# Ανοικτό Πανεπιστήμιο Κύπρου

**Σχολή Θετικών και Εφαρμοσμένων Επιστημών**

**Μεταπτυχιακό Πρόγραμμα Σπουδών *Πληροφοριακά και Επικοινωνιακά Συστήματα***


## Μεταπτυχιακή Διατριβή

# Η Χρήση Βιοαισθητήρων στην Ανίχνευση του Στρες και Πειραματική Μελέτη του Σήματος GSR
# (Use of Biosensors for the Detection of Stress and Experimental Analysis of Galvanic Skin Response Signal)


**Αριστομένης Δημήτριος Τουρβάς**

**Επιβλέπων Καθηγητής**
**Χρήστος Γκουμόπουλος**



**Δεκέμβριος 2017**

# Ανοικτό Πανεπιστήμιο Κύπρου

**Σχολή Θετικών και Εφαρμοσμένων Επιστημών**

**Μεταπτυχιακό Πρόγραμμα Σπουδών *Πληροφοριακά και Επικοινωνιακά Συστήματα***


# Μεταπτυχιακή Διατριβή

## Η Χρήση Βιοαισθητήρων στην Ανίχνευση του Στρες και Πειραματική Μελέτη του Σήματος GSR (Use of Biosensors for the Detection of Stress and Experimental Analysis of Galvanic Skin Response Signal)


**Αριστομένης Δημήτριος Τουρβάς**

**Επιβλέπων Καθηγητής**
**Χρήστος Γκουμόπουλος**


Η παρούσα μεταπτυχιακή διατριβή υποβλήθηκε προς μερική εκπλήρωση των απαιτήσεων για απόκτηση μεταπτυχιακού τίτλου σπουδών στα Πληροφοριακά και επικοινωνιακά συστήματα από τη Σχολή Θετικών και Εφαρμοσμένων Επιστημών του Ανοικτού Πανεπιστημίου Κύπρου.

**Δεκέμβριος 2017**

BLANK PAGE

# Περίληψη

Το stress λαμβάνει διαστάσεις επιδημίας με σημαντικές κοινωνικό-οικονομικές επιπτώσεις. Η ηλεκτροδερματική δραστηριότητα (electrodermal activity), μεταξύ των άλλων βιο-σημάτων, παρουσιάζεται ως ένας υποσχόμενος δείκτης για την παρακολούθηση του stress, καθώς συσχετίζεται με την ενεργοποίηση του συμπαθητικού νευρικού συστήματος.

**Μέθοδοι** Διενεργήθηκε ανασκόπηση της υπάρχουσας βιβλιογραφίας αναφορικά με την χρήση των βιο-αισθητήρων στην ανίχνευση του stress με έμφαση στην κριτική αξιολόγηση των μεθοδολογιών που χρησιμοποιούνται για την καταγραφή και ερμηνεία της ηλεκτροδερματικής δραστηριότητας.

Μετά την εισαγωγική ανασκόπηση έπεται το ειδικό πειραματικό σκέλος που συνίσταται στην ανάλυση δεδομένων από είκοσι πέντε εθελοντές συνολικά, με επακόλουθη στατιστική επεξεργασία σε δύο ομάδες (n=7 και n=18 εθελοντές αντιστοίχως βάσει της συχνότητας δειγματοληψίας) σε συνθήκες ηρεμίας και stress. Η ταυτοποίηση και ο υπολογισμός των σχετικών παραμέτρων ηλεκτρο-δερματικής δραστηριότητας διενεργήθηκε με την γλώσσα προγραμματισμού Python, ενώ η στατιστική ανάλυση με τη γλώσσα προγραμματισμού R.

**Αποτελέσματα** Εντοπίστηκαν στατιστικά σημαντικές συσχετίσεις σε πολλαπλή γραμμική παλινδρόμηση μεταξύ της τονικής δραστηριότητας(συχνότητα Non SCR) και ηλικίας των συμμετεχόντων($p<0.01$), συχνότητας Non SCRs και φύλου($p<0.05$), συχνότητας Non SCRs και φυσικής δραστηριότητας($p<0.01$) για την πρώτη ομάδα. Για τη δεύτερη ομάδα εντοπίστηκαν στατιστικά σημαντικές συσχετίσεις μεταξύ ύψους SCR(amplitude) και ηλικίας($p<0.001$) καθώς και ύψους SCR(amplitude) και STAI2 ($p<0.001$) σε πολλαπλή γραμμική παλινδρόμηση. Η μη παραμετρική μέθοδος Spearman's rho εντόπισε στατιστικά σημαντικές σχέσεις στη δεύτερη ομάδα μεταξύ ύψους SCR(amplitude) και STAI1($p<0.001$), χρόνου επαναφοράς στο μισό του μέγιστου ύψους(half recovery time) και STAI1 ($p<0.001$), STAI2($P<0.05$), ηλικίας($p<0.05$). Επιπλέον η συχνότητα Non SCR παρουσίασε στατιστικά σημαντικές συσχετίσεις με την ηλικία($p<0.05$), το STAI1($p<0.001$) και το STAI2(<0.001) σε πολλαπλή γραμμική παλινδρόμηση στην ομάδα 2. Επίσης διαπιστώθηκε στατιστικά σημαντική διαφορά στην ομάδα 2 στον αριθμό των κορυφών (peaks) μεταξύ περιόδων stress και ηρεμίας ($p<0.05$, Wilcoxon signed rank test).

**Συμπέρασμα** Η ηλεκτροδερματική δραστηριότητα φαίνεται να συσχετίζεται με τα επίπεδα stress, προσφέροντας μια χρήσιμη μέθοδο διερεύνησης των ατομικών παραμέτρων που συμβάλλουν στη δημιουργία stress. Η προοπτική δημιουργίας σημαντικών πρακτικών εφαρμογών βασισμένων στην ηλεκτροδερματική δραστηριότητα για την πρόληψη και αντιμετώπιση του stress θα πρέπει να τύχει μελέτης.

# Summary

Stress is becoming an epidemic with significant socioeconomic implications. The utilization of bio signals in its detection is a promising research domain that could provide tools for prevention and management. Electrodermal activity(EDA), among the other bio signals, appears as a promising marker for stress monitoring, since it correlates with the activity of the sympathetic nervous system.

**Methods** The current thesis reviews the existing literature regarding the utilization of biosensors for stress detection with a focus on the critical appraisal of the methodologies employed in electrodermal activity recording and interpretation in relation to stress. The introductory review is followed by the experimental component , which involves data processing and analysis of volunteer derived electrodermal activity in calm and stress conditions. More specifically data from twenty five individuals (n=25) in total were processed with a subsequent two group statistical analysis (seven and eighteen volunteers respectively based on different data acquisition frequencies) for the investigation of possible correlations with volunteer specific variables. The extraction of relevant EDA metrics was performed with algorithms implemented in the Python programming language while the statistical analysis was performed with the R language and environment for statistical computing and graphics.

**Results** The results revealed statistically significant correlations in multiple regression between tonic activity (Non SCR frequency) and age($p<0.01$), Non SCR frequency and Gender($p<0.05$), Non SCR frequency and physical activity($p<0.01$) for the first group. For the second group statistically significant correlations were identified between SCR amplitude and Age($p<0.001$) as well as SCR amplitude and STAI2($p<0.001$) in multiple linear regression. Spearman's rho in group two additionally revealed statistically significant relationships between SCR amplitude and STAI1($p<0.001$), half recovery time and STAI1($p<0.001$), STAI2($p<0.05$), age($p<0.05$). Furthermore Non SCR frequency exhibited statistically significant correlations with age($p<0.05$), STAI1($p<0.001$) and STAI2($<0.001$) in multiple linear regression in group 2. A Wilcoxon signed rank test revealed a statistically significant difference between the number of EDA peaks during calm and stress phases($p<0.05$) in group2.

**Conclusion** Electrodermal activity appears to correlate with stress levels, providing a useful insight into the volunteer specific parameters that contribute to the genesis of anxiety. Significant practical applications in stress prevention and management should also be considered.

# Contents

# Chapter 1
# Introduction

Chronic stress is becoming an epidemic, with rising numbers of individuals experiencing its adverse effects on their everyday social and professional activities. The economic burden of mental and physical stress is also significant since those who suffer from it tend to have reduced performance at work, be less productive and in need of medical and/or psychological support [1]. Characteristically in 2002, work related stress cost in European Union(EU) based enterprises amounted to 20 billion euro [2] [3], while 51% of workers in the EU report experience stress in their working environment.

The definition of stress is not straightforward since a plethora of descriptions have been proposed:

1. The perception of stress as an agent, situation or variable that perturbs the normal functioning of an individual [4]. In the context of this definition stress can be sub-classified into stimulus-based and response-based.

2. The transactional model, which is based on the notion that stress stems not solely from the individual or the environment but from their transaction [5]. Transaction requires processing, meaning that the cognitive mechanisms of perceiving stress have to be investigated in order to understand stress and its implications [6].

3. The complex interaction between perceived demand, ability to cope and perception of the significance of managing to do so [7].

4. Another approach emphasizes the fact that ultimately stress could be just considered equivalent to time pressure, since limited time is the basic factor that initiates and propagates stress [8].

Common categorizations (although arbitrary) of stress are:

1. Survival Stress. Associated with increased activity of the sympathetic nervous system that enables the person to “fight” or “flight” regarding a stimulus perceived as an imminent threat [9].

2. Environmental Stress. Induced by environmental factors such as noise [10].

3. Work related. This source of stress is on the rise and has significant social and financial implications, since increased levels of stress have been reported to reduce performance with diverse subsequent complications [11].

4. Internal Stress. Mostly attributed to the modern hectic lifestyle that tends to prevail in modern societies [12].

Regardless of the exact definition and categorization, job stress is estimated to cost the U.S. economy 300 billion dollars annually due to diminished productivity, absence from work, and medical and insurance bills [1], further substantiating the fact that this phenomenon constitutes a public health crisis.

In this context, stress has additionally been implicated in the initiation of complex pathophysiological cascades contributing to the development of various medical conditions including cardiovascular diseases, diabetes and immunosuppression [13]. Stress-induced sudden cardiac death has been reported to be the most severe manifestation of psychosomatic interaction [14]. Furthermore, stress can also exacerbate preexisting diseases such as gastrointestinal reflux disease, back pain, and irritable bowel syndrome [15].

On the other hand, stress-free living has been associated with longevity and reduced morbidity when other confounding factors are matched [16]. Self-perceived well-being and a stress-free lifestyle are therefore of paramount importance in maintaining health and homeostasis [16].

At the human physiology level, stress leads to changes in the activity of the central nervous system and most notably the autonomous nervous system. More specifically, under stressful conditions the hypothalamus and adrenal glands are activated, imitating a hormonal cascade. The two main hormones involved are glucocorticoids (mainly

cortisol) and catecholamines (adrenaline and noradrenaline), both of which facilitate the ability of the human body to cope with the demanding conditions that have arisen [17].

The relative amount of the hormones produced is considered to be of paramount significance since the neuroendocrinological equilibrium can lead either to eustress or distress. Eustress is characterized by positive emotions arising from a stressful but pleasant stimulus (excitement) while distress is perceived as negative stress associated with fear or threat [18].

Measuring stress has traditionally been associated with the usage of weighted questionnaires, such as the relative stress scale [19] and the perceived stress scale [20]. The downside of these methods is that they are subjective, require manual recognition and are static failing to adjust to the continuous changes in human emotions and environmental conditions.

Continuous monitoring and classification of stress levels is very significant in order to address and limit its consequences. The recording of various physiological parameters such as blood pressure, heart rate, respiratory rate and electrodermal activity has been elaborated to achieve this goal [21].

The human skin has distinct electrophysiological characteristics that can be measured and analyzed [22]. The main determinant of the changes that occur in its electrical properties is sweat gland activity, since the production of sweat reduces skin resistance. This in turn depends on the function of the autonomous nervous system, which provides sympathetic innervation to the skin glands and regulates their function [23].

The most widely accepted model of electrodermal activity dates back to the 1980 [24] but the recording and analytic methodologies for its study have evolved over the years, leading to a revived interest in its use as a non-invasive method to diagnose psychological and somatic pathophysiology [23]. Mental and physical stress from various insults have a direct effect on autonomous nervous system and therefore this model appears promising for monitoring and interpreting stress activity [25].

## 1.1 Objectives and methodologies

The primary objectives of the current thesis are:

1. Reviewing the literature regarding the usage of biosensors for stress detection, with a focus on electrodermal activity(EDA) recording. More specifically the types of bio signals that are utilized, the methodologies employed to extract meaningful electrodermal activity data regarding stress as well as their interpretation are an essential part of this review.
2. The analysis of electrodermal activity data for the calculation of relevant metrics and subsequent statistical analysis for potential correlations with volunteer specific parameters.

As far as the methodological approaches are concerned, the review process involved searching Google Scholar, ScienceDirect, the IEEE Xplore Digital Library, and Pubmed with relevant keyword/phrases (electrodermal activity, bio signals, galvanic skin response, skin conductance, skin resistance, stress and electrodermal activity, stress and galvanic skin response) in order to identify the corresponding publications. Only publications written in English were considered for further evaluation.

The analysis of EDA data from volunteers was performed with the Python programming language (continuous wavelet transform (CWT)-based peak detection was employed) while the subsequent statistical analysis was achieved by using the R language and environment for statistical computing and graphics.

## 1.2 Potential contribution

The current thesis is expected to contribute to the better understanding of electrodermal activity and its practical applications in stress detection methodologies both in research and real-life scenarios. This will be facilitated not only by the critical appraisal of the existing scientific literature but also by the experimental component, which includes the analysis of electrodermal activity data from volunteers and their statistical processing and interpretation. The outcomes of the study could also trigger further research and rejuvenate interest over EDA and its applications in the field of bio signal monitoring. Furthermore stress prevention based on the bio signal technology

would be in line with the long term goal that has been set by the EU to personalize health care [26].

## 1.3 Thesis outline

Chapter two focuses on the physiological basis of stress detection via EDA recording and processing. The link between sudomotor activation, changes in skin conductance and stress is explained. Furthermore, other bio-signals that can be utilized according to the literature in stress detection are presented alongside their corresponding sensitivities and specificities.

Chapter three presents the technical aspect of EDA recording including the various methodologies applied, the different metrics employed, and basic nomenclature. In addition potential practical applications of EDA in relation to stress are summarized.

Chapter four analyzes the different determinants of EDA metrics, both person specific and technical. The difficulties of EDA recording, especially in the ambulatory setting are evaluated and methodologies for dealing with artifacts are presented.

Chapter five focuses on the interpretation of EDA metrics in relation to baseline volunteer characteristics and combined with other bio signals. The importance of the nature of applied stimuli is also underlined as well as the implications of this for research methodologies.

Chapter six presents the analysis and the results of the current study. More specifically the number of participants, the methodologies and statistical approaches are presented as well as the statistically significant correlations that were identified and their interpretation.

Chapter seven correlates the findings of the current study with results from the existing literature and provides potential interpretations the statistical relationships detected. Potential limitations of the study are also presented.

Chapter eight presents a justification for the plausibility of utilizing EDA metrics in stress detection based on the findings of the current study and the appraisal of the literature. The potential for future applications in personalized healthcare is also underlined.

Chapter nine provides (Appendix A) detailed information regarding the algorithms employed for the identification of EDA metrics as well as samples of the Python code that was utilized. In addition, relevant R code examples are included.

# Chapter 2
# Physiology, Biosignals and Stress

The skin consists of two main layers, the dermis (corium) and the epidermis. The latter comprises the surface of the skin and consists of epithelial cells. Dermis, which lies deeper, consists primarily of connective fibrous tissue and is followed by hypodermis (subcutis) which contains the majority of the secretory parts of sweat glands (some also lie in the dermis), fat and vasculature [27].

Sweat gland activity is of paramount importance for thermal auto-regulation. Sweat glands are categorized as eccrine, meaning that they depose their secretion (which contains no cytoplasmic material) directly onto the skin surface (Figure 1). Under stressful conditions sweat secretion can reach 2 L/hour, potentially leading to severe dehydration [28].

The biological significance of electrodermal activity (EDA) and increased sweat gland activation is considered to be associated with the survival advantage arising from the increased grip strength, mobility and protection from cuts that the hydration of palms and soles confer [29].

Sudomotor activation is mainly sympathetic, originating initially from the spinal sympathetic nerves. Each sweat gland is innervated by multiple sudomotor efferent fibers [30], with every fiber corresponding to a skin area of approximately 1.28 $cm^2$ [31]. When multiple fibers are activated concurrently, a nerve burst can be recorded in the form of a skin conductance response [32]. The involvement of the central nervous system in the production of EDA is crucial, since the limbic system, the basal ganglia and the reticular formation have all been implicated in sweat gland activation and elicitation of Galvanic Skin Response(GSR) [33].

Electrodermal activity is considered an appropriate indicator of autonomous nervous system function because:

1. The eccrine glands of the fingers receive innervation solely from the sympathetic part of the autonomous nervous system (no innervation from the parasympathetic system)

2. The postganglionic sympathetic nerves are cholinergic and not noradrenergic, which is in line with the other tissues that receive sympathetic innervation [33].

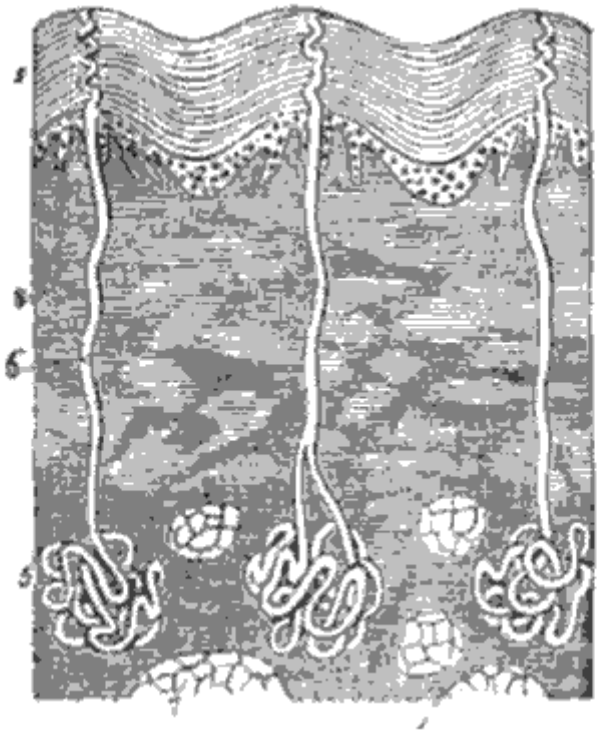

**Figure 1**. Relevant anatomy of the human skin depicting the sweat glands and their ducts [34].

## 2.1 Biosignals that can be utilized in stress monitoring

Apart from electrodermal activity [35], a variety of other biosignals have been reported to correlate with stress levels including the following:

1. Electrocardiogram (ECG) acquisition. ECG recording has been utilized for extracting heart rate variability, a parameter that has been found to correlate not only with stress but also with other physiological variables. It is recorded non-invasively through the usage of the corresponding leads and the consequent analysis can be automatically performed with appropriate software packages. Both time and frequency based domain methodologies have been applied for HRV analysis. The former is considered the simpler one, with its basic characteristic being that it preserves the temporal integrity of the signal while lacking in frequency resolution [36]. The latter one is based on time aggregation, preserving frequency composition but lacking in terms of temporal resolution [36].

2. Electroencephalogram (EEG). EEG (Electroencephalogram). This parameter depicts the spontaneous and occasionally induced brain activity recorded through electrodes [37]. The recording of brain waves correlates with the mental activity of a person and their type and frequency is indicative of the level of stress experienced by the person. In addition, the location of the scalp where the wave activity is detected is also characteristic of the emotions and mental state of the person [38]. The band category and frequency range of brain waves is very informative since Beta waves (13-30 Hz) are associated with anxiety and stress while Alpha waves are considered indicative of relaxation [39]. It has also been reported that the theta/beta brain wave ratio is analogous to the individual's stress levels [40].

3. Electromyogram (EMG). Muscle contractions and activity can also be used in the context of stress level monitoring [41], though less reliably due to difficulties that may arise in its interpretation and the existence of confounding factors and artifacts.

4. Photo-plethysmography is a technique that analyzes transmitted or reflected light in order to calculate heart rate, respiratory rate and even oxygen saturation. This

method is also non-invasive and provides continuous data. The combination of the above-mentioned parameters can be used to reach statistical conclusions regarding stress [42].

5. Pupil dilation. Changes in the diameter of the pupils have been reported to correlate with stress induction, although further validation is still pending [43].

6. Heart rate variability (HRV). The high frequency component of HRV in indicative of parasympathetic activity while the low activity correlates with the sympathetic system activation [44].

7. Respiratory system. More specifically the respiratory rate has been found to both correlate with heart rate and stress levels [45].

8. Speech. Neural network-based classifiers have been theorized to be of use in utilizing speech pattern for detecting stress [46].

The recording of each type of bio signal requires a different data acquisition technique while the anatomic site for sensoring should also be adjusted (Table 1). Furthermore, the sensitivity of the corresponding bio signals in detecting stress ranges from 79% to 97% depending on the nature of the stimuli applied and other methodological and investigational factors (Table 2).

Interestingly every bio signal has its own unique characteristics that provide specific metrics such as the various intervals in the ECG waves (Figure 2) and the frequency and morphology of EEG waves (Table 3).

| **Recording device** | **Bio signal** | **Anatomic site for sensoring** |
|---|---|---|
| GSR (Galvanic Skin Response) sensor | Skin resistance/conductance | Usually digits/wrist/arms/thorax |

| Recording device | Bio signal | Anatomic site for sensoring |
|---|---|---|
| **Electrocardiograph** | Electrocardiogram | Thorax |
| **Electroencephalograph** | Electroencephalogram/Brain waves | Scalp |
| **Electromyogram** | Muscle contractions | Muscle groups |
| **Electrooculograph** | Electrooculogram | Area surrounding eyes |
| **Inductive plethysmography** | Respiratory rate | Thorax |
| **Photoplethysmography** | Heart rate, oxygen saturation | Finger and ear |
| **Sphygmomanometer** | Blood pressure | Upper arm |

**Table 1.** Bio signal recording devices and anatomic sites [47], [48], [49]

| Biosignals | Stimulus | Maximum reported sensitivity |
|---|---|---|
| **EMG, ECG, EDA, RSP** | Driving | 97% |

| | | |
|---|---|---|
| **EDA, Blood Volume Pulse** | Stroop test variant | 90% |
| **EMG, ECG, EDA** | Driving (car racing) | 79% |

**Table 2.** Maximum reported sensitivities for stress detection by using specific biosignals. [50] [51] [52]

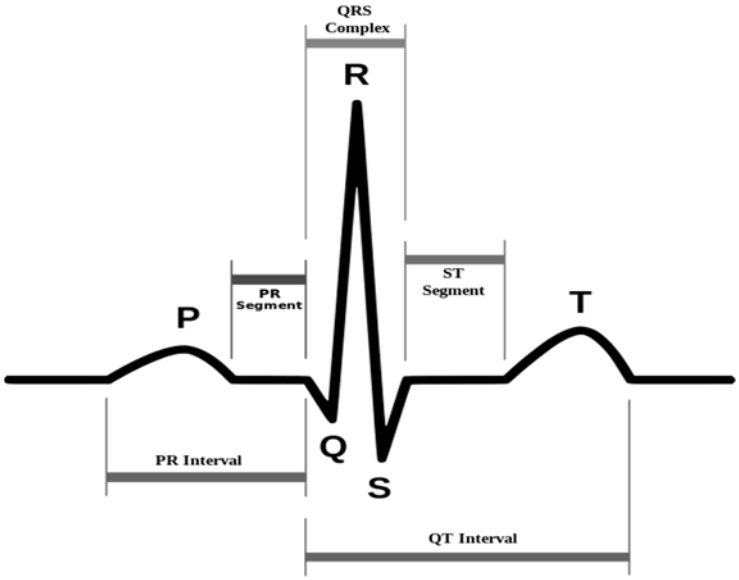


**Figure 2.** Electrocardiogram intervals. Heart rate variability can be calculated based on ECG trace and utilized in stress detection algorithms. [53]

| **Brain wave** | **Characteristics** |
|---|---|
| **Alpha** | Frequency range from 7 Hz to 14 Hz. Detected during eye closure and with relaxation. |
| **Beta** | Frequency range from 15 Hz to 30 Hz. Usually symmetrical distribution. Closely related to motor activity. Low-amplitude beta can be seen with busy or anxious thinking. |

| Brain wave | Characteristics |
|---|---|
| **Theta** | Frequency range from 4 Hz to 7 Hz. Usually recorded in young children and during meditation. Excess theta activity can indicate encephalopathy. |
| **Delta** | Frequency range up to 4 Hz. Usually observed during sleep. If it is recorded focal it can indicate subcortical brain lesions. |
| **Gamma** | Frequency range 30–100 Hz. Indicative of complex inter neuron interaction. |

**Table 3.** Brain waves that can be detected in an EEG recording and their characteristics [54].

## 2.2 Physiology of sympathetic skin response

Various terms have been used over the years to describe the electrical characteristics of the skin including electrodermal response, electrodermal activity, psychogalvanic reflex, galvanic skin response and sympathetic skin response [55]. Regardless of the term that is being used, galvanic skin response is a change in potential recorded from the surface of the skin that represents the result of increased sympathetic nerve activity that consequently leads to eccrine sweat gland stimulation.

Eccrine glands, located on the palms and the soles, have a distinctly different function than glands that are found elsewhere in the body, in the sense that they have no thermoregulatory function. On the contrary, they are activated in order to increase grip effectiveness from a phylogenetic point of view and are associated with a fight or flight reaction.

The autonomous nervous system is divided in two distinct parts: the sympathetic and parasympathetic components (Figure 3). The former is responsible for facilitating the so-called “fight or flight” reactions [56], meaning that when the human organism perceives

an external stimulus as dangerous then a cascade of events is initiated leading to preparations to either confront the insult (fight) or flee the scene (flight). In this context under stressful conditions the production of sweat is produced by the glands through the above-mentioned mechanism, leading to the creation of reduced resistance pathways and hence distinct skin electrophysiological results.

The basic afferent nerve pathway that controls sweat gland activation originates in the posterior hypothalamus which interacts with the medullary reticular formation and the pontine tegmentum of the brainstem. The pathway ends with the preganglionic sympathetic nerve in the spinal cord and postganglionic sudomotor innervation of the eccrine glands. Multiple interactions with the lateral prefrontal cortex, amygdala, cingulate and hippocampus also exist [33], raising the possibility of the existence of an autonomic regulation feedback loop.

The autonomous nervous system is excited by various stimuli such as visual, audial, thermal, working and exercising [57] creating a complex network of causality that need to be unraveled in order to create plausible scientific experiments.

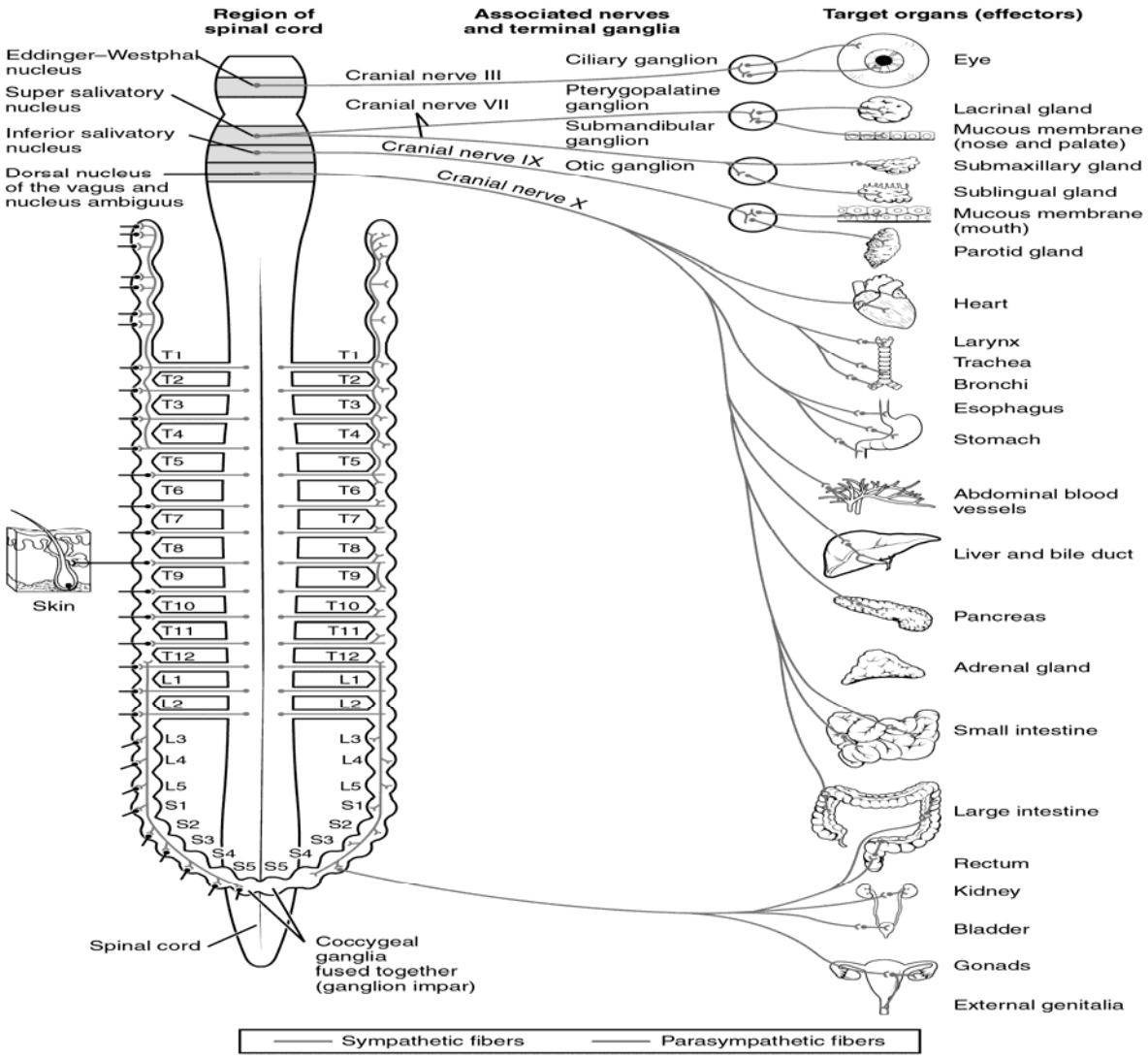


**Figure 3**. Relevant autonomic nervous system anatomy [58]

# Chapter 3
# Electrodermal activity and stress

According to Ohm's law, the current through a conductor between two points is proportional to the voltage across these two points. The mathematical equation that describes the above-mentioned relationship is:

$$I = V / R$$

where I is the current measured in units of amperes, V is the voltage measured in volts, and R is the resistance of the conductor expressed in ohms.

The law can be expressed as R=V/I if resistance is the investigated parameter.

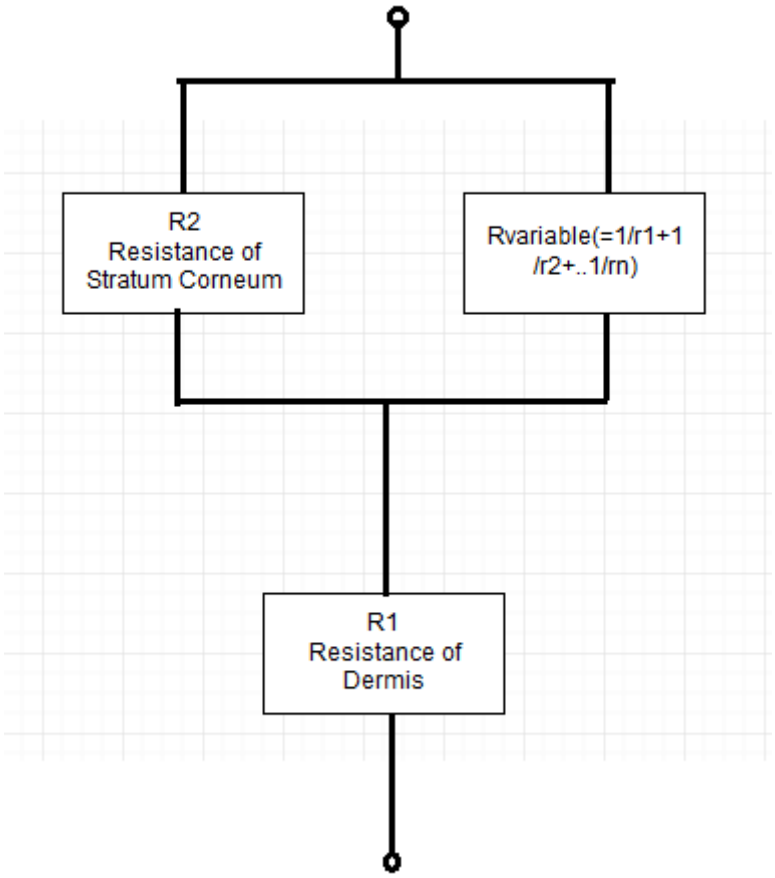


**Figure 4.** Model of skin resistance. r1,r2,….rn=sweat gland resistance

Skin can be viewed as an epidermal conduction pathway with interspersed sweat glands, connected externally to the applied electrode and at the other end to deeper dermal and connective tissues, creating a parallel resistor schematic.

As depicted above, constant current or constant voltage methods can be used in the context of electrodermal response. If current is kept stable, then voltage is directly proportional to skin resistance R [59].

Measuring skin conductance can be achieved by detecting the current that flows in the skin when a constant voltage is applied. The output of the EDA amplifier in this case is the skin's conductance (usually measured in microSiemens) [59].

A significant limitation is that Ohm's law holds only when the exosomatic electrodermal activity is recorded and current density does not exceed 10 μA/cm2 [59]. Higher current densities appear to decrease skin resistance level (SRL) and skin resistance response (SRR) and in this context constant current methodologies are preferentially elaborated.

However, in patients with considerably low resistance levels, current densities up to 75 μA/cm2 seem to produce valid results before non-linearity ensues [59].

## 3.1 Technical aspects of galvanic skin response recording

The two main methodologies that have been elaborated in the recording procedure of galvanic skin responses are the following [60]:

1. The application of a small electrical current between two electrodes in the skin surface and measurement of the changes in skin conductance with the use of a galvanometer when an external stimulus is applied to the individual (exosomatic method). If a DC current is applied, and voltage is kept constant, then EDA can be measured in conductance units (μS), while when the current is kept constant resistance units are applicable (Ω). AC measurements are more rarely used, but when this is the case impedance units apply when effective voltage is kept constant and admittance units when the effective current remains constant [61].

2. Measurement of natural differences in skin potential after the exposure of the individual to an external stimulus (endosomatic method).

There is no clear consensus regarding the site where the electrodes should be placed; however, the most common areas are palmar surface of the hand in medial and distal phalanges of the fingers and the thenar and hypothenar eminences. The movement of the hands can occasionally produce artifacts in certain experimental settings, in which case other areas such as the ventral sides of the distal forearms can be used.

There is a wide range of electrodes that can be elaborated in GSR recordings, however the Ag/AgCl type is the most common one. In this case, a suitable electrode paste is required (usually consisting of sodium chloride), since the contact medium should be isotonic to sweat [61].

In this context, the measurements that can be acquired are subdivided depending on the method applied as follows [60](Figure 5):

1. Skin resistance response (exosomatic)

2. Skin resistance level (exosomatic)

3. Skin conductance response (exosomatic)

4. Skin conductance level (exosomatic)

5. Skin potential response (endosomatic)

6. Skin potential level (endosomatic)

Conductivity is defined as $G = 1/R$, where R (resistance) equals the opposition of an element (skin in this occasion) to the passage of an electric current. Specific conductivity $\sigma = G \times (L/A)$, where L is the length of the column of liquid between the electrode and A is the area of the electrodes. In the context of galvanic skin response measurements sweat is considered as the liquid conductor since it has significantly higher conductivity from the surrounding fat and other tissues. The SI unit of electrical conductance is siemens (S) while that of electrical resistance is the ohm (Ω).

Conductance is considered the preferred expression for recording EDA activity, since it is reported to be more appropriate for averaging and statistical processing [60]. Phasic components are short lived fluctuations in GSR while tonic levels are generally less versatile. In this context, SCR is the measure of phasic activity while SCL corresponds to tonic EDA. The former appears to have a better temporal resolution and consequently the potential to reveal event related responses [62]. This is particularly important in order to exclude arousal that occurs due to thoughts unrelated to the experimental setting that could potentially lead to erroneous results. On the other hand, differential SCL recordings between two states of arousal (baseline and post stimulus) has the advantage of (even partially) addressing the problem of differential level dependency.

In the electrodermal measurement experimental setup, the stratum corneum of the skin may be considered as a large flat insulating layer (dielectric – usually 50,000 to 100,000 ohms due to moisture retained in the keratin layer). In the superficial side of this "insulating" material lies the electrode from the measurement device, while the inner

tissues with 300 to 1000 ohm resistance can be considered as another electrode in the context of the experimental design [63].

The internal resistance of the human body varies from approximately 300 ohms to 1,000 Ohms. Bone and fat have the greatest resistance while nerves and muscles have the lowest ones [64]. Resistance depends also on the location of the electrodes, since greater distance is associated with increased resistance, meaning that a configuration that uses adjacent finger electrodes will have greater conductivity in comparison to placing the two electrodes in the hand and foot.

Another important factor is the diameter of eccrine glands (maximum is ≤30 μm), which at any certain event is variable between the thousands of glands that exist in the skin surface, thus alternating conduction locally in a different manner [65]. Grip strength can also increase the quantity of sweat released in the surface leading to differentiated results that should be taken into account in order to increase the repeatability of the studies.

The elicitation of stress in research settings requires the utilization of an effective and reproducible stressor mechanism. In this context, the so-called Stroop test, has been widely accepted and validated as an appropriate means of inducing stress in a dependable and objectified manner [66]. More specifically, this test (in its classical version) demands from the user to name the color font of a word that designates a different color [66]. Interactive variations of the test have also been created, that are more practical in the era of electronics and computer technology [67].

Other stressors that have been occasionally elaborated include videogames, hyperventilation sessions as well as driver and pilot simulations [68] [69].

The delay time between the stimulus and the detection of a skin conductance change has been reported to be 1.5-2.5 sec [70].

The choice of location between the hands (Figure 7) and feet for the placement of the electrodes may also lead to small differences. More specifically, EDA peaks at the foot have been recorded to occur approximately 0.5 sec after those recorded in the hands [71]. Despite the disparities in the absolute values, a similar behavior is exhibited in the data pattern as manifested by the close correlation of the reported results.

The recording rates should also be appropriately adjusted in order to facilitate the research goal. In the context of an ambulatory measurement setting a rate of 1-5 samples per second could suffice [72], while during an event triggered analysis acquisition rates are expected to be considerably higher [73].

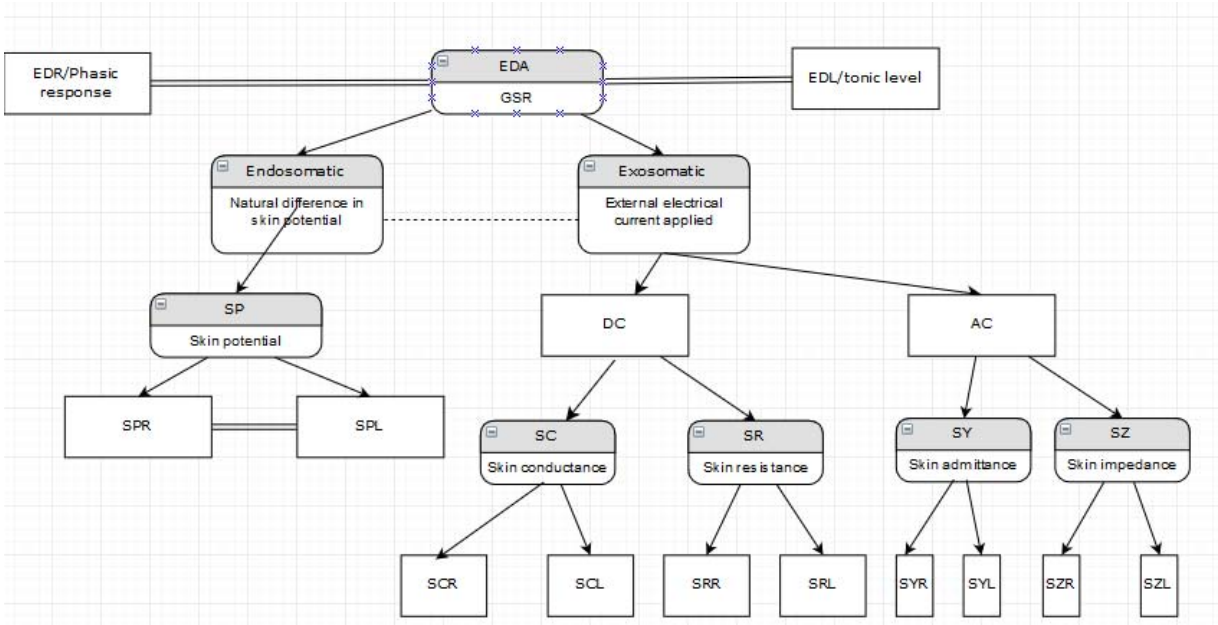


**Figure 5.** Electrodermal activity nomenclature

The first two letters in the acronyms refer to method applied (SP: skin potential, SR: skin resistance, SC: skin conductance, SZ: skin impedance, SY: skin admittance), while the third letter to response.

| **Parameter** | **Explanation** | **Normal/typical values** |
|---|---|---|
| **Skin conductance level** | Baseline skin electrical conductivity | 2-20μS |
| **SCR amplitude** | Phasic rise in conductance immediately following the application of stimulus | 0.1-1μS |

| Parameter | Explanation | Normal/typical values |
|---|---|---|
| **SCR latency** | Time internal between stimulus application and SCR initiation | 1-3 s |
| **SCR rise time** | Time interval between SCR initiation and SCR peak | 1-3 s |
| **Non-specific SCR** | Frequency of skin conductance responses not attributable to stimuli | 1-3 per min |
| **SCR half recovery time** | Time interval between SCR peak and fall to 50% of SCR amplitude | 2-10 s |
| **SCR habituation** | Rate of decrement in response amplitude with repetitions of the same stimulus | 0.01-0.5μS per trial |

**Table 4.** Based on [74] and [75]

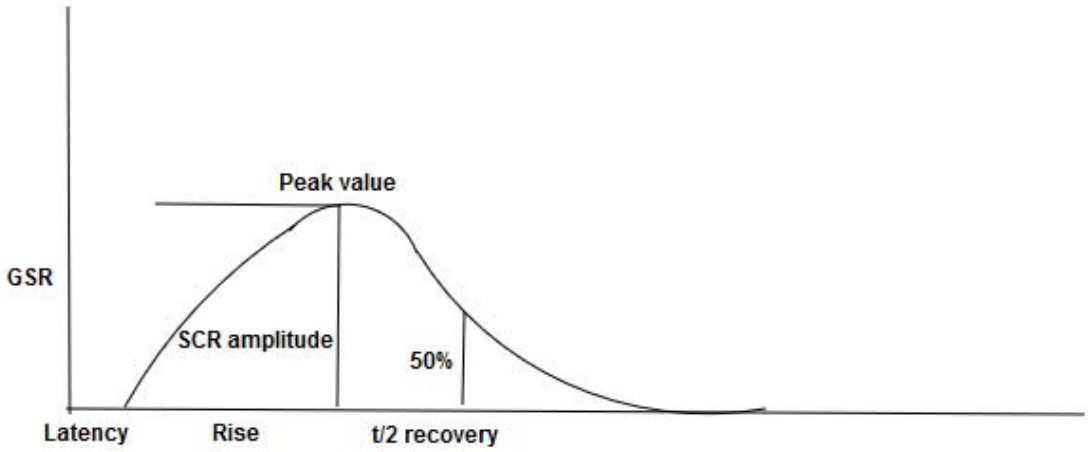


**Figure 6.** Galvanic skin response illustration

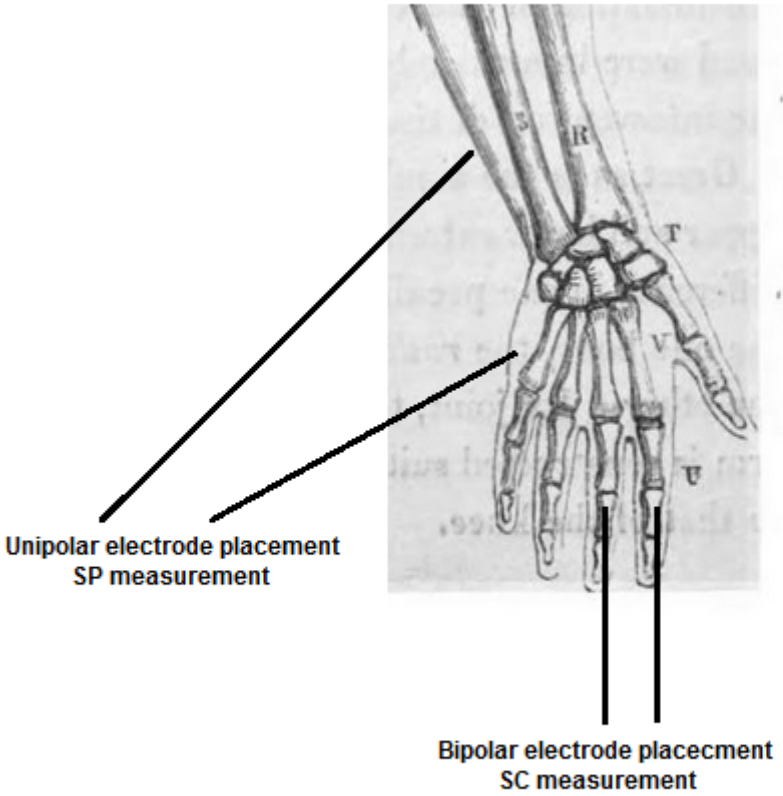


**Figure 7**. Common placement of electrodes for GSR measurement [76]. Modified by author.

## 3.2 Galvanic skin response, detection of stress and subsequent applications

The correlation of galvanic skin response and stress levels has been validated not only through the elaboration of questionnaires [77], but also biochemically. More specifically the levels of cortisol, a hormone that increases in stressful conditions have been found to correlate with GSR measurements, therefore indicating that there is a solid underlying physiological basis for its utilization in this context [78]. Radiological studies have also indicated that GSR values reflect the activity in brain areas associated with complex cognition patterns and stress perception [79].

It has been reported that financial traders experience significant predictable GSR changes correlating with stress levels during periods of market volatility [80]. The accuracy of GSR measurements for stress detection can reach 80%, especially when combined with other physiological indicators such as pupil size or heart rate [81].

Real world scenarios seem to validate the effectiveness of GSR measurements. Characteristically, individuals can be classified into distinct stress states with 97.4% accuracy when exposed to different stress levels during driving sessions, by utilizing GSR based algorithms [69].

These results have also been validated in real world and experimental settings involving arithmetic [82], reading [83] and visual tasks [84] with accuracy ranging from 80 to 90%.

These promising findings have led wearable device developers to incorporate GSR sensors in their new releases [85], indicating the potential applications of electrodermal activity in everyday life.

The incorporation of sensors in garments has attracted scientific attention in the recent years since this methodology allows the continuous non-invasive recording of physiological data indicative of stress. More specifically, chest straps [86], wrist/glove like devices [87] and T- shirts [88] have been manufactured for research purposes with the potential for wider implementations. With the advent of newer technologies and the evolution of the industry of electronics, these embedded galvanic detection systems have been refined to the point that they can be seamlessly incorporated in everyday

items/clothing while providing high quality data recording thanks to the application of textrodes [89].

The non-invasive nature of GSR recordings allows its application in various settings were stress level measurement is required including:

1. Perioperative stress detection and guidance of appropriate treatment [90].

2. Military applications [91]

3. Diagnosis of diseases that affect peripheral nerves [92]. Any condition affecting the peripheral nervous system could potentially influence GSR results. Most notably, diabetes, which is intrinsically associated with dis-regulation of the autonomous nervous system, has been a focus in GSR studies investigating the potential for early diagnosis and monitoring of disease progression. Interestingly, GSR amplitude has been found to be an objective and reproducible marker for peripheral nervous system dysfunction in diabetes patients [93] on the contrary to latency, which does not solely reflect peripheral c fibre activity.

4. Diagnosis of central nervous system conditions such as multiple sclerosis, Parkinson's disease and brain infarctions. Characteristically, as high as 75% of patients with multiple sclerosis exhibit deranged electrodermal activity, a sensitivity comparable to that of somatosensory evoked potentials, a method well validated and universally elaborated for monitoring these patients [94]. In the same context, sympathetic skin responses have been successfully utilized in the early diagnosis of Parkinson's disease [95] even when clinical findings are scarce. More specifically, it has been reported that suppression of the SSR amplitude is a marker of Parkinson's disease activity and response to medications [96]. As far as brain infarctions (strokes) are concerned, it has been suggested that hemispheral and brain stem lesions suppress the reflex activity of the sympathetic nervous system and hence reduce GSR amplitude [97].

5. Reducing road accidents by detecting operator dependent errors related to increased stress levels [98].

6. As a biofeedback tool in psychiatric disorders in the context of minimizing anxiety responses [99]. EDA based biofeedback training has also been reported to increase athletes' sport performance and promote their self-perceived well-being [100].

7. As a tool to improve video game experience and understand the complex behavioral patterns associated with gaming [101].

8. To assess cognitive load and optimize academic performance [102]

9. Studying sleep patterns (REM and non-REM) and improving its quality [103].

## 3.3 Galvanic skin response and other biosignals in the context of intelligent biofeedback systems

Biofeedback systems are an emerging method to promote stress control by providing quantifiable values of a specific physiological parameter as an indicator to guide the patients' efforts towards relaxation [104]. The monitored factors are usually non-invasively obtained and provided as feedback in real time. Heart rate, blood pressure and galvanic skin resistance have been successfully used in this context, since they correlate in a predictable manner with stress levels and they can be easily recorded and analyzed [105].

Characteristically the practicality of such applications has been exhibited in various medical conditions including:

1. Hypertension and achieving reduced need for medications upon usage of biofeedback systems [106]

2. Controlling epileptic activity and avoid heart arrhythmias [107]. More specifically galvanic skin response biofeedback training has been reported to achieve statistically significant less seizure frequency in the experimental group in comparison to controls [108].

3. Recovery from training and heavy competition circumstances that are associated with anxiety [109].

4. GSR biofeedback and the elaboration of relaxation techniques to reduce physiological indicators of stress such as the respiratory rate [110].

5. Control anxiety and avoid exacerbation of symptoms in psychiatric patients. The GSR profiles of each patient appear to be different, and for this reason an individualized follow up is preferential for monitoring mood disorders [111].

# Chapter 4
# Factors Affecting Galvanic Skin Response Measurement

Several baseline factors could potentially influence the results of individual parameters of the galvanic skin response including:

1. Age, height and gender. More specifically older individuals have been reported to produce a statistically significant lower amplitude with normal latency periods [112] although this notion has not been verified in other studies [113]. The same heterogeneity in results applies as far as height is concerned, with certain studies reporting an association of latency with height [114] [115] while others do not [116].

2. Skin and body temperature, with both parameters being linearly related to amplitude and latency values [117]. In this context, body temperature influences post ganglionic nerve conduction activity and neuroglandular interaction [118] leading to changes in the recorded measurements. In addition, the permeability of skin for water increases exponentially in relation to skin temperature, with skin permeability doubling for every 7 degrees' Celsius increase in skin temperature [119]. Appropriate room temperature and avoidance of local skin warming are of paramount importance in order to avoid these confounding factors.

3. Habituation. This term refers to the gradual decrease on the recorded potentials after repetitive stimulation [120]. This phenomenon may arise after as few as three repetitions [121]. Therefore, allowing for appropriate time intervals between repetitions and choosing a variable frequency of applied stimuli could contribute to managing this phenomenon.

## 4.1 External determinants of EDA signal recording

A variety of external factors may influence the data being recorded:

1. Relative humidity appears to be a significant confounding factor that should be taken into account. Both negative and positive correlations have been reported for different humidity levels [122], potentially differentiated between distinct age groups.

2. The influence of air pressure remains elusive, with studies indicating the existence of a correlation for the male gender [123].

3. The existence of artifacts is a major issue in EDA recordings since if they are not removed before the statistical analysis, erroneous results may occur. Disruptions of the skin electrode surface can arise due to mechanical pressures, flow of contact gel and wire drag. In addition, body movements and even the breathing pattern can be significant sources of artifact creation. In order to minimize artifacts, visual inspection of the recordings, is always desirable, if possible, while for longer recordings computer software can be used to remove the outlier values based on appropriate algorithms.

4. Medications can exert significant anti-cholinergic actions and therefore influence the EDA results. This applies to both prescription and over the counter drugs. Commonly used medications that could influence cholinergic activity include those given for allergic reactions, stomach upset, glaucoma as well as for psychiatric reasons (anti psychotics, antidepressants). Even caffeine has been reported to influence results and more specifically increasing arousal [124].

5. Statistical analysis. In this context, multiple statistical methodologies have been developed with varying validity [125] [126], meaning that depending on the researcher's choice significant divergence of the results and interpretative approaches could arise.

6. Form of applied stimuli. The changes in methodology have the potential to greatly influence the results. Bibliographically various modalities have been elaborated

ranging from specific breathing patterns (deep inspiration/forced expiration) [127], use of small intensity local currents [128] and mechanical effects [129] to sensory stimulation(optical/hearing) [130]. The extent of the variability of the reported findings attributed to the different applied methodologies remains elusive and further studies could contribute to objectifying the experimental procedures.

The aforementioned difficulties that may be encountered during the data recording can be overcome by various methodological and organizational approaches such as filtering, manual inspection, artefact removal(Table 5).

| **Proposed method** | **Study** |
|---|---|
| Inspect experimental conditions and recording equipment when rapid fluctuations in skin conductance levels arise, or amplitude increases beyond 40 μS/cm2, or falls below 1 μS/cm2 | [131] |
| Utilization of model-based filtering to remove noise from recorded data | [132] |
| Elaboration of automated active learning techniques | [133] |
| Using alternative non-hydrating electrolyte mediums that reduce noise generation | [134] |
| DC and AC simultaneous measurements from the same site allowing comparison of results | [135] |
| Use of devices that include an accelerometer in order to identify moments of increased physical activity with a propensity for artifact generation | [136] |

| Proposed method | Study |
|---|---|
| Wavelet-based motion artifact removal | [137] |

**Table 5**. Suggested methodologies for avoiding artifacts and erroneous results in EDA recordings

## 4.2 Ambulatory EDA recording

In most occasions EDA recording takes place in experimental conditions, when most external factors can be controlled. Furthermore, the duration of the recording is usually limited in the laboratory setting. Ambulatory monitoring offers the opportunity to record data under real life scenarios; however, their interpretation may be troublesome since the temporal correlation between the stimulus and the recorded results should be unraveled. The elaboration of video and audio recordings by the individual and the institution of intervening laboratory sessions can contribute to the delineation of the data.

Temperature, humidity and movement artifacts are major concerns in the ambulatory setting that should be addressed. The application of non-hydrating isotonic gels seems to produce better and more reliable results in these conditions [138]. Regardless of the type of gel used, after 24 hours the results start to lack the needed sensitivity and therefore ambulatory recordings beyond this period are discouraged.

A simple accelerometer sensor incorporated in the experimental device appears not to suffice for controlling for physical activity that the person undergoes [139]. More specifically, only strenuous activity seems to significantly increase sweating and SCL, which would require more robust techniques of measuring physical activity in a qualitative and quantitative manner.

Differences encountered during sleep awake cycles constitute an interesting aspect of ambulatory EDA monitoring. SCL appears to have lower values during sleep when the finger location is used for the electrodes [140]. At the wrist, prominent rises may also occur which may indicate thermal sweating caused by the REM- non REM sleeping cycle alterations.

Taking into account the above-mentioned considerations it becomes evident that multi-sensoring devices should be used for ambulatory EDA monitoring in order to simultaneously record multiple parameters allowing for eradication of artifacts and elucidation of causal relationships.

# Chapter 5
# Interpretation of biosignal data

The interpretation of biosignal data in order to quantify stress levels poses certain difficulties that have to be circumvented by elaborating appropriate statistical methodologies and improving experimental conditions. In addition, the transition from the experimental setting to a real-life scenario recording of biosignals is associated with multiple confounding factors such as the fact that the measurements are influenced by physical activity [132]. Characteristically individuals have a higher heart rate when standing in comparison to sitting, so measuring the heart rare in an isolated manner to predict the levels of anxiety would be an imprecise method. Furthermore, artifacts from electrode placing or the individual's movements can produce nonsense "noise" data that lead to mistakes in interpretation.

In this context, combining data from different physiological parameters is expected to increase the sensitivity and specificity of these stress detection techniques while advanced statistical methodologies such as standard linear regression, wilcoxon signed-rank, paired samples t tests, k means analysis and other advanced techniques that can lead to better classification results [141].

GSR readings tend to gradually increase over time due to accumulation of sweat in the electrodes, and therefore it is crucial that linear de-trend of the data should be performed. Overall the main interest is focused on the local patterns instead of the overall trend of a large sequence of recorded events.

Event related SCRs can be grouped as following [142]:

1. Phasic orienting responses to simple (usually noise) stimuli

2. Defensive responses to stimuli perceived as threatening

3. Reactions to stimuli that require complex analysis and perception (eg emotional visual stimuli)

The innate characteristics of galvanic skin response include(Figures 6,8):

1. Shape of the response. The form of sympathetic skin response can be triphasic, biphasic (most commonly in the legs) and rarely monophasic. Depending on the maximum deflection the responses can be classified into P type (positive maximum deflection) or N-type (negative maximum deflection), with the former being the most commonly encountered [143].

2. The latency of the GSR response, meaning the time interval between the stimulus and the first deflection from the baseline. Latency tends to be shorter in the hands compared to the feet [115]. The physiological stages of latency include afferent conduction (approximately 20ms), central nervous system processing time (milliseconds), and efferent conduction in autonomic nerve fibers. The majority of the GSR latency is attributed to the efferent nerve conduction and the activation of sweat glands. Normal latency is expected to lie in the vicinity of 1.3-1.5 sec in the hands and 1.9-2.1 sec in the soles [144].

3. The amplitude of the response, which is usually higher in the hands compared to the legs [115].

4. Reproducibility of the shape of the response. The rate of reproducibility in the same individual has been reported to be relatively stable at 23.9% [145].

The tonic EDA component is always changing in each individual and therefore it has been proposed that SCL on its own does not provide useful information [146]. In this context, subtracting the amplitude of SCR from the tonic signal as well as additionally recording outside stimulation events is considered crucial in analyzing data. The calculation of the frequency and amplitude of non-significant (not attributable to stimulation) SCRs is another important marker that should be taken into account, as they have been suggested to reflect more reliably background arousal in comparison to SCL [146]. One of the most significant difficulties that arise during GSR analysis is determining whether a SCR is event related (caused by a stimulus) or not. Failing to properly categorize SCRs can lead to

misinterpretation of the findings and erroneous results. This discrimination can be facilitated by acquiring a baseline recording period in order to determine the frequency and amplitude of NS-SCRs and also SCL. Hyper and hypo-respondents have distinct baseline measurements that may be of value during the final interpretation of the results.

The number of NS-SCRs depends on the amplification factors and amplitude thresholds that are being utilized [147], ranging from zero to ten per min during rest, while in active periods they lie in the vicinity of twenty per minute [147].

Skin conductance has certain limitations that should be taken into account when data are analyzed. More specifically habituation varies significantly between individuals, while as high as 15% of people studies may be classified as non-responders, meaning that no clear change in the SCR can be recorded after the exposure to a stimulus [148].

Another confounding factor that complicates the analysis of GSR is the fact that SCRs may be superpositioned. Researchers have traditionally calculated the difference of the SC values at its peak and preceding levels [149], with SCRs arising at an arbitrary time frame after the stimulus considered as event related [150]. Alternative approaches such as the curve-fitting decomposition and deconvolution have been proposed and applied by various researchers in order to deal with this problem [151] [152].

GSR activity is indicative not only of stress but also of mental effort or emotional changes and therefore its interpretation is not always straightforward. It has been suggested that greater GSR activity is associated with more effective word learning [153]. Interestingly, words that stimulate higher GSR activity appear to be characterized by a better long-term recall ability, raising the possibility that memory systems can be affected through this pathway [153].

If homogeneity or skew variance problems arise with the statistical analysis of the SCR data, then transformations can be performed including the square root or logarithmic transformations of the initial values.

The concept of transforming data into standard values has also been supported by researchers since the need for utilizing range corrected methods and normalization are obviated [154]. The transformation into z scores is one the prevailing methodologies in

this context, that addresses both the aforementioned practicalities. The mean SCR value and standard deviation of SCRs are utilized to create a normal random variable of a standard normal distribution.

A **z-score** indicates how many standard deviations an element is from the mean. A z-score can be calculated as follows:

$z = (X - \mu) / \sigma$

z =z-score,

X =value of the element,

μ=population mean

σ =standard deviation.

- A z score of zero indicates that the value of the element is equal to the mean value
- A z score of less than zero indicates a value less than the mean
- A z score of zero greater than zero indicates a value greater than the mean
- The z score indicates how many standard deviations the value of the element is greater or less than the mean value

Another approach would be to divide each SCR with mean SCR, providing an alternative standardization [155].

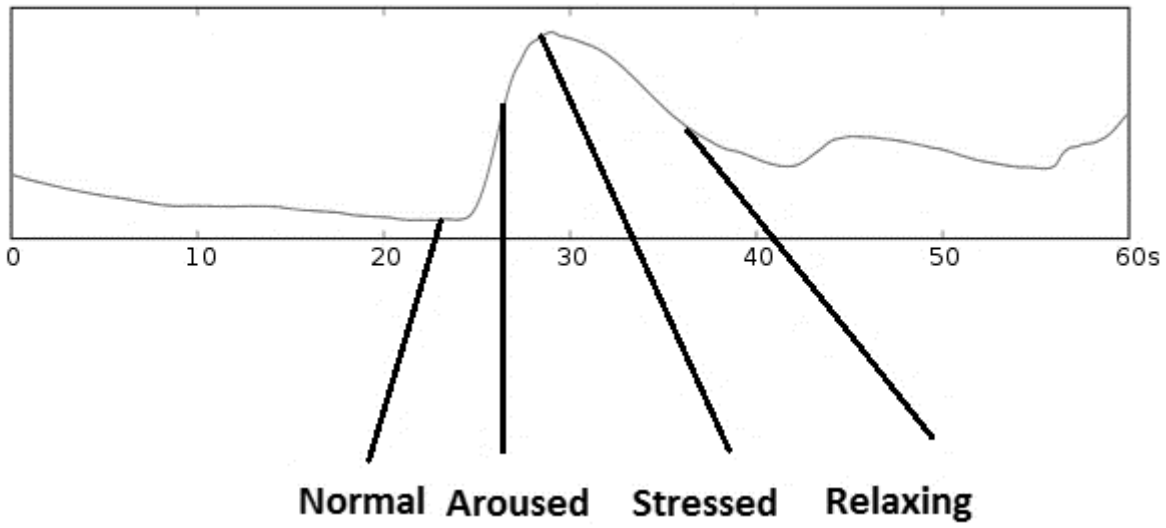


**Figure 8**. Example of acute stress pattern indicating the sequence of relevant phases. [156] Modified by author.

# Chapter 6
# Analysis and results of experimental data

The data for the current analysis stem from two groups of volunteers with seven and eighteen participants respectively. The first group consisted of one male and six female individuals(age range 56-66) while the second one of three women and fifteen men(age range 20-40). GSR recording was performed with a Shimmer GSR unit during calm and stress periods ,with the latter phases being facilitated by corresponding stroop and memory tests.

The recording frequency in the first group was 1.98 Hz and in the second group 32Hz. Taking into account the different sampling frequencies and age distributions of the two populations it was decided to undergo separate statistical analysis.

The participants of the second group were asked to fill the Spielberger State-Trait Anxiety Inventory (STAI) for adults questionnaires. Since they produce numeric results they were included in the statistical analysis along with the other demographic and physical data available.

The identification of NonSCRs, SCRs(with corresponding amplitudes) and Half Recovery times was performed using the python programming language(with application of continuous wavelet transform (CWT)-based peak detection)(Appendix A) while the subsequent statistical analysis was performed with the R language and environment for statistical computing and graphics(Appendix A).

Transformations to Z scores where employed where applicable in order to standardize data and eliminate differences in baseline sympathetic arousal. Figure 9 shows an example of Z transformed GSR versus time with peaks indicated.

The tonic electrodermal activity of each participant was evaluated by the calculation of Non SCRs per minute(Appendix A), which is considered an appropriate measure for this goal.

Multiple linear regression models and Spearman's Rho correlation coefficient where the primary statistical methods employed, since they do not require normal distribution of the data.

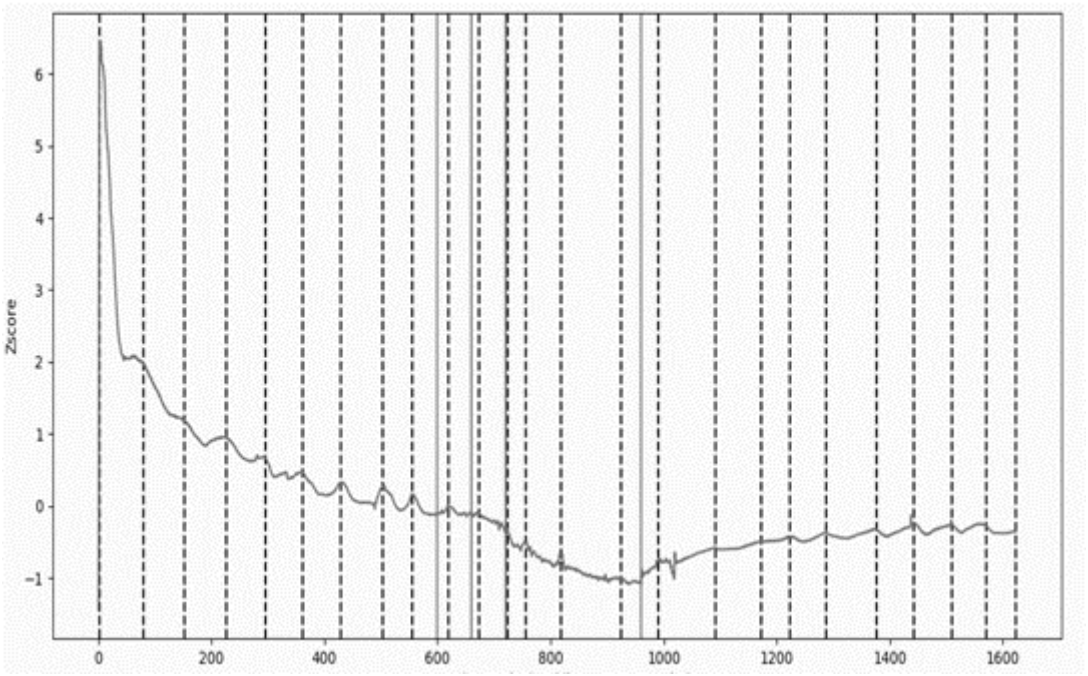


**Figure 9.** Example of Z transformed GSR versus time(in seconds) with peaks indicated with vertical dotted lines. The solid vertical lines indicate stress periods(patient ID9)

The statistical analysis of the data from the first group identified statistically significant correlations from the multiple regression analysis between the frequency of NonSCRs(regarding non stress time intervals) as a measure of tonic activity and age($p<0.01$), gender($p<0.05$) and physical activity($p<0.05$)(Table 6). More specifically increasing age appears to reduce the tonic EDA, which is in line with the literature which suggests that advancing age leads to a reduction both in the number and the activity of skin sweat glands [147]. The female gender is statistically associated with an increase in Non SCRs frequency, a finding also commonly encountered in studies [147].

```
Call:
lm(formula = group1$Frequency_nonscrs ~ group1$Age + group1$Gender +
    group1$physicalactivity, data = group1)

Residuals:
     Min       1Q   Median       3Q      Max
-0.43998  0.00000  0.00000  0.09692  0.11330

Coefficients:
                          Estimate Std. Error t value Pr(>|t|)
(Intercept)               2.93124    0.69469   4.219 0.000464 ***
group1$Age               -0.03006    0.01046  -2.874 0.009711 **
group1$Gender             0.38616    0.14239   2.712 0.013829 *
group1$physicalactivity -0.31706    0.11284  -2.810 0.011184 *
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 0.1577 on 19 degrees of freedom
Multiple R-squared:  0.402,     Adjusted R-squared:  0.3076
F-statistic: 4.258 on 3 and 19 DF,  p-value: 0.01847
```

**Table 6.** Multiple linear regression model for group 1(the estimate coefficients represent the difference in the predicted value of the dependent variable for each one-unit difference in the independent variable, if all other variables remain constant.).

The statistical analysis of group 2 yielded a plethora of statistically significant results. More specifically the multiple linear regression with SCR amplitude(z transformed-by definition during stress intervals) as the dependent variable and identified an association with the independent variables age($p<0.001$) and STAI2($p<0.001$)(Table 7). The association with age is analogous to the one found in group 1 for the tonic component, and can similarly be attributed to changes in sweat gland reactivity with age. STAI2 as a measure of "trait" anxiety is expected to positively correlate with SCR activity, a notion which is line with the current results.

```
Call:
lm(formula = zscramplitude ~ group2$Age. + group2$STAI1. + group2$STAI2.,
    data = group2)

Residuals:
     Min       1Q   Median       3Q      Max
-0.14188 -0.08056 -0.02544  0.03074  0.69672

Coefficients:
                Estimate Std. Error t value Pr(>|t|)
(Intercept)    1.144e-01  3.451e-02   3.314 0.000965 ***
group2$Age.   -3.722e-03  9.844e-04  -3.781 0.000169 ***
group2$STAI1. -5.497e-05  5.497e-04  -0.100 0.920380
group2$STAI2.  2.465e-03  5.799e-04   4.251  2.4e-05 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 0.1178 on 726 degrees of freedom
  (7 observations deleted due to missingness)
Multiple R-squared:  0.04233,   Adjusted R-squared:  0.03837
F-statistic:  10.7 on 3 and 726 DF,  p-value: 6.92e-07
```

**Table 7.** Multiple linear regression with amplitude as the dependent variable(the estimate coefficients represent the difference in the predicted value of the dependent variable for each one-unit difference in the independent variable, if all other variables remain constant.).

Spearman's rank correlation rho detects a significant relationship(rho 0.1430246, $p<0.001$) between SCR amplitude and STAI1, which expresses current state anxiety(Figure 10).

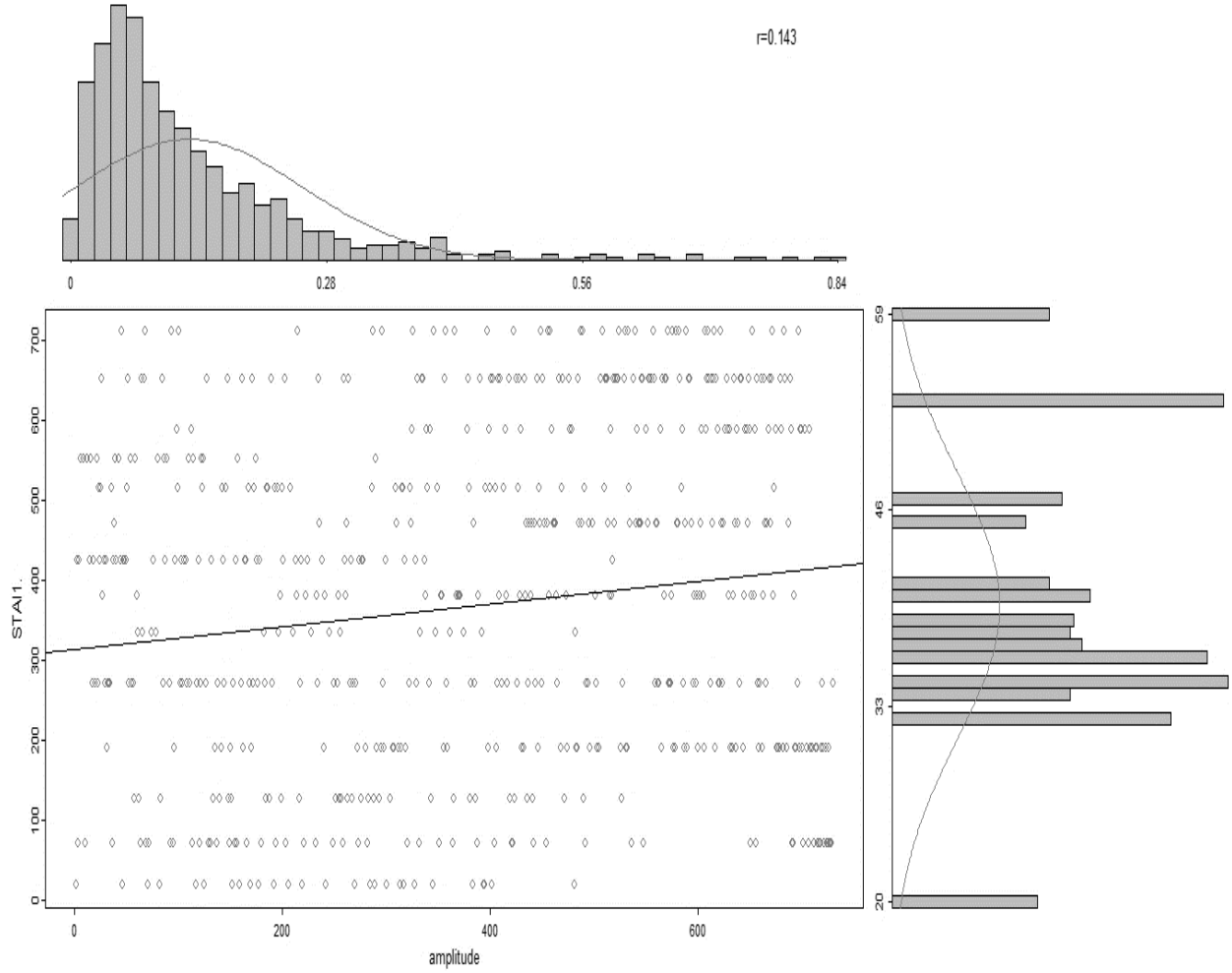


**Figure 10.** Spearman's rho SCR amplitude, STAI1( plotting of the ranks of the data, while the distributions of the raw data are also depicted.)

Spearman's rho also validates the results of the linear regression as far as the association between STAI2 and amplitude is concerned(rho 0.14471, $p<0.001$)(Figure 11).

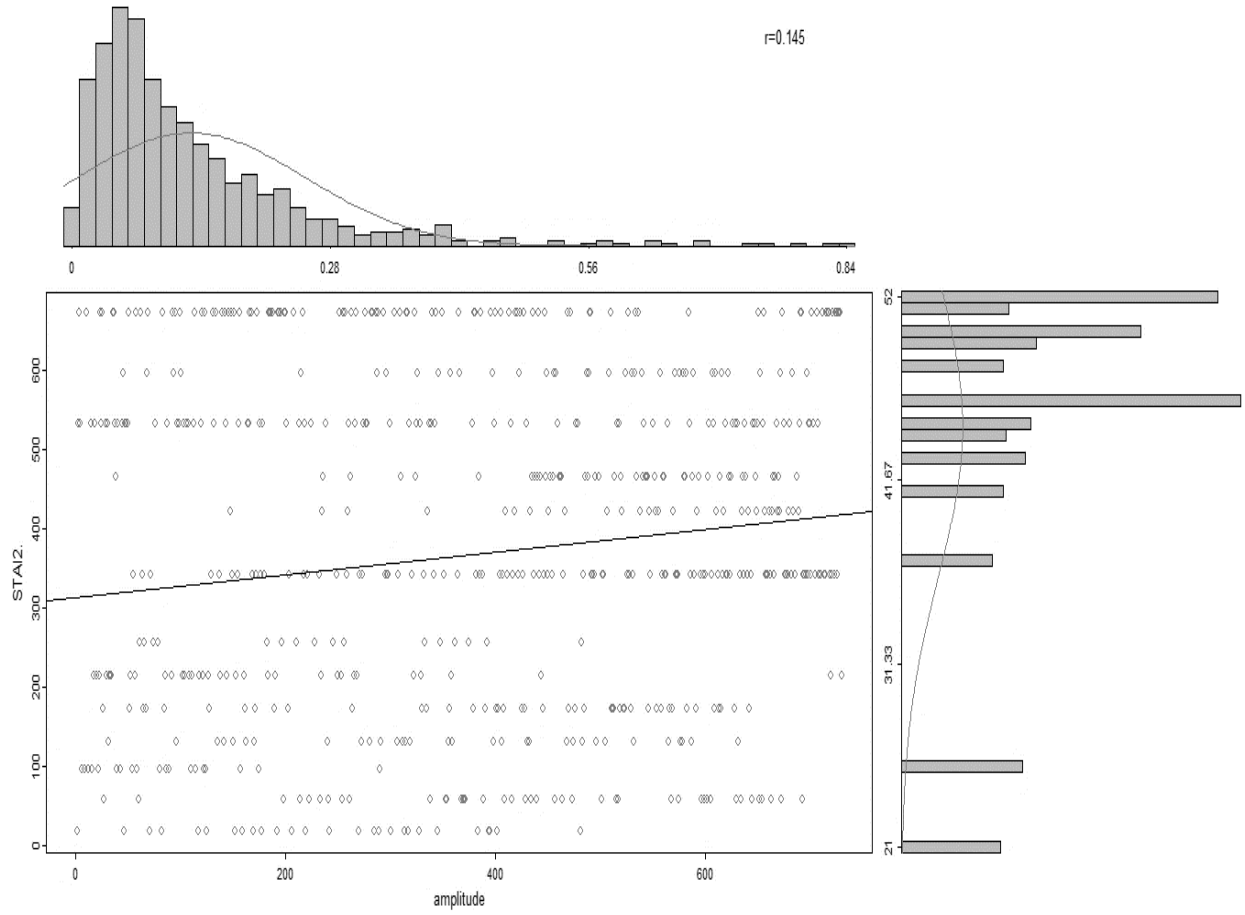


**Figure 11.** Spearman's rho between STAI2 and amplitude(plotting of the ranks of the data, while the distributions of the raw data are also depicted).

Finally Spearman's rho also detects the significant relationship between age and amplitude(-0.1033661, $p<0.005$)(Figure 12).

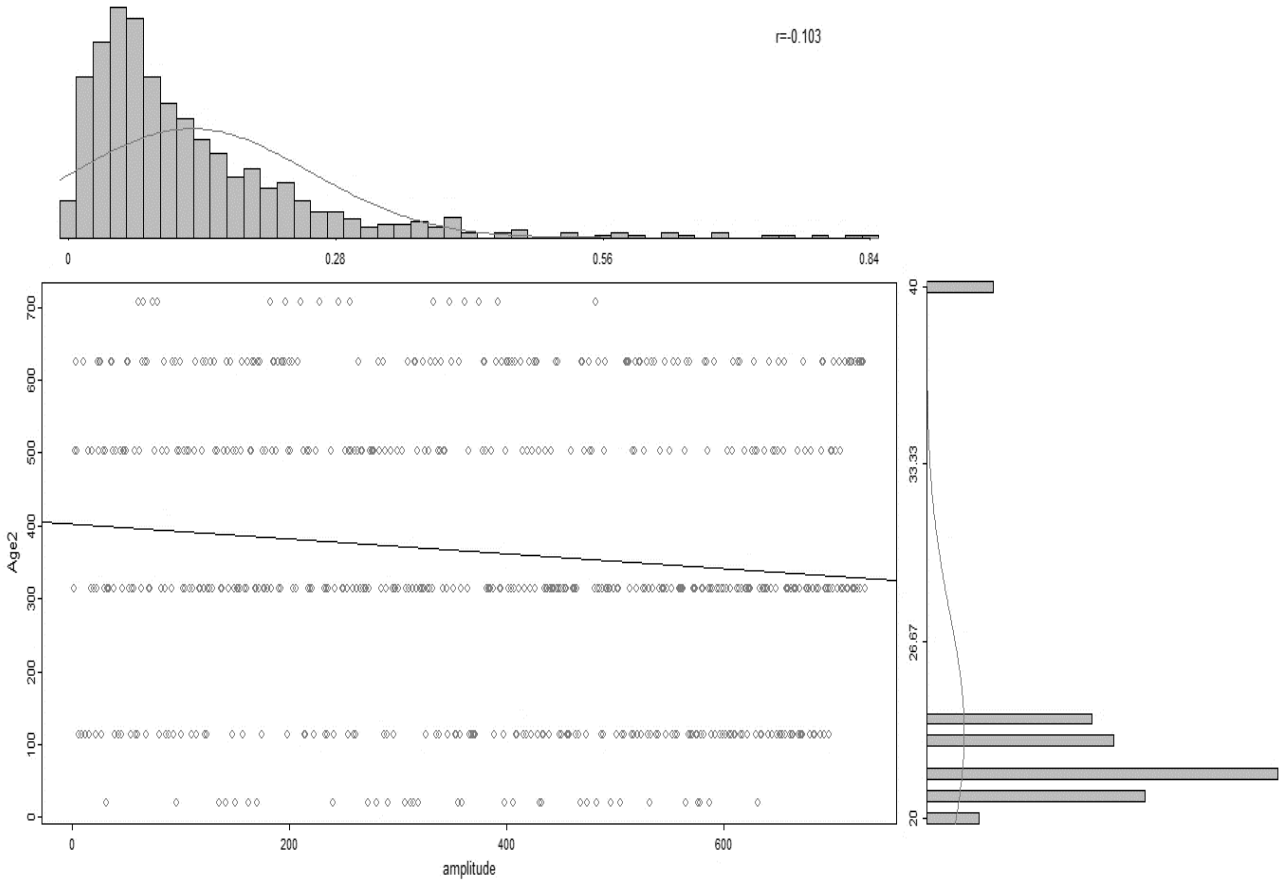


**Figure 12.** Spearman's rho between age and amplitude (plotting of the ranks of the data, while the distributions of the raw data are also depicted).

The multiple regression model in group 2 with Non SCR frequency as dependent variable detects the same relationship with age as described for group1($p<0.05$)(Table 8). STAI2 increase appears to lead to an increase in the dependent variable, which is reasonable taking into account that it is a marker of trait anxiety in the same way that tonic activity expresses baseline arousal($p<0.001$)(Table 8). Interestingly STAI1 appears to lead to reduction in the independent variable($p<0.001$)(Table 8). However since STAI1 expresses current anxiety it is generally expected to correlate with SCR amplitude and not with tonic activity, meaning that this finding is not unreasonable.

```
Call:
lm(formula = group2$nonscrfrequency ~ group2$Age + group2$STAI11 +
    group2$STAI2, data = group2)

Residuals:
     Min       1Q   Median       3Q      Max
-2.05072 -0.58591 -0.00985  0.90855  1.14638

Coefficients:
               Estimate Std. Error t value Pr(>|t|)
(Intercept)    7.527963   0.264589  28.452  < 2e-16 ***
group2$Age    -0.015708   0.007526  -2.087   0.0372 *
group2$STAI11 -0.015653   0.004187  -3.738   0.0002 ***
group2$STAI2   0.032704   0.004449   7.350 5.29e-13 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 0.9016 on 733 degrees of freedom
Multiple R-squared:  0.07047,   Adjusted R-squared:  0.06666
F-statistic: 18.52 on 3 and 733 DF,  p-value: 1.367e-11
```

**Table 8.** Multiple linear regression with Non SCR frequency as the dependent variable(the estimate coefficients represent the difference in the predicted value of the dependent variable for each one-unit difference in the independent variable, if all other variables remain constant.)

Spearman's rho validates the correlation of Non SCR frequency with STAI2 with a value of 0.0743554($p<0.05$)(Figure 13).

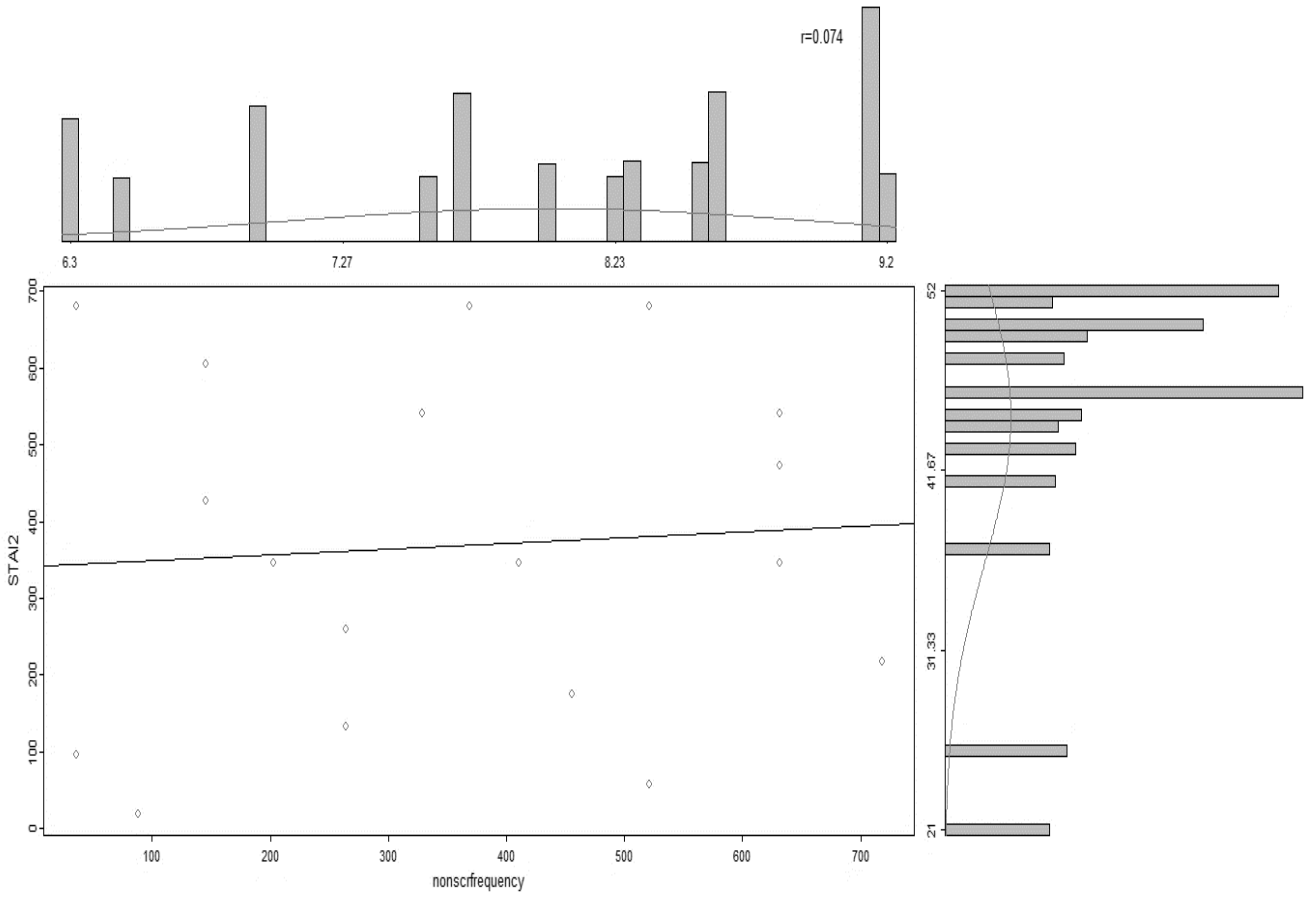


**Figure 13.** Spearman's rho. Non SCR frequency and STAI2(plotting of the ranks of the data, while the distributions of the raw data are also depicted).

Spearman's rho has also detected a negative statistically significant relationship between half recovery time and age(-0.08847413, $p<0.05$)(Figure 14). This interesting finding could be attributed to the fact that according to the literature advancing age confers a more optimistic attitude towards knowledge/information based stimuli, and a more pronounced one to socioeconomic triggers, leading to an artificial reduction in half recovery time [157]. Since the stimuli in this case are facilitated with a stroop test, this hypothesis appears plausible.

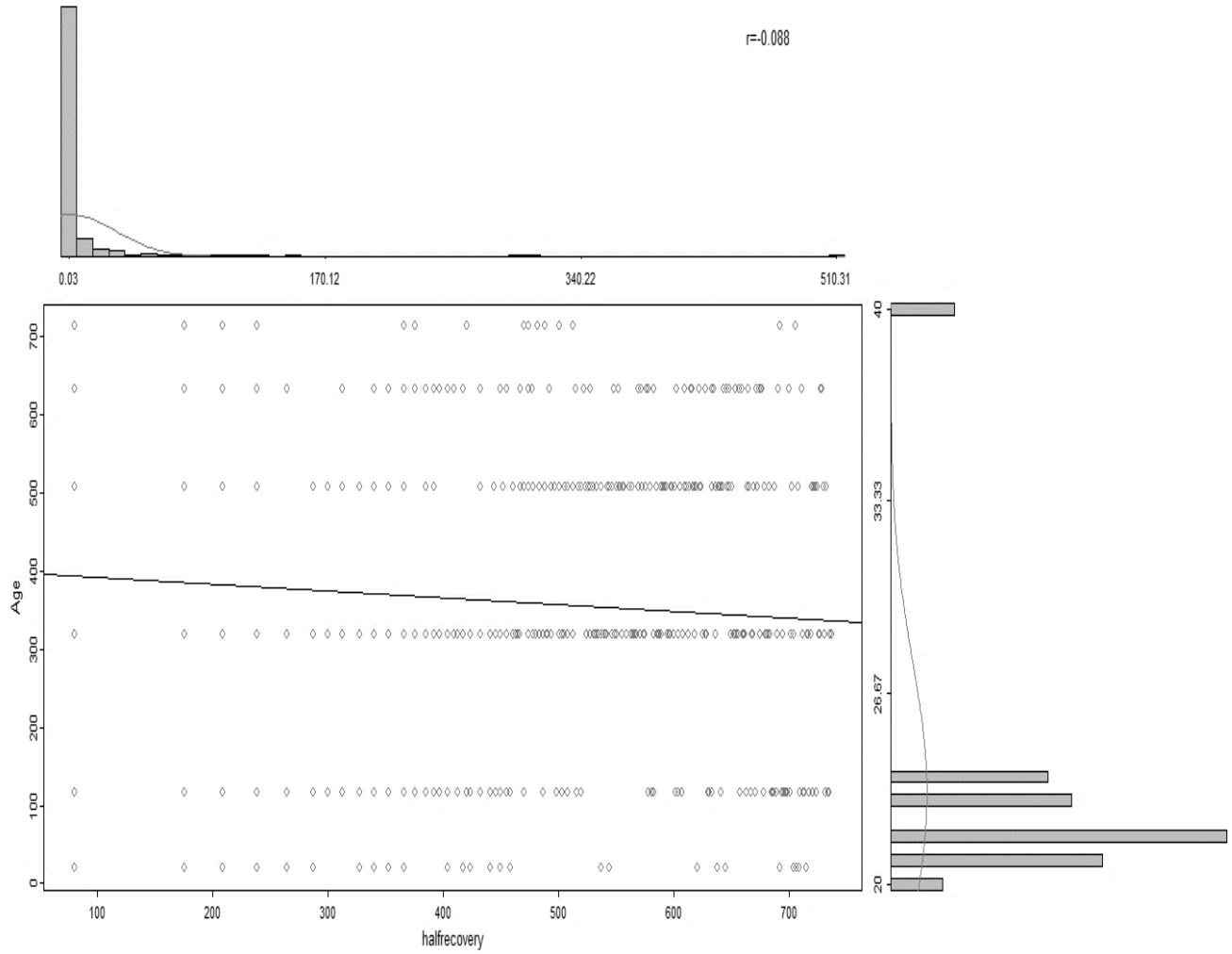


**Figure 14.** Spearman's rho between half recovery time and age(plotting of the ranks of the data, while the distributions of the raw data are also depicted).

Another interesting finding from non-parametric analysis is that half recovery time appears to positively correlate with both STAI1(0.1515905,$p<0.001$)(Figure 15) and STAI2(0.0743554, $p<0.05$)(Figure 16). The explanation could be that increased anxiety as expressed by STAI1 and STAI2 leads participants to a more slow return to their baseline GSR levels.

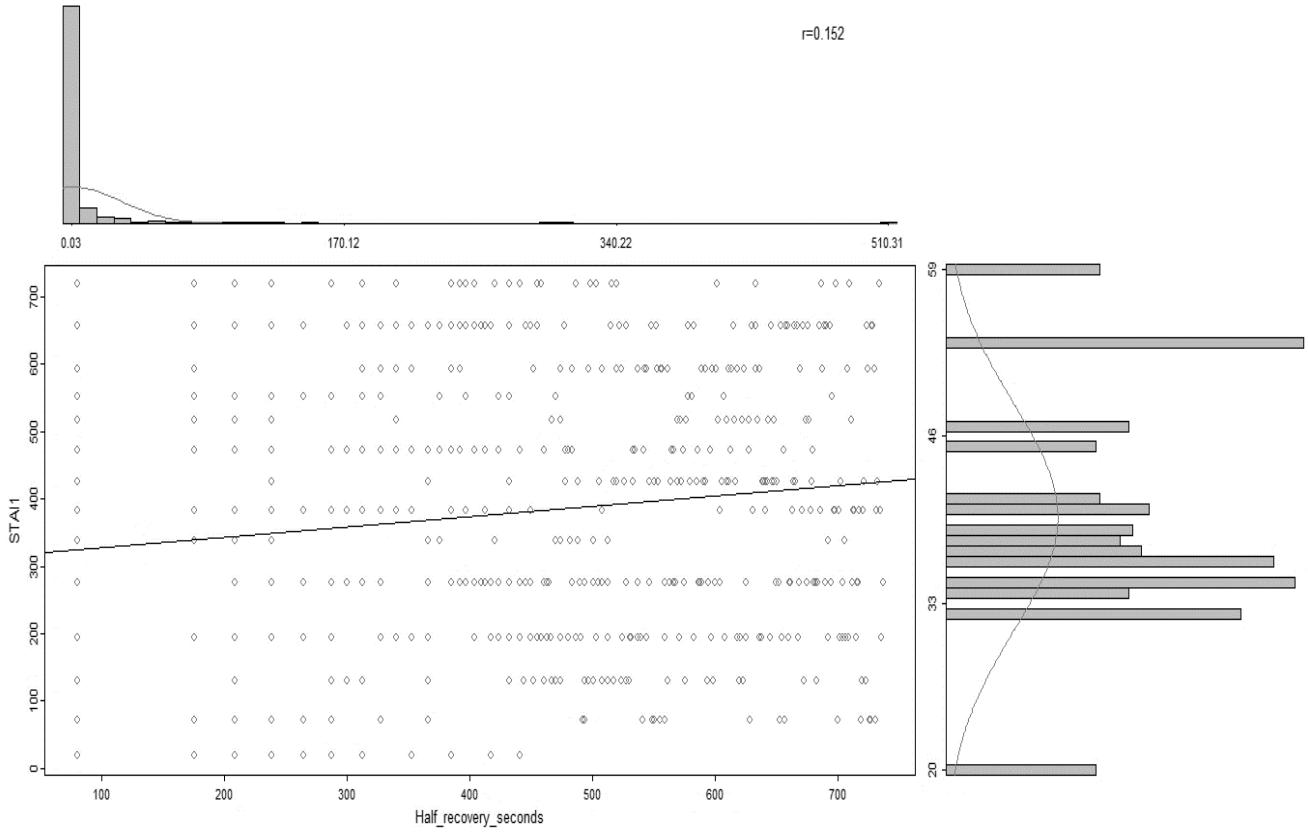


**Figure 15.** Spearman rho between half recovery time and STAI1(plotting of the ranks of the data, while the distributions of the raw data are also depicted).

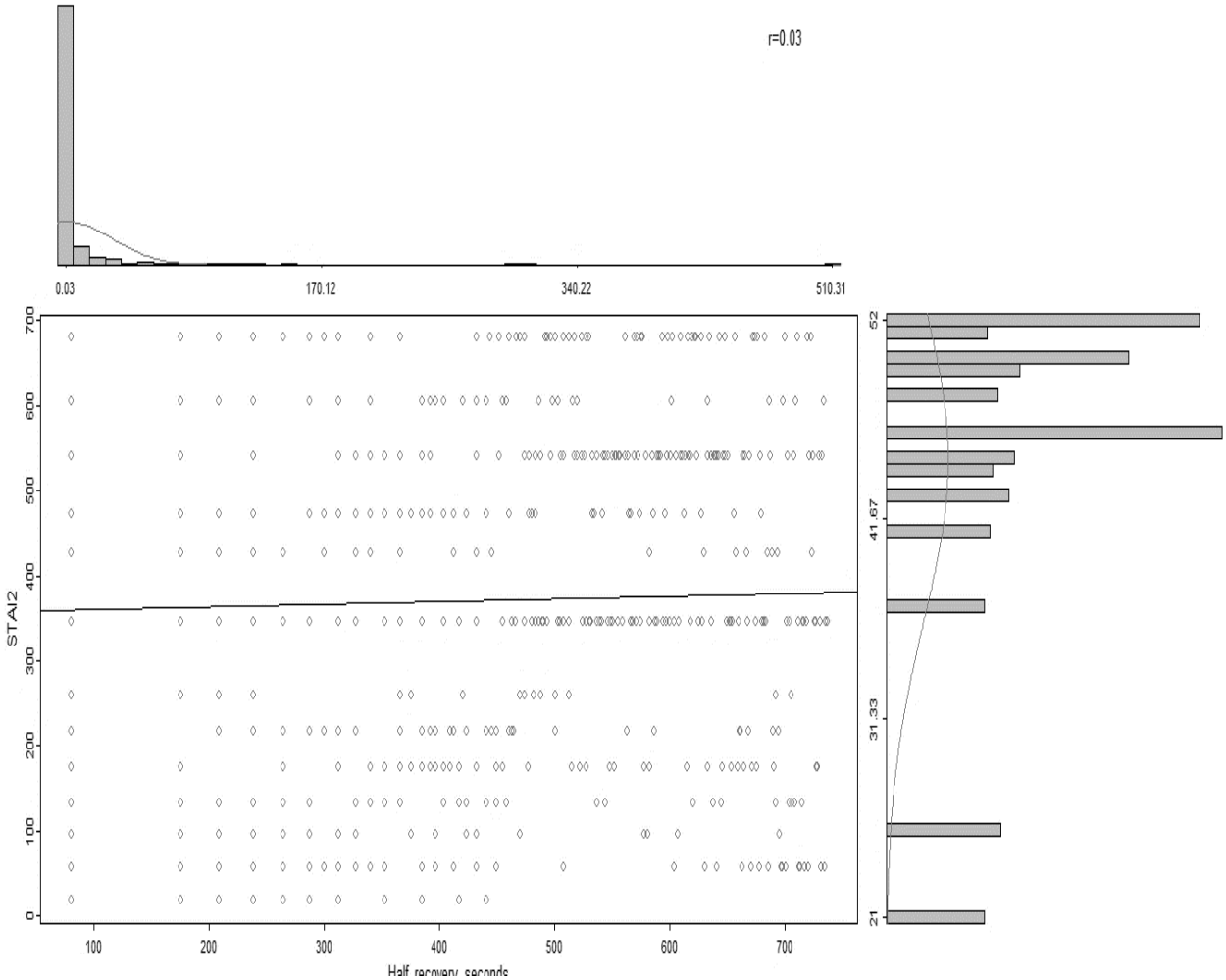


**Figure 16.** Spearman's rho between half recovery time and STAI2(plotting of the ranks of the data, while the distributions of the raw data are also depicted).

Finally, in order to compare peak frequency between stress and non stress periods, a Wilcoxon signed rank test was performed in group 2, which has the highest recording rate(32Hz) and population number. The analysis revealed statistically significant differences($p<0.05$) between peak frequency in non-stress and stress periods, with median values 8.1 and 8.2 respectively(Table 9).

```
        Wilcoxon signed rank test with continuity correction

data:  peaks_non_stress and peaks_stress
V = 39, p-value = 0.04491
alternative hypothesis: true location shift is not equal to 0
```

**Table 9.** Wilcoxon signed rank test between frequency of peaks in non-stress and stress periods indicating a statistically significant difference

# Chapter 7
# Discussion

Electrodermal activity is considered a marker of sympathetic function [152], since it depends on skin sweat gland activity which in turn is controlled by the autonomic nervous system. The EDA metrics are influenced both by person specific characteristics(such as age, gender, diseases, medications received, current mood ) and the quality of the applied stimuli(such as visual, auditory, neutral, emotional) [158]. Interestingly, it has been suggested that EDA responses may be partially genetically controlled by multiple genes [159].

SCR amplitude is generally considered an appropriate measure of phasic EDA activity [160] while tonic activity can be expressed by the frequency of non-specific skin conductance responses [161]. These two EDA metrics were included in the current analysis to investigate potential correlations and statistically significant associations.

In the current study the frequency of the Non SCRs appears in both groups to be correlated with age. More specifically advancing age appears to lead to less Non SCRs. This finding is reported in the literature and although the exact cause remains elusive, reduced sweat gland reactivity is considered to play a role [147].

The analysis from the first group of data also identified a negative relationship between increasing physical activity and frequency of Non SCRs. Regularly engaging in physical activity is considered to reduce the person's baseline anxiety levels [162] and therefore it would be plausible to hypothesize that these individuals exhibit reduced SCL.

The incorporation of STAI1 and STAI2 as markers of current and trait anxiety respectively in the data of the second group provided the opportunity to explore potential statistical relationships with both SCR amplitude and Non SCRs. The State-Trait Anxiety Inventory questionnaires have been used extensively in the literature for assessing the presence and severity of current anxiety as well as the general propensity of the individual to be anxious

[163]. Reliability and validity tests that have been performed confirmed the robustness of this tool and its usefulness in the evaluation of stress levels in research and clinical settings [164].

As far as SCR amplitude is concerned, there appears to be a positive correlation with STAI1(spearman's rho) and STAI2(spearman's rho and regression). An increase in state anxiety is reasonably expected to correlate with SCR amplitude as they both correlate with acute sympathetic system activity. Trait anxiety increases have been reported to lead to increases in SCL [165], while the correlation with EDA amplitude appears to follow an inverted U shape [166].

The frequency of Non-significant SCRs(independent variable) as a measure of tonic activity appears to have a statistically significant positive association with STAI2(dependent variable). This finding is reasonable as STAI2 expresses trait anxiety, which in turn manifests as tonic electrodermal activity. Individuals with increased anxiety appear to have more spontaneous EDA fluctuations and hence Non SCRs [167].

Half recovery time as a characteristic EDA metric has been occasionally evaluated in the literature as a marker of conditioning, with faster times being associated with enhanced information processing [168]. In the current study there appears to be a positive correlation of half recovery with STAI1 and STAI2. This could be attributed to the fact that patients with high anxiety levels (especially the trait component) may have developed increased processing skills, allowing them to return faster to their baseline autonomous nervous system state [169].

Interestingly age appears to have a negative correlation with half recovery time based on the current results. However, studies indicate that increasing age is associated with less pronounced physiological responses when the stimuli are knowledge/information based in comparison to socio-economic stimuli [157]. In this context, the above mentioned finding appears plausible, since the stimuli in the current study were generated via the stroop and memory test.

Furthermore and in order to directly validate that EDA metrics differ between stress and non stress periods a Wilcoxon signed rank test between frequency of peaks in non-stress

and stress time intervals was performed. The results indicated that there a statistically significant difference, with a higher median value for stress than non stress periods.

A potential limitation of the current study could be the lack of other bio signal data that could have been analyzed concurrently in order to detect differences in sensitivity and specificity of stress detection. This would facilitate the study of how different baseline volunteer characteristics can modify different bio signals that can assess stress as well as correlation analysis between the various signals. Despite this limitation, the current analysis has provided a plethora of data regarding electrodermal activity and its correlation with stress and the effect of age, gender, physical activity and trait anxiety. In addition it offered the opportunity to correlate EDA stress metrics with standardized anxiety questionnaires, which could prove useful for future validation purposes.

# Chapter 8
# Conclusion

The primary objectives of the current thesis were to review the current literature in the field of bio signal based stress detection and analyze EDA data from volunteers in order to infer meaningful correlations between the different variables studied.

The review component was conducted by searching electronic databases with relevant keyword/phrases and critically appraising the gathered scientific articles.
The experimental analysis component included EDA data processing from two groups of volunteers with seven and eighteen participants respectively. Volunteer specific characteristics such as age, gender, physical activity, and questionnaires for quantifying current and trait anxiety were utilized as variables. The identification of the relevant EDA metrics(SCRs,Non-SCRs, SCR frequency, half recovery times) was achieved with the continuous wavelet transformation methodology for peak detection, applied in Python.

The statistical analysis that followed was based on multiple linear regression and Spearman's rho, performed with the R programming language for statistical analysis.
The results that were produced through the above mentioned process revealed multiple statistically significant correlations.

As revealed by the Wilcoxon signed rank test in group 2(chosen due to the 32 Hz recording and the greater sample size) there appears to be a statistically significant difference between frequency of peaks in non-stress and stress periods.

Another finding of the current study is that advancing age seems to be associated with reduced EDA levels(both tonic and phasic), a finding which has several potential explanations. Furthermore advancing age appears to reduce half recovery time, which again could be explained by the fact that older individuals return faster to their baseline anxiety levels when exposed to information based stimuli (such as stroop/memory tests)

, which do not perceive as very significant. The fact that age is a significant determinant of EDA response as indicated in the current study supports the need for baseline age related adjustments during data interpretation, and provides insight in how changing physiology affects stress reactions.

A significant correlation between the STAI2 questionnaire and tonic activity(expressed as Non-SCR frequency) was also detected. In addition the amplitude of SCRs and STAI1 have been shown to have a statistically significant correlation in Spearman's rho, which indicates an association of EDA with state(current) anxiety too. In this context it is of paramount importance that EDA appears to be able to quantify both state and trait anxiety, in other words not only the tendency of the person to be anxious and stressed before the application of stimuli but also the amplitude of the reaction during the stimulation. Based on these findings it appears that the potential of using EDA for stress quantification and recognition is significant.

The current study also indicated that half recovery time(the time to return to half the value of the SCR amplitude) reduces when age advances. Furthermore it appears to increase with higher STAI1 and STAI2, a finding that indicates that the more stress someone has the more time it takes to return to baseline levels. Half recovery time is generally rarely studied in the literature and the fact that the current findings show an association with variables such as stress questionnaires and baseline volunteer characteristics could rejuvenate interest towards this EDA metric.

The correlations that have been detected between the aforementioned EDA metrics and both innate characteristics(age, gender) and acquired traits(trait anxiety, physical activity) of individuals, create a base for potential incorporation of galvanic skin responses to personalized health monitoring systems. In this context a real time EDA recording system could provide early detection of anxiety attacks or stress related sympathetic system activation, allowing for appropriate management and lifestyle modifications. This application would also contribute to the understanding of the underlying mechanisms of the genesis and propagation of stress.

# Appendix A
# EDA Detection Algorithms and Statistical Analysis

The continuous wavelet transform is a useful tool for analyzing time series signals in the time-frequency domain that works by connecting wavelet local maxima points to sequences that converge to a peak [170]. The CWT algorithm appears to work well in noisy data [171], offering a significant advantage in comparison with other approaches in signal processing. The Python function scipy.signal.find_peaks_cwt was used in the current study to detect the relevant SCR peaks throughout the EDA signal. In this context a sample of the code that detected the peaks is:

```
indexes = find_peaks_cwt(new_list, np.arange(1, 200))  #detection of indexes of peaks

for b in indexes:

  if (b*(1/recording_frequency)<780 and b*(1/recording_frequency)>600) or (b*(1/ recording_frequency)<1080 and b*(1/ recording_frequency)>840):

        significant_SCR.append(new_list[b])   #detecting  SCRs
```

In the above mentioned example the index b multiplied by the time that each single value measurement requires(1/recording_frequency) equals the total time elapsed until this point. The recording frequency was 1.98Hz for the first group(in which the volunteer of the example belonged) and 32 Hz for the second group. The time intervals (600 sec, 780 sec, 1080 sec, 840 sec) are those corresponding to the stress periods of the specific volunteer and they differed among the group members.

The calculation of the amplitudes was performed by subtracting from the peak SCR value the preceding minima. The calculation of the recent local minima required the use of scipy.signal.argrelextrema but confined in a specific area of the data:

```
minimal=argrelextrema(slice2_list, np.less)

mini_list=slice2_list[minimal]

mini_mini=min(mini_list)

amplitude.append(new_list[b]-mini_mini)
```

Non specific SCRs are the SCRs occurring outside of the stress periods. The calculation of the frequency of Non SCRs is then calculated by dividing with the corresponding time duration. In this context the following code with the volunteer specific stress periods was utilized:

```
for b in indexes:

  if b * (1 / 1.98) >1080 or b * (1 / 1.98) < 600 or (b * (1 / 1.98)>780 and b * (1 /1.98)<840):

    Non_SCR.append(new_list[b])

NonSCR_last_index=len(Non_SCR)-1

NonSCRs_frequency=NonSCR_last_index/time
```

The statistical analysis was performed with the R Language for Statistical Analysis, which has been extensively used in the literature for facilitating data processing [172].

Performing a linear regression analysis was achieved by following the corresponding syntax:

```
 fit <- lm(y ~ x1 + x2 + x3, data=EDA_data)

 summary(fit)
```

The calculation of Spearman's rho was done by applying the syntax: cor.test(x2,y2,method="spearman", exact=FALSE)

Obtaining a graphical representation required the code: spearman.plot(cbind(Half_recovery_seconds,Age), col="red", lhist=50)**,** for which the fifer package is required. The latter allows the plotting of the ranks of the data, while the distributions of the raw data are also depicted.

The calculation of Wilcoxon signed-rank test was achieved with the code: wilcox.test(a,b, paired=TRUE), with appropriate substitution for the a, b variables.

# Appendix B
## List of abbreviations

| | |
|---|---|
| **EDA** | Electrodermal activity |
| **GSR** | Galvanic Skin Response |
| **Non-SCR** | Non significant Skin Conductance Response |
| **SCR** | Significant Skin Response |
| **SC** | Skin Conductance |
| **SR** | Skin Resistance |
| **SP** | Skin Potential |
| **SZ** | Skin Impedance |
| **SY** | Skin Admittance |
| **STAI1** | State-Trait Anxiety Inventory 1 |
| **STAI2** | State-Trait Anxiety Inventory 2 |
| **Spearman's rho** | Spearman rank-order correlation coefficient |
| **ECG** | Electrocardiogram |
| **EMG** | Electromyogram |
| **EEG** | Electroencephalogram |
| **HRV** | Heart Rate Variability |

# References


[1] P. Adams, M. Rabbi, T. Rahman, M. Matthews, A. Voida, G. Gay, T. Choudhury and S. Voida, "Towards personal stress informatics: Comparing minimally invasive techniques for measuring daily stress in the wild," in *Proceedings of the 8th International Conference on Pervasive Computing Technologies for Healthcare*, 2014.

[2] M. Milczarek, E. Schneider and E. Gonzàlez, "OSH in figures, stress at work, facts and figures," *Tech. rep.,* 2009.

[3] European Agency for Safety and Health at Work, "Campaign guide: managing stress and psychosocial risks at work," European Agency for Safety and Health at Work, 2013.

[4] A. F. Stokes and K. Kite, "On grasping a nettle and becoming emotional," in *Stress, workload, and fatigue*, P. A. Hancock and P. A. Desmond, Eds., 2001.

[5] R. S. Lazarus, "Theory-based stress measurement," *Psychological inquiry,* vol. 1, no. 1, pp. 3-13, 1990.

[6] P. Dewe, M. O'Driscoll and C. Cooper, Coping with work stress: A review and critique, Chichester: Wiley-Blackwell, 2010.

[7] M. M. McGrath, "Group preparation of pediatric surgical patients," *Journal of Nursing Scholarship,* vol. 11, no. 2, pp. 52-62, 1979.

[8] S. J. Lupien, B. S. McEwen, M. R. Gunnar and C. Heim, "Effects of stress throughout the lifespan on the brain, behaviour and cognition," *Nature reviews neuroscience,* vol. 10, no. 6, pp. 434-445, 2009.

[9] M. K. Taylor, K. P. Sausen, L. R. Mujica-Parodi, E. G. Potterat, M. A. Yanagi and H. Kim, "Neurophysiologic methods to measure stress during survival, evasion, resistance, and escape training," *Aviation, space, and environmental medicine,* vol. 78, no. 5, pp. B224-B230, 2007.

[10] W. S. Helton, G. Matthews and J. S. Warm, "Stress state mediation between environmental variables and performance: The case of noise and vigilance," *Acta psychologica,* vol. 130, no. 3, pp. 204-213, 2009.

[11] L. Murphy, "Stress management in work settings: a critical review of the health effects," *American Journal of Health Promotion,* vol. 11, no. 2, pp. 112-135, 1996.

[12] A. M. Alsentali and M. H. Anshel, "Relationship between internal and external acute stressors and coping style," *Journal of Sport Behavior,* vol. 38, no. 4, p. 357, 2015.

[13] J. T. Cacioppo, L. G. Tassinary and G. G. Berntson, "Psychophysiological science.," in *Handbook of psychophysiology*, vol. 2, 2000, pp. 3-23.

[14] D. Morse, "Brain wave synchronizers: A review of their stress reduction effects and clinical studies assessed by questionnaire, galvanic skin resistance, pulse rate, saliva, and electroencephalograph," *Stress and Health,* vol. 9, no. 2, pp. 111-126, 1993.

[15] H. Mönnikes, J. J. Tebbe, M. Hildebrandt, P. Arck, E. Osmanoglou , M. Rose, B. Klapp, B. Wiedenmann and I. Heymann-Mönnikes, "Role of stress in functional gastrointestinal disorders," *Digestive Diseases,* vol. 19, no. 3, pp. 201-211, 2001.

[16] E. Diener and M. Y. Chan, "Happy people live longer: Subjective well-being contributes to health and longevity," *Applied Psychology: Health and Well-Being,* vol. 3, no. 1, pp. 1-43, 2011.

[17] J. Henry, "Biological basis of the stress response," *Integrative physiological and behavioral science,* vol. 27, no. 1, pp. 66-83, 1992.

[18] U. Lundberg and M. Frankenhaeuser, "Pituitary-adrenal and sympathetic-adrenal correlates of distress and effort," *Journal of Psychosomatic Research,* vol. 24, no. 3, pp. 125-130, 1980.

[19] I. Ulstein, T. Bruun Wyller and K. Engedal, "The relative stress scale, a useful instrument to identify various aspects of carer burden in dementia?," *International Journal of Geriatric Psychiatry,* vol. 22, no. 1, pp. 61-67, 2007.

[20] S. Cohen, T. Kamarck and R. Mermelstein, "A global measure of perceived stress," *Journal of health and social behavior,* pp. 385-396, 1983.

[21] A. Fernandes, R. Helawar, R. Lokesh, T. Tari and A. V. Shahapurkar, "Determination of stress using blood pressure and galvanic skin response," in *2014 International Conference on Communication and Network Technologies (ICCNT)*, 2014 (December).

[22] R. Vahey and R. Becerra, "Galvanic skin response in mood disorders: A critical review," *International Journal of Psychology and Psychological Therapy,* vol. 15, no. 2, pp. 275-304, 2015.

[23] S. Andrianome, J. Gobert, L. Hugueville, E. Stéphan-Blanchard, F. Telliez and B. Selmaoui, "An assessment of the autonomic nervous system in the electrohypersensitive population: a heart rate variability and skin conductance study," *Journal of Applied Physiology,* 15 June 2017.

[24] R. Edelberg, "Electrodermal Recovery Rate, Goal-Orientation, and Aversion," *Psychophysiology,* vol. 9, no. 5, pp. 512-520, 1972.

[25] R. E. Noble, "Diagnosis of stress," *Metabolism,* vol. 51, no. 6, pp. 37-39, 2002.

[26] R. Draghia-Akli, "Enabling personalized medicine in Europe: a look at the European Commission's funding activities in the field of personalized medicine research.," *Personalized Medicine,* vol. 9, no. 2, pp. 151-155, 2012.

[27] P. F. Millington and R. Wilkinson, Biological structure and function 9, skin, R. J. Harrison and R. M. McMinn, Eds., Cambridge: Cambridge University Press, 1983, pp. 83-98.

[28] G. E. Folk and A. Semken, "The evolution of sweat glands," *International Journal of Biometeorology,* vol. 35, no. 3, pp. 180-186, 1991.

[29] K. Hugdahl, Psychophysiology: The mind-body perspective, Harvard University Press, 1995, p. 104.

[30] W. R. Kennedy, G. Wendelschafer-Crabb and T. C. Brelje, "Innervation and vasculature of human sweat glands: an immunohistochemistry-laser scanning confocal fluorescence microscopy study," *Journal of Neuroscience,* vol. 14, no. 11, pp. 6825-6833, 1994.

[31] M. Schmelz, R. Schmidt, A. Bickel, H. E. Torebjörk and H. O. Handwerker, "Innervation territories of single sympathetic C fibers in human skin," *Journal of neurophysiology,* vol. 79, no. 4, pp. 1653-1660, 1998.

[32] V. G. Macefield and B. G. Wallin, "The discharge behaviour of single sympathetic neurones supplying human sweat glands," *Journal of the autonomic nervous system,* vol. 61, no. 3, pp. 277-286, 1996.

[33] M. Fredrikson, T. Furmark, M. T. Olsson, H. Fischer, J. Andersson and B. Långström, "Functional neuroanatomical correlates of electrodermal activity: a positron emission tomographic study," *Psychophysiology,* vol. 35, no. 2, pp. 179-185, 1998.

[34] J. Marshall, Outlines of physiology, human and comparative, F. G. Smith, Ed., H.C. Lea, 1868.

[35] S. A. Pakarinen, J. Korpela and J. Torniainen, "Quantifying acute stress with heart rate variability (HRV) and electrodermal activity (EDA) in real world conditions," *International Journal of Psychophysiology,* vol. 108, pp. 73-74, 2016.

[36] G. G. Berntson, K. S. Quigley and D. Lozano, "Cardiovascular psychophysiology.," *Handbook of psychophysiology,* vol. 3, pp. 182-210, 2007.

[37] J. F. Alonso, S. Romero, M. R. Ballester, R. M. Antonijoan and M. A. Mañanas, "Stress assessment based on EEG univariate features and functional connectivity measures," *Physiological measurement,* vol. 36, no. 7, p. 1351, 2015.

[38] X. Hou, Y. Liu, O. Sourina, Y. R. E. Tan, L. Wang and W. Mueller-Wittig, "EEG based stress monitoring," in *Systems, Man and Cybernetics (SMC) in 2015 IEEE International Conference (October)*, 2015.

[39] N. Sulaiman, M. N. Taib, S. A. M. Aris, N. H. A. Hamid, S. Lias and Z. H. Murat, "Stress features identification from EEG signals using EEG Asymmetry & Spectral Centroids

techniques," *IEEE EMBS Conference on Biomedical Engineering and Sciences (IECBES),* pp. 417-421, November 2010.

[40] D. J. Schutter and J. Van Honk, "Electrophysiological ratio markers for the balance between reward and punishment," *Cognitive Brain Research,* vol. 24, no. 3, pp. 685-690, 2005.

[41] U. Lundberg, R. Kadefors, B. Melin, G. Palmerud, P. Hassmén, M. Engström and I. Elfsberg Dohns, "Psychophysiological stress and EMG activity of the trapezius muscle," *International journal of behavioral medicine,* vol. 1, no. 4, pp. 354-370, 1994.

[42] M. Huiku, K. Uutela, M. Van Gils, I. Korhonen, M. Kymäläinen, P. Meriläinen, M. Paloheimo, M. Rantanen, P. Takala, H. Viertiö-Oja and A. Yli-Hankala, "Assessment of surgical stress during general anaesthesia," *British journal of anaesthesia,* vol. 98, no. 4, pp. 447-455, 2007.

[43] S. Baltaci and D. Gokcay, "Stress Detection in Human–Computer Interaction: Fusion of Pupil Dilation and Facial Temperature Features," *International Journal of Human–Computer Interaction,* vol. 32, no. 12, pp. 956-966, 2016.

[44] J. Morales, J. M. Álamo, X. García-Massó, J. L. López, P. Serra-Añó and L. M. González, "Use of heart rate variability in monitoring stress and recovery in judo athletes," *The Journal of Strength & Conditioning Research,* vol. 28, no. 7, pp. 1896-1905, 2014.

[45] R. Kuboi, K. Jimi, M. Inoue and I. Matsunami, "Estimating stress states using respiratory monitoring by 24GHz wideband radar," in *IEEE 5th Global Conference on Consumer Electronics*, 2016 (October).

[46] J. H. Hansen and B. D. Womack, "Feature analysis and neural network-based classification of speech under stress," *IEEE Transactions on Speech and Audio Processing,* vol. 4, no. 4, pp. 307-313, 1996.

[47] H. P. Da Silva, A. Lourenço, A. Fred , N. Raposo and M. Aires-de-Sousa, "Check Your Biosignals Here: A new dataset for off-the-person ECG biometrics," *Computer methods and programs in biomedicine,* vol. 113, no. 2, pp. 503-514, 2014.

[48] A. DeLongis, S. Folkman and R. S. Lazarus, "The impact of daily stress on health and mood: psychological and social resources as mediators," *Journal of personality and social psychology,* vol. 54, no. 3, p. 486, 1988.

[49] S. H. Seo, "Detection of Chronic Stress using Bio-Signals," *Indian Journal of Science and Technology,* vol. 9, no. 46, 2016.

[50] J. A. Healey and R. W. Picard, "Detecting stress during real-world driving tasks using physiological sensors," *IEEE Transactions on intelligent transportation systems,* vol. 6, no. 2, pp. 156-166, 2005.

[51] J. Zhai and A. Barreto, "Stress detection in computer users through non-invasive monitoring of physiological signals," *Biomedical sciences instrumentation,* vol. 42, pp. 495-500, 2006.

[52] C. D. Katsis, N. Katertsidis, G. Ganiatsas and D. I. Fotiadis, "Toward emotion recognition in car-racing drivers: A biosignal processing approach," *IEEE Transactions on Systems, Man, and Cybernetics-Part A: Systems and Humans,* vol. 38, no. 3, pp. 502-512, 2008.

[53] A. Atkielski, "Sinus Rhythm Labels," 13 January 2007. [Online]. Available: https://commons.wikimedia.org/wiki/File:SinusRhythmLabels.svg. [Accessed 8 July 2017].

[54] W. O. Tatum, Handbook of EEG interpretation, 2nd ed., Demos Medical Publishing, 2014, pp. 1-57.

[55] M. Christie, "Electrodermal activity in the 1980s: a review," *Journal of the Royal Society of Medicine,* vol. 74, no. 8, p. 616, 1981.

[56] A. S. Jansen, X. Van Nguyen, V. Karpitskiy, T. C. Mettenleiter and A. D. Loewy, "Central command neurons of the sympathetic nervous system: basis of the fight-or-flight response," *Science,* vol. 270, no. 5236, p. 644, 1995.

[57] S. D. Kreibig, "Autonomic nervous system activity in emotion: A review," *Biological psychology,* vol. 84, no. 3, pp. 394-421, 2010.

[58] OpenStax, Anatomy & Physiology, 2014: OpenStax CNX.

[59] W. Prokasy, Electrodermal activity in psychological research, Elsevier, 2012, p. 65.

[60] J. L. Andreassi, Psychophysiology: Human behavior & physiological response, Psychology Press, 2013.

[61] A. Theodoros, "Electrodermal activity: Applications in perioperative care," *International Journal of Medical Research & Health Sciences,* vol. 3, no. 3, pp. 687-695, 2014.

[62] A. Bechara, A. R. Damasio, H. Damasio and S. W. Anderson, "Insensitivity to future consequences following damage to human prefrontal cortex," *Cognition,* vol. 50, no. 1, pp. 7-15, 1994.

[63] J. C. Westland, "Electrodermal response in gaming.," *Journal of Computer Networks and Communications,,* 2011.

[64] U. G. Kyle, I. Bosaeus, A. D. De Lorenzo, P. Deurenberg, M. Elia, J. M. Gómez, B. L. Heitmann, L. Kent-Smith, J. C. Melchior, M. Pirlich and H. Scharfetter, "Bioelectrical impedance analysis—part I: review of principles and methods.," *Clinical nutrition,* vol. 23, no. 5, pp. 1226-1243, 2004.

[65] L. Rittié, D. L. Sachs, J. S. Orringer, J. J. Voorhees and G. J. Fisher, "Eccrine sweat glands are major contributors to reepithelialization of human wounds," *The American journal of pathology,* vol. 182, no. 1, pp. 163-171, 2013.

[66] J. R. Stroop, "Studies of interference in serial verbal reactions," *Journal of experimental psychology,* vol. 18, no. 6, p. 643, 1935.

[67] P. Renaud and J. P. Blondin, "The stress of Stroop performance: Physiological and emotional responses to color–word interference, task pacing, and pacing speed," *International Journal of Psychophysiology,* vol. 27, no. 2, pp. 87-97, 1997.

[68] C. Chin and A. Barreto, "Performance comparison of electromyogram-based computer cursor control systems," *WSEAS Transactions on Biology and Biomedicine,* vol. 3, no. 2, pp. 118-124, 2006.

[69] J. A. Healey and R. W. Picard, "Detecting stress during real-world driving tasks using physiological sensors," *IEEE Transactions on intelligent transportation systems,* vol. 6, no. 2, pp. 156-166, 2005.

[70] V. Rice, Handbook of stress, coping, and health: Implications for nursing research, theory, and practice, Sage, 2012, p. 106.

[71] C. Kappeler-Setz, F. Gravenhorst, F. Schumm, B. Arnrich and G. Tröster, "Towards long term monitoring of electrodermal activity in daily life," *Personal and ubiquitous computing,* vol. 17, no. 2, pp. 261-271, 2013.

[72] M. V. Villarejo, B. G. Zapirain and A. M. Zorrilla, "A stress sensor based on Galvanic Skin Response (GSR) controlled by ZigBee.," *Sensors,* vol. 12, no. 5, pp. 6075-6101, 2012.

[73] R. P. Tripathi and R. Mishra, "Study and Analysis of Galvanic Skin Response in Stressful Condition and Validation and Validation through ECG," *International Journal of Technical Research and Applications,* no. 42 (AMBALIKA), pp. 121-124, March 2017.

[74] M. E. Dawson, A. M. Schell and D. L. Filion, "The electrodermal system.," *Handbook of psychophysiology,* vol. 2, pp. 200-223, 2007.

[75] W. T. Roth, A. Ehlers, C. B. Taylor, J. Magraf and W. S. Agras, "Skin conductance habituation in panic disorder patients," *Biological psychiatry,* vol. 27, no. 11, pp. 1231-1243, 1990.

[76] H. Warren, Aristic anatomy of the human figure, 13th ed., Winsor and Newton, 1852.

[77] R. Duncko, A. Makatsori, E. Fickova, D. Selko and D. Jezova, "Altered coordination of the neuroendocrine response during psychosocial stress in subjects with high trait anxiety," *Progress in Neuro-Psychopharmacology and Biological Psychiatry,* vol. 30, no. 6, pp. 1058-1066, 2006.

[78] S. D. Vanderark and D. Ely, “Cortisol, biochemical, and galvanic skin responses to music stimuli of different preference values by college students in biology and music,” *Perceptual and motor skills,* vol. 77, no. 1, pp. 227-234, 1993.

[79] H. D. e. a. Critchley, “Neural activity relating to generation and representation of galvanic skin conductance responses: a functional magnetic resonance imaging study,” *Journal of Neuroscience,* vol. 20, no. 8, pp. 3033-3040, 2000.

[80] A. W. Lo and D. V. Repin, “The psychophysiology of real-time financial risk processing,” *Journal of cognitive neuroscience,* vol. 14, no. 3, pp. 323-339, 2002.

[81] J. Zhai, A. B. Barreto, C. Chin and C. Li, “Realization of stress detection using psychophysiological signals for improvement of human-computer interactions,” pp. 415-420, April 2005.

[82] D. Conway, I. Dick, Z. Li, Y. Wang and F. Chen, “The effect of stress on cognitive load measurement,” in *Human-Computer Interaction-INTERACT 2013*, Springer, 2013, pp. 659-666.

[83] J. D. Montagu and E. M. Coles, “Mechanism and measurement of the galvanic skin response,” *Psychological Bulletin,* vol. 65, no. 5, p. 261, 1966.

[84] C. S. Ikehara and M. E. Crosby, “Assessing cognitive load with physiological sensors,” *System Sciences. HICSS'05. Proceedings of the 38th Annual Hawaii International Conference on* , pp. 295a-295a, January 2005.

[85] “Empatica embrace product website,” [Online]. Available: https://www. empatica. com/product-embrace/.

[86] J. C. Márquez, F. Seoane and K. Lindecrantz, “Textrode functional straps for bioimpedance measurements-experimental results for body composition analysis,” *European journal of clinical nutrition,* vol. 67, pp. S22-S27, 2013.

[87] F. Axisa, C. Gehin, G. Delhomme, C. Collet, O. Robin and A. Dittmar, “Wrist ambulatory monitoring system and smart glove for real time emotional, sensorial and physiological analysis,” *Engineering in Medicine and Biology Society, 2004. IEMBS'04. 26th Annual International Conference of the IEEE,* vol. 1, pp. 2161-2164, September 2004.

[88] P. Grossman, “The LifeShirt: a multi-function ambulatory system monitoring health, disease, and medical intervention in the real world,” *Stud Health Technol Inform,* vol. 108, pp. 133-141, 2004.

[89] F. Seoane, J. Ferreira, L. Alvarez, R. Buendia, D. Ayllón, C. Llerena and R. Gil-Pita, “Sensorized garments and textrode-enabled measurement instrumentation for ambulatory assessment of the autonomic nervous system response in the atrec project,” *Sensors,* vol. 13, no. 7, pp. 8997-9015, 2013.

[90] H. Storm, K. Myre, M. Rostrup, O. Stokland, M. D. Lien and J. C. Raeder, "Skin conductance correlates with perioperative stress," *Acta Anaesthesiologica Scandinavica,* vol. 46, no. 7, pp. 887-895, 2002.

[91] S. P. Orr, Z. Sololmon, T. Peri, R. K. Pitman and A. Y. Shalev, "Physiologic responses to loud tones in Israeli veterans of the 1973 Yom Kippur War," *Biological psychiatry,* vol. 41, no. 3, pp. 319-326, 1997.

[92] B. T. Shahani, J. J. Halperin, P. H. Boulu and J. Cohen, "Sympathetic skin response--a method of assessing unmyelinated axon dysfunction in peripheral neuropathies," *Journal of Neurology, Neurosurgery & Psychiatry,* vol. 47, no. 5, pp. 536-542, 1984.

[93] B. Soliven, R. Maselli, J. Jaspan, A. Green, H. Graziano, M. Petersen and J. P. Spire, "Sympathetic skin response in diabetic neuropathy," *Muscle & nerve,* vol. 10, no. 8, pp. 711-716, 1987.

[94] T. Yokota, T. Matsunaga, R. Okiyama, K. Hirose, H. Tanabe, T. Furukawa and H. Tsukagoshi, "Sympathetic skin response in patients with multiple sclerosis compared with patients with spinal cord transection and normal controls," *Brain,* vol. 114, no. 3, pp. 1381-1394, 1991.

[95] S. e. a. Fusina, "Sympathetic skin response asymmetry in early stage idiopathic Parkinson's disease," *Clinical neurophysiology,* vol. 110, no. 2, pp. 358-366, 1999.

[96] T. H. Haapaniemi, J. T. Korpelainen, U. Tolonen, K. Suominen, K. A. Sotaniemi and V. V. Myllylä, "Suppressed sympathetic skin response in Parkinson disease," *Clinical Autonomic Research,* vol. 10, no. 6, pp. 337-342, 2000.

[97] J. T. Korpelainen, U. Tolonen, K. A. Sotaniemi and V. V. Myllylä, "Suppressed sympathetic skin response in brain infarction," *Stroke,* vol. 24, no. 9, pp. 1389-1392, 1993.

[98] V. Rajendra and O. Dehzangi, "Detection of distraction under naturalistic driving using Galvanic Skin Responses," in *IEEE 14th International Conference on Wearable and Implantable Body Sensor Networks (BSN)*, 2017 (May).

[99] L. Poppy, A. Schoenberg and A. S. David, "Biofeedback for psychiatric disorders: a systematic review," *Applied psychophysiology and biofeedback,* vol. 39, no. 2, p. 109, 2014.

[100] N. Pusenjak, A. Grad, M. Tusak, M. Leskovsek and R. Schwarzlin, "Can biofeedback training of psychophysiological responses enhance athletes' sport performance? A practitioner's perspective," *The Physician and sportsmedicine,* vol. 43, no. 3, pp. 287-299, 2015.

[101] L. E. Nacke, "Games user research and physiological game evaluation," in *Game user experience evaluation* , Springer International Publishing, 2015, pp. 63-86.

[102] O. Nepal, S. Shrestha, B. Timalsina, M. Bade and M. K. Jha, "Detection of Sympathetic Activation by Skin Conductance for a Cognitive Load of Mental Subtraction Task in Medical Undergraduates," *International Journal of Health Sciences and Research (IJHSR),* vol. 6, no. 3, pp. 139-144, 2016.

[103] A. Sano, R. W. Picard and R. Stickgold, "Quantitative analysis of wrist electrodermal activity during sleep," *International Journal of Psychophysiology,* vol. 94, no. 3, pp. 382-389, 2014.

[104] T. J. Palekar, M. G. Mokashi, S. Anwer, A. L. Kakrani, S. D. Khandare and A. H. Alghadir, "Effect of galvanic skin resistance-aided biofeedback training in reducing the pulse rate, respiratory rate, and blood pressure due to perceived stress in physiotherapy students," *Age (years),* vol. 19, no. 2.98, p. 18, 2015.

[105] J. E. Lewis, L. Lantigua, S. E. Atlas, J. Lopez, A. Mendez, S. Goldberg, S. Medici, J. Konefal, J. M. Woolger, E. Tiozzo and K. H. Aliffe, "A cross-sectional assessment to detect type 2 diabetes with endothelial and autonomic nervous system markers using a novel system," *Journal of Diabetes & Metabolic Disorders,* vol. 13, no. 1, p. 118, 2014.

[106] E. Paran, M. Amir and N. Yaniv, "Evaluating the response of mild hypertensives to biofeedback-assisted relaxation using a mental stress test," *Journal of behavior therapy and experimental psychiatry,* vol. 27, no. 2, pp. 157-167, 1996.

[107] E. R. Bleecker and B. T. Engel, "Learned control of cardiac function in Wolff-Parkinson-White syndrome," *N Engl Med,* vol. 288, p. 560–562, 2005.

[108] Y. Nagai, L. H. Goldstein, P. B. Fenwick and M. R. Trimble, "Clinical efficacy of galvanic skin response biofeedback training in reducing seizures in adult epilepsy: a preliminary randomized controlled study," *Epilepsy & Behavior,* vol. 5, no. 2, pp. 216-223, 2004.

[109] E. F. Pierce, " Exercise dependence syndrome in runners.," *Sports Medicine,* vol. 18, no. 3, pp. 149-155, 1994.

[110] A. Khanna, M. Paul and J. S. Sandhu, "A study to compare the effectiveness of GSR biofeedback training and progressive muscle relaxation training in reducing blood pressure and respiratory rate among highly stressed individuals," *Indian Journal of Physiology and pharmacology,* vol. 51, no. 3, p. 296, 2007.

[111] R. Vahey and R. Becerra, "Galvanic skin response in mood disorders: A critical review.," *International Journal of Psychology and Psychological Therapy,* vol. 15, no. 2, pp. 275-304, 2015.

[112] V. E. Drory and A. D. Korczyn, "Sympathetic skin response Age effect.," *Neurology,* vol. 43, no. 9, pp. 1818-1818, 1993.

[113] M. Baba, Y. Watahiki, M. Matsunaga and K. Takebe, "Sympathetic skin response in healthy man," *Electromyography and clinical neurophysiology,* vol. 28, no. 5, p. 277, 1988.

[114] J. Fagius and B. G. Wallin, "Sympathetic reflex latencies and conduction velocities in normal man," *Journal of the neurological sciences,* vol. 47, no. 3, pp. 433-448, 1980.

[115] B. Elie and P. Guiheneuc, "Sympathetic skin response: normal results in different experimental conditions," *Electroencephalography and clinical neurophysiology,* vol. 76, no. 3, pp. 258-267, 1990.

[116] W. Knezevic and S. Bajada, “Peripheral autonomic surface potential: a quantitative technique for recording sympathetic conduction in man,” *Journal of the neurological sciences,* vol. 67, no. 2, pp. 239-251, 1985.

[117] D. Claus and R. Schondorf, “Sympathetic skin response,” in *Recommendation for the Practice of Clinical Neurophysiology: Guidelines of the International Federation of Clinical Neurophysiology*, 2nd edition ed., E. 277285, Ed., 1999.

[118] T. Deltombe, P. Hanson, J. Jamart and M. Clérin, “The influence of skin temperature on latency and amplitude of the sympathetic skin response in normal subjects,” *Muscle & nerve,* vol. 21, no. 1, pp. 34-39, 1998.

[119] D. Fowles, “The eccrine system and electrodermal activity,” *Psychophysiology: Systems, processes, and applications,* vol. 1, pp. 51-96, 1986.

[120] M. Toyokura, “Waveform and habituation of sympathetic skin response.,” *Electroencephalography and Clinical Neurophysiology/Electromyography and Motor Control,* vol. 109, no. 2, pp. 178-183, 1998.

[121] M. Raszewa, I. Hausmanowa-Petrusewicz, M. Błaszczyk and S. Jabłońska, “Sympathetic skin response in scleroderma,” *Electromyography and clinical neurophysiology,* vol. 31, no. 8, pp. 467-472, 1991.

[122] P. Venables, “The relationships between PGR scores and temperature and humidity.,” *Quarterly Journal of Experimental Psychology,* vol. 7, no. 1, pp. 12-18, 1955.

[123] M. A. Wegner and T. D. Cullen, “Some problems in psychophysiological research: III. The effects of uncontrolled variables.,” in *Psychophysiological correlates of psychological disorder*, Ressler and N. S. Greenfield, Eds., Madison, University of Wisconsin Press, 1962, pp. 106-114.

[124] R. A. Davidson and B. D. Smith, “Caffeine and novelty: effects on electrodermal activity and performance,” *Physiology & behavior,* vol. 49, no. 6, pp. 1169-1175, 1991.

[125] M. P. Tarvainen, A. S. Koistinen, M. Valkonen-Korhonen, J. Partanen and P. A. Karjalainen, “Analysis of galvanic skin responses with principal components and clustering techniques,” *IEEE transactions on bio-medical engineering,* vol. 48, no. 10, p. 1071, 2001.

[126] P. Karthikeyan, M. Murugappan and S. Yaacob, “Descriptive analysis of skin temperature variability of sympathetic nervous system activity in stress.,” *Journal of Physical Therapy Science,* vol. 24, no. 12, pp. 1341-1344, 2012.

[127] B. T. Shahani, J. J. Halperin, P. H. Boulu and J. Cohen, “Sympathetic skin response--a method of assessing unmyelinated axon dysfunction in peripheral neuropathies,” *Journal of Neurology, Neurosurgery & Psychiatry,* vol. 47, no. 5, pp. 536-542, 1984.

[128] B. Elie and J. P. Loubo'Jtin, “Sympathetic skin response (SSR) is abnormal in multiple sclerosis,” *Muscle & nerve,* vol. 18, no. 2, pp. 185-189, 1995.

[129] M. Denislic and D. Meh, "Sympathetic skin response in parkinsonian patients.," *Electromyography and clinical neurophysiology,* vol. 36, no. 4, pp. 231-235, 1996.

[130] B. C. Hellerud and H. Storm, "Skin conductance and behaviour during sensory stimulation of preterm and term infants," *Early human development,* vol. 70, no. 1, pp. 35-46, 2002.

[131] F. Shaffer, D. Combatalade, E. Peper and Z. M. Meehan, "A Guide to Cleaner Electrodermal Activity Measurements," *Biofeedback,* vol. 44, no. 2, pp. 90-100, 2016.

[132] C. Tronstad, O. M. Staal, S. Sælid and Ø. G. Martinsen, "Model-based filtering for artifact and noise suppression with state estimation for electrodermal activity measurements in real time," in *Engineering in Medicine and Biology Society (EMBC), 2015 37th Annual International Conference of the IEEE*, 2015 (August).

[133] V. Xia, N. Jaques, S. Taylor, S. Fedor and R. Picard, "Active learning for electrodermal activity classification," in *Signal Processing in Medicine and Biology Symposium (SPMB)*, 2015 (December).

[134] S. L. Dormire and J. S. Carpenter, "An alternative to Unibase/glycol as an effective nonhydrating electrolyte medium for the measurement of electrodermal activity," *Psychophysiology,* vol. 39, no. 4, pp. 423-426, 2002.

[135] S. Grimnes, A. Jabbari, Ø. G. Martinsen and C. Tronstad, "Electrodermal activity by DC potential and AC conductance measured simultaneously at the same skin site," *Skin Research and Technology,* vol. 17, no. 1, pp. 26-34, 2011.

[136] T. Westeyn, P. Presti and T. Starner, "ActionGSR: A combination galvanic skin response-accelerometer for physiological measurements in active environments.," in *2006 10th IEEE International Symposium on Wearable Computers*, 2006 (October).

[137] W. Chen, N. Jaques, S. Taylor, A. Sano, S. Fedor and R. W. Picard, "Wavelet-based motion artifact removal for electrodermal activity," in *Engineering in Medicine and Biology Society (EMBC), 2015 37th Annual International Conference of the IEEE*, 2015 (August).

[138] W. Boucsein, F. Schaefer and T. Sommer, "Electrodermal long-term monitoring in everyday life. Progress in ambulatory assessment," pp. 549-560, 2001.

[139] S. Doberenz, W. T. Roth, E. Wollburg, N. I. Maslowski and S. Kim, "Methodological considerations in ambulatory skin conductance monitoring," *International Journal of Psychophysiology,* vol. 80, no. 2, pp. 87-95, 2011.

[140] W. T. Roth, M. E. Dawson and D. L. Filion, "Publication recommendations for electrodermal measurements.," *Psychophysiology,* vol. 49, no. 8, pp. 1017-1034, 2012.

[141] D. R. Bach, G. Flandin, K. Friston and R. J. Dolan, "Time-series analysis for rapid event-related skin conductance responses," *J. Neurosci. Methods,* vol. 184, pp. 224-234, 2009.

[142] W. Boucsein, Electrodermal Activity, Berlin: Springer, 1992.

[143] M. Toyokura, “Waveform and habituation of sympathetic skin response,” *Electroencephalography and Clinical Neurophysiology/Electromyography and Motor Control,* vol. 109, no. 2, pp. 178-183, 1998.

[144] G. Deuschl and A. Eisen, *Recommendations for the practice of clinical neurophysiology: guidelines of the International Federation of Clinical Neurophysiology,* Elsevier Science B.V., 1999.

[145] M. Toyokura and H. Takeda, “Waveform of sympathetic skin response in diabetic patient,” *Clinical neurophysiology,* vol. 112, no. 7, pp. 1229-1236, 2001.

[146] W. Boucsein, D. C. Fowles, S. Grimnes, G. Ben-Shakhar, W. T. Roth, M. E. Dawson and D. L. Filion, “Publication recommendations for electrodermal measurements,” *Psychophysiology,* vol. 49, pp. 1017-1034, 2012.

[147] W. Boucsein, “Electrodermal activity,” *Springer Science & Business Media,* 2012.

[148] M. M. Bradley and P. J. Lang, “Affective reactions to acoustic stimuli,” *Psychophysiology,* vol. 37, no. 2, pp. 204-215, 2000.

[149] R. Edelberg, “Electrical properties of the skin,” *Methods in psychophysiology,* pp. 1-53, 1967.

[150] D. F. Levinson and R. Edelberg, “Scoring criteria for response latency and habituation in electrodermal research: A critique,” *Psychophysiology,* vol. 22, no. 4, pp. 417-426, 1985.

[151] C. L. Lim, C. Rennie, R. J. Barry, H. Bahramali, I. Lazzaro, B. Manor and E. Gordon, “Decomposing skin conductance into tonic and phasic components,” *International Journal of Psychophysiology,* vol. 25, no. 2, pp. 97-109, 1997.

[152] D. M. Alexander, C. Trengove, P. Johnston, T. Cooper, J. P. August and E. Gordon, “Separating individual skin conductance responses in a short interstimulus-interval paradigm,” *Journal of neuroscience methods,* vol. 146, no. 1, pp. 116-123, 2005.

[153] H. L. Puckhaber, “New research on biofeedback,” Nova Publishers, 2006, p. 7.

[154] Y. Hulovatyy, S. D'Mello, R. A. Calvo and T. Milenković, “Network analysis improves interpretation of affective physiological data,” *Journal of Complex Networks,* vol. 2, no. 4, pp. 614-636, 2014.

[155] G. Ben-Shakhar, “Standardization within individuals: A simple method to neutralize individual differences in skin conductance,” *Psychophysiology,* vol. 22, no. 3, pp. 292-299, 1985.

[156] 24 December 2005. [Online]. Available: https://commons.wikimedia.org/wiki/File:Gsr.svg. [Accessed 8 July 2017].

[157] Carstensen, Gottman and Levenson, “Emotional behavior in long-term marriage,” *Psychology and aging,* vol. 10, no. 1, p. 140, 1995.

[158] Mendoza-Denton, Eisenhauer, Wilson and Flores, "Gender, electrodermal activity, and videogames: Adding a psychophysiological dimension to sociolinguistic methods," *Journal of Sociolinguistics,* vol. 21, no. 4, pp. 547-575., 2017.

[159] Vaidyanathan, Isen, Malone, Miller, McGue and Iacono, "Heritability and molecular genetic basis of electrodermal activity: A genome-wide association study," *Psychophysiology,* vol. 51, no. 12, pp. 1259-1271, 2014.

[160] Hinson, Jameson and Whitney, "Somatic markers, working memory, and decision making," *Cognitive, Affective, & Behavioral Neuroscience,* vol. 2, no. 4, pp. 341-353, 2002.

[161] Zahn, Rumsey and Van Kammen, "Autonomic nervous system activity in autistic, schizophrenic, and normal men: effects of stimulus significance," *Journal of abnormal psychology,* vol. 96, no. 2, p. 135, 1987.

[162] Salmon, "Effects of physical exercise on anxiety, depression, and sensitivity to stress: a unifying theory.," *Clinical psychology review,* vol. 21, no. 1, pp. 33-61, 2001.

[163] Julian, "Measures of anxiety: State-Trait Anxiety Inventory (STAI), Beck Anxiety Inventory (BAI), and Hospital Anxiety and Depression Scale-Anxiety (HADS-A)," *Arthritis care & research,* vol. 63, no. s11, pp. S467-72, 2011.

[164] Vitasari, Wahab, Herawan, Othman and Sinnadurai, "Re-test of State Trait Anxiety Inventory (STAI) among engineering students in Malaysia: reliability and validity tests," *procedia-Social and Behavioral Sciences,* vol. 15, pp. 3843-3848, 2011.

[165] Hofmann and Kim, "Anxiety goes under the skin: Behavioral inhibition, anxiety, and autonomic arousal in speech-anxious males. Personality and individual differences," *Personality and individual differences,* vol. 40, no. 7, pp. 1441-1451, 2006.

[166] S. Panju, J. Brian, A. Dupuis, E. Anagnostou and A. Kushki, "Atypical sympathetic arousal in children with autism spectrum disorder and its association with anxiety symptomatology," *Molecular autism,* vol. 6, no. 1, p. 64, 2015.

[167] Toone, Cooke and Lader, "Electrodermal activity in the affective disorders and schizophrenia," *Psychological Medicine,* vol. 11, no. 3, pp. 497-508, 1981.

[168] Raine, Venables and Williams, "Better autonomic conditioning and faster electrodermal half-recovery time at age 15 years as possible protective factors against crime at age 29 years," *Developmental Psychology,* vol. 32, no. 4, p. 624, 1996.

[169] Schwerdtfeger, "Trait anxiety and autonomic indicators of the processing of threatening information: A cued S1–S2 paradigm," *Biological psychology,* vol. 72, no. 1, pp. 59-66, 2006.

[170] Du, Kibbe and Lin, "Improved peak detection in mass spectrum by incorporating continuous wavelet transform-based pattern matching," *Bioinformatics,* vol. 22, no. 17, pp. 2059-2065, 2006.

[171] French, Zimmerman, Schilling, Gibson, Miller, Townsend, Sherrod, Goodwin, McLean and Tabb, "Wavelet-Based Peak Detection and a New Charge Inference Procedure for MS/MS Implemented in ProteoWizard's msConvert," *Journal of proteome research,* vol. 14, no. 2, pp. 1299-1307, 2014.

[172] Ihaka and Gentleman, "R: a language for data analysis and graphics," *Journal of computational and graphical statistics,* vol. 5, no. 3, pp. 299-314, 1996.

[173] D. T. Lykken and P. H. Venables, "Direct measurement of skin conductance: A proposal for standardization.," *Psychophysiology,* vol. 8, no. 5, pp. 656-672, 1971.