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The electrical activity map of the human skin indicates strong differences between normal and diabetic individuals: A gateway to onset prevention

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ABSTRACT

The human skin is not only the largest organ, but also the most important candidate for novel non-invasive methods of investigation. Here we describe a large-scale prototype for determining the real-time distribution of the electrical activity from the surface of the human skin. A collection of 200 sensors have been placed across the entire trunk surface. The output of each sensor was remotely inserted into a 20 × 10 LED matrix for a parallel capture of the signals. Continuous observations of the electrical activity pattern were made above the LED matrix by a digital camera in an obscure environment. A total of 5.2 million measurements (25,920 maps) have been recorded as light intensities from the LED matrix and converted into percentages for evaluation. A total of 36 individuals were divided equally into two groups and subjected to a short glucose tolerance test for 1 h; one group with established *Type 2 Diabetes* (T2D) and the other group without diabetes. The electrical activity pattern and the average signal intensity of normal individuals (37% ± 8.1) and diabetic individuals (58% ± 7.8), showed a significant difference of 21%. The average signal intensity on the ventral side (VS) and dorsal side (DS) of the torso exhibited different behaviors in diabetics and non-diabetics. On average, diabetic individuals have shown an electrical activity of higher intensity on DS (DS = 60%, VS = 55%), while the normal group has shown a higher intensity on VS (DS = 36%, VS = 39%).

1. Introduction

Some organs of the human body often gained favor for more complex research because of their clear roles and immediate medical significance. In contrast, other organs with mixed and partly uncertain roles received less attention. The human skin is the *organum miraculos* as it has multiple roles and can be considered an important indicator for many disorders (Proksch et al., 2008; Si et al., 2015). More often than not, this organ has been brought to the forefront of diabetes for non-invasive diagnostic methods (Murphy-Chutorian et al., 2013; Duff et al., 2015; Nwabudike and Tatu, 2018). External chemical and biological fuels and the reuse of *self* molecular parts are the main energy components used by the body (Galgani and Ravussin, 2008; Hall et al., 2012). Environmental parameters force the human body to use unique behavioral patterns for energy intake (Carreiro et al., 2016). Thus, the manner in which these resources are used by the body over time dictate the behavior of the metabolic machine and the impact of this behavior on homeostasis (Han et al., 2015; Savir et al., 2017). For a large proportion of the human population, certain mechanisms in the metabolic chain are only partially adapted to the variability of the environmental parameters due to genetic susceptibility and inheritance or *de novo* somatic mutations (Karaderi et al., 2015; De Silva and Frayling, 2010). A low adaptation to a broad range of environmental conditions implies a predisposition of the body to certain diseases, which are triggering only under specific conditions (Ionescu-Tîrgovişte et al., 2015). More often, particular deviations of the metabolic behavior can trigger diseases such as type 2 diabetes (Galgani and Ravussin, 2008; Hall et al., 2012). A non-invasive method to probe the metabolic behavior is represented by the electrical activity that can be sampled from the surface of the skin (Nuccitelli et al., 2011; Thorell et al., 2013). However, the lack of useful imaging methods for in vivo studies of metabolic diseases would be the main rationale behind our current investigation. Diabetes

Abbreviations: BMI, Body Mass Index; ECG, Electrocardiograph; EDA, Electrodermal Activity; EEG, Electroencephalograph; HbA1C, Glycated hemoglobin; LED, Light-Emitting Diode; T2D, Type 2 Diabetes; VSL, Vertical Sensor Lines

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implications on the global metabolic status of the body served as our initial hypothesis for a detailed exploration of the electrical activity of the skin. Ions from individual cells and moving fluids are the origin of the electrical signals (potentials and currents) generated by the human body. Sodium (Na^+) and potassium (K^+) are the most important examples of monovalent cations with a single positive charge or calcium (Ca^{2+}), which is a divalent cation that carries a double positive charge. Thus, the electrical activity represents the change in electric current produced by the sum of an electrical potential difference across a specialized tissue, organ or cell system. By our knowledge, a high resolution of sensors for macro-detection of electrical fluctuations of the skin has not been used in past investigations. Here we propose a novel prototype for direct observations on the subtle metabolic processes through high resolution electrical activity patterns. In our approach the electrical activity is observed through a large collection of 200 sensors located over the surface of the trunk. Thus, a high resolution of the electrical activity generated by the trunk is obtained and analyzed comparatively between normal and diabetic individuals.

2. Materials and methods

In order to make direct observations on the subtle metabolic processes in normal and disease conditions, we built a prototype measuring device called „Vesta" (Gagniuc et al., 2018). The system was composed of a coat equipped with 200 sensors and a signal recording box that was able to transfer the data to a computer in real-time. Changes in the electrical signal patterns over time during a short glucose tolerance test, have been the main objective of this experiment (Fig. 1).

2.1. Sensor internals & organization

Eight electronic parts have been attached to a printed circuit board (PCB) for each sensor: three BC546B general-purpose NPN bipolar junction transistors (Q1,Q2, and Q3) arranged in a Darlington triplet, an electrode wire (L = 2 cm,d = 0.5 mm), three resistors, R1(1 MΩ), R2 (100 kΩ), R3 (100 Ω), and L1, a *Light-Emitting Diode* (LED) that resides outside the PCB of the sensor (Fig. 1a). A coat without sleeves that molds over the human torso was chosen in order to allow the skin an optimal exchange with the environment (Supplementary material 1). 200 sensors were arranged and sewn on the outer part of the vest in 16 *Vertical Sensor Lines* (VSL). The electrode of each sensor penetrated through the vest material and established a physical contact with *stratum corneum*. The VSL consisted of 11–13 sensors arranged linearly on the vest, in accordance with the anatomy of the human torso. The ventral and dorsal side of the torso were covered by 8 VSL each. Thus, the torso VSL coverage was made between T1 and L4 or L5 vertebrae. Sensor labeling was made by using the number associated with a VSL, followed by the sensor number along the VSL (Fig. 1b,c).

Supplementary material related to this article can be found online at doi:10.1016/j.bios.2018.08.057.

2.2. LED matrix organization and signal encoding

The 200 LEDs have been positioned outside of the vest environment by using insulated copper wires. The LEDs of the sensors have been arranged on a PCB into a 20 × 10 LED matrix of 12 × 6 cm in size. 100 LEDs of VSL from the dorsal side of the torso were encoded (positioned) on the first half of the LED matrix (left side) whereas the 100 LEDs of VSL from the ventral side have been encoded on the second half (Fig. 1d). The encoding was made in a zigzag pattern starting from the right to the left, for both sides of the LED matrix.

2.3. The electric diagram of the vest

The main electrode and the positive/negative terminals represented the input of each sensor (S_1, S_2 … Sn, where n = 200). Thus, VSL were powered in parallel using a DC power supply (7.5 V). The electrode had the task of collecting and transmitting the local biological signal to the base of the Q1 transistor for further amplification. The output of each sensor was represented by the signal from the collector of the Q3 transistor and it was connected remotely to the corresponding LED anode by an insulated copper wire. The positive terminal (+) of the DC power supply was connected to the VSL and to the cathode of each LED in the matrix. The negative terminal (-) of the DC power supply was grounded and also connected to the emiter of each Q3 transistor from the VSL. The connection between the vest and the signal recording box was made through a total of 232 insulated copper wires. Of which, 200 wires bring the amplified signal from each sensor to the LED matrix and 32 wires feed the VSL.

2.4. The black box & data acquisition

In the absence of ambient light, a digital camera (320 × 240 pixels) was used as a light detector. A digital camera supported by a duralumin skeleton, was targeted at 15 cm above the LED matrix inside an opaque box (Fig. 1e). A dedicated opensource software was developed for the video camera and used to retrieve the images of the LED matrix at discrete time intervals. The optimal setting for our experiment was established at 60 min with an interval of 5 s, which resulted in a constant series of 720 images/subject (25920 images for the entire experiment). These images were stored on a computer for further analysis.

2.5. Presentation of groups

A total of 36 individuals were divided into two groups: the normal group (-); composed of 5 normal females (F-) and 13 normal males (M-) and a diabetic group (+); consisting of 8 diabetic females (F+) and 10 diabetic males (M+). *Glycated hemoglobin* (HbA1C) values and prior diagnosis of T2D metabolic syndrome were the main parameters for inclusion into the group. The diabetic group included individuals with HbA1C values above the 6.5% threshold whereas individuals with values below 5.9% were associated with the normal group. On average, individuals belonging to the diabetic group (+) showed a HbA1C value of 7.82 ± 0.7 (F(+) = 7.88 ± 0.7 and M(+) = 7.77 ± 0.73), and the normal group (-) showed a HbA1C value of 5.45 ± 0.25 (F (-) = 5.46 ± 0.27 and M(-) = 5.44 ± 0.26). The *Body Mass Index* (BMI) was calculated in order to observe the balance between female and male groups (Supplementary material 2). Diabetic females F(+) showed an average age of 66 ± 8.9 years and a BMI of 32.41 (*height* = 156 ± 9, *weight* = 79 ± 15), while diabetic males M(+) showed an average age of 63.9 ± 8.8 years and a BMI of 29.87 (h = 173.3 ± 7.6, w = 89.7 ± 17.4). In the normal group, females F (-) showed an average age of 52.6 ± 16.14 years and a BMI of 30.71 (h = 165 ± 10.2, w = 83.6 ± 38.3), while normal males M(-) showed an average age of 37.38 ± 16.73 years and a BMI of 26.51 (h = 181.46 ± 9.48, w = 87.31 ± 11.59).

2.6. Experiment design

Volunteer patients participated in the experiment in a dry fasting state. Each experiment was conducted in the morning (3 subjects/day). To avoid an increase in the apparent temperature of the body, constant temperature (25 °C) and relative humidity (40%) have been preserved around the experimental setup. During the experiments, the subjects had to wear the vest and sit comfortably and immobile for 1 h on a chair without a backrest. In order to closely observe the metabolic response, two oral doses of 37 g glucose have been administered to the subjects (Fig. 1f). The first dose was administered after 15 min and the second dose after 30 min (75 g in total). Each participant was carefully monitored for blood glucose levels in *milligrams per deciliter* (mg/dL) at 15-

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