrotherapy, hypnosis, therapeutic massage, music therapy and osteopathy.

Skin conductance can become a popular way of measure the psychological anxiety level. There are already simple and inexpensive sensors. SC if free from artifacts is reliable. But SC data analysis face a complex mix of superposed discrete reactions over a tonic component. New software helps old methods like trough to peak analysis that are generally used to extract characteristics from raw SC data. The scoring of SCRs that occur close to each other is complicated because the second SCR will be distorted by the recovery slope of the preceding SCR. The level of distortion is dependent on both amplitude and proximity of the previous SCR. If the recovery slope cannot be withdrawn, the peak latency and the amplitude of the subsequent SCR can be miscalculated. Two SCRs can be layered over each other and appear as one. This is a particular problem with short stimulus intervals. A flat SCR can occur if sweat ducts are filled to their limits and intraductal pressure causes a hydraulic diffusion of sweat in the stratum corneum.

5.1 Future work

The complexity of a future system will be the computation of the signal in realtime, giving a clean output, free from noise and artifacts. The star plot idea diagram of presenting sensor data could potentially be used in a tablet or smartphone. The current trend is the construction of body area network systems. This system could monitor different physiological parameters and be adapted to emotional states during the dental appointment. Already the camera of mobile phones can monitor accurately breathing rate and heart rate [94]. Non-contact imaging photo plethysmography can be used for measure the heart rate with no discomfort for the patient [95][96]. This type of sensors could be operated remotely and always be updated with the latest emotional detection algorithms. This is a possible niche for a trending market of services in the health field. Nevertheless this would require more computational power for the analysis of the two or more sensor data sets.

The EDA sensor for dental anxiety assessment need more clinical design and testing in real situations. There were already studies with a pulse rate monitor that gave direct results to stress in dental patients during treatment [97]. The ability to measure the anxiety of patients with disabilities may also benefit from leveling anxiety during appointments.

Besides the focus on the measure of anxiety, it may be useful to proceed with advances in the environmental hardware i.e. ambient intelligence (AmI) system, to cope with different ways to relax and distract the anxious patient. More studies on how to incorporate a digital anxiety scale in a clinical system should be addressed in the future. This gives rise to future challenges of assembling a system easy to control and use by non-advanced users like health care professionals in the daily practice. The system could even detect what would be the reaction of the patient to a given treatment by using neural networking decision making [98]. The manufacturers could develop a more robust clinical sensor, with more sensitivity in dry or wet skin. The new ambulatory biosensor would allow flexible and robust measuring in order to improve signal raw measurement, with better accuracy and precision [99]. This would require the implementation of a new order of complexity in the AmI system design and the introduction of additional specifications to the sensor analysis software.

Emotional reading is and will most likely be an unsolvable computational challenge in the near future. User interfaces must be adapted to the frequency of affective readings. Facial reading is a promising way to assess anxiety. Smartphone evolver every 6 months and can potentially “read minds and understand emotions” [32]. These mobile systems that can use physiological data always rise privacy concerns about storing and accessing personal data.

The future work should focus on design of the components of the system for a clinical everyday use: smaller design and mobility. A good bet could use open source hardware, such as Arduino, the base of the Portuguese hardware low cost sensor Bitalino. Already there is research in systems that employ a wearable interface with a variety of physiological sensors, including SC, RFID, wireless Bluetooth modules, Atmega microprocessors with Arduino's environment [100]. There is also some work in connecting SC sensor to an iPhone[101]. Thermal and humidity sensors could compensate ambient temperature that interferes with production of sweat and gives erroneous EDA recordings. Accelerometers sensors coupled with EDA sensors would prevent the micro movements artifacts.

Dental anxiety distraction with music could be made without earphones, using bone conduction to play sounds. This would allow patient communication with health professionals and at the same hearing music during appointments.

Chapter 6 References

Hardware:

Nexus 4, NeXus Skin Conductance Bluetooth Sensor and Biotrace+ Software for Nexus-4
Version:2012C, Mind Media BV, Netherlands

Software:

G*Power 3, Universität Düsseldorf, Germany

Ledalab, Austria; Germany

MATLAB, The MathWorks, Inc., Natick, Massachusetts, United States.

Microsoft Excel. Microsoft, Redmond, Washington, United States

SPSS Statistics for Windows, Armonk, NY: IBM Corp

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Appendix 1 - MDAS Questionnaire

Este é um **pequeno e rápido** questionário (5 perguntas) para um trabalho sobre *ansiedade* no consultório dentário.

Este questionário é impessoal e **confidencial**, tendo a garantia de não ser possível identificar a resposta e mantendo a **privacidade** durante a recolha e tratamento dos dados.

A resposta é **livre e voluntária**, embora o questionário só é **válido** se responder às 5 questões.

CONSEGUE INDICAR-NOS O QUANTO FICA ANSIOSO
(SE É QUE FICA ANSIOSO) COM A SUA IDA AO DENTISTA?

POR FAVOR, COMUNIQUE, ASSINALANDO A RESPECTIVA OPÇÃO COM A **LETRA**.

P1. Sabendo que hoje tinha consulta no dentista como se sentiu ONTEM?

P2. Hoje está aqui sentado na SALA DE ESPERA (à espera de tratamento), como se sente?

P3. Se lhe estivessem prestes a BROCAR UM DENTE, como se sentiria?

P4. Se lhe estivessem prestes a fazer uma DESTARTARIZAÇÃO E POLIMENTO (limpeza), como se sentiria?

P5. Se estivesse prestes a receber uma INJEÇÃO DE ANESTESIA LOCAL na sua gengiva, como se sentiria?

			E - Extremamente Ansioso
		D - Muito Ansioso	
	C - Moderadamente Ansioso		
	B - Um pouco Ansioso		
A - Nada Ansioso			

Figure 25 MDAS Questionnaire

Appendix 2 - MDAS Dataset

Table 48 MDAS Questionnaire Responses

Date	Age	Man	Woman	Q1	Q2	Q3	Q4	Q5	Qx SUM	HIGH >13	VERY H.>19
11/11/2010	27	0	1	2	2	3	2	4	13	1	0
11/11/2010	34	1	0	2	2	2	2	2	10	0	0
11/11/2010	40	1	0	1	1	2	2	2	8	0	0
11/11/2010	30	0	1	1	2	2	2	2	9	0	0
11/11/2010	27	0	1	2	1	2	2	3	10	0	0
11/11/2010	29	0	1	1	1	2	2	3	9	0	0
11/11/2010	31	0	1	3	3	3	3	3	15	1	0
11/11/2010	34	0	1	2	2	2	3	3	12	0	0
11/11/2010	27	1	0	1	2	2	3	3	11	0	0
11/11/2010	38	1	0	2	3	3	3	5	16	1	0
11/11/2010	31	1	0	2	2	2	2	3	11	0	0
11/11/2010	20	0	1	2	2	3	2	3	12	0	0
11/11/2010	51	1	0	1	2	3	3	3	12	0	0
11/11/2010	47	1	0	3	3	3	2	4	15	1	0
11/11/2010	32	0	1	2	2	3	4	4	15	1	0
11/11/2010	30	0	1	2	2	3	2	4	13	1	0
11/11/2010	22	0	1	2	3	3	2	5	15	1	0
11/11/2010	35	1	0	2	2	3	2	4	13	1	0
11/11/2010	38	0	1	3	3	3	2	5	16	1	0
11/11/2010	39	1	0	3	3	3	3	5	17	1	0
11/11/2010	30	0	1	2	2	2	2	4	12	0	0
11/11/2010	26	0	1	1	2	2	2	3	10	0	0
11/11/2010	27	0	1	1	2	2	3	4	12	0	0
11/12/2010	35	1	0	2	2	2	3	4	13	1	0
11/12/2010	33	1	0	3	3	4	3	5	18	1	0
11/12/2010	31	1	0	3	3	4	4	5	19	1	1
11/12/2010	23	0	1	3	3	3	4	5	18	1	0
11/12/2010	27	0	1	2	2	4	3	2	13	1	0
11/12/2010	25	1	0	2	2	3	2	3	12	0	0
11/12/2010	30	0	1	2	2	3	2	3	12	0	0
11/12/2010	31	1	0	1	2	3	2	4	12	0	0
11/12/2010	48	1	0	1	1	2	2	3	9	0	0
11/12/2010	53	1	0	2	2	2	2	3	11	0	0
11/12/2010	50	1	0	1	1	1	2	4	9	0	0
11/12/2010	47	0	1	1	1	1	2	4	9	0	0
11/12/2010	43	1	0	2	2	1	1	3	9	0	0
11/12/2010	30	1	0	2	2	2	2	3	11	0	0
11/12/2010	23	0	1	2	2	2	1	3	10	0	0
11/12/2010	26	0	1	2	2	2	1	3	10	0	0
11/12/2010	28	0	1	2	2	2	2	3	11	0	0
TOTAL	40 Patients	19	21	76	83	99	93	141			

Appendix 3 - EDR Informed Consent

Formulário de Consentimento Informado

Investigador Principal (PI):	Dr. Pedro Peres
Contato do PI:	9 [REDACTED]
Título do Estudo Clínico:	Medição da ansiedade dentária através de um sensor de condutividade da pele
Duração esperada da participação no estudo	10 minutos

Quais são os objetivos principais do estudo?

O objectivo principal do estudo é tentar quantificar a ansiedade dentária através da medição da condutividade da pele. A condutividade da pele é a capacidade da pele conduzir a electricidade devido à produção de suor pelas glândulas existentes na zona palmar das mãos.

Porque fui convidado a participar?

Foi convidado a participar por estar na sala de espera para uma consulta dentária. Este estudo pretende que seja feito a recolha de dados com o paciente sentado num equipamento dentário.

O que será exigido de mim?

Será feito um questionário de três questões acerca de tratamentos dentários. Durante o questionário será medida a condutividade da pele e ao mesmo tempo registada a resposta à pergunta feita.

Quais são os riscos envolvidos, a probabilidade de que ocorram e o que será feito para minimizá-los? Quais são os custos envolvidos

Este estudo é gratuito e não envolve nenhum risco para a saúde.

Procedimento	Medição da Condutividade dérmica
• Risco	Poderá haver um risco ligeiro de contaminação cruzada pelo uso dos sensores. No entanto a frequência e gravidade será praticamente nula.
• Segurança	Os dedos da mão e os sensores são individualmente desinfetados antes de cada utilização
• Procedimento de investigação	Este é um procedimento de investigação que não faz parte de um tratamento clínico de rotina.
• Custo	Não terá qualquer custo associado.

Qual será o meu papel no estudo: voluntário não ansioso ou paciente ansioso?

Pacientes ansiosos e não ansiosos fazem parte do estudo e só serão classificados após a análise dos dados.

Há probabilidade de que o estudo me beneficie diretamente? Quais são os possíveis benefícios para outras pessoas?

Este estudo servirá de base a um sistema que ainda terá de ser construído e poderá levar ainda algum tempo. O participante não vai beneficiar diretamente da informação recolhida no estudo. No entanto no futuro outras pessoas que sofrem de ansiedade poderão beneficiar dos dados recolhidos neste estudo. Com estes dados talvez seja possível encontrar um método para diagnosticar e tratar pessoas ansiosas ou uma maneira para prevenir este problema. Também existe a possibilidade de que não exista qualquer benefício resultante deste estudo.

Figure 26 EDR Informed Consent 1/2

Quero mesmo participar neste estudo? A participação é voluntária?

A sua participação é voluntária. É importante que esteja bem informado e tenha confiança na sua participação. Antes de tomar uma decisão para participar leia este consentimento com atenção e discuta quaisquer questões com os investigadores. Se participar no estudo, é livre de desistir a qualquer momento. Se não quiser pode não responder às perguntas ou pode parar a qualquer momento. A sua decisão não vai afetar os cuidados de saúde oferecidos nesta instituição presentes ou futuros. Igualmente não haverá penalidade ou perda de benefícios aos quais tenha direito atualmente.

Quantas pessoas serão convidadas a participar?

Estimamos que cerca de 50 pessoas irão participar neste estudo. Como o estudo será realizado noutros locais, esperamos que o número total final suba até 100.

Quanto tempo durará a minha participação?

Este estudo tem a duração de uma sessão única com um tempo previsto de 10 minutos.

Serei compensado monetariamente por participar no estudo?

Não irá ser compensado por participar no estudo.

Como será protegida a minha informação pessoal?

O estudo é anónimo e não será recolhida informação pessoal. A informação dos indivíduos nunca será identificável nas publicações ou apresentações baseados nesta investigação. A informação recolhida será guardada de forma segura e não será partilhada com terceiros. Faremos o possível para proteger os dados recolhidos mas não poderemos garantir 100% de confidencialidade e.g. os registos podem ser inspecionados para verificar que o estudo está a ser realizado corretamente.

E se sentir algum efeito secundário relacionado com a minha participação?

Se sentir algum efeito anormal deve avisar o investigador principal logo que possível. O estabelecimento onde decorre o estudo não oferece cuidados de saúde gratuitos.

Alguém me pode impedir de participar neste estudo?

O investigador principal pode parar a sua participação se se detetar que não existe resposta à leitura da condutividade dérmica pelos sensores colocados nos dedos.

E se tiver outras questões?

Se tiver outras questões, problemas ou preocupações relacionadas com a investigação, deve contactar com o investigador principal (PI). É encorajado a fazer perguntas até estar completamente esclarecido antes de decidir participar no estudo. Se tiver perguntas sobre os seus direitos pode contactar o gabinete de ética do estabelecimento onde realiza o estudo.

Consentimento para participar:

Ao assinar o consentimento, o participante ou tutor legal reconhece que leu, ou ouviu este consentimento, falou com o pessoal de investigação, teve oportunidade de fazer perguntas e obter respostas satisfatórias e consente voluntariamente em participar no estudo com descrito neste formulário. Terá acesso à sua participação e mudar de ideias a qualquer momento.

Papel	Iniciais do nome	Assinatura / Data
Investigador	Assinar o anexo após consentimento	Assinar o anexo após consentimento
Participante ou tutor legal e/ou testemunha se aplicável	Assinar o anexo após consentimento	Assinar o anexo após consentimento

Figure 27 EDR Informed consent 2/2

ANEXO AO CONSENTIMENTO INFORMADO

CONSENTIMENTO INFORMADO N°

ASSINADO PELO PACIENTE OU UM REPRESENTANTE LEGAL

EU, [INICIAIS DO NOME] _____ compreendi as explicações prestadas pelo Clínico relativamente à natureza, finalidade do questionário proposto e que me foram esclarecidas todas as dúvidas que me ocorreram, pelo que autorizo a realização do procedimento indicado

DATA: _____, ASSINATURA: _____

CONSENTIMENTO INFORMADO N°

ASSINADO PELO PACIENTE OU UM REPRESENTANTE LEGAL

EU, [INICIAIS DO NOME] _____ compreendi as explicações prestadas pelo Clínico relativamente à natureza, finalidade do questionário proposto e que me foram esclarecidas todas as dúvidas que me ocorreram, pelo que autorizo a realização do procedimento indicado

DATA: _____, ASSINATURA: _____

CONSENTIMENTO INFORMADO N°

ASSINADO PELO PACIENTE OU UM REPRESENTANTE LEGAL

EU, [INICIAIS DO NOME] _____ compreendi as explicações prestadas pelo Clínico relativamente à natureza, finalidade do questionário proposto e que me foram esclarecidas todas as dúvidas que me ocorreram, pelo que autorizo a realização do procedimento indicado

DATA: _____, ASSINATURA: _____

CONSENTIMENTO INFORMADO N°

ASSINADO PELO PACIENTE OU UM REPRESENTANTE LEGAL

EU, [INICIAIS DO NOME] _____ compreendi as explicações prestadas pelo Clínico relativamente à natureza, finalidade do questionário proposto e que me foram esclarecidas todas as dúvidas que me ocorreram, pelo que autorizo a realização do procedimento indicado

DATA: _____, ASSINATURA: _____

Figure 28 EDR Signature Form

Appendix 4 - EDR Questionnaire

INFORMAÇÕES GERAIS SOBRE O ESTUDO

No âmbito do Mestrado sobre **Ansiidade no Consultório Dentário** tenho este pequeno **questionário** que demora cerca de **1 minuto** para responder. Responda com **sinceridade**, não existem respostas certas ou erradas, o que é **importante é a sua experiência**.

A medição da ansiedade é feita passivamente por dois **sensores** que se colocam em dois dedos de uma das mãos não sentido qualquer desconforto.



A participação no estudo é **voluntária**, e a **confidencialidade** é sempre mantida.

Mesmo que as conclusões do estudo sejam publicadas, a **identificação dos participantes não será divulgada** mantendo a sua **privacidade**.

Com os melhores cumprimentos, Dr. Pedro Peres

Ansiidade no Consultório Dentário

Figure 29 EDR Questionnaire 1/4

QUESTIONÁRIO 1/3

1. **Sexo:** Masculino Feminino

2. **Idade:**

3. **1X no Dentista:** Sim Não

P1 - Como se sente em relação à injeção de anestesia durante a consulta?

0 – Não sei

1 – Nada ansioso

2 – Um pouco ansioso

3 – Moderadamente ansioso

4 – Muito ansioso

Ansiedade no Consultório Dentário

Figure 30 EDR Questionnaire 2/4

QUESTIONÁRIO 2/3

P2 - Como se sente em relação ao tratamento de desvitalização?

0 – Não sei
1 – Nada ansioso
2 – Um pouco ansioso
3 – Moderadamente ansioso
4 – Muito ansioso

Ansiedade no Consultório Dentário

Figure 31 SC Questionnaire 3/4

QUESTIONÁRIO 3/3

P3 - Como se sente em relação ao barulho de brocar um dente durante a consulta?

0 – Não sei
1 – Nada ansioso
2 – Um pouco ansioso
3 – Moderadamente ansioso
4 – Muito ansioso

FIM
OBRIGADO

Ansiedade no Consultório Dentário

Figure 32 EDR Questionnaire 4/4

Appendix 5 - EDR Hardware



Figure 33 Nexus 4 Unit



Figure 34 Nexus 4 Sensor and Bluetooth dongle

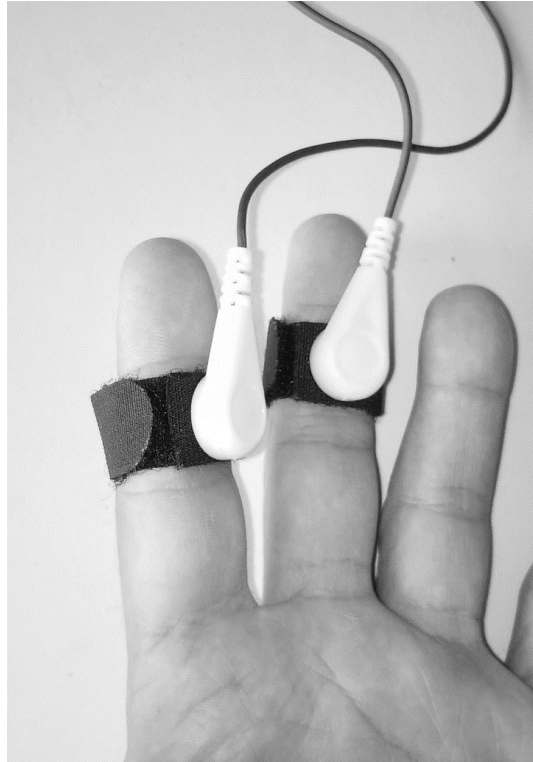


Figure 35 EDR Electrodes usage

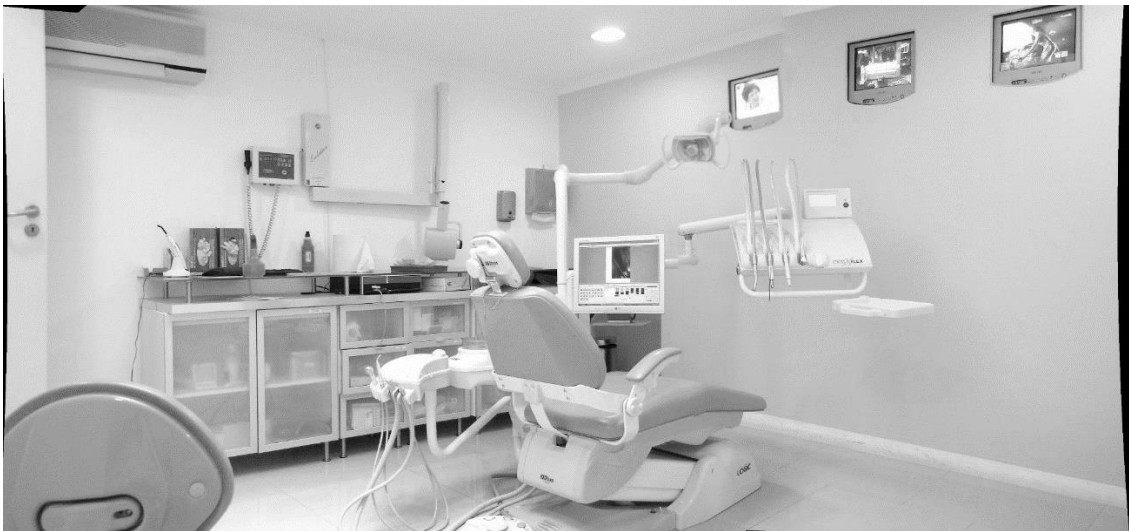


Figure 36 Dental Setting Example

Appendix 6 - Sample Clinical Trial Permission Letter

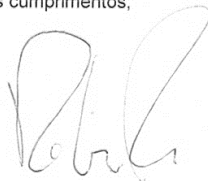
Exmo Sr
Director da Faculdade de Medicina
Dentária da Universidade de Lisboa

No âmbito do Mestrado que estou a realizar na Faculdade de Ciências da Universidade de Lisboa, venho por este meio pedir autorização para realizar um pequeno questionário (anexo 1) aliado à medição em paralelo da condutância dérmica (anexo 2) para uma amostra aleatória de população que se dirija à consulta de medicina dentária. A amostra deverá ser constituída preferencialmente, de primeiras vezes.

O trabalho é orientado pelo Prof Dr Nuno Guimarães e pela Prof. M Fernanda Diamantino da Faculdade de Ciências da Universidade de Lisboa.

Com os melhores cumprimentos,

Pedro Peres



Lisboa, 18 de Março de 2011

*Autorizado, desde
que o preâmbulo do
questionário seja reformu-
lado de modo a ser
compatível com os
direitos. 21/03/2011
Guimarães*

Pág 1/3

Appendix 7 - EDR Informed Consent Signed Example

CONSENTIMENTO INFORMADO

NºSÉRIE 38

ASSINADO PELO PACIENTE OU UM REPRESENTANTE LEGAL

EU, [INICIAIS] ACC compreendi as explicações prestadas pelo DR PEDRO PERES_ relativamente à natureza, finalidade do questionário proposto e que me foram esclarecidas todas as dúvidas que me ocorreram, pelo que autorizo a realização do procedimento indicado,

DATA: 17/02/2011, ASSINATURA: ACC

CONSENTIMENTO INFORMADO

NºSÉRIE 32

ASSINADO PELO PACIENTE OU UM REPRESENTANTE LEGAL

EU, [INICIAIS] CM compreendi as explicações prestadas pelo DR PEDRO PERES_ relativamente à natureza, finalidade do questionário proposto e que me foram esclarecidas todas as dúvidas que me ocorreram, pelo que autorizo a realização do procedimento indicado,

DATA: 17/02/2011, ASSINATURA: Carolina J. Freitas

Figure 37 Field Trial Informed Consent

Appendix 8 - EDR Dataset

Table 49 SRR Sample Clinical Trial Dataset

Q1	Q1NA	Q1	Q1A	Q2	Q2NA	Q2	Q2A	Q3	Q3NA	Q3	Q3A
3	-1.7293	4	-0.9734	1	-0.6824	4	1.49635	2	0.30822	5	-1.0995
2	0.91705	4	1.39741	1	0.34292	5	0.96814	2	-2.4185	4	-2.292
2	-0.9128	4	-1.1327	2	1.23913	4	-0.8738	2	0.58252	4	-1.4226
3	0.81287	4	-1.833	3	-0.6781	5	-1.3476	2	-0.8242	5	-1.9764
2	1.44621	5	-1.2862	1	1.38426	4	0.9234	2	1.05022	4	-0.704
2	-1.4608	4	-1.5862	3	1.28571	5	-2.0919	2	-0.4454	4	-0.9025
3	-1.028	4	0.6123	1	-0.4032	4	1.48428	3	1.08326	5	-0.8928
2	-1.5588	4	-1.2533	2	1.95861	5	-1.3621	3	-1.3264	5	-0.9604
2	-1.2957	5	-1.5767	3	-1.0802	5	-1.1602	2	-6.3379	4	-1.9927
3	0.96734	4	-1.3315	1	-1.4297	5	0.83908	1	1.22814	5	-1.497
2	-1.6549	5	-1.2882	3	-1.2703	4	-1.1126	2	1.14173	5	-2.1846
3	-1.2397	4	-2.1385	3	-9.0733	4	0.0625	1	-0.8202	4	-2.0811
3	-1.0982	5	-1.6085	3	-0.9667	4	1.16444	2	0.26857	4	-1.1035
2	0	4	-1.092	3	1.88405	4	0.02304	3	-1.6069	4	0.12908
2	-1.6386	5	-1.3398	2	-2.6992	4	0.77604	2	1.56549	4	1.78374
3	-0.069	4	-1.748	3	-1.0713	4	-1.4189	3	-1.209	4	0.3234
3	-1.1713	5	-1.4295	3	-1.8493	4	-1.6636	3	-1.343	4	-1.5041
2	0.5935	4	-1.1915	2	0.94757	4	1.08076	1	1.82022	4	-1.2691
1	1.63062	5	-0.7729	3	-1.7522	5	-1.85	3	-2.6486	4	0.96094
3	-0.8836	4	1.95652	3	-1.5757	4	-1.7632	2	-1.0484	5	-0.8361
2	1.5964	5	-0.6968	1	-2.1197			2	-0.1789	4	-1.6592
2	-0.7246			3	-3.2819			1	0.09302	4	-1.7173
1	-1.7729			1	1.51919			1	-1.215	5	-1.2497
3	-0.2271			1	1.67093			1	-0.913	4	-1.1579
2	-1.111			3	-1.322			3	-1.4988	5	-1.2992
2	0.12957			1	1.16935			2	1.48113	5	-0.8795
3	-1.4249			2	-1.4255			1	-0.9474	5	-1.2874
3	-1.5023			1	1.65039			1	-1.6745	4	-0.75
3	-0.2123			1	1.33095			3	-0.972	4	-0.3888
2	0.35612			3	-1.493			2	-0.9831	4	0
1	0.66398			2	1.15774			1	-1.1	4	-0.6202
2	1.025			1	-0.5953			3	-0.5402	4	-1.7703
1	-2.3256			1	-0.4973			2	-0.9656	5	-3.2645
1	-0.6185			1	0.76093			1	0.91398	4	2
3	0.17143			1	-1.8588			3	0.31731		
2	1.22344			3	-1.2444			1	-1.2642		
2	1.29545			3	-1.4658			2	1.78159		
3	-2.092			1	-1.234			3	-1.7308		
1	-3.4979			2	-1.4043						
3	0.28188			1	-0.0299						
2	1.05674			1	0						
1	-1.748			2	1.08475						
3	-0.6179			1	-1.5976						
2	-0.9385			3	1.54407						
2	1.41989			2	-1.4377						
3	0.10893			2	-1						
2	-1.7613			1	-1.5584						
2	1.29817			2	-1.1762						
1	-1.5071			1	1.02198						
2	-1.8889			1	0.22955						
3	-1.1228			2	-0.2914						
				2	1.08588						