Quantitative assessment of learning process from EEG and ECG signals during training in laparoscopic surgery using a simulator

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QUANTITATIVE ASSESSMENT OF LEARNING PROCESS FROM EEG AND ECG SIGNALS DURING TRAINING IN LAPAROSCOPIC SURGERY USING A SIMULATOR

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ABSTRACT

Laparoscopic surgery has become the first option to perform procedures that involve abdominal cavity. This minimally invasive technique requires the surgeon to acquire special skills and abilities to work without tactile and depth perception. Therefore, surgeons training has been taken out of the operating room to laboratories with the use of instruments such as training boxes, videos and simulators. Of the above, virtual reality simulators have become an important part of training and have shown to improve the performance of residents in operating room. The assessment of resident training involves several aspects including skill acquisition, interaction with instrumental and cognitive assessment. Of all aspects to be evaluated, one of those that have not been approached in an effective way, because it does not include quantitative strategies, is the cognitive evaluation throughout learning process. Analysis of neurophysiological signals such as electroencephalography (EEG) and electrocardiography (ECG) allows to evaluate the cognitive state under which the subject is performing an activity. Its effectiveness has been demonstrated in a wide range of applications ranging from the evaluation of performance during a task execution, to training in flight simulators and air traffic controllers. This doctoral thesis it is proposed to obtain quantitative information about changes in the EEG and ECG signals associated with learning progress throughout the training period in general surgery residents.

LIST OF PAPERS

1**. Changes in brain activity of trainees during laparoscopic surgical virtual training assessed with electroencephalography**
J. X. Suárez, K. Gramann, J. F. Ochoa, J. P. Toro, A. M. Mejía, and A. M. Hernández
Brain Research, vol. 1783, p. 147836, May 2022, doi: 10.1016/j.brainres.2022.147836.

2. Neurophysiological changes associated with training in laparoscopic surgery using EEG: a pilot study
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3. **Changes in Electrocardiographic Signals During Training in Laparoscopic Surgery Simulator: A Preliminary Report**
J. Suárez, A. Ruiz, J. Toro, A. Mejía, A. Hernández
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4. **Electroencephalographic functional connectivity in laparoscopic surgery training**
J. Suárez, J. Ochoa, J. Toro, A. Mejía, A. Hernández
Pending for Publication

Other relevant publications and works:

1. **Validation of EEG Pre-processing Pipeline by Test-Retest Reliability**
J. Suárez, J. Ochoa, C. Tobón
Applied Computer Sciences in Engineering. WEA 2018. Communications in Computer and Information Science, Medellín, Colombia, October 17-19, 2018

2**. Resting-state EEG alpha/theta ratio related to neuropsychological test performance in Parkinson's Disease**
A. Jaramillo, J. Suarez, J. Ochoa, et al.
Clinical Neurophysiology, vol. 132, no. 3, 2021, doi: 10.1016/j.clinph.2021.01.001.

3. **Automatic Classification of Subjects of the PSEN1-E280A Family at Risk of Developing Alzheimer's Disease Using Machine Learning and Resting State Electroencephalography**
F. J. García Pretelt, J. X. Suárez Relevo, D. Aguillón, F. Lopera, J. F. Ochoa, and C. A. Tobón Quintero
Journal of Alzheimer's Disease, vol. Preprint, pp. 1–16, 2022, doi: 10.3233/JAD-210148.

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ABBREVIATION LIST

BOLD	Blood oxygenation level dependence
ECD	Equivalent Current Dipole
ECG	Electrocardiography
EEG	Electroencephalography
EOG	Electrooculography
fMRI	functional Magnetic Resonance Imaging
fNIRS	functional Near-Infrared Spectroscopy
gICA	group Independent Component Analysis
HR	Heart Rate
HRV	Heart Rate Variability
IC	Independent Component
ICA	Independent Component Analysis
LD	Linearly Distributed
M1	Primary motor cortex
MEG	Magnetoencephalography
PCA	Principal Component Analysis
PFC	Prefrontal cortex
SMA	Supplementary motor area
VR	Virtual Reality
wICA	wavelet ICA
wMNE	Weighted Minimum Norm Estimation

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1. INTRODUCTION

1.1 Problem statement

In 2016, an estimated of 251,000 annual deaths in the United States were associated with medical errors, making medical errors the third leading cause of death [1]. In Colombia, four out of ten patients are harmed in primary health care and outpatient services. Unsafe surgical procedures cause complications in up to 25% of patients, leading to 1 million deaths annually during or immediately after surgery [2]. This has led to a greater emphasis on patient safety and reduction of medical errors, conducting to greater awareness about training and surgeons' education.

Laparoscopic surgery has become the standard for patients who need abdominal surgery. This technique allows the abdomen through small incisions, where surgical instruments are introduced, and it is used an optical device connected to a video camera and a monitor to visualize the abdominal cavity [3]. Laparoscopy is part of the minimally invasive techniques, which imply a lower incidence of complications such as: risk of infection, pain and difficulties in patient recovery [4].

The advent of laparoscopic surgery has created challenges that did not exist in traditional open surgery. Depth perception is significantly affected by the transformation of a three-dimensional surgical space into a two-dimensional video image. Surgeons must learn to adapt to this new visual interface to determine spatial relationships between structures. The fulcrum effect, caused by fixed trocar sites for instrument access, represents another psychomotor challenge for trainees, as it requires the surgeon's hand to move in an opposite direction to that of the instrument. In addition, the use of long instruments that separate the surgeon's hand from the anatomical structures, reduce the tactile feedback [5]. The implication of these changes requires that apprentices receive an adequate training in which they acquire basic skills before reaching the operating room, to preserve patient safety and reduce medical errors [6], [7].

Training of basic skills such as psychomotor performance, depth perception, and spatial judgment has been shown to be independent of the operating room and can be performed inside laboratories with the aid of models and simulators [8]. Simulation in surgical education has evolved dramatically over the past two decades and has gained wide acceptance as a valuable educational tool. This method provides the opportunity for novices to learn in a controlled environment free from any adverse consequences to real patients [9].

Among the models and simulators used for laparoscopic surgery training are animal and cadaver models, training boxes, and virtual reality simulators [5]. Of the above, virtual reality simulators have become an increasingly important part of training programs, since they are a safe, ethical and a repeatable alternative. Among its main advantages are avoiding injury to the patient, reducing the costs associated with the use of corpses and animals, and offering the possibility of repeating surgical procedures as many times as necessary to learn them correctly, while they offer the revision of the procedures performed [10]. Its use produces objective measures of performance, allows feedback to students, and does not necessarily require regular supervision by the coach [11]. Several studies have shown the effectiveness of these type of devices, mainly to improve student skills with specific exercises [12], and to show how the skills acquired are transferred to the operating room environment [13]. Surgical skills training prior to the surgery has demonstrated more efficient learning in the operating room, allowing the trainee to focus attention on technical details of the procedure, without the need to learn all of these for the first time on a patient [7].

There is great interest in measuring surgical skills and performance during surgeon's training process. The acquisition of surgical competence is a complex and multifactorial process that can take years of experience and training [3]. Having an objective evaluation tool that qualifies the performance and progress of students allows to improve learning experience and failures of the training program [14], [15].

Traditional methods of resident evaluation depend on student supervision during repeated practice. Here, one or more experts rate the surgical procedure by direct observation or video. However, this type of evaluation is expensive, since it requires the expert to be at the training site and, although there is the possibility of evaluating a video later, it is important that the student have real-time feedback [16]. Faced with this, more objective evaluations have been developed in which times and errors in task performance are quantified [13]. This method is easy to implement on simulation devices and is useful for evaluating the overall performance. Its main drawback is that it is not very specific to evaluate complex tasks.

There are also scales that evaluate the resident skills in a surgery based on parameters such as depth perception, bimanual dexterity, efficiency, tissue management and autonomy. Scales like OSATS (Objective Structured Assessment of Technical Skills) and GOALS (Global Operative Assessment of Laparoscopic Skills) provide a global performance rating that may be able to differentiate training levels [17], [18]. Although these scales provide a more objective evaluation, they are also carried out by experts.

Another way of evaluation is the use of optical, electromagnetic or mechanical tracking and monitoring systems for the instruments, which allow to measure speed and execution of useless movements when performing an exercise [16]. The above in order to evaluate movement economy, indicating the skill degree, operational focus and general experience [8].

There are several behavioral aspects that are crucial for safe performance of minimally invasive surgery, and one of these is cognition. Although the use of performance measures (speed, economy of movement, errors) and ergonomic evaluations are relatively well established, the evaluation of participants cognitive commitment during training is not so frequent and has been mainly based on questionnaires [19]. The main drawback of these questionnaires is that they cannot be applied during the execution of the task, but are evaluated at the end of it, which compromises the accuracy and reliability of the measurement itself. Furthermore, these methods suffer from subjective biases, from the evaluator's dependent judgment.

Cognition has been assessed by measuring knowledge or decision making. However, these aspects are the product of a process of perception, attention, information processing, storage and retrieval of this information at the appropriate time to make a decision [9]. During training, the allocation of cognitive resources changes. In the early stages of learning, considerable cognitive activity is required, since the subject is trying to find out how to carry out the task. Once the basic skills are acquired, the associative stage begins, and the subject can direct her attention towards the performance rather than the strategy [20]. Throughout learning, neural processes for the execution of activities have been shown to move from cortical areas to basal ganglia structures, subcortical area for automated process [21].

An interesting question is to know if it is possible to follow such changes in brain activity during training, using neuroimaging techniques. This would provide additional and objective evidence related to the skills acquisition. Neuroimaging methodologies could track the reassignment of cognitive resources during practice, providing an independent metric about the quality of the task performed [22].

Brain electrical activity measured by electroencephalography (EEG) is one of the most useful tools, since it provides the time resolution required to track brain activity during task execution. Furthermore, the cost associated with acquisition and analysis is less than other neuroimaging techniques, such as Magnetoencephalography (MEG) or functional magnetic resonance imaging (fMRI) [23]. However, a drawback for EEG is the poor spatial resolution, since electrodes measure electrical activity at the scalp, it is difficult to know whether the signal was produced near the cortex or from a deeper region. Various analysis techniques have been proposed to improve its resolution, but it remains a challenge for EEG research.

EEG effectiveness has been proven in a wide range of applications ranging from performance evaluation of a task [24]–[26], to training in flight simulators and air traffic controllers [22], [27], [28]. Along with EEG recordings, other physiological signals such as electrocardiography (ECG) which measures the activity of the autonomous nervous system, and electrooculography (EOG), an indirect measurement of central nervous activity are also analyzed. Studies suggest that an increase in heart rate could be related to an increase in mental workload and stress, while blink rate would be inversely correlated [22], [29].

EEG-specific frequency bands have been associated to learning process, such as theta and alpha bands. Theta has been linked to memory consolidation processes [30]. In particular, the increase in cognitive effort during a task performance has been related to an increase in theta power [31]. Likewise, variations in this band have been found mainly in frontal regions during training in flight simulation tasks [22], [32]. These changes show increases during the first training sessions, followed by a power decrease when an optimal performance level is reached.

The alpha band has been related to the level of attention. Alpha suppression is associated with increased focused attention (particularly on visual stimuli) [33]. This suppression suggests an inhibition of cortical structures irrelevant to the task [34]. In the evaluation of training in flight simulation tasks, Borghini et al. reported a decrease in alpha rhythm at the beginning of practice, related to greater mental effort, followed by an increase in the last sessions when the subject performed better [22].

In addition to spectral analysis, another important analysis to consider and that has not been evaluated in previous studies is functional brain connectivity analysis. Functional connectivity defines the temporal dependence of neuronal activity between anatomically separate brain regions [35], [36]. Connectivity measures evaluate the interactions between brain regions from measures such as correlation, covariance, spectral coherence, or phase block [37]. Through this approach the brain can be understood as a highly complex structural and functional network [38], [39] and using graph theory, these networks can be described and quantified, reducing them to a set of nodes and connections.

Langer et al. [40] analyzed functional brain networks organization in fronto-parietal regions and how their topology is modified by training in working memory tasks. This work showed that task performance correlates with power in theta band. Additionally, they found that better task performance is associated with greater small-world topology. Another work published by Kong et al. [41] evaluated changes in phase synchronization measures when drivers going from an alert state to mental fatigue during their training in a simulator. Their main finding was that synchronization in delta and alpha bands of frontal and parietal regions increases significantly as the driver's mental state changes from alertness to fatigue.

Taking into consideration the findings discussed in this section, training processes of surgery residents could obtain benefits from cognitive related quantitative measures, and additionally there are brain activity analysis techniques that have not yet been used to evaluate surgeons training but have been shown to be useful in other applications; this doctoral thesis proposed to obtain quantitative information on the degree of progress in the learning process throughout the training period in laparoscopic surgery based on neurophysiological signals. By means of spectral and connectivity analysis of EEG signals, and heart rate analysis of ECG signals, it is expected to find indices that quantify the learning process of different tasks to be performed in the simulator and that it can be correlated with residents' performance data.

1.2 Research objectives

The general objective of this thesis is to evaluate, from EEG and ECG signals, the learning process in surgery residents during laparoscopic surgery training using a simulator. The specific aims are:

1. Design and implement a protocol for the acquisition of EEG and ECG signals for quantitative evaluation of laparoscopic surgery residents training in a simulator.

2. Perform spectral and functional connectivity analysis on EEG signals.
3. Perform heart rate and heart rate variability analysis on ECG signals.
4. Corelate the neurophysiological measures with performance data provided by the simulator.

1.3 Methodology

Figure 1.1 shows a general scheme of the followed methodology. This consists of an initial phase in which the signal recording protocol was designed and tested with a first pilot study to observe changes in neurophysiological measures from the training sessions. In a next phase, EEG signal pre-processing pipelines were evaluated, including the use of a pipeline previously validated in repeatability studies, and another based on ICA for the extraction of neuronal activations. Spectral power measurements at the level of channels and neural sources were extracted using previous pre-processed signals. Based on the results found in the power spectrum analysis, a functional connectivity analysis was carried out on those brain areas related to motor training. Then was carried out the analysis of the ECG signals, values of HR and HRV were extracted from the signals recorded in the different tasks and training sessions.

Statistical analysis was performed cross-sectionally in all phases of the project, from the exploratory analysis in the pilot study to the analysis of changes in neurophysiological measures with training. Likewise, correlation tests were carried out to look for relationships between the neurophysiological measurements and tasks performance.

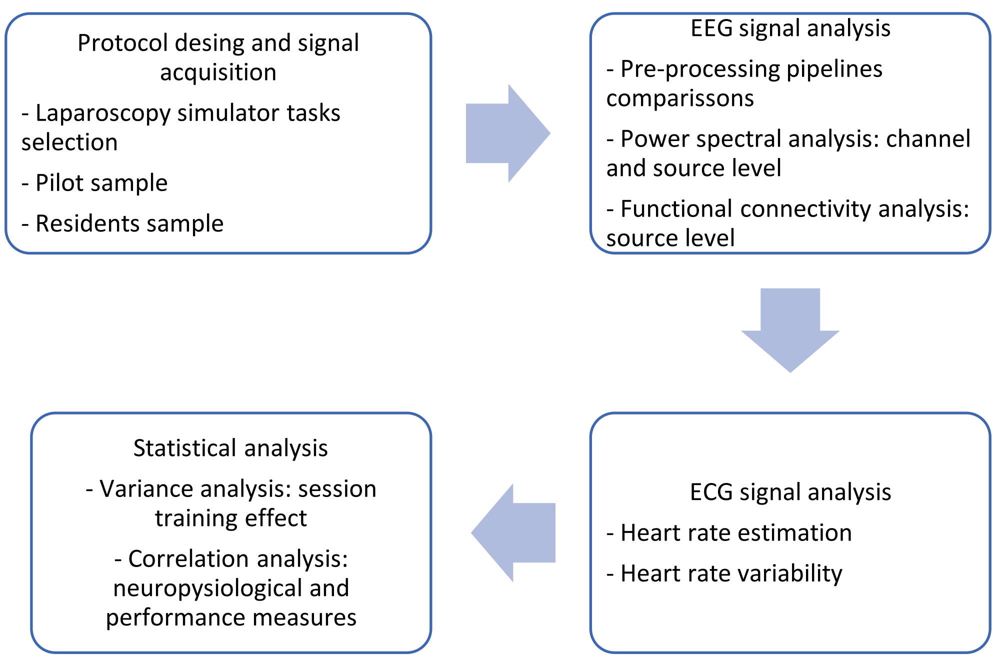

Figure 1-1. Implemented methodology.

1.3.1 Participants

For this project two groups of subjects were collected: an initial sample to evaluate the recording protocol that consisted of 8 students from bioengineering program (pilot test), and the sample of surgical residents from medicine faculty (residents database). Informed consent approved by the bioethics committee of Universidad de Antioquia (Act 18-19-787, March 9, 2018) was obtained from all participants.

Pilot test

Eight healthy volunteer subjects (age: 23 ± 3.6 years old, right-handed, 5 females) from Bioengineering program of Universidad de Antioquia.

Residents database

17 first year surgery residents from the Universidad de Antioquia (age: 28.3 ± 2.3 years, right-handed, 10 females).

1.3.2 Protocol design

The experimental protocol consisted in participants learn to execute a series of tasks in the VR simulator LapSim® (Surgical Science Ltd., Göteburg, Sweden), during 4 sessions training, one per week. In each session, subjects performed three repetitions of each task. Signals recording was performed during the first task execution for the pilot test. Given that during this pilot test it was observed that participants tried to remember the procedures carried out in the previous session, it was decided to take the record during the second execution for the residents group, since in this execution participants had more clarity on how to perform the task. Figure 1.2 shows schemas for the experimental protocol in both studies.

Prior to tasks execution recordings, a reference condition was recorded during 2 min while the participant was in a standing position in front of the simulator with closed eyes following by 2 min with opened eyes looking a blank screen.

Finally, at the end of each session, participants filled the National Aeronautics and Space Administration-Task Load Index (NASA–TLX) questionnaire [42], in order to assess the perception of workload across training sessions. The total NASA-TLX score ranges from 0 to 100 and it is calculated as an average of six factors: Mental Demand, Physical Demand, Temporal Demand, Performance, Effort and Frustration.

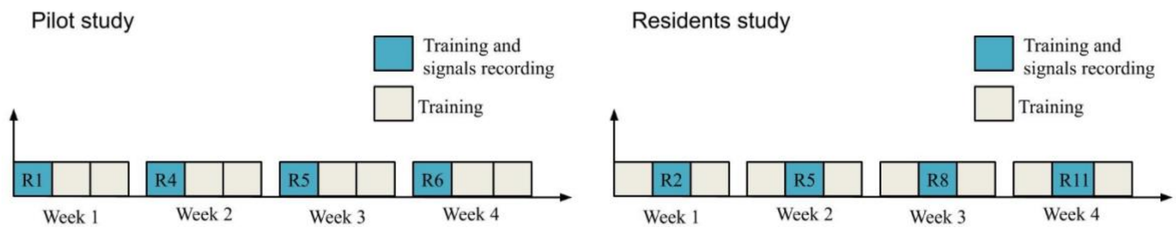

Figure.1-2. Experimental setup for pilot and residents' studies. The boxes with R correspond to the number of repetitions of the task.

1.3.3 Signals Acquisition

The neurophysiological signals were recorded using the digital monitoring system Natus® Quantum™ (Natus Neurology Incorporated, Wisconsin, USA) at a sampling frequency of 1024 Hz.

A cap with 60 AgCl electrode was used for EEG recording with mastoid bone reference and AFZ as ground. ECG electrodes were placed in Lead II (left leg as positive and right arm negative). Vertical and horizontal EOG activity was recording by bipolar electrodes. Horizontal EOG electrodes were put in the outer canthus of each eye and vertical EOG in the supraorbital and suborbital region of right eye. Figure 3.2 shows the electrode diagrams.

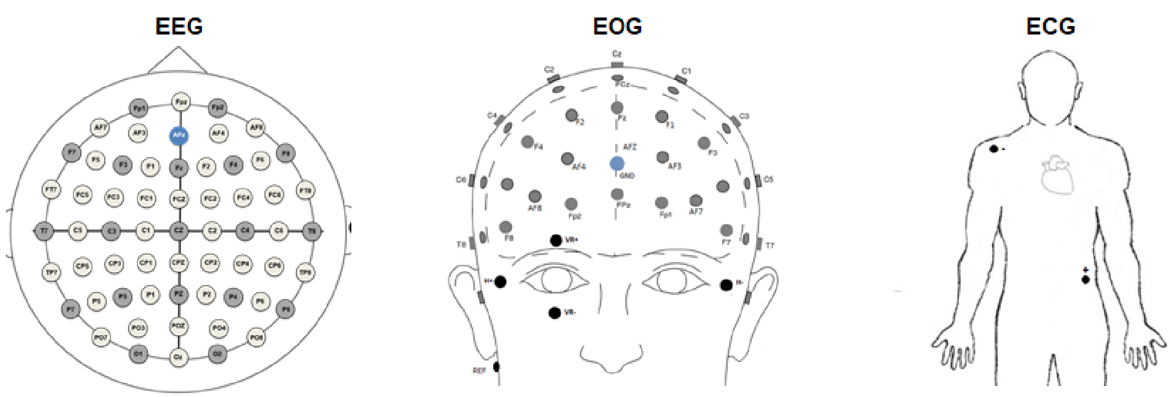

Figure.1-3. Electrode position. Shown from left to right are the electrode arrangements for EEG, EOG and ECG.

Recording conditions

In order to keep the homogeneity of subject internal conditions, volunteers should follow the following recommendations:

- Avoid alcohol approximately 12 hours before each experimental session.
- Avoid caffeine, tea or heavy meals, as well as smoking for at least one hour before each session.
- Avoid extreme physical activity before the session.

To guarantee homogeneity of external conditions, light intensity and room temperature were kept under control. Likewise, to avoid variability given by the circadian cycle, all recordings were carried out in the afternoon, between 1:00 and 5:00 pm.

1.3.4 LapSim tasks

Three tasks with incremental difficulty grade were selected according to the LapSim®. Coordination, grasping and cutting tasks were selected for pilot test. From the performance analysis, it was found that there were not significant increases for the cutting task, participants stated the procedure involved a high difficulty level. Due to the above, the last task was changed for peg transfer, which is part of the Fundamentals of Laparoscopic Surgery (FLS) program. This task was proposed as the one with the highest level of difficulty, as it integrates more psychomotor skills such as picking and transferring between dominant and non-dominant hands. Tasks are described below (Figure 1.4):

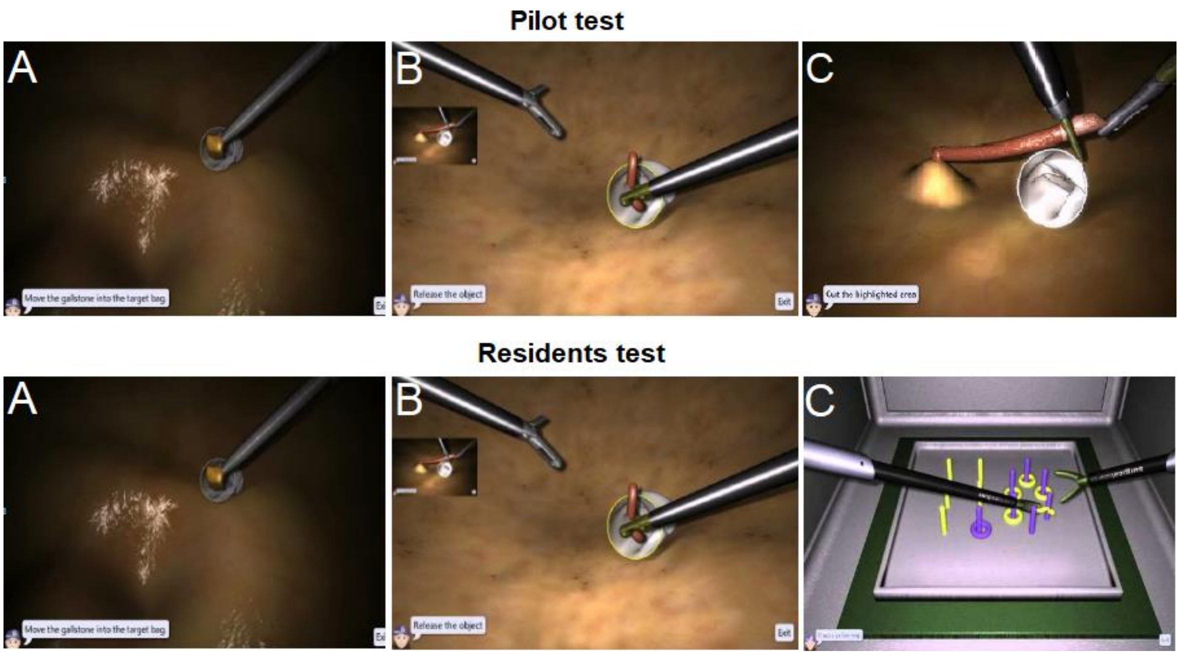

Figure 1-4. LapSim task. Pilot test: A) Coordination, B) Grasping, C) Cutting. Residents test: A) Coordination, B) Grasping, C) Peg transfer.

Coordination: combines the use of camera and one instrument. It requires the participant to hold the camera with one hand and locate ten randomly appearing objects, pick them up with the instrument and transfer them to a target that appears instantaneously.
Grasping: intermediate-level task that involves grasping six vertical pipes or appendices, pull them from the ground and transport them to a target with alternating hands.
Cutting: the aim is learning how to grasp and manipulate an object by holding and cutting it with a pair of ultrasonic scissors which are activated with a pedal.
Peg transfer: workspace consists of a board with 12 pegs (two sets of six pegs each one) and six rings. The task requires the user to lift each ring from a peg, then transfer it between hands and place it in a designated peg on the other set.

1.3.5 EEG signal analysis

EEG signal analysis was covered in 3 studies described in chapters 3, 5 and 6. In the pilot study (Chapter 3) a previously validated pre-processing pipeline in test-retest analysis was used [43], [44]. This pipeline covers the use of the MATLAB PREP toolbox and ICA enhanced by wavelet (wICA) analysis to correct eye blinks and muscular artifacts. On clean data, power spectrum measurements in theta, alpha and beta bands were obtained using the multitaper spectral estimation method in MATLAB chronux library [45].

With the study done in Chapter 5, another pre-processing pipeline was applied to extract neural activations from ICA and source localization techniques. ICA decomposition was performed using the adaptive ICA mixture model algorithm (AMICA) [46], and an equivalent dipole model was computed to estimate the location of IC sources. In order to identify equivalent brain components across subjects, a clustering analysis was done. This pipeline allowed obtaining cortical neuronal activations and estimated changes in frontal theta and parietal alpha power associated with training.

Finally, the connectivity analysis was carried out in chapter 6. Here another technique of inverse solutions based on wMNE algorithm [47] was used to estimate cortical activity. On regions found in the previous power analyzes and others involve motor learning, functional connectivity was estimated by means of coherence measures. The annex to chapter 4 shows the HRV analyses performed in residents group.

1.3.6 ECG signal analysis

Chapter 4 covers ECG signal analysis by studying HR. Data pre-processing includes: filtering, down sampling and a peaks-detection algorithm to identify the number of beats per minute (RR signal). HR was calculated by the mean beat per minute in each condition (resting and tasks). In this work, HR changes through training, task difficulty and gender of the participants were analyzed.

HRV analysis is performed from the RR signal obtained with the peak detection algorithm. The RR signal is cleaned by removing and interpolating outliers [48]. Subsequently, the computation of power spectral density is performed using the Welch periodogram. Power values are extracted in low frequency (LF: 0.04-0.15 Hz) and high frequency (HF: 0.15-0.4 Hz) ranges, the LF/ HF ratio is also obtained.

1.4 Thesis framework

This thesis is a compendium of four articles, chapters 3 to 6, all of them published or hold, waiting for some external condition to be submitted. All these papers are aligned with the main objectives of the work. In chapter 3 is describing an exploratory analysis on EEG power spectrum density, in which improvements in laparoscopic simulation task performance are associated with power changes in theta, alpha and beta bands. Then, chapter 4 covers the study of ECG signals in an initial sample of surgical residents, where changes in HR related to the complexity of the task and a gender effect on the HR changes with the training session were found. On the other hand, chapter 5 shows the extraction and study of neural activations derived from EEG during the training of the residents group. With this study it was possible to obtain changes of brain activations related to working memory, mental workload and visual attention processes. Finally, with chapter 6, the analysis of functional connectivity is covered. Here the interactions between previously found brain regions and those associated with motor training were evaluated. Changes in frontoparietal interactions were associated with the increase in task performance.

The papers mentioned are a result of a collaborative work between the following research groups: Bioinstrumentation and Clinical Engineering Research Group (GIBIC) and Neuropsychology and behavior group (GRUNECO) from Universidad de Antioquia, and Biological Psychology and Neuroergonomics from Technical University in Berlin, Germany, under the supervision of professor Klaus Gramman.

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2 THEORETICAL FRAMEWORK

The following chapter describes the definition, use and limitations of EEG and ECG signal analysis techniques in the evaluation of learning processes and motor training. Analysis of HR and HRV in ECG signals have shown association with stress, mental fatigue and level of motor skills. Regarding to EEG, changes in frequency bands such as theta and alpha are associated with learning, as well as changes in functional interactions between frontal and parietal regions.

2.1 Learning Assessment

Learning consists of acquiring and memorizing solutions to specific situations [1]. With enough practice, long-term memory will have many domain-specific knowledge structures, hierarchically organized schemes that allow to categorize different problem states and decide the most appropriate solution actions. These schemes can operate under automatic processing instead of a controlled one. Automatic schema processing requires minimal working memory resources and allows problem solving to be done with less effort [2].

Cognitive load theory states that an adequate allocation of available cognitive resources is essential for learning [3]. When a novice is acquiring new skills such as those required for laparoscopic surgery, he or she must use his attentional resources to consciously monitor what his/her hands are doing, in addition to spatial judgments and operational decision-making. Simulation training allows many of psychomotor skills and spatial judgments to be automated, meaning that fewer attentional resources will be employed, allowing resident to focus more on learning the surgery steps and how to manage complications rather than waste time on initial technical skills refinement [4].

Automation process is due to two consecutive phenomena. At the beginning, procedure memorization, which allows substituting general knowledge for specific (procedural) knowledge. Subsequently, there is a decrease in the involvement of attentional system, since processes are carried out automatically. The more innate surgeon's visual, perceptual and psychomotor ability, the faster he/she will automate surgical skills, requiring fewer attention resources to monitor the basics of his/her performance [5].

The amount of cognitive resources used in a motor-cognitive task execution, such as driving a car, changes from the first time it is carried out until the moment when mastery of the activity is reached [6]. Throughout learning, it has been shown that neural processes for execution of activities shift from cortical areas to subcortical structures such as basal ganglia for automated process [1]. This shift of neuronal processes into subcortical structures allows an increase in cortical resources that could eventually be involved in the control of other present tasks. Using neuroimaging techniques, it is possible to track the reassignment of such cognitive resources during training phase, providing an independent metric about the quality of task performed [7].

A review of brain imaging studies in surgeons by Modi et al. [8] shows that technical skills acquisition is related to brain areas of attention and judgment, motor planning and execution. First phases of training include a greater activation in prefrontal cortex (PFC), and with practice, PFC activity attenuates as performance improves. It has also been seen that novices exhibit greater PFC activation than expert surgeons. Regarding motor planning and execution, less primary motor cortex (M1) activation in expert surgeons compared to novices has been shown, implying learning-related movement efficiency. But also, experts have showed greater activation in motor and parietal regions [9]. Finally, laparoscopic tasks led to enhanced activation of cerebellum in expert surgeons compared to novices [10].

Diagnostic imaging-based methods such as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) are excellent tools for evaluating how the brain adapts in response to repeated practice or exposure to tasks. However, their limitations in terms of cost, space and invasion make them unsuitable for real work environments, where less invasive approaches would be preferable and costs for their implementation and use are limited. Functional near-infrared spectroscopy (fNIRS) is an indirect optical brain imaging technique that is more portable than fMRI and which captures hemodynamics brain changes with improved spatial resolution compared with EEG and MEG [11]. The use of this technique assessing laparoscopic surgery skills has shown to discriminate levels of expertise, showing novices have greater PFC activation and lower functional activation in M1 and supplementary motor area (SMA) compared to experts. Also, after a 11-day training, skilled trainees exhibited increased cortical activation in M1 and SMA and decreased PFC activation compared to unskilled trainees [12].

Along with fNIRS, EEG allows to evaluate neural activity during a task execution in a more portable way with fewer restrictions. Furthermore, this technique is a direct measure of neural activity, with a temporal resolution close to the timescale of neuronal dynamics [13].

2.2 Electrocardiographic signal analysis

Electrocardiogram (ECG) is the record of electrical activity generated by the heart. ECG signals are typically in the range of ± 2mV and a frequency band of 0.05 to 150Hz. ECG analysis has allowed differentiation and diagnosis of cardiovascular disease and metabolic disturbances [14].

Figure 2.1 shows the schematic representation of a cardiac cycle. The first wave of the cycle corresponds to P wave, which represents the activation of atrium. There is a relatively isoelectric short segment after P wave. Once ventricles are excited, a large and rapid deviation of the signal is observed. This wave seems to have several components. An initial downward deformation called Q wave, followed by an upward deviation or R wave, and a terminal deflection called S wave. The above is referred as QRS complex. After QRS complex, there is another relatively short isoelectric segment. After this segment, ventricles return to electrical rest state, and a repolarization wave called T wave is seen as a low-frequency signal.

In some individuals a small peak occurs at the end or after T wave and is called U wave. Its origin is not fully established, but it is believed to be a repolarization potential [15].

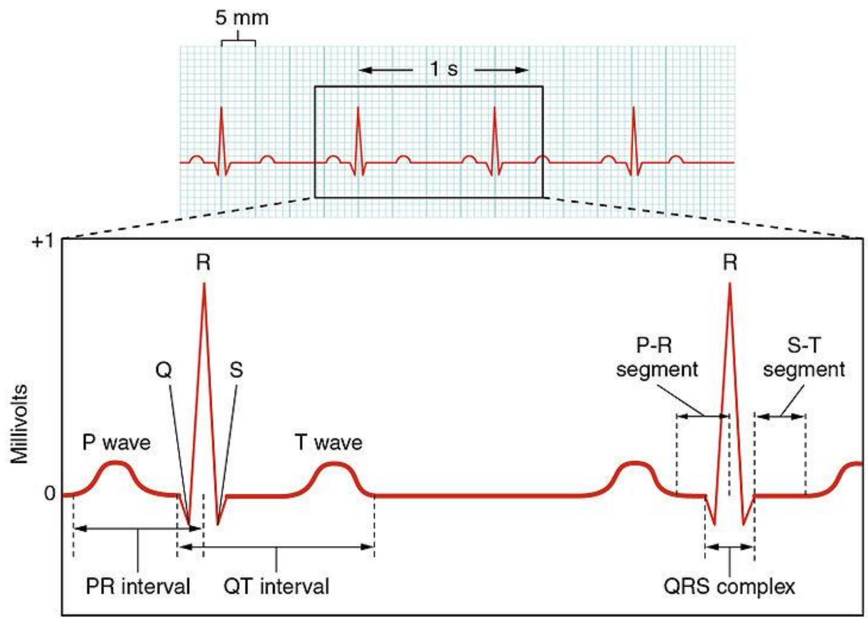

Figure 2-1. Schematic representation of a cardiac cycle (Creative Commons).

2.2.1 Heart rate

Heart rate (HR) corresponds to 60,000 divided by the time in ms between adjacent beats. Variations in HR have been found to be related to variation in emotional states. For this reason, the role of HR in evaluating the mental state of a subject during a task performance has been investigated [16]. In flight simulation tasks training, a reduction in HR was found throughout the training sessions [5]. Johnson et al. showed that heart rate of experts is lower than novices while performing a military training task. Additionally, an increase in HR in both groups is reported when going from a resting condition to task execution. The increase in task difficulty also seems to be directly related to an increase in HR [17].

2.2.2 Heart rate variability

Heart rate variability (HRV) refers to variations in instantaneous heart rate and series of intervals between consecutive peaks of R wave. This variation is considered as a mean of indirect observation of autonomic nervous system (ANS) [18]. HRV is under control of ANS, which through parasympathetic and sympathetic branches, is responsible for adjusting HRV in response to external or internal physical or emotional stimuli. Sympathetic activity is mainly related to preparing the body for action, as well as stressful situations. Alternatively, parasympathetic activity, active in resting situations, compensates for effects of sympathetic activity in bringing the body to a resting state. In normal situations, there is a balance between these two activities [19].

From measurements obtained in time and frequency domain, studies have shown the use of HRV in the evaluation of parasympathetic and sympathetic nervous systems, and their association with stress [20]. HRV measurements in time domain include statistics such as mean of RR intervals, standard deviation, and the square root of the mean square difference of successive R-R. Frequency analysis of short signal segments include characteristics such as low-frequency power (LF, 0.04 – 0.15 Hz), high-frequency power (HF, 0.15 – 0.4 Hz) and the ratio LF/HF [18].

Assessment of temporal measures shows that with a higher mental workload, standard deviation of the R-R intervals (SDNN) decreases significantly [21]. A study developed by Heine et al. evaluated a series of characteristics obtained from ECG signals to discriminate levels of mental load in drivers [22]. Here it was found that mental load leads to an increase in HR along with a decrease in SDNN. Regarding the frequency measurements, during acute mental stress, increases in LF, decrease in HF and increases in the LF/HF ratio have been reported [16]. In the field of sport and exercise psychology, HRV analysis has had extensive studies on topics such as stress, overtraining, anxiety, biofeedback, cognitive performance, and sporting performance [23]. However, given the variability of results and interpretations of HRV indices, there are several aspects to consider such as recording length, quality of the recorded signal, breathing methods and participant variables (age, gender, cardio-related medication) [24].

2.3 Electroencephalographic signal analysis

Electroencephalography (EEG) is a non-invasive technique that provides a representation of brain electrophysiological activity with a high temporal resolution (< 1 ms) [25]. EEG signals provide relevant information about dynamic brain processes responsible for cognitive functions, which allows to evaluate different cognitive processes associated with a particular task [26]. Figure 2.2 shows the setup of an EEG recording.

Figure 2-2. EEG electrode montage.

Quantitative EEG (qEEG) refers to mathematical processing of EEG data in order to more accurately quantify specific parameters of the signal [27]. qEEG analysis have identified phase, amplitude, and power characteristics that reflect unique aspects of brain function. Five groups of oscillations are distinguished by their different frequency ranges: delta (1 - 4 Hz), theta (4 - 8 Hz), alpha (8 - 13 Hz), beta (13 - 30 Hz) and gamma (30 - 50 Hz) [28].

Most cognitive processes have been linked to at least one of the traditional frequency bands [29]. Delta oscillations are related to inhibition process associated with attention, with sources of this oscillation located in areas of frontal and cingulate cortex [30]. Theta rhythm is commonly associated with memory processes, reflecting communication with the hippocampus, and it is seen primarily in the frontal cortex [31], [32]. Alpha band is modulated during sensory stimulation, reflects memory and attentional processes [33]. Alpha oscillations have been shown to exhibit an inverse correlation with cognitive performance, suggesting the inhibition of task-irrelevant cortical structures [34]. Modulation of beta oscillations has been observed mainly during motor task performance or cognitive tasks that require sensorimotor interaction [35]. Gamma band reflects cortical activation and is related to attentional information processing, active maintenance of memory contents, and conscious perception [36].

Likewise, changes in EEG rhythms have been described in a wide variety of diagnoses of neurological diseases, such as epilepsy, brain tumors, head injury, sleep disorders and dementia. Psychiatric disorders including depression, attention deficit-hyperactivity disorder, autism, bipolar disorder, anxiety, post-traumatic stress disorder and schizophrenia have also been associated with patterns of power changes within specific frequency bands. However, these alterations are not exclusive to a single disorder, and they do not always reflect the same trend [37]. This leads to a cautious interpretation of the results, considering the methodological limitations.

2.3.1 Spectral analysis in training and motor learning

Two types of qEEG studies have been observed regarding evaluation of learning: analysis of performance during a task execution between experts and novices, and monitoring of a training process.

Theta and alpha bands have been primarily related to learning. During execution of a rifle marksmanship task, significant increases in theta power were observed in a group of experts relative to novices. Increase in this activity was observed mainly in areas of anterior and medial frontal cingulate cortex [38]. In another application, neurophysiological measures were evaluated to distinguish experts from novices during decision-making process in a military training task [17]. Suppression of the alpha rhythm was evidenced compared to rest periods, and an increase in theta power of experts compared to novices.

Works carried out by Borghini et al., have evaluated qEEG measurements during training in flight simulation tasks [5], [39]. Changes in frontal theta and parietal alpha are reported, finding that with better performance in the task execution, power in theta band tends to decrease and alpha band tends to increase. During the first phases of training, an increase in theta and a decrease in alpha were observed, related to a greater mental effort. These changes were reversed in the last sessions, with a decrease in theta and an increase in alpha.

Borghini et al. it also reported results in other applications such as air traffic management tasks and robot-assisted surgery. In these, same changes were observed in theta band over frontal electrodes, increases at the beginning of training followed by a decrease at the end, and an alpha power decrease over parietal electrodes [40]. Additionally, a progressive decrease is reported on theta band in parietal electrodes during training in the robot-assisted surgery task [41].

Specific applications in motor learning show changes in alpha and beta rhythms over sensorimotor areas. Reduction in beta rhythm as a result of training is reflected in groups of subjects with different ages [42]. Pre-movement low beta activity is associated with motor adaptation performance [43]. In this way, medial frontal theta activity is associated with a context-dependent adaptation model process, and sensorimotor alpha and beta both are representative of error processing [44].

2.3.2 Functional connectivity

Analysis of spectral measurements in EEG reflects the activation or deactivation of brain regions during the development of a task. However, the brain is a complex system that involves a network of interacting subsystems. This has led a shift from search for locally activated cortical areas towards the identification of functional networks related to a task [45]. Network communication is carried out through the synchronization of neuronal activity, which constitutes an important physiological mechanism for functional integration [46].

Functional connectivity defines the temporal dependence of neuronal activity between anatomically separated brain regions [47]. It is highly time-dependent and allows statistical interdependence to be measured without an explicit reference to cause-effect relationships. For its estimation, measures such as correlation or coherence between the temporal patterns of neurophysiological events can be used [48]. In this way, the degree of statistical dependence between neurophysiological variables is associated to the degree of connectivity.

The data on which functional connectivity is evaluated are essentially of temporal nature such as fMRI, EEG and MEG data [49]. FMRI has high spatial resolution (1–10 mm), but limited temporal precision (> 1s), mainly due to limitations of hemodynamic response. Therefore, it has been used to map anatomically accurate functional networks, even at the voxel level, operating at low frequencies (<0.5 Hz). EEG and MEG data contain information about electromagnetic activity in the brain over a wide range of frequencies (~ 1 to 100 Hz), with high temporal resolution (< 1ms), but low spatial resolution (1-10 cm) [50]. Compared to other techniques, EEG has high temporal resolution and is low cost, which makes it a more accessible tool to evaluate functional connectivity in a reliable way during resting state or while performing a task [51].

2.3.3 Functional Connectivity Estimation

Neurophysiological techniques such as EEG and MEG have high temporal resolution and are therefore more suitable for identifying synchronization across frequency bands in large-scale functional networks. In EEG recordings, synchronization is typically quantified through linear measures such as coherence or through nonlinear measures such as those based on phase synchronization or generalized synchronization.

- Coherence

The most important linear correlation measure is coherence. Considered as a generalization of the correlation, coherence describes the correlation between two time series as a function of frequency and depends both on the consistency of the phase difference and the power of the two signals [52]. However, this technique has several limitations, including the problem of conductive volume and the use of a common reference electrode that can introduce interdependencies between the electrodes that are not actually present in the signals.

Coherence between two signals is given by their cross spectral density function S_{xy} normalized by their individual spectral density functions. However, due to finite size of neuronal data, it is necessary to estimate the true spectrum, known as the periodogram, using smoothing techniques [53].

$$K_{xy}^2 = \frac{|\langle S_{xy}(f)\rangle|^2}{|\langle S_{xx}(f)\rangle||\langle S_{yy}(f)\rangle|} \qquad (2.31)$$

Where $\langle\cdot\rangle$ indicates the average of windows. The estimated coherence for a given frequency ranges from 0 (no coupling) to 1 (maximum linear interdependence).

- Multitaper spectral estimation method

Electrophysiological signals represent a stochastic process, where a single trial or epoch represents only one noisy performance of the process of interest. Therefore, a single sample from a process does not provide a reliable estimation of its spectral properties [54].

These problems are often overcome by an average over many realizations of the same event (Periodogram). However, this method is unreliable with small data sets, and not suitable when it is not desired to attenuate signal components that vary between assays. Instead of the joint average, the multitaper method reduces estimation bias by obtaining multiple independent sources from the same sample. Each taper is multiplied element by element by the signal to provide a windowed test from which the power is estimated. Since each taper is orthogonal to all the others, the spectrum estimates will be independent. The final spectrum is obtained by averaging all the spectra [55].

Considering a stationary stochastic process of dimension p and with zero mean:

$$X(t) = [X(1,t), X(2,t), \dots, X(p,t)]^T \qquad (2.32)$$

Where *T* denotes the transpose and *p* refers to the number of channels. The multitaper spectral estimator between channel *l* and *m* is the average of *K* crossed spectral estimators between the same pair of channels:

$$\hat{S}^{lm}(f) = \frac{1}{K}\sum_{k=0}^{K-1} \hat{S}_k^{lm}(f) \qquad (2.33)$$

Where $\hat{S}_k^{lm}(f)$ is given by:

$$\hat{S}_k^{lm}(f) = \frac{1}{N\Delta t}\left[J_k^l(f)\right] * [J_k^m(f)] \qquad (2.34)$$

Where:

$$J_k^l(f) = \sum_{t=1}^{N} h_{t,k} X(l,t) e^{-i2\pi f t \Delta t} \qquad (2.35)$$

The sequence $\{h_{t,k}\}$ is the taper data for the spectral estimator. These data are chosen in a way to provide good protection against spillage. Slepian sequences (discrete elongated spheroidal sequences) are usually chosen. The maximum order *K* is chosen in such a way that it is less than the Shannon number $2NW\Delta t$. The *2W* quantity defines the bandwidth resolution $W \in (0, f_N)$ [55].

- Phase synchronization

The synchronization is based on the interaction of chaotic oscillators. It can be understood as an adjustment of the rhythms of oscillating objects due to their interaction. Phase synchronization (PS) is most observed in large-scale gamma-frequency oscillations that enter precise phase lock for a limited time period when the subject is engaged in cognitive tasks [56]. A representative method capable of obtaining a statistical measure of PS strength in different brain areas is the Phase Locking Value (PLV) [50].

The PLV approach posits that two dynamical systems can have their phases synchronized, even if their amplitudes are uncorrelated. PS is defined as the blocking of the phases associated with each signal:

$$\left|\phi_x(t) - \phi_y(t)\right| = const \qquad (2.36)$$

In order to estimate the instantaneous phase of a signal, the Hilbert transform (HT) can be used to form the analytic signal H(t) as:

$H(t) = x(t) + i\tilde{x}(t)$ (2.37)

Where $\tilde{x}(t)$ is the HT of $x(t)$, defined as:

$$\tilde{x}(t) = \frac{1}{\pi} PV \int_{-\infty}^{\infty} \frac{x(t\prime)}{t-t\prime} dt' \qquad (2.38)$$

where PV denotes the Cauchy principal value. The phase of the analytical signal is defined as:

$$\phi(t) = arctan \frac{\tilde{x}(t)}{x(t)} \qquad (2.39)$$

Therefore, for two signals $x(t)$, $y(t)$ of equal duration, with instantaneous phases $\phi_x(t)$, $\phi_y(t)$, the bivariate PLV metric is defined as:

$$PLV = \left| \frac{1}{N} \sum_{j=0}^{N-1} e^{i(\phi_x(j\Delta t) - \phi_y(j\Delta t))} \right| \qquad (2.40)$$

Where Δt is the sampling period and N is the number of samples of each signal. PLV takes values within the interval $[0,1]$, where 1 indicates perfect phase synchronization and 0 indicates lack of synchronization.

- Generalized synchronization

Generalized Synchronization (GS) represents how the neighborhoods (i.e., recurrences) of one chaotic attractor map onto another. Attractor mapping is considered a robust way to assess GS range, even if it is prone to stationarity deficiencies [57]. To form such attractors from the raw EEG data, delay vectors must be constructed from the time series using the following procedure known as time delay embedding[50]:

$$x_n = (x_n, \dots, x_{n-(m-1)\tau}),\ y_n = (y_n, \dots, y_{n-(m-1)\tau}) \qquad (2.41)$$

Where $n = 1, \dots, N$ and m and τ are the embedded dimension and the time delay. Let $r_{n,j}$ and $S_{n,j}, j = 1, \dots, k$ denote the time indices of the k nearest neighbors of x_n and y_n, respectively. For each x_n the mean squared Euclidean distance to its k neighbors is defined as:

$$R_n^{(k)}(X) = \frac{1}{k} \sum_{j=1}^{k} (x_n - x_{r_{n,j}})^2 \qquad (2.42)$$

and the Y-conditional mean squared Euclidean distance $R_n^{(k)}(X|Y)$ is defined by substituting the nearest neighbors for the equal time partners of the nearest neighbors of y_n. If the set of reconstructed vectors (point cloud x_n) has a mean square radius:

$$R(X) = \frac{1}{N} \sum_{n=1}^{N} R_n^{(N-1)}(X) \qquad (2.43)$$

Then
$R_n^{(k)}(X|Y) \approx R_n^{(k)}(X) \ll R(X)$ when the systems are strongly correlated, while $R_n^{(k)}(X|Y) \approx R(X) \gg R_n^{(k)}(X)$ if they are independent. Therefore, a measure of interdependence is defined as:

$$S^{(k)}(X|Y) = \frac{1}{N}\sum_{n=1}^{N}\frac{R_n^{(k)}(X)}{R_n^{(k)}(X|Y)} \qquad (2.44)$$

Since $R_n^{(k)}(X|Y) \gg R_n^{(k)}(X)$ by construction, S ranges between 0 (indicating independence) and 1 (indicating maximum synchronization). Another normalized and more robust version of S is defined as [58]:

$$N^{(k)}(X|Y) = \frac{1}{N}\sum_{n=1}^{N}\frac{R_n(X)-R_n^{(k)}(X|Y)}{R_n(X)} \qquad (2.45)$$

- Techniques based on information theory

Information-based techniques are sensitive to both linear and nonlinear statistical dependencies between two time series. The most representative method is the cross-mutual information (CMI) that measures the mutual dependence between two signals by quantifying the amount of information obtained about one signal from the measurement of the other, as a function of the delay between them [59]:

The mutual information between two random variables X y Y is defined as:

$$I(X;Y) = H(X) + H(Y) - H(X,Y) \qquad (12)$$

$$H(X) = \sum p(x_i)log_2 p(x_i) \qquad (13)$$

Where $H(i)$ is the Shannon entropy of variable i and $H(X,Y)$ is the join entropy of X and Y.

2.3.4 Inverse solution analysis

EEG is a powerful tool to capture brain function in the time frame in which these processes occur (miliseconds). However, this technique suffers from a poor spatial resolution that makes it difficult to infer the sources of the neuronal activity measured on the scalp [60].

The localization of brain signal sources from EEG has been an active research area during the last decades. Radiological imaging techniques have been widely used for this purpose. However, these techniques are expensive and difficult to access for all patients. This has led to the use of algorithms which use MR image templates to anatomically localize activity by brain sources. Source location based on scalp potential requires a solution to an inverse problem. The signal recorded on the electrodes might come from different distributions of brain currents. In electromagnetic theory, this fact is considered as an ill-posed problem, since the current distribution in a conductor cannot be unequivocally found starting from the fields and potentials in its exterior [61].

The selection of a particular solution requires a priori knowledge of brain physiology and the subject state. Assumptions are made about the nature of the sources, i.e., number of sources, anatomical and neurophysiological constraints, prior probability density functions, norms, smoothness, correlation, covariance models, spatial extent constraints, etc [62].

- Source model

Two general approaches of mathematical models have been proposed: equivalent current dipole (ECD) model and linearly distributed approach (LD). Inverse methods using the dipole source model consider sources to be a small number of magnetic dipoles located at certain locations over three-dimensional space within the brain [28]. However, reliable estimation of nonlinear dipole localization parameters becomes difficult when the number of sources increases.

In LD methods, there is no need for any knowledge about the number of sources. In general, this problem is considered as an indeterminate inverse problem. An L_p norm solution is the most common regulation operator to solve this problem. This regularized method is built on minimizing the cost function:

$$\psi = \|Lx - m\|_p + \lambda\|Wx\|_p \qquad (2.36)$$

Where x is the vector of source currents, L is the lead field matrix, m is the EEG measurements, W is a diagonal location weighting matrix, λ is the regulation parameter, and the norm $1 \leq p \leq 2$ is the measure in the Banach vector space [28].

- Weighted Minimum Norm Estimation (WMNE)

This method is part of the LD approaches. The solution is regularized by imposing some constraints regarding to anatomical and physiological information on the general cost function. Quadratic error costs are weighted based on spatial and temporal properties. In this approach, the sources are assumed to be sufficiently distributed and oriented orthogonally to the cortical lamina [28].

The EEG source localization problem using a multivariate linear model and the observations, X, as the electrode potentials, is formulated based on the observation model:

$$X = \mathfrak{I}(r, J) + V \qquad (2.37)$$

Where $X = [x(1), x(2), \dots, x(T)]$ has dimension $n_e \times T$, T represents the data length in samples and n_e is the number of electrodes, r and $J = [j_1, j_2, \dots, j_T]$ are, respectively, the locations and moments of the sources, and V is the added noise matrix. $\mathfrak{I}$ is the binding function of the sources to the electrode potentials. For the calculation of $\mathfrak{I}$, a three-layer head model is normally considered [63].

A structural MR image of the head can be segmented into three isotropic regions with the same conductivity: brain, skull, and scalp. Most of these models consider the head as a sphere for simplicity. However, EEG sources are modeled by a fixed and uniform three-dimensional grid of dipoles spread throughout the entire brain volume.

The problem is also an indeterminate linear problem [28]:

$$X = LJ + V \qquad (2.38)$$

Where L is the directed field matrix that interrelates the dipoles to the electrode potentials. To achieve a unique solution to the indeterminate equation, some restrictions must be imposed. The proposed regularization method constrains the reconstructed source distribution by joint minimization of a linear mixture of some weighted norm $\|H_j\|_2$ of current sources j and the principal cost function of the inverse solution. Assuming that the noise is Gaussian with a covariance matrix C_v then:

$$\hat{J} = \arg min_j \left[\left\| C_v^{-\frac{1}{2}}(Lj - x) \right\|_2^2 + \lambda^2 \|Hj\|_2^2 \right] \qquad (2.39)$$

Where the Langrage multiplier λ is adjusted to make a balance between the main cost function and the constraint $\|H_j\|_2$. The covariance matrix is scaled such as $trace(C_v) = range(C_v)$. This can be formulated as an overdetermined least squares problem. The solution to the minimization of equation (2.39) for a given λ is of the form:

$$\hat{J} = BX \qquad (2.40)$$

Where:

$$B = \left[L^T C_p^{-1} L + \lambda^2 (H^T H)\right]^{-1} L^T C_p^{-1} = (H^T H)^{-1} L^T \left[L (H^T H)^{-1} L^T + \lambda^2 C_p\right]^{-1} \qquad (2.41)$$

These equations describe the weighted minimum norm (WMN) solution to the localization problem. However, they are not complete unless an appropriate spatial or temporal constraint is imposed. In theory, any number of constraints can be added to the main cost function. However, assumptions like those about the covariance of the sources must be implicit in order to effectively find L, which includes the information about the directions and the dipoles. An assumption can be $[diag(L^T L)]^{-1}$, which is proportional to the covariance components, must be normalized. Another restriction is based on the spatial information of fMRI that appears as blood oxygenation level dependence (BOLD) when the sources are active. Evoked responses can also be used as time constraints [28].

2.3.5 Independent Component Analysis - ICA

EEG signals recording at each electrode are the sum of activities in brain areas, as well as electrical artifacts from muscles, eyes, electrodes, movements, and the electrical environment. ICA is a blind decomposition technique, which descompose multi-channel EEG data into maximally independent component processes. Each independent component (IC) can be either particularly brain generated EEG activities or some type of non-brain artifacts (environmental noise, eye blinks, eye movements, scalp or heart muscle activity) [64].

- ICA model

ICA performs a blind separation of the data matrix (X) based only on the criterion that resulting source time courses (U) are maximally independent. ICA finds a unmixing matrix (W) that, when multiplied by the original data (X), yields the matrix (U) of IC time courses [64].

$$U = WX \qquad (2.42)$$

Where X and U are $n \times t$ matrices, and W is $n \times n$. Equation (2.42) implies that:

$$X = W^{-1}U \qquad (2.41)$$

W^{-1} is the mixing matrix whose columns contain the relative weights which the component projects to each of the scalp channels (IC scalp map). The starting point for ICA is the assumption that the components of U are statistically independent. It is also assumed that the independent component must have non-Gaussian distributions.

2.3.6 Functional connectivity analysis during training and learning

Few studies have evaluated functional connectivity from EEG during task training. Langer et al. [65] analyzed the organization of functional networks in the fronto-parietal region and how their topology is modified by training in working memory tasks. The networks were obtained from coherence measures, and graph analysis was carried out to evaluate the small-world property of the network. Their results showed that task performance correlates with power in theta band. Additionally, they found that a better performance in the task is associated with a higher small world topology in the network.

Performing a resting-state functional connectivity analysis, Lasaponara et al. evaluated a 12-week training with the Quadrato Motor Training (QMT) paradigm, used to increase cognitive flexibility, creativity and spatial cognition [66]. From analysis of cortical sources and the computation of linear connectivity in the alpha band, they observed increases in limbic and fronto-temporal connectivity in the resting condition with eyes open, after 6 weeks of training. Increases were also seen for the resting condition with eyes closed in the occipital network after 12 weeks of training.

Another recent work published by Kong et al. [67], evaluated the changes in measures of phase synchronization that occur when drivers going from a state of alertness to a state of mental fatigue during their training in a simulator. Their main finding was that synchronization in the delta and alpha bands in the frontal and parietal regions increases significantly as the driver's mental state changes from alertness to fatigue. Distinctive patterns of connectivity over frontal regions and motor areas have been found in other studies evaluating mental fatigue [68].

2.4 References

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3 NEUROPHYSIOLOGICAL CHANGES ASSOCIATED WITH TRAINING IN LAPAROSCOPIC SURGERY USING EEG: A PILOT STUDY

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Abstract: Laparoscopy is a minimally invasive technique that requires surgeons to acquire special motor skills derived from an extensive training. This work focuses on exploring the neurophysiological changes associated with motor learning. Electroencephalographic (EEG) signals were recorded from eight subjects while performing a bimanual coordination task in a laparoscopic simulator. Spectral power measurements in theta, alpha and beta bands during four training sessions were calculated. Power indices, task score and perception of mental workload were evaluated using analysis of variance to show the effect of training session. Results show improvements in task performance and changes in power measurements associated with the training process. This work opens the possibility to assess the training performance of surgical residents using electrophysiological recordings.

3.1 Introduction

Laparoscopic surgery has become the standard for patients who need surgical intervention at the abdominal level [1]. Laparoscopy requires that the surgeon and his assistants acquire special skills, related to depth perception and video-hand-eye coordination, mainly associated with a long learning curve and extensive training [2]. The training of basic skills including psychomotor performance, depth perception and spatial judgment can be carried out in laboratories with help of models and simulators [3]. Virtual reality simulators represent a safe, ethical and repeatable option for training programs since they avoid injuries to the patient, reduce costs associated with the use of cadavers and animals, and offer the possibility to repeat surgical procedures as many times as necessary to learn them correctly, while offering the review of the procedures performed [4], [5]. The assessment of surgical training is a research field in growth [6], [7], and the use of a tool that allows to quantify the performance and learning progress of the residents helps to improve the learning experience and the training program [8]. The acquisition of surgical skills involves many aspects to evaluate such as: performance [9], [10], ergonomics [11], stress or fatigue, and cognition [12]. Cognition encompasses a series of processes of perception, attention, processing of information, storage and retrieval of this information at the appropriate time to make a decision and execute a movement [13]. Thus, an interesting question is to know if it is possible to track the neurophysiological changes underlying the skill acquisition. The foregoing will provide additional and objective evidence related to the acquisition of a skill during the training phase.

Brain electrical activity measured by electroencephalography (EEG) is one of the most useful tools, since it provides the temporal resolution required to follow brain activity throughout the execution of a task [14]. Several applications has proven its effectiveness such as training in flight simulators and air traffic controllers [15], [16]. Studies have shown that theta and alpha frequency bands are related to the learning process. Theta band has been linked to memory consolidation processes [17]. Particularly, the increase of cognitive effort during the performance of a task has been related to an increase in theta power [18]. Likewise, variations in this frequency band have been found mainly in frontal regions [16], [19]. The alpha band has been related to the level of attention. Suppression of alpha is associated with an increase in focused attention (particularly in visual stimuli) on posterior regions [20]. In addition to the two previous bands, it is important to consider beta rhythms, modulated during cognitive tasks that require sensorimotor interaction [21]. Principally on central regions (supplementary motor area - SMA) [22]. With this work we attempt to carry out an exploratory study of neurophysiological, performance and behavioral measures during students training in a laparoscopy virtual reality simulator based on the previously reported frequency bands that change during training. We recorded EEG signals while subjects executed a task of bimanual coordination in the simulator and spectral power measurements in theta, alpha and beta bands were extracted. We evaluated the effect of the training session over variation of power indices, task performance and perception of mental workload.

3.2 Methodology

3.2.1 Subjects and experimental protocol

Eight healthy volunteer subjects (23 ± 3.6 years old, right handed, 5 females) from Bioengineering program of Universidad de Antioquia participated in this study. Informed consent approved by the bioethics committee of the Universidad de Antioquia was obtained from all participants. Subjects had no knowledge in laparoscopy, neither prior contact with the VR simulator LapSim® (Surgical Science Ltd., Göteburg, Sweden). The experimental protocol consisted in subjects learn to execute tasks in the simulator, during 4 sessions training, one per week. In each session, subjects performed three repetitions of the task, and the EEG recording was done during the first execution. At the end of each session, volunteers were asked to fill the National Aeronautics and Space Administration-Task Load Index (NASA–TLX) questionnaire [23], in order to assess the perception of the workload across the training sessions. The workload score (ranging 0 – 100) was calculated as combination of six factors which include Mental Demand, Physical Demand, Temporal Demand, Performance, Effort and Frustration.

3.2.2 LapSim training

LapSim® Haptic System is a virtual reality laparoscopic simulator that contains Basic Skills, Task Training and Camera Anatomy Training modules. Coordination task of the Basic Skills module was selected for the study. Participants hold the camera with left hand and the instrument with right hand, then they have to search out ten appearing objects, lift them with the instrument and transfer them to a bag (Figure 3.1). Default settings of the exercise were used. The overall score (%) was calculated based on parameters such as total time of execution, errors, instrument out of sight, path length instruments and tissue damage.

Figure 3-1. LapSim coordination task.

3.2.3 EEG recording and pre-processing

Electroencephalographic signals were recorded using Natus® Quantum™ (Natus Neurology Incorporated, Winsconsin, USA) amplifier with a sampling frequency of 1024 Hz. A cap with 64 AgCl electrode with mastoid bone reference was used.

The pre-processing pipeline used in this paper has been applied in a previous work showing good test-retest reliability [24]. First, PREP [25] pipeline was used to remove 60 Hz noise line and to apply a robust average reference where bad channels are detected and interpolated. Then, data were filtered using a high pass filter (4 Hz) with the eegfiltnew EEGLAB function [26] to eliminate the noise produced by subject movement. Filtered data were segmented in 2s epochs and ICA enhanced by wavelet (wICA) analysis was done to correct eye blinks and muscular artifacts in each epoch [27]. Finally, a low-pass filter (50 Hz) was applied to remove high frequency noise.

3.2.4 EEG power analysis

Relative power in theta (4 – 8 Hz), upper alpha (10 – 13 Hz) and beta2 (18 – 21 Hz) bands was computed over the first 16 artifact-free epochs in each recording. This number of epochs refers to the shortest execution time (~32 s) of the task among all subjects and sessions. The above was chosen to avoid the influence of the recording length on the analysis. Power spectral measures were computed using the MATLAB Chronux toolbox and the multitaper spectral estimation method [28]. Relative power mean values over frontal region (AF3, AF4, F5, F3, F1, FZ, F2, F4, F6) for theta, posterior region (CP5, CP3, CP1, CPZ, CP2, CP4, CP6, P5, P3, P1, PZ, P2, P4, P6) for alpha, and central region (C5, C3, C1, CZ, C2, C4, C6) for beta band were selected for the analysis. The previous electrode groups were chosen according to the previous literature described in the first section [16], [19]–[21].

3.2.5 Statistical analysis

Five one-way repeated measures ANOVA analysis were used to evaluate the effect of training session (4 levels) on overall task score, NASA-TLX score, frontal theta, posterior alpha, and central beta (significant p-value < 0.05). The normality of the data was verified using the Kolmogorov-Smirnov test. Mauchly's test was used to assess the sphericity assumption and Greenhouse-Geisser correction was employed when the assumption was not met. Marginal means comparisons were performed with p-values corrected by means of Bonferroni method.

3.3 Results

3.3.1 Task performance

ANOVA analysis shows significant effect of training session on total score ($F(3,21) = 12.454$; $p = 0.000$; $\eta^2 = 0.640$). Post-hoc analysis shows a significant increase in the score from first to second session and between first and fourth session (Figure 3.2).

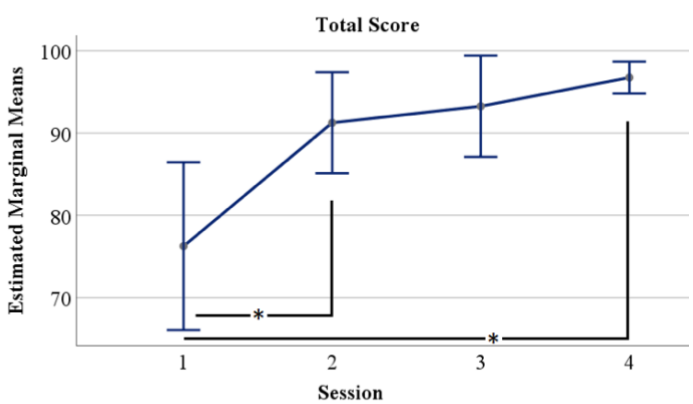

*Figure 3-2. Means of total score task. With * is indicated the sessions in which score presented statistically significant differences (p < 0.05, corrected for multiple comparisons).*

3.3.2 EEG power measures

ANOVA analysis on frontal theta band shows a significant effect of training session ($F(3,21) = 3.243$; $p = 0.043$; $\eta^2 = 0.317$). There is a significant increase of power in second training session compared to the first session (Figure 3.3). Regarding posterior alpha, the analysis also shows significant effect of training session ($F(3,21) = 5.790$; $p = 0.005$; $\eta^2 = 0.453$). Here, there is a significant power increase from first to fourth session (Figure 3.4). Finally, in central beta results show a significant effect of training session ($F(3,21) = 4.230$; $p = 0.017$; $\eta^2 = 0.377$), and a significant power decrease is observed between sessions 1 and 4 (Figure 3.5).

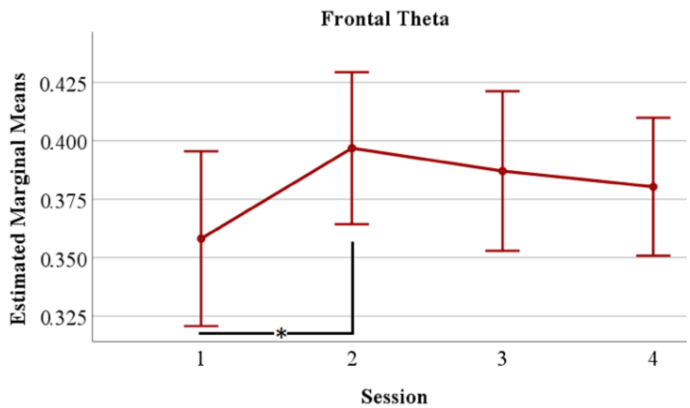

*Figure 3-3. Means comparision of frontal theta power. * indicates the sessions in which power presented statistically significant differences (p < 0.05, corrected for multiple comparisons).*

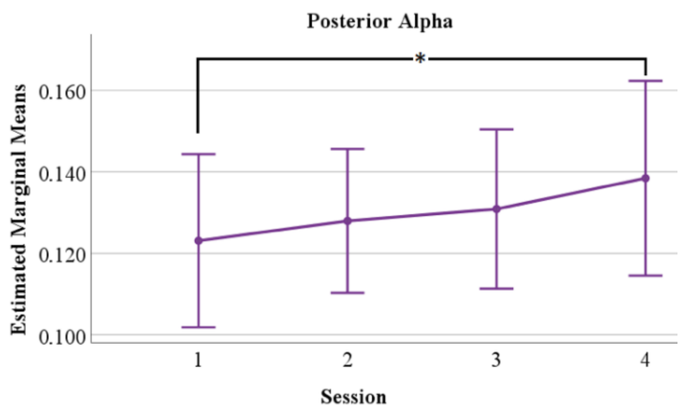

Figure 3-4. Posterior alpha power. A significant increase between 1 and four training session was found (p < 0.05, corrected for multiple comparisons).

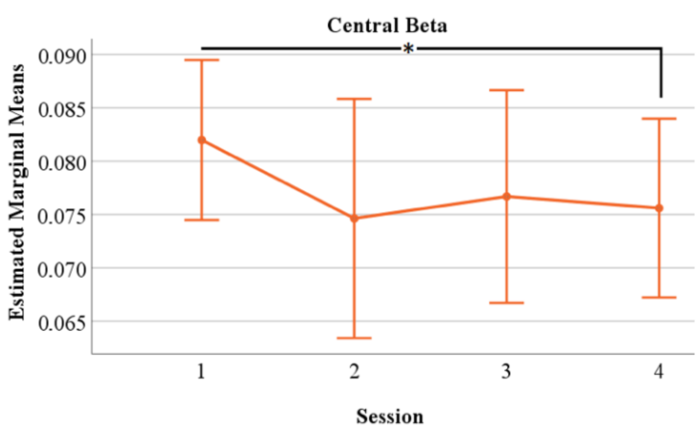

*Figure 3-5. Means of central beta power. * indicates the sessions in which a statistically significant difference was presented (p < 0.05, corrected for multiple comparisons).*

3.3.3 Perceived workload index

ANOVA analysis does not show a significant effect of training session on workload total score ($F(3,21) = 1.964$; $p = 0.156$). However, as shown in Figure 3.6 it is observed a decrease in workload index throughout the training sessions.

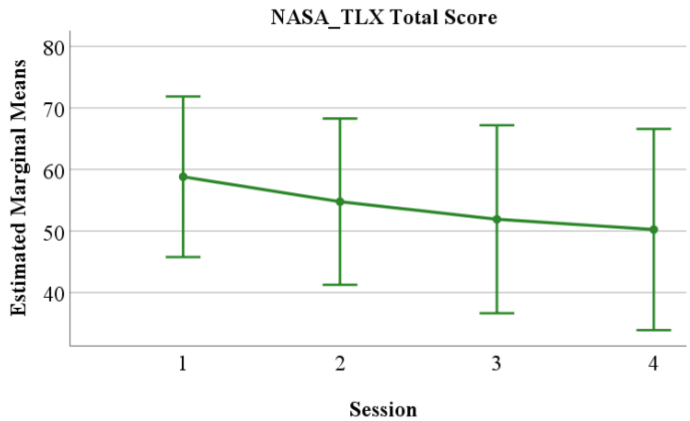

Figure 3-6. NASA- TLX total score. ANOVA analysis does not show significant effect of training session.

3.4 Discussion

In this work we described neurophysiological changes related to training in a laparoscopic surgery simulator. We explored power spectral measurements in theta, alpha and beta bands, performance and workload index through four training sessions of a bimanual coordination task. The results show that the score obtained in the task improves with training session from second session and reaching the highest score in the last one. EEG analysis show changes related to training in theta, upper alpha and beta2 bands. Frontal theta increases from first to second training session, posterior alpha increases between first and fourth session, and central beta decreases from first to fourth session.

Variations in frontal theta and parietal alpha have been found in flight training using simulation [16], [19], [29]. These changes show an increase in theta power on the first training sessions, followed by a decrease when an optimum level of performance is reached. On the contrary, in alpha band is observed a decrease at the beginning of training followed by an increase in the last sessions. The findings show as in the early stages of learning (session 2), considerable cognitive activity is required (reflecting the increase in theta band), where the subject is trying to find out how to achieve the task. In the following sessions, the allocation of cognitive resources changes and the subject can direct his attention towards the performance rather than the strategy [30]. It has been shown that during motor learning the neural processes shift from the cortical areas to subcortical area such as basal ganglia for the automated process [31]. This automation means that it will take less attention resources, which may indicate the progressive increase in alpha band. Upper alpha rhythms are related to cognitive processing of stimuli, and the power decrease is related to its disinhibitory action to enable the processing of information [21]. This shift of activation to subcortical regions may also explain the decreases in beta waves over cortical regions. Walz et al. using fMRI found that long-term hand motor training leads to a decrease in the cortical motor area activation and an increase in cerebellar and striatum activation [32]. Although our results show a relationship with the previous literature, it is important to consider the limitations of the EEG technique in terms of spatial resolution, which would not make it comparable with fMRI studies. However, analysis like inverse solutions can be applied to improve the special resolution and anatomically locate the activity generated by brain sources [33]. Also, it should be noted that EEG spectral measurements reflect the activation or deactivation of brain regions during the development of a task. However, the brain is an extremely complex system that involves a network of interacting subsystems [34]. Therefore, it is required investigation of brain networks and connectivity patterns related to surgical training.

Our work is just an exploratory study aimed to show changes in spectral EEG measurements during training in a laparoscopic simulator. An investigation with a larger number of subjects, in this case residents of surgery, and with deeper quantitative analyzes such as functional connectivity over cortical areas will be carried out.

3.5 Conclusion

The training processes of surgery residents do not have quantitative measures to evaluate the cognitive state of the trainees. Changes in neurophysiological measures have been shown to be related to the processes of learning and acquisition of motor skills. Using spectral measurements in EEG, this work shows significant changes in frequency bands related to motor training. Future analyzes should include the study of the sources that cause the neuronal activation and the interaction between the brain regions involved.

3.6 Acknowledgment

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4 CHANGES IN ELECTROCARDIOGRAPHIC SIGNALS DURING TRAINING IN LAPAROSCOPIC SURGERY SIMULATOR: A PRELIMINARY REPORT

The following study shows an exploratory analysis of changes in HR for the LapSim training of an initial sample of surgical residents. According to the exposed antecedents, it was considered to evaluate the effects of gender, together with the training session and the difficulty of the task. Results found show a variation of HR with task difficulty level exhibiting an increased HR in peg transfer task. Although HR measurements were normalized with resting condition, high variability was observed in the data, which makes it difficult to find statistically significant differences across sessions.

Regarding the HRV analysis, an appendix to this chapter shows the analyzes carried out. Estimation of spectral density was made from the RR signals obtaining normalized LF, HF and ratio LF/HF measurements. However, no statistically significant changes were obtained with training sessions. The main limitation of these analyzes may be in the recording length obtained, since according to the literature, HRV analysis is performed on long-term recordings (24 h), although it is possible to have short-term segments of 5 min. Our recordings length was, on average, of 1 min for coordination, 1.3 min for grasping and 3.5 min for peg transfer task.

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Book: Applied Computer Sciences in Engineering.

Abstract. The aim of this work is attempting to identify physiological characteristics of the learning process in surgery residents. As an exploratory approach, we are interested in determining statistically significant changes in electrocardiographic (ECG) signals recorded while a group of eleven first year general surgery residents were performing three basic skills tasks from the virtual reality (VR) laparoscopic simulator LapSim®. These signals were processed and heart rate (HR) was calculated to analyze it along with the overall score for each exercise. Statistical analysis was performed by means of analysis of variance showing the effects of training session, difficulty of the task and participants gender on heart rate and performance. Our preliminary experimental results show that the score obtained in the tasks improves with training session, being in the women where significant changes occur. HR analysis showed that it increases with the complexity of the task. Besides, the effect of gender on HR showed that in male group there were the significant changes with the difficulty of the task, and a decrease with the training session in the intermediate level of difficulty task.

Keywords: ECG, HR, Laparoscopic Surgery Training, Simulation.

4.1 Introduction

Laparoscopic surgery has become the first option to performing surgeries that involve the abdominal cavity [1]. This minimally invasive technique implies a lower incidence of complications such as risk of infection, pain and difficulties in patient recovery [2]. Laparoscopy requires the surgeon to acquire special skills and abilities to operate without tactile and depth perception [3]. In order to preserve patient safety and reduce medical errors, apprentices must receive an adequate training in which they acquire basic skills before arriving in the operating room [4], [5].

It has been shown that skill training such as psychomotor performance, depth perception and spatial judgment does not depend on the operating room and can be done in laboratories with the help of models and simulators [6], [7]. Virtual reality (VR) simulators have become an important part of training for being a safe, ethical and repeatable alternative [8], [9]. Its use produces objective measures of performance, allows feedback to students, and does not require regular supervision [10].

There is a rising interest in the assessment of surgical and performance skills in laparoscopy during the surgeon's training process [11]. Acquisition of surgical competence is a complex and multifactorial process that can take years of experience and training [1]. Having a quantitative evaluation tool that qualifies the performance and progress of the students allows improving the learning experience and reducing failures of the training program [12]. The assessment of residents training involves several aspects including technical skills acquisition through the supervision of an expert [13], [14]; interaction with instrumental using tracking systems of optical, electromagnetic or mechanical monitoring [15]; and behavioral aspects like cognition, stress or fatigue [16], [17]. One of the above aspects, the evolution of cognitive performance throughout learning process, has not been approached in an effective way since it does not include quantitative strategies [18].

Analysis of physiological signals such as electrocardiography (ECG) allows to objectively evaluate the mental state under which the subject is performing an activity [19]. It has been seen that variations in heart rate (HR) can be related to the variation of emotional states. During training in flight simulation tasks, a reduction of the HR was found through the training sessions [20]. It has also been found that heart rate is lower in experts than in novices during the performance of a military training task. Additionally, an increase of HR in both groups has been also reported when going from a resting to task condition. The difficulty of a task also seems to be directly related to an increase in HR [21].

By acquisition of ECG recordings from surgery residents during training sessions in a VR simulator, we attempted to identify physiological features of the learning process. The goal of the current study is to explore changes in residents' ECG signals through training sessions and tasks. The obtained results show effects of training session and participants gender on their tasks performance, and an effect of task difficulty and gender on changes in heart rate.

4.2 Materials and Methods

4.2.1 Participants

A total of eleven young healthy adults (5 females, 6 males; 9 right handed; mean age: 28 ± 2.9 years, no significant differences in age between men and women) first year general surgery residents in the Universidad de Antioquia participated in the study. Subjects had no significant prior knowledge in laparoscopic surgery, neither previous contact with the VR simulator. The nature of the study was explained to all subjects prior to enrolment, they gave written informed consent approved by the bioethics committee of the Universidad de Antioquia. In addition, they were asked if they had skills in other domains (arts, music, video games).

In order to maintain uniform conditions for quantitative evaluation training, volunteers were asked to avoid alcohol at least 12 hours before each session, as well as to avoid smoking, caffeine, tea, heavy meals right before the experiments; likewise, they were asked to avoid extreme movements over the entire experimental protocol.

4.2.2 Experimental protocol

The experimental protocol consisted in four training sessions developed one every week. In each session volunteers performed three basic skills tasks in the VR laparoscopic simulator LapSim® (Surgical Science Ltd., Göteburg, Sweden). Instructions have been provided to each subject on the first day of training. In order to investigate possible trends and changes of the physiological signals across the experimental sessions, heart electrical activity was recorded using a biopotential amplifier. Each session consisted in three repetitions (a total of 12 repetitions at the end of the study) of the same tasks series in which the volunteers also were evaluated with the LapSim® measurements. Nevertheless, physiological signals were recorded only in the second repetition of each session, furthermore before LapSim® exercises recordings, subjects were recorded in resting condition for 2 minutes. They were in standing position in front of the simulator looking at a blank screen. Figure 4.1 shows a general schema of the experimental protocol, in which can be observed the repetitions where ECG signals were recorded.

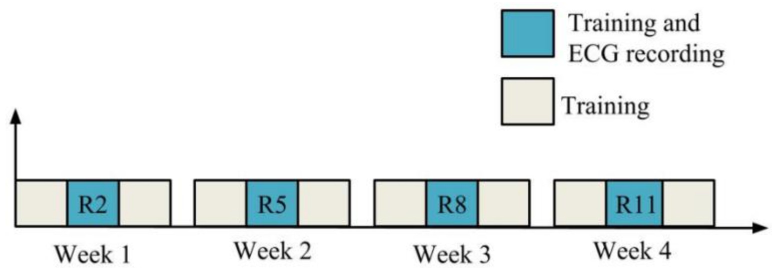

Figure 4-1. Experimental protocol. Each square represents a set of three tasks.

4.2.3 Signals acquisition

Electrocardiographic signals (ECG) have been recorded by the digital monitoring system Natus® Quantum™ (Natus Neurology Incorporated, Winsconsin, USA) at a sampling frequency of 1024 Hz. Electrodes were placed in Lead II and referenced to the right mastoid bone.

4.2.4 LapSim Tasks

LapSim® Haptic System is a virtual reality laparoscopic simulator that comprehends a LapCam, a separate laparoscope, a Basic Skills training package containing Basic Skills, Task Training and Camera Anatomy Training modules. Three tasks with incremental difficulty grade were selected according to the LapSim® Basic Skills and Task Training modules. Each assignment was explained and shown to the participants at the beginning of the first session, due to volunteers had no prior contact with the simulator. The default design of each exercise was determined by the software. The overall score (%) for each exercise was evaluated against predefined parameters based on tissue damage, maximum damage, span time, angled or straight navigation, etc. Figure 4.2 shows three selected exercises that included:

Coordination. This task combines the use of the camera and one instrument. It requires the participant to hold the camera with one hand and locate ten randomly appearing objects, pick them up with the instrument and transfer them to a target that appears instantaneously.

Grasping. This is an intermediate-level task that involves grasping six vertical pipes or appendices, pull them from the ground and transport them to a target with alternating hands.

Peg transfer. In this exercise the workspace consists of a board with 12 pegs (two sets of six pegs each one) and six rings. The task requires the user to lift each ring from a peg, then transfer it between hands and place it in a designated peg on the other set.

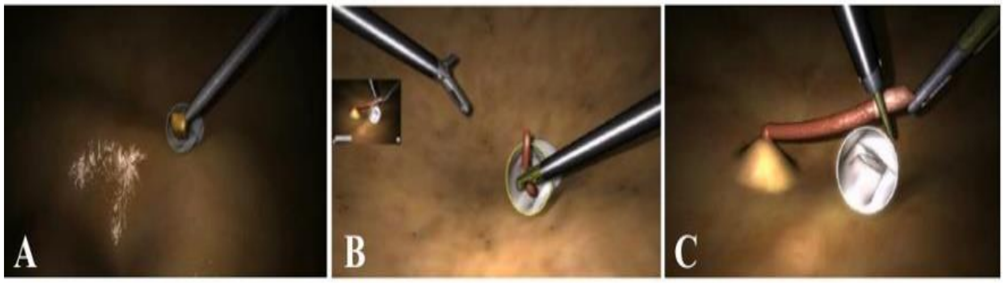

Figure 4-2. LapSim® task. A: Task 1: coordination. B: Task 2: grasping. C: Task 3: peg transfer.

4.2.5 Signals Processing

The first step was decimation of the ECG signals to a sampling frequency of 256 Hz as well as digitally band-pass filtered by a 4th order Butterworth filter (low-pass filter cut-off frequency: 50 Hz, high-pass filter cut-off frequency: 0.8 Hz) [22]. Once the pre-processing stage was achieved, it was applied a peaks-detection algorithm to iden-tify the number of beats per minute, then HR was calculated by the mean beat per minute from each signal on every recording and finally HR obtained values were normalized with reference to the resting condition.

4.2.6 Statistical analysis

A statistical analysis was accomplished in order to evaluate changes in heart rate and performance in the simulator tasks through the total score obtained in each one. Data were analyzed with the Statistical Package for the Social Sciences version 25 (SPSS, Chicago, IL). For HR analysis a mixed design ANOVA was used with gender (2 levels) as inter-subject factor, and training session (4 levels) and task (three levels) as intra-subject factors. Global score was analyzed using a mixed design ANOVA with gender as inter-subject factor and training session as intra-subject factor for each task. The sphericity assumption was tested with Mauchly's test, and Greenhouse-Geisser correction was used in cases where the assumption was not met. A p-value < .05 was considered statistically significant. Marginal means comparisons were carried out without correcting the p-values due to the exploratory nature of the study.

4.3 Results

4.3.1 LapSim® Task Score

Table 4.1 shows the results of the ANOVA for the global scores obtained in each task. Tasks 1 and 2 had a significant effect of session and the interaction session x gender factors, which indicates that the score obtained in the tasks through the sessions be-haves differently in men and women. In the task with the highest level of difficulty (task 3), analysis showed only significant effect of session, indicating that there are not differences in the evolution of task performance according to gender.

Table 4-1. ANOVA results for global score.

Task	Significant effect	F	p-value	η2
Task 1 (Coordination)	Gender	F (1,9) = 0.593	0.461	0.062
	Session	**F (3,27) = 15.856**	**0.001**	**0.638**
	Session x Gender	**F (3,27) = 4.452**	**0.048**	**0.331**
Task 2 (Grasping)	Gender	F (1,9) = 3.195	0.107	0.262
	Session	**F (3,27) = 17.298**	**0.000**	**0.658**
	Session x Gender	**F (3,27) = 3.376**	**0.033**	**0.273**
Task 3 (Peg Transfer)	Gender	F (1,9) = 0.003	0.958	0.000
	Session	**F (3,27) = 6.972**	**0.001**	**0.437**
	Session x Gender	F (3,27) = 0.183	0.907	0.020

Analysis of mean comparisons show significant differences between training sessions for women in tasks 1 and 2, and at a general level in task 3 (see Figure 4.3). For easy and intermediate tasks, there are significant differences between session 1 with sessions 2, 3 and 4, and between session 2 and session 4. These differences show an increase in the score from session 2 (compared with session 1) and a subsequent increase in session 4 (compared with session 2). On the other hand, for the most difficult task, the significant differences are between session 1 with sessions 3 and 4, and session 2 with session 3. The above indicates that the score improves significantly after the third training session. It is important to note that there were no significant differences between men and women in any session for any task.

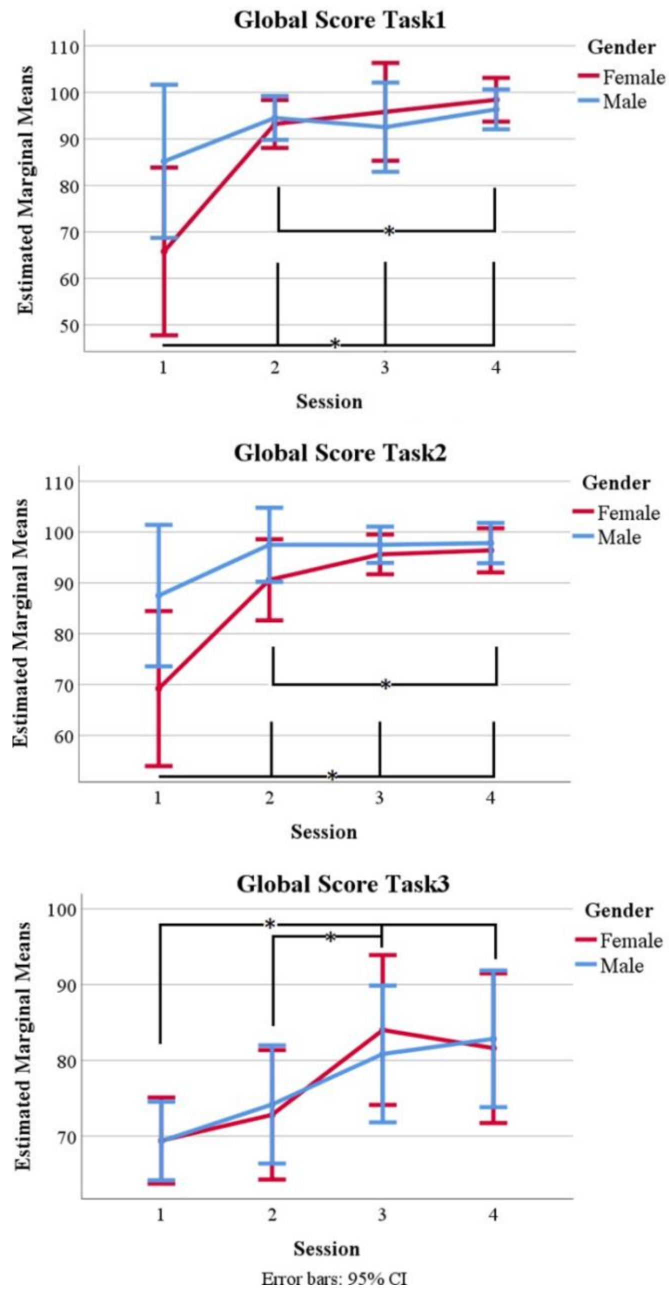

Figure 4-3. Estimated marginal means for global score. Significant differences are marked with black lines. In tasks 1 and 2 differences between sessions were in female group. Differences in task 3 occurred at a general level (linking groups of men and women).

4.3.2 Heart Rate

The results of the ANOVA test for the normalized heart rate are shown in Table 4.2. A significant effect of the task and task x gender was found, no significant effects of session were found. Figure 4.4 shows HR through the training sessions for the three tasks for each gender group. In male group, task 3 had higher HR compared to the other two tasks (easy and intermediate level) throughout all sessions. When comparing between sessions, no significant differences were found in any task for women group. For men group, there was a significant decrease in HR from session 2 to session 3 in task 2. Comparing means between men and women, there were no significant differences in any session for any task.

Table 4-2. ANOVA results for HR.

Significant effect	F	p-value	η2
Session	F (3,27) = 0.182	0.908	0.020
Gender	F (1,9) = 1.125	0.316	0.111
Session x Gender	F (3,27) = 0.696	0.563	0.072
Task	**F (2,18) = 7.974**	**0.003**	**0.470**
Task x Gender	**F (2,18) = 4.510**	**0.026**	**0.334**
Session x Task	F (6,54) = 0.860	0.530	0.087
Session x Task x Gender	F (6,54) = 0.933	0.479	0.094

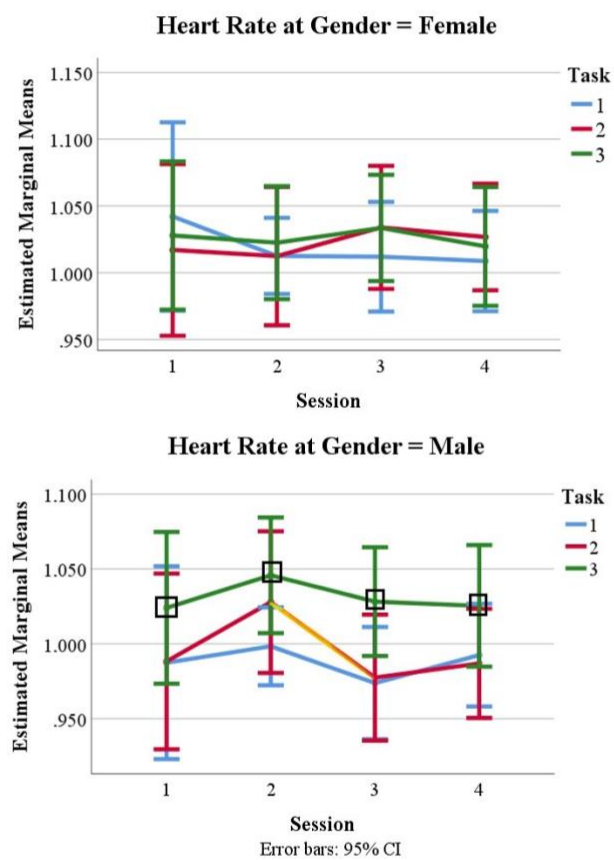

Figure 4-4. Estimated marginal means for normalized heart rate. In male group, significant differences were found in sessions 2 and 3 for task 2 (marked with a yellow line), and task 3 showed the highest HR in all sessions (marked with black squares).

4.4 Discussion

This paper describes the results of changes in heart rate obtained through training sessions of surgery residents using a laparoscopic surgery simulator. As a preliminary study, we decided to perform an exploration of the data, by means of analysis of variance showing the effects of training session, difficulty of the task and participants gender on heart rate and performance.

The results show that the score obtained in the tasks improves with training session, but that it does not have the same behavior for both genders, being in the women where significant changes occur. Additionally, it is shown that for tasks with easy and intermediate level of difficulty, improvement in performance is achieved since the second session, while for the task of greater difficulty more training sessions could be required to improve.

In the acquisition of surgical skills, male medical students performed better and studies found the greatest gender differences in the visuospatial abilities and speed. However, surgical training eliminated initial gender differences [23]. There may also be a cultural influence, as males may be more likely to have played video and ball games during their childhood, which could help develop their visuospatial abilities [24], [25].

In our study, all male participants have affirmed they played video games some-times or always, instead of female volunteers, where only two of them have said they play sometimes. Thus, significant differences between training sessions for women global scores in tasks 1 and 2, may be due they were acquiring new visuospatial skills that men had acquired while playing video games.

Grantcharov et al. [26] evaluated the influence of factors such as gender, hand dominance and experience with computer games in surgeons performance using a VR laparoscopic surgery simulator. They found that men take less time to complete tasks and subjects who used computer games had fewer errors than those who did not use them. In addition, they showed that right-handed subjects performed fewer unnecessary movements. In our study we do not consider differences in hand dominance since only two residents (one woman and one man) were left-handed. Likewise, due to the shortage of residents with previous experience using video games, we do not consider the effects of this variable. We hope that for future analysis we can count with more subjects to also analyze the influence of these factors.

Regarding to heart rate analysis, it was found that HR increases with the complexity of the task. The effect of gender on HR showed that in male group there were significant changes, increases in HR with the difficulty of the task, and a decrease with the training session in the grasping task (intermediate level of difficulty). The male participants showed a high level of HR in task 3 compared to the other two tasks (easy and intermediate level) throughout all sessions; while in female participants no significant differences were found in any task.

The increase in HR with the difficulty of the task is consistent with previous studies [21]. A greater difficulty in the task increases participant's effort to deal with the task demands and this leads to an increase in the mental workload [27], and the mental workload can increase the heart rate [28]. However, a decrease in HR was also expected with the training session and the results obtained were not significant, there is not effect of session on HR. This may be due to the great variability observed in the measurements, both for men and for women groups, even though measurements were normalized by the resting condition. Perhaps, analysis of other signal characteristics such as heart rate variability (HRV) may show better indications, since this is an indirect measure of the autonomic nervous system and it has seen its association with stress [29]. Future studies should include this analysis.

4.5 Conclusion

This work showed an initial exploratory analysis of performance and heart rate data obtained during four training sessions in a laparoscopic surgery simulator of general surgery residents. Our results showed changes in the performance of the task influenced by the training session and gender, indicating that a better performance is achieved in both men and women. The analysis of physiological signals showed an increase in the heart rate associated with the difficulty of the task, but not a decrease with the training session. From these changes, future studies should include analysis of more variables such as HRV, factors such previous experience with video games and hand dominance, as well as other performance features, such as span time and errors, which can be correlated better with the gender differences found here. Our results suggest that it is possible to develop a quantitative surgical training assessment from analysis of performance and physiological signals.

4.6 Acknowledgment

This work was supported by Departamento Administrativo de Ciencia, Tecnología e Innovación (COLCIENCIAS), announcement N. 757 Doctorados Nacionales, and Convenio Jóvenes Investigadores e Innovadores N. 761 through the project Fortalecimiento de la plataforma tecnológica para la formación especializada en el área de la salud y el desarrollo de tecnología biomédica / Ruta N 139C.

4.7 References

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4.8 Appendix: HRV analysis

4.8.1 HRV estimation

Figure 1 shows a scheme of the steps performed to extract HRV measurements. HRV analysis is performed from the RR signal obtained with a peak detection algorithm. The RR signal is cleaned by removing and interpolating outliers (values with a deflection greater than 3 standard deviations from the mean value). Subsequently, the computation of power spectral density is performed using the Welch periodogram. Power values are extracted in low frequency (LF: 0.04-0.15 Hz) and high frequency (HF: 0.15-0.4 Hz) ranges, the LF/ HF ratio is also obtained. These values were normalized by the resting condition of each session.

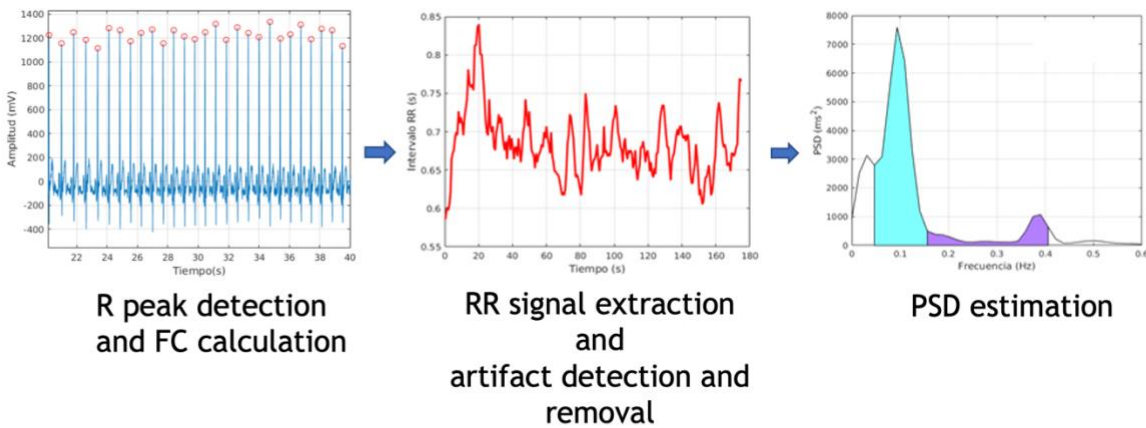

Figure 5. Workflow for the estimation of HRV measurements.

For each of the measures of LF, HF, and LF/HF ratio in each task, a repeated measures ANOVA of 2 factors was performed: Session (4), Gender (2) with a comparison of marginal means (p-values without correct). Sphericity assumption was tested with Mauchly's test, and Greenhouse-Geisser correction was used in cases where the assumption was not met. A p-value < .05 was considered statistically significant.

4.8.2 Results

Table 1 shows the results obtained for LFn measurement. No significant interaction effects between session and gender were found for any of the tasks. However, for the coordination task a significant effect of gender was found, and for women, a significant decrease in LF from session 1 to sessions 2, 3 and 4 was found (Figure 2).

Table 3. ANOVA results for LFn

Task	Effect	F	P-value
Coordination	Gender	F(1, 15) = 4.851	0.044
	Session	F(1.554, 23.308) = 2.887	0.087
	Session x Gender	F(1.554, 23.308) = 1.773	0.196
Grasping	Gender	F(1, 15) = 2.879	0.110
	Session	F(3, 45) = 0.688	0.564
	Session x Gender	F(3, 45) = 0.718	0.546
Peg transfer	Gender	F(1, 15) = 2.543	0.132
	Session	F(3, 45) = 0.719	0.546
	Session x Gender	F(3, 45) = 0.315	0.814

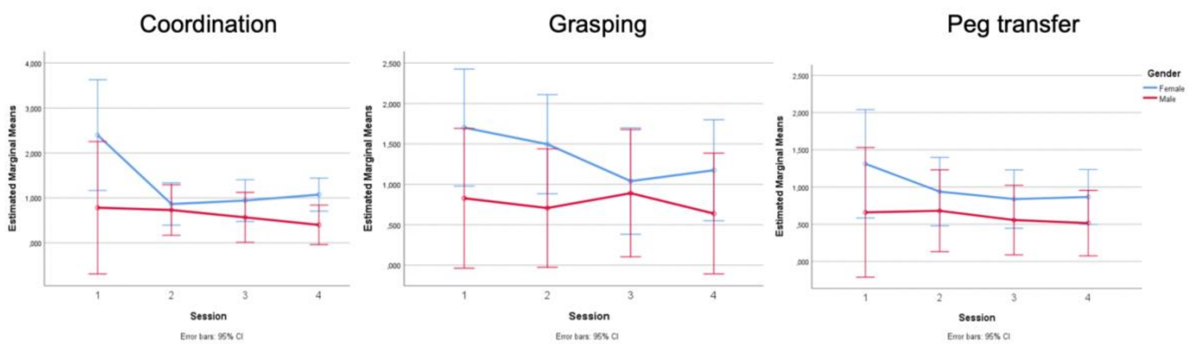

Figure 6. Estimated marginal means for LFn.

Table 2 shows the results obtained for HFn. No significant interaction effects between session and gender were found for any of the tasks, neither significant effect of gender nor session. In multiple comparisons, a significant decrease from session 2 to session 3 in women was found (Figure 3).

Table 4. ANOVA results for HFn

Task	Effect	F	P-value
Coordination	Gender	F(1, 15) = 1.333	0.266
	Session	F(1.089, 16.333) = 0.862	0.468
	Session x Gender	F(1.089, 16.333) = 1.261	0.283
Grasping	Gender	F(1,15) = 0.584	0.457
	Session	F(1.056, 15.846) = 0.768	0.401
	Session x Gender	F(1.056, 15.846) = 0.964	0.346
Peg transfer	Gender	F(1, 15) = 0.009	0.926
	Session	F(1.668, 25.017) = 1.098	0.339
	Session x Gender	F(1.668, 25.017) = 0.823	0.431

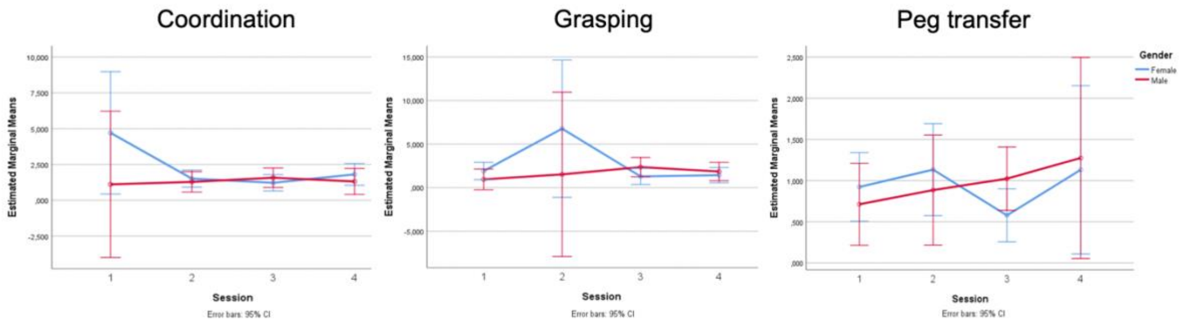

Figure 7. Estimated marginal means for HFn.

Table 3 shows the results obtained for LF/HF ratio. No significant interaction effects were found. For peg transfer task, a significant effect of gender was found. In multiple comparisons, a significant decrease from session 1 to session 2 and 3 was found for men and women in grasping task (Figure 4).

Table 5. ANOVA results for LF/HF

Task	Effect	F	P-value
Coordination	Gender	F(1, 15) = 3.719	0.073
	Session	F(1.643, 24.644) = 0.796	0.440
	Session x Gender	F(1.643, 24.644) = 0.228	0.755
Grasping	Gender	F(1,15) = 2.482	0.136
	Session	F(1.240, 18.604) = 1.435	0.254
	Session x Gender	F(1.240, 18.604) = 1.177	0.305
Peg transfer	Gender	F(1, 15) = 5.188	0.038
	Session	F(3, 45) = 0.514	0.675
	Session x Gender	F(3, 45) = 1.916	0.141

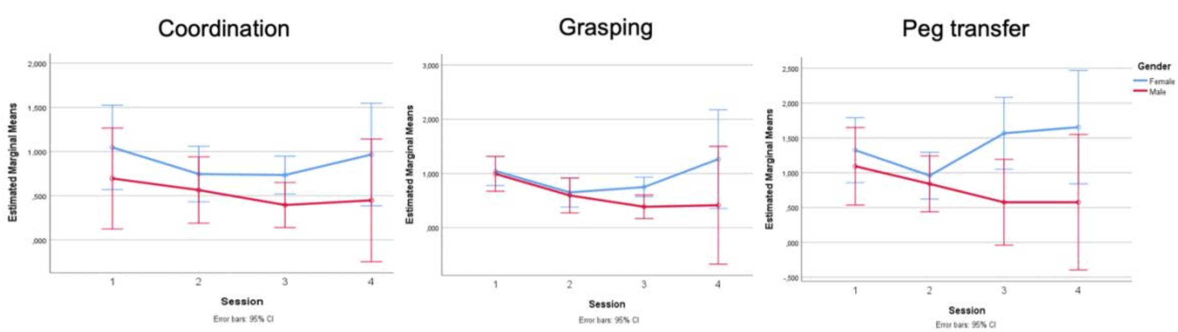

Figure 8.Estimated marginal means for LF/HF.

5. CHANGES IN BRAIN ACTIVITY OF TRAINEES DURING LAPAROSCOPIC SURGICAL VIRTUAL TRAINING ASSESSED WITH ELECTROENCEPHALOGRAPHY

The main challenge of this thesis was to extract neuronal activity from the recorded signals. In any kind of setting (stationary or mobile), EEG recordings are contaminated with noise that must be removed so data can be correctly interpreted. In the pilot test (chapter 3), a signal pre-processing involving robust referencing, filtering and ocular and muscular artifacts remotion by wavelet ICA was initially considered. Although this pipeline cleans the signals obtained at the channel level, the question remains whether the resulting data corresponds to neuronal activity. This is how spatial filters methods such as ICA were chosen, which allows differentiating between the different sources that integrate EEG recorded. Additionally, source localization techniques such as dipole model, allow us to locate the neural sources. Although experiment conditions do not allow us to evaluate specific cognitive processes, we might associate certain brain areas with processes involved in training motor skills. With the analysis carried out in this chapter, it was possible to extract neuronal components such as frontal midline theta and parietal alpha related to working memory, mental workload and visual attention, and evaluate activation changes associated with tasks training.

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Abstract

Objective: Evaluate changes in brain activity of trainees during laparoscopic surgical training from electroencephalographic (EEG) signals in an ecological scenario with few restrictions for the user.

Design: Longitudinal study with two follow-up measurements in the first and last session of a 4-week training with LapSim laparoscopic surgery simulator. Variables analyzed include EEG neuronal activations in theta and alpha bands, tasks performance measures, and subjective measures such as perception of mental workload.

Setting: Medical School, Universidad de Antioquia, Medellin, Colombia.

Participants: First-year surgical residents (n = 16, age = 28.0 ± 2.6 years old, right-handed, 9 females)

Results: Significant improvements in tasks performance were found together with changes in neuronal activity over frontal and parietal cortex. These changes were also correlated with task performance through training sessions.

Conclusions: The use of neurophysiological measures such as electroencephalography combined with source separation techniques allows evaluating neural changes associated with motor training. The experiment proposed in this work establishes less controlled recording conditions leading to a more realistic analysis scenario to cognitive assessment in residents training.

Keywords
Electroencephalography, Independent Component Analysis, Laparoscopic Surgery, Simulation Training, Quantitative Evaluation

5.1 Introduction

Due to the adverse effects linked to operator errors (Kohn et al., 1999) and the cost associated with surgeons training in the operating room (Bridges and Diamond, 1999), greater emphasis has been placed on surgical teaching inside laboratories. Learning basic skills such as hand-eye coordination, depth perception and spatial judgment can be carried out with help of models and simulators (Tsuda et al., 2009). Virtual reality (VR) simulators represent a safe, ethical and repeatable alternative for training programs since they avoid injuries to the patient, reduce costs associated with the use of cadavers and animals, and offer the possibility to repeat surgical procedures as many times as necessary to learn them correctly, while offering the review of the procedures performed (Alaker et al., 2016; Sabench Pereferrer et al., 2013).

Quantifying the performance and learning progress of medical residents helps to improve the learning experience and the training program (Usón-Gargallo et al., 2013). Acquisition of surgical skills involves various aspects to evaluate such as: performance (Martin et al., 1997; Vassiliou et al., 2005), ergonomics (Janeiro, 2007), stress or fatigue, and cognition (Vedula et al., 2017). Of these, cognitive aspects are usually assessed using questionnaires which heavily rely on subjective reflection (Oropesa et al., 2011). Therefore, more analytical and less subjective methods are required to gain better insights into the cognitive processes involved. Cognition encompasses many different processes including perception, attention, transformation of information, storage and retrieval at the appropriate time to make a decision and execute a movement (Madani et al., 2017). Thus, using surgical simulations for training of (future) surgeons allows to address specific aspects of cognition by systematically manipulating parameters of the training task. For example, tissue perception and identification or haptic feedback allows to manipulate the perceptual and motor aspect of the task, respectively. Behavior like errors and time on task provide more insights than subjective measures would allow. However, they provide limited detail regarding the cognitive processes that underpin them. Tracking the neurophysiological changes associated with changes in behavior and cognitive processes during training would provide additional and objective evidence related to the acquisition of new skills.

Neuroimaging methods such as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) have shown neural changes in response to practice (Kelly and

Garavan, 2005). At the beginning of training, activations in attentional and control areas (prefrontal cortex (PFC), anterior cingulate cortex (ACC) and posterior parietal cortex (PPC)) are presented. After practice, activation increases are observed over task-specific areas such as primary and secondary motor or sensory cortices. The study of these changes in laparoscopic skills training has been tested using functional near-infrared spectroscopy (fNIRS) (Nemani et al., 2018). This work showed that activation decreased over PFC and increased over primary motor cortex (M1) and supplementary motor area (SMA) as motor skill proficiency increased.

Along with fNIRS, surface electroencephalography (EEG) is a brain mapping technique that allows to assess neural activity performance of tasks that require active behavior without constraining and interfering with its execution. Furthermore EEG provides high temporal resolution close to the timescale of neuronal dynamics (Unturbe et al., 2008). Several works have demonstrated its applicability in performance evaluation during complex tasks such as military training (Johnson et al., 2014), training in flight simulators (Borghini et al., 2016b), traffic controllers (Borghini et al., 2014) and robot-assisted laparoscopic surgery (Borghini et al., 2016a) as well as in visuomotor training for prosthetic control (Parr et al., 2019). Results from the aforementioned studies show changes in power spectral density measures, relating alpha (8 – 13 Hz) and theta (4 – 8 Hz) bands with learning. These variations occur over frontal channels for theta and over parietal channels for alpha band. Enhancement in frontal theta power has been associated with cognitive effort, task difficulty and working memory (WM) processes (Cavanagh and Frank, 2014; Gevins et al., 1997). Parietal alpha band is related to attentional processes (Klimesch, 1999), linking the request for attentional resources to alpha desynchronization and therefore power reduction (Lopes da Silva, 1991).

The analyses described in the previous studies were carried out at the channel level, and, although EEG has advantages in terms of portability, cost and temporal resolution compared to other techniques such as fMRI, this technique has limitations in spatial resolution. Thus, EEG does not allow for a precise anatomical localization of brain sources in the millimeter range. However, previous simulations and invasive approaches have shown that the EEG is able to provide source localization accuracy down to 1 to 2 cm (Akalin Acar and Makeig, 2013; Smith et al., 1985). Using distributed source reconstruction approaches further require high density recordings to allow for reliable source reconstruction (Michel et al., 2004). Independent component analysis (ICA) provides an approach for decomposing the recorded scalp signals into instantaneously independent time source activations even in EEG recordings in actively behaving participants (Gramann et al., 2014, 2011; Makeig et al., 2009). The associated scalp maps allow for an estimate of their anatomical localization even with lower spatial densities (Klug and Gramann, 2020) using equivalent dipole modelling to reconstruct physically distinct compact cortical areas (Hyvärinen, 2013). Representative brain components can subsequently be identified based on their cortical localizations, scalp maps projections, time courses and power spectral features. Some of these sources are reliably identified as originating from the parietal cortex exhibiting alpha band activity as well as frontal midline areas demonstrating task-related theta band activity (Delorme et al., 2012; Gramann et al., 2010; Onton et al., 2005). These activations have been detected both at rest and tasks such as visual event-related potentials (ERPs) (Jungnickel and Gramann, 2016; Makeig et al., 2002) and working memory (Onton et al., 2005).

The current study attempts to investigate cortical oscillatory dynamics during training in laparoscopic surgery using EEG recordings in conjunction with ICA and subsequent source localization techniques (Delorme et al., 2011). We expected that training cause activation changes in the independent components (IC) described above (frontal theta and parietal alpha), based on their association to cognitive processes involved. Since the increase in frontal theta is related to effort in working memory and task difficulty (Langer et al., 2013; Onton et al., 2005), and the decrease in alpha with increases in visual attention, we presume that training will cause a decrease in theta band and an increase in alpha band over frontal and parietal regions respectively.

5.2 Experimental Procedure

5.2.1 Subjects and experimental protocol

Sixteen first-year surgical residents (28.0 ± 2.6 years old, right-handed, 9 females) of Medical School of Universidad de Antioquia participated in this study. All participants signed informed consent approved by the bioethics committee of the Universidad de Antioquia (Act: 18-19-787, 2018). Residents were complete novices to surgical tasks in general and had no previous contact with the simulator before starting the study.

The experiment consisted in a 4-week training program with the VR simulator LapSim® (Surgical Science Ltd., Göteburg, Sweden), one session per week, where residents performed three consecutive tasks. Each series of tasks was executed three times. The EEG recordings were taken during the second repetition of each task. One of the researchers manually controlled the start and end of the acquisition while the resident started and finished the execution of the task. On average, the recordings length was: Task 1: 61.42 ± 25.84 s; Task 2: 88.81 ± 45.24 s; Task 3: 236.94 ± 95.27. The analyses presented in this work was performed on the first (S1) and last (S4) training sessions, since we expected to find the most pronounced changes between the beginning and the end of the training. Before executing the tasks, a reference condition was recorded during a 2 min baseline while the subject was in a standing position in front of the simulator with closed eyes following by 2 min with opened eyes looking a white screen. During the signals recording, participants were asked to remain as still as possible, not to make head movements and not to speak.

Additionally, at the end of each session, participants filled the National Aeronautics and Space Administration-Task Load Index (NASA–TLX) questionnaire (Hart and Staveland, 1988), in order to assess the subjectively experienced workload across training sessions. This questionnaire has been also adopted in the evaluation of mental workload in surgical research (Moore et al., 2015). The total NASA-TLX score ranges from 0 to 100 and it is calculated as an average of six factors: Mental Demand, Physical Demand, Temporal Demand, Performance, Effort and Frustration. In order to maintain similar experimental conditions during sessions, the experiments were run in the afternoon (1:00 - 5:00 pm) and participants were asked to avoid alcohol, caffeine and non-ordinary workout routines before each training session.

5.2.2 LapSim VR simulator

Three tasks from the LapSim® Basic Skills and Task Training modules were chosen for the study. In the first session, each task was explained and shown through an explanatory video to the participants. The default design and assessment parameters of each exercise was determined by the software. The overall score (%) for each task was calculated according to parameters based on total time of execution, errors, tissue damage and instrument path length (Surgical Science, 2016). The tasks included are (Figure 5.1):

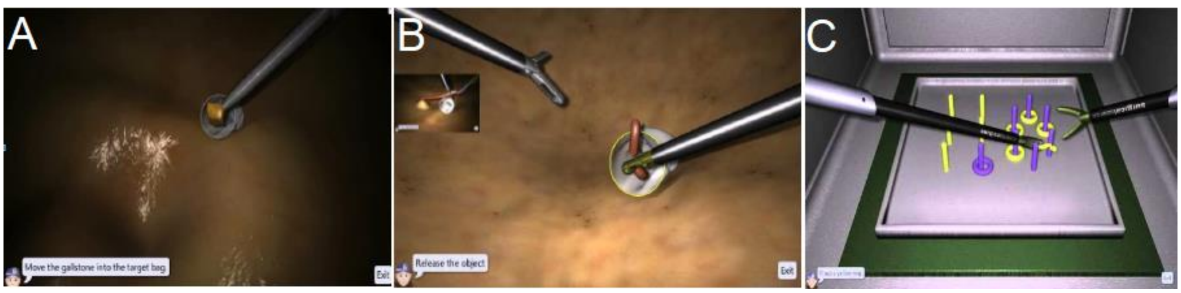

Figure 5-1. LapSim tasks. A: coordination; B: grasping; C: peg transfer.

Coordination: combines the use of the camera with left hand and one instrument with right hand. Participants hold the camera and locate ten randomly appearing objects, pick them up with the instrument and transfer them to a target.

Grasping: involves grasping six vertical pipes or appendices, pull them from the ground and transport them to a target. Each appendix must be taken with the hand indicated by the software.

Peg transfer: consists of a board with 12 pegs (two sets of six pegs) and six rings. The task requires the user to lift each ring from a peg, transfer it between hands and place it in a designated peg on the other set.

5.2.3 EEG recordings

Electroencephalographic signals were recorded using a Natus® Quantum™ (Natus Neurology Incorporated, Winsconsin, USA) amplifier with a sampling frequency of 1024 Hz. A cap with 60 AgCl channels positioned according to the 10-10 system was used. Right mastoid bone was used as reference and AFZ as ground. Additionally, the vertical and horizontal electrooculographic activity (EOG) was recording by bipolar electrodes. Horizontal EOG electrodes were put in the outer canthus of each eye and vertical EOG in the supraorbital and suborbital region of right eye.

5.2.4 EEG signal pre-processing

The pre-processing pipeline was based on established algorithms of the EEGLAB toolbox, an open-source toolbox based on Matlab (Delorme and Makeig, 2004). Due to the short length of the records in the different conditions, which affects analysis techniques such as ICA (Makeig et al., 2004), resting and tasks recordings were concatenated. The data was imported, down sampled to 512 Hz, and filtered between 4 and 50 Hz (Hamming windowed sinc FIR filter, order = 846, zero phase shift). Bad channels and artifactual time periods, such as head movements, disconnections or impedance jumps were removed by visual inspection without considering eye movements as artifacts since these add information to following analysis. Subsequently, the data was re-referenced to a common average reference and bad channels removed were interpolated. Then, ICA decomposition was performed on the concatenated data using the adaptive ICA mixture model algorithm (AMICA) (Palmer et al., 2008, 2006) with default settings. To estimate the location of IC sources, an equivalent dipole model was computed for each IC using a boundary element head model (BEM) based on the MNI brain (Montreal Neurological Institute, MNI, Montreal, QC, Canada) implemented by DIPFIT toolbox (Oostenveld and Oostendorp, 2002).

The weights and spheres returned from the AMICA decomposition, and their equivalent dipoles were copied to the original continuous EEG data after down sampling, filtering, bad channel rejection, re-reference and bad channel interpolation. This way, the full data range was used and potential artifacts on the sensor level were removed independently from the preprocessing for ICA decomposition. The channels removed and interpolated were identical as those detected in the concatenated recordings. Then, recordings were segmented into 2 s epochs with a 0.5 s of overlap. Finally, an automatic artifactual epochs rejection was applied, including detection of fluctuations greater than 1000 µV and unlikely activity with a threshold of 5 SD, rejecting a maximum of 5 % of total trials per iteration.

5.2.5 IC clustering analysis

Two EEGLAB studies were created combining the five recording conditions of all subjects in each session (S1 and S4). One study was created for each training session in order to group the largest number of subjects in each study. Brain ICs were selected using the EEGLAB plug-in for automatic IC classification (ICLabel) (Pion-Tonachini et al., 2019). ICLabel classifies the components into seven categories (brain, muscle, eye, heart, line noise, channel noise, other), calculating the probability of each IC for each class. Scalp topographies, power spectral densities and dipole location are the IC features used as input to an artificial neural network that computes the labels. A threshold of 75% probability to be a brain component was established. A total of 210 ($\mu = 13.1 \pm 4.1$ per subject) and 228 ($\mu = 14.3 \pm 5.2$ per subject) brain components were obtained in the first and last training session respectively.

In order to identify equivalent brain components across subjects, an IC clustering analysis was performed (Onton and Makeig, 2006). Using the EEGLAB preclustering function, distances between all ICs were calculated based on weighted measures of power spectrum (frequency range: 4 – 50 Hz), components scalp maps and their equivalent dipole model locations. For power spectrum and scalp maps measurements, the dimension was reduced to the first 10 principal components (PCA), dipole location has three dimensions. The subsequent measures were normalized and weighted to then be combined into the cluster positions vectors. A factor of 10 was used for dipole locations in order to have tight clusters and to compensate for its low dimensionality. Spectral measures were weighted by a factor of 3 since they contain relevant information related to the component activation. Finally, the standard weight of 1 was used for scalp maps. An additional reduction of 10 PCA was used for the final dimension of the cluster position vectors.

K-means algorithm implemented in EEGLAB was used for clustering. The number of clusters was set as the number suggested by the software (mean of ICs over all subjects) minus one in order to retain the largest number of components in each study (S1 = 13; S4 = 14 clusters). Outlier clusters were formed with ICs whose distances were greater than 3 SDs to the mean of any cluster centroid. When the cluster contained more than one IC per subject, the IC with the smallest residual variance of the equivalent dipole model was selected. Finally, clusters which including frontal midline theta (4 – 8 Hz) activity and central parietal alpha band (8 – 13 Hz) were identified for the analysis. To find an overlap of the clusters between the two studies, average scalp maps for both cluster solutions from session 1 and session 4 were correlated and the clusters that had the highest correlation between sessions were selected (see supplementary material).

5.2.6 Power spectrum analysis

Power spectrum analysis over channels and individual IC activations in each cluster was computed using the multitaper spectral estimation method available in MATLAB Chronux toolbox (Mitra and Bokil, 2008). According to the literature described in the introduction section, relative power values in theta band (4 – 8 Hz) over frontal channels (AF3, AF4, F5, F3, F1, FZ, F2, F4, F6) and for the frontal midline cluster were calculated. Likewise, alpha power (8 – 13 Hz) over central parietal channels (CP5, CP3, CP1, CPZ, CP2, CP4, CP6, P5, P3, P1, PZ, P2, P4, P6) and for the central parietal cluster was computed. Mean power values were calculated across a minimum of clean epochs in each condition (resting: 50 epochs, coordination and grasping: 20 epochs, peg transfer: 50 epochs). The numbers above refer to the shortest recording length among all subjects and sessions. In order to reduce variability between subjects, task power measurements were normalized with respect to closed eyes resting condition.

5.2.7 Statistical analysis

A repeated measures ANOVA with two factors: Session (2 levels) and Task (3 levels) was used to evaluate the spectral power variation across sessions and tasks. One ANOVA analysis was performed for each measurement: task total score, and power values in channels and IC clusters. For perceived workload index only a paired t-test was performed. Mauchly's test was used to evaluate the sphericity assumption, and correction of the degrees of freedom was made with the Greenhouse-Geisser procedure. Multiple comparison analyses were performed between the sessions using paired t-tests. A p value < 0.05 was established as significant. Further, in order to provide complementary information to the p-value, Cohen's d (Cohen, 1977) measure was calculated to assess the effect size of the differences. According to Lakens et al., a value greater than 0.5 will be considered as medium and a value greater than 0.8 as a large effect (Lakens, 2013). Spectral power measurements were also correlated with task performance using repeated measures correlation (rmcorr) (Bakdash and Marusich, 2017). This correlation determines the common within-individual association for paired measures assessed on two or more occasions for multiple individuals. After removing measured variance between-participants, rmcorr provides the best linear fit for each participant using parallel regression lines (the same slope) with varying intercepts.

5.3 Results

5.3.1 Performance

Figure 5.2 shows the means of the total score in each task and session. ANOVA showed a statistically significant effect of session ($F(1,15) = 42.943$, $p < 0.001$) and task ($F(2,30) = 15.982$, $p < 0.001$) factors. Multiple comparisons analyses showed a significant improvement in performance with training session in all tasks (Table 5.1).

Table 5-1. Tasks performance. Paired sample t-test, p-value and Cohen d effect size.

	Coordination	Grasping	Peg transfer
t	-4.634	-4.295	-3.969
P-value	0.001	0.001	0.001
Cohen d	-1.434	-1.217	-1.203

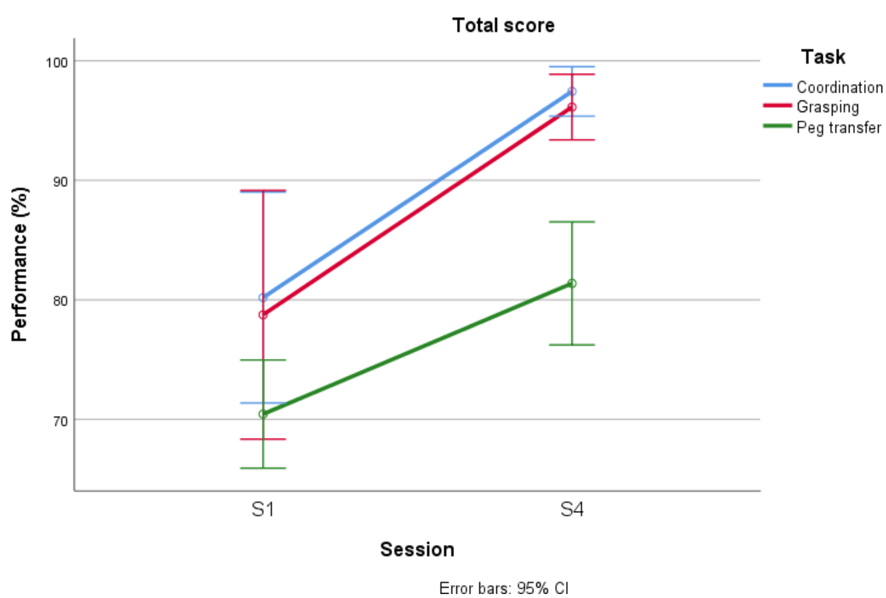

Figure 5-2. Means graph of tasks performance.

5.3.2 Electrophysiological data

Channel measurements

Figure 5.3 shows the mean graphs for theta power in frontal channels and alpha power in central parietal channels. ANOVA showed a statistically significant interaction effect between session and task ($F(2,30) = 5.893$, $p < 0.05$) for theta band. Instead for the alpha band there was only statistically significant effect of task ($F(1.396,20.945) = 15.615$, $p < 0.001$). Table 5.2 shows the multiple comparison analyses for the two groups of channels.

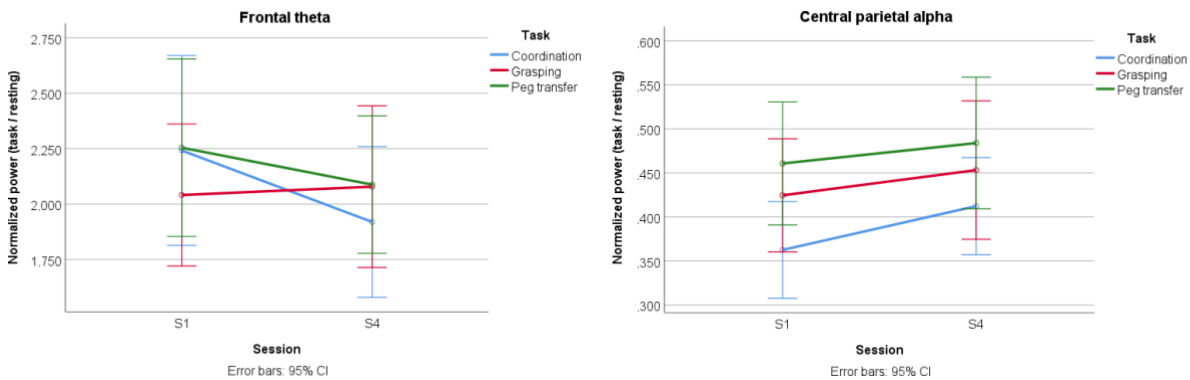

Figure 5-3. Means comparison in channels power spectrum analysis

Table 5-2. Statistical analysis of channels power spectrum measures.

Channels		Coordination	Grasping	Peg transfer
Frontal theta	t	1.972	-0.238	1.170
	P-value	0.067	0.815	0.260
	Cohen d	0.444	-0.058	0.248
Central parietal alpha	t	-1.671	-0.684	-0.611
	P-value	0.115	0.504	0.551
	Cohen d	-0.481	-0.213	-0.171

IC clusters

Table 5.3 presents information corresponding to the clusters analyzed: the number of subjects within each cluster and the centroid localization, which is an approximation of the origin of the cortical sources, limited by the source localization method and the use of standard electrode positions and head model. Subjects that were present in both sessions 1 and 4 in each cluster were taken for further analysis (frontal midline: 10 subjects; central parietal: 8 subjects). Figure 5.4 shows the mean scalp maps and dipoles of each cluster.

Table 5-3. Clusters location.

IC cluster	Session	Number of subjects	Talairach coordinates (x, y, z)	Gray Matter nearest to
Frontal midline	S1	14	-1, 7, 39	Left Cerebrum, Limbic Lobe, Cingulate Gyrus, Gray Matter, Brodmann area 32, Range=1
	S4	11	-6, -1, 32	Left Cerebrum, Limbic Lobe, Cingulate Gyrus, Gray Matter, Brodmann area 24, Range=1
Central parietal	S1	14	0, -46, 23	Left Cerebrum, Limbic Lobe, Posterior Cingulate, Gray Matter, Brodmann area 23, Range=1
	S4	10	13, -33, 47	Right Cerebrum, Frontal Lobe, Paracentral Lobule, Gray Matter, Brodmann area 5, Range=1

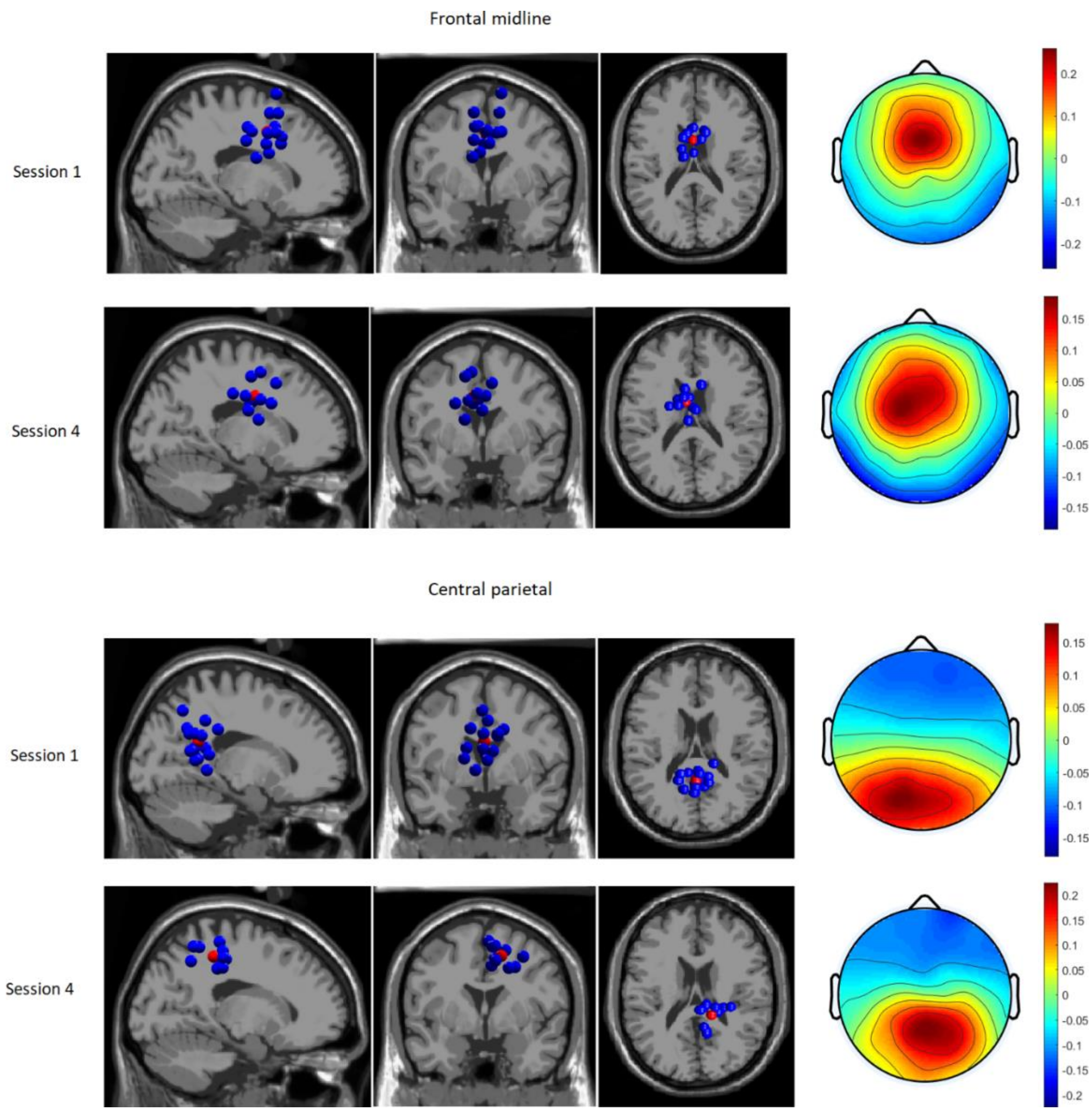

Figure 5-4. Dipoles (left) and mean scalp maps (right) of frontal midline and central parietal clusters across training sessions.

IC power spectrum

For theta band, ANOVA did not show statistically significant effects of session or task. On the contrary, for the alpha band there was a statistically significant effect of the session ($F(1,7) = 7.340$, $p < 0.05$). When performing the multiple comparisons, significant increases in alpha power were found for the central parietal cluster (Table 5.4). Although, for theta band the differences were not statistically significant, the Cohen's d values showed a medium effect size (> 0.5). Figure 5.5 shows the mean graphs for these measurements.

Table 5-4. Statistical analysis of IC power spectrum measures.

Cluster		Coordination	Grasping	Peg transfer
Frontal midline theta	t	1.556	1.178	1.975
	P-value	0.154	0.269	0.080
	Cohen d	0.554	0.514	0.691
Central parietal alpha	t	-3.111	-1.725	-3.065
	P-value	0.017	0.128	0.018
	Cohen d	-1.240	-0.717	-0.945

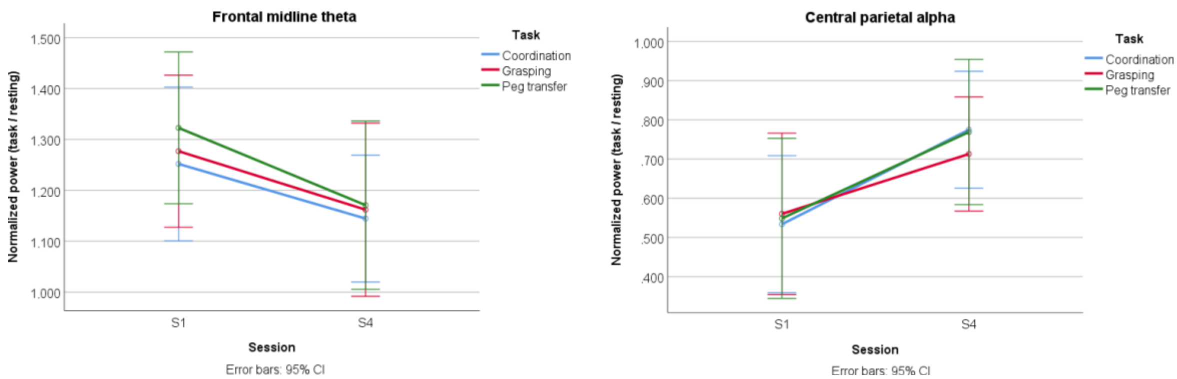

Figure 5-5. Means comparison in IC power spectrum analysis.

5.3.3 Correlations with performance

Table 5.5 shows the correlation results. Statistically significant positive correlations were found for frontal midline theta in coordination and peg transfer tasks (Figure 5.6). A significant negative correlation was also found between central parietal cluster and coordination task.

Table 5-5. Correlation analysis between power spectrum measures and task performance. Highlighted in bold are shown significant coefficients (p-value < 0.05).

Cluster		Coordination	Grasping	Peg transfer
Frontal midline theta	r	-0.623	-0.549	-0.606
	P-value	0.041	0.080	0.048
Central parietal alpha	r	0.740	0.595	0.430
	P-value	0.023	0.091	0.248

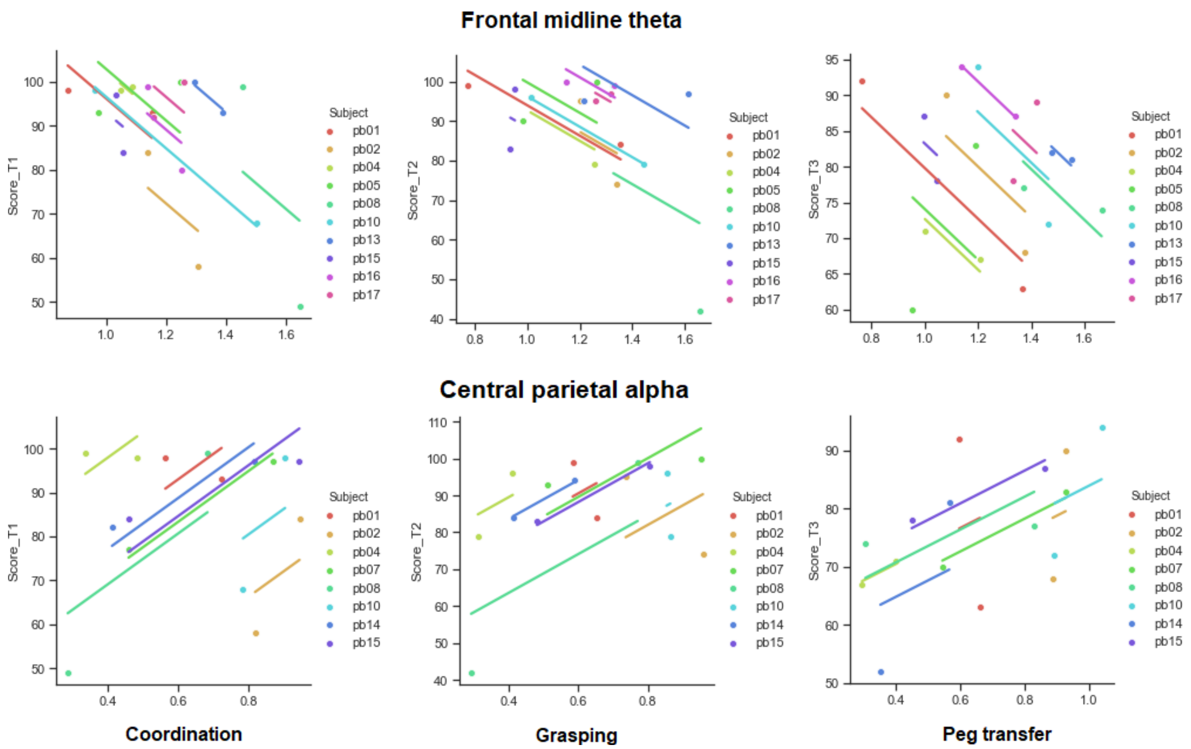

Figure 5-6. Repeated measures correlation graphs.

5.3.4 Perceived workload

There was no statistically significant difference in the perceived workload total score. However, analyzing by test factors, significant differences were found in temporal demand and perceived performance of NASA_TLX test (Table 5.6). Residents perceive a decrease in temporal demand along with an increase in performance with training (Figure 5.7).

Table 5-6. NASA_TLX results.

	Total score	Temporal demand	Performance
t	1.119	2.683	-2.734
P-value	0.281	0.017	0.015
Cohen d	0.317	0.714	-0.804

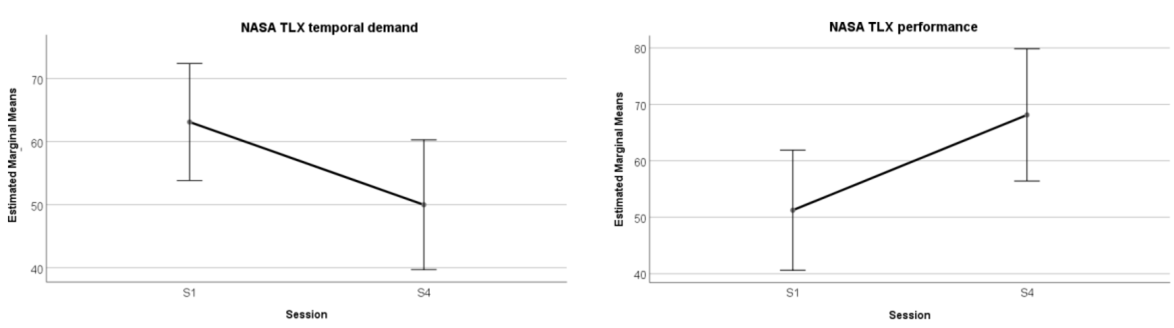

Figure 5-7. Temporal demand and performance of NASA_TLX questionnaire.

5.4 Discussion

This study evaluated neural adaptations related to improvement in laparoscopic surgical training with VR. With the aim to provide new insights about motor training from ICA analysis, in this work we compared the changes that occur at channels level with the activations at components level. Channel level analysis of power indicated slight differences observed at the beginning and at the end of the training. The differences were elicited in the theta and alpha rhythms for coordination task, the one with the lowest level of difficulty. This visuospatial task was the first contact with the simulator. The changes exhibited a decrease in theta power over frontal channels and an increase in alpha rhythm over central parietal channels. ICA analysis improved previous results and enabled localization of neural sources, showing a decrease in theta power in or near the ACC and an increase in alpha rhythm in the parietal lobe for all tasks. IC power changes were also correlated with task performance, showing a positive correlation with frontal midline theta and a negative correlation with central parietal alpha. In addition, the adopted subjective measures demonstrated changes in the perceived mental workload, such as reduction in temporal demand and increase in perceived performance.

The current experiment evaluated brain activity in an ecologically setting, with few restrictions for the user. Assuming that our hypothesis is true, the results found in this work show that it is likely that the changes in brain rhythms are related to different cognitive processes involved in training and skill acquisition. Reduction in the activation of control areas such as ACC was associated with learning and has been consistent in both neuroimaging (Kelly and Garavan, 2005; Nemani et al., 2018) and electrophysiological studies with the analysis over frontal channels (Borghini et al., 2016b, 2013). ICA analysis allowed for localizing the source of activity to originate in or near ACC and associating the frontal midline power modulation with visual WM load (Onton et al., 2005). It is suggested that with task performance improvement, the mental workload and cognitive effort will decrease, leading to frontal theta reduction (Zander et al., 2017). This was also observed with the negative correlations obtained between frontal midline theta activation and performance.

Studies have shown that during motor learning an automatization process occurs where neural processes shift from cortical areas to subcortical areas such as basal ganglia (Kelly and Garavan, 2005). Automation requires less attentional resources, and it might indicate the progressive alpha increase. The alpha rhythm seems to act as a modulatory gate for information process with a decrease in power enabling attentional processes (Klimesch et al., 2007). Therefore, it is assumed that when the operator learns to perform a task, attention load decreases and alpha power increases (Jaquess et al., 2018). The positive correlation between central parietal alpha with performance obtained in the present study support this association.

There are several constrains that must be considered in this work, such as sample size and aspects of the experimental setup. The number of participants that were recorded was limited by the new residents who were admitted by the faculty (7 – 8 per year). Expanding the sample size is one of the main challenges in this project, since it could increase the observed differences. Also, the lack of a control group makes it unclear whether the same effects could have occurred only due to adaptation to the VR simulator. Including a control group or making a long-term measurement that accounts for the skill acquisition over time are aspects to consider for future research. Second, due to less controlled experimental setup, in which EEG recordings were done without time control in tasks execution and as a continuous data record without event marks, it does not allow us to make inferences to specific cognitive processes. However, it was possible to show neural changes that might be related to processes involved in training such as attention, working memory and motor skill acquisition. A recent review shows the need to consider the processes that may be involved in motor control tasks: muscular effort, working memory and sensorimotor feedback (Parr et al., 2021).

The amount of data recorded (signal length) poses problems with EEG analysis techniques that are highly dependent on the quantity and quality of data (Makeig et al., 2004). The reduced amount of data available in the present study was the reason why it was necessary to concatenate the different recording conditions to obtain a good ICA decomposition. Also, the use of source analysis methods provides an approximation to the anatomical location where cortical activity is generated. This approximation is limited by the use of standard electrode locations and head models. Although a cap with channels positioned according to a standard system, variability in head shape and size between subjects makes the approach less reliable. One solution is to measure channels location per subject (Michel and Brunet, 2019).

It is also important to consider that the low number of electrodes used in this work affects the accuracy of sources estimation. It is known the higher number of electrodes, the smaller the regions of interest in the estimation of the EEG source (Song et al., 2015). A 60-channel montage was selected based on setup time and costs as the minimum viable to obtain acceptable results. However, recent work shows that using empirical mode decomposition to clean and reconstruct neural EEG signals, even fewer electrodes may be sufficient to obtain good source estimation (Soler et al., 2020). With the calculation of the equivalent electric dipole on the independent components with the highest probability of being neural, we think we have a better source estimation.

Finally, clustering analysis allowed us to find similar components between subjects and analyze them as a group. However, as it was seen in the results, different subjects contributed to different clusters, and, since the analysis was performed for each training session, the groups obtained differed both in topographic maps and in the centroid location between sessions. Reason why correlation analysis was used to find an overlap between the clusters of the two studies. Clustering involves tuning different parameters (measure weights, number of clusters, etc..), which can reduce objectivity of the analysis and reproducibility of the results (Bigdely-Shamlo et al., 2013).

Despite the above concerns, we could show that the use of neurophysiological measures such as electroencephalography combined with source analysis techniques allow evaluating neural changes associated with surgical training. The experiment proposed in this work establishes less controlled recording conditions leading to a more realistic analysis scenario to cognitive assessment in residents training. This could provide a starting point for the evaluation of medical training in simulation that can be extended to the operating room, and it would lead to broader applications such as the evaluation of interventions in motor rehabilitation, or the development of classifiers to determine the skill level of a subject.

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5.7 Supplementary

5.7.1 Cluster selection

Figures 1 and 2 show the average scalp map for all clusters obtained in sessions 1 and 4 respectively. In session 1, clusters 7 and 15 were identified as frontal midline theta, and cluster 14 was selected as central parietal alpha activity. On the previous topographical maps, 2-D correlation coefficients were calculated with all average maps of session 4. Table 1 shows the correlation values. Clusters from session 4 with the highest correlation values were selected (clusters 14, 10 and 13).

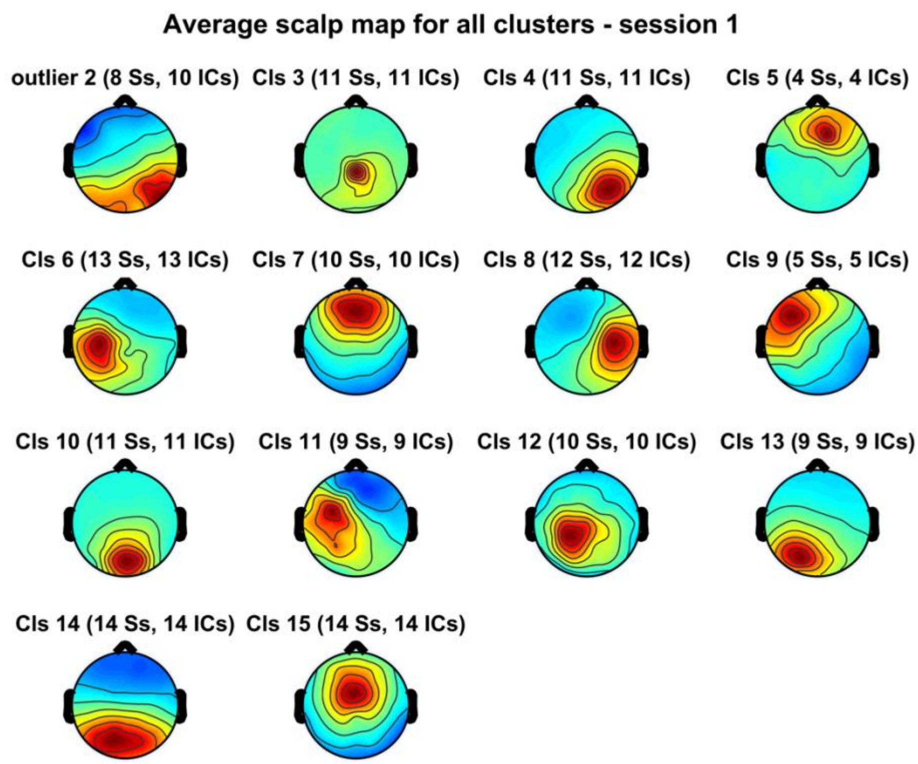

Figure 8. Mean scalp maps session 1. Clusters 7 and 15 were identified as frontal midline and cluster 14 as central parietal activity.

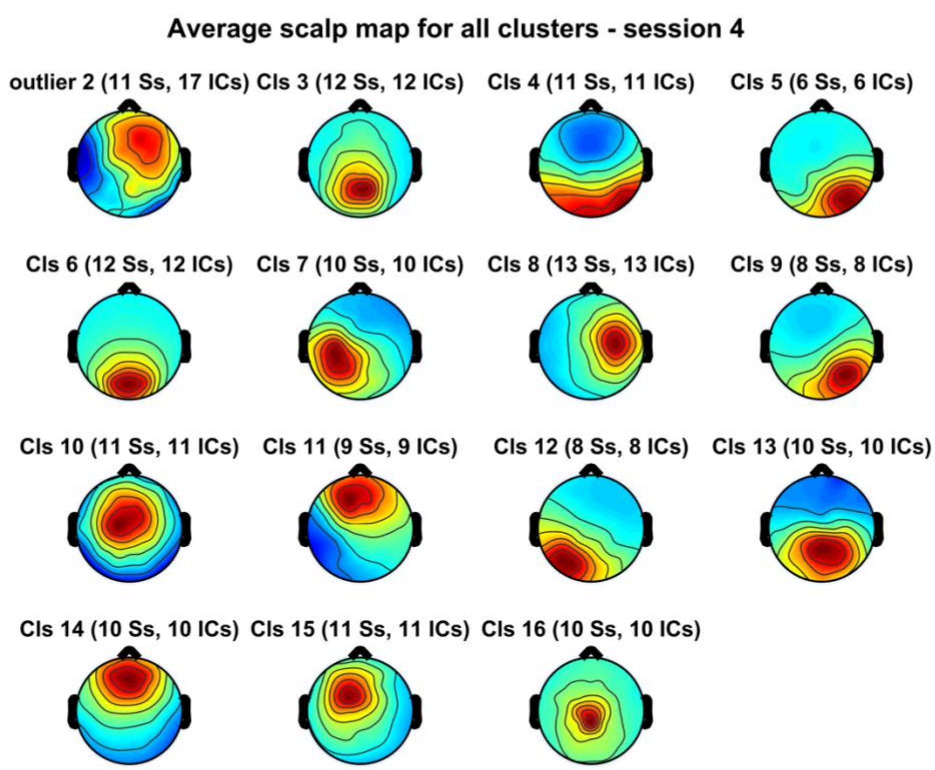

Figure 9. Mean scalp maps session 4. Clusters 14, 10 were selected as frontal midline and cluster 13 as central parietal respectively.

Table 7. Correlation coefficients between clusters of sessions 1 and 4.

Session 4	Session 1			
	Cls 7	**Cls 14**	**Cls 15**	**Cls 10**
Cls 3	-0.278	0.682	0.035	0.784
Cls 4	-0.874	0.887	-0.813	0.671
Cls 5	-0.638	0.676	-0.588	0.666
Cls 6	-0.563	0.883	-0.387	**0.982**
Cls 7	-0.476	0.639	-0.123	0.373
Cls 8	0.136	-0.219	0.257	-0.070
Cls 9	-0.721	0.724	-0.632	0.664
Cls 10	0.643	-0.400	**0.951**	-0.220
Cls 11	0.912	-0.780	0.691	-0.457
Cls 12	-0.636	0.858	-0.469	0.572
Cls 13	-0.706	**0.911**	-0.409	0.810
Cls 14	**0.994**	-0.777	0.798	-0.511
Cls 15	0.707	-0.419	0.905	-0.291
Cls 16	-0.041	0.293	0.413	0.342

5.7.2 Other clusters analysis

Table 2 presents information corresponding to the clusters analyzed: the number of subjects within each cluster and the centroid localization. Subjects that were present in both sessions 1 and 4 in each cluster were taken for statistical analysis (frontal theta: 10 subjects; occipital: 8 subjects). Figure 3 shows the mean scalp maps and dipoles of each cluster.

ANOVA analysis did not show significant effects of session or task for any cluster. In theta band, session: $F(1,6) = 0.219$, $p = 0.656$, task: $F(2,12) = 2.839$, $p = 0.098$. For alpha band, session: $F(1,7) = 0.119$, $p = 0.740$, task: $F(2,14) = 0.857$, $p = 0.446$. Figure 4 shows the mean graphs for these clusters.

Table 8. Clusters location.

IC cluster	Session	Number of subjects	Talairach coordinates (x, y, z)	Gray Matter nearest to
Frontal theta	S1	10	7, 32, 10	Right Cerebrum, Limbic Lobe, Anterior Cingulate, Gray Matter, Brodmann area 24, Range=1
	S4	10	5, 32, 6	Right Cerebrum, Limbic Lobe, Anterior Cingulate, Gray Matter, Brodmann area 24, Range=0
Occipital alpha	S1	11	6, -88, 26	Right Cerebrum, Occipital Lobe, Cuneus, Gray Matter, Brodmann area 19, Range=0
	S4	12	3, -82, 19	Right Cerebrum, Occipital Lobe, Cuneus, Gray Matter, Brodmann area 18, Range=0

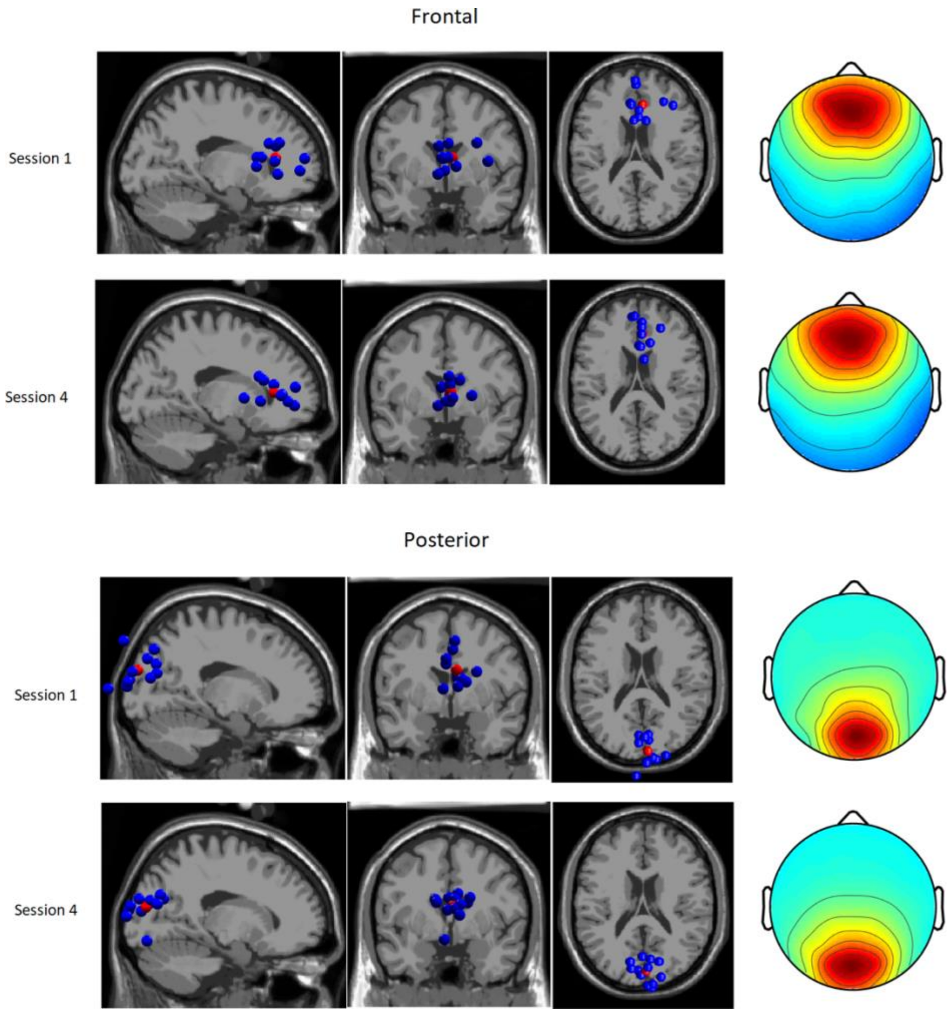

Figure 10. Dipoles (left) and mean scalp maps (right) of frontal midline and posterior clusters across training sessions.

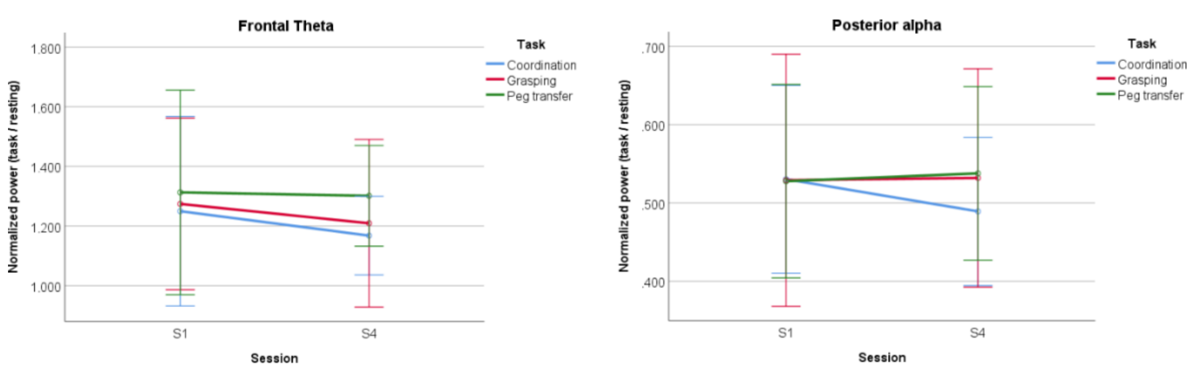

Figure 11. Means comparison in IC power spectrum analysis.

6. ELECTROENCEPHALOGRAPHIC FUNCTIONAL CONNECTIVITY IN LAPAROSCOPIC SURGERY TRAINING

This chapter describes the study of the functional brain interactions during training. Since clustering analysis performed in chapter 5 did not allow us to have the same subjects in each IC cluster, it was decided to extract cortical signals using an inverse solution approach with wMNE algorithm. Here, brain functional connectivity was evaluated on those regions not only related to previous work activations, but also associated with motor learning (PFC, M1 and SMA). Result showed changes in the interactions between ACC and SMA with parietal cortex in alpha band. Fronto-parietal interactions seem to play an important role in processes such as working memory and mental workload.

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Document in preparation.

Abstract

Objective: Finding performance markers in a laparoscopic task from functional EEG connectivity measures.
Design: Two follow-up measurements in the first and last session of a 4-week training with LapSim laparoscopic surgery simulator. Coherence in theta, alpha and beta bands was calculated as a measure of functional connectivity between cortical wMNE solutions of regions related with motor learning. Changes in connectivity were related to changes in performance using repeated measures correlation.
Setting: Medical School, Universidad de Antioquia, Medellin, Colombia.
Participants: First-year surgical residents (n = 16, age = 28.0 ± 2.6 years old, right-handed, 9 females)
Results: Significant increase in task performance with training sessions was associated with a decrease in functional connectivity between frontal (ACC, SMA) and parietal region (PPC).
Conclusions: alpha connectivity play a critical role in motor training.

Keywords

Electroencephalography, Functional Brain Connectivity, Coherence, Laparoscopic Surgery Skills, Simulation Training, wMNE.

6.1 Introduction

Surgical training is essential to ensure patient safety and reduction of medical errors. Procedures such as laparoscopic surgery requires surgeons learn to adapt to a new visual two-dimensional interface without depth perception and reduce tactile feedback [1]. Virtual reality simulation offers the opportunity for novices to learn in a controlled environment free from any adverse consequences to real patients [2]. Basic technical skills such as hand-eye coordination can be improved and transferred to operating room environment [3].

There are several metrics for performance evaluation in a surgical training related to behavioral aspects (errors, time) and cognition (knowledge, fatigue) [4]. Cognitive assessment is often done through questionnaires that are applied at the end of the procedure and presents subject bias [5]. Thus, there is a need for more analytical, and objective evaluation methods. Provide insights about motor skills improvement from a neuroscience perspective, which would be related to changes in the underlying neural activity, is an objective and robust way to improving our understanding in surgical training.

Among noninvasive functional brain imaging techniques, electroencephalography (EEG) offers the ability to monitor and quantify functional brain activity with high temporal resolution and without constraining and interfering with task execution [6]. Quantitative EEG analysis has been used in a wide range of applications ranging from performance evaluation of a task [7]–[9], to training in flight simulators and air traffic controllers [10]–[12]. In these works, EEG-specific frequency bands such as theta and alpha have been associated to learning process.

Analysis of spectral measurements in EEG reflects the activation or deactivation of brain regions during the development of a task. However, brain is a complex system that involves a network of interacting subsystems [13]. Functional connectivity defines the temporal dependence of neuronal activity between anatomically separated brain regions [14]. To our knowledge, there are no studies evaluating functional connectivity during surgical training. Some as Langer et al. [15] analyzed functional brain networks organization in fronto-parietal regions during training in working memory tasks, showing increased small-worldness with high performance. Another work published by Kong et al. [16] founded increases in delta and alpha phase synchronization in frontal and parietal lobe when drivers going from an alert state to mental fatigue during their training in a simulator.

In this study, we are interested in exploring functional connectivity changes underlying surgical training task performance. Using algorithms to improve the spatial resolution of the EEG, we calculated coherence measures on a cortical level over previously reported regions associated with motor learning [17], [18]. Interactions between prefrontal cortex (PFC), anterior cingulate cortex (ACC), primary motor cortex (M1), supplementary motor area

(SMA), and parietal posterior cortex (PPC) are evaluated during training of a coordination task. We founded changes in alpha coherence as a function of task performance.

6.2 Methodology

6.2.1 Subjects and experiment

Subjects described in this work belongs to previously published analysis [19]. The sample consisted of sixteen first-year surgical residents (28.0 ± 2.6 years old, right-handed, 9 females) of Medical School of Universidad de Antioquia. Residents had no prior laparoscopic experience or with the simulator. This study was approved by a bioethics committee (Act: 18-19-787, 2018) and all the participants involved signed an informed consent.

Residents attended a 4-week training program with the VR simulator LapSim® (Surgical Science Ltd., Göteburg, Sweden), one session per week, where performed a coordination task (Figure 6.1). The task was executed three times in each session and EEG recordings were taken during the second repetition. The coordination task consisted of to hold the camera with left hand and locate ten randomly appearing objects, pick them up with the instrument in the right hand and transfer them to a target.

Figure 6-1. LapSim coordination task

The start and end of the acquisition were manually controlled by a researcher while the resident started and finished the execution of the task. On average, recordings length was: 61.42 ± 25.84 s. The participants were asked to remain silent and not to make unnecessary movements. Acquisitions were made in the afternoon (1:00 - 5:00 pm) and participants were asked to avoid alcohol, caffeine and non-ordinary workout routines before each training session.

At the end of each session, participants were asked to fill the National Aeronautics and Space Administration-Task Load Index (NASA–TLX) questionnaire [20] to assess the subjectively experienced workload across training sessions. The total NASA-TLX score ranges from 0 to 100 and it is calculated as an average of six factors: Mental Demand, Physical Demand, Temporal Demand, Performance, Effort and Frustration.

The analysis presented in this work was performed on the first (S1) and last (S4) training sessions. Before executing the tasks, a reference condition was recorded during a 2 min baseline while the subject was in a standing position in front of the simulator with opened eyes looking a white screen.

6.2.2 EEG signals acquisition and processing

A Natus® Quantum™ (Natus Neurology Incorporated, Winsconsin, USA) amplifier with a sampling frequency of 1024 Hz were used to capture EEG using a cap with 60 AgCl channels positioned according to the 10-10 system. Right mastoid bone was used as reference and AFZ as ground. Additionally, the vertical and horizontal electrooculographic activity (EOG) was recording by bipolar electrodes. Horizontal EOG electrodes were put in the outer canthus of each eye and vertical EOG in the supraorbital and suborbital region of right eye.

The pre-processing pipeline was based on the EEGLAB toolbox, a Matlab open-source toolbox [21]. Data was imported, down sampled to 512 Hz, and filtered between 4 and 50 Hz (Hamming windowed sinc FIR filter, order = 846, zero phase shift). Bad channels and artifactual time periods, such as head movements, disconnections or impedance jumps were removed by visual inspection. Then, recordings were re-referenced to a common average reference and bad channels removed were interpolated. Later, recordings were segmented into 2 s epochs with a 0.5 s of overlap. Finally, an automatic artifactual epochs rejection was applied, containing detection of fluctuations greater than 1000 µV and unlikely activity with a threshold of 5 SD, rejecting a maximum of 5 % of total trials per iteration.

6.2.3 Source analysis

Inverse solutions analysis was carried out with the Matlab Electrophysiological Connectome (eConnectome) tool [22].The applied method uses the wMNE algorithm together with the boundary element technique. A high-resolution cortical surface is segmented and reconstructed, consisting of 41136 triangles for viewing MR images of the brain template from the Montreal Neurological Institute (MNI). The cortical surface is resampled with 7850 dipoles to form the source space. The dipoles are restricted to the gray matter with their orientations perpendicular to the cortical surface. The scalp, skull, and brain surfaces are segmented and reconstructed from the MNI template. The scalp surface with 2054 triangles forms the sensor space. A high resolution directed field matrix (2054 × 7850) is precomputed to link all scalp triangles to the sources. A specific directed field matrix for the electrode setup used (60 channels, 10-10 system) is constructed as a subset of the precomputed directed field matrix to solve the inverse problem. The solution of the inverse problem gives an estimation at each time point for the cortical sources.

90 regions of interest (ROI) were reconstructed according to the AAL (Automated Anatomical Labeling) atlas that provides a cortical parcellation of the cerebral sulci [23]. The signal of each ROI is calculated as the average of the cortical sources in each ROI.

6.2.4 Functional Connectivity Estimation

Estimation of functional connectivity on cortical signals was done using the coherence function. Coherence was calculated by means of multitaper spectral estimation method available in Matlab's Chronux tool [24].

From the AAL ROIS, five regions were taken in each hemisphere for functional connectivity estimation: anterior cingulate gyrus (ACC), superior frontal gyrus dorsolateral (dPFC), superior parietal gyrus (PPC), precentral gyrus (M1) and supplementary motor area (SMA).
Coherence was calculated between all pairs of ROIs (45 interactions) in three frequency bands: theta (4-8), alpha (8-13), and beta (13-30). The computation was performed for each epoch, obtaining, in each frequency band and per subject, 10 x 10 x epochs matrices. Subsequently, the coherence values were averaged through the first 50 epochs, resulting in 10 x 10 matrices.

6.2.5 Statistical analysis

A repeated measures ANOVA with two factors: Session (2 levels) and Connection (45 levels) was used to evaluate functional changes across sessions for each frequency band. Paired t-test for task score and perceived workload index were performed. Mauchly's test was used to evaluate the sphericity assumption, and Greenhouse-Geisser correction of the degrees of freedom was made in cases where the assumption was not fulfilled. Multiple comparison analyses were performed between the sessions using paired t-tests with a p value < 0.05 established as significant. P-values were corrected for multiple comparisons using the false discovery rate (FDR) method. Those statistically significant functional connections were then correlated with task performance using the repeated measures correlation (rmcorr) [25].

6.3 Results

6.3.1 Performance and workload index

There was a significant increase in task performance from the first to the last training session ($T(15) = -4.634$, $p < 0.001$, Hedges $g = -1.398$). Regarding to perceived workload there was no statistically significant difference in the total score ($T(15) = 1.119$, $p = 0.281$, Hedges $g = 0.309$). Figure 6.2 shows a boxplot for total score and workload index in each session.

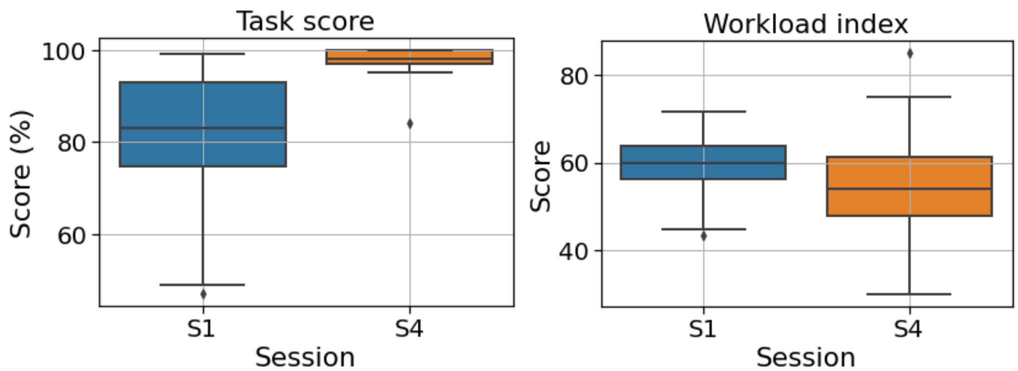

Figure 6-2. Task score and Workload index boxplots. There was a significant increase in task score with training. However, there are no statistically significant changes for the perceived mental workload index.

6.3.2 Functional connectivity

For theta band, ANOVA did show statistically significant effects only for connection factor (F(44,660) = 3.4373, p = 0.0051). For alpha band there was a statistically significant effect of session (F(1,15) = 20.3337, p = 0.0004) and connection (F(44,660) = 2.3074, p = 0.02957). When performing multiple comparisons analysis, significant decreases in alpha coherence were found for connections between right AAC with PPC, and right PPC with left SMA (Table 6.1 and Figure 6.3). Finally, for beta coherence, only connection factor had a statistically significant effect (F(44,660) = 2.8202, p = 0.0117).

Table 6-1. Paired t-test for alpha coherence.

Connection	T-value	P corr-value	Hedges
ACCr_PPCl	4.062	0.027	1.106
ACCr_PPCr	3.983	0.027	0.919
SMAl_PPCr	3.655	0.035	0.963

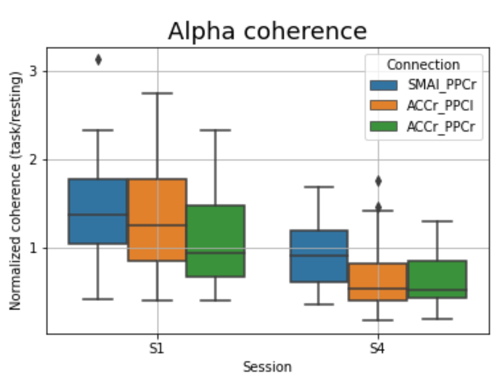

Figure 6-3. Means comparison for alpha coherence.

6.3.3 Correlations with performance

Table 6.2 shows the correlation results. Statistically significant negative correlations with task score were found for ACCr-PPCl, ACCr-PPCr, SMAl-PPCr connections (Figure 6.4).

Table 6-2. Correlation analysis between alpha coherence and task performance.

Connection	r	P-value	power
ACCr_PPCl	-0.691	0.002	0.903
ACCr_PPCr	-0.583	0.014	0.725
SMAl_PPCr	-0.761	0.001	0.968

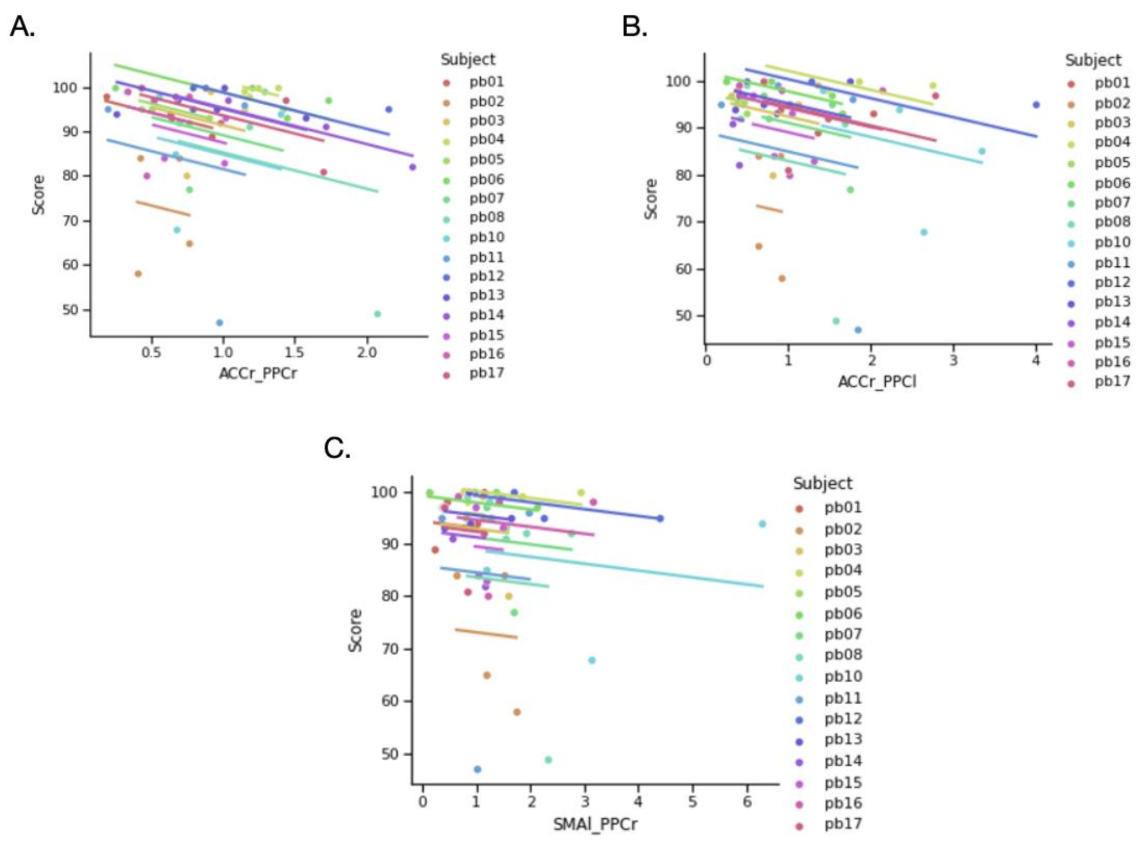

Figure 6-4. Repeated measures correlation graphs. Significant negative correlations were found for ACCr-PPCr (A), ACCr-PPCl (B) and SMAl-PPCr (C) connections with task score.

6.4 Discussion

This study evaluated functional connectivity changes related to improvement in laparoscopic surgical virtual training. Coherence measures in theta, alpha and beta bands were evaluated between five regions interactions: PFC, ACC, M1, SMA, and PPC, areas associated with strategy, planning, and control of motor tasks [18]. Of those, statistically significant decreases for alpha connectivity between ACCr-PPCr, ACCr-PPCl, and SMAl-PPCr were found, which were correlated with increase in task performance.

As far as we know, there are no studies evaluating functional connectivity during surgery training. Some works have related learning and performance in motor tasks with alpha connectivity. For example, using resting functional connectivity, Manuel et al. [26] shows reduced alpha connectivity between parietal cortex and the rest of the brain after training of computerized mirror drawing task. Similarly, alpha coherence between left premotor cortex (PMC) and sensorimotor cortex (SM1) and left cerebellar crus I was decreased during a sequence learning of the serial reaction time task [27]. Alpha connectivity between T7-Fz channels has also been reduced with training with a prosthetic hand simulator [28]. In accordance with the reports mentioned, our results might suggest that changes in alpha at functionally relevant sites may play a critical role in motor training. Alpha oscillations have been associated to working memory [29] and long-term memory processes [30]. As well as decreases in the mu rhythm with motor sequence learning and motor memory consolidation [31], [32].

This work has several constrains related to small sample size and experimental setup. The number of residents was limited by admission to the faculty (7 – 8 per year). Increase sample size or include a control group could have increase the observed differences and clarify whether the same effects could have occurred only due to adaptation to the VR simulator. EEG recordings were done without time control in task execution and without event marks, it does not allow us to make inferences to specific cognitive processes. Therefore, the results shown allow us to associate different cognitive processes involved motor training, such as attention, working memory and motor skill acquisition. It is also important to consider that the accuracy of source estimation algorithm is affected by the low number of electrodes [33]. However, acceptable results can be obtained using a 60-channel montage based on setup time and costs, even fewer electrodes may be sufficient to obtain good source estimation according to recent work [34].

In summary, this work allowed us to calculate functional interactions between cortical areas functionally related to motor learning. The EEG allows us to have good temporal resolution, and inverse solutions analysis brings us closer to better spatial resolution so we can compare the results with other neuroimaging techniques such as fNIRS. Our work contributes to the evaluation of future surgeons, next steps can be focused on skill level assessment metrics and potentially provide predictive models of skill acquisition. In addition, these methodologies can be applied to other applications such as rehabilitation and brain computer interfaces.

6.5 References

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7. RESULTS AND CONCLUSIONS

The main purpose of this thesis was to evaluate, from EEG and ECG signals, the learning process in surgery residents during laparoscopic surgery training using a simulator. This goal was divided into four specific objectives related with design and implementation of a protocol for the acquisition of EEG and ECG signals, spectral and functional connectivity analysis on EEG signals, heart rate and heart rate variability analysis on ECG signals, and correlations of neurophysiological measures with tasks performance.

7.1 Protocol for EEG and ECG acquisition

To meet this objective, a pilot test with 8 students from the bioengineering program was performed. The purpose was to obtain a signal acquisition scheme that allows monitoring the training in the simulator. In this sense, a longitudinal study was proposed, in which the EEG and ECG signals were recorded during the execution of 3 tasks (coordination, grasping, cutting). From an EEG power spectrum analysis, significant changes were obtained between sessions on EEG bands related to processes involved in motor learning for coordination task.

From the performance analysis, it was found that there were not significant increases for the cutting task, participants stated the procedure involved a high difficulty level. Due to the above, the last task was changed for peg transfer, which is part of the Fundamentals of Laparoscopic Surgery (FLS) program. This task was proposed as the one with the highest level of difficulty, as it integrates more psychomotor skills such as picking and transferring between dominant and non-dominant hands.

Likewise, due to the high variability found in neurophysiological measurements (EEG and HR), data normalization involving a baseline recording was considered. This was a resting condition with the participant standing in front of the simulator, first, looking at a blank screen and then with closed eyes. Finally, another aspect to consider in the protocol was the recording during the first task execution. In the first contact of the participant with the simulator, an adaptation period can be given, which is expected to decrease in the second task execution. Therefore, was decided to take the recordings during the second repetition of each task.

The experiment proposed in this thesis provides a signal recording in a more real scenario, with fewer restrictions for the subject. Complex tasks such as laparoscopy training tasks require more portable equipment and set up that can be carried out in different environments, from the simulation to a real scenario such as an operating room.

7.2 EEG analysis: power spectrum and functional connectivity

The main challenge of this work was to extract neuronal activity from the recorded signals. In any kind of setting (stationary or mobile), EEG recordings are contaminated with noise that must be removed so data can be correctly interpreted.

In the pilot test (chapter 3), a signal pre-processing involving robust referencing, filtering and ocular and muscular artifacts remotion by wavelet ICA was initially considered. Although this pipeline cleans the signals obtained at the channel level, the question remains whether the resulting data corresponds to neuronal activity. This is how spatial filters methods such as ICA were chosen, which allows differentiating between the different sources that integrate EEG recorded. Additionally, source localization techniques such as dipole model and wMNE, allow us to locate the neural sources. Although experiment conditions do not allow us to evaluate specific cognitive processes, we might associate certain brain areas with processes involved in training motor skills.

With the analysis carried out in chapter 5, it was possible to extract neuronal components such as frontal midline theta and parietal alpha related to working memory, mental workload and visual attention, and evaluate activation changes associated with tasks training. Since clustering analysis performed in this work did not allow us to have the same subjects in each IC cluster, it was decided to extract cortical signals using an inverse solution approach with wMNE algorithm. In chapter 6, brain functional connectivity was evaluated on those regions not only related to previous work activations, but also associated with motor learning (PFC, M1 and SMA) [1]. Results showed changes in the interactions between ACC and SMA with parietal cortex in alpha band. Fronto-parietal interactions seem to play an important role in processes such as working memory and mental workload [2], [3] .

It is important to note that consistent results were obtained from the different analyzes performed. Going from channels to cortical regions, it was possible to determine brain changes (activations or interactions) associated with motor training, mainly focused on frontal and parietal regions. Assuming that our hypothesis is true, the results found show that it is likely that the changes in brain rhythms are related to different cognitive processes involved in training and skill acquisition. Neuroimaging and electrophysiological studies have shown reduction in the activation of ACC with learning, a control area associated to visual WM load and cognitive effort [1], [4]. From EEG studies, theta power over frontal channels and frontal midline IC has been shown to modulate WM load[5], the improvement in task performance leads to frontal theta reduction [6].

Regarding to alpha, seems like this rhythm play as modulatory gate for information flow through enabling attentional processes, reflected as a reduction in alpha power [7]. Studies have shown that during motor learning an automatization process occurs where neural processes shift from cortical areas to subcortical areas such as basal ganglia [4]. Automation requires less attentional resources, and it might indicate the progressive alpha increase.

7.3 Heart rate and heart rate variability

Variations in HR and HRV can be related to the variation of emotional states and stress [8]. With the work done in chapter 4, we expected a modulation of HR with training sessions. However, results only showed a variation of heart rate with task difficulty level exhibiting an increased HR in peg transfer task. Although heart rate measurements were normalized with resting condition, high variability was observed in the data, which makes it difficult to find statistically significant differences.

Regarding the HRV analysis, frequency analysis was made from the RR signals obtaining normalized LF, HF and ratio LF/HF measurements. However, no statistically significant changes were obtained with training sessions. According to literature, HRV analysis is performed on long-term recordings (24 h), although it is possible to have short-term segments of 5 min [9]. This might be the main limitation in our analyses, since recordings length was, on average, of 1 min for coordination, 1.3 min for grasping and 3.5 min for peg transfer task.

7.4 Correlations of neurophysiological measures with tasks performance

Both power and connectivity measures that had significant changes with training session were significantly correlated with performance. In contrast, no significant correlations were obtained with ECG-derived measurements. For power analysis (Chapter 5) it was found a positive correlation between frontal midline theta and performance of coordination and peg transfer task, and a negative correlation between central parietal alpha and coordination task performance. On the other hand, the connectivity analysis showed negative correlations between frontal-parietal alpha connections and coordination task performance.

Negative correlation of frontal theta power with performance could reflect decreased mental workload and mental effort with training [6]. Likewise, positive correlation in alpha band could be associated with attention load decreases [10]. On the other hand, functional connectivity analysis shows that frontal-parietal interactions in alpha have a different behavior and synchronization decreases with training. Linear correlation analysis works for measurements with two time points, but in the evaluation of the 4 sessions a non-linear regression analysis would be more appropriate, since activations changes are non-linear. However, since the greatest changes occurred between the beginning and the end of training, linear measurements were chosen.

7.5 Limitations and future work

The main constrains of this work have to do with sample size and experimental setup. The number of participants who were recruited was limited, as the general surgery program accepts 7 to 8 residents per year. Likewise, the inclusion of a control group would have allowed us to clarify whether the same effects could have occurred only due to adaptation to the VR simulator. Second, with this experiment it is not possible to evaluate a specific cognitive process, therefore, the results shown here only allow us to make associations of activations or interactions with previously described cognitive processes that would be involved in training with the simulator such as working memory and sensorimotor feedback [11]. Third, recorded signals were of short length, which affects analysis such as ICA for EEG or HRV for ECG. Although some strategies were applied, such as data concatenation in EEG, increasing tasks length and have the same amount of data recorded in all the tasks and sessions would be a good alternative to consider in future analysis. Finally, EEG source analysis methods provides an approximation of where cortical activity is generated. The use of standard electrode locations and head models limits the algorithm, due to variability in head shape and size between subjects. Could be considered for further work to measure channel location per subject [12].

The experiment and methodology proposed in this thesis can be expected as a starting point for recordings during the execution of complex tasks. Considering the limitations exposed here will allow to propose better acquisition. An improvement to the developed protocol should include, in addition to the above considerations, recording and analysis of multimodal data such as of EMG and movement tracking, as exposed in works of Mobile Brain / Body Imaging [13].

7.6 Concluding remarks

This thesis shows the development of a protocol for the acquisition and evaluation of neurophysiological measurements during training in laparoscopic surgery using a simulator. EEG and ECG are non-invasive, portable, low cost and easy-to-implement tools that allow obtaining neurophysiological information related to the activity performed by a subject without constraining and interfering with its execution.

The results found in the different analyzes suggest that it is possible to develop a quantitative surgical training assessment from analysis of performance and physiological signals. Starting from variations in heart rate with ECG, to changes in neuronal activations with EEG, results suggest that these changes could be associated to processes involved in training motor skills such as working memory and attention.

The experiment proposed in this work establishes less controlled recording conditions leading to a more realistic analysis scenario to cognitive assessment in residents training. This could provide a starting point for the evaluation of medical training in simulation that can be extended to the operating room, and it would lead to broader applications such as the evaluation of interventions in motor rehabilitation, or the development of classifiers to determine the skill level of a subject.

7.7 References

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