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EXECUTIVE SUMMARY OF THE THESIS

Assessment of children emotional state during robot-based gait rehabilitation: from patients' self-evaluation to bio-signals processing

TESI MAGISTRALE IN BIOMEDICAL ENGINEERING – INGEGNERIA BIOMEDICA

AUTHOR: ANNA FALIVENE

ADVISOR: EMILIA AMBROSINI

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1. Background and rationale of the study

Robotic rehabilitation is nowadays an established intervention aimed at recovering walking abilities in patients with neurological disorders.
Robot-assisted therapeutic methods demonstrate multiple advantages with respect to conventional therapy, such as increased efficacy, intensity and modulation of the therapy. Among robot-assisted devices, one of the most used is the Lokomat system (Hocoma), which is a driven gait orthosis that combines body weight support system and treadmill training.
Most traditional approaches investigate the effectiveness of therapy focusing mainly on the motor aspects, ignoring patients' psychophysiological state, which can greatly contribute to the outcome of the therapy. To the best of my knowledge, estimation of emotional and psychophysiological states with both quantitative and semi-quantitative methods has never been performed in children with neurological disorders during Lokomat rehabilitation therapies.
Therefore, the aim of the present Master thesis was to objectively characterize the psychophysiological state of the patient before and throughout the therapy with Lokomat, combining the monitoring of the activation of the autonomic nervous system (ANS) through the analysis of bio-signals, such as blood volume pulse and electrodermal activity, with the therapist's evaluation and patients' self-assessment. In particular, the first specific objective of the study was to develop a (semi)automatic algorithm for the extraction of emotion-related features from patients' bio-signals, recoded with the E4 wearable wrist medical device (Empatica®, Milan, Italy). The secondary objective was to investigate whether the extracted features correlate with the therapists' evaluation, collected during the rehabilitation session, and/or with the patients' self-evaluation about their emotional state. The final objective was to assess if and how children's emotional state changes throughout the rehabilitation period.

2. Methods

2.1. Test protocol and participants

The project in which the present Master thesis is included aims to enrol 40 subjects; inclusion criteria are: subjects who receive 15/20 sessions (30-45 minutes each session) of Lokomat gait training

at IRCCS Medea, as prescribed by the reference clinician and parents signing the informed consent. Exclusion criteria is the presence of skin problems in the wrist area, where the sensorized bracelet is supposed to be worn.
Enrolled patients were asked to wear the E4 wristband before, during and after two rehabilitation sessions (one at the beginning, one among the last five sessions, distant from each other at least 5/7 days). Before the training, patients were asked about their emotional state through a visual analogue scale (VAS) *ad hoc* questionnaire (see section 2.5). This was followed by the rehabilitative exercises on the Lokomat system, during which the physiotherapist was asked to fill in an *ad hoc* questionnaire that collects a reliable evaluation about patients' well-being condition (see section 2.5). At the end of the rehabilitation, patients were asked again about their emotional state through the VAS *ad hoc* questionnaire. The instants corresponding to the start and the end of the Lokomat training were registered on the bio-signals by means of a flashing light recorded by a camera synchronized with E4 wrist sensor.

2.2. Bio-signals extraction

E4 wearable wrist device records non-invasively patients' physiological signals such as blood pressure volume (BVP), heart rate, electrodermal activity (EDA), skin temperature and acceleration data. In particular, BVP and EDA bio-signals are considered the most informative markers of the psychophysiological and emotional state in the presence of physical effort induced by walking [1].
BVP signal, recorded with the E4 photoplethysmogram sensor, reflects changes in the blood volume that occurs between the systolic and diastolic phases of the cardiac cycle. The ideal BVP waveform is indeed characterized by a diastolic point, a systolic peak, and a dicrotic notch followed by a second wave. Considering two adjacent diastolic points, inter beat intervals (IBI) can be computed. However, E4 wrist sensor provides IBI only for ideal waveforms.

EDA represents the variations of skin electrical properties as a reaction to sweat secretion. The raw signal, measured by two silver-coated (Ag) electrodes embedded on the wristband, can be divided into tonic (EDL: electrodermal level) and phasic phenomena (EDR: electrodermal response).

Electrodermal responses (μS) are recognizable as short-lasting variations of EDA signal that can be either elicited by an external stimulus (event-related electrodermal responses ER.EDRs), or spontaneous responses that cannot be traced to any specific stimulation (non-specific electrodermal responses NS.EDRs). In the present work, the focus was on non-specific responses since during the Lokomat sessions no established a priori stimuli were imposed, of which the response could be studied.

Since parts of bio-signals acquisition was performed during Lokomat training, the signals were affected by motion artefacts. Therefore, pre-processing algorithms were developed in MATLAB and applied to the signals as described in the following paragraph.

2.3. Signal pre-processing

In order to clean the BVP signal from noise and motion artifacts a band pass filter was applied, exploiting the acceleration signal. The cut off frequencies were computed specifically for each patient and for each session in order to have a customized filter. Starting from the IBI spreadsheet provided by the E4 device, artefacts-free segments of the BVP were identified in an automatic way considering at least 10 consecutive negative peaks. The power spectral density (PSD) of both BVP segment and the corresponding acceleration segment were then computed with a Fast Fourier transform (FFT) method and then normalized with respect to their maximum amplitude value. Finally, the PSD of acceleration signal was subtracted to the PSD of BVP to identify the motion-free fundamental frequency for each segment. These steps were performed for each artefacts-free segment of the BVP. Only frequencies belonging to the physiological range of the cardiac frequency (1-3 Hz, i.e. 60-180 bpm) were kept and saved in a new vector. The maximum (MAX) and minimum (MIN) values of this new vector of fundamental frequencies were then computed and the cut off frequencies for the whole signal were imposed as in Equation (1), where Δ is a safety margin set arbitrarily to 0.1 Hz.

$$f_l = MIN - \Delta \quad (1a)$$

$$f_u = MAX + \Delta \quad (1b)$$

A Butterworth bandpass filter between f_l and f_u was finally applied to the BVP signal, from which the new diastolic points were identified, and the new inter-beat-intervals were computed.

As for EDA processing, the signal decomposition into its tonic and phasic components was performed using a convex optimization method (*cvxEDA algorithm)* implemented by [2]. Before *cvxEDA* application, a moving average across a 1-second window was applied to smooth the raw signal. In addition, a z-score normalization was performed, as suggested by [2] for standardization purposes and to increase the velocity of the optimization procedure. To address motion artifacts issues, the stationary Haar wavelet transform was applied for detecting artefacts characterized by sudden changes of the signal and recognized applying an adaptive threshold to wavelet coefficients each 1000s-time-window. Coefficients higher than three times their standard deviation in the current time-window were considered artefacts-related. The detected artefacts were the visually inspected so to accept or reject them as artefactual. Once all portions containing artefacts were detected, they were excluded from the feature extraction process.

2.4. Feature extraction procedure

Features extraction was performed for both BVP and EDA signal as described below. For each patient, features were collected for the self-evaluation questionnaire-filling phases and the Lokomat-active training for two rehabilitative sessions.
Following the BVP pre-processing phase, Heart Rate Variability (HRV) parameters were extracted. The HRV time domain parameters computed were the mean inter-beat interval (IBI) and the corresponding mean heart rate. In addition, the square root of the mean squared differences of successive inter-beat intervals (RMSSD) and the standard deviation of all IBI intervals (SDNN) were computed. As for HRV frequency domain parameters, Low Frequency (LF, [0.04–0.15] Hz) and High Frequency (HF, [0.15-0.40] Hz) power were normalized with respect to the total power minus the Very-Low Frequency (VLF) component. Moreover, the ratio LF/HF was computed as the sympathovagal balance index.
Reduced values of RMSSD, SDNN and HF parameters and increased values of LF and LF/HF features are typically associated with higher mental stress condition and negative emotional states. [3]
As for EDA time domain parameters, the following features were computed: the mean value of the tonic data, the number of phasic peaks (i.e non-specific responses), the distance peak-to-peak parameter, and the indices related to the magnitude of the response (Mean amplitude and Area Under the Curve parameters). The minimum amplitude that qualifies a non-specific response as effective was set to 0.015 μS, according to [4].
EDA frequency parameters were computed considering the Very-Low-Frequency band (VLF, [0–0.045] Hz), the Low Frequency band (LF, [0.045-0.15] Hz), the High Frequency range (HF_1, [0.15-0.25] Hz; HF_2, [0.25-0.4] Hz), and the Very-High-Frequency band (VHF, [0.4-0.5] Hz) normalized with respect to the total power.
Greater mean electrodermal level, number and magnitude of the response are typically related to an increased sympathetic nervous system arousal. In addition, a decreasing of power in VLF band, and a corresponding increased power for [0.045-0.5] Hz range, are typically found in response to increased mental workload. [5]

2.5. Processing of self-evaluation and therapist's evaluation questionnaires

Self-assessment questionnaires were structured with six questions related both to positive and negative emotions (Q1-"*Are you worried?*"; Q2-"*Are you happy?*"; Q3-"*Are you sad?*"; Q4-"*Are you angry?*"; Q5-"*Are you scared?*"; Q6-"*Are you bored?*"), to which possible answer were: *not at all, a little, very much*.
Therapists 'evaluations were collected in an *ad hoc* questionnaire, structured with 12 items, listed below, about subjects' experience during the training.

Q1. "*The patient is passive/ proactive*";
Q2. "*The patient is fearful/in control of the situation*";
Q3. "*The patient is anxious/relaxed*";
Q4. "*The patient is impulsive /thoughtful*";
Q5. "*The patient is distracted /focused*";
Q6. "*The patient is hyperactive/quiet*";
Q7. "*The patient underestimates/overestimates his/her abilities*";
Q8. "*The patient is not/ is persistent*";
Q9. "*The patient is concerned/does not care about failure*";

Q10. *"The patient is unable/able to derive satisfaction from success"*;
Q11. *"The patient manages emotions in a negative/positive manner"*;
Q12. *"The patient does not/does actively seek information to learn and update"*.
The therapist gave an evaluation to each item with a numerical score ranging from -3 to 3, where the lowest value is associated with negative emotional state, while the maximum score is related to maximal well-being condition.

For statistical analysis, responses from both self-evaluation questionnaires were converted into a numerical score from 1 to 3, while the therapist's evaluations were converted from 0 to 6.
In addition, for each item of the self-evaluation and therapist' evaluation the median and interquartile range values of the responses were computed.

2.6. Statistical analysis

First, to identify parameters that may be indicative of the subject's emotional state (second specific objective of the present study), correlation between HRV/EDA features, acquired during the Lokomat exercises, and all the questionnaires' responses were performed evaluating the Kendall's τ coefficient. Moreover, to assess the patient's emotional state in the first recorded session and detect any changes from the beginning to the end of the treatment (third specific objective), differences between the two considered sessions were investigated, for both questionnaires' responses and HRV/EDA parameters.

Data were not normally distributed, as verified with the Kolmogorov-Smirnov test. Therefore, first, a Friedman test was used to assess potential differences in terms of self-evaluation answer among 4 timepoints (pre/post of the two sessions). Then, a Wilcoxon test was used to look for potential differences in terms of therapist's evaluation. Finally, a Wilcoxon test was used to compare HRV/EDA parameters during Lokomat active training. Before any statistical analysis, E4 feature extracted during Lokomat training were normalized subtracting the data collected during the last phase of the recording (after the conclusion of the active Lokomat training). This was indeed the most reliable phase in terms of signals according to the literature and visual inspection.

3. Results

A total of 16 subjects were recruited in the present thesis. These subjects (9 male and 7 female), ranging in age from 5 to 23 years old (10.06±5.31; mean±SD), suffered from cerebral palsy, acquired brain injury or hereditary spastic paraplegia.
With respect to the first specific objective, the pipeline of the analysis was implemented and tested. Then, the bio-signals of the 16 patients were acquired and processed. Figure 1 shows how the raw BVP signal was successfully filtered with the pre-processing algorithm implemented during the present work, for motion artefacts removal and feature extraction.

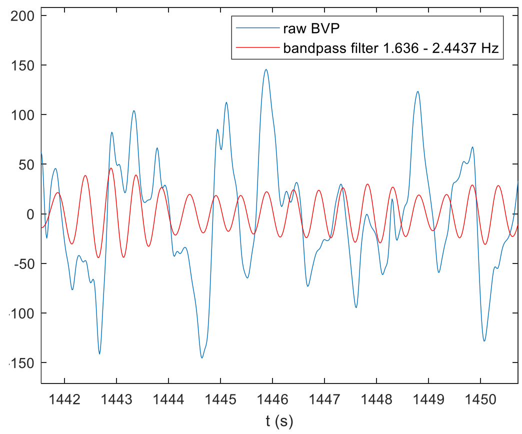

Figure 1: Example of raw (blue) and filtered (red) BVP signal

As for EDA processing results, the decomposition into tonic and phasic component is shown in Figure 2.

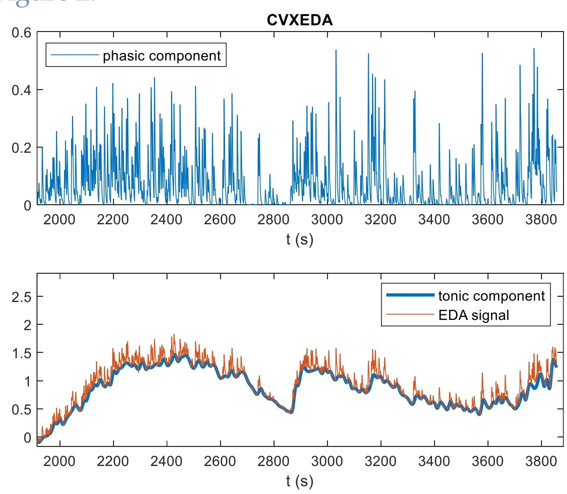

Figure 2: Outcome of the *cvxEDA algorithm*: decomposition into phasic and tonic component.

In addition, efficacy of the artefacts-detection algorithm implemented is shown in Figure 3.

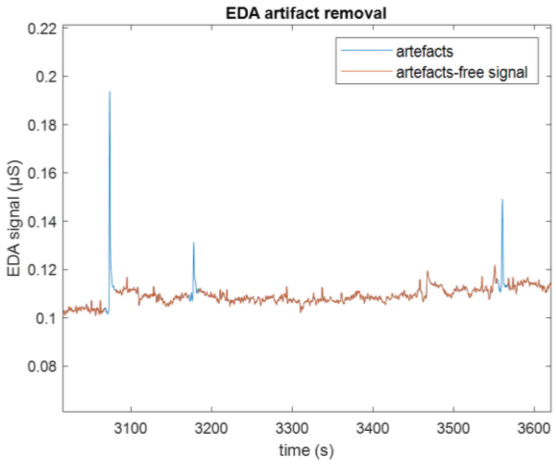

Figure 3: Artefacts identification: artefact-free signal (orange) and artefacts segment (blue).

To identify parameters that may be indicative of the subject's emotional state (second objective), correlation between Lokomat-features and all the questionnaires' responses were investigated: a moderate correlation (Table 1 and Table 2) was found between EDA frequency parameters and self-evaluation responses, in particular those related to feelings of sadness and worry (Q3 and Q1).

	Q1	Q2	Q3[↑]	Q4	Q5	Q6
VLF[↓]	-0.07	0.10	-0.28	0.03	-0.02	-0.03
LF[↑]	0.07	-0.07	0.26	-0.03	0.05	0.03
HF_1 [↑]	0.06	-0.13	0.27	-0.01	0.00	0.02
HF_2 [↑]	0.07	-0.18	0.35	-0.05	0.01	0.05
VHF[↑]	-0.01	-0.25	0.34	-0.14	-0.01	-0.03

Table 1: Kendall's τ coefficients between EDA frequency parameters and Pre-Lokomat self-evaluation responses. Significant correlations are highlighted: darker the colour, higher the correlation. The arrows explain the direction of the correlation.

	Q1[↑]	Q2	Q3	Q4	Q5	Q6
VLF[↓]	-0.28	0.01	0.08	0.07	-0.13	-0.06
LF[↑]	0.27	0.01	-0.07	-0.07	0.12	0.09
HF_1 [↑]	0.29	-0.01	-0.08	-0.06	0.16	0.07
HF_2 [↑]	0.30	-0.08	-0.05	-0.10	0.13	0.01
VHF	0.23	-0.16	-0.05	-0.15	0.01	-0.11

Table 2: Kendall's τ coefficient between EDA frequency parameters and Post-Lokomat self-evaluation responses. Significant correlations are highlighted. The arrows explain the direction of the correlation.

Interestingly, the same features were found to be moderately correlated (Table 3) also with the therapist assessments, particularly those about emotion handling (item Q11). In details, VLF was positively correlated to positive emotional state while the other frequency bands to negative emotional states.

No other significant correlations were found.

Patients' emotional state was then assessed considering their self-evaluation responses in all the proposed questionnaires: from their answers it is clear that a feeling of happiness prevailed in patients during both the previous and post-Lokomat phases (Figure 4). The Friedman test on self-evaluation questionnaire did not reveal any statistically significant differences among the four time-points considered (for all *p* >.194).

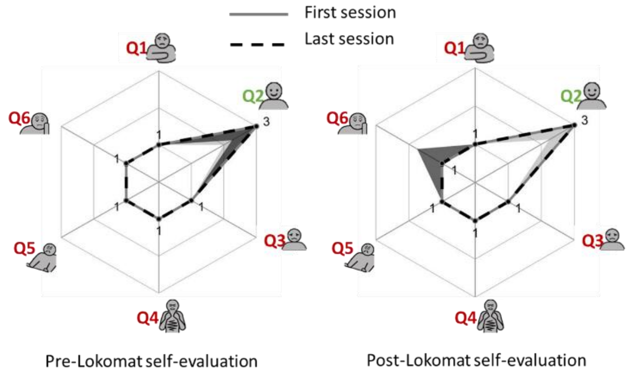

Figure 4: Radar plot of self-evaluation responses. Labels $Q_1 - Q_n$ were assigned as in section 2.5. The continuous line represents median values of the first session, while the dotted line accounts for the second session. Interquartile ranges are shown with the brighter gray area for the first session and the darker area for the second session.

Moreover, statistical analysis on differences between the two sessions yielded no significant differences (for all parameters and responses $p >$ 0.05) considering both the therapist responses, that underlined a general feeling of wellbeing during the treatment (e.g. assigned scores to item Q3: First session median value: 4.75, interquartile range: 1; Second session median: 5, iqr: 1.5) and the HRV/EDA parameters during Lokomat rehabilitation (third objective).

4. Discussion

The aim of this Master thesis was to assess the emotional states of children/adolescents that perform Lokomat-assisted gait training. Self-assessment responses suggested that walking with the Lokomat system was perceived as a positive experience by the subjects, who mostly expressed a feeling of happiness at the beginning and at the end of treatment. This was also confirmed by the therapist's evaluation and by the bio-signals features during Lokomat sessions, which showed no significant variations in the subjects' emotional state during the rehabilitation treatment.

Furthermore, the correlation results demonstrated that emotional states can be detected by analyzing EDA frequency parameters that correlate, even if moderately, with questionnaire responses and therapists' evaluation. More in details, the results suggest that the VLF spectral content increases with the patient wellbeing (while LF and HF spectral contents decrease), according to [5].

	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11[↑]	Q12
VLF[↑]	0.06	-0.07	0.11	0.02	0.04	-0.01	0.19	0.12	0.08	0.00	0.23	0.18
LF[↓]	-0.05	0.07	-0.10	-0.01	-0.04	0.02	-0.19	-0.14	-0.06	0.00	-0.23	-0.20
HF_1 [↓]	-0.04	0.08	-0.10	-0.04	-0.04	-0.03	-0.22	-0.10	-0.09	-0.01	-0.23	-0.17
HF_2 [↓]	-0.06	0.10	-0.10	0.00	0.02	0.02	-0.17	-0.09	-0.06	-0.01	-0.26	-0.17
VHF[↓]	-0.05	0.12	-0.09	0.05	0.10	0.05	-0.03	-0.04	-0.01	-0.07	-0.26	-0.09

Table 3: Kendall's τ coefficient between EDA frequency parameters and therapists' evaluation. Significant correlations are highlighted. The arrows explain the direction of the correlation.

5. Conclusions

Some limitations are present in this research: the first one is related to the signal processing, that is not fully automatic and visual inspection is often necessary. Hence, future developments should focus on total automation of these tools for possible real-time data extraction and analysis.

Another point to highlight is the small sample size: 16 participants were included during the present work, while at the end of the research a sample size of 40 subjects is estimated, leading to more robust results. Lastly, some modifications should be introduced to the experimental protocol, although the complexity of not interfering with the rehabilitation session is recognized: it is suggested to introduce a baseline period during the Lokomat rehabilitation phase to be considered as low-stress reference. Moreover, it might be useful to determine, with the help of physiotherapists, which game challenged the patient the most during rehabilitation, so that it could be taken as a stress-level reference.

Despite the above-mentioned study limitations, from these preliminary results, it can be concluded that it is possible to investigate the subjects' emotional state during the rehabilitation session through the BVP and EDA bio-signals, which were processed and analyzed according to the methodology presented above.

Future developments may lead to automatically identify any stressful or challenging situation during the rehabilitation session, so as to adjust the therapy not only to patient's physical performance but also to their psychological condition.

6. Bibliography

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