POLITECNICO DI TORINO

Dipartimento di Ingegneria Meccanica e Aerospaziale

Corso di Laurea Magistrale
in Ingegneria Biomedica

Tesi di Laurea Magistrale

Specific role of agency, prediction and movement in sensory attenuation: a SEP study with an ad hoc-developed platform

Relatore
Prof.ssa Gabriella Olmo
Correlatori
Prof. Giovanni Di Pino
Prof. Domenico Formica

Candidata
Chiara Casolani

Luglio 2018

The data and results of this work would not exist without the precious collaboration of the NEXTlab and the knowledge and devices provided by the professors Giovanni Di Pino and Domenico Formica.

INDEX

1. Introduction

The sensory attenuation or sensory cancellation is a phenomenon widespread in the animal world. The brain differentiates between self-induced stimuli, caused by our own movements and external stimuli, and according to many studies (which will be cited in details in the next paragraph), the first ones are more attenuated with respect to the second ones. This capacity is particularly important to cancel out unnecessary information and stress the attention on changes in the outer environment and consequentially be ready for any dangerous situation; in the animal wildlife, for example, every predator needs to be prepared not only for the hunt, but also for the escape if the need arises.

For what concerns humans, to understand how concrete the sensory attenuation is, many examples can be mentioned: the inability to tickle oneself, since the self-produced tickle is much less ticklish than the external one; other studies investigated the different responses in the patients with schizophrenia. In particular, patients with schizophrenia with symptoms such as auditory hallucination and passivity showed less intense sensory attenuation, as they do not recognise the difference between an external stimulation and a self-stimulation (Blakemore, Wolpert, & Frith, 2000)**.** A similar study was done on people with functional movement disorders (Macerollo et al., 2015), whose somatosensory evoked potentials (SEPs) showed relatively no differences between the external stimulus delivered with an electrical stimulation of the median nerve at a certain frequency and the self-administered stimulus consisting of a movement of the thumb, differently from what was observed in healthy subjects. In particular, the authors speculated that the suppression of SEPs in the healthy group can be related to the sensory attenuation.

The main aspects which play a role in the sensory attenuation are: agency (if the stimulation to the subject is self-exerted or externally given), prediction (if the subject is aware or not he is going to be stimulated) and movement (if the subject is moving while he is receiving the stimulation). Since the phenomenon is not clear enough to answer the question: "which is the cause of the sensory attenuation?" The guiding idea has been to distinguish all the possible combination of these three factors (Table 1.1) to understand the specific weight of every single component in determining sensory attenuation.

For the moment, only the first two combinations have been explored:

- 1- The subject pushes a button and receives a stimulus: agency component is present because he personally presses the pushbutton, prediction is present, since he knows when the stimulation is going to arrive, and movement as well, because he is doing the action.
- 2- The subject receives a stimulus from the external: no agency component is present, the subject is still (no movement), and no prediction is possible because the stimulation arrives at a random delay.

Many studies tried to identify the areas of the brain responsible for the phenomenon and at the same time deduce the main causes generating it and they will be described in the next paragraph.

ID	**Agency** *Am I the responsible for the stimulation?*	**Prediction** *Do I know I am going to receive the stimulus?*	**Movement** *Am I moving while I receive the stimulus?*
1	Yes	Yes	Yes
2	No	No	No
3	No	Yes	No
4	No	No	Yes
5	Yes	No	No
6	No	Yes	Yes
7	Yes	No	Yes
8	Yes	Yes	No

Table 1.1 Three variables needs to be taken into account: agency, prediction and movement, and there are eight possible combinations of these three. To examine which are the causes of the sensory attenuation all the possibilities should be examined.

1.1 State of the art

Blackemore et al. found in **prediction** and in the 'forward model', first articulated in 1976 by B. A. Francis and W. M. Wonham, the explanation of the sensory attenuation (figure 1.1). When the motor command is driven by the subject, who is aware he is going to stimulate his sensory-motor system, an **efferent copy** of the movement is produced, and since it's the subject himself that planned the action, there is little or nearly no discrepancy between the actual sensory feedback (**re-afference**) and the predicted one. This way the sensation becomes attenuated, and to resume the previous example, the tickling does not have effect. On the other hand, as the discrepancy gets bigger (for example because of a certain delay or a change in the orientation of the movement) or when the prediction is completely missing, the efferent copy does not correspond to the sensory feedback or it's not even created, as in the case of an external stimulus.

The consequence is that the sensory attenuation decreases proportionally to reach the minimum in case of externally generated sensations (Blakemore et al., 2000)

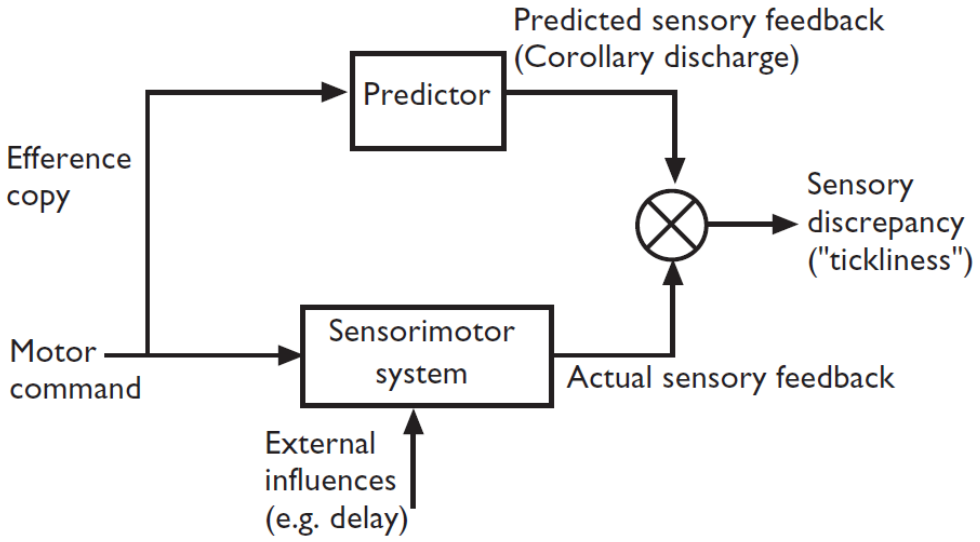

Figure.1.1 The forward model states how a movement can be predicted comparing the efference copy of a motor command with the sensory feedback. An example is the determination of the gaze direction: Helmoholtz (Helmholtz, 1867)proposed this model since eye muscles does not have receptors for this purpose. The brain creates an efferent copy of the movement of the eyes muscles to interpret the gaze direction and consequently locate the objects around us in the space. In fact, if the eyes are moved without using the muscles, for example soflty pushing the bulb, it seems like the world around is moving, because there is no efferent copy of the new position of the eyes, and the sensory discrepancy becomes significant.

This explanation was adopted also by **Shergill et al.** who stated that the sensory attenuation of self-generated stimuli deals with prediction. In particular, this research group studied the tit-for-tat phenomenon, a **force matching task** in which there are two people and one hit the other, then the second person is asked to hit back the first one with the same force he felt and the other person does the same thing afterwards in a loop. It can be noticed that the trend of intensity is growing and this confirms that the external stimulus is perceived as stronger than it actually is. Subsequently, the author sets two different experiments to evaluate the various aspects of the force matching task. The first one is represented in figure 1.2(A). Two subjects, one at a time, have to push with the index finger on a lever, while the other one has its own finger on the other side of the lever in order to feel the force exerted by the first one. A sensor embedded on the lever allows to record the magnitude of the force exerted. In the second experiment, a single subject undergoes two different conditions: in both of them, the subject exert the force and feels it as well. In the first condition the force is exerted by pushing the lever with the index finger of one hand and felt with the index of the other one positioned as shown in figure 1.2 B (upper side). In the other condition, the force is not exerted directly by pushing on the lever, but through a joystick, which acts as an actuator to deliver the force (figure 1.2(B) lower side). The first experiment showed the increasing trend expected in the exchange of forces between two subjects. In the second experiment, the comparison is between the self- and the externally induced stimuli and it shows that the forces match in a more precise way when the joystick is used as an actuator, because the predictive processes are not engaged and the stimulus is treated as if coming from an external source. This means that sensory attenuation is absent (Shergill, Bays, Frith, & Wotpert, 2003).

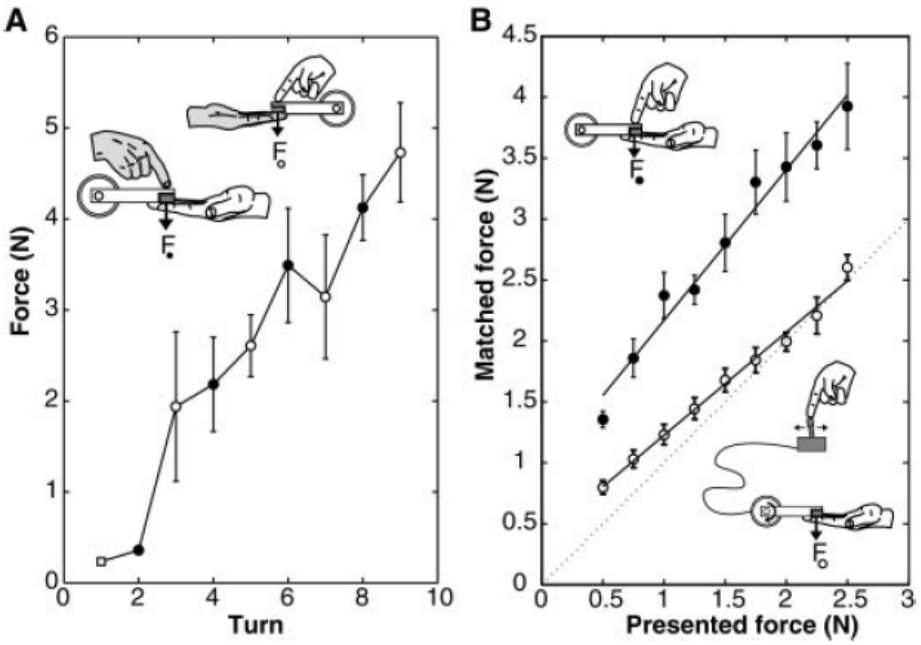

Figure 2.1 (A) the first experiment consists of matching the force perceived from the other subject pressing with the finger a lever. The trend is noticeably increasing. (B) in the second experiment the dotted line indicated the real behaviour of the force. There is only one subject in this case and the comparison is between the condition in which the subject has to match the force felt pressing directly with the other finger the lever and the condition in which the joystick is the actuator.

Pareés et al. interpreted this drop in the sensory attenuation of the second experiment as a lack of "voluntariness" of the action: the subject does not feel the stimulation as coming from himself even if he has the control of the joystick. This research group associated the sensory attenuation with the **agency**. When the sense of agency is missing because of the addition of this actuator between the movement and the sensation, the sensory attenuation tends to disappear. In fact, the subjects reported to feel these stimulations as involuntary, even if they were not (Pareés et al., 2014).

For what concerns **movement**, **Rushton et al.** wrote a long study that was recalled by **Angel et al.**. They concluded that if a digit is stimulated and simultaneously there is a movement, both active or passive, or even an external stimulus applied on the digit itself, two effects are obtained: the sensory threshold increases and the amplitude of the SEPs decreases. The authors conclude that the afferent information related to movement has a principal role in the modulation of somatosensory evoked potentials and in sensory attenuation (Angel & Malenka, 1982).

Some other groups found conflicting results attempting to eliminate variability and trying to understand which is the driving cause of the phenomenon. For example, **Voss et al.** stimulated the motor cortex of the subject with TMS (transcranial magnetic stimulator) to delay his voluntary movement. It is demonstrated that during the onset of a **movement** there is a decrease in the SEP, but it is not clear how the brain activity in the motor area can modify the perception of the movements, and in particular the sensory attenuation. In the experiment, it emerged that during the delay introduced by the TMS there was an attenuation even if the movement was absent, and this confirmed the hypothesis that the sensory attenuation depends on central signals involved in the preparation of the movement before the primary motor cortex intervenes. Moreover, they verified that the

extent of the attenuation is practically the same in these two conditions: with and without an added delay, and thus, with or without movement. This proves that the movement is not strictly necessary to generate the sensory attenuation (Voss, Ingram, Haggard, & Wolpert, 2006).

Another study which isolated the movement component, was conducted by **Hughes et al**. The authors introduced a delay of 400 ms between the movement (pressing a button) and the stimulus that in this particular experiment was visual. This delay was necessary to be sure no signal related to the movement was present together with the signal representing the visual stimulus. Both ANOVA and t-test confirmed that 400 ms was a sufficient delay to get rid of the effect caused by the motion. These tests have been done analysing four conditions: action to effect (that means an action linked to a certain stimulus, in this case visual), action to no effect (press the button but no visual stimulus), effect only and no effect. (Hughes & Waszak, 2011).

The first aim of this study was to find if an attenuation in visual ERP can distinguish self-triggered stimuli with respect to the external ones. This result did not emerged; the expected output was not found in correspondence to the electrodes in the occipital cortex but in the frontocentral areas and at long-latencies. In particular, 150 ms after the onset of the visual stimulus (in the condition action followed by effect) there is a reduction in the activity registered by the P3 electrode (figure 1.3 B). The hypothesis could be that in the condition "action to no effect" the subjects activated the visual area to the same extent with respect to the other situation because of a prediction of the stimulus. The late activation instead could be a subsequent evaluation of the stimulus.

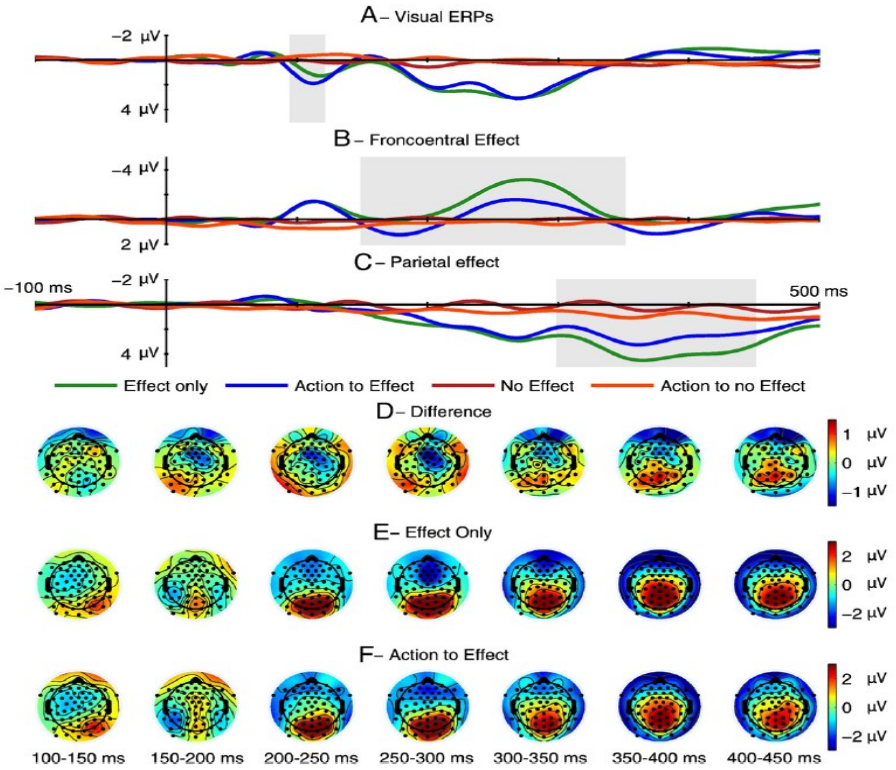

Figure 3.1 Averaged ERPs in the range of -100 ms to 500 ms of the four conditions analysed: effect only, action to effect, no effect and action to no effect. (A) electrode in the occipital cortex (activity in the visual area) (B) frontocentral area (C) parietal electrode. In (D), (E), (F) are present the topographical plots of two of the conditions (effect only and action to effect) and the difference between the other two (effect only minus action to effect).

The second aim has been to differentiate the activity on the basis of the presence or absence of prediction, and some differences were clear in the motor activity before (figure 3.1) and after the movement of the subject. These differences could represent the cerebral correlate of the creation of the "efferent copy" previously cited even by Blackemore.

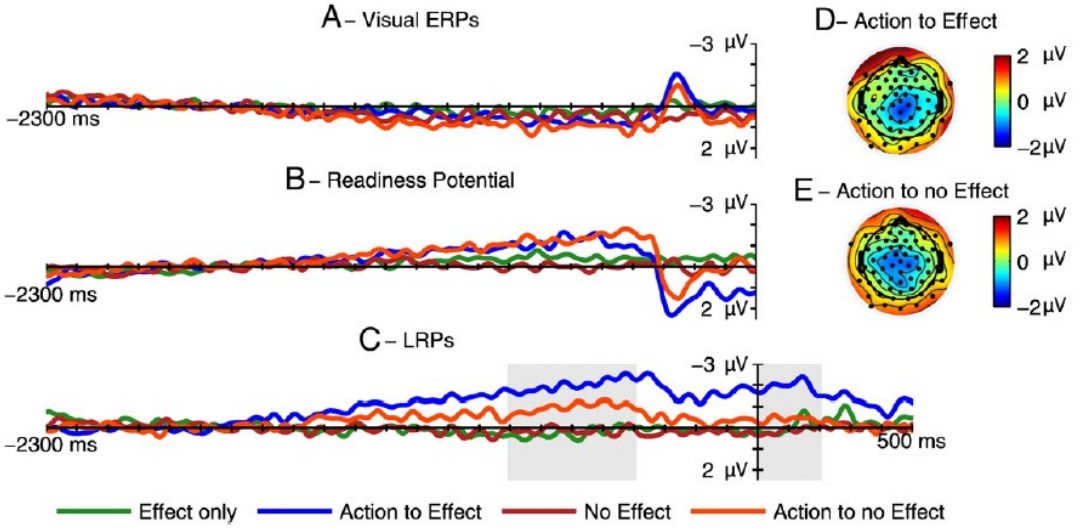

Figure 4.1 Pre-stimulus averaged ERPs (A) in visual cortex, (B) motor cortex, (C) lateralised readiness potentials and related topographic plots related to the conditions of (D) action to effect and (E) action to no effect.

It is clearly evident that lateralized readiness potentials (LRPs), which reflect the onset of any motor action on a certain side of the body, have a greater amplitude in the "action to effect" condition compared to the "action to no effect" case (figure 4.1 C). Since the differences are clear in the pre-stimulus phase of the experiment, the conclusion could be related to the forward model: the LRP probably plays an important role in the prediction of the effect of voluntary action, such as the creation of the efferent copy.

Kida et al. proposed an experiment in which the subject receives an electrical stimulation and eventually has to close his hand in correspondence with a warning auditory stimulus. The experiment is made up of three conditions: "movement", "no movement" and a control condition of "counting". When the subject perceives the auditory stimulus, he voluntary closes the hand (movement condition) and the prediction is present because of the forewarned stimulus. The analyses has been made both in early and delayed SEPs. Many research groups found that the short-latency SEPs are attenuated when the stimulation is followed by a voluntary action of the subject (among all Haggard et al.).

The differences that emerged in this study between the first two conditions are in the frontal electrodes (Fz, F3) at a latency of 30 ms, with a negative polarity (N30), and in the central ones (C3 for example), at a latency of 60 ms, with positive polarity (N60) (Figure 5.1). In both cases the "movement" condition in attenuated confirming the results found in the other studies and the "counting" condition didn't differentiate much from the "rest" condition, meaning that **attention** and **concentration** don't have an impact.

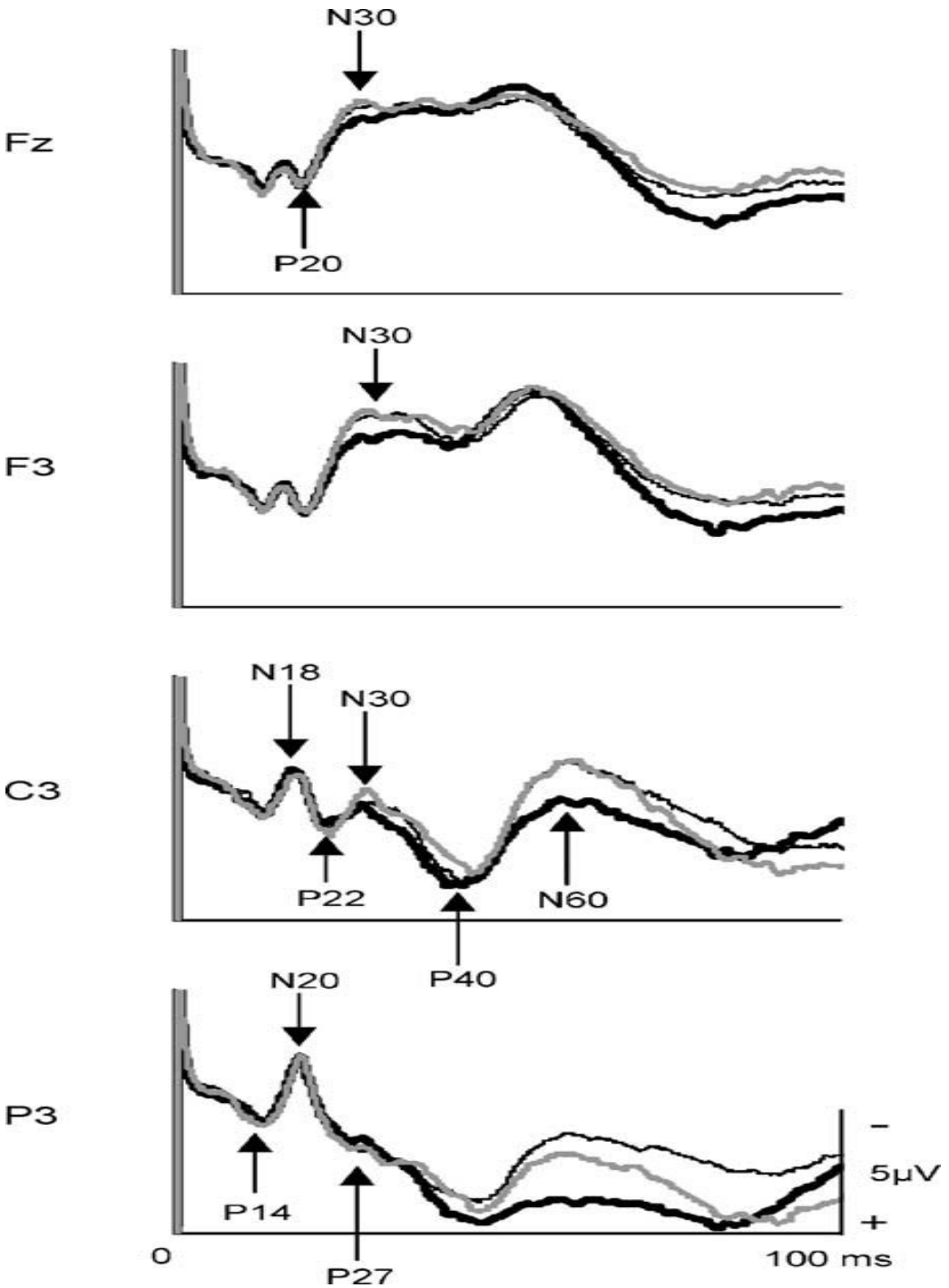

Figure 5.1 The condition in black is "movement", the thinner line is the condition of "no movement", and the grey one is the "counting condition".

For what concerns long-latency SEPs, there is less evidence in literature, and some results are discordant. In figure 6.1 the results showed a difference in amplitude in P80 and N140 , in Cz e Pz the trace representing the condition of movement is attenuated at 80 ms, while in Fz e Cz at 140 ms of latency.

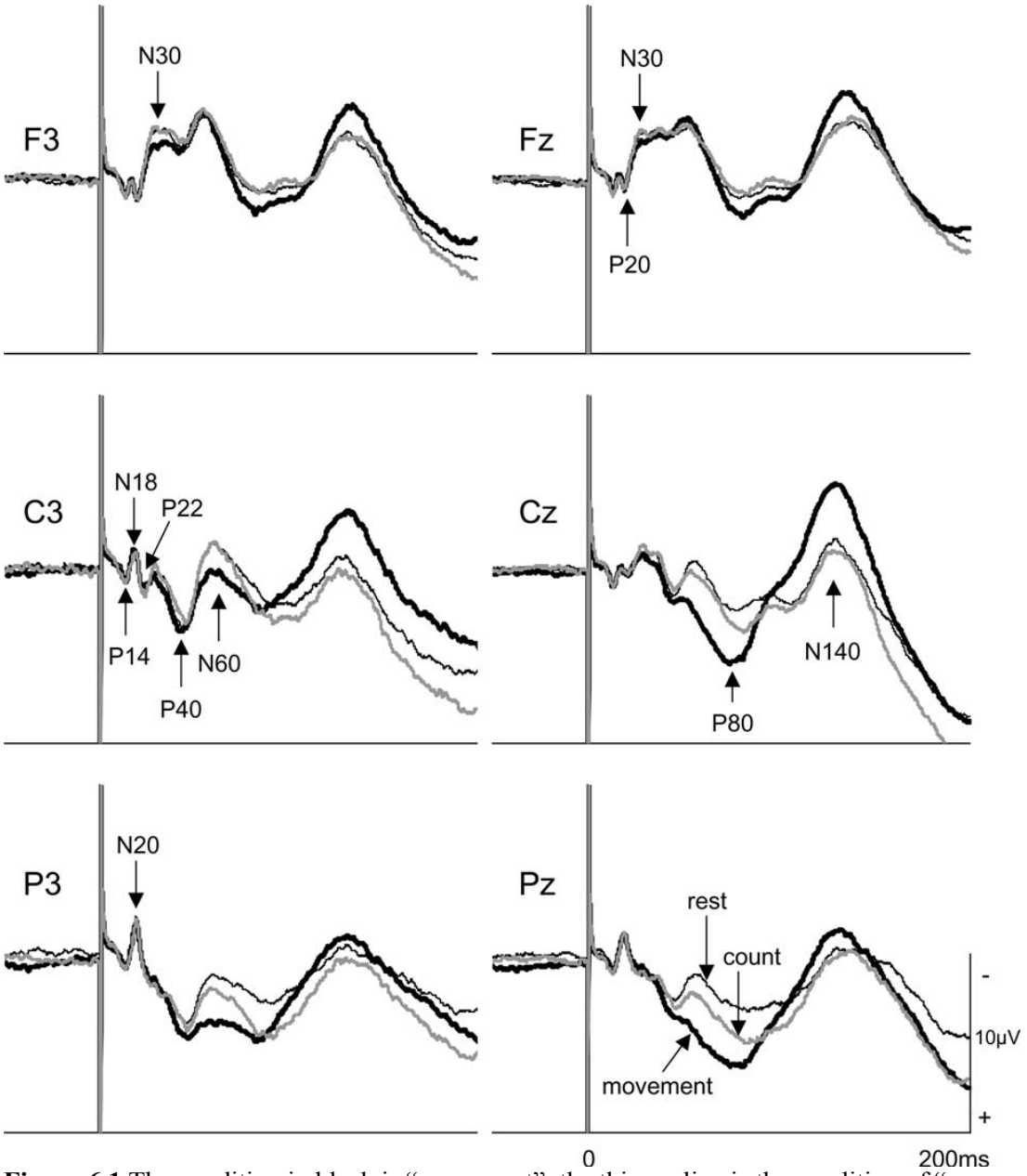

Figure 6.1 The condition in black is "movement", the thinner line is the condition of "no movement", and the grey one is the "counting condition".

The conclusion of the article is that the short-latency attenuations of the previously mentioned channels is due to efferent mechanisms, that means from motor controls outward, while the attenuations observed in long-latency waves could be determined both from efferent or afferent effects. (Kida, Nishihira, Wasaka, Sakajiri, & Tazoe, 2004).

Another work on evoked potentials analysed also by Hughes et al. was conducted by **Baess et al.**. The auditory evoked potentials result attenuated as well when the stimulus is self-initiated with respect to the external one, but the localisation of this type of stimulus is more difficult with respect to the visual one elicited by Hughes. In the experiment both the auditory middle latency responses and the evoked 40 Hz responses were tested and both resulted attenuated, as expected.

The conclusion is that this concur to an optimisation of the handling of outer acoustic events (Baess, Widmann, Roye, Schröger, & Jacobsen, 2009).

Sensory attenuation, as said before, is necessary to relieve the central nervous system from an excessive work. A peculiar aspect of this phenomenon is that the attenuation occurs at the level of the motor cortex even though the attenuated stimulus is not strictly related to the motor component. To explain this counterintuitive result, **Haggard et al.** proposed that the suppression involves all the sensory information concerning the movement, while there is an enhancement of all the inputs apt to the achievement of a target. (Haggard & Whitford, 2004)

To localise sensory attenuation in the brain **Blakemore at al.** conduced an experiment with fMRI and confirmed the hypothesis that the brain is activated more when the stimulus received is external with respect to a self-produced stimulus of the same intensity. In particular, the areas of the brain that seem involved are the somatosensory cortex and the anterior cingulate cortex, while the cerebellum could mediate the generation of the prediction (Blakemore et al., 2000).

Haggard et al. found that stimulating with TMS the supplementary motor area (SMA) extremely decreases the sensory attenuation felt by the subjects. For this reason, they gave to the SMA a fundamental role and discarded the hypothesis that the cerebellum is uniquely involved in prediction, without keeping out the possibility that it has a role in sensory attenuation (Haggard & Whitford, 2004).

In conclusion, there are many hypothesis about the origins of the sensory attenuation. The most supported hypothesis seems to be related to prediction, even though also agency could give a contribution. For what concerns the movement, different experiments seems to conclude that the amplitude of the SEPs decreases if the stimulation is given in correspondence with a voluntary action; on the other side a TMS-induced delay of the movement has been proven not to reduce the effect of sensory attenuation. These are the reasons why the phenomenon is still not clear enough and more studies will be needed to clarify the dynamics behind it.

2. Electroencephalographic signals

Neurons communicate through propagation of electromagnetic fields. These signals can be registered with two different techniques: electroencephalography, which registers the variation of the electric field generated from pyramidal neurons; magnetoencephalography which registers the changes in the magnetic field introduced by the variation in the electric field.

Electroencephalography (EEG) is a recording technique widely employed to study the functionality of the brain since it is non-invasive, relatively easy to use and the device is small and portable.

2.1 Neurophysiological overview

EEG signals are originated by a huge number of low voltage events which reflect the electrochemical activity of the brain. Although its volume is only around 1100/1300 cm^3, the brain is populated by around 86 billions neurons and an even greater number of support cells with metabolic functions, and this is made possible by the presence of gyri and sulci, which extend the contact surface of the brain. The magnitude of differential potentials registered on the surface is of the order of few to tens μV because there are many tissues between the electrons and the neurons such as skin, cranium and cerebral fluids.

The signal generated by the brain is casual, since it is the superimposition of many waveforms coming from many neurons at the same time; in fact, each electrode records the neural activity of the underlying area and the surrounding ones.

The **nervous system** is composed by the nervous cells or neurons, and the glial cells.

Among the glial cells we can cite: oligodendrocytes, which produce and maintain the neurolemma or sheath of Schwann, and the astrocytes, which regulate the chemical environment of the neurons and provide them with nutrients.

The neurons present four different morphological areas that can be distinguished: nucleus (soma), dendrites, axon and presynaptic terminals. The nucleus, which is inside the soma, contains the genetic information and two different structures originate from it: dendrites and the axon. Dendrites are the connections with the other neurons and since they receive the stimuli incoming they represent the “input” of the neuron.

The axon, which is longer, represents the “output”, since it carries the stimuli to the near nervous cells through the synapses.

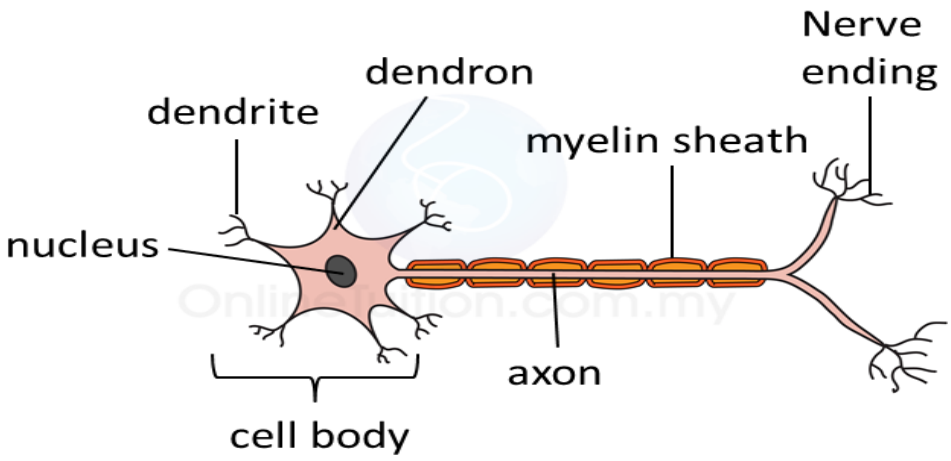

Figure 1.2 The structure of the neuron: nucleus (soma), dendrites, axon and presynaptic terminals.

2.1.1 Propagation of the action potential

The central nervous system receives a huge number of signals both from the external and from the internal receptors. These stimuli are transformed into electrochemical impulses, based on the difference of electrical potentials caused by the different concentration of ions. This process is called signal transduction. The impulses are the language of the brain and they can be transmitted through the brain thanks to another process called propagation.

A current flow is possible thanks to an electrical differential potential. In fact, in resting condition each neuron has a membrane potential equal to -70mV with the inside of the cell negatively charged. The difference is in the concentration of sodium (Na+) which is present in higher concentration in the interstitial liquid external to the neuron, and potassium (K+) ions more present in intracellular liquid. In the internal side of the neuron both chlorine ions (Cl-) and negatively charged proteins are contained in higher percentage.

Potassium is free to move following the gradient because there are specific channels through which it can cross the membrane, migrating from the internal side to the external side, while the sodium tends to remain in the extracellular side. This difference in permeability together with the activity of the sodium-potassium pumps (specific proteins able to actively move the sodium ions to the external side and the potassium ions to the internal with consumption of ATP) allow to keep stable the potential of the neuron.

The incoming stimulus changes the permeability of the membrane, opening many specific channels for the sodium, which enters in the cell altering the potential. When the threshold value of -55mV is reached, other voltage-dependent channels are opened, and the sodium potassium pumps are stopped. This leads to a quick depolarisation of the neuron until +35mV. The action potential is generated, as a result of the stimulus being transformed in an electrochemical impulse.

In the neuron, the action potential originates at the beginning of the axon and propagates until the end. The opening of voltage-dependent channel is caused by the depolarisation of the membrane, which spreads in the area near the starting point downstream, while

upstream the channels enter the refractory period, and do not open anymore, forcing the action potential to propagate in only one direction.

The modalities of propagation of the action potential (impulses with an amplitude of around 100 mV and with a length of 1 ms), depend on the presence or not of the myelin sheath constituted by oligodendrocytes. If it is not present the propagation is continuous, relatively slow, around 5m/s, and implies a consistent dispersion of current. Otherwise, if the myelin sheath is present the dispersion is minor because of the sheath insulating capacity. In this configuration some nodes are present, called Ranvier nodes, which interrupt the myelin sheath and in which the channels are located. In this case, the conduction is saltatory and faster, reaching 150 m/s.

The action potential travels until it reaches the synapses (meaning "conjunction"), highly specialised structure that allow the connection with another neuron or with the target efferent cell. There are two types of synapses: electrical and chemical. The electrical ones permit a direct passage of the ions between the two neurons thanks to the gap junctions, intercellular structures constituted by proteins called connexions, which permit electrical match. The characteristics of this first type of synapses are: high transmission speed, bidirectionality and synchronisation with electrical activity, and they are widely spread in the heart or in the digestive system. The chemical synapses are more numerous in mammals with respect to the electrical ones, and in this case, the transmission is unidirectional and goes from the presynaptic terminal, which belongs to the neuron which sends the message, to the postsynaptic membrane of the second neuron. Synaptic vesicles are present in the presynaptic terminal which contains the neurotransmitter, chemical substances and hormones which depolarizes the membrane and allows the transfer of the action potential. As soon as the impulse reaches the presynaptic terminal, the vesicles fuse and the exocytosis of the neurotransmitter in the synaptic fissure occurs. At this point, the neurotransmitter can reach the receptors positioned in the postsynaptic membrane and combine to them specifically, while unused portion is reabsorbed or degraded. Depending on the type of answer the synapses can be excitatory or inhibitory. In the first ones the sodium-potassium channels are opened and the permeability of the postsynaptic membrane changes in such a way to permit the depolarisation and a new action potential. In the second ones the channels which open are specific for the potassium which exits the cell and for the chlorine which enters and has a negative charge. This decreases the intensity of the propagating potential, making more difficult to generate a new action potential.

2.2. Cerebral cortex

Although the morphology of the cerebral cortex is very variable from subject to subject, the functional organisation is practically identical for everyone. Two fundamental aspects need to be reminded: each hemisphere deals with the contralateral side of the body; the two hemispheres are not exactly symmetric nor equivalent.

In each hemisphere four lobes can be distinguished (figure 2.2):

- the *frontal* lobe or associative cortex, which was studied at the beginning in relation with aphasia. In fact, in this region is included Broca's area, essential in the articulation of sentences and in expressing ideas. This lobe is involved in the elaboration of the thought and the interaction with the external world, emotion, behaviours, short-time memory and control of the movement.

- the *temporal* lobe, is fundamental to understand the language since Wernicke's area is included. Further studies in epileptic subjects with the seizure in this area, demonstrated also the relationship with emotional control that was altered in correspondence of the event. Functions linked to the processing of sensory stimuli and long term memories are asserted as well.

- the *occipital* lobe, is involved in elaborating visual stimuli. Here the primary visual cortex carries out different functions: each group of neurons is specialised in the recognition of a certain stimulus such as orientation or colour

- the *parietal* lobe, has implications in somatic sensations and in the formation on the body image and the characterisation of the extra-personal space

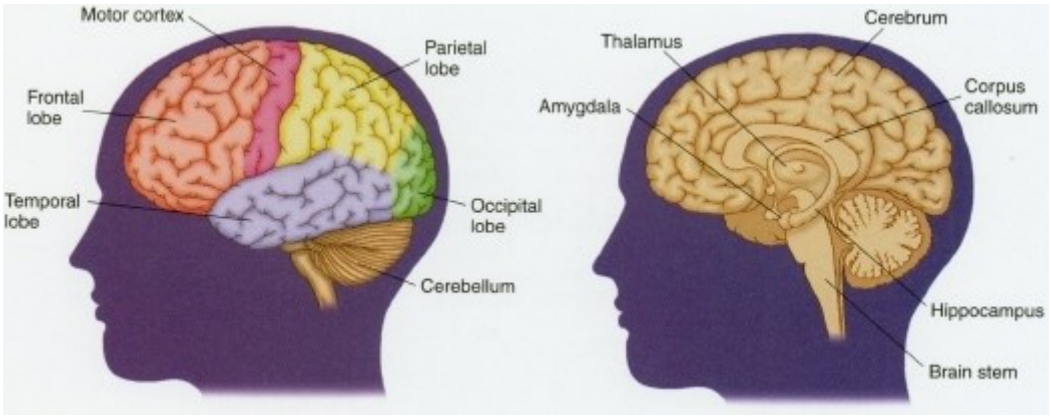

Figure 2.2 Lateral view of the cerebral structures of the brain with lobes in evidence.

Each lobe, in its turn, is characterised by some cortical areas, which are designate to a specific function. (Figure 2.3)

- Primary motor cortex: beginning of voluntary movements
- Broca's area: speech, from the thoughts to the elaboration of the spoken words
- Orbitofrontal cortex: feelings and problems resolution
- Primary olfactory cortex (deep)
- Primary auditory cortex
- Wernike's area: comprehension of the language
- Primary visual cortex: simple visual stimuli recognition (colours, light intensity…)
- Visual association area: elaboration of visual information
- Primary gustatory cortex
- Somatosensory association cortex: elaboration of complex somatosensory information
- Primary somatosensory cortex: identification of somatosensory information

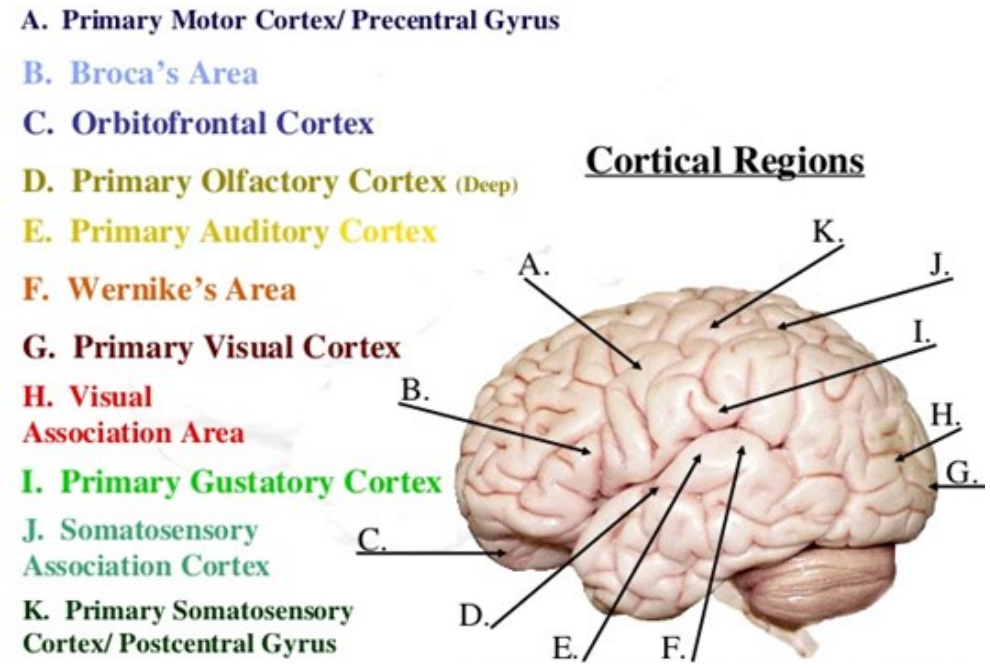

Figure 3.2 Cortical areas of the brain each one designates to a specific function.

The majority of the functions are executed by neurons from different regions, this means that, since functions are related to certain areas, some areas have a stronger correlation with a certain activity with respect to another, but different areas are connected among each other with associative cortex and cooperate to the achievement of the objective.

2.3 EEG signal spectra

Two fundamental parameters to describe an EEG signal are the amplitude and the frequency oscillation.

The amplitude can variate between 10 and 500 μV, and the signal can be divided in:

- EEG low amplitude: < 30 μV
- EEG medium amplitude: 30-70 μV
- EEG high amplitude: >70 μV
- The frequency oscillation, instead, has a range that goes from 0.5 to around 40 Hz. Inside this range it is possible to distinguish some sub-bands (Table 2.1):

Frequency Band	Frequency	Brain condition
Delta δ	0.5-3 Hz	Very deep sleep, pathological condition
Theta θ	4-7 Hz	Sleep
Alpha α	8-12 Hz	Very relaxed, passive attention
Beta β	13-35 Hz	Attention, concentration, cortical areas activated
Gamma γ	>35 Hz	Deep concentration and muscular effort

Table 1.2 Frequencies bands in EEG signals related to brain states

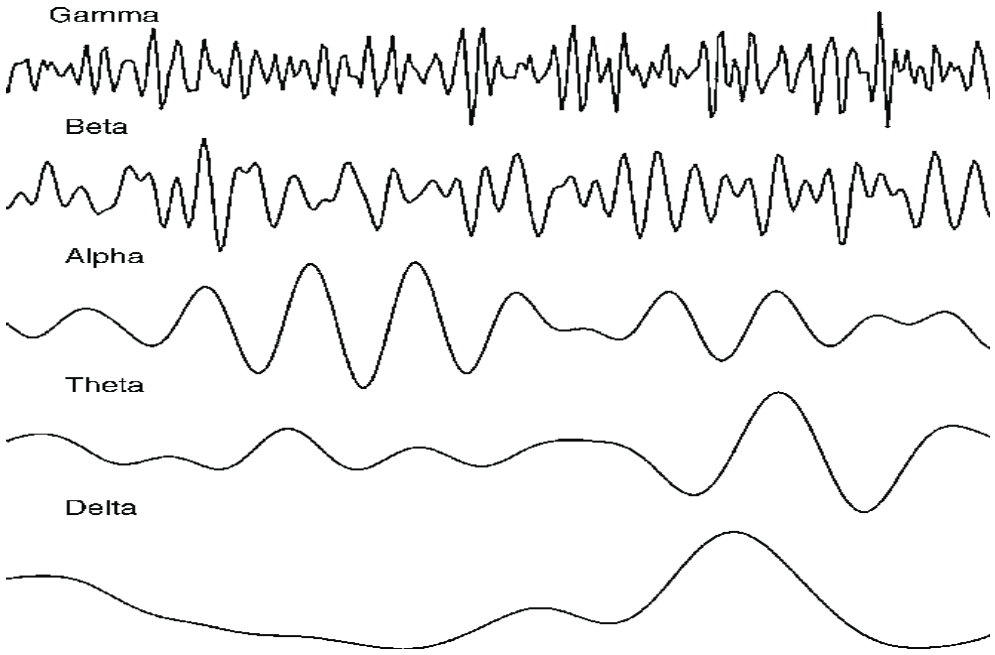

Figure 4.2 Brain waves graph in order of increasing frequency.

- Delta waves (δ): band between 0.5-3 Hz and an amplitude less than 100 μV. This very slow waves are associated with pathological conditions or a very deep sleep. In this phase the brain relaxes and reorganises ideas.
- Theta waves (θ): band between 4-7 Hz and amplitude less than 100 μV. Those waves are usually associated with sleep.
- Alpha waves (α): band between 8-12 Hz and amplitude less than 10 μV. These waves describes a condition of relax, for example when a person is falling asleep. In the occipital area the amplitude of alpha waves increases when eyes are closed and decreases rapidly when they are opened.

In the same range of frequency there are also the μ waves, correlated to the movement or the intention of the movement. They are present exclusively in the motor cortex of humans and Primates and are very often elicited for development of specific brain computer interfaces (BCIs).

- Beta waves (β): band between 13-35 Hz with an amplitude smaller than 20 μV. They are usually present when the subject is in the middle of a mental or motor activity and it is possible to register them in frontal, central e parietal areas. There are more sub-bands because the lower bands are related to attentional tasks, while the higher are related to operative tasks.
- Gamma waves (γ): band that goes over 35 Hz. This band is characterised by a deep concentration of the subject and a high muscular effort.

2.4 Event-Related potentials

Event-Related potentials (ERP) describe responses of the brain when a change in the environment occurs. In cognitive experiments the EEG of the subjects is registered to study the cerebral response to certain events or stimuli. The ERPs are defined as the mean of the signal over all the epochs, (intervals of fixed length the time trend is divided into), and this means that for each electrode there is a correspondent ERP.

ERPs can be extrapolated by the EEG since they are deterministic signals, and therefore have a precise and repeatable shape, with certain latencies, amplitudes and polarities (that

can be positive 'P' or negative 'N'). To be able to collect these signals, epochs or trials are computed in correspondence to a specific event. For each epoch the subject receives a stimulation and depending on the type of stimulus these potentials can be distinguished in: visual (VEP), auditory (AEP) and somatosensory(SEP), which will be explained in details in the next pages (Schomer & Silva, 2015). The duration of the epoch has to be set long enough to register all the potentials desired. Usually the beginning of the epoch is set a few millisecond before the stimulus and the end is dependent on the type of study. Long latency ERP investigation will need a longer epoch with respect to a study focused on short-latency ERPs only.

Since their amplitude is quite low, ranging from less than a μV to tens of them, and are often hidden by noise, detecting the signal requires certain processes. ERPs can be analysed both in time and in frequency, but the most diffused protocol followed is in **time,** through a technique called 'averaging'.

This process consists of stimulating the subject a certain number of times, and calculating the average of the epochs (correspondent to the stimulations). Since the SEPs are localised always at the same temporal delay with respect to the onset of the stimulus and have a repeatable shape (deterministic signal), averaging the data means that only the noise (which is casual) is deleted. The principal assumptions that make this technique reliable are:

- The signal has to be deterministic and localised in time, and this hypothesis is valid for the evoked potential signal;
- The signal has to recur a sufficient number of times dependent on the improvement of the signal required and the length of the signal. This is based on the experience (we set at least 500 stimuli, to have a good reliability). In the next pages it will be show that the quality of the signal is proportional to the number of epochs averaged;
- The noise is casual, uncorrelated, wide sense stationary and ergodic
  - Uncorrelated: the cross correlation function is zero between each couple of signals;
  - Wide sense stationary: the first two statistical moments, mean and variance are independent from time;
  - Ergodicity: the signal is completely characterised taking a single observation, and this hypothesis is always assumed by definition for biological signals.

For each stimulus an epoch signal is acquired. The i^{th} epoch can be expressed with the additive model (signal acquired seen as the sum of the signal desired plus noise,) as:

$$x_i = s(t) + n_i(t)$$

From the hypothesis the signal s(t) is not dependent on the epoch, but remains equal to itself, while the noise can vary from epoch to epoch, since it is casual. Calculating the mean:

$$\bar{x}(t) = \frac{1}{N}\sum_{i=1}^{N} x_i(t) = s(t) + \frac{1}{N}\sum_{i=1}^{N} n_i(t)$$

To verify the quality of the increased signal, the signal to noise ratio SNR, that is the ratio between the power of the signal and that of the noise needs to be calculated. Taking into account the characteristics of the signals considered, it is possible to calculate the SNR evaluating the amplitude (A_s) for the deterministic signal and the standard deviation

(σ_n) for the casual noise, instead of calculating the power. The difference from the standard definition of SNR, in this case, is a factor of two since $P = {A_s}^2$ and $P = \sigma_n^2$

$$SNR = \frac{A_s}{4\sigma_n}$$

The power of noise is also equivalent to the squared mean of the signal, and the noise from the first equation can be seen as the difference between the mean of the whole signal registered and the signal of interest.

$$E[\bar{x}(t) - s(t)]^2 = \frac{1}{N^2} E\left[\sum_{i=1}^{N} n_i(t)\right]^2$$

Being Σ and E linear operators, the previous equation can be written as:

$$\frac{1}{N^2} E\left[\sum_{i=1}^{N} n_i(t)\right]^2 = \frac{1}{N^2} \sum_{i=1}^{N} E[n_i(t)]^2$$

Since the noise has null mean value the variance is defined in this way $\sigma_n = \frac{[\sum_{i=1}^{N} n_i(t)]^2}{N}$ and the previous equation becomes:

$$\frac{1}{N^2} \sum_{i=1}^{N} E[n_i(t)]^2 = \frac{\sigma_N^2}{N}$$

Calculating the new SNR

$$SNR = \frac{A_s}{4\sigma_n}\sqrt{N}$$

It is clear that the improvement of the signal is directly proportional to $\sqrt{N}$, being N the number of mediated epochs. This estimate is valid as long as the hypothesis of uncorrelated signals holds. In fact, if there is a correlation in the noise signal, another factor contributes to the power and correspond to the autocorrelation of the EEG activity. Usually this happens when a robust, regular rhythm is present, such as alpha waves.

Another aspect to take into account is the periodicity of the stimulation. In fact, it has been demonstrated by Ruchkin that a non-periodic stimulation can reduce the variance in the ERP, which is considered a measure to evaluate the quality of the signal. In particular, if the distribution of the inter-stimuli intervals is exponential, the variance is closer to a null value (Ruchkin, 1965).

The **analysis in the frequency domain**, instead, is particularly employed in two cases: 1. the ERP does not appear at a specific latency related to the trigger; 2. the stimulation is continuous. The cross-correlation or the cross-power spectrum function between the stimulus and the EEG is calculated, and not only the amplitude but also the change of the phase pre and post-stimulus are taken into account. In fact, it emerged that the reaction to a certain stimuli decrease the variance of the phase for certain frequencies.

In this case, to show the ERP obtained it is useful to decompose the EEG signal in frequency components and average the power for each component, depending on the trigger. Then, with the help of an ANOVA, it can be evaluated if there are specificity in

the signal or if the changes are casual. Sayers et al. described this phenomenon as a reorganisation of the phase spectra of the normal spontaneous brain activity.(Liss & Slater, 1974)

Finally, the last approach is the **time-frequency** one which integrates both domains. Vijn et al. explained that ERPs are not only added signals superimposed on the EEG, in fact visual stimulation, for example, reduces the amplitude of the EEG signal. As explained before, the effect of the stimulus is also that of a reduction of the phase variance for some frequencies and this consists of a "phase resetting", because some phase components of the EEG tend to align. The method developed to investigate these aspects is based on three steps: the first one is running the independent component analysis (ICA) to separate the EEG components in time, which is a method similar to PCA, but without the requirement of orthogonality for the components. Then, it is necessary to calculate the spectral power for each component and finally the inter-trial phase coherence (ITC) can be calculated, which can be defined as a "phase averaging".

2.4.1 Somatosensory Evoked Potentials (SEPs)

Somatosensory evoked potentials (SEPs) are deterministic signals which represent the electrical response of the brain to a touch stimulus or even to a bipolar electrical stimulus exerted transcutaneously on peripheral nervous fibres. Electrical stimulation generate a potential difference through the membrane of the nervous fiber and depolarise the area around the cathode. Depending on the thickness of the nerve, and the characteristics of the skin, the intensity of the stimulation can vary greatly. Usually, in SEP studies an intensity equal to three or four times the sensory threshold is selected as stimulus intensity. This is usually sufficient to generate a detectable twitch of the muscle.

In addition to the type of stimulus exerted, it is important to take into account several factors: the baseline, the recurrent frequencies, the cortical areas involved and the activity changes they show.

Usually the median nerve is elicited when the stimulation is on the upper limb, as in our case.

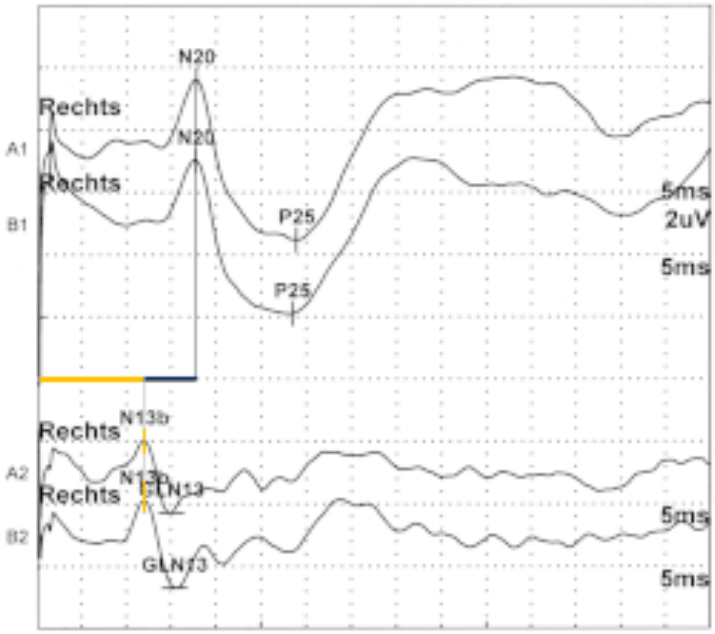

Figure 5.2. The typical behaviour of a SEP driven by the stimulation on the median nerve.

Non pathologic aspects which can alter the shape of the SEP are: age, body height and gender, skin and core temperature, attention, sleep and use of drugs.

SEPs analysis is useful for clinical assessment since patients with focal hemispheric lesions show atypical frontal and parietal behaviour of the SEPs. This suggests that, not only the somatosensory cortex (SI), but also the prerolandic cortex should have a role in the phenomenon of sensory attenuation, but this topic is still controversial. Many studies try to combine the information content of SEPs with that of medical imaging, especially functional magnetic resonance (fMRI) or positron emission tomography (PET).

2.4.1.1 Early latency SEPs

The early latency SEPs are those which are visible around 18 and 35 ms, and the frequency of the stimulation that let them emerge is usually quite low and does not exceed 2 Hz. In the case of the present experiment it is even lower than 1 Hz, to allow a better randomisation. The principal cortical areas involved and analysed to detect the SEP waves are the cortical and the frontocentral ones, in particular in the contralateral side to the stimulation.

Evoked potentials have **near field** and **far field** components. In the first ones the recording electrode is relatively near the nervous fibres which propagate the action potentials, while far field evoked potentials reflect the changing of the physical characteristic of the medium through which the potentials travel, or a sudden change in the direction, for example when the signal travels through the bend underarm to the ribcage.

Among the subjects there are some differences but the quality of the signal can be assessed considering that the profile and amplitude voltage is symmetric in each hemisphere of the same subject. In order to eliminate the differences among the subjects, related to physical characteristics like height and arm length, the interval should be calculated from the peak P14 of the far field.

N20 - P20 potentials

The waves N20 is present in the parietal area around 20 ms after the stimulation, and the P20, which is exactly the specular one, can be observed at the same latency but in the frontal cortex. They are recorded in the contralateral cortex relatively to the stimulation and are the first potentials generated when the stimulus is on the median nerve. In particular, the electrodes used to observe the N20 wave have been the P4 and eventually the CP4, and F4 for the P20, all in the right hemisphere since the stimulation was on the left.

The studies based on electrical or magnetic field generation, in addition to the cortical recordings on the scalp, show that the N20-P20 waves are generated by a dipolar source which is tangent to the scalp surface and reflects the response of the cutaneous stimulation. This finding was proved with the evidence that the N20-P20 response is absent in the case of passive finger movements.

There are still some debates about the existence or not of some independent waves, such as the P22, which being very near to this complex of waves is not always considered as generated by a distinct source.

P-24/27 – N24 and N30 potentials

The wave in the parietal region following the N20 is known as P24 or P25 or even P27 because the latency at which it appears is variable, but is usually included between 24 ms and 27 ms after the stimulation. Sometimes two waves are present both at 24 and 27 ms. This wide range of variation is determined by the fact that at these latencies many sources overlap in the parietal region. Also these potentials are observed in the contralateral side with respect to the stimulation. The P24 potential has a correspondence in the frontal region that is the N24.

The frontal N30 potential is a commonly studied SEP because it seems to have a direct connection with some motor disorders. It is registered in the contralateral side of the stimulation, as the others, but tends to spread in the ipsilateral frontal region and in the midfrontal one.

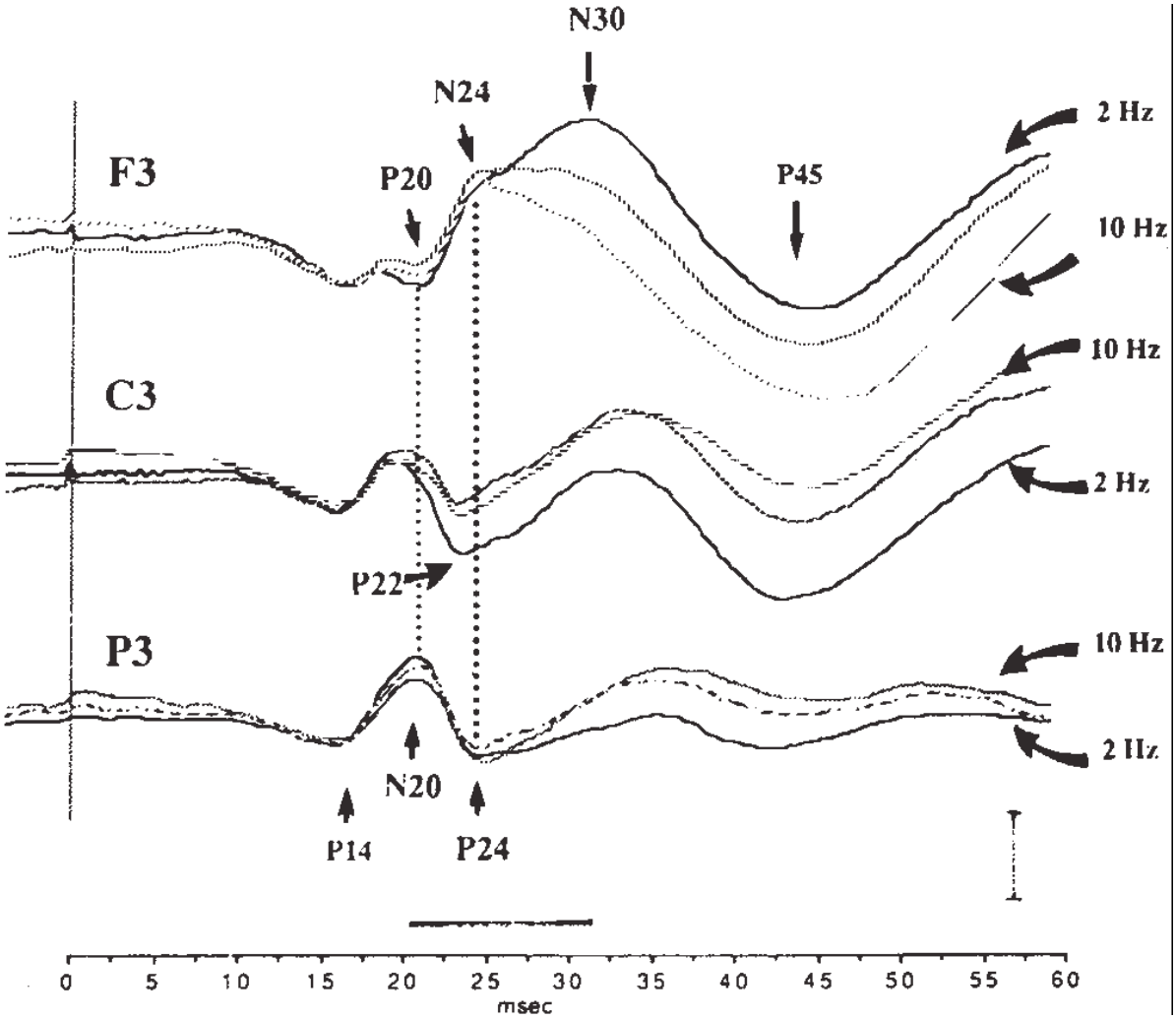

Figure 6.2 The early cortical SEPs in F3, C3 and P3 with the most significant waves in evidence.

3. Experimental Setup

The aim of the experiment is to evaluate the different effect on somatosensory evoked potentials (SEP) of self- vs. externally-induced electrical stimulation. In particular, during the experiment the participants received electrical stimuli on the median nerve either by pushing a button placed in front of him/her or by an external trigger. In the first case, the participant was moving during the stimulation (movement), had prediction of the stimulus (prediction) because he /she was also the cause of the stimulus (agency); whereas in the second case he /she received passively the stimulus (without movement, control of the stimulus and knowledge about the time of stimulation) (Table 1.3).

ID	Condition	Agency Am I the responsible for the stimulation?	Prediction Do I know I am going to receive the stimulus?	Movement Am I moving while I receive the stimulus?
1	The subject pushes the button and provides the stimulus	Yes	Yes	Yes
2	The subject receives a stimulus from the external trigger (which pushes the button)	No	No	No

Table 1.3 This table shows the two protocols followed for this experiment

3.1 Platform for stimulation and EEG recording

During the experiment, two participants sit at the two sides of a table, one in front of each other, but they can see each other only from the shoulders up, since there is a wooden panel which divide them. Both wear an EEG cap each: one is a 64 electrodes from g.Tec, and the other is not for registering purpose but it is used to create a correspondence between the conditions of the two subjects. The fake subject will be called “mirror” from now on, and act as the external trigger for the stimulus. At the beginning both the caps were used for registration (two subjects were recorded at the same time figure 2.3), but due to technical issues with the second cap, we opted for a single registering cap. On each side of the panel there is a green LED light, and fixed on each side of the table there is a pushbutton. The two participants have their right hand on their own pushbutton, whereas on the left arm of each of them two electrodes connected to electro-tactile stimulator (Digitimer, DS) are placed. The aim of the electrode is to stimulate the median nerve when triggered via the pushbutton.

The EEG channels are recorded together with ECG and EOG, in order to monitor eventual artefacts.

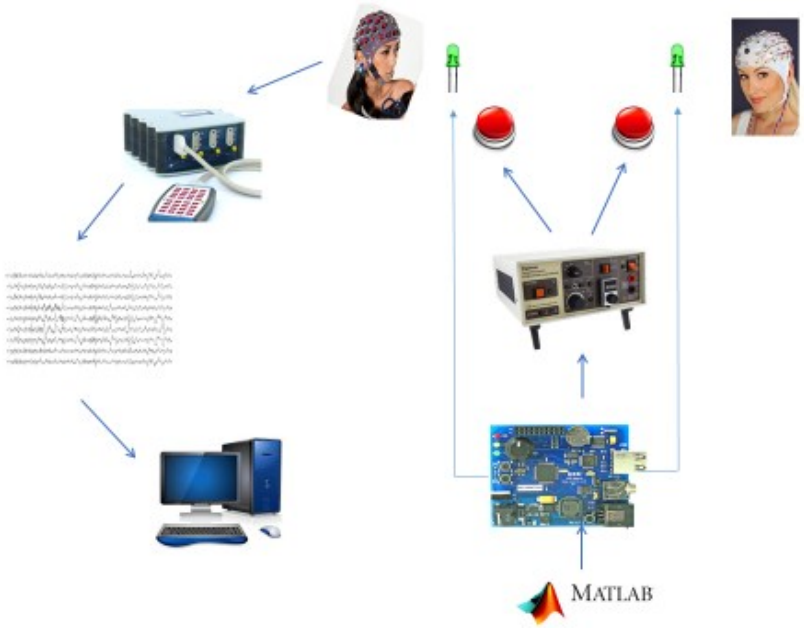

Figure 1.3. Schema of the experimental setup, the two subjects in front of each other, one with its workstation and connected to the electrical stimulator, in the middle of the figure and the other wearing a cap but without registering. Everything managed by the PIC microcontroller.

A PIC microcontroller (USBmaster, CCS Inc.) manages all the devices. This is connected by a serial port to the PC from which receives a list of 0 and 1 generated and sent by *Matlab* software, which corresponds to the condition 1 or 2 of the experiment (see Table 1.3). The subject and the mirror subject are both required to do the same task: pressing the pushbutton when they see the green led on. Depending on the received input, the PIC can switch on the LED which advices the participant to push the button. In the condition 1, the trigger is activated when the subject pushes the button. In the case 2, the trigger is activated by the mirror subject. When the trigger is active in both condition, the electro-tactile stimulator stimulates the median nerve of both participants: one of them will feel it as self-stimulated whereas the other one will be unaware of the incoming stimulus. Two different triggers (related to the condition) are sent to each amplifier of the EEG recorder to identify the two different events on EEG traces.

3.1.1 Pic microcontroller

The PIC microcontroller has been programmed in C language (Appendix A). It is connected to the PC through the SR232 port from which receives a list of random numbers generated in *Matlab*. In particular, this list is composed by 1010 events, since the minimum number required to get an appreciable SEP (somatosensory evoked potential) is 500 events per condition, and ten more to have the possibility to exclude any eventual noisy epochs (Appendix B).

In addition to this, a specific function has been used to let the list be equally composed by 0 and 1.

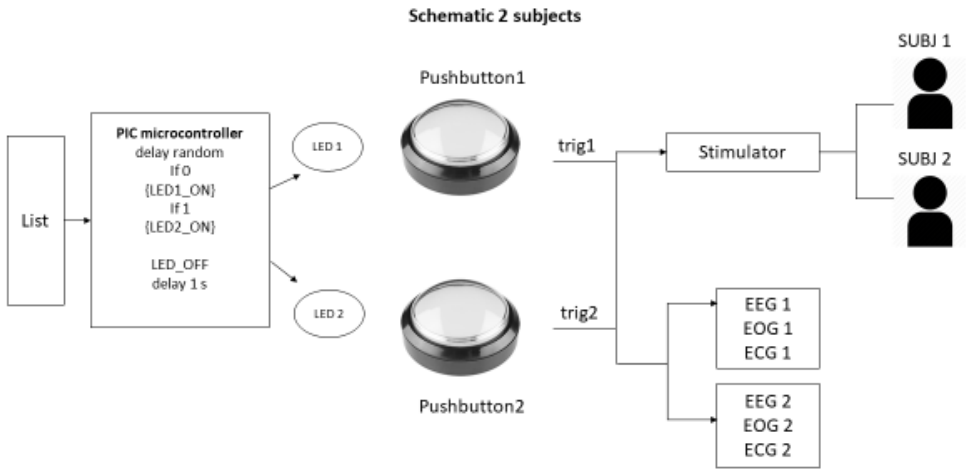

Figure 2.3 The schematic of the experiment with two subjects

As we can see from figure below (Figure 3.3), there are two green LED activated dependently on the list, two pushbutton enabled only if the correspondent LED is on and a third red LED which switches on at the end of the experiment, when the event list is over. There are three other outputs named "trig1" and "trig2" which are the triggers related to each condition of the experiment, that will be sent to both the EEG devices, and the "stim" output which will be sent to the Digitimer as input.

There is another pushbutton, embedded in the PIC to control the timing at which the experiment begins. In fact, until the pushbutton is pushed the list will not be sent.

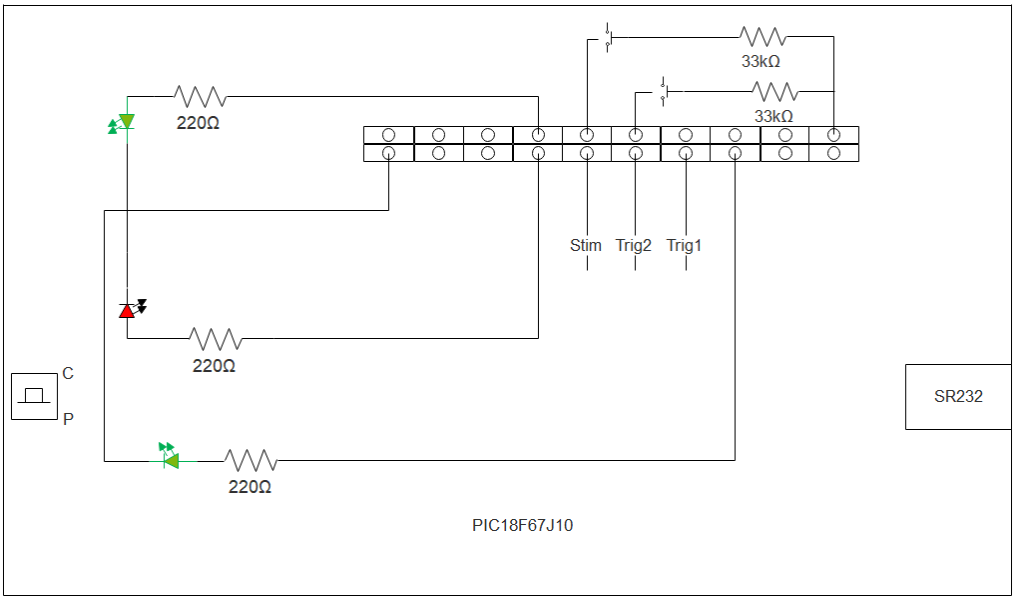

Figure 3.3 Electric scheme of the PIC microcontroller

3.1.2 Digitimer

The electrical stimulator receives one trigger input (TTL, transistor-transistor logic) from the PIC microcontroller and gives as output an electrical stimulus (a monophasic current-controlled, squared electrical waveform with pulse width equal to 200 μs) that will be split between the two subjects. To be sure the stimulation is on the median nerve, at the beginning the twitch of the thumb is induced in both the participants separately, then the intensity of the stimulus is lowered to match the sensitive threshold of both the participants without any involuntary motor component. Since the impedance characteristics of each participant can vary among individuals, the amplitude of the stimulus is variable.

3.1.3 EEG systems

3.1.3.1 EEG electrodes

The electrical potential on the scalp is registered through the electrodes. Normally silver/silver chloride (AgCl) electrodes are chosen for clinical use, since they are easy and cheap to prepare and are also stable, and quite robust. On the other hand a layer of gel or electrolytic paste between the electrode and the scalp is always needed to lower the impedance that should be always between 5 kΩ and 10 kΩ (Meziane, Webster, Attari, & Nimunkar, 2013). The preparation of the skin and the use of the conductive substance extend the time required for the experiment as the number of the electrodes increases.

Electrodes can be classifies in:

- Dry or wet: depending on the necessity or not of the gel/paste to decrease the impedance of contact
- Active or passive: Electrodes which deal with skin-electrode impedance using a circuit of preamplification and/or buffer downstream are known as active, the ones without this system are, instead, passive (Mathewson, Harrison, & Kizuk, 2017).

If a wet electrode is used, it is important to take in account that the progressive dry out of the gel can modify the impedance, and an excessive use of gel could build a bridge between two adjacent electrodes and create a short circuit (Fonseca et al., 2007).

There are also wet electrodes embedded with a circuit of preamplification, but this makes the system more expensive.

The EEG cap from g.Tec used in the experiment, is composed by 64 wet active channels. As mentioned before, there are 6 more electrodes for the first setup: these are used for EOG (4 of them) and ECG (2 in the first system) and are wet passive paramagnetic electrodes.

3.1.3.2 International system 10/20

The system usually used to position the electrodes in multichannel recordings is the 10/20 that considers as reference four points:

- nasion: at the bridge of the nose between the eyes;
- inion: projecting part of the occipital bone at the base of the skull;

- right and left pre-auricular points;

Nasion and inion together cover the anteroposterior area while the two pre-auricular points cover the latero-lateral area. The system is defined 10/20 because the electrodes are positioned at a distance that is 10% or 20% of the anteroposterior or latero-lateral distance.

The specific nomenclature for the electrodes consists in assigning to each electrode a letter which depends on the location: A stands for auricolar, C for central, P for parietal, F for frontal, FP for fronto-parietal, O for occipital; and a even number if the electrode is on the right hemisphere or odd if it is on the left (Trans Cranial Technologies Ltd., 2012).

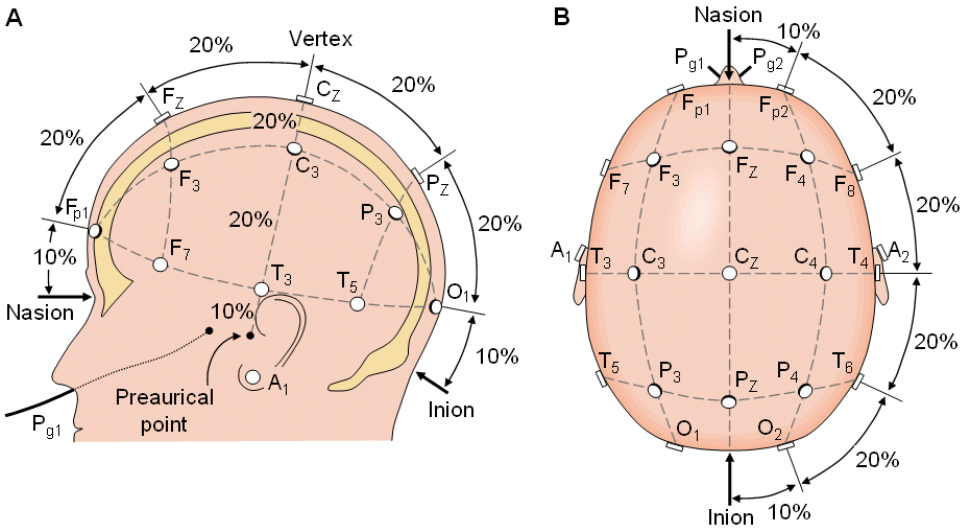

Figure 4.3 Standard 10-20 for the positioning of brain electrodes

The cap is in the right position if the central electrode, that is Cz, is exactly at the half point between nasion and inion and the two preauricolar-points (Trans Cranial Technologies Ltd., 2012).

The electrooculography signal measurement, known as EOG, detect the position of each eye through a measurement of the resting potential. There is a voltage between each couple of electrodes and assumed as constant the frontal position, as the eye rotates toward the electrode the potential becomes positive or negative depending on the electrode. Regarding the placement of the EOG electrodes we use a cross-channel method which assures a better accuracy with respect to the conventional positioning (Tamura, Yan, Sakurai, & Tanno, 2016).

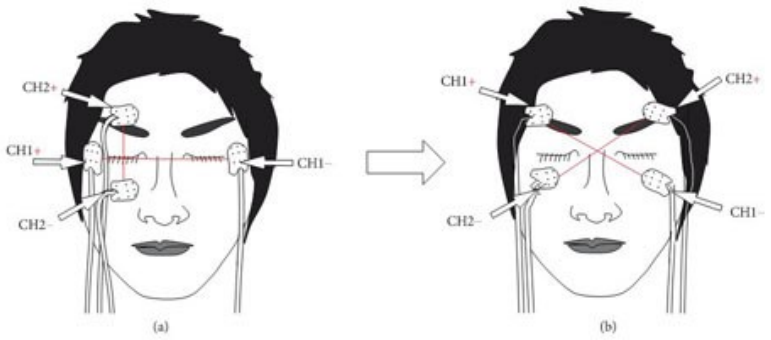

Figure 5.3 Conventional electrodes positioning for EOG on the left, cross-channel positioning on the right.

The montage to register the ECG has been done with 3 electrodes, one on the right mid-clavicular line and one on the specular position on the left. The ground, as mentioned before, for the g.Tec device was embedded on the cap. In the figure below the correspondence is in the Lead I.

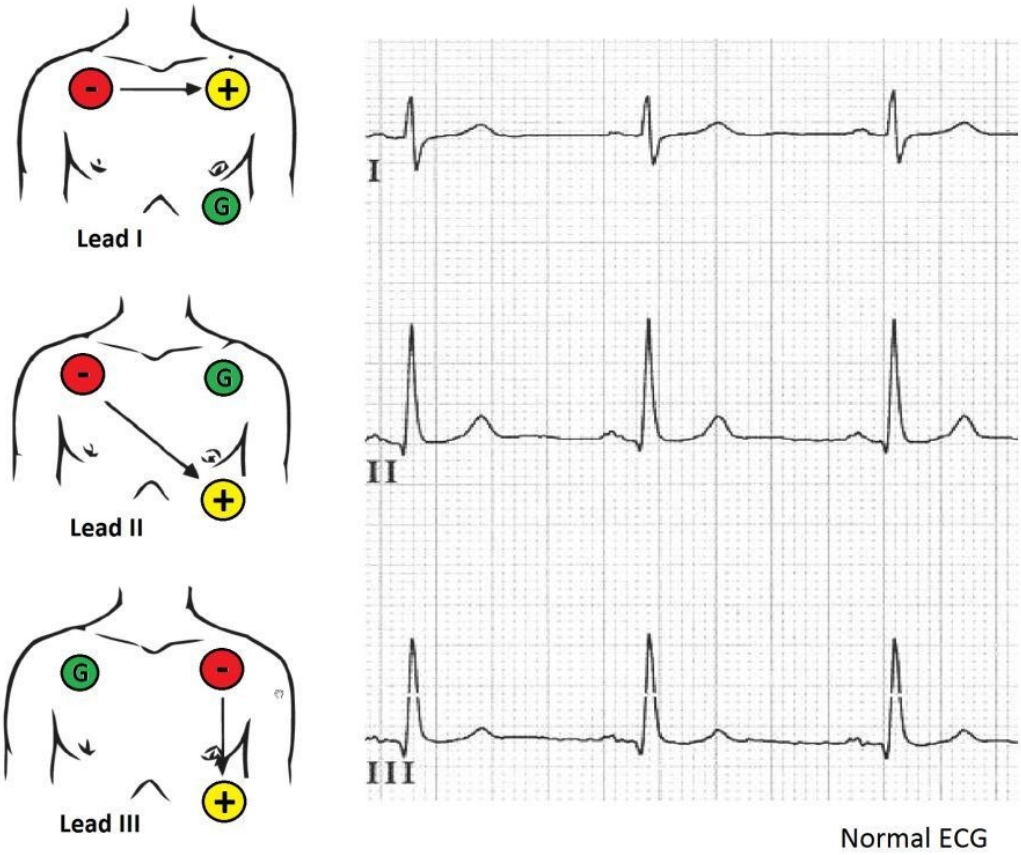

Figure 6.3 Different positionings of the electrodes to register ECG signal

3.1.3.3 Montage

Two electrodes, one used as a reference and the other to collect the signal, register each cerebral signal on the scalp. The two electrodes are, then, sent to the amplifier, which has two inputs: one is inverting and the other one is non-inverting.

There are two main configurations:

- monopolar: is the mainly used especially because it allows to register the signal in the deeper structures of the brain. One electrode is positioned on the electrically active tissue and the other upon the reference tissue, where there should not be variation of the potential. In the acquisition of EEG, for example, the reference electrode can be positioned on the median line of the scalp near Cz, Fz or Pz, on the neck, on the earlobes or on the mastoid.

- bipolar: two electrodes positioned on the electrically active tissue of the scalp and the difference between them is registered. The signal registered comes from the more external areas of the brain because the deeper sources are considered as common mode from the amplifier. Bipolar registration is more localised with respect to the monopolar one and for

this reason, it is usually more widespread. In our case the g.Tec cap employs a monopolar montage, there are 64 electrodes registering the signal and the 64th is the reference for all the channels, put on the earlobe, ipsilateral to the stimulation (on the left).

Electrodes employed in ECG and EOG are bipolar, instead.

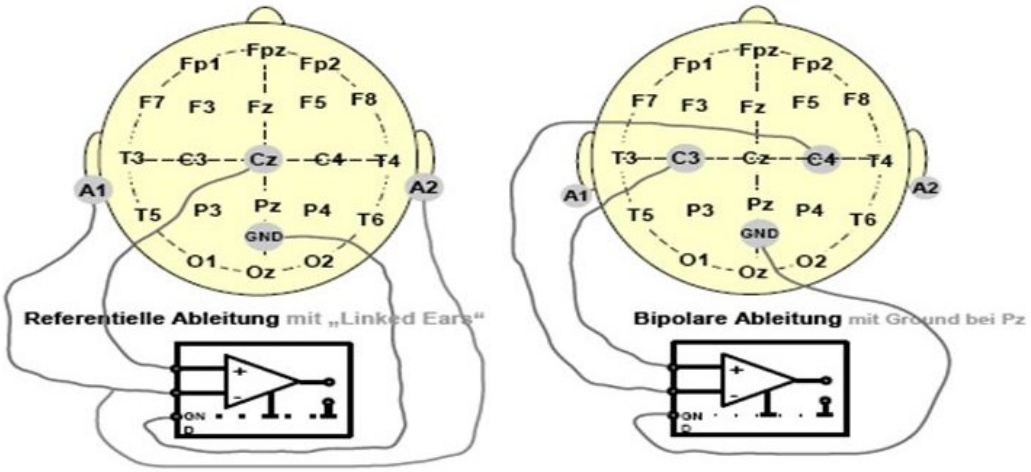

Figure 7.3: Monopolar montage on the left, bipolar montage on the right.

3.1.3.4 Sampling

Every analogical signal has to be converted to digital by an analogical/digital converter (ADC) before being analysed. There are two processes done by the ADC

- sampling: the signal has to be transformed from continuous-time to discrete-time
- quantisation: the real number that constitutes the signal has to be replaced by discrete values

Both these two operation depend on some values that the user can choose and that depend on the complexity of the signal we are dealing with, those are: the sampling rate and the number of bit with which the quantisation is done.

As said before, to choose these parameters it is necessary to know the signal we are analysing

- sampling rate: for EEG signals the bandwidth is around 30-40 Hz (if we are not considering the HFO). If the analysis includes also evoked potentials the band considered increases till at least 200 Hz. Following Nyquist rule the minimum sampling frequency to avoid the aliasing should be the double of the bandwidth, but usually the ratio is preferred to be not less than 4:1.

the number of bits depends on the instrumentation, and the quantisation gives a direct correlation with the resolution

In our case, the sampling rate chose was 4800 Hz with the idea of future analysis even in high frequencies

Our instrumentation has a number of bit for the quantisation that is 24 bit. Depending on the level of tensions in input, which in the EEG case would be between 10 and 500 μV

$$Resolution = \frac{Ampliture\ voltage\ range}{2^{n\_bit}}$$

This means resolution for g.Tec is around 30 pV.

4. Analysis of the data

The recorded data have been analysed with EEGLAB toolbox. The effort was focused on maintaining a standardised analysis for the different subjects. Here, it has been listed the operations done for every dataset but with some changes and adjustments dependent on each case. In general the procedure has been:

- Loading of the setup
- Inserting the channel location
- Epoching the signal
- Rejecting the artefact due to stimulation and the noisy channels
- Filtering the data
- Visual inspection of the noisy epochs
- Re-reference the data to the average of all the channels
- Running Independent component analysis (ICA)
- Rejecting bad ICA components

Some of these steps will be described in details in the following paragraphs.

4.1 Channel locations

The first step to perform, after the loading of the data, consists on inserting the channel location. This means to associate the channel number to the spatial position of each electrode on the scalp.

The g.Tec device provides as output the channel locations in a .xml file (figure 1.4), whereas in EEGLAB the polar angle, the polar radius and the Cartesian coordinates (x, y, z) are required for each channel as a file .ced (figure 4.2). The missing polar coordinates, required as input for EEGLAB, has been extrapolated from the .xml file through a change of coordinates in *Matlab*.

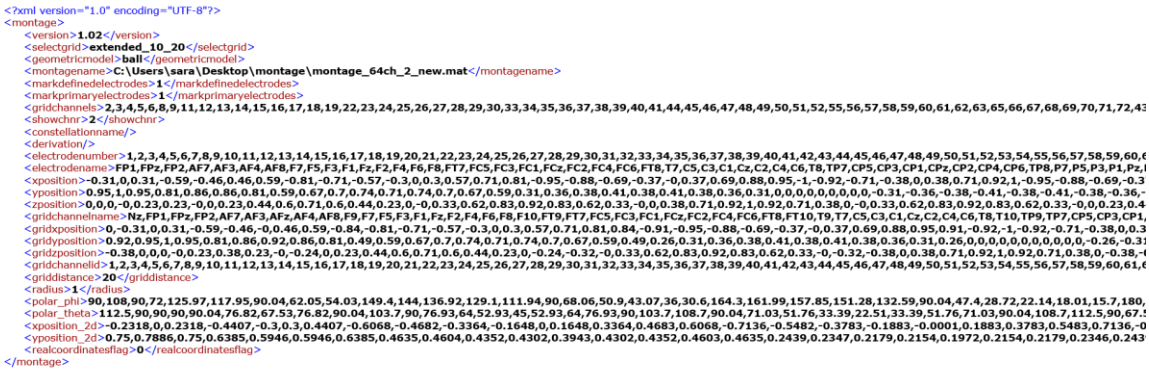

Figure 1.4 Channel location exported directly from the g.Tec software.

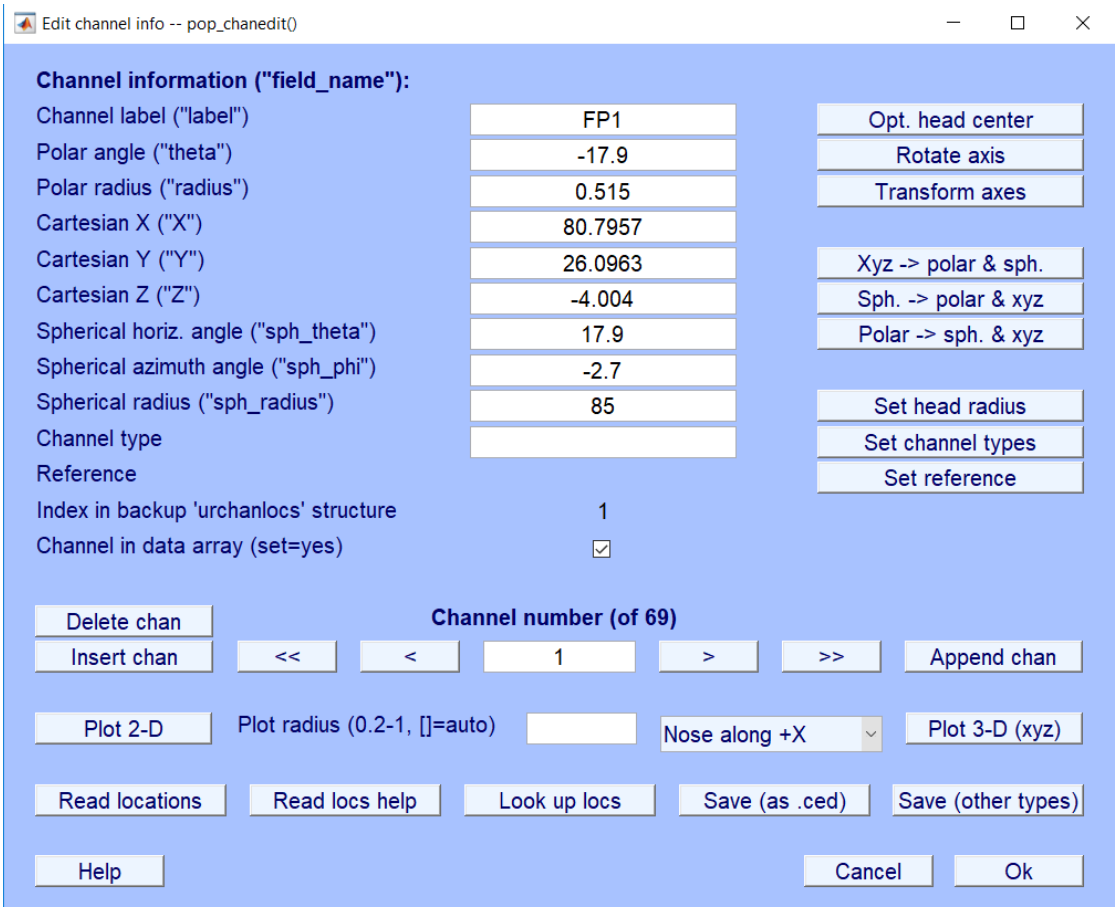

Figure 2.4 The channel information required from EEGLAB. The information can be inserted manually channel by channel or can be created a file .ced which can be imported.

After recreating the EEG channels (62 plus the reference), six more channels have been added, two for the ECG recording and four for EOG (as explained in chapter 2). The final result is shown in figure 3.4 where only the first 63 channels of the EEG are visible on the scalp.

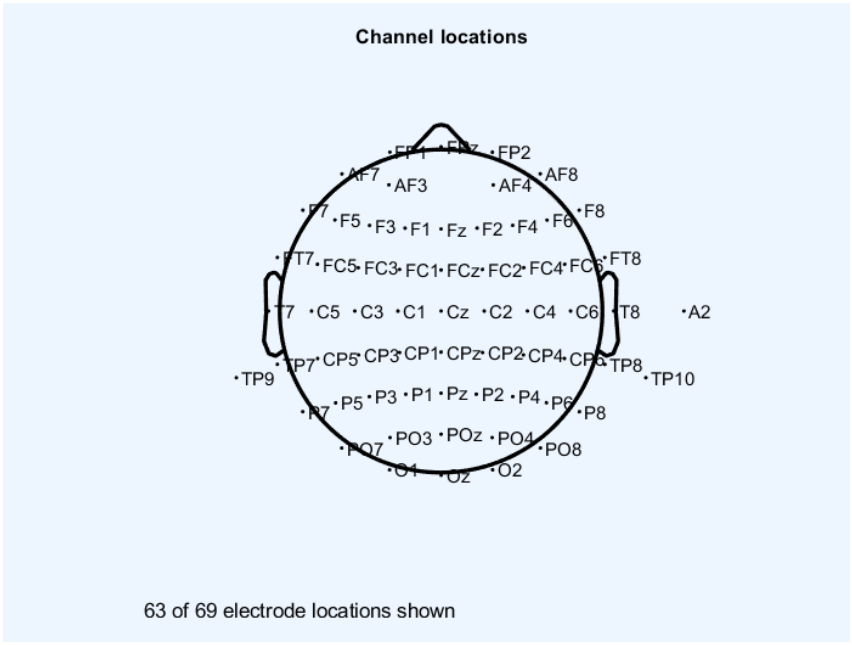

Figure 3.4 The scalp map with the electrodes localised in the correct position.

4.2 Epoching the signal

The range of the epoch has been set 1 s long, in particular, between -100 ms to 900 ms with respect to the trigger. The script, which manages the timeline of the triggers, allows to assure no superimposition of any couple of epochs, since a fixed delay of 1 s plus a random extra delay is set. This is fundamental to avoid biases in the statistical model and misinterpretation of the SEP waves.

Two options have been considered: epoching the signal before or after the application of the ICA algorithm. The ICA algorithm has been a necessary choice in order to limit the noise of the signal. In fact, the task is performed with eyes opened and it is subjected to involuntary muscular contribution of the subject because of its long duration (at least 45 min), which makes it difficult for the participant to remain perfectly still for the entire experiment.

Epoching the signal before the ICA is time saving but, introducing many discontinuities in the signal ("boundaries"), the ICA algorithm could result less accurate. Some consideration regarding the signal explains why it has been decided that epoching the signal before had more positive than negative aspects:

- The amount of data is consistent even cutting many segments of the signals between an epoch and the other, because the registration lasts around 45 minutes.
- ICA requires that the signal is stationary, and epoching the data increases the stationariness, this means that the same statistical model generates all time points.
- The epochs can be extrapolated long enough because of the delay between a trigger and the other. This assures a sufficient amount of data for the ICA without introducing the variability, which would decrease the stationariness.

To epoch the signal it has been used a plugin of EEGlab whose name is ERPlab. There are three fundamental steps to follow:

- Create an event list: for each trigger it is assigned an "ecode", that is an integer number, if the original "labels" were constituted by alphabetic characters. The file can be exported and saved as a .txt file (elist). An example is in the figure 4.4, and it is shown that in the first part of the list there is a summary of the principal characteristics of the dataset and then the list of all the events where the temporal delays are specified.

```
1  #  Non-editable header begin ------------------------------------------------------------------------------
2  #
3  #  data format..............: continuous
4  #  setname..................: Chiara_art_rej_elist
5  #  filename.................: none_specified
6  #  filepath.................: none_specified
7  #  nchan....................: 69
8  #  pnts.....................: 12964703
9  #  srate....................: 4800
10 #  nevents..................: 1008
11 #  generated by (bdf).......:
12 #  generated by (set).......: Chiara_art_rej_elist
13 #  reported in .............:
14 #  prog Version.............: 7.0.0
15 #  creation date............: 07-May-2018 15:12:30
16 #  user Account.............:
17 #
18 #  Non-editable header end --------------------------------------------------------------------------------
19
20
21
22
23 # item   bepoch   ecode           label        onset          diff      dura   b_flags    a_flags    enable        bin
24 #                                             (sec)          (msec)    (msec)    (binary)   (binary)
25
26
27 1       0           2        Trigger2        0.7692          0.00      0.0     00000000     00000000      1    [       ]
28 2       0           1        Trigger1        3.2817       2512.50      0.0     00000000     00000000      1    [       ]
29 3       0           1        Trigger1        5.7708       2489.17      0.0     00000000     00000000      1    [       ]
```

Figure 4.4 The elist created in ERPLAB. To each trigger is associated a code, a latency and is calculated the difference in ms between one trigger and the previous one

- Assign bins: in the previous figure the "bin" field is empty, and since the epochs are computed in relationship with this field, the next step is to fill the space between the brackets. A document called "binlister" (figure 5.4) has to be uploaded to fulfil this task

Figure 5.4 The binlister that associates to each ecode 1 (of the elist) the event 1; and to each ecode 2 the event 2

In this case the binlister associates to the ecode 1 the bin 1 and to the e code 2 the bin 2. Nevertheless, there is the possibility with some syntax rules to select the events that occur at certain latencies or events which occur only with certain relationships between each other, however, in this experiment it was unnecessary to set similar rules.

After this step another .txt file with the bin field filled can be exported and saved.

- Compute bin-based epochs: this operation, as said before, simply computes the epochs referring to the bin previously assigned.

4.3 Stimulation artefact removal & bad channels removal

The first required step is aimed to reject the stimulation artefact, which is a biphasic wave, present in all the channels, with a quite variable amplitude among all the channels and among the subjects usually not less 0.2 mV (figure 6.4). The operation has been made visually inspecting the signal and cutting the milliseconds of signal affected and substituting it with an interpolation of the remaining signal. This depends on some factors: the spreading of the current from the electrode to the nerve and the surrounding tissues, that are conductive. The displacement current, due to an imperfect isolation between the stimulator and the subject, also called "escape current" because of the impedance of both is capacitive. Finally, the electromagnetic coupling which arises because of a capacitance between the stimulator and the leads (Scott, McLean, & Parker, 1997). In addition to this operation, the bad channels are rejected.

The bad channels are all the channels which present a noisy signal because of an high impedance of the electrode, which can be due to a bad fitting of the cap (which has a certain size and resulted quite large for some subjects), or to a detachment of the electrode or also to the dry out of the gel.

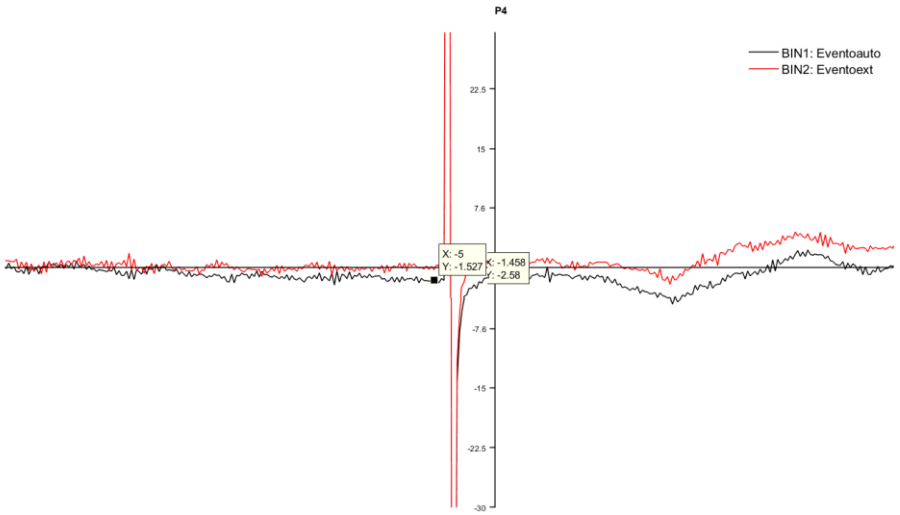

Figure 6.4 An example of artefact stimulation on the channel P4. The onset of the artefact is around -5 ms and the end around -1 ms.

4.4 Filtering the data

There is a wide debate in literature about the possibility of filtering the EEG data for SEP analysis.

Van Rullen proposed not to filter the biological signal at all to avoid distortions on the temporal dynamic and wrong evaluation of waves latencies, since he observed a widening of the signal after the application of the filter (VanRullen, 2011).

Widman and Schröger explain that the results obtained by Von Rullen are biased by a bad choice of the filter. The authors selected the standard EEGlab FIR filter, which is based on the *Matlab* function *firls*, which has least square fitting coefficients, this means that tends to minimise the weighted, integrated squared error between the ideal function and the magnitude response of the filter. The authors assert that this filter has more than one negative aspect: the attenuation is not optimised, in the bandpass ripples introduce artefacts and the transition bands are defined as "do not care regions" (Widmann & Schröger, 2012).

In addition to this, a filter can be chosen **causal** or **non-causal**. In the first case the output comes from the past and present inputs, if the dependence also includes future inputs the filter is said non-causal. The choice between these two is based on the application, for example in any real-time analysis, the filtering should be causal. When the filter is designed like an IIR, applying a non-causal filter is usually preferred to overcome the problem of the phase distortion and to obtain symmetrical impulse.

Rousselet (Rousselet, 2012) affirms that the ideal filter to study ERP waves should be a causal one. The reason behind is that filtering the signal in both directions, introduce side lobes just before the onset of the signal (figure 7.4). Although even non-causal filters could give acceptable performances if the cut-off frequencies (i.e. the frequency boundary at which the energy of the signal presents the first attenuation,) are distant enough from the frequency of interest. This is another aspect to taken in account to rebut Van Rullen's choice of the filter, which was a zero-phase one, that means the filtering is applied forward and backward (non-causal).

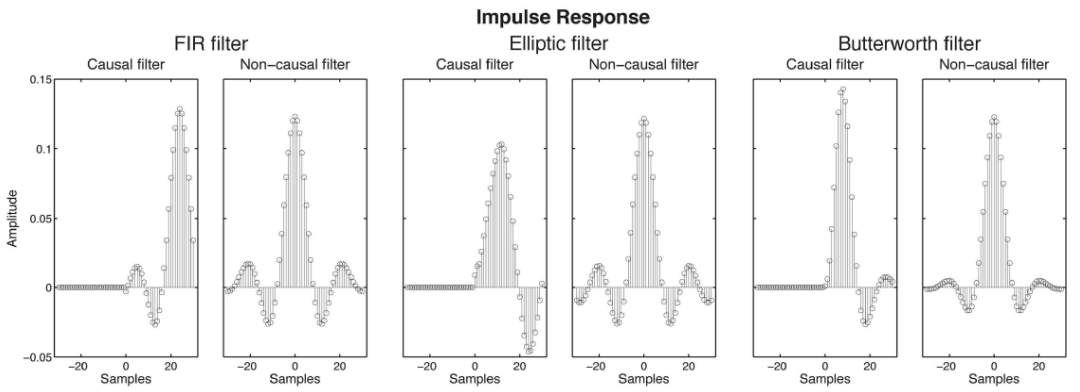

Figure 7.4 How the choice of casuality of the filter can vary the output in different filters: FIR, elliptic and Butterworth.

Widmann agrees with the idea that casual filtering introduces less energy leakage, but he adds that also using FIR filters the phase distortion is not avoidable. He affirms that IIR filters are more efficient, since are shorter (the order required is smaller), and the roll-off (which is the steepness of the magnitude of the transfer function, which measures how fast the filter attenuates the signal beyond the cut-off frequency) is slow with respect to FIR filters, this is considered as a positive aspect because minimises distortion. On the other hand, using IIR filters the signal would require non-causal filtering to achieve zero-phase.

In the debate emerged different approaches with respect to the problem; in this study the effort has been to check which filter has the best performances without changing the shape of the waves. We tested the default filters in ERPlab, which proposes an IIR (Butterworht), a FIR (sinc-shaped function) and a Parks-McClellan notch filter. Both the IIR and FIR filters are implemented by the plugin as non-causal filters (zero-phase shift).

- **IIR butterworth** filter: which has no ripples in both the stop and pass bands and presents a steep roll-off, even though it requires higher order to reach the steepness of other IIR filters like Chebyshev or the elliptic one. However, with respect to the other cited filters the phase response is more linear (figure 8.4).

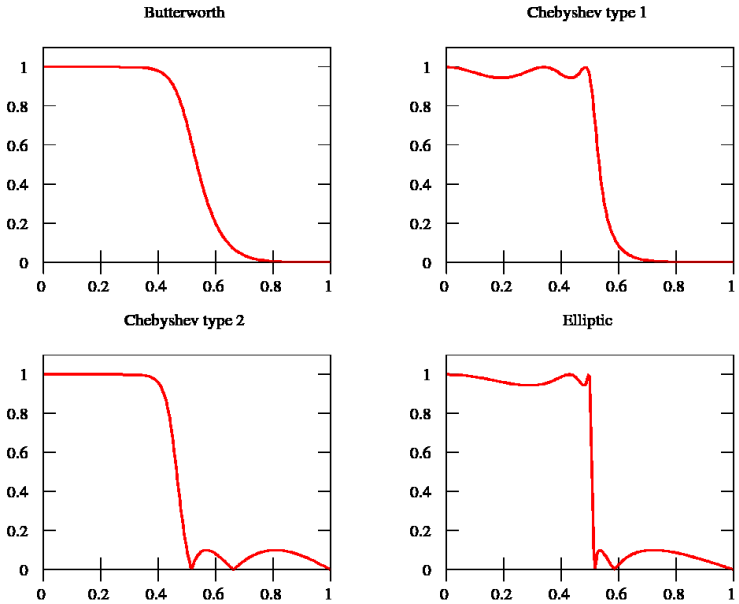

Figure 8.4 Examples of the behaviour of different IIR filters. Both the roll-off and the presence or not of ripples in band pass or attenuated band can vary a lot.

For these reasons among all the IIR filters this was the most versatile for treating the ERPs.

- **FIR** with sinc-shaped function: if the chosen order is very low, for example around 20, the filter is very slow but the waves are not deformed in time. On the other hand, if the order is increased, around 200 the roll-off is better, but could introduce an oscillation in the recorded data.

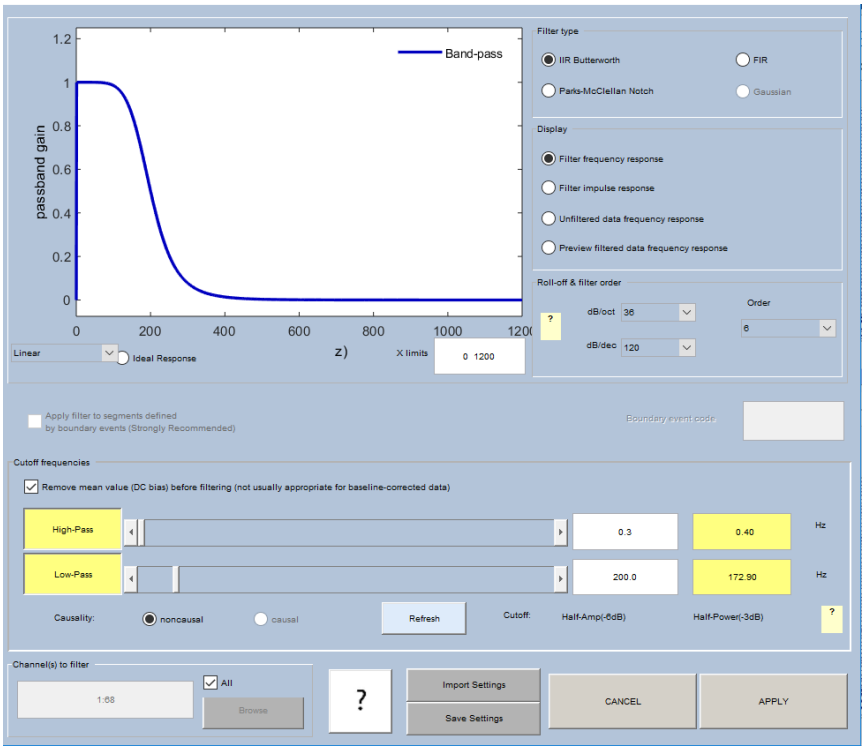

Figure 9.4 The GUI of ERPLAB for the designing of the filter. Here, it is shown the response of a band-pass, IIR Butterworth filter.

In the GUI (figure 9.4) dedicated to filter the EEG, the first option to set is the type of filter, and the different options have been previously mentioned. Then the choice is among high-pass, low-pass or even band-pass filtering (selecting both the filters together), depending on frequency band it has to be attenuated. The cut-off or the cut-offs, in the case of the pass-band, at half-amplitude (-6 dB) have to be set from the user, while the corresponding half-power cut-offs (-3 dB) are automatically calculated. The order is advised by the GUI, but can be always decreased and sometimes also increased if it does not affect the stability of the filter. On the bottom of the page can be set also the channels interested in the filter, but by default are all selected.

Another option is the possibility to remove the baseline (DC offset) before filtering, this is particularly useful when the lower frequencies are eliminated with an high-pass (as in this case, since it has been chosen a pass-band equal to 0.3-200 Hz for the reasons that will be explained in the next paragraphs). It is not advisable to remove DC offset if the filtering is done on a dataset already epoched in which the baseline is previously removed. In the case of this study the DC offset is removed because the filtering is done on the epoched data without any baseline removal (because the DC offset removal is included in this operation).

The final comparison has been done with these two settings:

- Passband FIR filter 0.3-200 Hz, order 16, with DC bias removed, and in all channels (figure 10.4)

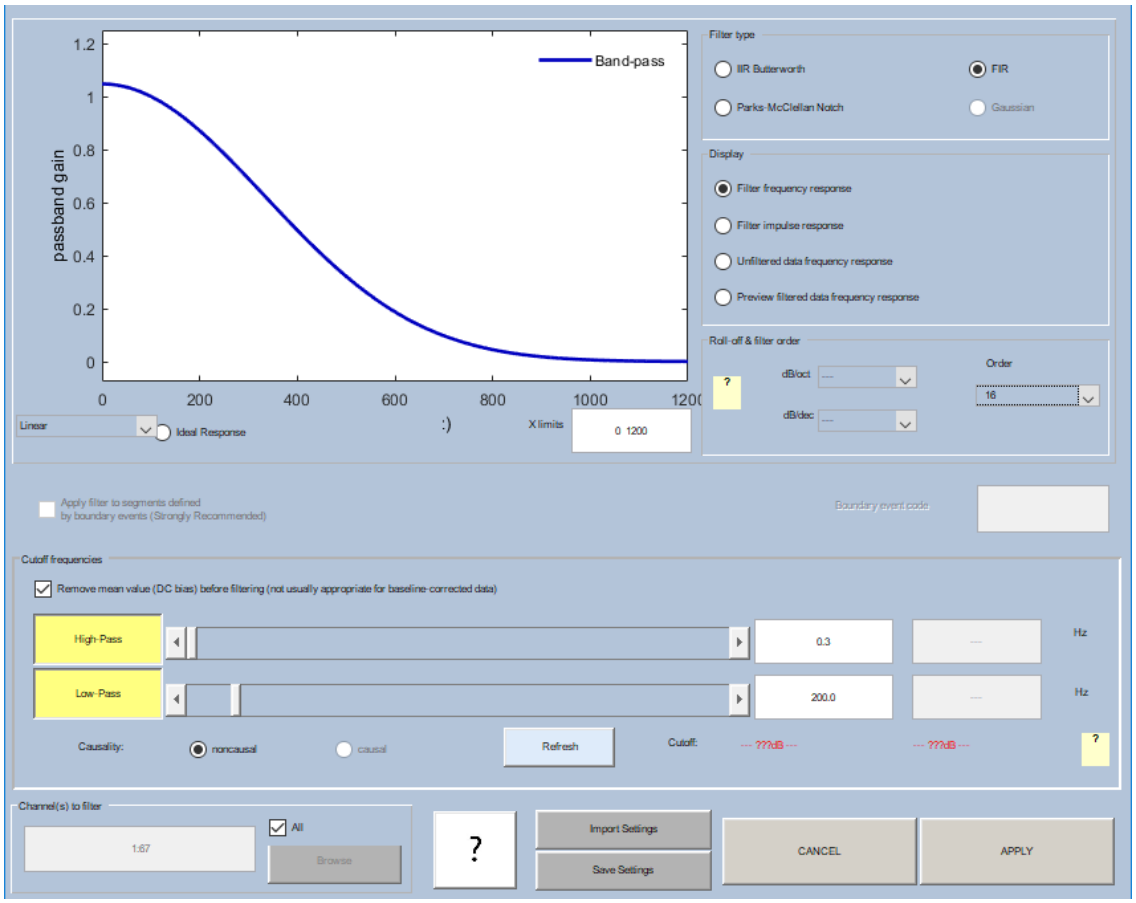

Figure 10.4 The GUI of ERPLAB for the designing of the filter. Here it is shown the response of a band-pass, FIR filter. It is worth to note, that the high-pass is not shown nor implemented even though no error poped-up.

- Passband IIR 0.3-200 Hz, order 6, with DC bias removed, and in all channels (figure 9.4)

The graph of the FIR and at the order (16) which is very low, were very suspicious and it has been hypnotised that even though no error has been pointed out, the toolbox could not handle the high-pass. This hypothesis was confirmed with another attempt of high-pass at 0.3 Hz.

In the figure 11.4 it is shown the error: the order required would be too high with respect to the potentiality of the toolbox.

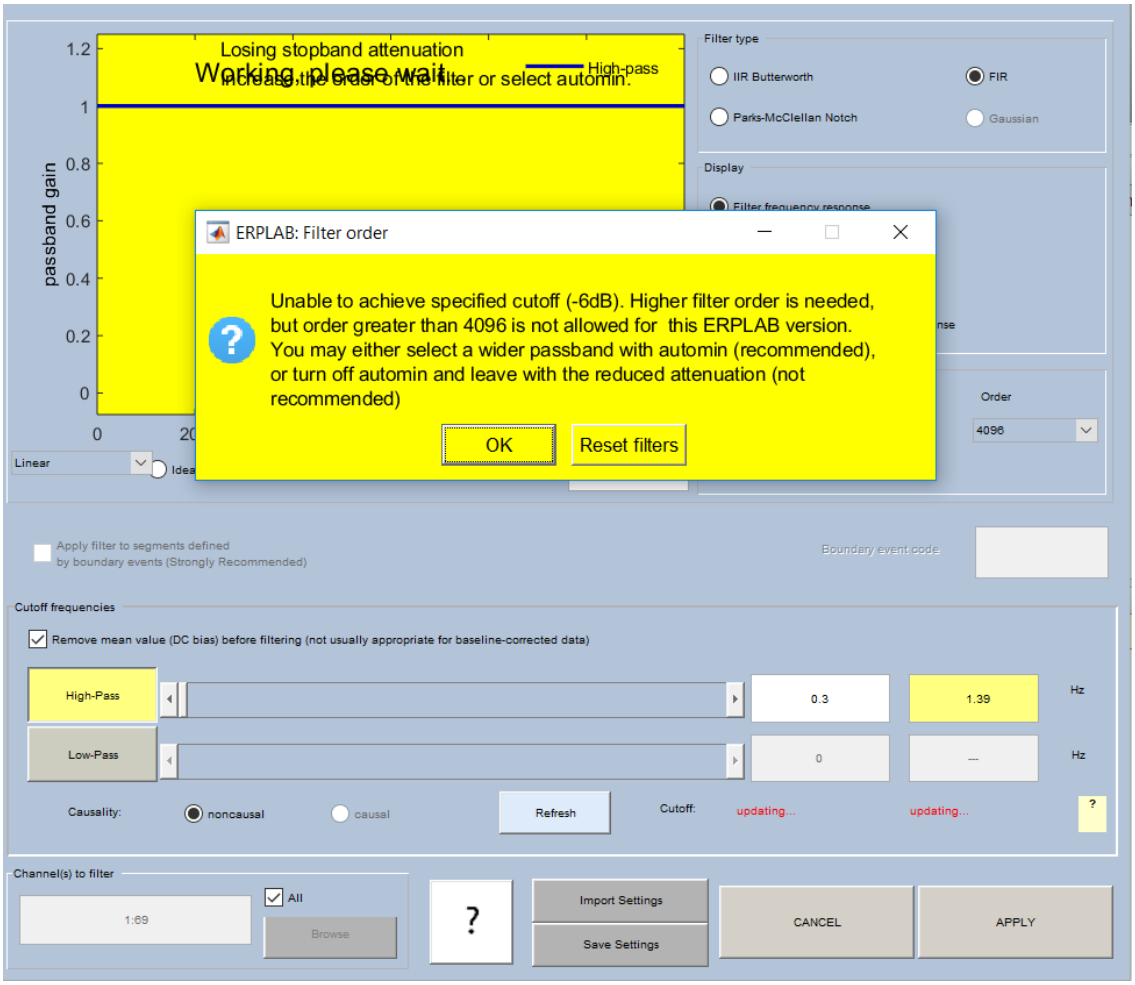

Figure11.4 An attempt of high-pass 0.3 Hz. The filter requested result impossible to obtain with a FIR filter with this toolbox.

Considering these evidences and also the recommendation of the ERPLAB creators to use the Butterworth filters it has been used the IIR.

For what concerns the **frequency band** of the signal (Rousselet, 2012) reported that high pass higher that 0.4 Hz distort the signal, in particular cut-off frequencies between 0.4 and 0.5 Hz shorten the ERP onset and above 1 Hz change drastically the shape of the wave. That is the reason why it has been elicited a cut-off frequency below 0.3 Hz. Rousselet reported that the low pass filter seems to have negligible effects on the temporal dynamics of the signal, in contrast to the evidences found by Van Rullen (Rousselet, 2012). This is the reason why it has been elicited a frequency band of 0.3-200 Hz.

Another aspect to take into account is that the filtering is always applied to continuous data, and not across boundaries. This means that epoching the signal or rejecting some portions of the signals (through the rejection by visual inspection process previously operated) introduces some variability. However, in the analysis, it was considered a long epoched window of signal with high sampling frequency (4800 samples), and a distortion of the signal was not identified by visual inspection.

4.5 Rejection by visual inspection and re-reference

Removing the major artefacts, peaks or EMG related noise, is preferable before ICA algorithm to avoid the presence of not repeatable noise and make the signal more homogeneous. The EEGlab interface allows to select the portions to remove in the continuous data or select the noisy epochs if the signal is already divided into segments. When the selected data is removed in the continuous signal, it is substituted by an event marked as "boundary" to indicate that in that segment the continuous data has been cut and merged. The problem is overcome if the operation is made after epoching, in this case the epoch can be simply highlighted on the panel and selected for future rejection.

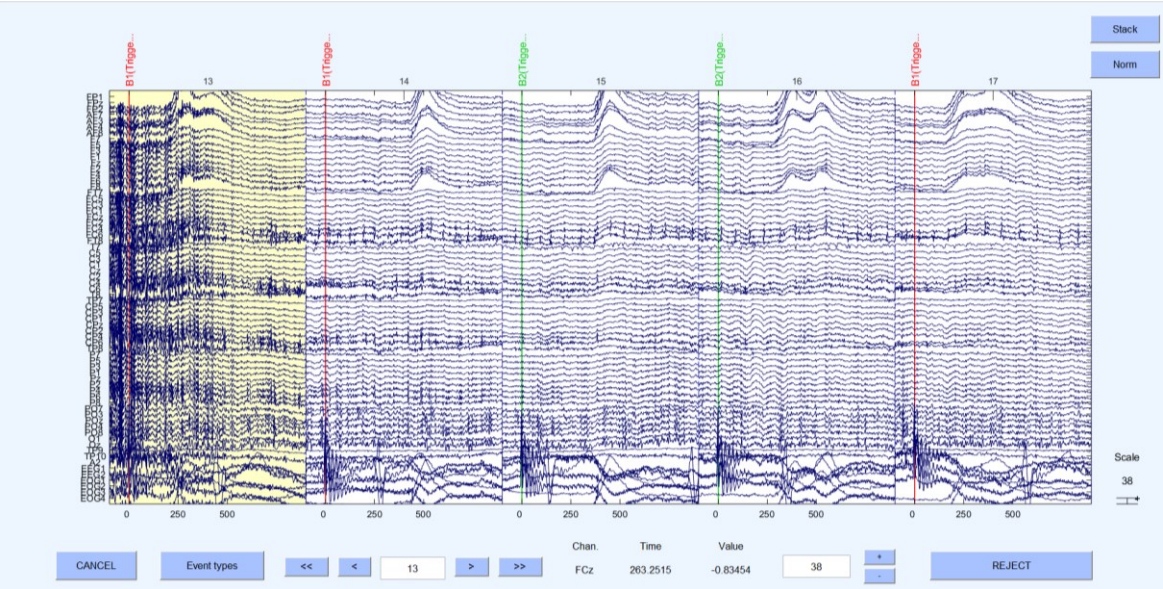

Figure 12.4 The visual inspection of the epoched epochs is very simple in the GUI since it consists of selecting all the bad epochs and reject them pressing the "Reject" option. Here the example shows a very noisy epoch number 13.

In figure 12.4 the noise is widespread along all the channels, this is due to a movement of the head of the subject. While the high peaks especially accentuated in the frontal channels (the first seven) are the eye-blink artefacts and they will be eliminated in the next steps through the independent component analysis, for this reason they are not considered in this phase of epoch removal.

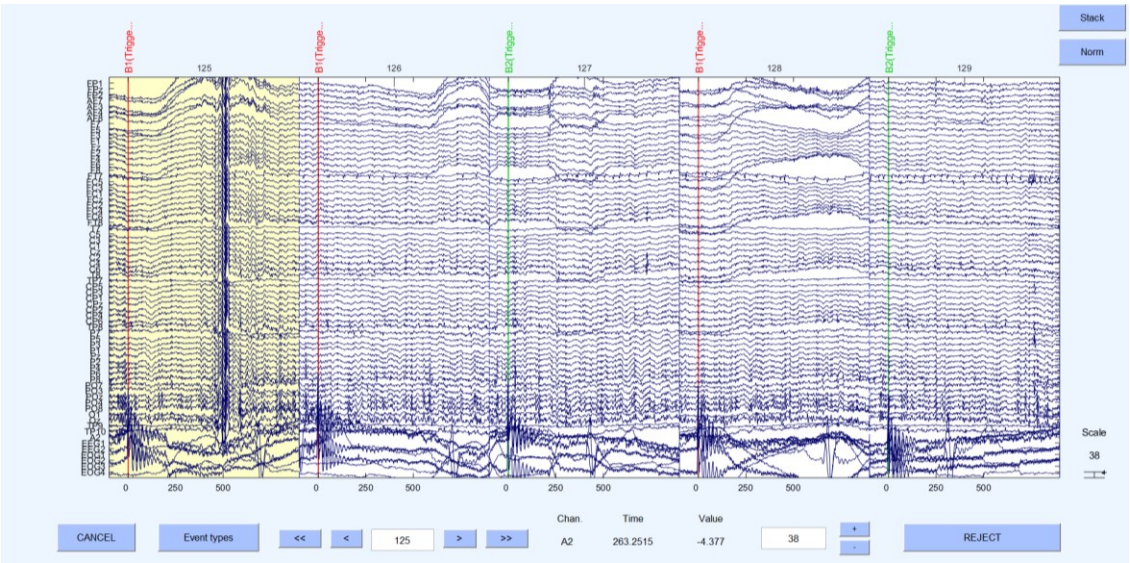

Figure 13.4 The visual inspection of the epoched epochs is very simple in the GUI since it consists of selecting all the bad epochs and reject them pressing the "Reject" option. Here the example shows a very noisy epoch number 125.

In the figure 13.4, another example of movement of the subject, even if it is more concentrated, is shown. While the drifts in the other epochs, longer in latency with respect to the eye-blink previously noticed, are the lateral eye movement and will be eliminated with the independent component analysis.

After this step the re-reference of the data to the average of all the channels is requires, this step reduces the noise, allowing to make the SEP more identifiable in amplitude.

4.6 Independent component analysis (ICA)

Some noise can be not eliminated by only filtering the data (as said in the previous paragraphs). In particular, hardware artefacts or biological artefacts are the most common. Among the biological artefacts it can be mentioned the lateral eye movement, eye blinking (which causes changes in the electrical potentials of the order of 50 μV), pulse artefact, ECG and EMG.

Many methods can be applied to reject these types of noise:

- Rejection methods: which consist of rejecting part of the signal visually or automatically for example setting a certain threshold. With this method, the risk is to reject a lot of data or not all the artefacts, because of the strong dependency on the choice of the threshold. In general, it depends on the application and the positioning of the electrodes (a good approach is to place them far from the eyes and muscles). (Croft & Barry, n.d.)
- Subtraction methods: derived by the consideration that the EEG is a signal which can be modelled as the linear combination of neural signals or "sources". The EOG signal, registered together with the EEG, can be subtracted to the channels affected by the noise. Recent methods instead have the aim to recognise each source having only the combined signals, the methodology is named Blind Source Separation (BSS).

This separation of the sources has been developed with the Independent Component Analysis (ICA), a statistic method which decomposes the EEG channels blindly (figure 14.4). The objective of the algorithm is to extract N sources from the raw signal (which is a linear combination of the sources), finding the linear projections of the data which maximise the mutual independence without alter the information. Once obtained the different components, the ones representing the noise can be eliminated.

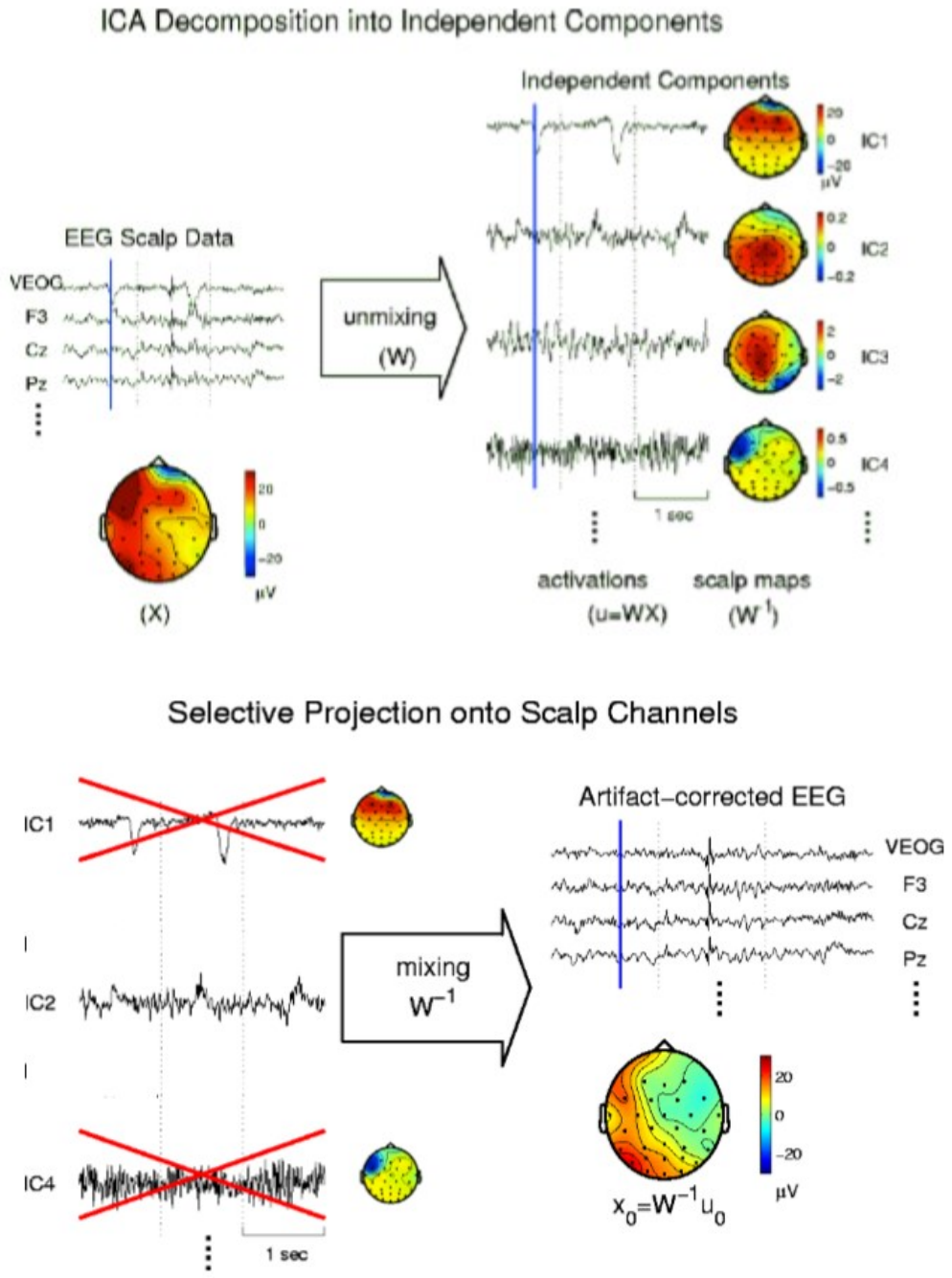

Figure 14.4 All the steps of the ICA: registering the data, finding the weights, extrapolate the components, eliminate the bad components and obtain the artefact-corrected EEG.

4.6.1 Blind Source Separation

Taking m independent casual signals $s_1(t)$,$s_2(t)$, $\ldots s_m$ (t) combined linearly and a number n of sensors, at least equal to the number of sources (n ≥ m), it has been registered a number of signals equal to n $x_1(t)$, $x_2(t)$,…,$x_n(t)$. The model for the signal output is $\vec{x}(t) = A\vec{s}(t)$ where A is the mixing matrix with dimension equal to n x m.

The BSS consists of the estimation of the sources $\vec{s}(t)$, hypothesising their mutual independence and knowing only the signals $\vec{x}(t)$. The problem would have been easily solved, if A were squared and known:

$\vec{s}(t) = W\vec{x}(t)$ $\quad\quad$ $W = A^{-1}$ is the unmixing matrix.

but usually this does not happen. In any case, knowing signal $x_1(t)$, $x_2(t)$… and assuming that $s_1(t)$, $s_2(t)$… are linearly independent the parameters a_{ij} can be estimated.

An example of BBS is presented in the next paragraph (i.e. the cocktail party)

4.6.2 Cocktail party problem

In a room in which two people are speaking at the same time, there are two microphones available in two different positions. The microphones gives two signals at a specific time instant: $x_1(t)$ and $x_2(t)$ while $s_1(t)$ and $s_2(t)$ are the voices emitted by the two people.

If it is considered the same situation but with many groups of people who talk together in addition with some background noise, for example music, and other ambient noise, and a certain number of microphones, it is very difficult to distinguish each conversation (figure 16.4).

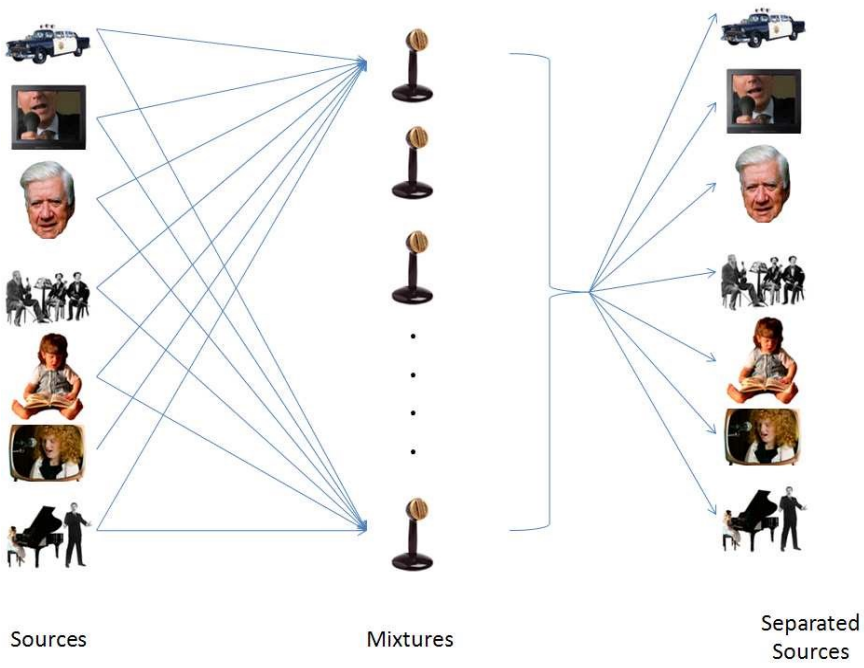

Figure 15.4 The cocktail party problem explained easily: different sources of sounds, which mixed in different ways in the microphones. The ICA algorithm disentangle the mixtures to obtain the sources again.

There are some unavoidable aspects to take in account to have some chances to discern among the different inputs:

- there have to be more signals than sources (n>=m), this means the number of microphones in our room has to be at least greater than the number of people speaking in addition to music speakers and any other noise source. This assumption is quite easy to satisfy in our example, but referring to biological signals, like the EEG, it is not so easy to determine the appropriate number of electrodes
- the sources and the sensors have to be stationary among each other in our example people are not supposed to move around the room, while referring to the registration of EEG it is important to avoid the movement of the cap due to muscular activity or any kind of sliding of the electrodes. Since electrodes are fixed on the cap the relative motion among them is unlikely.
- The sources are linearly mixed in each instant each microphone collects a linear combination of the sounds coming from all the sources. The delay introduced by the different location of the electrodes in correspondence to the sources is considered negligible because of the assumption that the impedance of the tissues during EEG can be modelled as purely resistive. In other words, this impedance is not dependent on the frequency of the sources, and the viscous components of the tissue are considered negligible.
- Sources are statistically independent even a small temporal discrepancy between the two signals can be sufficient to separate the sources.
- The distribution is non-Gaussian, given two independent sources whose joint probability distribution is Gaussian, and calculating the probability distribution of the signals (multiplying for mixing matrix A), it can be noticed that the distribution of the two variables is completely symmetric. For this reason no information can be deduced about the directions located by A, and A itself can't be estimated. ICA can still be estimated if only one component is Gaussian and the others are not.
- The mixing matrix (A) is of full column rank: it implies that the columns of A are linearly independent. If this is not true, the mixed signals would be linear multiples one of the other.

4.7 Rejecting components

The result of the independent component analysis is a set of N components, each of them has a time course and is associated with N weights, where N is equal to the number of electrodes. There are two ways the ICA components can be used: to obtain the noise components and subtract them to the signal (pre-processing); or to analyse the resulting components to distinguish among the dynamics of the different cortical areas and the relationships among them ("analysis", which has not been developed).

Before removing the bad independent components, i.e. they are the components not due to the brain activity, it is useful to plot them in time (figure 16.4), and visualise the scalp map of the activations as well (figure 17.4). For the selection of the component to be eliminated, two aspects have to be considered: the first is that the components have mixed activity, both brain signal and noise. The second is the number of the component to be eliminated, because the components are ordered in terms of how much variance they

introduce in the data. If the electrodes are 64, electrode 40 would introduce low variance in the data and it is practically negligible to eliminate it, this is the reason why in the figure 17.4 are plotted only the first 35 components.

As said before, the number of components is at most equal to the number of channels, but in this experiment the number of channels is variable among subjects because of different pre-processing ad hoc for each case (due to eventual channel removal).

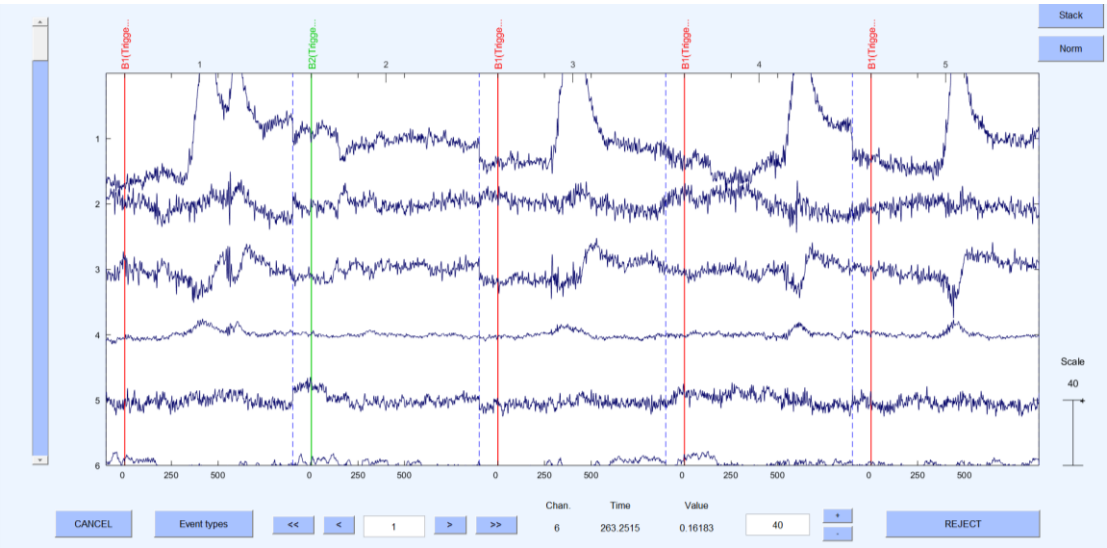

Figure 16.4 The first 5 independent components plotted in time, epoch by epoch.

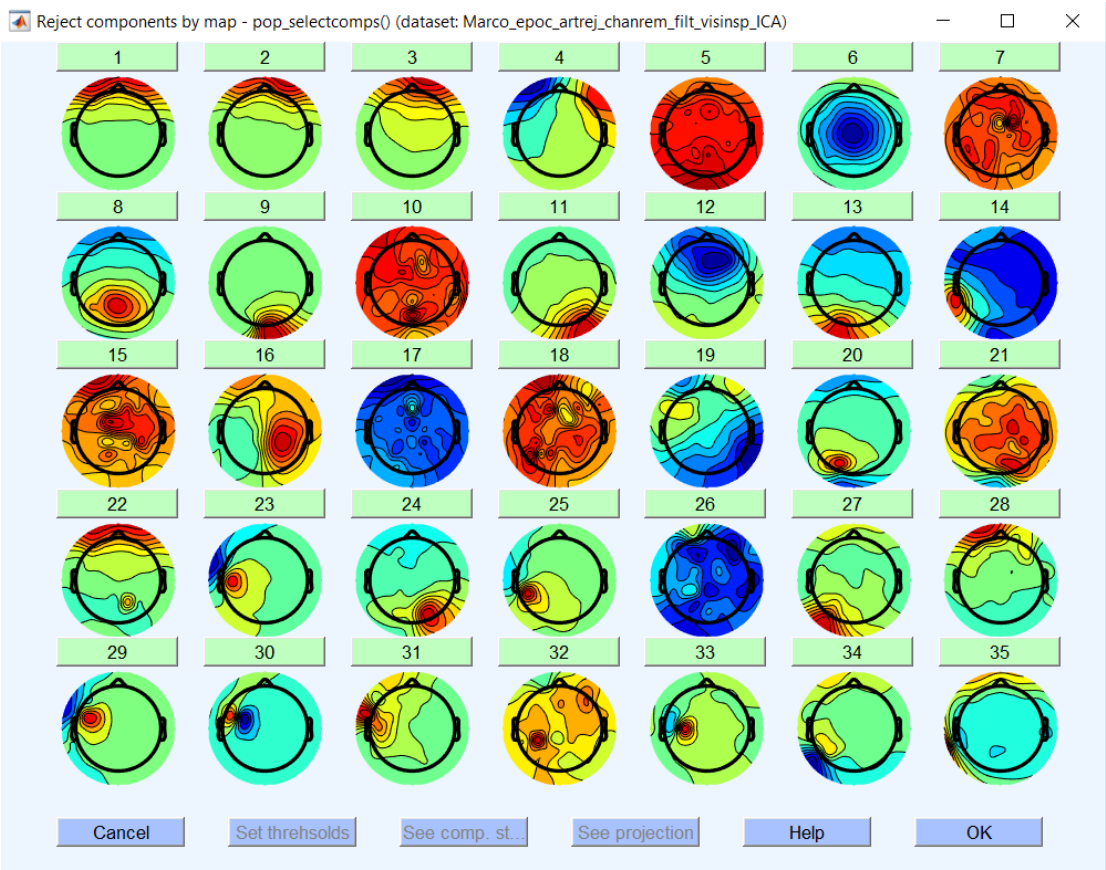

Figure 17.4 All the activation maps of the independent components.

The eye-blink component can be identified because it is the most prominent with eye-peaks predominant in frontal electrodes, in the figure 17.4 corresponds to the first one. Selecting the desired component among the topographic plot (topoplot) presented in the panel shown in figure 17.4, a pop-up figure with two additional graphs is open: one graph is the activity of each epoch along time and the other is the activity power spectrum. In the right upper side of the figure 18.4 which corresponds to the first component, the red spots are all the blinks for each trial, because their amplitude is definitely higher than the rest. Right behind there is the mean of all the trials plotted in blue, it can be noticed that is not time related and the shape is different with respect to an EEG component.

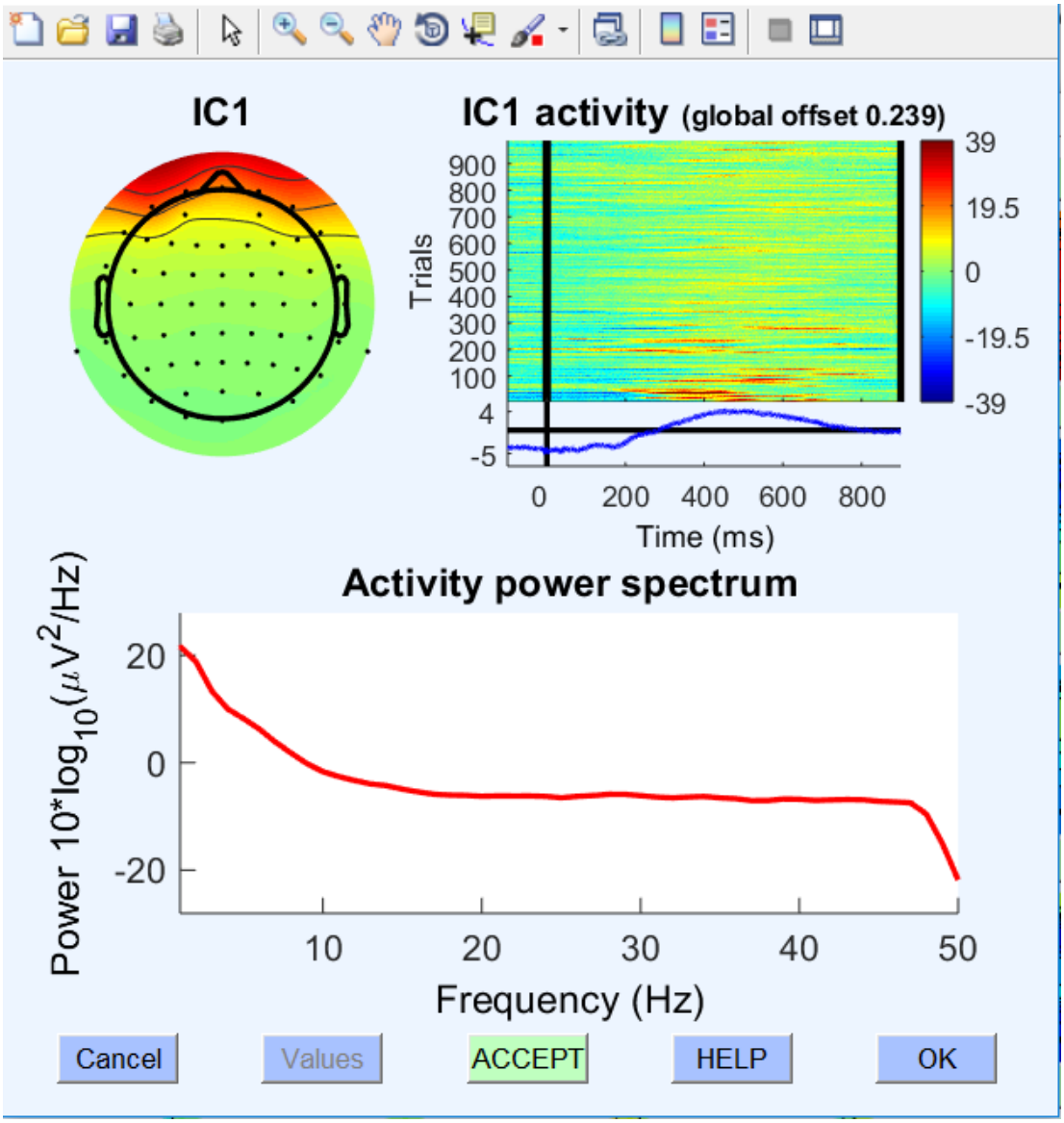

Figure 18.4 The first independent component in detail: both from the scalp map activation and from the activity plot it can be deduced it is the eye-blink component.

In the figure 19.4 it is shown the lateral eye noise. This can be recognised because it is always composed by two dipoles, one positive and the other negative, and the activity is concentrated on the frontal position. As in the other case, looking at the activity over time there are several red spots which represent the movements, usually with longer latencies with respect to the eye blink.

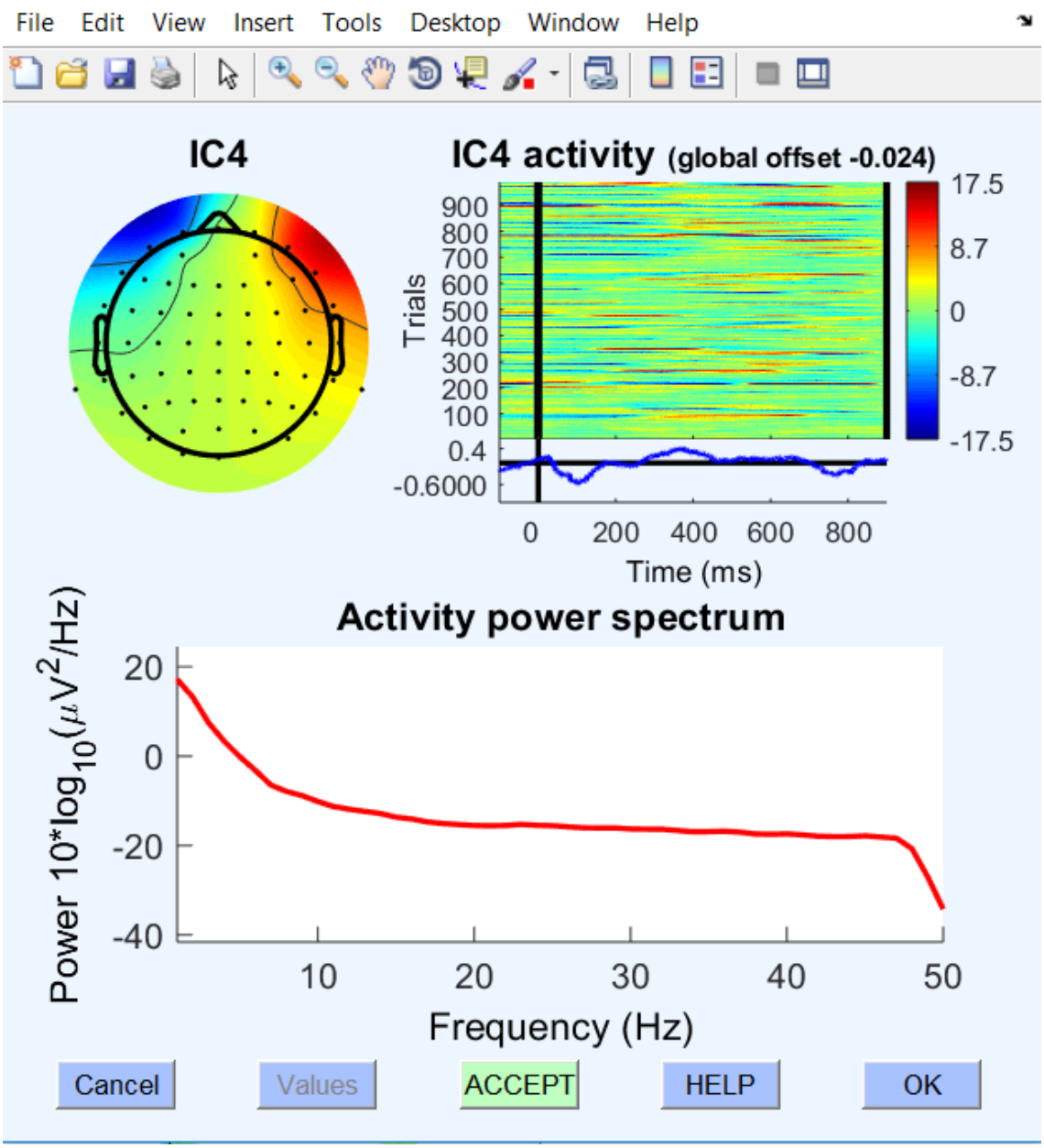

Figure 19.4 The fourth independent component in detail: both from the scalp map activation and from the activity plot it can be deduced it is the lateral-eye movement component.

In figure 20.4 component 9 is quite suspicious over time, because the frequency is high and the peaks are large. Looking at the scalp map activity (figure 21.4), the topography is practically driven by one electrode, because the rest of the scalp is green and this means that the weights are around zero. In the time domain there is not a task related response, this means it would have been impossible to locate the zero of the timeline if it had not been plotted.

The trend of the power spectrum around 5 Hz drops and then rises again and this is typical of the EMG activity. This components can be also eliminated with some confidence.

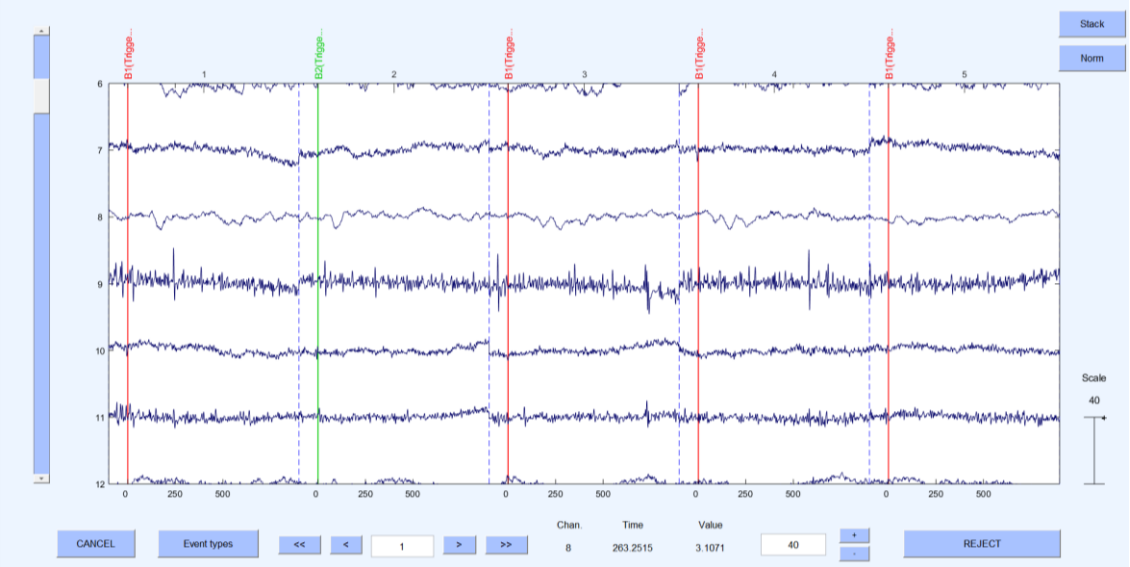

Figure 20.4 The independent components from 7 to 11 plotted in time, epoch by epoch.

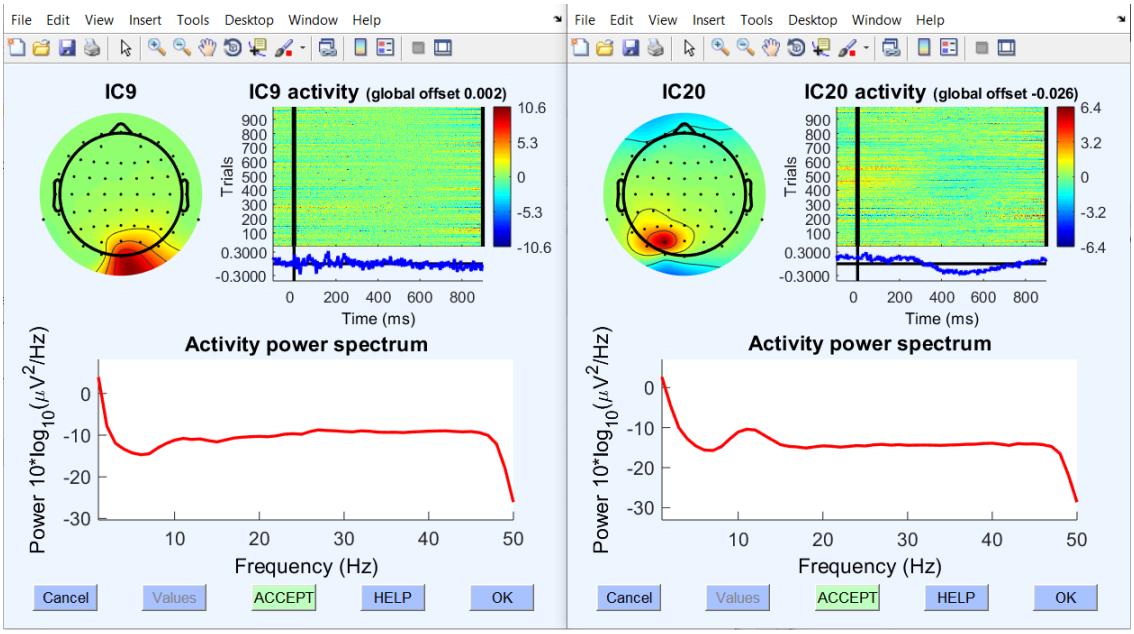

Figure 21.4 The ninth and twentieth independent component in detail: both from the scalp map activation and from the activity plot it can be deduced they are muscle activation components.

From another dataset it has been taken the next example. This component is not present in all the subjects because represent the pulse artefact, which is only present if there is a vein that pulses in correspondence of the electrode.

The activity spectrum in this case is quite peculiar because it presents two peaks between 5 and 10 Hz. The activity over time is spiking, and this can be noticed both from the scroll component activities plot (figure 22.4) and also from the trials over time plot (figure 23.4).

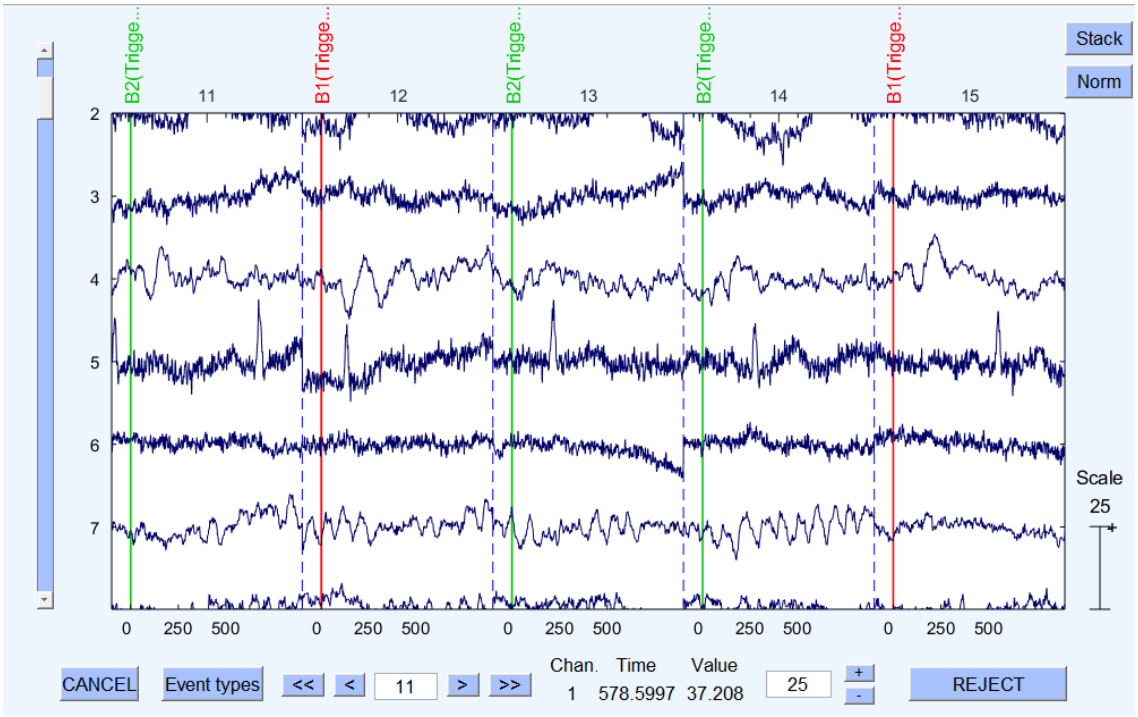

Figure 22.4 The independent components from 3 to 7 plotted in time, epoch by epoch.

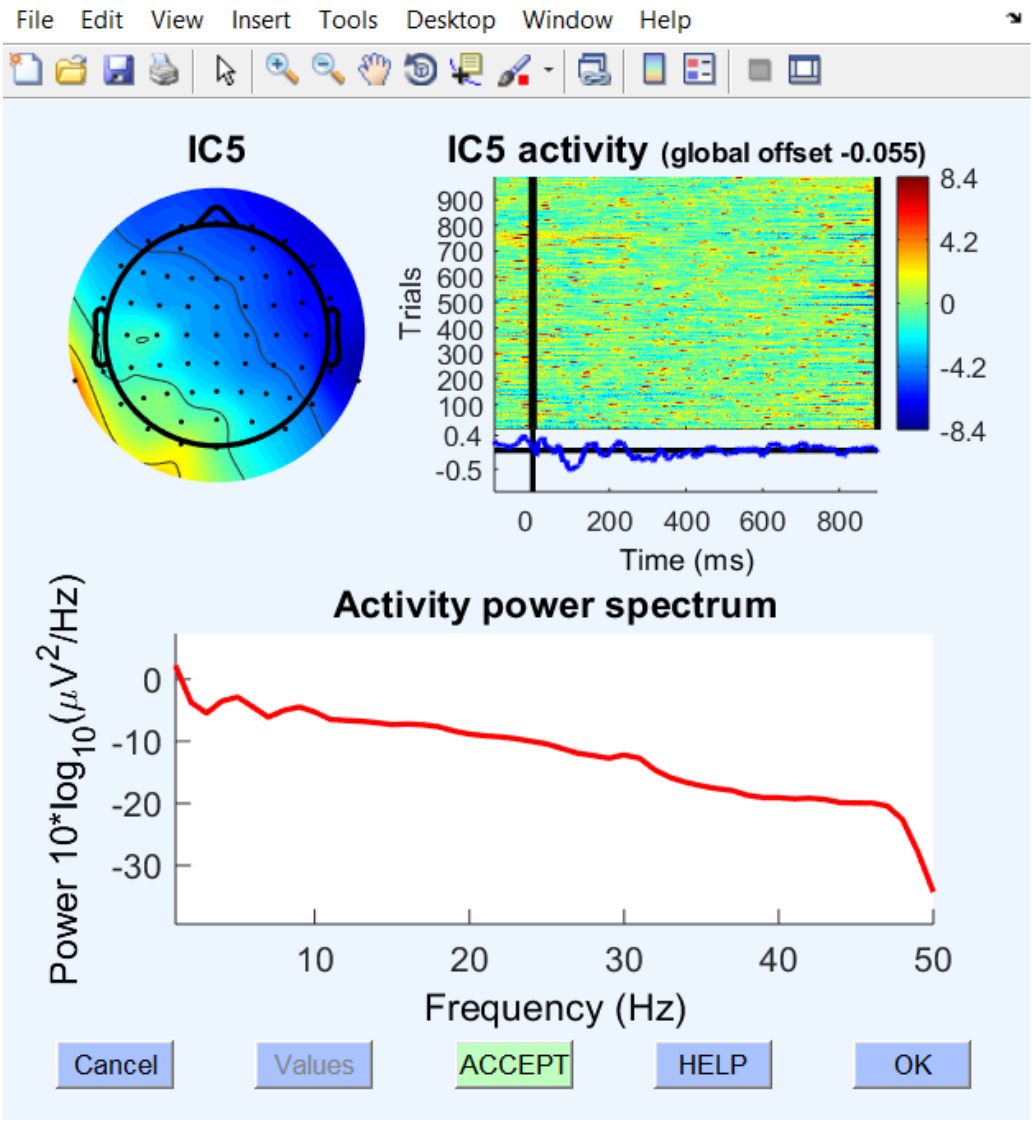

Figure 23.4 The fifth independent component in detail: both from the scalp map activation and from the activity plot it can be deduced it is the pulse component.

For what concerns the good ICs (in which the source is clearly recognisable) an example is in figure 4.24. The intensity in the scalp map draws concentric circles and the trials over time plot is very synchronous among the trials and with the trigger. In this particular case, the component is in the parietal cortex, where it is well know that the SEP present a negative peak at a latency of around 20 ms and a positive one at a latency of around 30 ms.

In fact, in figure 4.24 the average of all the trials is zoomed in and can be noticed that the trend of the peaks is coherent with the location of the component (even if the polarity at 30 ms should be negative), and probably represent one of the component which mainly represent the right parietal electrodes.

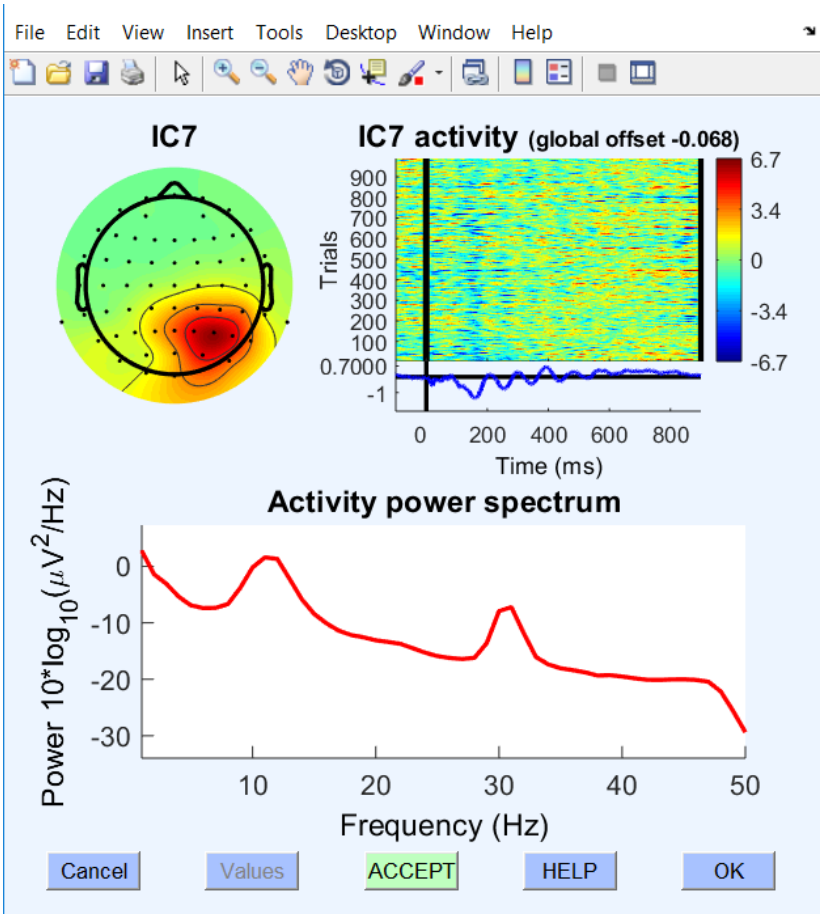

Figure 24.4 The seventh independent component in detail: both from the scalp map activation and from the activity plot it can be deduced it is a good component.

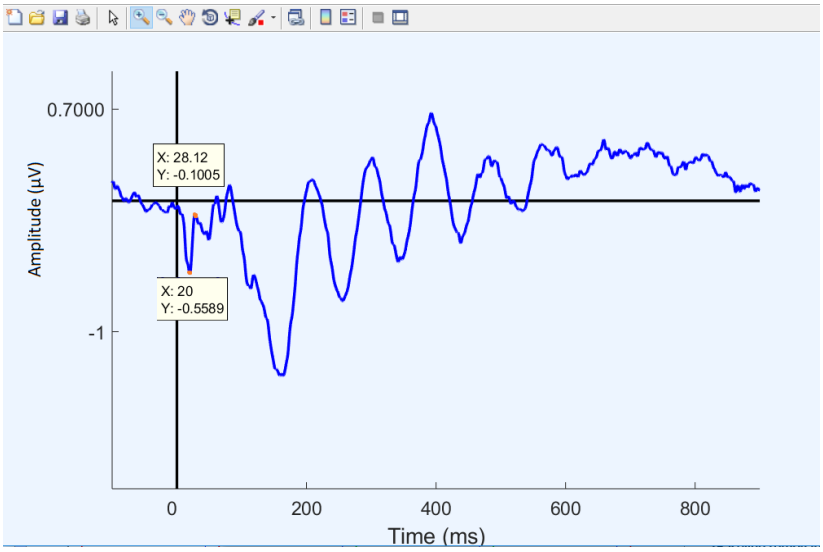

Figure 25.4 The seventh independent component plotted in time, like an average of all the trials. The peaks reveal that this component is very consistent with the usual activation of parietal cortex during SEPs.

4.8 Retrieving SEPs

Once epoched the signal it is possible to compute the SEPs through the averaging technique. This operation is usually done after each step to be sure the signal is not changing from the original after the mentioned operations. It is possible to do it both with EEGlab and with ERPlab, usually has been made through ERPlab because thanks to this toolbox it is possible to get at the same time the ERP changing in time and in frequency (figure 26.4).

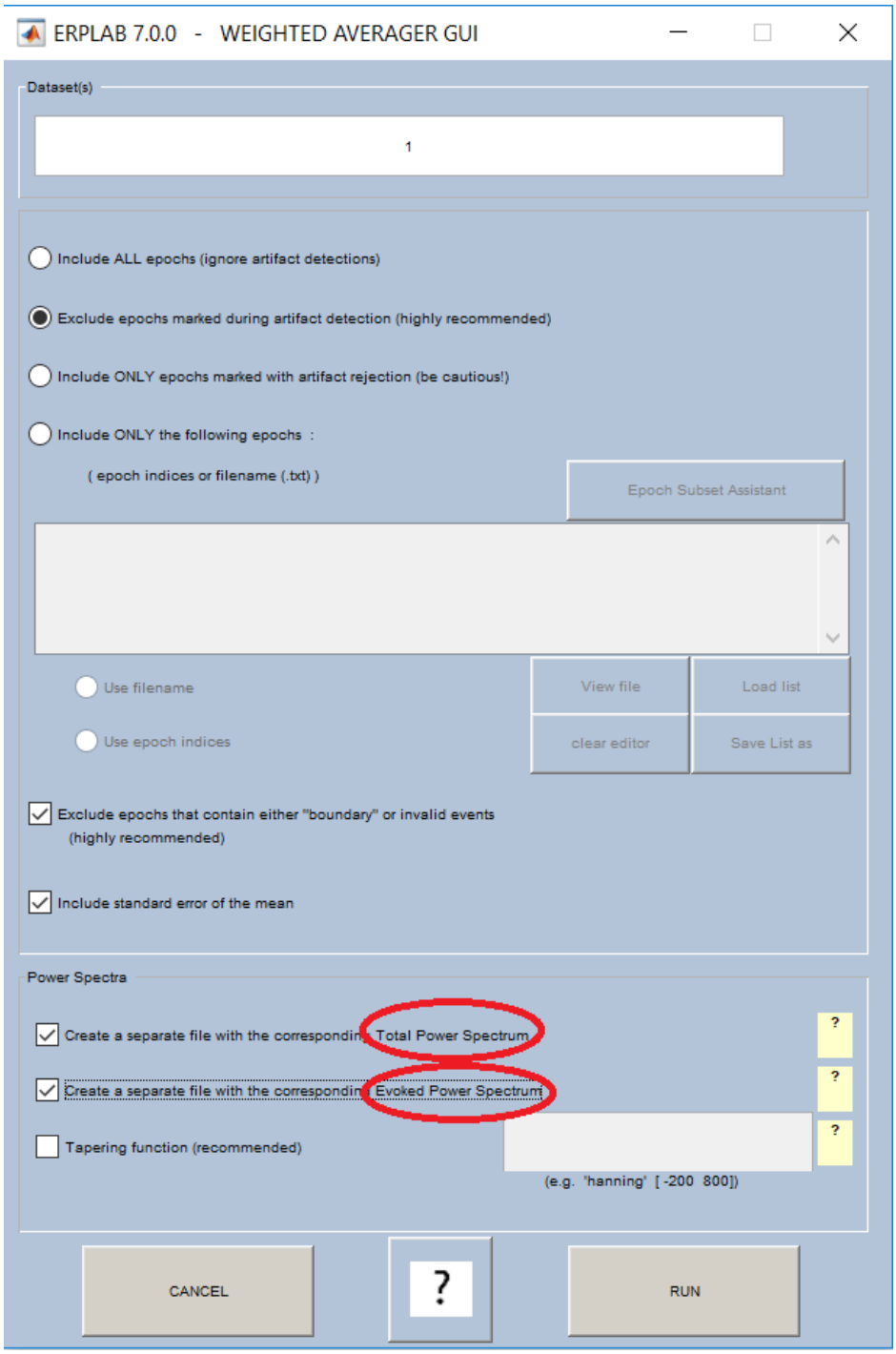

Figure 26.4 The ERPLAB GUI to compute average ERP. ERPs are created by default in time, but there is the possibility to plot them in frequency too.

In addition to this, ERPlab toolbox is more portable to choose which channels to plot, the scales, and the temporal window. It is also possible to add a baseline correction only in visualisation. At the end of all the operations, the ERPset can be exported and saved (figure 27.4).

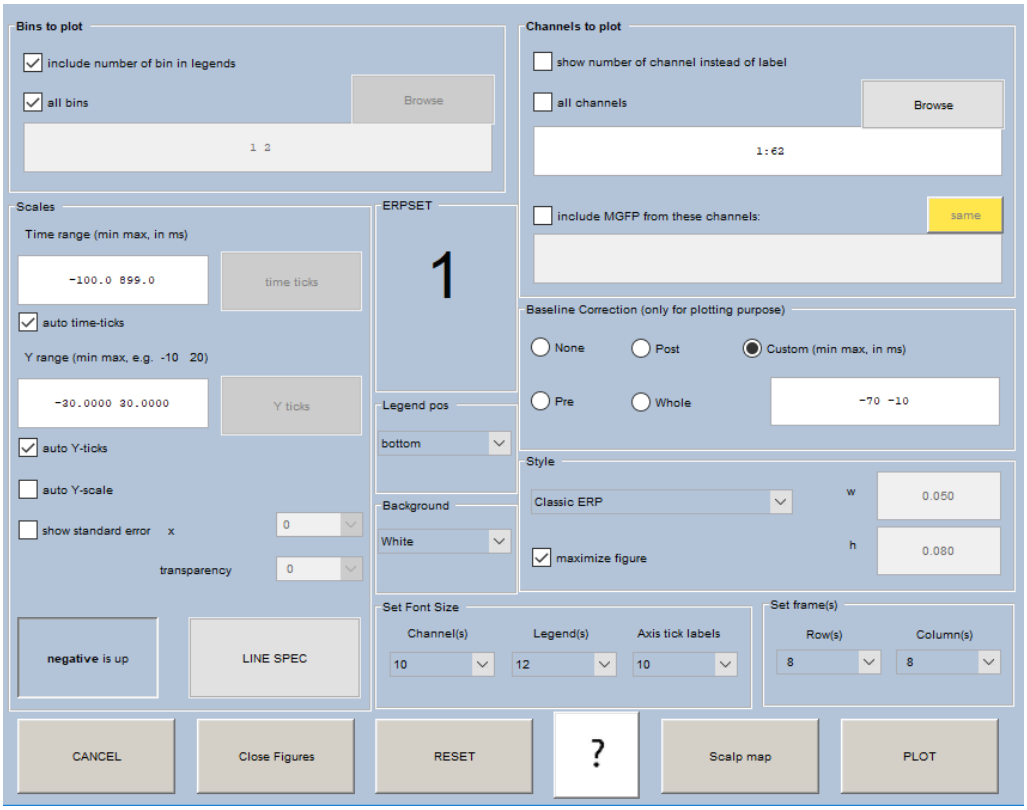

Figure 27.4 The ERPLAB plotting GUI in which can be chose the channels to plot, the time range and scale, and there is the possibility to plot the ERP with baseline correction.

In figure 28.4 it is shown the SEPs after all described processing. The average of all the event related to the auto-induced stimulation are plotted in black, the average of the events with the externally-triggered stimulation are in red. The trend of the signal in the two cases is usually congruent, but zooming in especially at long latencies some differences can be pointed out.

In figure 28.4 and figure 29.4 the channels P4 and F4 are respectively represented. The behaviour of the two channels should be mirrored from the literature, and this can be evinced, confirming that the analysis did not distort the behaviour of the signal. The latencies of the waves seem to be respected too, and especially in P4 the N20 and P27 are quite evident.

In the next paragraphs the latencies and amplitudes of the signals have been statistically analysed in order to highlight difference between the two events among the subjects.

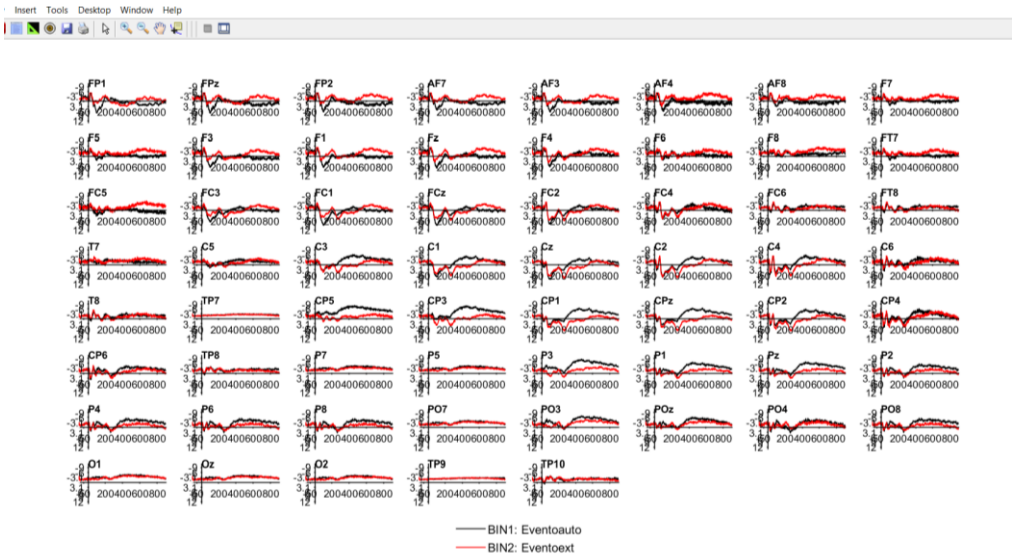

Figure 28.4 The two SEPs signal (one derived from auto stimulation and one from external one,) for each channel

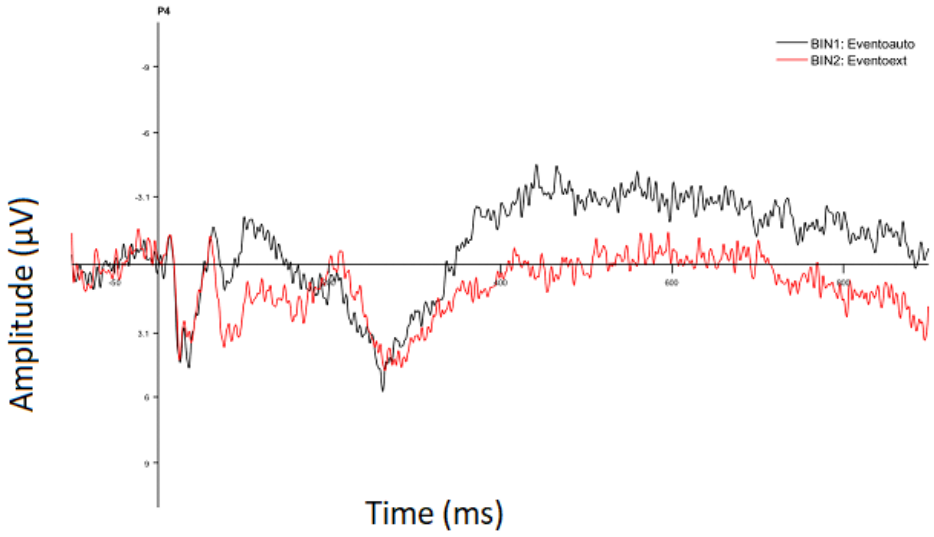

Figure 29.4 A zoom of the channel P4. It is clearly shown the first wave at a latency of around 20 ms (N20). The y axis is negative up for convention.

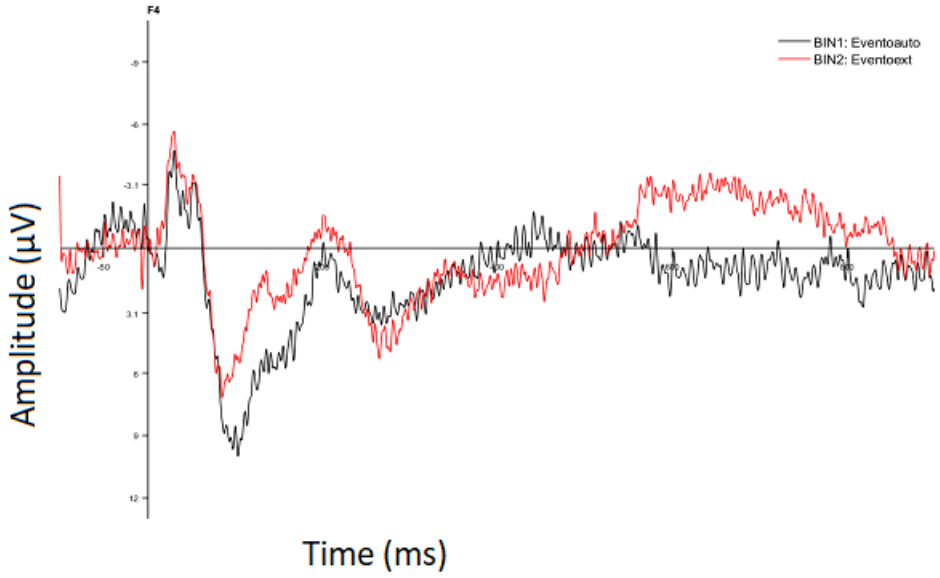

Figure 30.4 A zoom of the channel F4. The y axis is negative up for convention.

4.9 Statystical analysis on the waves

The further analysis has been performed on the waves analysed in chapter 2, the N20 in the channel P4 and N30 in channel F4 (figure 31.4 and figure 32.4). Running the ad hoc functions (Appendix C), some parameters: latencies, amplitudes, areas of the curve and mean amplitudes of the peaks have been found. The function takes as arguments the data, the channel of interest, the time window in which the waves have to be found (identified through visual inspection for each subject) and returns the desired measurements. Two vectors has been constructed for each of these parameters, one relative to bin1 and one relative to bin2.

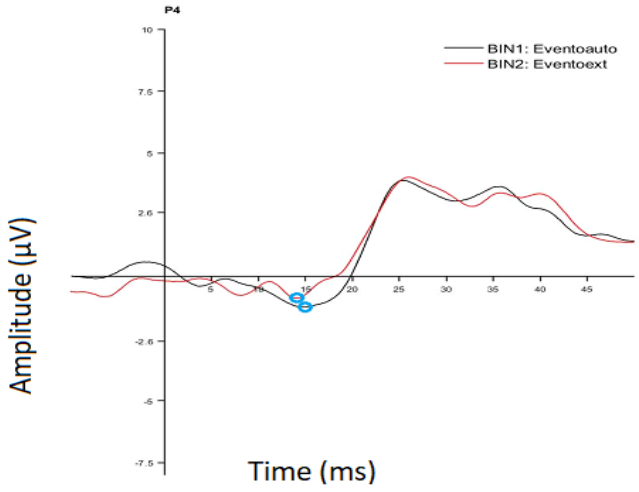

Figure 31.4 The P4 channel for one subject, the two bins are superimposed and in blue are circled the N20 waves for the two cases.

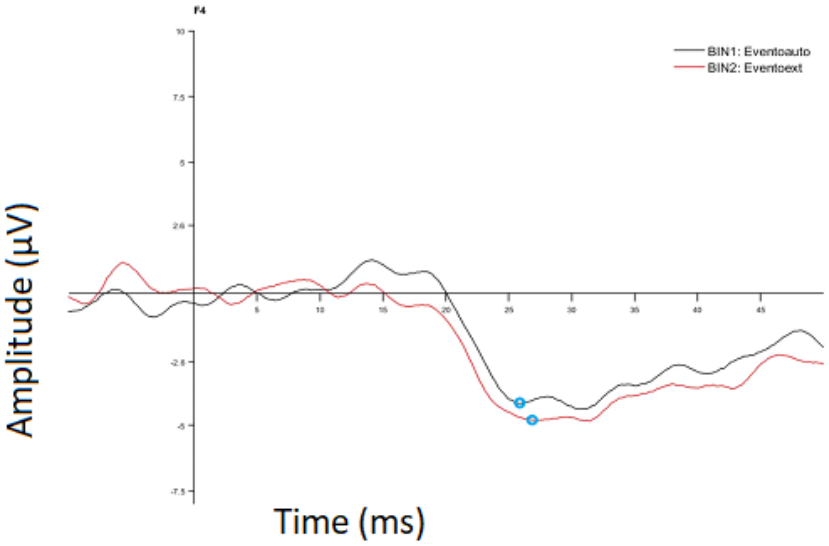

Figure 32.4 The F4 channel for one subject, the two bins are superimposed and in blue are circled the N30 waves for the two cases.

As it was expected the parameters retrieved are quite variable among all the subjects; this is the reason why a statistical analysis has been conducted to verify the significance of the data (i.e. the difference between the groups is not related to chance). Among the statistical methods, the t-test has been chosen. The general aim of this method is to compare two groups of data computing the mean of each group and verify how statistically different they are between them. The t-test can be of three types:

- **Independent samples t-test**: the samples are not dependent among each other, for example because they are subjected to different conditions or are extrapolated from two different groups.
- **Paired sample t-test**: in which the samples are dependent between each other, could be the same group of subjects in two different conditions, or at different times.
- **One sample t-test**: a single group compared with a certain mean.

In this case, the paired sample t-test has been chosen, since the comparison is between the two different conditions (auto and external) in the same subject.

There are two possibilities: accept or reject the null hypothesis:

- The null hypothesis is usually accepted by default, this means that there is no association between the two groups (**h = 0**)
- If the null hypothesis is rejected this means that the data are in contrast with the null hypothesis and another hypothesis is needed (**h = 1**).

To assess how different the two groups are, a **t-score** is calculated as the ratio between the dissimilarity between two groups and inside each group. A high t-score indicated that the two groups are dissimilar, whereas a low t-score means the opposite. A t-score of n indicates that the variation between the groups is n times more different with respect to the variability inside the group. Each t-score is associated to a **p-value** which evaluates the probability the data are related to coincidences; this can range from **0** to **1** (0% to 100%). The lower the p-value is, the more significant the difference between the groups is. Usually p-values lower than 0.05 (only 5% of the result is biased by chance,) are considered acceptable to validate the data.

5. Results

As explained in the previous chapter, the parameters retrieved for the statistical analysis are: the latencies, the amplitudes, the area behind the curves and the mean amplitude. Some of these parameters (latency and amplitude) have been taken into account by Macerollo et al. in his study about sensory attenuation which compares healthy subjects with patients with functional movement disorders. He found significant results running an ANOVA which compared the ratio between the movement condition (onset of the movement) and rest in the two groups. (Macerollo et al., 2015)

Kida et al. proposed an ANOVA to compare the amplitude in three conditions: rest, movement and count (condition used to test the role of the concentration in the experiment). Other studies (Hughes & Waszak, 2011), (Baess et al., 2009) conducted tests with the maximum amplitude or mean amplitudes with ANOVA to have the possibility to combine more parameters in the same analysis or because the conditions to analyse were more than two.

The results obtained in this study are not coherent with those which studied the role of the movement in the modulation of the waves (Kida et al., 2004), (Abbruzzese, Ratto, Favale, & Abbruzzese, 1981). In these experiment the comparison is usually between a condition in which the subject moves and a rest condition, and the results show that the evoked potentials decrease their amplitude in the presence of the movement. For what concerns this experiment, being the first experiment which combines movement, agency and prediction studying them with SEPs with this precise modalities: auto induced and externally induced stimuli, the results should be re-interpreted after the comparison with other future studies.

In this experiment, as previously said, the t-test has been chosen as a first exploratory step (Appendix D).

The t-test has been run for each parameter in the different channels, to find statistical differences between the two bins: bin 1 corresponds to auto-induces events, and bin 2 to external events; and it is reported in the last column (table 1.5 and table 2.5).

		P4 (N20)								
		S1	S2	S3	S4	S5	S6	S7	S8	
Latency	**bin 1**	13,75	15,625	15,20833	15	16,25	20,20833	16,875	12,91667	
	bin 2	13,75	15,41667	14,58333	14,58333	16,25	20,41667	16,25	13,75	**n.s.**
Amplitude	**bin 1**	0,360364	1,163437	1,218346	1,940662	1,680694	2,288977	-1,6153	0,557815	
	bin 2	1,035716	0,517332	0,866568	0,808175	0,977033	1,072592	0,382647	0,633506	**n.s.**
Area curve	**bin 1**	1,267344	4,592154	6,107802	9,169152	5,980783	11,34489	9,188762	2,639535	
	bin 2	4,554594	1,490287	3,816023	3,332323	3,084433	4,780818	1,320362	3,005239	**0,048797**
Mean amplitude	**bin 1**	-0,24372	-0,91843	-1,14521	-1,71922	-1,1392	-2,16093	1,786704	-0,52791	
	bin 2	-0,87588	-0,2908	-0,7155	-0,62481	-0,45449	-0,91063	-0,23456	-0,60105	**n.s.**

Table 1.5 The values of the latencies, amplitudes, areas of the curve and mean amplitudes of the peak N20 in channel P4, for each bin: bin 1 corresponds to auto-induced events, and bin 2 to external events. The last column represent the p-value.

		F4 (N30)								
		S1	S2	S3	S4	S5	S6	S7	S8	
Latency	**bin 1**	30	26,25	26,04167	27,08333	31,25	28,125	31,45833	26,04167	
	bin 2	28,125	26,45833	27,29167	26,875	31,875	28,95833	29,79167	30,83333	**n.s**
Amplitude	**bin 1**	3,374827	3,545218	4,18192	5,421169	3,314581	1,823596	4,838786	1,77943	
	bin 2	1,49624	2,811832	4,815967	3,494996	3,757812	1,760456	1,525542	1,386235	**n.s**
Area curve	**bin 1**	17,11475	17,88577	19,62348	27,06288	13,89583	7,075224	24,5102	7,086166	
	bin 2	7,478046	13,78109	22,98266	17,15465	14,95176	6,737075	7,755879	4,44325	**n.s**
Mean amplitude	**bin 1**	-3,25995	-3,35358	0	-5,07429	-2,77917	-1,41504	-4,66861	-1,41723	
	bin 2	-1,42439	-2,58395	-4,59653	-3,2165	-2,99035	-1,34742	-1,47731	-0,88865	**n.s**

Table 2.5 The values of the latencies, amplitudes, areas of the curve and mean amplitudes of the peak N30 in channel F4, for each bin: bin 1 corresponds to auto-induced events, and bin 2 to external events. The last column represent the p-value.

In table 1.5 it is shown that the only significant value ($p < 0.05$) is related to the area of the curve in the parietal channel (P4). It has been calculated the mean of the values representing the curve of the area and for bin 1 corresponds to 6.2863 and 3.1730 for bin 2. This difference can be interpreted as a mean increment of the area in the case the stimulus is auto-induced. The mean of the amplitude gives coherent results (mean for bin 1 is 0.9493 and mean for bin 2 is 0.7866). For what concerns the dispersion of the data the bin 2 is less dispersed with respect to bin 1, a result that could be predicted because the bin 1 corresponds to the auto-triggered stimulus, which is more subjected to noise.

In addition to this, even if in table 2.5 it is reported that the area of the curve in the frontal channel (F4) is non-significant, actually the value corresponds to 0.08 which is nearly significant. Also in this channel both the mean and the dispersion resulted higher for bin 1 with respect for bin2 (respectively 16.7819 against 11.9105 for the mean and 7.2838 against 6.3501 for the standard deviation).

5.1 Conclusions

From the previous results it can be deduced that the most stable parameter considered in our experiment is the area of the curve (which is significant in the channel P4 and nearly significant for the channel F4). This result could be biased by the fact that the number of subjects tested is only eight, which is scarce.

For what concerns the latencies, it is known from the literature that the delay of the waves always shows a subject dependency related to height and physical characteristics and this aspect together with a small group of datasets might have contributed to give non-significant results.

Another aspect that has influenced the results in a negative way is the presence of a bigger drift in the auto-induced trigger group (highlighted by the higher standard deviation of that bin), which has diminished the possibility to obtain relevant statistically significant differences in the amplitude of the two bins. Unfortunately, as explained in the data analysis chapter a more aggressive filtering has been discouraged to avoid deformation of the waves.

It has to be said that one of the datasets resulted quite noisy with respect to the others, and could have altered the results of the statistics, but it has been included at this stage of the study to expand the sample.

The idea in the future is to increase the sample of subjects. To do this, since the experiment is quite long in time, it could be useful to register the signal of both the

participants to the experiment (both the subject and the “mirror”). Even tough, from our experience, in this case the best scenario would be to have the same EEG cap for both, eventually with more electrodes if a more reliable esteem of the cerebral connectivity will be required. In addition to this, the different combination of agency, prediction and movement are planned to be experimented to better define the phenomenon of sensory attenuation as mentioned in the introduction.

Various experiment related to social behaviours can be imagined, linking the experiment of sensory attenuation to the personal relationship between the two participants and also different responses between right handed and left handed people could be investigated.

The experiment here presented represents the first step towards a wider study of the cerebral mechanisms of sensory attenuation. Defining the mechanisms that surround such phenomenon could be useful to understand and identify the parameters that affect the interaction between self and external environment in humans, and could be employed to establish the relationship among the models of motor prediction, agency and self-perception.

Appendix

A-The programme in the PIC microcontroller:
1-initialisation of the pins and variables

```
5
6   #include <18F67J10.h>
7   #device ICD = TRUE
8   #fuses HS, NOWDT
9
10  #include <stdio.h>
11  #include <stdlib.h>
12  #include <string.h>
13
14  #define delay_seconds
15  #use delay(clock = 10000000)
16  #use rs232 (baud = 230400, xmit=PIN_G1, rcv=PIN_G2)//115200
17
18  #define LED1 PIN_A1
19  #define LED2 PIN_A2
20  #define LEDR PIN_B5
21  #define BUTTON1 PIN_C1
22  #define BUTTON2 PIN_C3
23  #define EXT_STIM PIN_C0
24  #define TRIG1 PIN_C4
25  #define TRIG2 PIN_C2
26  #define PULSANTE PIN_D6
27
28  char ch[1010];
29  int16 i;
30  int32 n;
31  int16 maxdel = 2000;
32  int16 del;
33  int16 min_del=500;
34  int1 ctrl = 0;
35  int16 count = 0;
36
37
```

2- initialisation of the timer employed to read the data coming from the serial port, a character at a time at a frequency of around 1KHz (reading function invoked by the interrupt).

The tension level of the PIN_C5 was used for debugging (by reading the output by the oscilloscope) and assuring the correctness of the data loading.

```
38
39  #int_timer3 //timer used to control the data which arrives to the serial port
40  void reading()
41  {
42     set_timer3(63582);//1kHz
43     ch[i] = getc();
44     if (ctrl) //controllo del caricamento
45     {
46     output_high(PIN_C5);
47     }
48     else
49     {
50     output_low(PIN_C5);
51     }
52     ctrl++;
53     i++;
54  }
55
```

3- functions used in the main programme:

- The “light_led” function lights one of the LED on depending on the list coming from the serial port: if the received character corresponds to 0 the first LED is switched on, otherwise the second.
- The “wait_for_one_press” function waits that the subject pushes the button in front of him and the corresponding LED is switched off when it happens.
- The “wait_sec” function waits one second after each stimulus, and this is necessary for registration.
- The “create_delay” function creates a delay random in ms that varies from half a second till 2 s.

```
56  void light_led(int led){
57     switch(led) {
58        case 0: output_high(LED1); break;
59        case 1: output_high(LED2); break;
60     }
61  }
62  void wait_for_one_press(int button){
63     switch(button){
64     case 0:
65        while(input(BUTTON1));
66        output_low(LED1);
67        break;
68     case 1:
69        while(input(BUTTON2));
70        output_low(LED2);
71        break;
72     }
73  }
74  void wait_sec(){
75     output_low(LED1);
76     output_low(LED2);
77     delay_ms(1000);
78  }
```

```
79  void create_delay(){
80     del = (rand() % (maxdel-min_del+1))+min_del;
81     delay_ms(del);
82  }
83
```

4- In the main function, when the embedded pushbutton is pressed the interrupt is enabled, invoking the “reading” function and the vector “ch” is filled by the data coming from the serial port (i.e. an array constituted by zeros and ones in random order).

```
84  void main() {
85        output_low(LED1);
86        output_low(LED2);
87        while(input(PULSANTE));
88        setup_timer_3(T3_INTERNAL | T3_DIV_BY_1);
89        enable_interrupts(int_timer3);
90        set_timer3(63582);
91        i=0;
92        enable_interrupts(global);
93        while(i < 1020);
94        disable_interrupts(global);
95
96        n = 0;
```

5-finally, the data contained in the vector “ch” is used to switch on the LEDs, enable the pushbuttons, and send the trigger to the relative subject on basis of the value (0 or 1) while the stimulation is always given in both situations.

```
98        while (n<1010){
99           if (ch[n] == '0'){
100             light_led(0);
101             wait_for_one_press(0);
102             output_high(EXT_STIM);
103             delay_ms(5);
104             output_low(EXT_STIM);
105             count ++;
106             output_high(TRIG1);
107             delay_ms(5);
108             output_low(TRIG1);
109             wait_sec();
110             create_delay();
111             }
112          if (ch[n] == '1'){
113             light_led(1);
114             wait_for_one_press(1);
115             output_high(EXT_STIM);
116             delay_ms(5);
117             output_low(EXT_STIM);
118             count ++;
119             output_high(TRIG2);
120             delay_ms(5);
121             output_low(TRIG2);
122             wait_sec();
123             create_delay();
124             }
125          n++;
```

6-if the number of stimulation is equal to the length of the vector “ch”, a red LED is switched on and this sets the end of the experiment.

```
126         if (count == 1010){ //control on the nuber of stimulations
127             output_high(LEDR);
128
129           }
130       }
131   }
132
```

B – Send a list of numbers through a serial port with MATLAB

The list is created with the command *“randperm”* which offers the possibility to create a random list distributing equally the elements, in this case having an equal number of 0 and 1. Then, the list is sent through the port one character at a time in form of string.

```
1   clear all
2   close all
3   clc
4
5   %% create list
6   lista = mod( reshape(randperm(1010*1), 1010, 1), 2 );
7
8   %% send list
9   s = serial('COM4');
10  set(s,'BaudRate',230400);
11  fopen(s)
12
13  for i=1:length(lista)
14      x = int2str(lista(i))
15      fprintf(s,'%c',x);
16      pause(0.015)
17  end
18
19  fclose(s)
```

C – Findpeaks N20 in channel P4 and N30 in channel F4

the “my_findpeaks_N20_N30” function finds the peaks (the maximum) N20 and N30 in EEG channels. The arguments of the function are the averaged EEG signals, the time intervals (two extreme values for each peak) and the number of the channels in which the peak has to be found, in this case the channels which correspond to P4 o F4.

The outputs are the eight amplitudes of the peaks (four for each bin: auto or external), and eight latencies of the peaks (four for each bin: auto or external).

```
function [ maximum_value1, maximum_value2, maximum_value7,...
    maximum_value8, index_N20_P4_bin1,index_N20_P4_bin2, ...
    index_P30_F4_bin1, index_P30_F4_bin2 ] = my_findpeaks_N20_P30(erp,low_N20,high_N20,low_P30,high_P30,ch_P4, ch_F4)



fc = 4800;

bin1_P4 = erp(ch_P4,1:1000,1);
bin2_P4 = erp(ch_P4,1:1000,2);
bin1_F4 = erp(ch_F4,1:1000,1);
bin2_F4 = erp(ch_F4,1:1000,2);

bin1_P4_corrected = bin1_P4;
bin2_P4_corrected = bin2_P4;
bin1_F4_corrected = bin1_F4;
bin2_F4_corrected = bin2_F4;
low_extreme_N20 = round(low_N20*4.8);
high_extreme_N20 =  round(high_N20*4.8);

low_extreme_P30 = round(low_P30*4.8);
high_extreme_P30 =  round(high_P30*4.8);


%% N20 in P4

[maximum_value1,index_maximum1]=max((-bin1_P4_corrected(low_extreme_N20:high_extreme_N20)));
index_N20_P4_bin1=index_maximum1+low_extreme_N20-1;


[maximum_value2,index_maximum2]=max((-bin2_P4_corrected(low_extreme_N20:high_extreme_N20)));
index_N20_P4_bin2=index_maximum2+low_extreme_N20-1;

%%  N30 in F4

[maximum_value7,index_maximum7]=max((-bin1_F4_corrected(low_extreme_P30:high_extreme_P30)));
index_P30_F4_bin1=index_maximum7+low_extreme_P30-1;

[maximum_value8,index_maximum8]=max((-bin2_F4_corrected(low_extreme_P30:high_extreme_P30)));
index_P30_F4_bin2=index_maximum8+low_extreme_P30-1;

```

```
%% to verify
figure
subplot(2,2,1)
plot(bin1_P4_corrected)
hold on
stem(index_N20_P4_bin1,-maximum_value1,'*');
ylabel('P4 bin1')

subplot(2,2,2)
plot(bin2_P4_corrected)
hold on
stem(index_N20_P4_bin2,-maximum_value2,'*');
ylabel('P4 bin2')

subplot(2,2,3)
plot(bin1_F4_corrected)
hold on
stem(index_P30_F4_bin1,-maximum_value7,'*');
ylabel('F4 bin1')

subplot(2,2,4)
plot(bin2_F4_corrected)
hold on
stem(index_P30_F4_bin2,-maximum_value8,'*');
ylabel('F4 bin2')


end
```

Below, an example of how the function is used in a dataset: the dataset of the subject is loaded, the inputs are set case by case after a visual analysis of the signal and the function is recalled. 16 vectors corresponding to the latency, the maximum amplitude, the area of the curve and the mean amplitude of the peak for each channel and bin (auto and external) are filled with the information provided by each output of the function, and they will be update after each subject. These vectors will be used for the statistical analysis.

```
%% Soggetto 1
ERP = pop_loaderp( 'filename', 'Alessandra_epoc_artrej_chanrem_filt_vi_cr_ar_ICA_postIca_basecorr.erp', 'filepath',.
 'C:\Users\CHIARA\Desktop\dataset' );
k=1;
erp1=ERP.bindata;
low_N20=112.5;
high_N20=115;
low_N20_samples=round(low_N20*4.8);
high_N20_samples=round(high_N20*4.8);

low_P30=128;
high_P30=132;
low_P30_samples=round(low_P30*4.8);
high_P30_samples=round(high_P30*4.8);

ch_P4 = 50;
ch_F4= 14;

[maximum_value1, maximum_value2, maximum_value3, maximum_value4, maximum_value5, maximum_value6, maximum_value7, max
    index_P30_P4_bin1, index_P30_P4_bin2, index_N20_F4_bin1, index_N20_F4_bin2, index_P30_F4_bin1, index_P30_F4_bin2

%N20
latenza_N20_P4_b1(k)=index_N20_P4_bin1;
ampiezza_N20_P4_b1(k)=maximum_value1;
area_N20_P4_b1(k)=sum(abs(erp1(ch_P4,low_N20_samples:high_N20_samples,1)))/(high_N20-low_N20);
mean_amplitude_N20_P4_b1(k)=mean(erp1(ch_P4,low_N20_samples:high_N20_samples,1));

```

```
27
28 -   latenza_N20_P4_b2(k)=index_N20_P4_bin2;
29 -   ampiezza_N20_P4_b2(k)=maximum_value2;
30 -   area_N20_P4_b2(k)=sum(abs(erp1(ch_P4,low_N20_samples:high_N20_samples,2)))/(high_N20-low_N20);
31 -   mean_amplitude_N20_P4_b2(k)=mean(erp1(ch_P4,low_N20_samples:high_N20_samples,2));
32
33    %P30
34 -   latenza_N30_F4_b1(k)=index_P30_F4_bin1;
35 -   ampiezza_N30_F4_b1(k)=maximum_value7;
36 -   area_N30_F4_b1(k)=sum(abs(erp1(ch_F4,low_P30_samples:high_P30_samples,1)))/(high_P30-low_P30);
37 -   mean_amplitude_N30_F4_b1(k)=mean(erp1(ch_F4,low_P30_samples:high_P30_samples,1));
38
39 -   latenza_N30_F4_b2(k)=index_P30_F4_bin2;
40 -   ampiezza_N30_F4_b2(k)=maximum_value8;
41 -   area_N30_F4_b2(k)=sum(abs(erp1(ch_F4,low_P30_samples:high_P30_samples,2)))/(high_P30-low_P30);
42 -   mean_amplitude_N30_F4_b2(k)=mean(erp1(ch_F4,low_P30_samples:high_P30_samples,2));
```

D – Statystical analysis

The outputs of the function “my_findpeaks_N20_N30” (maximum amplitude, latency of the peak, mean amplitude of the wave and area of the wave) are the parameters for which the t-test between the two groups (bin 1 and 2) has been calculated (in *Matlab*).

```
1    %% samples to seconds
2    latenza_N20_P4_b1s = (latenza_N20_P4_b1/4.8)-100;
3    latenza_N20_P4_b2s = (latenza_N20_P4_b2/4.8)-100;
4    latenza_N30_F4_b1s = (latenza_N30_F4_b1/4.8)-100;
5    latenza_N30_F4_b2s = (latenza_N30_F4_b2/4.8)-100;
6
7    %% T-test
8    [AN20_P4H, AN20_P4P]  = ttest(ampiezza_N20_P4_b1,ampiezza_N20_P4_b2);
9    [AN30_F4H, AN30_F4P] = ttest(ampiezza_N30_F4_b1,ampiezza_N30_F4_b2);
10
11   [LN20_P4H, LN20_P4P] = ttest(latenza_N20_P4_b1s,latenza_N20_P4_b2s);
12   [LN30_F4H, LN30_F4P] = ttest(latenza_N30_F4_b1s,latenza_N30_F4_b2s);
13
14   [AreaN20_P4H, AreaN20_P4P]  = ttest(area_N20_P4_b1,area_N20_P4_b2);
15   [AreaN30_F4H, AreaN30_F4P] = ttest(area_N30_F4_b1,area_N30_F4_b2);
16
17   [MeanamplitudeN20_P4H, MeanamplitudeN20_P4P] = ttest(mean_amplitude_N20_P4_b1,mean_amplitude_N20_P4_b2);
18   [MeanamplitudeN30_F4H, MeanamplitudeN30_F4P] = ttest(mean_amplitude_N30_F4_b1,mean_amplitude_N30_F4_b2);
19
```

Moreover, for each group of the two channels has been calculated also the mean and the standard deviation (in each group separately) and the mean and the standard deviation of the difference of values of the two groups (difference between a condition and the other of the same subject).

```
20   %% Mean and standard error of latencies
21   MEAN_LN20_P4_b1 = mean(latenza_N20_P4_b1s);
22   STD_LN20_P4_b1 = std(latenza_N20_P4_b1s);
23
24   MEAN_LN20_P4_b2 = mean(latenza_N20_P4_b2s);
25   STD_LN20_P4_b2 = std(latenza_N20_P4_b2s);
26
27   MEAN_LN30_F4_b1= mean(latenza_N30_F4_b1s);
28   STD_LN30_F4_b1= std(latenza_N30_F4_b1s);
29
30   MEAN_LN30_F4_b2 = mean(latenza_N30_F4_b2s);
31   STD_LN30_F4_b2 = std(latenza_N30_F4_b2s);
32
```

```
%% Mean differences between latencies and amplitudes
N=length(latenza_N30_F4_b2s);

for j=1:N

    DIFF_LN20_P4(j)= latenza_N20_P4_b1s(j)-latenza_N20_P4_b2s(j);
    DIFF_LN30_F4(j)= latenza_N30_F4_b1s(j)-latenza_N30_F4_b2s(j);

    DIFF_AN20_P4(j)= ampiezza_N20_P4_b1(j)-ampiezza_N20_P4_b2(j);
    DIFF_AN30_F4(j)= ampiezza_N30_F4_b1(j)-ampiezza_N30_F4_b2(j);

end

MEAN_DIFF_LN20_P4=mean(DIFF_LN20_P4);
STD_DIFF_LN20_P4=std(DIFF_LN20_P4);

MEAN_DIFF_LN30_F4=mean(DIFF_LN30_F4);
STD_DIFF_LN30_F4=std(DIFF_LN30_F4);

MEAN_DIFF_AN20_P4=mean(DIFF_AN20_P4);
STD_DIFF_AN20_P4=std(DIFF_AN20_P4);


MEAN_DIFF_AN30_F4=mean(DIFF_AN30_F4);
STD_DIFF_AN30_F4=std(DIFF_AN30_F4);

```

Source of the images

Acknowledgements

My heartfelt thanks to my family for the tireless support, to my friends and my housemates for the precious time spent together in this training path despite the anxiety and the problems. My gratitude goes also to Giulia and the PhD students Mattia and Marco for the help in the compilation of this thesis, and to all the people working in the NEXTlab for the teachings and laughs of the past seven months.

Bibliography

Abbruzzese, G., Ratto, S., Favale, E., & Abbruzzese, M. (1981). Proprioceptive modulation of somatosensory evoked potentials during active or passive finger movements in man. *Journal of Neurology Neurosurgery and Psychiatry*, *44*(10), 942–949. https://doi.org/10.1136/jnnp.44.10.942

Angel, R. W., & Malenka, R. C. (1982). Velocity-dependent suppression of cutaneous sensitivity during movement. *Experimental Neurology*, *77*(2), 266–274. https://doi.org/10.1016/0014-4886(82)90244-8

Baess, P., Widmann, A., Roye, A., Schröger, E., & Jacobsen, T. (2009). Attenuated human auditory middle latency response and evoked 40-Hz response to self-initiated sounds. *European Journal of Neuroscience*, *29*(7), 1514–1521. https://doi.org/10.1111/j.1460-9568.2009.06683.x

Blakemore, S.-J., Wolpert, D., & Frith, C. (2000). Why can't you tickle yourself? *NeuroReport*, *11*(11), R11–R16. https://doi.org/10.1097/00001756-200008030-00002

Croft, R. J., & Barry, R. J. (n.d.). Removal of ocular artifact from the EEG: a review.

Delorme, A. (2010). ICA components reliability.

Fonseca, C., Silva Cunha, J. P., Martins, R. E., Ferreira, V. M., Marques De Sá, J. P., Barbosa, M. A., & Martins Da Silva, A. (2007). A novel dry active electrode for EEG recording. *IEEE Transactions on Biomedical Engineering*, *54*(1), 162–165. https://doi.org/10.1109/TBME.2006.884649

Haggard, P., & Whitford, B. (2004). Supplementary motor area provides an efferent signal for sensory suppression. *Cognitive Brain Research*, *19*(1), 52–58. https://doi.org/10.1016/j.cogbrainres.2003.10.018

Helmholtz, H. von. (1867). Handbuch der physiologischen Optik.

Hughes, G., & Waszak, F. (2011). ERP correlates of action effect prediction and visual sensory attenuation in voluntary action. *NeuroImage*, *56*(3), 1632–1640. https://doi.org/10.1016/j.neuroimage.2011.02.057

Kida, T., Nishihira, Y., Wasaka, T., Sakajiri, Y., & Tazoe, T. (2004). Differential modulation of the short- and long-latency somatosensory evoked potentials in a forewarned reaction time task. *Clinical Neurophysiology*, *115*(10), 2223–2230. https://doi.org/10.1016/j.clinph.2004.04.017

Liss, P. S., & Slater, P. G. (1974). © 1974 Nature Publishing Group.

Macerollo, A., Chen, J. C., Parés, I., Kassavetis, P., Kilner, J. M., & Edwards, M. J. (2015). Sensory attenuation assessed by sensory evoked potentials in functional movement disorders. *PLoS ONE*, *10*(6), 1–6. https://doi.org/10.1371/journal.pone.0129507

Mathewson, K. E., Harrison, T. J. L., & Kizuk, S. A. D. (2017). High and dry? Comparing active dry EEG electrodes to active and passive wet electrodes. *Psychophysiology*, *54*(1), 74–82. https://doi.org/10.1111/psyp.12536

Meziane, N., Webster, J. G., Attari, M., & Nimunkar, A. J. (2013). Dry electrodes for electrocardiography. *Physiological Measurement*, *34*(9). https://doi.org/10.1088/0967-3334/34/9/R47

Pareés, I., Brown, H., Nuruki, A., Adams, R. A., Davare, M., Bhatia, K. P., … Edwards, M. J.

(2014). Loss of sensory attenuation in patients with functional (psychogenic) movement disorders. *Brain*, *137*(11), 2916–2921. https://doi.org/10.1093/brain/awu237

Rousselet, G. A. (2012). Does filtering preclude us from studying ERP time-courses? *Frontiers in Psychology*, *3*(MAY), 1–9. https://doi.org/10.3389/fpsyg.2012.00131

Ruchkin, D. S. (1965). An Analysis of Average Response Computations Based Upon Aperiodic Stimuli ! Okj I < Tm, 87–94.

Schomer, D. L., & Silva, F. L. da. (2015). *Niedermeyer's Electroencephalography: Basic Principles, Clinical Applications, and Related Fields*. https://doi.org/10.1016/B978-0-7020-3369-8.00001-X

Scott, R. N., McLean, L., & Parker, P. a. (1997). Stimulus artefact in somatosensory evoked potential measurement. *Medical & Biological Engineering & Computing*, *35*(May), 211–215. https://doi.org/10.1007/BF02530040

Shergill, S. S., Bays, P. H., Frith, C. D., & Wotpert, D. M. (2003). Two eyes for an eye: The neuroscience of force escalation. *Science*, *301*(5630), 187. https://doi.org/10.1126/science.1085327

Tamura, H., Yan, M., Sakurai, K., & Tanno, K. (2016). EOG-sEMG Human Interface for Communication. *Computational Intelligence and Neuroscience*, *2016*(Dc). https://doi.org/10.1155/2016/7354082

Trans Cranial Technologies Ltd. (2012). 10 / 20 System Positioning Manual. *Technologies Trans Cranial,* (1), 20. Retrieved from http://www.trans-cranial.com/local/manuals/10_20_pos_man_v1_0_pdf.pdf%5Cnwww.trans-cranial.com%5Cnwww.trans-cranial.com

VanRullen, R. (2011). Four common conceptual fallacies in mapping the time course of recognition. *Frontiers in Psychology*, *2*(DEC), 1–6. https://doi.org/10.3389/fpsyg.2011.00365

Voss, M., Ingram, J. N., Haggard, P., & Wolpert, D. M. (2006). Sensorimotor attenuation by central motor command signals in the absence of movement. *Nature Neuroscience*, *9*(1), 26–27. https://doi.org/10.1038/nn1592

Widmann, A., & Schröger, E. (2012). Filter effects and filter artifacts in the analysis of electrophysiological data. *Frontiers in Psychology*, *3*(JUL), 1–5. https://doi.org/10.3389/fpsyg.2012.00233