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Chapter # - will be assigned by editors

THE ROLE OF SERIOUS GAMES IN ROBOT EXOSKELETON ASSISTED REHABILITATION OF STROKE PATIENTS

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Abstract: This chapter describes how serious games can be used to improve the rehabilitation of stroke patients. Determining ideal training conditions for rehabilitation is difficult, as no objective measures exist and the psychological state of patients during therapy is often neglected. What is missing is a way to vary the difficulty of the tasks during a therapy session in response to the patient needs, in order to adapt the training specifically to the individual. In this chapter, we describe such a method. A serious game is used to present challenges to the patient, including motor and cognitive tasks. The psychological state of the patient is inferred from measures computed from Heart Rate Variability (HRV) as well as breathing frequency, skin conductance response, and skin temperature. Once the psychological state of the patient can be determined from these measures, it is possible to vary the tasks in real time by adjusting parameters of the game. The serious game aspect of the training allows the virtual environment to become adaptive in real time, leading to improved matching of the activity to the needs of the patient. This is likely to lead to improved training outcomes and has the potential to lead to faster and more complete recovery, as it enables training that is challenging yet does not over-stress the patient.

Key words: Robot exoskeleton, stroke rehabilitation, physiological measurements, closed loop difficulty

1. BACKGROUND

This chapter describes an application of serious games to stroke rehabilitation. Serious games have been defined in terms of their function as achieving a specific goal by using entertainment as a means to reach that goal rather than forming the primary goal of the game (Rego et al., 2011). Games are now recognized as one of the technologies that can be used to assist with aged care (Vichitvanichphong 2014). Serious games have been applied to rehabilitation as they can provide motivation for patients, to encourage compliance with exercises, and therefore assist recovery (Wiemeyer 2012). When applied to stroke recovery, serious games have been shown to improve engagement (Burke, 2009).

Tasks that form part of a game can be finely tuned in terms of difficulty, duration and repetition. When the game is adopted for a serious or therapeutic purpose it becomes a serious game. Such serious games incorporating virtual task environments have been used in neurorehabilitation with good outcomes and can provide the basis for improvement or neurorehabilitation practice. The benefits of serious games have shown as transferable to the requirements of activities of daily living in patients with stroke (Adamovich et al., 2009; Holden 2005). The degree of active participation and motivation, as a function of task difficulty, has been explored by several authors. This degree of

participation is difficult to assess and is often dependent on the interpretation of the physical therapist (Maclean et al., 2002). Serious gaming can be a useful adjunct as an edutainment device, which can provide different training scenarios and set an appropriate task difficulty level. Numerous methods exist that try to achieve this in real time. How to provide this adaptation to the patients' needs is the subject of this chapter.

1.1 Rehabilitation

Stroke rehabilitation aims to return patients to an optimal level of activity through a combination of progressively improving motor and cognitive tasks. The goal of rehabilitation is often to reduce motor related impairments, increase participation in activities of daily living and improve quality of life. Spontaneous recovery of motor skills after a stroke plateaus at approximately three months. However, rehabilitation based improvements beyond spontaneous recovery have been demonstrated even in chronic stroke patients, inspiring research and application of long term therapies. Determining ideal training conditions for rehabilitation that provides optimal active mental engagement and a physical challenge to individual patients is difficult, as no objective measures exist. Technology assisted rehabilitation including robot-assist training and the use of virtual reality (VR) is becoming a practical component of rehabilitation, with increasing availability and ease of use. Combining robot-assist technology with VR can address mental engagement and increasing repetitions, as well as greatly increasing the reach and effectiveness of today's healthcare system (Saposnik et al., 2010).

Gait is one area often affected by stroke, requiring robot-assist devices linked with a treadmill where patients retrain to walk. Robot-assisted treadmill training is an established intervention to improve motor function and walking ability in neurologically impaired patients. Treadmill training is an established treatment for gait rehabilitation in neurological patients such as stroke survivors, or people with spinal cord or traumatic brain injury (Dietz & Duysens, 2000; Harro et al., 2014). To improve the rehabilitation outcome in those patients, an increasing number of Driven Gait Orthosis (DGO) devices are available, which automate gait training; amongst them are the Lokomat, the Autoambulator, the LOPES and the Gaittrainer (Colombo et al., 2000;; Arazpour, 2014; Stauffer et al., 2009; Veneman et al., 2007; Winchester & Querry 2006).

The work described in this chapter used Lokomat (Hocoma, Switzerland). Parts of this work have previously been published in Koenig et al., (2011). The Lokomat assists locomotion at the knee and ankle joint as well as providing support for foot drop. The device allows assisted locomotion on a treadmill by guiding the participant's legs along a predefined trajectory. The training is assisted by providing the participant with an interactive serious game facilitated by video screens placed in front of the Lokomat, as shown in Figure 1.

Figure 1. The experimental setup described in this chapter, showing the Lokomat and video screens used for the interactive serious game.

Training involves learning motor skills associated with balance and walking. Ideally, these activities should be challenging to the patients, yet not too challenging, as this can lead to increased stress and despair. Learning and exercise can be exceptionally challenging for stroke patients (Jelinek et al., 2011). It is important to ensure that rehabilitation and exercise are safe for the patient and at the same time, it is essential to select a suitable training protocol that brings the most benefit in terms of improved functionality. Measures that can inform the clinician of any risk for the individual, such as a sluggish or rapid physiological or psychological response to abrupt changes or specific challenges, would improve safety for the patient. Active biomechanical engagement of the patients in rehabilitation training has been shown to be an important factor for successful rehabilitation results (Lotze et al., 2003); the

patient's biomechanical effort can be quantified by torque and force sensors. This information is used to assess the patient's level of physical activity (Banz et al., 2008).

1.2 Psychological state

Despite the fact that attention has been shown to play a role in training success, psychological responsiveness to task difficulty and motivational levels at task onset have not been routinely measured. Active mental engagement and a positive emotional state are the prerequisites for optimal learning in rehabilitation programs of stroke patients. In order for patients to realize the full potential of rehabilitation, it is important to establish and maintain an ideal motor learning situation combining appropriate cognitive, emotional, and physical aspects of the training (Adamovich et al., 2009; Meyer, 2014).

This chapter describes an approach to automatically estimate and classify a patient's psychological state, i.e. his/her mental engagement, in real time, during gait training. In this work, participants engaged in a virtual task with varying difficulty levels that was shown to induce a feeling of being bored, excited and over-stressed.

1.3 Measurement of Psychological State

To obtain an objective measure of the current psychological state, psychophysiological measurements of heart rate (HR), breathing frequency, skin conductance and skin temperature may be used. Skin conductance responses and skin temperature can be used as markers for psychological states in the presence of physical effort induced by walking. In stroke patients, there are often impaired responses in the involuntary nervous systems (also known as the autonomic nervous system), which are responsible for regulation of breathing, heart rate, swallowing and other bodily functions. The sympathetic branch of the system is responsible for arousal or the "fight-or flight" response, while the parasympathetic or vagal is responsible for resting and feeding. Generally, sympathetic activity increases heart rate and decreases variability, whereas parasympathetic activity decreases heart rate and increases variability (Berntson et al., 1997). These can be assessed using heart rate variability (HRV) and interpreted to provide information on the relative emotional state of the patient (Gunther et al., 2010). Acute stroke leads to increased HR but lower variability, with some improvement over time post-stroke (Lakusic et al., 2003). Although the magnitude of HRV is influenced by differences in underlying illness, injury, or a result of therapies including

medications, HRV reflects adaptation of the organism to physical, cognitive, and emotional conditions (Thayer et al., 2009). HRV has been shown to correlate well with EEG measures of cognitive involvement as well as to motivation levels determined using a psychological test battery (Andreassi, 2007).

In practice there is always some variability in the HR, due to imbalances in the activity levels of the sympathetic and parasympathetic nervous systems. Hence, any HR cannot increase or decrease indefinitely but instead will be followed by an opposite trend. The speed at which the HR increases or decreases is variable, which implies that the periods of increasing or decreasing inter-beat intervals are also not equal. As a result, heart rate asymmetry (HRA) should be a common phenomenon present in the healthy heart (Porta et al., 2008; Jelinek, 2014). The asymmetry in consecutive beat-to-beat intervals can be represented by three different asymmetry indices, namely Guzik's, Porta's and Ehlers' index (Porta et al., 2008), and indicates sympatho-vagal balance (Jelinek et al., 2011).

In this work HRA was calculated from the Percentage Index (PI, defined in Section 2.2, equation 1) of the normalized probability of the accelerations and decelerations within the time series. Heart periods (inverse of HR) are either shorter or longer on a beat-by-beat basis following acceleration associated with sympathetic activation and inhibition due to vagal activation.

Signals from the Autonomic Nervous System (ANS) that could indicate mental engagement are primarily signals that respond to mental stress or relaxation (Andreassi 2007). However, in addition to psychological processes, physical effort, such as walking on a treadmill, can influence the psychophysiological measurements. Physiological effort and psychological stress have an influence on the short-term variation of HR. HRV was shown to decrease during physical effort (de la Cruz, 2008) and mental stress (Delaney & Brodie, 2009). Galvanic skin response is used as a direct measure for arousal (Hirshfield, 2014). From the galvanic skin response, skin conductance response (SCR) and skin conductance level (SCL) are computed. The SCR, measured as a number, is a sensitive indicator for emotional strain (Brown, 2014). In recent research, SCL was found to increase during demanding tasks compared to a rest period (Dawson et al., 2007). The breathing frequency was found to increase during stress (Suess et al., 2007) and mental effort (Carroll et al., 1986) and also during physical activity (Doberenz, 2011; Mackersie, 2011). Skin temperature decreased during mental work stress in a study by Ohsuga (2001) but increased with physical activity (Mancuso & Knight, 1992).

The challenge is how to combine these various indicators in order to provide one variable that describes mental engagement. To solve this problem, one can turn to the methods offered by machine learning.

1.4 Machine Learning

Machine learning has the potential to assist with the identification of mental engagement in a training scenario. Machine learning treats a variety of problems including supervised learning, or classification, which is the concern of this work. Here the key is to determine some relationship between a set of input vectors that represent measurements, and a corresponding set of values on a nominal scale that represent category or class. The relationship is obtained by applying an algorithm to training samples that are 2-tuples $\langle \mathbf{u}, z \rangle$, consisting of an input vector $\mathbf{u}$ and a class label z . The learned relationship can then be applied to instances of $\mathbf{u}$ not included in the training set, in order to discover the corresponding class label z (Dietterich, 1995). A variety of techniques, including Artificial Neural Networks (Duda, 2012), have been shown to be very effective for solving such problems. A related problem is to determine the optimum set of measures, by selecting from those available, in order to maximize the performance of the classifier.

A neural network is a mathematical abstraction of some function of neural tissue, but greatly simplified and used to form a complex model relating dependent and independent variables. It can be regarded as a kind of piecewise linear regression model (Nguyen & Widrow, 1988). The problem described in this chapter that requires the use of machine learning is how to determine the current state of mental engagement, without having to continuously administer a questionnaire. This is difficult within a training environment because of the movement required by the participant, as well as the concentration required for the task. The inputs that are available are measurements of HR, breathing frequency, skin conductance and skin temperature. Is it possible from these to determine a classification of engagement as baseline, under-challenged, challenged or over-challenged? In the work described here a neural network was used to investigate the possibility of identifying the current state of mental engagement directly from physiology. This is necessary in order that the video game can be adjusted to vary the difficulty of the task without stressing the patient.

1.5 Implementation

Experiments used a definition of three different levels of mental engagement according to the circumplex model of affect (Koenig, 2011; Russell, 1980) (Figure 2), in which emotions are defined by two dimensions: valence (ranging from unpleasant to pleasant) and arousal (ranging from deactivation to activation). The virtual environments were used during robot assisted gait training to induce different levels of mental engagement in participants.

In the present state of the art, mental engagement of participants is quantified via questionnaires – motivation for example can be quantified via the “Intrinsic Motivation Inventory” (McAuley et al., 1989). During gait rehabilitation, questionnaires are not appropriate for continuous, objective assessment of the psychological state of the patient. In addition, neurological patients with severe cognitive deficits or aphasia (language disorder) might not be able to understand and respond appropriately to the questions.

Figure 2. Levels of mental engagement according to the circumplex model of affect.

Here the goal is to determine if a patient is mentally engaged during the training in order to maximize motor learning during rehabilitation. From motor learning theory it is known that the learning rate is maximal at a task difficulty level that positively challenges and excites participants while not being too stressful or boring (Guadagnoli & Lee, 2004). A task which is too easy for the participant will be perceived as boring, a task which is too difficult will overstress the participant, while an optimally challenging task should induce maximal mental engagement and optimal physical participation.

The new approach described here focused on measuring the activity of the ANS, as real-time measurement and analysis of signals from the Central

Nervous System (CNS) during walking in a robotic device are in general not feasible due to noise and motion artefacts.

2. EXPERIMENTAL PROTOCOL

The studies described in this chapter were conducted at two locations. Measurements with healthy participants were conducted at the Spinal Cord Injury Center Balgrist, Zurich, Switzerland. Measurements with participants who experienced stroke were conducted at the Neurologische Klinik Bad Aibling, Germany. The latter group suffered from neurological gait impairment due to their illness. All participants were selected and approved for participation in the study by a clinical expert to ensure that the participants were able to follow the instructions and respond accordingly. Approval for both studies was obtained from local ethics committees, and all participants or their legal representative gave written informed consent before data collection.

All participants were made secure in the machine and given 30% body weight support. The feet of the participants were passively lifted by elastic foot straps to prevent foot drop. The speed of the system was kept at a constant 2km/h and cadence adjusted to suit each participant. The virtual environment was projected on to screens and auditory signals projected to an appropriate speaker system. Participants were challenged to differing degrees during navigation through the virtual environment.

2.1 Task

Participants were given serious game objectives that required a simultaneous mechanical and cognitive response. The mechanical task was to pick up items by walking to them, which involved a change of walking direction in the virtual environment. To change the walking direction, participants had to perform an active push-off. To turn left, the participants had to increase activity in the right leg during stance (Zimmerli et al., 2009). As the required physical effort to change walking direction was set individually, the challenge was to navigate through the virtual environment and collect items. In order to provide for different task difficulty levels, the distance between virtual items involved in the task was adjustable. Furthermore, the distance between the barrels as well as their speed were adjustable. The cognitive task was to jump over barrels which rolled towards subjects as they walked. As it was not possible for stroke patients to physically jump, barrels were negotiated by

clicking a computer mouse button. Points were scored for each collected item and subtracted if items were not collected or not jumped over.

Participants were given an initial training session, then completed five levels of the game: standing with harness; walking with harness; and three levels of difficulty/challenge whilst walking. The difficulty was related to the distance between barrels and the speed at which they were moving (Koenig et al., 2011). In the first difficulty level participants were under-challenged, as all objects were easily collected without major changes in the walking direction. In the second difficulty level, participants were challenged by varying the distance settings between items and their distribution, so that only 80-90% of objects could be collected. In the third difficulty level, participants were over-challenged as objects were distributed to reduce score to less than 10% of the maximum possible score. These three challenge levels correlated with three levels of mental engagement and cortical response: under-challenge is equivalent to boring, correctly challenged is equivalent to excitement and over-challenged is synonymous with the feeling of being over-stressed.

Task difficulty was specific to each participant and determined during the initial training session using the Self-Assessment Manikin questionnaire (SAM) (Bradley and Lang, 1994). The SAM is used to measure emotional response to different stimuli (Bradley and Lang, 1994), in particular the emotional response arousal and valence. This allows an individualized program that increases in task difficulty to be developed and the extent of engagement/emotion/stress experienced by the participant to be determined using HRV analysis (Koenig, 2011; Morris, 1995). In this work, SAM was used to verify the hypothesis that the three conditions in the virtual task really resulted in a feeling of boredom, excitement and of being over-stressed.

Participants were asked to respond to a 5-point scale by selecting a number which best represented their current emotion. The value of 1 represented the lowest valence (“unhappy”) and arousal (“sleepy”) and 5 represented the highest valence (“very happy”) and arousal (“excited”) (Morris, 1995). The SAM was administered after each task. This nonverbal, pictorial questionnaire was chosen so as not to disturb the breathing frequency analysis by speaking, and also to reduce the complexity of responding for aphasic stroke patients or patients with cognitive impairments. Results of the SAM were compared to the predictions made by the neural network, in order to assess the accuracy of the latter. Statistical methods are described at the end of Section 2.2

Each subsequent level lasted five minutes. The last minute of each level was regarded as a steady state for purposes of data analysis, and the difference

between the last minute of one level and the first minute of the following level was regarded as a transition period.

The sequence of one training session was:

- Practice time: participants became acquainted with the effects of their movements upon the system (controlling the system). The walking speed for the baseline and the balance of the measurement interval was maintained at 2 km/h. The task difficulty levels were set individually for each participant as described above.
- Five minute walking baseline: physiological signals were recorded in the Lokomat with body weight support of 30 % and without the virtual environment tasks.
- Three task conditions in the virtual environment: the three task conditions were arranged in increasing levels of difficulty, each with duration of five minutes. Five minutes was determined as a tradeoff between the time required to reach a steady state in the physiological signals and also to keep the exercise portion of the experiment time below 45 minutes for the participants who are patients, since it has been informally reported by physiotherapists to be the maximum time for patients to exercise in the Lokomat. After the walking baseline and after each scenario, the participants were requested to respond to the SAM. During the questionnaire response time, the virtual environment was turned off.

The entire experiment can therefore be summarized according to these steps:

1. Practice
2. Baseline Walking
SAM
3. Under-challenging task
SAM
4. Challenging task
SAM
5. Over-challenging task
SAM

2.2 Measurement

Objective measures (ECG, breathing, skin conductance and skin temperature) were used to assess different levels of mental engagement. Using a thermistor flow sensor placed underneath the nose, breathing of participants was

measured and breathing frequency was computed using a peak detection algorithm. Changes in SCR and skin temperature were also measured.

HR was computed from ECG using a real time R-wave detection algorithm (adapted from (Christov, 2004), R wave peaks were determined using the algorithm first suggested by Tomkins (Hamilton & Tompkins 1986). HRV was computed as a discrete time series of consecutive RR intervals.

Inter-beat variation and complexity was determined from the ECG using time domain measures such as the Root Mean Square of Successive Differences in the RR interval (RMSSD) and the Tone-Entropy (Karmakar, 2013). Frequency domain measures included the number of RR intervals in the high frequency band (HF_n) (Malik & Camm, 1995), and parameters of the Poincaré plot. The Poincaré plot of the HRV signal is constructed by plotting consecutive points of RR interval time series against the previous RR interval. Figure 3 illustrates this. The technique to quantify the Poincaré plot is to fit an ellipse to the shape of the plot and measure the dispersion along the major and minor axis of the ellipse. SD1 (minor axis) provides a numeric expression of the parasympathetic, that is short-term correlation between inter-beat intervals, whereas SD2 describes the sympatho-vagal balance (Brennan et al., 2002).

Fig. 3. Poincaré plot for a sequence of RR intervals allows the estimation of SD1 and SD2.

The Complex Correlation Measure (CCM) measures the variability in the temporal structure of the Poincaré plot, which can characterize or distinguish plots with similar shapes (Karmakar et al., 2011). The CCM measures the point-to-point variation of the signal rather than the gross description of the Poincaré plot. It is computed in a windowed manner, which embeds the temporal information of the signal. A moving window of three consecutive points from the Poincaré plot are considered and the temporal variation of the points are measured. CCM is more sensitive than SD1 and SD2 to changes of parasympathetic activity (Karmakar et al., 2011).

HRA is determined from the RR intervals as the probability index of accelerations and deceleration of the HR and derived from the calculation of tone and entropy (Khandoker et al., 2010). Heart period data or RR intervals are first transformed into the percentage index (PI) time series by:

$$PI(n) = [H(n) - H(n - 1)] \times 100 / H(n) \quad (1)$$

where $H(n)$ is a heart period time series, and n a serial number of heart beats. The tone is defined as a first order moment (arithmetic average) of this PI time series as:

$$\frac{1}{N} \sum_n PI(n) \quad (2)$$

where N is a total number of PI terms. The tone represents the balance between accelerations ($PI > 0$) and inhibitions ($PI < 0$) of the heart rhythm and represents the sympatho-vagal balance (Amano et al., 2005). The entropy is defined from the PI probability distribution by using Shannon's formula:

$$- \sum p(i) \log_2 p(i) \quad (3)$$

where $p(i)$ is a probability that $PI(n)$ has a value in the range, $i < PI(n) < i+1$, where i is an integer. The entropy evaluates total acceleration–inhibition activities, or total heart period variations (Rosenblueth, 1984). Acceleration of the HR is, therefore, expressed as a plus difference, inhibition as a minus difference.

From the PI series the positive and negative difference periods were separated. The calculation $PI(n) = 0$ was omitted because it is neither acceleration nor inhibition. Then the entropy of the positive and negative differences of the PI

time series was calculated. The HR asymmetry is given by the following formula:

$$\text{HRA} = \frac{\text{Entropy of positive difference part of PI time series}}{\text{Total entropy of PI time series}} \quad (4)$$

HRA has a value of 0.5 when there is symmetry between the positive and negative parts of the PI time series.

The neural network was used to investigate the possibility of identifying the current state of mental engagement directly from physiology. For automatic classification of mental engagement from physiological recordings, the effectiveness of a neural network was evaluated. As a classifier, a data fitting neural network was trained using the Neural Network Fitting Tool in Matlab (Mathworks, www.mathworks.com), containing 30 hidden layer neurons. The neural network provided an estimation of the current state of mental engagement, based on the physiological recordings. Twenty percent of the data was taken as training data, 20% as validation and 60% as testing data. This ensures that the neural network was always tested on unseen data, in order to avoid over-fitting bias in the model, which could lead to overly optimistic results. As neural networks require labeled data during the training phase, the training data was labeled as 1=“baseline”, 2=“under-challenged”, 3=“challenged” or 4=“over-challenged”. Learning was performed with the Levenberg-Marquardt back-propagation algorithm (Moré 1997).

2.3 Feature Selection

The attachment of sensors for physiological recordings on the participant's body is time consuming for a clinical application, demanding resources of the therapist and also reducing the time a participant can exercise in the Lokomat. To improve clinical applicability of this approach, it is important to determine whether all recorded physiological signals are necessary to perform classification of mental engagement or if the recorded data contained information from dependent variables. It could, for example, be possible that HR and breathing frequency would show a strong correlation. In this case, one of these signals could then be omitted in future recordings without degrading classification performance. Principal component analysis (PCA) allows identification of those signals that explain most of the variance in the data (Pearson, 1901). PCA is a mathematical technique that takes a set of measures, some of which could be correlated, and converts them to another, usually smaller, set of measures that are guaranteed to not be correlated. In the process

of doing this, the original measures have scores attached to them that describe how much variance they contribute to the overall dataset. In the context of feature detection, such measures can be used to select those features that represent less variance so can be omitted with little consequence.

PCA was applied to each participant individually using five minutes of data for each of the four training conditions. Inputs to the PCA were HR, a discrete time series of HRV, a discrete time series of the number of SCR events, SCL, skin temperature and a discrete time series of breathing frequency. PCA provides combinations of the inputs, where the first axis (or first principal component) explains most of the variance. The second PC explains the second most important variance, etc.

The number of factors k that were necessary to explain more than 80% of the variance in all participants was computed ($k \in [1, n]$, where n is the dimensionality of original data, i.e. 6). A factor rotation on these first k PCs was performed to obtain a clearer picture of which input signals provided the largest variance. Factor rotation is a mathematical transformation that does not alter the subspace spanned by the PCs, but shifts the weight of an input e.g. from the first PC to the second, while maintaining the orthogonality between the components.

Descriptive statistics were used to investigate which physiological signals changed significantly between the different task level conditions. Only the last minute of each 5 minute condition was analyzed to ensure that steady state had been reached. All conditions were tested using the Friedman test followed by a Wilcoxon test for paired comparison. Bonferroni correction corrected multiple errors caused by the paired comparison. The significance level was set at $p < 0.05$. The performance of the classifier was assessed by means of the mean squared classification error for two sets of input data. The first set was the 6 raw physiological data streams, while the second was a reduced dataset that contained only the physiological recordings that were dominant in the first k PCs ($k < n$).

3. RESULTS

Results for HRA indicated that at rest, stroke patients are anxious. This is indicated by a higher value for HRA, which indicates that the entropy of positive changes in HR has higher entropy than that of the negative changes. The HRA inverts in patients when the tasks increase in complexity, leading to

a value less than 0.5, indicating that the entropy of the negative changes in HR dominates during the challenged condition. This high probability of deceleration (0.45 ± 0.07) returns towards a more balanced response during the over-challenged condition (0.47 ± 0.04). The control group showed a steady increase in acceleration, peaking at the challenged condition (0.62 ± 0.17), then returning towards baseline during the over-challenged condition as well.

These differences are shown graphically in figure 4. It can be seen that the differences between stroke patients and healthy participants are not statistically significant. However the data suggest the difference in control of heart rhythm between the two groups with respect to task condition. In figure 4, the 0.5 line indicator is the reference value of HRA. Values greater than 0.5 indicate an accelerating influence, whereas values below 0.5 indicate slowing of the HR.

Figure 4. Heart rate variability recorded at different stages of the experiment.

Healthy participants revealed statistically significant differences in several physiological signals (Table 1). HR increased significantly from baseline for all conditions with the virtual task and for the conditions challenged and over-challenged compared to the condition under-challenged. The same significant

changes were found for breathing frequency. Similar results were also found for the SCR. For all virtual task conditions, the SCR increased significantly compared to baseline. In addition, the SCR increased significantly for the over-challenged condition compared with the under-challenged condition.

RMSSD decreased significantly from baseline for the conditions challenged and over-challenged. Furthermore, a significant decrease was found for the over-challenged condition compared with the under-challenged condition. In the frequency domain, no significant changes were found. A significant decrease was also found in skin temperature. The skin temperature during conditions under-challenged and challenged were significantly decreased when compared with the baseline and the over-challenged conditions.

Table 1. Statistical results of physiological recordings in healthy participants. The table shows Median and 95% confidence interval (CI) of heart rate (HR), breathing frequency (BF), skin conductance response (SCR), square root of the mean squared differences of successive normal-to-normal intervals (RMSSD), and skin temperature. (Data previously presented in Koenig et al. 2011)

	HR [bpm]		BF [cpm]		SCR [SCR/min]	
Baseline	73.3 ^{b,c,d}	CI: 60.3-81.8	21.6 ^{b,c,d}	CI: 20.3-24.5	0.2 ^{b,c,d}	CI: 0.0-0.6
Under-challenged	81.3 ^{a,c,d}	CI: 68.0-91.2	23.0 ^{a,c,d}	CI: 22.2-26.1	1.0 ^{a,d}	CI: 0.2-3.7
Challenged	94.1 ^{a,b}	CI: 77.8-103.0	27.5 ^{a,b}	CI: 24.9-30.3	3.1 ^a	CI: 0.6-5.3
Over-challenged	96.4 ^{a,b}	CI: 76.3-102.9	27.8 ^{a,b}	CI: 25.0-29.4	3.3 ^{a,b}	CI: 0.4-6.2
	RMSSD [ms]		Skin temperature [°C]			
Baseline	30.0 ^{c,d}	CI: 19.4-49.9	32.5 ^{b,c}	CI: 31.7-32.9		
Under-challenged	27.5 ^d	CI: 6.8-37.3	30.8 ^{a,d}	CI: 29.1-32.1		
Challenged	25.5 ^a	CI: 5.0-60.2	31.5 ^{a,d}	CI: 30.5-32.5		
Over-challenged	15.3 ^{a,b}	CI: 4.7-63.0	32.0 ^{b,c}	CI: 31.3-32.7		

^a = Significant different from the baseline ($p < 0.05$); ^b = Significant different from the under-challenged condition ($p < 0.05$); ^c = Significant different from the challenged condition ($p < 0.05$); ^d = Significant different from the over-challenged condition ($p < 0.05$)

The results for stroke patients were very different. Compared with the very robust and variable physiological signals in healthy participants, only three significant changes were found in patients. HR increased significantly for the challenged condition (+7.6%) and for the over-challenged condition (+6.2%) compared with baseline (median 89.7 bpm, CI: 77.5-103.2). Breathing frequency decreased significantly for the over-challenged condition (-5%) compared to the challenged condition (median 27.7 cpm, CI: 24.8-29.8). This highlights the need for Principal Components Analysis (PCA) to discover variables that can discriminate these mental states.

PCA was able to directly separate the four conditions baseline, under-challenged, challenged and over-challenged, in spite of the fact that the statistical analysis of the physiological data was unclear.

Evaluation of the results of the PCA revealed the importance of skin temperature and SCL in both groups. HRV played a lesser role. Breathing frequency was not dominant in healthy participants, but it was for patients.

Although only two significant differences were found in all physiological recordings over all conditions of patient data, the classification of the different psychological states using a neural network was possible for healthy participants and also for those who had suffered from stroke. The classification results were evaluated for a neural network for two different sets of input data: on the one side with six physiological parameters extracted, on the other side using only the physiological signals dominant in the first three PCs. Mean classification error was 1.4% for the full and 2.5% for the reduced dataset in healthy participants and 2.1% for the full and 4.7% for the reduced dataset for patients (Figure 5).

Figure 5. Classification error by means of the root mean square error (RMSE) for all 17 healthy subjects (left) and all 10 patients (right), using all six physiological

signals (full dataset) and using only the three signals that were dominant in the first three PCs (reduced dataset).

3.1 Changes During the Training Session

Turning to an examination of how some of these measures change during the training session, we examine the 4 transitions in healthy participants:

- Transition 1 – standing to walking;
- Transition 2 – walking to under-challenged;
- Transition 3 – under-challenged to challenged;
- Transition 4 – challenged to over-challenged.

Table 2 shows the result of investigating the level of adaptation, which is an important component in task performance. The HRV parameters shown are:

- SDNN – standard deviation of RR intervals;
- RMSSD – square root of the mean squared differences of successive RR intervals;
- HFn – normalized high frequency power,
- SD1 - Poincare short time correlation parameter;
- CCM – complex correlation measure of Poincare plot.

Only the nonlinear measures, SD1 and CCM differentiated between the level of adaptation. Specifically only transition 1 and transition 3 were significant, which is found from calculating the gradient of changes for those parameters.

Table 2. Adaptation to transitions, as manifested in changes of different HRV parameters. All values are mean $\pm$ standard error. Transitions between standing to walking and between under-challenged to challenged show significant difference at $p < 0.05$, and so are indicated by an asterisk.

stages	SDNN	RMSSD	HFn	SD1	CCM
Transition 1	0.40 $\pm$ 0.07	0.57 $\pm$ 0.12	0.5 $\pm$ 0.05	0.24 $\pm$ 0.08*	0.71 $\pm$ 0.12*
Transition 2	0.44 $\pm$ 0.07	0.51 $\pm$ 0.13	0.57 $\pm$ 0.08	0.27 $\pm$ 0.08	0.70 $\pm$ 0.09
Transition 3	0.59 $\pm$ 0.07	0.56 $\pm$ 0.08	0.67 $\pm$ 0.1	0.39 $\pm$ 0.10*	0.81 $\pm$ 0.07*
Transition 4	0.46 $\pm$ 0.06	0.61 $\pm$ 0.09	0.49 $\pm$ 0.09	0.37 $\pm$ 0.09	0.74 $\pm$ 0.13

4. DISCUSSION

Experiments using a serious game to enhance robot assisted treadmill training in healthy participants and stroke patients, yielded data and objective measurements that were fully sufficient to detect the current psychological state of a participant. This is an important result, since one would question whether it is possible to detect psychological state from such simple physiological measures as those used. This work suggests that this is indeed the case. The difficulty of a virtual task during the rehabilitation training was set as under-challenging, challenging and over-challenging to induce a feeling of boredom, challenge, or stress. During training the ECG, breathing frequency, skin temperature and the galvanic skin response were recorded. The psychological state of a participant could be classified using a combination of PCA with a neural network. Variables chosen were HR, SCL and skin temperature, which can be used as markers for psychological states in the presence of physical effort.

Evaluation of questionnaires from healthy participants confirmed that virtual tasks of different difficulty levels can indeed induce, or result in, different levels of mental engagement, i.e. of being bored, challenged or over-stressed. Also in healthy participants, descriptive statistics suffice to distinguish between different levels of mental engagement. The automatic classification worked in all but two participants with less than 2% classification error. This is a promising result that provides confidence in the ability to deduce mental engagement from simple measures.

In patients, neither questionnaires nor physiological signals showed a picture as clearly as in healthy participants. While therapists anecdotally reported that the virtual task bored, challenged or over-stressed the participant, the questionnaires did not confirm this observation. A possible explanation of the results showing lower clarity from questionnaires is that patients with cerebral lesions might suffer from cognitive deficits, which might prevent them from assessing, expressing, and verbalizing their level of mental engagement during rehabilitation. This was consistent with reports by the therapists. In addition, it was reported that patients did not usually admit if they experienced the task as too difficult, because they were very ambitious and determined to solve the task successfully. Although the questionnaire showed only few changes, the predefined scores (success rate of 100% for the under-challenged condition, of 80-90% for the challenged condition and of 10-20% for the over-challenged condition) were achieved by every patient. Another explanation might be the fact that walking with the help of the DGO was an experience that is positively perceived by patients who may be otherwise unable to walk well on their own.

The significance of this finding is that the difficulty in identifying mental engagement by questionnaire might be overcome if the appropriate numerical measures are used.

Despite the heterogeneous and unclear nature of the picture in the descriptive statistical analysis of the physiological data of patients, the classification of the various conditions in the virtual environment was possible with less than 8% classification error in all patients. In this context, a real time automatic classification algorithm applied to physiological recordings seems to allow an objective estimation of mental engagement for the benefit of the patient in clinical applications, and in particular, when compared with the sometimes conflicting and often unreliable subjective information obtained from other sources. This provides a pathway to move beyond subjective measures and to allow reliable assessment of mental engagement through numerical means.

PCA was used to identify the minimum set of physiological signals that would be necessary to perform classification of mental engagement while not degrading the performance of the classifier. In both, healthy participants and participants who suffered from neurological injuries, skin temperature and SCL were the main psycho-physiological responders to this intervention. Also, HRV did not contribute significantly to the first three PCs. As discussed above, HRV might have been reduced due to the physical effort involved in walking. It might be possible that more advanced analysis based on HRV will provide measures that will have more success in the automatic classification of mental engagement.

Previously, virtual environments in rehabilitation did not provide patient-specific and adaptive features, with the ability to adjust levels of difficulty that correlated with mental engagement. The long-term goal of this work is to perform closed loop control of psychological states during robot-assisted rehabilitation – to objectively determine the psychological state of the patient, and then by automatically or by enabling the therapist to adjust the attributes of the system, to stimulate a desired level of mental engagement during rehabilitation. The goal of approaching optimal mental engagement during exercise in rehabilitation is consistent with evidence that attention to task and mental engagement improve outcomes of rehabilitation efforts for patients in the training of motor skills. Previously, researchers have used closed loop control of psycho-physiological measurements to control stress.

This approach is not limited to a particular gait orthosis, and not even to rehabilitation of the lower limbs. In robot assisted arm rehabilitation, as

performed with the ARMin (Nef et al., 2007; 2009), the HapticMaster (Houtsma et al., 2006) or the MIT Manus (Aisen et al., 1997), the absence of physical effort induced by walking might even improve the results obtained from healthy as well as neurologically impaired participants.

5. CONCLUSION

A stroke can be a devastating event in a person's life, leading to severe loss of mobility, cognitive impairment, inability to participate in various activities of daily living, and associated loss of independence. The goal of rehabilitation is often to reduce motor related impairments beyond spontaneous recovery, to increase participation in activities of daily living and improve quality of life. Effective rehabilitation relies upon an appropriate level of physical and emotional engagement during task practice involving learning a motor skill.. The use of serious games in this context can be shown to assist in stroke rehabilitation, by providing an environment which can be tailored to meet the needs of each patient. The challenge in the past, to provide a system that is responsive to the changing needs of each patient, has been how to easily and in real time objectively assess physical ability and psychological state of the patient, to dynamically adapt the task in order to suit the current state of the patient, and to do this in a way that does not complicate the scene.. The use of real time physiological measurement has been demonstrated to provide feedback indicating the psychological state in real time, during the training and while the patient is engaged by the serious game. This means that cumbersome questionnaires can be omitted, and replaced with feedback from an effective objective measure taken from patients in real time that does not interrupt the training activity or burden the therapist. Consequently the virtual environment can be adapted in real time to meet the needs of the patient, in order to provide training that is challenging yet does not over-stress the patient. In this way the serious game would enable optimal personalized rehabilitation conditions.

Future work will focus on improving the classifier system so that the patient psychological state can be identified with even more accuracy. There is a large number of classifier algorithms available and these should be investigated to determine their relative performance. In order to validate the findings, the system will be tested on a larger number of patients. In addition, the use of multiple measurements to determine the psychological state may be unnecessary. The ability to eliminate the measures that are less useful should allow the environment to be simplified, leading to a more accessible training

environment that could be adopted more widely in stroke rehabilitation and extended to other areas of physical rehabilitation.

It is our aim that through these advances, a generic training framework using a serious game would become mainstream and enhance rehabilitation options available, meeting the needs of the largest possible number of patients with safe, effective, personalized therapies.

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