Discrimination of neuropsychiatric disease using EEG and Neurophysiological Biomarker Toolbox (NBT)

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In the Name of Allah, the Most Gracious, the Most Merciful.

Parise be to Allah, the Cherisher and Sustainer of the worlds

Abstract

Electromyogram (EMG) contamination has been shown to affect electroencephalogram (EEG) signals. Therefore, methods of isolating and removing EMG contamination are a focus of research. One of the most common ways to eliminate this contamination is through independent component analysis (ICA). Also, surface Laplacian (SL) has been proven to isolate the distant sources of EEG signals. The objective of this thesis is to demonstrate the effects of EMG contamination on EEG signals using the Neurophysiological Biomarker Toolbox (NBT) and the impact of applying ICA, and ICA + SL on raw data. In this thesis, the method for preparing the data is ICA with an auto-pruned method and SL using a flexible spherical spline. The thesis has two main sections designed to demonstrate the objective. The first describes the use of random sampling of subjects who were assigned three tasks during EEG recording (eyes closed, eyes open, and solving a maze) and comparing them, under three types of data pre-processing, using Student's paired t-test and normalised amplitude of delta (1–4 Hz), alpha (8–13 Hz), and gamma (30–45 Hz). Second, machine learning was used to classify three neuropsychiatric diseases (anxiety, depression, and epilepsy) against control subjects under the three types of data pre-processing and raw data + SL. The data has been split into one second segments and classified according to features extracted from the NBT, which are the amplitude and the normalised amplitude for all frequency bands. Principal component analysis (PCA) was used for reducing the features, and 10x10-fold cross-validation and artificial neural networking were the methods used for the classification.

The results in the first section show that EMG contamination affected the EEG signal in the gamma bands, that ICA eliminated the EMG contamination, and that ICA + SL improved the reading of brain signals; and the delta and alpha bands were not affected by ICA or ICA + SL. The results in the second section show a high percentage of accuracy in ICA + SL in all frequency bands. However, ICA in general has a percentage quite similar to the raw data, while SL, as well as ICA with a small percentage improved more than ICA and raw data. Overall, the gamma band for both amplitude and normalised amplitude in ICA + SL showed the best results, with accuracy over 87%, when comparing it with all disease classifications. Both results indicate that ICA + SL eliminate and isolate EMG contamination. However, the classification of ICA shows no significant change in the percentage of accuracy.

Declaration

I certify that this thesis does not incorporate without acknowledgment any material previously submitted for a degree or diploma in any university; and that, to the best of my knowledge and belief, it does not contain any material previously published or written by another person except where due reference is made in the text.

fayez

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Chapter 1

Introduction

Currently, the activities of the brain are non-invasively recorded with the help of an electroencephalogram, or EEG. An EEG offers exceptional temporal resolution and usability, which is why it is frequently used for brain-computer interface (BCI) research. BCI is a technology that offers differently abled people control over artificial communication and motor devices without the help of conventional mechanisms, such as nerves or peripheral muscles (Wolpaw et al. 2000; Bashashati et al. 2007).

It is important for a user to yield different patterns of brain activity to be able to control the EEG-based BCI. These patterns are recorded by electrodes that are attached to a person's scalp, and the outcomes are commands that are derived from algorithms and data that is mined from the EEG signals. As far as EEG signals are concerned, noise is ubiquitous because of functional variations and disparities present in the EEG, measurement inaccuracies, and elements like muscle movements and eye blinks. An unsuitable imaging of a motorised image-based BCI can also result in noise. The technologies for classification and extraction of features that are employed in BCIs are reviewed by Bashashati et al. (2007) and Garrett et al. (2003). Nonetheless, these elements can be eliminated, if ICA is used (Oja & Nordhausen 2001; Kachenoura et al. 2008), or excluded by criteria or thresholds.

On the other hand, ICA is a technique for processing signals that originated from blind source separation (Bell & Sejnowski 1995; Lee et al. 1999). Since then, ICA has frequently been applied in a number of fields, like speech processing, communication, and biomedical signal processing. ICA can decompose the observed multichannel signals into a number of autonomous constituents using an optimisation algorithm, which is driven by the principle of statistical independency. Neither of these techniques can identify the sound produced by incorrect selection of patterns of imaging because the information provided on the label is not considered (Sannelli et al. 2009). The ICA algorithm, on the other hand, needs visual inspection for the selection of artificial components that make its application impossible in an automatic BCI system.

Continuous EEG signals in clinical applications can be separated into numerous rhythms depending on their frequency: delta rhythm (0.3–4 Hz), theta rhythm (4–8 Hz), alpha rhythm (8–13 Hz), beta rhythm (13–30 Hz), and gamma rhythm (30–45 Hz).

Cerebral diseases, such as cerebrovascular diseases, migraine and epilepsy, and EEG signals have a close correlation as the EEG of humans reflects the activity carried out by the nervous system. Hence, the method of processing and investigation of EEG signals in order to yield the hidden structures essential for curing and diagnosing diseases is frequently used. The EEG is therefore deemed a vital means for analysing brain function.

When electrical activity is recorded from the scalp, that recording contains electromyogram, or EMG, and the EMG is considered a serious contaminant of EEGs recorded from the scalp (Goncharova et al. 2003; McMenamin et al. 2010; Shackman et al. 2009). Stereotypically, EMG contamination is known to have large amplitude, which is why it is easily recognisable both visually and algorithmically. Moreover, it is generally the contaminated periods of EEG that are excised and discarded. However, constant weak contractions yield low amplitude impurities that are very stubborn in nature and difficult to detect visually. This continual contamination has spatial and spectral properties that are low power and difficult to recognise through the scalp recordings, but comparable to the contaminates cused by movement (Pope et al. 2009; Whitham et al. 2008). Temporary cranial, neck muscle and facial contractions result in electrical signals of very high amplitude with spectral features that overlap similar EEG bands. In addition, it has been established that recordings through the scalp and the range of incidences in the EMG interconnect, and as a result contaminate with the movement from muscles or EMG of the cranium and neck (Goncharova et al. 2003; Kumar et al. 2003).

The spatial resolution of the potential distributions is significantly reduced by the spatial smearing caused by the head volume conduction. For that reason, neck and face muscles have affected EEG signals recorded, and based on this, each electrode can be read for close and distant sources. Furthermore, surface Laplacian (SL) is sensitive to local sources as well as sources that are located close to the recording places and are impermeable to distant locations. Likewise, the SL diminishes enormously with the spatial smearing of the potential, which acts as a high-pass spatial filter (Nunez 1989). SL converts the existing scalp density with the help of data from all active scalp electrodes (Nunez & Srinivasan, 2006).

This thesis will investigate the EMG contamination of the EEG signal. Raw data will be processed to clean it of EMG contamination by using ICA, and we will apply SL on the ICA data. Therefore, three kinds of data pre-processing will be used in each section to clarify the effect of EMG contamination on the EEG signal. The study will be divided into two major sections, both working on pre-processing the data. The first section will use the Neurophysiological Biomarker Toolbox (NBT) to statistically analyse and clarify the EMG effect on random subjects (patients and controls) who were performing three tasks (eyes closed, eyes open, and solving a maze) during data recording. NBT will compare between eyes closed and open and maze-solving tasks with different pre-processing of the data. The second section will use artificial neural network (ANN) to classify neuropsychiatric diseases (anxiety, depression, and epilepsy) and control subjects based on the NBT features and for each type of pre-processing separately.

Chapter 2

Literature review

2.1 EEG concepts

The EEG, developed by Richard Caton over 140 years ago (Caton 1875), grew quickly into a tool for clinical diagnosis (Berger 1925), and since the 1950s has been used to study brain activity by employing it in the practice of meditation (Das & Gastaut 1955).

The concept of the EEG signal and the ways that it is used to work follow. Kaur and Kaur (2015) mention that the human brain has fluctuations of the order of a few microvolts that are consequences of ionic currents that flow between the brain and neurons. Furthermore, EEG signals represent synchronously the activity of a large number of neurons in the brain (Kaur & Kaur 2015). Moreover, non-invasive and invasive methods can be used for recording EEG signals (Kunjan et al. 2016). These authors have explained that the difference between the non-invasive and invasive methods is that in non-invasive methods, electrodes are attached to the scalp surface, whereas in invasive methods they are implanted. Ball et al. (2009) and Whitham et al. (2007) indicate that the non-invasive method is contaminated by signals from other sources, such as eye movements, head movements, and muscle activities. The non-invasive method is widely used because of its lower cost and high temporal resolution (Kunjan et al. 2016). EEG caps give accurate positioning of electrodes on the scalp (Kunjan et al. 2016). The brain has different regions that produce various kinds of waves based on brain activity (Schomer & Da Silva, 2012). Each electrode that is placed on the scalp records a number of waves, each with different characteristics, which is how the EEG signal is captured (Teplan, 2002). The EEG signal can be recorded for many tasks, such as eyes open/closed, photic stimulation, auditory stimulation, auditory oddball, visual rotation, visual discrimination, subtraction, reading, finger tapping, verbal working memory, meditation, and maze solving.

Each task has different results in the EEG signal. For example, Barry et al. (2007) have done an experiment to find out the difference between eyes closed and eyes open tasks. These authors have found that delta band has a reduction from eyes closed to eyes open, especially in the frontal regions, and most of the brain has significantly different levels. The alpha band showed that power decreased from eyes closed to eyes open; however, there were no significant changes in topography. Moreover, the difference between the tasks in the delta band showed most of the brain had significantly different levels, but the alpha band recorded non-significant activity between the tasks (Barry et al. 2007).

EEG features have wide ranging content because the EEG signal contains a lot of features, of which we will mention some. Amplitude, frequency and time-domain parameters have been used to find the difference between subjects (16 subjects, 10 sessions during 1 year) (Grosveld et al. 1976). They had a classification accuracy of 81%. They found that inter-individual variation was large compared to intra-individual variation. Moreover, Greene et al. (2008) compared 21 features to find the features more suitable to be used in a neonatal seizure detection algorithm. The features were divided into three main categories: frequency domain, time domain, and entropy-based features. Each of these categories had a number of features in it. The comparison was made between the individual features. Some examples of the features that have been used in this study are bandwidth (BW), peak frequency, spectral edge frequency (SEF), root mean-squared EEG amplitude (RMS Amp), minima and maxima, and Shannon entropy (HSH). They found that RMS Amp was the best performing.

Studying EEG signals led the researchers to implement toolboxes that were used to analyse signals. While here, we will mention some of these toolboxes.

EEGLAB is an open source toolbox using the MATLAB environment that was developed in 2004 by Arnaud Delorme and Scott Makeig (Delorme & Makeig 2004). EEGLAB uses an interactive user interface that allow users to process signals through it without writing code (Delorme et al. 2011). It implements the common methods for analysis of an EEG signal, such as ICA and time/frequency analysis (Delorme et al. 2011). EEGLAB is more reliable in the features that give users more options to choose what they want to do with data, and since it is open source, users can modify the code (Delorme & Makeig 2004).

FieldTrip is a MATLAB toolbox used to analyse Magnetoencephalography (MEG), EEG and other electrophysiological data that began to be developed in 2003. FieldTrip is open source software under the GNU General Public License (Oostenveld et al. 2011). It consists of approximately 108 high-level and 858 low-level functions (Oostenveld et al. 2011). In FieldTrip, there is no GUI for interaction between the user and the toolbox, but the user can interact directly with the functions on the MATLAB command line (Oostenveld et al. 2011).

NBT uses MATLAB software to implement its functions. NBT provides details based on brain activity. It was developed in 2008 and opened to the public in 2012. The aim of NBT is to provide a toolbox that can process EEG signals with easy-to-use features. NBT provides a GUI for user interaction. Multiple biomarkers are provided to analyse the EEG signal by NBT. The website (https://www.nbtwiki.net/) has information and tutorials for downloading and using the toolbox, with datasets that can be used to learn to use the toolbox.

Current Source Density (CSD) is a toolbox that implements a spherical spline algorithm (Perrin et al. 1989) using MATLAB software (Kayser, 2009). CSD computes scalp SL or current source density estimates for surface potential (EEG/ERP) (Kayser 2009). This author has claimed that this toolbox is registered for the GNU General Public License.

2.2 Artefact removal methods

There are various computational methods for the reduction of EMG artefacts. For example, General Linear Model (Shackman et al. 2009) removes variances in a neurogenic band of interest. Shackman et al. (2009) have enumerated the technique features, such as automatic, performing separate correction at each site and not requiring dedicated EMG channels. Another example is linear or non-linear low-pass filtering (Goncharova et al. 2003), for which they found that ICA performs more effectively to remove EMG contamination than linear or non-linear low-pass filtering. ICA (Jung et al. 2000, Shackman et al. 2009, Makeig et al. 1996) and Adaptive Mixture of Independent Component Analysers (AMICA) (Delorme et al. 2012) use the same concept with each source being an independent source. Parallel factor analysis (PARAFAC) is another example for EMG filtering (De Vos et al. 2007a, De Vos et al. 2007b). They describe it as having "reliably separated a seizure atom from the noise and background activity with a sensitivity of more than 90%".

2.2.1 Independent component analysis (ICA)

EEG signals are affected by some artefacts, such as eye movements, blinks, muscle noise, heart signals and line noise, that make it difficult to read and reduce accuracy for data analysis (Sanei & Chambers 2007). ICA is a method that can deduct the artefacts from the signal. Researchers are using the ICA method widely in their research to remove artefacts from EEG signals. Multichannel data mixtures with independent time courses are identified by ICA (Delorme et al. 2012). These authors also claim that ICA therefore directly models each source of the EEG signals in a scalp sensor. Each are independent sources that give clear signals without artefacts and without interference from other scalp sensors

The class of algorithms that using higher-order statistical properties with effective separating signals from an arithmetic mixture of signals, known as independent component analysis (ICA) (Delorme & Thorpe 2001; Delorme et al. 2007; Fitzgibbon et al. 2007; Fitzgibbon et al. 2016). Akhtar and James (2009) have mentioned that the artefacts cannot be removed by cutting the signal that contains them, because it may contain important data that is masked by artefacts, so using ICA and wavelet denoising (WD) improves the EEG signal pre-processing. In this study, they proposed a new approach for removing artefacts by using the concept of spatially-constrained ICA (SCICA) to cut only the signal that contains artefacts from the EEG signal and use WD to extract the brain activity from the artefacts, then return the brain activity to the EEG signal, so they have clean EEG data. The main advantage of using this method is computational efficiency. Vorobyov and Cichocki (2002) explained that in their experiment they used a modified version of data that was obtained through ICA. Furthermore, the experiment projected data to the sensor level, that is each sensor measured the noisy mixture of original source signals. They worked with two methods to show the effectiveness and validity of the proposed approach: simulations and the real application results for EEG signal noise removal. This study has a hypothesis to determine whether ICA is truly beneficial and gives some reasons for finding independent components (ICs) that characterise noise or artefacts in comparison to direct analysis of the originally measured EEG signals. As a result of this study, they found that the "inner" structure of observed signals is the key point for making the ICA technique important and effective for the blind noise-reduction problem. Moreover, they applied a procedure taken from the Hurst exponent calculation to detect ICs that contain "interesting" signals and used the subspace filtering method to filter "interesting" ICs after separation of the mixture. Both simulation and real application of the proposed method have demonstrated the effectiveness of this approach. On the other hand, the special structure of measured signals cannot be taken by direct application of filters as sequences that do “not allow us to obtain acceptable results of noise reduction”. FastICA is an ICA algorithm that, because of possible parallel implementation, is often used in real time applications (Sahonero-Alvarez et al. Taha 2010).

When we talk about methods of using ICA, there are several, but the most prominent is AMICA. Delorme et al. (2012) say AMICA is currently the one of the best the different ICA methods and generally preferred. Also, they have mentioned that using flexible modelling of source signal densities allows it to achieve better solutions for EEG data. Moreover, non-stationarities can be captured in a principled manner because multiple models can be learned. In this study, the criteria used were “the amount of mutual information reduction (MIR) between the recovered component time courses relative to the recorded data channels (in kbits/sec), the mean remaining pairwise mutual information (PMI) between pairs of component time courses (in kbits/sec), and the ‘dipolarity’ of the decomposition defined as the number of returned components whose scalp maps can be fitted to the scalp projection of a single equivalent dipole with less than a specified error threshold (specified as percent residual variance)” (p.2, Delmore et al, 2012). They have applied their study to 14 subjects and 71 channels on the human scalp. They have compared 22 methods. The results were that AMICA produced the highest mutual information reduction. In addition, AMICA and 18 other methods returned many similarities in components in the two other criteria. Moreover, Leutheuser et al. (2013) compared two methods to reduce EMG contamination: AMICA and InfoMax. Both methods use mathematical transforms to find the statistically independent sources inside a mixture of sources. These authors found that the AMICA algorithm performed better for removing EMG contamination than the InfoMax algorithm.

Whitham et al. (2007), Whitham et al. (2008), Pope et al. (2009) and Yilmaz et al. (2014) mentioned that frequencies above than 20 Hz have led EMG to have an impact on spectra. EMG exceeds EEG power 10-fold in the 20–80 Hz range (Aoki et al. 1999; Bertrand & Tallon-Baudry 2000) and it can exceed EEG power by more than 200-fold at 100 Hz. A software package has been developed by Moretti et al. (2003) for (i) electrooculographic (EOG) artefact detection and correction, (ii) EMG analysis, (iii) EEG artefact analysis, and (iv) optimisation of the ratio between artefact-free EEG channels and trials to be rejected. The results have shown to be approximately 95%

accurate for EOG artefact detection both vertical and horizontal, hand EMG response for a cognitive-motor paradigm, involuntary mirror movement detection, and EEG artefacts. Fitzgibbon et al. (2016) have worked to identify persistent EMG with a simple heuristic based on the gradient of the power spectrum of ICs. They have tested the heuristic and have seen that the spectra have gradients greater than a certain threshold. Moreover, the components where the spectra have power that decreases faster than the threshold are kept, and those where the power decreases slower than the threshold are rejected because they are EMG. As a result, for this simple technique (auto-pruned), it is valid to exclude EMG-containing components (Fitzgibbon et al. 2016). Combining two methods, the wavelet threshold denoising method with ICA decomposition, to separate the effects of EMG and Electrocardiography (ECG) from the signal was proposed by Zhou and Gotman (2004). The result showed the method is less difficult based on it not needing to calculate the higher-order statistics of the signal and it can efficiently remove the EMG and ECG artefacts from the EEG signal.

2.2.2 Surface Laplacian

The surface Laplacian technique is a popular technique used with EEG signals to determine a local relationship between the underlying flow of electric current caused by brain activity and SL of scalp potentials (Carvalhaes & de Barros 2015). Ohm's law is the basis of SL. SL has been used by a number of researchers in several different studies, such as generators of event-related potentials (Kayser & Tenke 2006b,a), quantitative EEG (Tenke et al. 2011), and spectral coherence (Srinivasan et al. 2007; Winter et al. 2007); however, here we will examine deeply what appears in Fitzgibbon et al. (2013), as it relates directly to the use of the SL technique in sensitivity to muscle contamination.

As is known, SL is more accurate for reading EEG signals as each electrode reads the signal from the nearest source in the scalp while ignoring the signals from distant sources. Fitzgibbon et al. (2013) tested the central channel because they knew that the middle of the scalp does not contain muscles, which means any muscle contamination would be caused by distant muscles. This study was conducted on 6 people, one of them a female. All were aged between 28 and 73 years. Recording was done twice: the first without neuromuscular paralysis and the second after full paralysis. They used 115 channels, and the recording was made in several different tasks including closed eyes, left eye open, submaximal jaw clenching (bite) and frowning (frown).

The result of this study is that SL succeeded in removing the influence of muscles on the central channel, although at high frequencies of more than 20 Hz, which may not be useful in clinical trials. However, SL is expected to be useful for investigators to use in the development and testing of algorithms to separate signals from the brain and the muscles. In the other study done by Fitzgibbon et al. (2015), they investigated whether combining ICA with SL can eliminate EMG. The data and systematic methodology they used in this study to evaluate EMG decontamination is the same they used in the previous research (Fitzgibbon et al. 2013; Fitzgibbon et al. 2014). Moreover, these researchers performed ICA processing by using AMICA, then spherical spline SL after that to remove EMG. Fitzgibbon et al. (2015) concluded that the combination of the two methods contributed significantly to their results. ICA is very sensitive to local temporal and cranial muscles and works to remove the contamination, but other muscles, like the postural muscles of the neck, are considered beyond the range of ICA, so therefore cannot be assembled and cleaned. Thus, the task of SL is to compile signals from the nearest source so the signals from these distant muscles are excluded.

2.3 Machine learning

Machine learning makes a machine learn a specific task and do it automatically. Mistakes often occur during analysis or with establishing relationships between multiple features when done by humans (Kotsiantis et al. 2007). However, machine learning can often solve this issue and is successfully applied to these problems, improving the efficiency of systems (Kotsiantis et al. 2007).

Choosing the learning algorithm is an important step in classification. Kotsiantis et al. (2007) reported that at least three techniques are used to calculate the accuracy of classification. The first technique is to split data into thirds and use two thirds for training and the other third for estimating performance (Kotsiantis et al. 2007). The second technique is cross-validation, which divides the training set into equally sized subsets, and each subset is the training classifier for the union of all the other subsets. Average error rate of each subset is estimated by the error rate of the classifier. The third technique is leave-one-out validation, which is a special case of cross-validation with all test subsets consisting of a single sample.

Machine learning has provided many competing tools that enables us to analyse EEG signals in real time (Sebastiani 2002). Müller et al. (2008) have represented two applications that use EEG signals in the real word, which are Hex-o-Spell and the online monitoring of arousal. Hex-o-Spell is a text entry system used for communication, and online monitoring of arousal reflects the concentration ability of subjects. They have used Machine learning uses a number of classification techniques to classify EEG signals, such as artificial neural network (ANN), support vector machine (SVM) and k-Nearest Neighbors (kNN).

Researchers have widely suggested ANN to diagnose epileptic diseases (Srinivasan et al. 2005). The ANN method was proposed by Weng and Khorasani (1996) using methods that were proposed by Gotman and Wang (1991). Inputs to an adaptive structured neural network will be: average EEG duration, average EEG amplitude, dominant frequency, coefficient of variation, and average power spectrum (Srinivasan et al. 2005). The LAMSTAR network is a neural network model proposed by Nigam and Graupe (2004), and it is used to detect epilepsy. Srinivasan et al. (2005) have used ANN for detection of epilepsy. The test pattern contains a pre-processing EEG segment of one second. Three features of frequency domain and two features of time-domain have been used in evaluating the performance of ANN. Five types of training schemes have been used in training the ANN. The result shows a 99.6% accuracy rate even with a single input feature. Moreover, Srinivasan et al. (2005) have researched the use of ANN to detect epilepsy by using frequency-domain and time-domain features. Their study was conducted on normal and epileptic subjects, with 100 single channel EEG segments for each set. The experiment used 10 subjects, 5 were controls and recorded the EEG signal while relaxed and with eyes open, and the other 5 were epilepsy patients, and the EEG signal was recorded during occurrences of epileptic seizures. The study used 5 different features, 3 frequency-domain and 2 time-domain, to evaluate the performance of the neural networks. The result has shown an accuracy rate of 99.6% of epilepsy detection, even with a single feature (Srinivasan et al. 2005).

SVM is a classifier formally defined by a separating hyperplane. It is widely used due to its good performance and computational efficiency. The task for SVM is to take a training set of data and estimate the input-output functional relationship (Zhang 2001). As an example of using SVM, Trambaiolli et al. (2011) have used it in their study. Their study was to use machine learning to diagnose Alzheimer’s disease (AD) using SVM. The study was applied to search for differences in EEG signals between AD patients and controls. The study recorded EEGs from 19 normal subjects (14 females and 5 males, mean age 71.6 years) and 16 AD patients (14 females and 2 males, mean age 73.4 years). The accuracy of the result was 79.9%, and sensitivity was 83.2%. For each individual patient, the diagnosis reached an accuracy of 87.0% and sensitivity of 91.7%. Kunjan et al. (2016) used SVM for predicting cognitive work load using EEG data. They applied classification for pre-processing data to prove the improvement in EEG features by removing EMG contamination. They conducted the study on 9 subjects performing an oddball task during the recording. As discussed above in the ICA section, the auto-pruned method used to eliminate EMG contamination (Fitzgibbon et al., 2016). A 10-fold cross-validation technique was used, then SVM on training and testing data. The result achieved was pre-processing the data improved the cognitive work load predictive power with an accuracy of nearly 100%.

2.4 Diseases

Neurological disorder diseases (NDDs) are widespread around the word. The global burden of disease (GBD) shows that neurological disorder diseases have increased over the past 25 years (Feigin et al. 2017). These diseases lead to death and disability, with 16.8% of global deaths being caused by NDDs and represented 10.2% of the global leading cause group of disability adjusted life years (DALYs) in 2015. Tension-type headaches (about 1,500 million cases) are the most prevalent NDDs, the next is migraine (about 1,000 million), then Alzheimer's and other dementias (about 46 million cases) (Feigin et al. 2017). They also report that 36.7% is the increase in death and 7.4% in DALYs due to NDDs between 1990 and 2015. The main two reasons for this increase are the life expectancy has increased from 1990 to 2015, so people live longer suffering from dementia, and the growing population. However, comparing cases per 100,000 people between 1990 and 2015, 26% and 29.7%, respectively, are the decreases in age-standardised rates of deaths and DALYs caused by NDDs (Feigin et al. 2017).

Depression is a neurological disorder disease where the patient feels sad, moody, or low all the time. Jorm et al. (2013) have said "depression affects how people feel about themselves". People with depression lose interest in hobbies, work, or anything they may enjoy (Jorm et al. 2013). These authors also report some depression behaviours, such as no longer going out, stopping doing things at work/school, not being close to family or friends, and not doing usual enjoyable activities.

Anxiety is a neurological disorder disease where the patient feels more than stress or worry. An anxiety patient maybe be under stress or worried without any reason (Bartik et al. 2001). These authors also have mentioned some anxiety behaviours, for instance feeling frightened, overwhelmed, panicked, heart racing, muscle tension, butterflies in the stomach, or shaky hands. The common feature of anxiety is thinking about things a lot more than usual, and this may be about unnecessary things, but the patient is unable to stop thinking about them, therefore, it leads to being anxious all the time (Bartik et al. 2001).

Epilepsy is a central nervous system (neurological) disorder that causes brain activity to become abnormal, seizures, or unusual behaviour for periods of time. Seizure symptoms are common, even in people without epilepsy. The signs for people with epilepsy are simply staring blankly for a few seconds or repeatedly twitching their arms or legs during a seizure (Mayo_Clinic_Staff 2018). This clinic has listed some of the causes of epilepsy, such as genetic influence, head trauma, brain conditions, prenatal injury and developmental disorders (Mayo_Clinic_Staff 2018). Moreover, epilepsy usually happens because of abnormal brain activity that may affect any process that the brain is responsible for. The Mayo Clinic report mentioned some symptoms for epilepsy; for example, "temporary confusion, a staring spell, uncontrollable jerking movements of the arms and legs, loss of consciousness or awareness or psychic symptoms such as fear, anxiety or deja vu".

EEG signals have been used widely in research although they have been used to determine a number of diseases that have relationships with the brain. Lyapunov indicated the use of EEG signals for identification of epileptic seizures (Swiderski et al. 2005). By feeding discrete wavelet transform (DWT) number of EEG signals into a modular neural network structure, it detected epileptic EEG signals (Subasi 2007). Moreover, the Kiymik et al. (2004) study compared the performances of a continuous wavelet transform (CWT) and of a short time Fourier transform (STFT) by using the Labview program to analyse epileptic seizures. They found that STFT is useful for real-time diagnosis; however, CWT has a high resolution, which is effective for clinical interpretation. When we talk about other diseases, such as dementia, Ktonas et al. (2007) have reported the differences between dementia patients and normal subjects in sleep spindle instantaneous frequency dynamics by using the time-frequency technique of complex demodulation. Another study shows that patients who have dementia have a lower spectral index than normal “awake” subjects (Renna et al. 2003). Studies have shown the decrease in fast wave and the increase in slow wave activity of the EEG for patients with Alzheimer’s disease or vascular dementia (Subha et al. 2010). Brunovsky et al. (2003) proposed a method that can estimate the degree of cognitive impairment caused by Alzheimer’s disease from the EEG quantitative indicators. They have shown that increase in delta coherence and decrease in alpha coherence were connected to the degree of dementia. Subjects with autism diseases and normal subjects have been classified in the study by Sheikhani et al. (2007). That was done with calculated, short time Fourier transform (STFT), Bispectrum transform and STFT at bandwidth of total spectrum (STFT-BW) for 21 channels of EEG. This study achieved an 82.4% accuracy between normal and autism subjects by using STFT-BW.

2.5 Summary

The literature review has reviewed the concept of EEG signal and the ways of recording data. Tasks that used during recording data has been reviewed and put up an example of the difference between tasks. Moreover, EMG contamination and the effect on EEG signal has been widely researched and investigated a number of ways. EMG contamination removal has been reviewed and the main effective ways that it is widely performed such as ICA and SL, both have proved their effectiveness to eliminate and isolate the EMG contamination. Furthermore, machine learning and classification methods have been reviewed and explain the different methods that can used to classify data. We have also mentioned the studies that have used the different classification methods. Neuropsychiatric diseases also have reviewed and both the definitions of those diseases and the effects on the person as well as the difference between them with some studies that have done the classification on them.

The above review has given the knowledge that will used in this thesis to investigate the effect of EMG contamination on EEG signal and using different data pre-processing will eliminate EMG contamination. The next chapter looks at the hypothesis of the study and the expected result. Chapter 4 investigates the main hypothesis by comparing between different tasks. As well as Chapter 5 will use machine learning to investigate the main hypothesis by classifying neuropsychiatric diseases Chapter 6 has summarises the finding, highlights limitations that were faced, and future work.

Chapter 3

Hypothesis

The study uses two methods to find the effects of EMG contamination on the EEG signal. The first section will compare maze solving and eyes closed or open for random subjects and the second section will use classification to distinguish neuropsychiatric diseases (anxiety, depression and epilepsy) and control subjects. Each section has different pre-processing data, which are raw data, ICA (auto-pruned) data and ICA + SL. The study hypothesis is divided into three expected results, as shown in Table 1. The expected result (1) shows whether a difference in the data is caused by the muscles, so the brain activity has no differentiation between these tasks or diseases when applying muscle cleaning. For the second expected result (2), the brain has the same activity and muscles have no effect on brain activity, so all the results will be the same in each of the different data stages. In the expected result (3), the difference between these pre-processing types will increase with contaminated EMG. In this case, brain activity has been hidden by muscle contamination. Therefore, reading the EEG signal will be affected by the muscles. For example, we might expect that in the maze task there is more muscle contamination, so we would expect to see some like result 3 where the pre-processing methods reduce EMG contamination.

Table 1 Expected result at three different data pre-processing stages.

<table>
<tr><td>Pre-processing data</td><td>Expected result (1)</td><td>Expected result (2)</td><td>Expected result (3)</td></tr>
<tr><td>Raw data</td><td>Difference between tasks is higher than difference between them in ICA or ICA + SL.</td><td rowspan="3">Difference between tasks has not affected by muscles and has no different overall the data pre-processing.</td><td>Tasks has no different in this stage.</td></tr>
<tr><td>ICA data</td><td>Difference between tasks is higher than difference between them in ICA + SL.</td><td>Difference between tasks is higher than difference between them in Raw data.</td></tr>
<tr><td>ICA + SL</td><td>Tasks has no different in this stage.</td><td>Difference between tasks is higher than difference between them in raw data or ICA data.</td></tr>
</table>

Chapter 4

Using NBT toolbox to compare between different EEG signal recording tasks

4.1 Methods

In this section of the study, we will examine the effect of EMG contamination on EEG signals by comparing different tasks for a random sampling who have recorded EEG signals under several tasks. We have chosen eyes closed and eyes open tasks to compare with a maze solving task. The comparison will be under three different stages of data filtering: raw data, data with applying ICA, and data with a combination of ICA and SL. Moreover, we expect this comparison will give a result.

4.1.1 Experimental subjects

The subjects that we used were collected by The Brain Signals Lab (Whitham et al. 2007; Whitham et al. 2008). The experiment selects subjects randomly (subjects with different diseases, as well as control subjects). During EEG recording, participants performed a number of tasks (DeLosAngeles 2010; Whitham et al. 2007; Whitham et al. 2008) including eyes open/closed, photic stimulation, auditory stimulation, auditory oddball, visual rotation, visual discrimination, subtraction, reading, finger tapping, verbal working memory, meditation, and maze solving. In this study, tasks selected were eyes closed, eyes open and maze solving. The numbers of subjects are 50 recorded with the eyes closed task, 40 recorded with the eyes open task, and 50 recorded with the maze solving task. During the study, to compare between the eyes open and the maze, we randomly chose 40 subjects' maze signals to compare with the 40 subjects' eyes open signals. All the subjects were recorded with 124 channels and with 1000 Hz sample frequency. The Brain Signals Lab provided raw EEG signals. The Clinical Research Ethics Committee of the Flinders University and Flinders Medical Centre have given the approval for all experiments, and all subjects gave written informed consent.

4.1.2 Preparation of the data

In this stage, this study has used two different stages of filtering to remove EMG contamination. The first filter is the ICA auto-pruned algorithm, used to remove EMG contamination. The auto-prune algorithm uses AMICA for calculating the independent components (ICs) that are used to prune the data. The second filter is SL. We will use spherical spline SL to determine the local source of the electrode.

4.1.2.1 Independent components analysis (ICA)

This study uses ICA filtering to remove EMG contamination. We will use an auto-pruned algorithm by using the Adaptive Mixture Independent Component Analysis (AMICA) method. This study has used the same processing that has been used by Fitzgibbon et al. (2015) with AMICA. For each subject, AMICA (Delorme et al. 2012) was performed on tasks separately. While the EEGs were being recorded, participants performed a number of tasks (DeLosAngeles 2010; Whitham et al. 2007 2008). Only three tasks are mentioned here (maze solving, eyes closed, and eyes open). Due to electrode drift, a 1 Hz high-pass filter was applied to each task prior to merging to eliminate large offsets (Fitzgibbon et al. 2015). Also, for each of the individual tasks, ICA weights from the merged data were used. Moreover, auto-pruned works with components are calculated, spectra is calculated for each component. The linear slope of each spectral component is calculated. Those components that have a spectral slope exceeding a predefined threshold (which was set to -0.3) are excluded and the remaining components are projected back to EEG sensor space.

4.1.2.2 Surface Laplacian

In this work, spherical spline SL (Kayser & Tenke 2006) has been used. It was provided by CSD Toolbox (Kayser 2009). SL has been applied to the EEG signal prior to the ICA auto-pruning. SL permits manipulation of the flexibility of the spherical spline in the CSD Toolbox. Legendre polynomial used a constant ‘m’, with a lower value giving more flexibility and a higher value giving more rigid splines (Perrin et al. 1989). Perrin et al. (1989) recommended m = 4 when they evaluated the value of m = 2–6. However, m = 3–5 under different circumstances is recommended by Tenke and Kayser (2012). In this study, we evaluate splines using flexibility of m = 2–6 for their capability to remove EMG contamination (Fitzgibbon et al. 2015).

4.1.3 Statistical analysis

This study uses the Neurophysiological Biomarker Toolbox (NBT) (https://www.nbtwiki.net/). This is an EEG toolbox that uses the MATLAB program for computation and integration of neurophysiological biomarkers. Moreover, the Student paired t-test is used in this study to compare two population means, which are in two samples: observations in one sample can be paired with observations in the other sample (Shie 2004). Statistical significance was assumed for $p < 0.05$.

NBT has several of computing biomarker that we have been tried to calculate the difference between tasks such as Coherence, Phase Locking Value, phase looking value and Detrended fluctuation analysis (DFA) , however, the most of them have non-different between tasks in that computed biomarker. Therefore, in this study, normalised amplitude has been used.

EEG signals will be categorised in classical frequency bands: delta (1–4 Hz), theta (4–8 Hz), alpha (8–13 Hz), beta (13–30 Hz) and gamma (30–45 Hz). Normalised amplitude computes the integrated amplitude for each of these frequency bands. However, the result will focus on three frequency bands, delta (1–4 Hz), alpha (8–13 Hz), and gamma (30–45 Hz). These bands were chosen because muscle activity will appear in the gamma frequency band and the delta and alpha bands will determine whether the ICA and SL have an effect on any brain activities (Fitzgibbon et al. 2015).

NBT has different scale ranges each time the t-test is applied between two tasks. The different scales will affect the comparison; therefore, we have changed the scale to be fixed in the three stages of testing. The selection of the scale was based on calculating the average between the three different scales resulting from applying the t-test between two tasks in each stage. For example, applying normalised amplitude on the gamma frequency band between maze solving and eyes closed tasks gives a scale range as the following for the three stages:

Table 2 Calculating the average between the three different scales to use in comparisons of the pre-processing data.

Stage	Raw data	ICA data	SL	Calculate average
Scale range	-5.56–5.56	-2.55–2.55	-3.63–3.63	-3.91–3.91

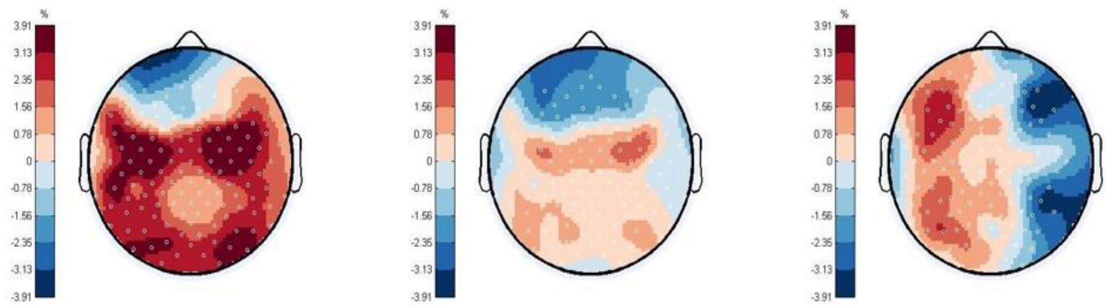
4.1.4 Study processing

The raw data that was provided by The Brain Signals Lab (Whitham et al. 2007; Whitham et al. 2008; DeLosAngeles 2010) will be processed to clean it by using the ICA filtering that we mentioned earlier. EMG contamination is removed by using AMICA first then using auto-pruned data. This data will be processed again using SL.

In this step, the data will be in three different stages of EMG contamination that is marked data (raw data), auto-pruned data, and data with AMICA, auto-pruned and SL. Each stage will be computed with amplitude normalisation biomarker under frequency bands delta (1–4 Hz), alpha (8–13 Hz), and gamma (30–45 Hz). The final process is to compare eyes closed subjects and maze solving in each stage, such as by applying the Student paired t-test on raw data for eyes closed subjects with raw data for maze solving subjects under each frequency band, at all stages. Also, we apply all the processes to compare eyes open and maze solving as well. Therefore, eyes open with raw data is compared to raw data with maze solving, ICA data for both eyes open and maze solving will be compared, and ICA with SL for those tasks will be compared as well. The results will be analysed to see whether muscles affect brain EEG recording.

4.2 Results

In this section, we will explain our findings by applying the NBT statistical computing program (https://www.nbtwiki.net/), by using the Student paired t-test on the data and finding the differences between eyes closed and maze solving with the three main frequency bands, delta (1–4 Hz), alpha (8–13 Hz), and gamma (30–45 Hz), as well as the differences between eyes open and maze solving, with the same frequency bands.



Marked data (Raw data) **ICA** **ICA + surface Laplacian**

Figure 1 Grand average for maze solving minus eyes closed for gamma frequency band (30–45 Hz), in raw data, after applying ICA, and after applying ICA and SL. The scale has represented the red colour with non-significant different and when it comes down to the blue it means that it has a significant different.

4.2.1 Eyes closed versus maze solving

With SL in combination with ICA, significant differences were observed in the brain. As shown in Figure 1, the gamma frequency band (30–45 Hz), the grand average for maze solving minus eyes closed marked data shows that the raw data has most of the brain not significantly different, with the percentage in the range 0.78%–3.91%, except the FP1 and FP2 electrodes have a small part that is significantly different. However, we have applied ICA to it with auto-pruned and the result for the grand average for maze solving minus eyes closed showed a reduction in the non-significant difference in the majority of the brain to be 0%–0.78% and the small area 0.78%–1.56%, as shown in Figure 1. In this stage, the significantly different area in the FP1 and FP2 electrodes increased to include a bigger area in the FP1 and FP2 electrodes. Comparison between ICA and SL has given a result as shown in Figure 1. SL, as known, cancels out distant sources and keeps the local sources only (Nunez & Srinivasan 2006); therefore, the grand average for maze solving minus closed eye tasks has a different result for the F4, F8, T4 and T6 electrodes, which are the electrodes of the highly significant difference in the range -0.78%–3.91%, and the F3 and P3 electrodes have the most non-significant different, however, F7, Pz, O1 and C3 electrodes have less non-significant different than F3 and P3 electrodes.

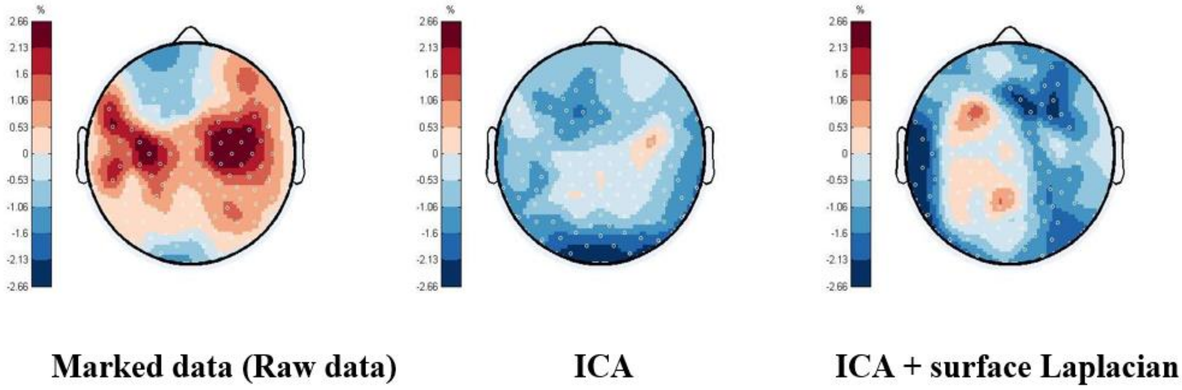


Figure 2 Grand average for maze solving minus eyes open for the gamma frequency band (30–45 Hz), in raw data, after applying ICA, and after applying ICA and SL. The scale has represented the red colour with non-significant different and when it comes down to the blue it means that it has a significant different.

4.2.2 Eyes open versus maze solving

Applying the Student paired t-test to the raw data of eyes open and maze solving under the gamma frequency band (30–45 Hz) has shown the grand average for maze solving minus eyes open has most of the brain with non-significant differences Figure 2. The percentage of non-significant difference is different between scalp areas. However, the big area is in the range 0.53%–2.66%. EMG contamination has hidden the differences between maze solving and eyes open. This appeared after applying ICA to the data and finding the grand average for those tasks, as shown in Figure 2. This shows most of the brain has a small range of difference (-1.06%–0%) between those tasks, except the O1 and O2 electrodes have more significant differences. SL and ICA together have changed the result to give us the local areas of the brain that have significant differences and those without. Figure 2 represents the Pz and F3 electrodes with non-significant differences in the range 0%–10.6%, and the F4 and T3 electrodes with significant differences, more than the rest of the brain with differences in the range -2.13%–0%.

4.2.3 EMG contamination

The variance between raw data and ICA with SL is obvious in the grand average for maze solving and eyes closed. In Figure 1, the variation between them is clear, and we can see how the non-significant difference has been limited by using both ICA and SL. Moreover, EMG contamination played a role in hiding the differentiation between tasks. By looking at the ICA + SL, the most significant difference and the non-significant difference areas will be apparent.

The difference between the maze solving and eyes open tasks is observable in Figure 2. When looking at raw data, there appears to be no difference between those tasks in the brain activity; however, ICA + SL gives us the positions of the differences in brain activity between those two tasks. These results explain that EMG contamination can affect EEG signals.

Both Figures 1 and 2 represent the same concept of results. Raw data in both figures shows most of the brain has non-significant differences. There are two major points of the scalp that have the most non-significant differences in these figures. By applying ICA, both results have the same reaction with EMG contamination, which is reducing non-significant differences, as shown in these figures. Moreover, ICA + SL has shown that the areas of the brain that have non-significant differences are quite similar between them.

4.2.4 Brain activities

Brain activity has not been affected by applying ICA and SL, as shown in Figures 3 and 4. The delta and alpha frequency bands for all stages in this study have the same result. In other words, in the delta frequency band, the grand average for maze solving minus eyes closed in the raw data has shown non-significant differences between them as well as by using ICA and ICA + SL. Furthermore, the same grand average for maze solving and eyes open tasks has similar results to maze solving and eyes closed, with no effect after applying ICA and SL. This result shows the brain activity isn't affected by applying ICA and SL. Furthermore, the alpha frequency band is also not affected in any stages, as shown in Figures 3 and 4, where the grand average for maze solving with eyes closed and maze solving with eyes open are the same for all stages, with the outcome of only brain activities, which means in the gamma frequency band, the differentiation that we have mentioned earlier has been applied to the EMG contamination without losing any brain activities.

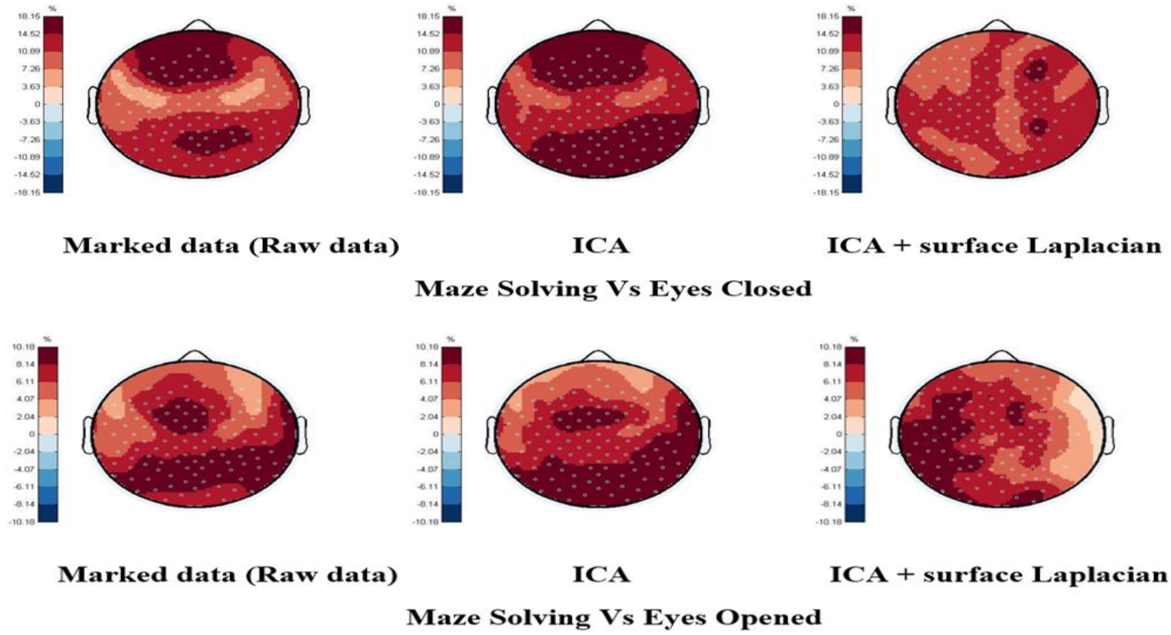


Figure 3 Grand average for maze solving minus eyes closed and eyes open for the delta frequency band (1–4 Hz) in raw data, after applying ICA, and after applying ICA + SL. The scale has represented the red colour with non-significant different and when it comes down to the blue it means that it has a significant different.

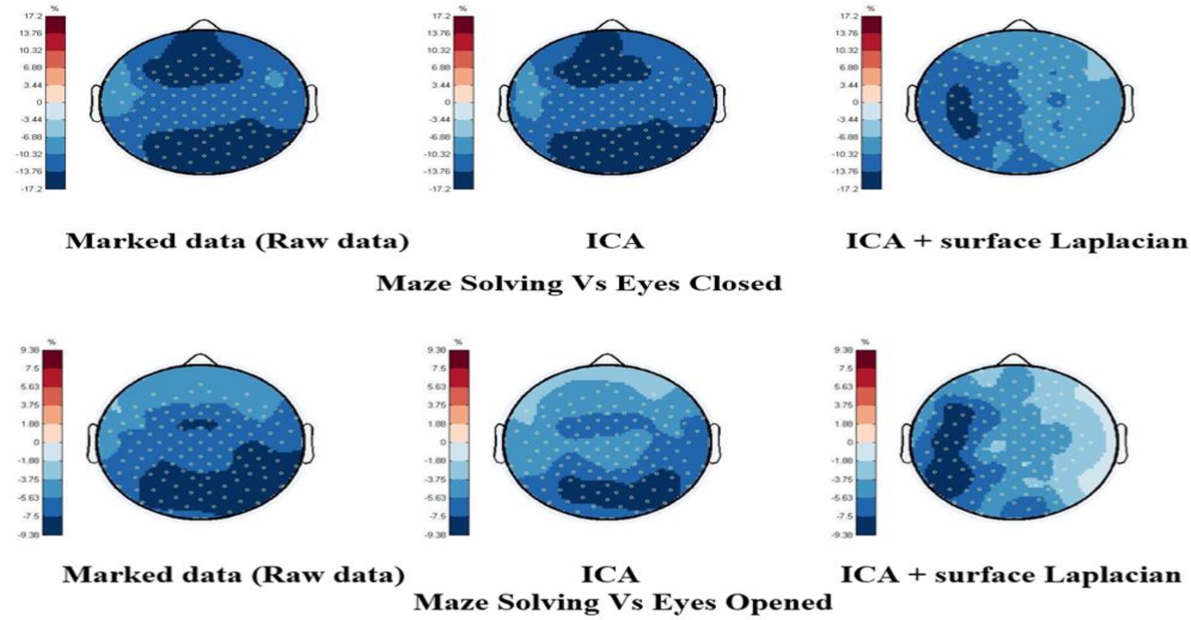


Figure 4 Grand average for maze solving minus eyes closed and eyes open for the alpha frequency band (8–13 Hz) in raw data, after applying ICA, and after applying ICA + SL. The scale has represented the red colour with non-significant different and when it comes down to the blue it means that it has a significant different.

4.3 Discussion

In this section, we will discuss the findings in this study from many different angles. The subjects that we have used have been recorded performing different tasks. Some have different diseases and some are normal people. All the data has the same processing, using the same methods to remove the EMG contamination. The ICA has been used previously in Fitzgibbon et al. (2016), Delorme et al. (2012), and Fitzgibbon et al. (2015), using the AMICA method; therefore, it has shown good performance with different datasets. We applied auto-pruned by using the AMICA method for calculating the independent component, as shown in Fitzgibbon et al. (2016). Referring to the results that we have in Figure 1 for applying ICA, it appears the ICA has contaminated EMG without affecting the brain activity, as shown in Figures 3 and 4. It has been mentioned that EMG contaminates the data above 20 Hz (Whitham et al. 2007); therefore, delta and alpha have seen no activity change after applying ICA, which means ICA contaminates EMG by keeping brain activities.

The combination of ICA and SL gives a result different from applying ICA only. With ICA only, the region of non-significant difference is less than with ICA + SL. This phenomenon may be due to SL giving the local electrode records and by applying differentiation between those tasks, SL distinguishes between the electrodes that have significant differences in activity and those that do not. This phenomenon has appeared after applying SL on ICA with two different comparisons (eyes closed versus maze solving and eyes open versus maze solving). As shown in Figures 1 and 2, the difference between applying ICA and applying ICA + SL is that SL eliminates the distant effects of EMG and the distant electrode effects.

Eyes closed and eyes open are different tasks for recording an EEG signal. According to Barry et al. (2007), eyes closed and eyes open have differences in brain activity. Also, differences between the tasks are seen in the delta frequency band for most of the brain, while no differences are seen in the alpha frequency band. This study shows this by comparing eyes closed with maze solving and eyes open with maze solving to confirm the reduction when reducing EMG contamination. Using two different tasks with different categories, as proved in Barry et al. (2007), and getting results by using ICA has reduced EMG, and ICA + SL gives the actual position of the brain difference for those tasks, which is evidence that EMG contamination affects the EEG signal.

The result has shown that the delta frequency band has non-significant differences between raw data and the auto-pruned method in both kinds of comparison Figure 3. This was proved by Fitzgibbon et al. (2016), where they have proved there was no significant difference between data contaminated by EMG and data after applying auto-pruned methods. As well, the alpha band frequency Figure 4 has non-significant differences between raw data and data after applying the auto-pruned method. That was proved also in Fitzgibbon et al. (2016), which found similar results with data contaminated by EMG and data after applying the auto-pruned method. This has proved the ICA used in this study has no effect on the EEG signal.

ICA enables us to isolate and remove EMG sources and leave EEG free from EMG contamination. Moreover, SL deals with current source density (CSD) space that transforms EEG voltage. CSD is not sensitive to distant EMG contamination. Therefore, the combination of ICA and SL limits the impact of EMG contamination on EEG signals, with ICA isolating and removing the EMG contamination, and SL dealing with CSD to locate sources of EEG signals, therefore, stopping the data effect from distant muscles.

Chapter 5

Using classification method to classify neuropsychiatric diseases

5.1 Methods

EEG signals are usually used with neuropsychiatric diseases; therefore, this section examines the difference between those with neuropsychiatric diseases and control subjects. These diseases are anxiety, depression, and epilepsy. The study will compare each disease with controls under the three stages: raw data, data after applying ICA and data with combination of ICA and SL. In this section, the comparison will use machine learning to analyse data under NBT features. This section covers one of the main three expected results (Table 1).

5.1.1 Experimental subjects

This study uses data from subjects collected by The Brain Signals Lab (Whitham et al. 2007; Whitham et al. 2008). The subjects were chosen based on their diseases. Data was recorded with many tasks (Whitham et al. 2007; Whitham et al. 2008; DeLosAngeles 2010); however, eyes closed is the task that we chose for this study. The number of subjects in this study is 34, 10 were controls, 10 had depression, 10 had epilepsy and 4 had anxiety. Raw EEG signals were provided by The Brain Signals Lab. The Clinical Research Ethics Committee of the Flinders University and Flinders Medical Centre have given the approval for all experiments, and all subjects gave written informed consent (Fitzgibbon et al. 2016). All the data was recorded with 124 channels and 1000 Hz sample frequency. Data was prepared by applying ICA (auto-pruned method) on raw data and applying SL on data with ICA, which will be explained further later in this chapter.

5.1.2 Preparing the data

In this stage, this section has used the two stages of filtering to remove EMG contamination as used in the first section. The first filter is the ICA auto-pruned algorithm used to remove EMG contamination. The auto-pruned method uses AMICA for calculating the ICs that are used to prune the data. Then, the second filter is SL. We will use spherical spline SL to determine the local source of the electrode. As we have mentioned earlier, ICA isolates and removes EMG contamination; however, it may be affected by distant muscle sources, so SL collects the local sources of electrodes and rejects the distant sources. The combination of them isolates and removes the local and distant EMG contamination. In this section of the study, SL is applied to raw data as well to ensure the good results will only be affected by the SL or by the combination of ICA + SL.

The data was divided into one second segments because the samples were limited due the numbers of subjects with the studied diseases. Recording was done using 124 channels. Dividing data into one second segments will extend the data to be a large data set; therefore, machine learning will have a large data set for training and testing as shown in Table 3.

Features that will be used to examine the data are prepared by using NBT (https://www.nbtwiki.net/). NBT provides different kinds of computing biomarkers. The computing biomarkers that are used in this study are amplitude for some frequency bands (delta (1–4 Hz), theta (4–8 Hz), alpha (8–13 Hz), beta (13–30 Hz), and gamma (30–45 Hz)) and normalised amplitude for some frequency bands (delta (1–4 Hz), theta (4–8 Hz), alpha (8–13 Hz), beta (13–30 Hz), and gamma (30–45 Hz)). Each feature of these has used with 124 features that have given by the electrodes, therefore, each time of the classification has 124 features.

Table 3. The number of actual subjects and the number of one second segments subjects for each disease and the control

	Anxiety	Depression	Epilepsy	Control
Actual number of subjects	4 subjects	10 subjects	10 subjects	10 subjects
Number of one second instances	142 instances	360 instances	285 instances	348 instances

5.1.3 Statistical analysis

Principal component analysis (PCA) is a method used for dimensionality reduction and feature extraction (Subasi & Gursoy 2010). PCA is used to represent the d-dimensional data in a lower-dimensional space that will minimise the degree of freedom and time complexities (Subasi & Gursoy 2010). Therefore, we have used PCA to reduce features, in some cases, to 9 features from 124 to get better and quicker results.

The evaluate the generalisation error of the classifier a 10x10 cross-validation method is used. The division of the folds uses a stratified randomly sampling to produced ten mutually exclusive subsets for each fold. Artificial neural network (ANN) is a MATLAB toolbox that performs a particular function of training a neural network by adjusting the values of the connection between elements (Demuth & Beale 1992). The subsets were entered into ANN to train the network using the Feed-Forward Neural Networks (FFNN) method (Levenberg 1944; Marquardt 1963). This method works in one direction, which means there are no cycles or loops in the network (Zell 1994). FFNN has 1 hidden layer with 10 nodes. The algorithms used in this study are random data division, Levenberg-Marquardt to train the network, and Mean Squared Error in performance. Levenberg-Marquardt is an algorithm to solve the problem of minimising a non-linear function and is suitable for small and medium sized problems (Wilamowski & Yu 2010).

5.1.4 Study processing

The data used in this study was collected by The Brain Signal Lab (Whitham et al. 2007; Whitham et al. 2008; DeLosAngeles 2010) for the eyes closed task. Data is isolated and EMG contamination is removed by applying ICA, then by applying SL to remove distant muscle effects. Therefore, each kind of disease (anxiety, depression, and epilepsy) and the control data have four different kinds of data pre-processing: raw data, data with ICA, data with both ICA and SL, and raw data with SL. This data has been computed with the biomarkers (amplitude and normalised amplitude for different frequency bands (delta (1–4 Hz), theta (4–8 Hz), alpha (8–13 Hz), beta (13–30 Hz), and gamma (30–45 Hz)). The data has fewer subjects; therefore, we divide it into one second, non-overlapping segments to extend the data. PCA was applied to reduce the number of features, in some cases from 124 features to 9. The was training method was applied ten times (10x10 CV) to gain enough data to perform a statistical analysis.

5.2 Results and discussion

ANN was applied to classify the three neuropsychiatric diseases (anxiety, depression, and epilepsy) with control subjects under the four different types of data pre-processing (raw data, ICA data, ICA + SL, and raw data + SL) and with different features given by the NBT (https://www.nbtwiki.net/).

Table 4. Accuracy percentages and biomarkers informedness of classification of anxiety v control for each band with amplitude and normalised amplitude. The following symbols indicate significant differences: * from Raw, + from ICA, # from SL, ^ from ICA+SL

	Raw data		ICA data		ICA + SL		SL	
Frequency bands	Accuracy %	BM	Accuracy %	BM	Accuracy %	BM	Accuracy %	BM
Amplitude								
Delta (1–4 Hz)	$72^{+\#\wedge}$	0.07	$71^{*\#\wedge}$	0.01	$96^{*+\#}$	0.87	$79^{*+\wedge}$	0.32
Theta (4–8 Hz)	$77^{\#\wedge}$	0.28	$77^{\#\wedge}$	0.30	$98^{*+\#}$	0.96	$89^{*+\wedge}$	0.66
Alpha (8–13 Hz)	$80^{+\#\wedge}$	0.39	$82^{*\#\wedge}$	0.48	$98^{*+\#}$	0.93	$95^{*+\wedge}$	0.87
Beta (13–30 Hz)	$89^{+\#\wedge}$	0.69	$91^{*\#\wedge}$	0.37	$99^{*+\#}$	0.97	$96^{*+\wedge}$	0.90
Gamma (30–45 Hz)	$92^{\#\wedge}$	0.79	$93^{\#\wedge}$	0.80	98^{*+}	0.97	98^{*+}	0.94
Normalised Amplitude								
Delta (1–4 Hz)	$71^{+\#\wedge}$	0.06	$71^{*\#\wedge}$	0.67	$92^{*+\#}$	0.81	$85^{*+\wedge}$	0.63
Theta (4–8 Hz)	$71^{\#\wedge}$	0.01	$71^{\#\wedge}$	0.03	$90^{*+\#}$	0.75	$81^{*+\wedge}$	0.50
Alpha (8–13 Hz)	$76^{+\#\wedge}$	0.28	$75^{*\#\wedge}$	0.21	$93^{*+\#}$	0.79	$87^{*+\wedge}$	0.60
Beta (13–30 Hz)	$75^{+\#\wedge}$	0.24	$71^{*\#\wedge}$	0.06	94^{*+}	0.88	95^{*+}	0.87
Gamma (30–45 Hz)	$96^{+\#\wedge}$	0.88	$86^{*\#\wedge}$	0.61	100^{*+}	0.99	100^{*+}	1.00

5.2.1 Anxiety versus control

Table 4 shows the accuracy of classifying anxiety patients versus control subjects under the four different types of data pre-processing. The result shows no huge difference between raw and ICA data. The difference is usually 1%–2%. For example, the delta band in marked data gives higher accuracy (72%) than ICA data (71%) by 1%. Accuracy in the alpha band differed from ICA, which had higher accuracy (82%) than marked data (80%) by 2%. Also, for the gamma band, marked data had 92% accuracy in marked data and 93% in ICA data. On the other hand, the difference between SL and

ICA + SL was obvious, especially in the delta and theta bands. However, the accuracy percentages were closer for the alpha and beta bands and similar in the gamma bands, which both had 98% accuracy. Table 4 shows the obvious differences between the ICA + SL and both raw data and ICA in all frequency bands. Therefore, the good accuracy percentage for ICA + SL is based on both ICA + SL, even if ICA has not given a good result by itself.

Normalised amplitude gave a result quite similar to amplitude for the raw and ICA data, where there were no differences for the delta and theta bands and small differences between the alpha and beta bands. However, the gamma band has a huge difference in accuracy between them, where raw data has 96% accuracy and ICA has 86%. For amplitude, ICA + SL has no differences in accuracy apart from in the beta band, where SL is 1% higher than ICA + SL.

In general, ICA + SL has given the best results in all bands, where the accuracy was greater than 95% for amplitude and greater than 90% for normalised amplitude. However, the best result was given by the gamma band for normalised amplitude for both ICA + SL and SL, which was 100% accuracy.

Table 5. Accuracy percentages and biomarkers informedness for classification of depression v control for each band for amplitude and normalised amplitude. The following symbols indicate significant differences: * from Raw, + from ICA, # from SL, ^ from ICA+SL

	Raw data		ICA data		ICA + SL		SL	
Frequency bands	Accuracy %	BM	Accuracy %	BM	Accuracy %	BM	Accuracy %	BM
Amplitude								
Delta (1–4 Hz)	$59^{+\#\wedge}$	0.18	$62^{*\#\wedge}$	0.24	100^{*+}	0.99	70^{*+}	0.40
Theta (4–8 Hz)	$66^{\#\wedge}$	0.33	$65^{\#\wedge}$	0.30	$98^{*+\#}$	0.97	$73^{*+\wedge}$	0.47
Alpha (8–13 Hz)	$55^{+\#\wedge}$	0.10	$57^{*\#\wedge}$	0.15	$100^{*+\#}$	1.00	$75^{*+\wedge}$	0.50
Beta (13–30 Hz)	$84^{\#\wedge}$	0.67	$84^{\#\wedge}$	0.68	$100^{*+\#}$	1.00	$90^{*+\wedge}$	0.81
Gamma (30–45 Hz)	$88^{\#\wedge}$	0.76	$90^{\#\wedge}$	0.79	$99^{*+\#}$	0.99	$94^{*+\wedge}$	0.89
Normalised Amplitude								
Delta (1–4 Hz)	$61^{\#\wedge}$	0.21	$61^{\#\wedge}$	0.21	$93^{*+\#}$	0.85	$65^{*+\wedge}$	0.30
Theta (4–8 Hz)	$55^{+\wedge}$	0.11	$57^{*\wedge}$	0.14	$92^{*+\#}$	0.85	$57^{\wedge}$	0.14
Alpha (8–13 Hz)	$56^{+\#\wedge}$	0.12	$57^{*\#\wedge}$	0.13	$92^{*+\#}$	0.84	$68^{*+\wedge}$	0.36
Beta (13–30 Hz)	$62^{\#\wedge}$	0.23	$61^{\#\wedge}$	0.22	$94^{*+\#}$	0.87	$72^{*+\wedge}$	0.44
Gamma (30–45 Hz)	$73^{\#\wedge}$	0.45	$74^{\#\wedge}$	0.48	$99^{*+\#}$	0.97	$88^{*+\wedge}$	0.75

5.2.2 Depression versus control

The result of classification of the depression patients and control subjects is shown in Table 5. Amplitude features have shown small differences between marked and ICA data. For example, the delta band had 59% accuracy in the marked data and ICA 62%; for the theta band, marked data had 66% accuracy and ICA 65%; and marked data had 55% and ICA 57% in the alpha band, while there was improvement in accuracy in the gamma band between marked data and ICA data, from 88% to 90%. Moreover, SL data had better results than raw and ICA data, as shown in Table 5; however, the ICA + SL gave the best result in all bands for amplitude. The delta, alpha and beta bands for amplitude gave 100% accuracy, and the gamma gave 99% accuracy.

The normalised amplitude results showed that the percentages are quite similar between the raw, ICA and SL data. For instance, the theta band in raw data gave 55%, whereas ICA and SL gave the same accuracy, 57%. The gamma band is the one where raw and ICA data gave large differences, with SL raw data achieving 73% accuracy and ICA 74%; whereas SL had 88%. Overall, ICA + SL gave the best result for normalised amplitude, where all bands had above 90% accuracy.

The gamma band for both amplitude and normalised amplitude gave 99% accuracy for ICA + SL data, as well as in this data the accuracy was similar or converged in other bands. For example, amplitude has three bands with the same 100% accuracy, and the rest approached 100%. Also, for normalised amplitude, the bands approached 93%, except the gamma band has greater accuracy than the others.

Table 6. Accuracy percentages and biomarkers informedness for classification of epilepsy v control for each band for amplitude and normalised amplitude. The following symbols indicate significant differences: * from Raw, + from ICA, # from SL, ^ from ICA+SL

	Raw data		ICA data		ICA + SL		SL	
Frequency bands	Accuracy %	BM	Accuracy %	BM	Accuracy %	BM	Accuracy %	BM
Amplitude								
Delta (1–4 Hz)	$64^{+\#\wedge}$	0.28	$67^{*\wedge}$	0.16	$84^{*+\#}$	0.60	$69^{*\wedge}$	0.38
Theta (4–8 Hz)	$66^{+\#\wedge}$	0.32	$71^{*\#\wedge}$	0.34	$83^{*+\#}$	0.59	$77^{*+\wedge}$	0.54
Alpha (8–13 Hz)	$64^{\#\wedge}$	0.28	$66^{\#\wedge}$	0.16	$82^{*+\#}$	0.57	$74^{*+\wedge}$	0.48
Beta (13–30 Hz)	$85^{\#}$	0.70	$85^{\#}$	0.66	$86^{\#}$	0.63	$82^{*+\wedge}$	0.65
Gamma (30–45 Hz)	$93^{+\#\wedge}$	0.86	$92^{*\wedge}$	0.82	$96^{*+\#}$	0.91	$92^{*\wedge}$	0.84
Normalised Amplitude								
Delta (1–4 Hz)	$60^{+\#\wedge}$	0.19	$64^{*\#\wedge}$	0.12	$77^{*+\#}$	0.47	$68^{*+\wedge}$	0.36
Theta (4–8 Hz)	$62^{\#\wedge}$	0.25	$62^{\#\wedge}$	0.05	$66^{*+\#}$	0.19	$67^{*+\wedge}$	0.35
Alpha (8–13 Hz)	$59^{+\#\wedge}$	0.17	$64^{*\#\wedge}$	0.12	$77^{*+\#}$	0.46	$67^{*+\wedge}$	0.34
Beta (13–30 Hz)	$70^{\#\wedge}$	0.39	$71^{\#\wedge}$	0.28	$80^{*+\#}$	0.55	$74^{*+\wedge}$	0.48
Gamma (30–45 Hz)	$82^{+\#\wedge}$	0.64	$76^{*\#\wedge}$	0.43	$87^{*+\#}$	0.69	$91^{*+\wedge}$	0.82

5.2.3 Epilepsy versus control

For this classification, the reduction in accuracy of all results was apparent when compared with the other classifications. Moreover, the accuracy percentages for the delta to gamma bands do not differ from those of the other classifications, as shown in Table 6. For example, raw data in the delta band has 64% accuracy, and gamma has 93%. However, the alpha band for each type of pre-processing for amplitude is less accurate than the theta band, which did not occur for the other classifications (Tables 4 and 5). For instance, for raw data, the theta band has 66% accuracy, and alpha has 64%; for ICA data, the theta band has 1% accuracy, and alpha has 66%. For amplitude at all frequency bands, ICA + SL gave the best result of all data pre-processing. The gamma band with ICA + SL gave 96% accuracy, the highest accuracy of all bands.

The disparity between pre-processing is not great, especially between raw, ICA and SL data. For example, the delta band raw data got 64% accuracy, ICA 67%, and SL 69%. While the disparity between them and ICA + SL is obvious in the lower bands, it is not as great in the higher bands. For instance, the delta band ICA + SL had 84% accuracy, which is great in comparison with the others; however, the beta band ICA+ SL had 86%, while raw data and ICA data had 85% and SL had 82%.

Normalised amplitude had different results from amplitude, with disparities in accuracy between the bands for each type of pre-processing. For example, raw data for the alpha band had 59% accuracy, while delta had 60%, and theta had 62%. Also, for ICA and ICA + SL, delta and alpha have the same accuracy percentages, while theta is less accurate. SL gave the highest accuracy in the gamma band, where it was 91%. The gamma band ICA + SL was less accurate than SL, which is due to the disparity between raw data and ICA data, where raw data had 82% while ICA data had 76%.

5.2.4 T-test

Student’s t-test has been used for statistically analysing the results. The t-test was calculated for each band in both amplitude and normalised amplitude frequency bands between the pre-processing data. Tables 4, 5 and 6 show the significant differences and non-significant differences between the data pre-processing types for each classification ($p < 0.05$).

In delta and alpha bands over both amplitude and normalised amplitude usually give significant different level between data pre-processing. However, the other bands have different result from one classification table to other table.

The t-test results for raw and ICA data shows non-significant difference in more than one of the different frequency bands. Most of the time, the non-significant difference arose between those data pre-processing in all classification tables and over all bands, were 13 out of 30. ICA + SL has significant difference with each pre-processing over all bands in each Tables 4, 5 and 6. ICA+SL has proved that the combination between those pre-processing gives the best result overall all bands.

As mentioned previously, the SL has used to confirm that the ICA+SL is affected only by influence of SL or by the combination of both methods. The differences in the accuracy percentages have shown that as well as the t-test with the significant different in the almost all the t-test between ICA+SL and SL data pre-processing. Therefore, the ICA+SL is an effective combination of both methods

5.2.5 EMG contamination

Classification of diseases under the pre-processing data gave different accuracies, shown in Tables 4, 5 and 6. ICA data has non-significant differences with raw data more than other data pre-processing, which means ICA did not quite improve data, similar to in the first section. In this case, there may be two reasons for that. The first is the classification was performed on 124 channels on the scalp, and some have minimal muscle contamination (Fitzgibbon et al. 2016). Accuracy percentages for raw data and SL in Tables 4, 5 and 6 show small improvements over raw data and significant different in t-test in the most bands. Therefore, we can say that combination of ICA + SL improved both t-test and accuracy. As we mentioned in the first section, ICA is able to isolate and remove the EMG contamination and SL collects data from local sources. These features in the combination of ICA and SL proved the first reason. The second reason is the number of subjects in the study was limited. The number of subjects for training and testing the validation was limited, which may have affected identification of the features that were hidden by EMG contamination. SL makes the features that were hidden by EMG clear; hence, the best result was from ICA + SL.

Chapter 6

Conclusion

This thesis has demonstrated the effect of EMG on the EEG signal by comparing EEG signals under three different types of data pre-processing. The study was divided into two major sections and each of them had a goal to determine the effect of EMG contamination. The first section used three types of data pre-processing: raw data (no pre-processing), data after applying ICA, and data after applying ICA + SL. The second section used the same pre-processing as well as the raw data + SL.

The first section used NBT to determine the EMG contamination effect on the EEG signal. In this section, a random sample of subjects was used to expand the data. The tasks chosen were eyes closed, eyes open, and maze solving. The comparison was between eyes closed or open and maze solving. The Student's paired t-test was used to compare tasks under normalised amplitude as a computed biomarker for various frequency bands (delta (1–4 Hz), alpha (8–13 Hz), and gamma (30–45 Hz)). These frequency bands gave brain activity and the effect of EMG contamination. The result of the first section showed that brain activity in the gamma band is affected by EMG contamination. ICA cleans the data of EMG contamination and gives better brain activity. However, the combination of ICA + SL cleared the brain activity of EMG contamination and showed the brain activity positions and showed the difference between the tasks in the brain regions. The delta and alpha bands showed non-significant differences between tasks under all types of pre-processing, which means brain activity was not affected by applying ICA and SL. The gamma band proved the effect of EMG contamination and how ICA and SL isolated and removed it.

The second section used machine learning to classify those with neuropsychiatric diseases (anxiety, depression, and epilepsy) and control subjects under the four types of data pre-processing (raw data, ICA, ICA + SL, and SL). ANN was used for training data and testing validation. The features were extracted from NBT, which were amplitude and normalised amplitude for all frequency bands. Also, the Student's t-test was applied to discover the significant differences and non-significant differences between types of pre-processing for amplitude and normalised amplitude for all bands. The result was that SL had the highest accuracy for all the bands and had significant differences between it and raw data for anxiety v control and depression v control, and non-significant differences for epilepsy v control, with obvious differences in accuracy percentages in all bands. However, ICA had non-significant differences for all the classifications with raw data in the t-test and showed no improvement in accuracy percentages. Moreover, SL gave non-significant differences in the t-test with raw data; however, with the observed bands, accuracy percentages are improved.

In general, section one has proved the third expectation, which is that brain activity is hidden by EMG contamination, which means the isolation and removal of EMG contamination by ICA gave improvement in recordings between different tasks, and SL has further improved brain recordings and given the different positions between tasks on the scalp.

Section two has different data and methods used for classification, and the result was between the second and third expectations. ICA does not improve the accuracy percentages, which means the EMG contamination did not affect brain activity for the classification. However, ICA + SL improved the accuracy percentages, which means EMG contamination affects brain activity and by removing EMG contamination, the accuracy was improved. The effect of SL was not the only reason for the improvement in the accuracy, which was confirmed when we applied SL to raw data giving small improvements in accuracy. Therefore, ICA played role in improving the results when integrated with SL.

6.1 Study limitations

The NBT that we used is version 0.5.5-public, which has limitations in that some features cannot gives limitation in result whatever the data that has been computed. For example, Coherence, Phase Locking Value, phase looking value and Detrended fluctuation analysis (DFA) Also, for biomarker statistics we had to use the MATLAB version 2014a to display the figures. As well as the statistical tests some of them do not display figures such as one-way or two-way ANOVA, Wilcoxon paired sum test and Permutation test for paired mean difference. NBT does not provide multi-test correction and it choose to plot significance with the absence of effect size.

In the data set used in the first section, the subjects had different diseases, and some were control subjects, which may have affected the comparison because each disease had different brain activity. Moreover, the data set in section two had a small number of subjects for training the ANN and testing the validation, which may have affected the results.

This study used 124 channels to examine the entire scalp. Some of these channels are affected by EMG contamination, and some diseases are different from normal in specific regions of the brain while the rest has the same brain activity; therefore, we believe that has affected the results, especially for classification.

6.2 Future work

This study has used 124 channels from all the brain regions. However, in future work, the classification of neuropsychiatric diseases and control subjects must be specific on the regions of differentiation between each disease and the controls. As well, the number of subjects must be increased to give more accurate results.

Amplitude and normalised amplitude are the features that have been used in this study. However, it would be interesting to investigate further features such as bandwidth (BW), peak frequency, spectral edge frequency (SEF), root mean-squared EEG amplitude (RMS Amp), minima and maxima, and Shannon entropy (HSH).

The focus of this thesis was the different muscle reducing pre-processing methods and not necessarily the machine learning algorithms. It would be interesting to investigate further using the dataset with different machine learning algorithms such as SVM or even Deep Learning if the data is sufficiently large. As well as the numbers and sizes of hidden layers will be tried to see the result with different machine learning algorithms and different hidden layers.

Using the fusion of the classifiers for the 10 different band + normalised approaches, which may give much better result. More over using a diversity analysis would also be useful.

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