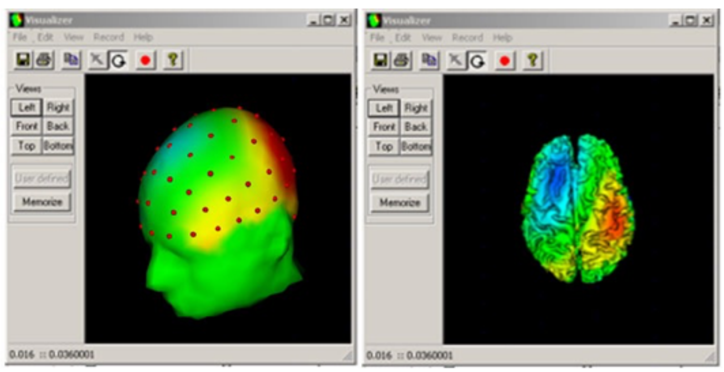
Chapter 4 – ERPs

Event Related Potentials (ERPs)

ERPs

"Making sense of the myriad linear and nonlinear features of EEG data requires careful analyses and clever thinking, not fancy or expensive equipment." Mike X Cohen (2017)

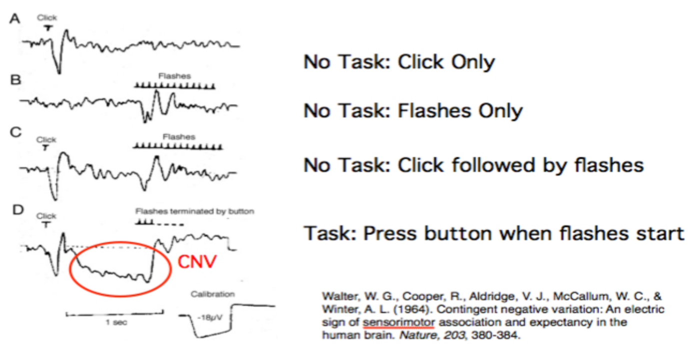


So far, we have talked about continuous Electroencephalography (EEG) recordings. After you have finished your recordings there are many types of analyses that can be applied that enable you to draw stronger conclusions and gain better insights from the millions of points of data that can come from each EEG recording session. Chapter 3 mentioned scalp topographies (fig 1.) which displays a map of where activations happen based on the activation, polarity and covariance of the activations from many electrodes. This can be done by looking at specific frequencies such as beta waves. We can also look at ratios of frequencies, temporal differences in frequency changes, or topographic changes of these frequencies.

One of the most popular analysis techniques for EEG to investigate perception and cognition is called Event Related Potentials (ERPs). ERPs has become popular because it enables us to correlate sensation, perception and cognition to brain processes. It also allows us to look at behavior through reaction times and accuracies (linked to behavior), to gain a direct understanding of what brain differences the behavioral changes evoke. ERPs are time-domain averaged EEG signals. They can be either time- or phase-locked in response to physical stimuli, in association with mental activity or in preparation of actions. This means that we only look at a set time interval before and after the stimulus was presented to observe how the average signal looks in relation to the event of interest.

An important aspect of ERPs is the behavioral paradigm. Ideally, a behavioral paradigm has already been established showing differences between conditions related to a psychological phenomenon of interest. By applying ERPs to this behavioral task, we can see how the behavioral differences between the conditions differ in the brain. We can gain an understanding of the stages of activation, their differences in amplitude, latency difference between potentials and interaction with other variables. ERPs is an effective tool to gain a deeper understanding of how a psychological phenomenon is expressed in the brain. It is a great starting point before applying more expensive and complicated technologies such as FMRI (see chapter 6).

History of ERPs



The ERP technique was first applied in 1939 by Pauline and Hallowell Davis. At one point, their work was funded by billionaire Alfred Loomis who set up an EEG laboratory in his personal home outside of New York and invited luminary scientists of the time. These discoveries slowed down during WWII as Loomis directed his focus to develop the radar to support the war instead. In the 1950s, Grey Walter made significant improvements and developed e.g., scalp topography (Walter, 1953). In the 1960's, he applied this technique to understand cognition in the brain (e.g., Walter, 1964). Since the 1970s the number of published ERP articles has grown exponentially every decade. Today, ERPs are one of the most common approaches to investigate cognition in the brain, but it is also applied to topics such as clinical diagnoses, brain-computer interfacing, awareness detection, and other areas. With the help of better computing power and sophisticated algorithms ERPs is becoming an even more powerful tool.

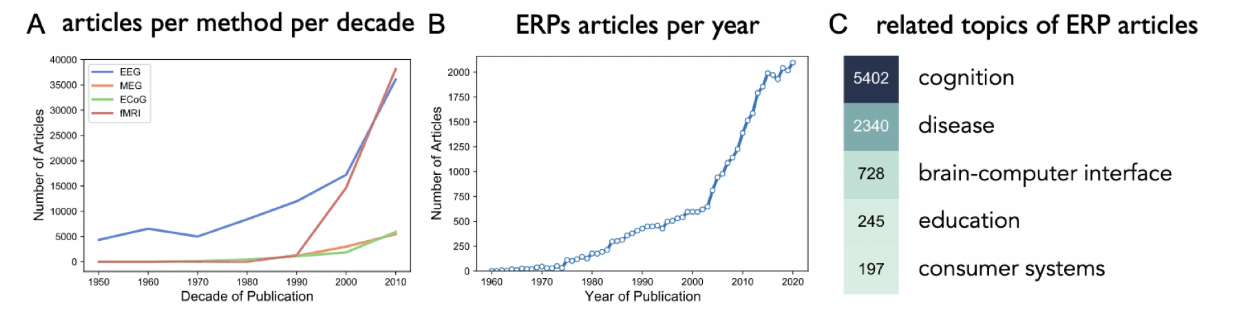
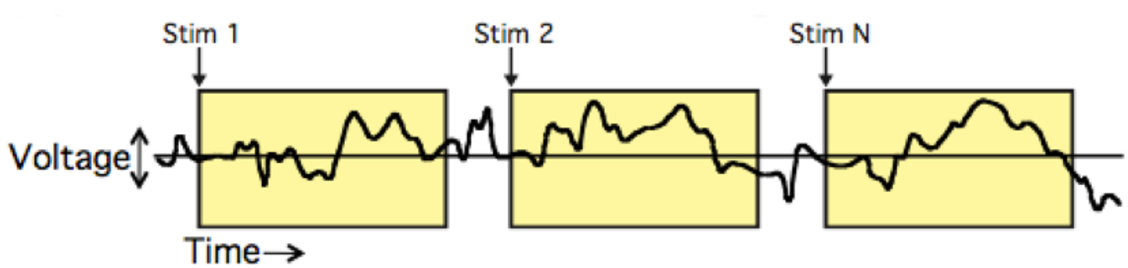


Figure 1. Prevalence of ERP research. (**A**) The number of articles across different methods for measuring brain activity, across decades. Note that each x-axis label reflects a decade (eg. "1950" reflects 1950–1959). (**B**) The number of articles on the topic of ERPs per year, measured as papers using the terms "event related potential", "ERP", or "evoked potential". (**C**) The number of ERP articles related to different topics, based on co-occurrence of ERP terms and listed association terms.

How does it work?

If you present a stimulus 100 times and look at the averaged EEG response pattern for one electrode over the subsequent 1000 ms you get an averaged waveform containing the ERPs. The process is represented by the picture below where a stimulus has been presented repeatedly at varying time intervals and we take time intervals (yellow boxes) and average their signals. The average waveform we get is the common waveform activation for that type of stimulus in the area of the brain underlying that specific electrode. The weakness with this approach is that we don't capture the idiosyncratic activations of each stimulus presentation. Things such as habituation for example might get lost in the averages. On the other hand, it can produce a much better signal to noise ratio. For early brain processes that are quite standard e.g., the visual processing pathway activation from presenting a blink from an LED this approach can be very valuable in shedding light on how these basic processes operate and interact with other basic cortical processes.



Experimental Design

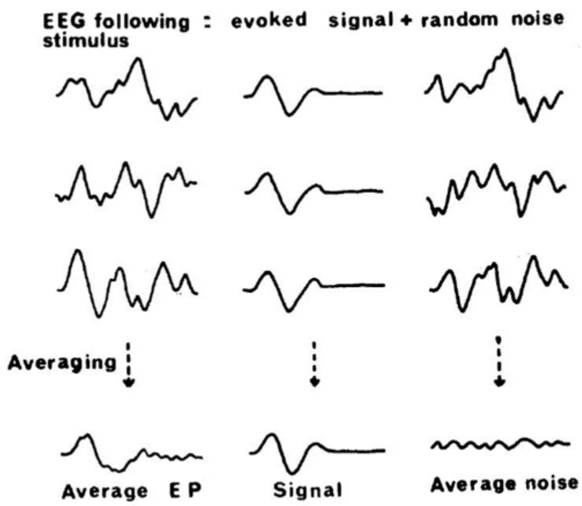
In order to properly study ERPs, it is important to carefully design the experimental protocol for your ERP study. This includes selecting appropriate stimuli, defining the timing of the stimuli (Inter-stimulus interval), and ensuring that the participant is properly prepared and positioned for EEG recording. Stimulus selection is a critical aspect of experimental design for ERP studies, as the stimuli are the events that elicit the brain activity being measured. The stimuli should be relevant to the research question being studied and should be presented in a controlled and standardized manner. This allows researchers to accurately and consistently compare brain activity across different conditions or groups. One factor is the type of stimuli, which can include visual, auditory, somatosensory, or other types of stimuli depending on the research question and the specific brain activity being studied. It is also important to carefully control for extraneous variables, such as the participant's physical and mental state, and the environment in which the experiment is conducted. One breakthrough for ERP research was by looking at attention in the brain. Attention enables researchers to have the same experimental and control conditions with the only difference being that attention is directed to the object of interest in the experimental condition. This experimental angle enabled researchers to overcome a difficult problem in brain imaging namely finding a good control condition. E.g., if you want to find the areas active when you see a picture of a dog you would have to compare it to something but what would be the best control condition? Is it the picture of a cat or a picture of a house? Presenting stimuli on the left side can be a good contrast to presenting stimuli on the right side, but it can get quite philosophical trying to establish the ideal "undog" as a contrast to a picture of a dog. As ERPs are sensitive to the timing of events, the timing of stimuli presentation and the intervals between stimuli should be carefully defined in the experimental protocol. By following a carefully designed experimental protocol, researchers can obtain reliable and valid results when studying ERPs. In addition to controlling for extraneous variables, it is also important to consider the sample size and sampling method when designing an ERP study. A larger sample size can increase the reliability and generalizability of the results, but it is also important to ensure that the sample is representative of the population being studied.

Practical EEG and Analysis

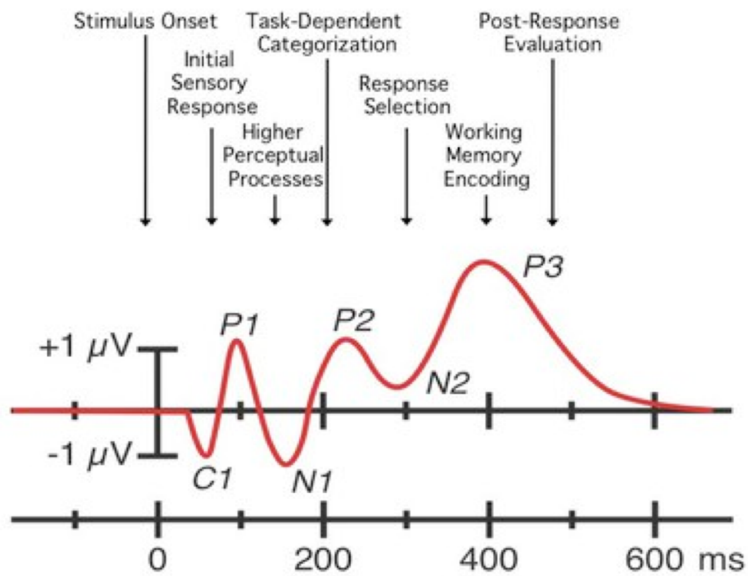
The method of extracting ERPs from a continuous EEG recording involves segmenting each section of interest. This commonly involves including segments 100ms before until 800 ms after stimuli were presented. The exact time interval varies by task and by preference. During preprocessing, baseline correction is applied so that all waveforms are aligned. Then we apply the filters explained in the last chapter (high-pass, low-pass, artifact rejection, eye-blink reduction). These are commonly performed using automated software that have functions for each of these modulations. Despite the software, it is important to be aware of each of the steps and the logic behind them. Finally, we average (epoch) all waveforms to get an average waveform for each electrode and plot them on a topographic map of the head. We do this for every experimental condition separately and compare them. The results enable us to see when and where differences in activation between experimental conditions occur.

What Can We See?

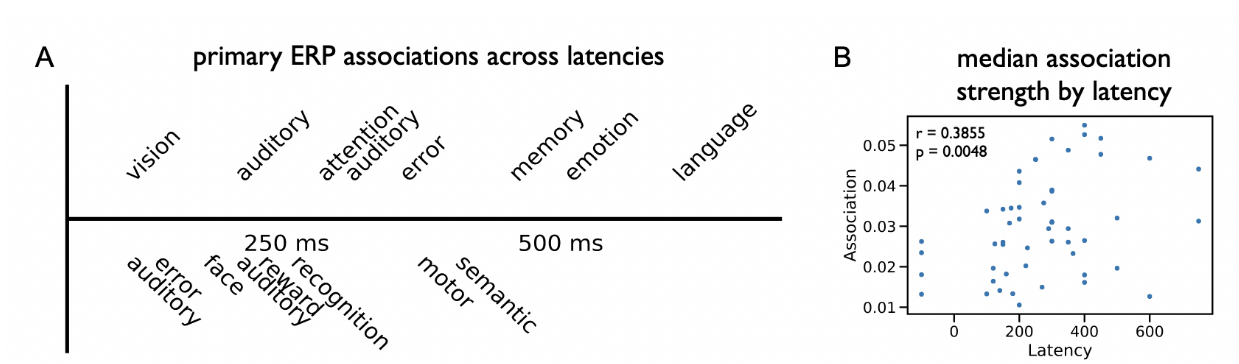
A lot of things happen in the brain in one second. We know the gist of a scene within 150-250 ms. We move our eyes every 200-500 ms. Eye movements include processes such as low-level sensory processing, focus attention, identification, working memory storage, finding the next saccade target and executing eye-movement. That's why the real-time (sub-millisecond) temporal resolution of EEGs is so valuable. The idea with ERPs is that through the averaging of many stimulus-synched segments of recording (below) the averaged signals will remain while the noise will cancel out. The average signals combined amplify the underlying brain activation while the noise averages out somewhere around the baseline. That leaves an average ERP that contains mostly brain signal, but with minor noise. If one wishes, smoothing filters can be applied to reduce some of the remaining noise. However, smoothing filters are mainly cosmetic improving the visuals, but not the underlying data. If you see ERPs that look very smooth (e.g., in textbooks) commonly smoothing and other filters have been applied.



From the ERP averaging, several characteristic potentials appear. If a stimulus was presented at zero milliseconds, we can record brain stem responses already around 20 ms. Early visual, auditory, and tactile ERPs look somewhat similar, but start in different areas of the brain (over visual, auditory, and tactile primary cortices). For visual stimulation, at 50 ms the C1 potential can be observed in electrodes over the visual cortex. While the subsequent potentials are named with a P for positive or an N for negative the C1 can be either positive or negative depending on if the visual stimulus was presented in the upper or lower visual field.. The potentials have a number depending on their order. The P1 is the first negative potential and the N2 is the second negative potential etc. Similarly, The N1 is the first positive potential and the P2 is the second positive potential. They can sometimes be named after their timing such as P100 or P200 since they roughly occur around that time. To further confuse us, some researchers insist on presenting negative potentials upwards, though most do not. The names of the ERPs have stuck as the technique has developed so they are not always exact e.g., the P300 commonly occurs between 350 and 550 ms, though it varies depending on task. There are many potentials depending on which experimental paradigm was applied. The picture below shows what the most common ERPs in a prototypical 600ms waveform commonly look like. In reality, some of these potentials occur strongest over different electrodes e.g., P300 (P3) is frontal and C1 is occipital, so in opposite parts of the cortex.



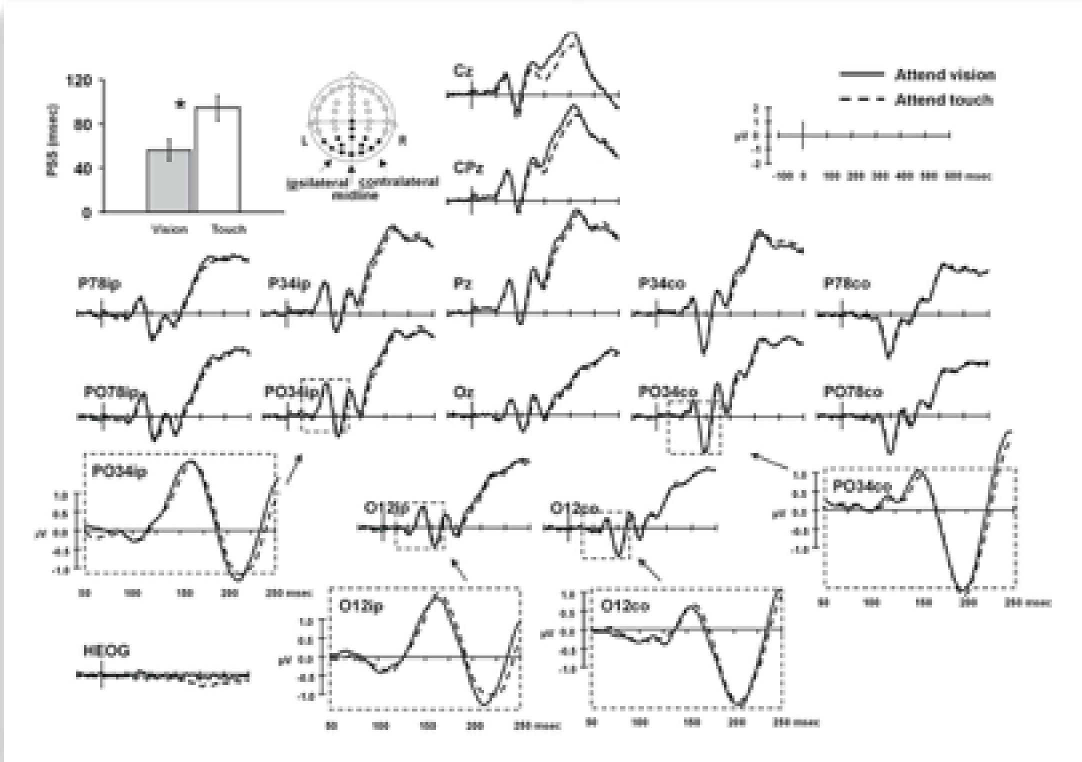
The brain has to perform a set of processes before we can recognize and act on a stimulus. Initially the brain performs lower-level processing followed by attentional focus, identification of a stimulus, remembering it, evaluating it, acting, and finding the next saccade and performing that next eye movement. All these activities happen within half a second. If a stimulus is presented at 0 ms, the gist of a scene is usually processed by the brain by 150-250 ms, spatial localization happens by about 200-300 ms, motor responses happen between 300-500 ms and language is interpreted somewhere around 400-600 ms (see fig xx). However, the order and precise timing of these processes depend on the type of task being performed.



<u>Different ERP components and their origin in the cortex</u>

The C1 potential originates in the primary visual cortex and is positive or negative depending on if the stimulus is presented in the upper or lower visual field. The P1 emanates from the extrastriate cortex and relates to visual feature processing and attention. The N1 potential is from extrastriate and parietal areas, is sensitive to spatial attention and may have several subcomponents. A sharp P2 commonly follows the N1 over anterior and central scalp sites around 150-275 ms. The P2 belongs to the most common peaks because it has high consistency within and between participants. P2 is linked to many tasks including selective attention, stimulus change, feature detection and short-term memory. The N2 component is less reliable than the P2 and varies between individuals (Pekkonen et al 1995). It is evoked by tasks including response orientation, stimulus discrimination, task demands, and target selection. It can include a family of components that differ based on task. For example, for auditory stimuli it occurs over fronto-central areas, while visual stimuli show occipito-parietal activations. The P3 amplitude depends on target probability and categorization. Its latency is tied to the time it takes to evaluate a stimulus. The P300 can contain many components such as P3a and P3b depending on the testing paradigm. Obviously with an approximate 86 billion neurons in the brain many activations can underlay components such as P300 and we gradually refine our understanding of these as the field and techniques evolve. These potentials are commonly seen in experiments, but latencies and amplitudes can vary depending on the testing paradigm.

Some potentials can be completely task specific, so it is important to interpret them within the existing literature. Some of these include the Error Related Negativity (ERN), Contingent Negative Variation (CNV), and the N400. It is not important to know all of the potentials, though you should know the basic ones presented here. It is more important to be familiar with the potentials that are relevant for your line of investigation. For ERPs we need to look at other similar studies and see what they found. We also look at these neuronal processes in light of FMRI work and single cell recordings to get the whole picture of what might be underlying the phenomenon we are investigating. The picture below is from Vibell (2007) and it looks at differences in the visual cortex when we attend to vision or touch. Here we can see that attention to vision and touch while looking at a visual stimulus presented repeatedly produced quite consistent waveforms. However, there are significant differences depending on how attention is directed. This enables us to gain an understanding of where and at what stage our attentional processes influence perceptual processing. It is via minute manipulations such as these that we can gradually paint the picture of how cognition influences brain processing.



Throughout the perceptual processing pathway new variance is introduced. There are 86 billion neurons, and they are very interconnected with an estimated 100 trillion connections. Thus, with stimuli time locked to point zero at each processing step backwards and forward connections can introduce a bit more variance. Once a visual signal has reached the frontal cortex for processing the signal can have quite a bit of variance. That means that intra- and intersubject reliability is greater and your statistics will be less reliable. Therefore, if you see many seasoned researchers test lower-level perceptual functions it may be because they are aiming for more reliable data. They may be just as interested as you and I in the brain differences that make someone a criminal or the brain activation underlying social skills, but have decided to solve the more lower level questions first. That is not to say that more complicated behaviors are not important to investigate, they are, but the statistics will be inherently less reliable making predictions more difficult.

ERPs are especially useful when you want to look at:

- Which area was influenced at what time and brain stage
- What was the onset time of the difference
- Which ERP component was affected by a manipulation
- The interaction between multiple neurocognitive processes
- Multiple ERP effects accompanying behavior
- Covert monitoring of processing

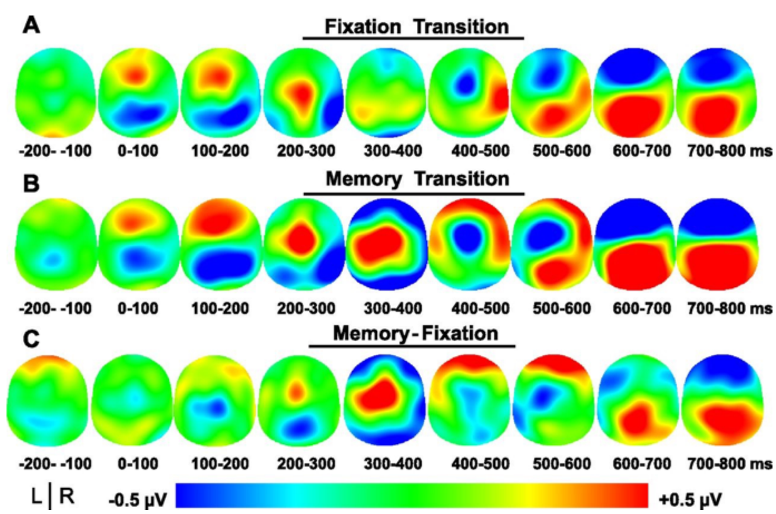
- Processing that can be measured without a behavioral response (or from subjects who cannot easily respond)
- Something that was not evident in behavior

ERPs are not useful when you want to look at:

- The precise neuroanatomical location of an effect
- Activity that is slow (>~2 s) or not time-locked to a sudden, observable event
- Small numbers of trials in each critical condition
- Stimuli with long period of time between trials
- Severe adaptation of response over trials
- Stimuli that startle subjects
- Something where subjects make frequent head, eye, or mouth movements during the time period of interest
- Conditions where participants need to speak (tongue has strong dipole)

Scalp Topographies and Source Analysis

In chapter 3 we talked about scalp topographies for looking at activations from EEG in different wavebands. Scalp topographies can also be applied to ERPs. The results can look something like the topographic map below. The resultant baseline topographies (a) and the experimental ones (b) are subtracted from each other to reveal the areas and timings of the differences in the brain resulting from the experimental manipulation (c). This approach is used to compare many mental processes including cognitive workload, vigilance, fatigue, attention, and memory.



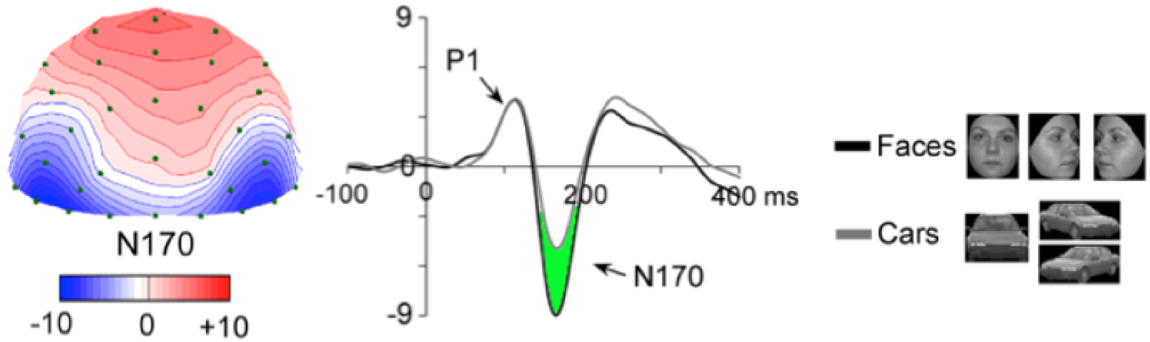
By using the covariance of activations between different electrodes we can gain a deeper understanding of where its source originates. Reasonably, if a source activates two electrodes similarly it should be located underneath both these electrodes. If a third electrode shows partial covariance, we know that this electrode too is above the source, albeit only partially. Via this principle we can apply a technique called independent component analysis to further home in on the source of a signal. Theoretically, an infinite number of sources could create the activations recorded on the surface of the scalp (See inverse problem). Still this technique likely gives us a stronger estimate of the true source of the signal though we must always be aware of any potential bias.

ERP Paradigms and Their Classic Potentials

As we have described above ERP research has to be evaluated within the context of relevant literature. There are many different paradigms and some of them have been explored deeply and widely. The classical paradigms provide a set of consistent activations which will give insight into how the brain works. Follow-up studies have evaluated the impact of many experimental manipulations and how these impact the paradigm specific potentials. It is important to have an understanding of these classical ERPs to understand how to apply the ERP method in novel ways. Some but not all activations transfer between paradigms.

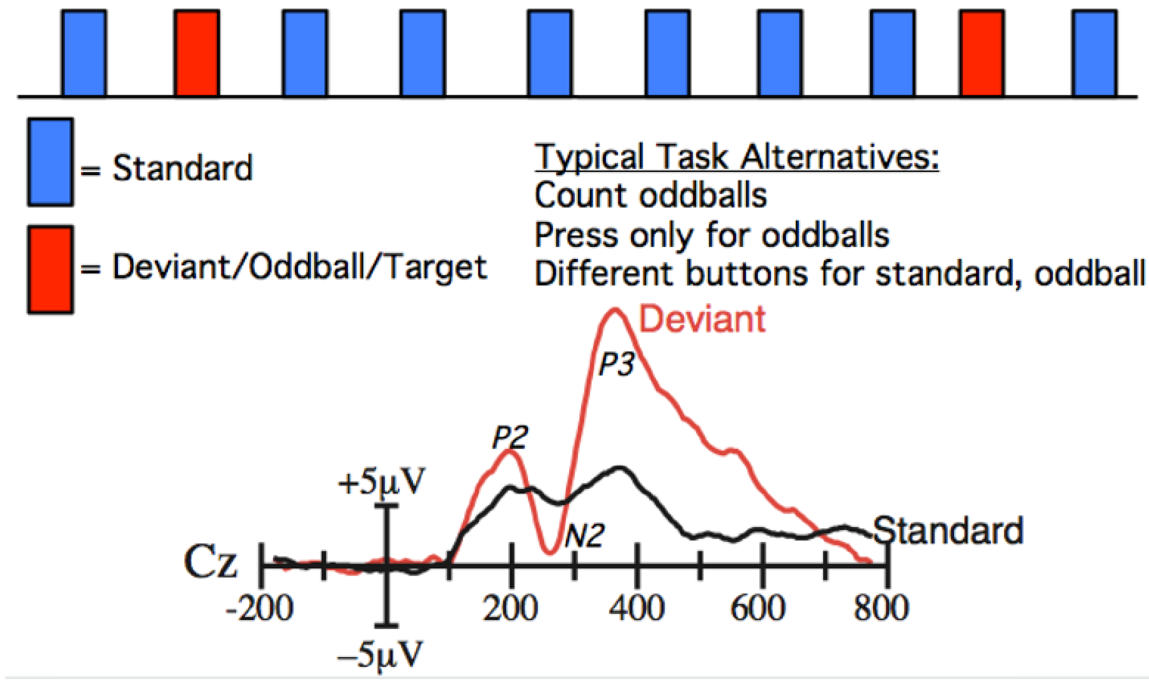
One way that brain activation can be compared is by presenting stimuli and comparing their activation when they are attended and not attended. Attention increases the amplitude of ERP potentials at the stage where the participant attends. The beauty of this approach is that the same attended stimulus can be its own control when attention is directed elsewhere. This can be used as a tool to see how different types of attention can influence different stages of perceptual processing. For example, attending to the shape, location or color of a visual stimulus can modulate different stages of these perceptual or cognitive processes in the brain and give us a good understanding of their place in the processing hierarchy and their specific latencies.

By presenting pictures of faces and comparing them to pictures of cars the ERP activation shows a specific potential (N170) that differs over extrastriate regions. This can lead us to the conclusion that there should be face-specific areas in the cortex somewhere underneath the recorded electrode. Convergent studies using FMRI and single cell recordings have revealed this area to be the fusiform face area. Oftentimes tools such as FMRI and single cell recordings are used in parallel with ERPs to provide convergent evidence of this specific function in the brain.

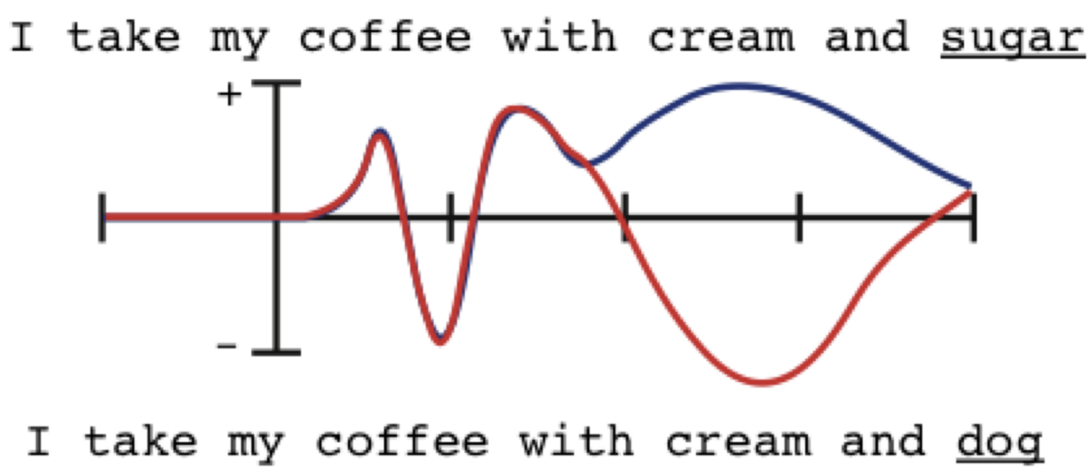


This difference reflects only brain activity that differentiates between faces and cars

One of the most common research paradigms is the oddball paradigm. The brain shows a strong and reliable activation for a rare stimulus presented in a string of more common stimuli. This happens regardless of how the stimulus is presented e.g., sounds, words, or LED lights. By presenting deviant stimuli (oddballs) and comparing them to standard stimuli we commonly see a strong P300 (P3) activation. This effect is usually strongest over fronto-central areas and is one of the most consistent ERP effects. It is applied in many research studies as well as in brain computer interfacing due to its reliability and broad strong activation. For example, it is a well-established diagnostic method for psychiatric disorders (Pfefferbaum, Roth & Ford, 1995). Acute ethanol intake as well as abstinence are also known to impact the P300 (Patrick, Bernat, Malone, Iacono, Krueger & Mcgue, 2006). In schizophrenic patients there is a robust P300 amplitude decrease and an increase in its latency. The P300 has also been linked to other psychiatric disorders such as bipolar disorder, depression, phobia, panic disorder and generalized anxiety disorder (Sur & Sinha, 2009).

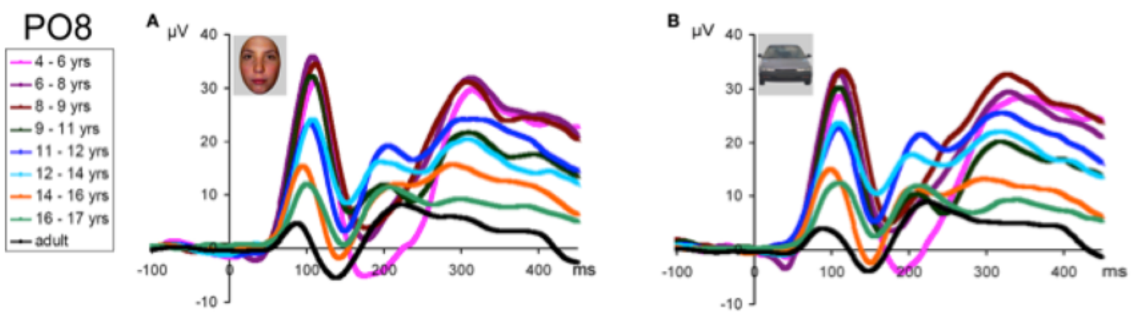


- Typical paradigm: Establish a semantic context and then violate it

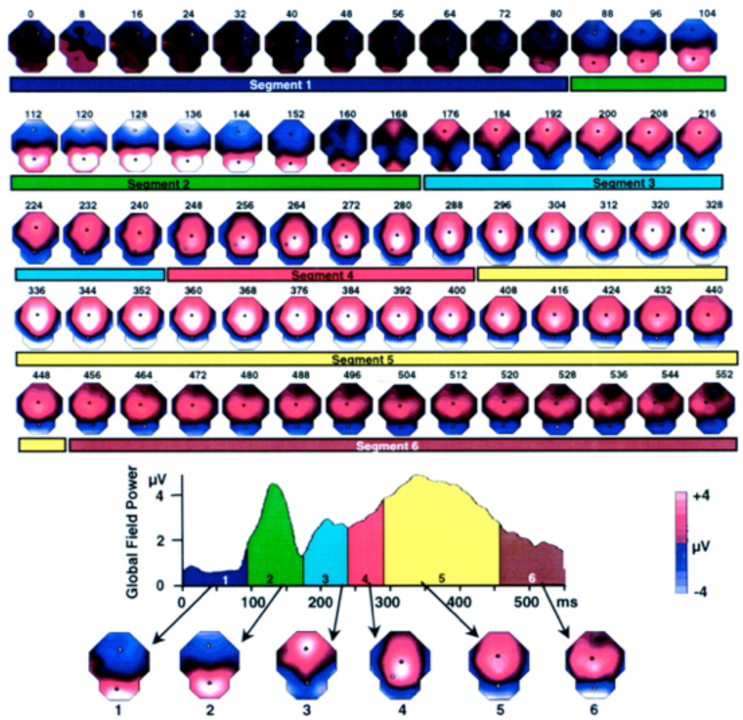


The N400 is a language related potential that is influenced if semantic context is violated. If a sentence is logical such as “I take my coffee with cream and sugar” the N400 is not activated, while a sentence such as “I take my coffee with cream and dog” would significantly impact the N400. The N400 is found over language related areas over left fronto-central regions. Many language-related studies show activations over these electrodes though it depends on which aspects of language we are looking at. Deciphering letters happens at earlier visual processing stages. However, the precise areas of activation by language also depends on how it was presented. If the letters were presented auditorily, auditory processing pathways are activated. Later cognitive processing such as grammar tends to activate e.g., Broca's areas over left fronto-central regions regardless of input method (hearing, touch, or vision). Thus, it is always important to be clear about which processing stages your specific paradigm manipulates and to interpret it in the context of similar studies.

Many factors play a role when processing stimuli in the brain. Age is one such factor. Adults (black lines) show less strong activations when processing faces and cars, while younger kids show increasingly strong potentials. Similar patterns arise for expertise where experts show smaller activations while non-experts show larger peaks and troughs. Thus, results can be somewhat non-intuitive and depend on a myriad of factors such as temperature, time of day, and the location of stimuli. All these factors may or may not impact your study so you need to have a strong understanding of all of the factors that can have an impact on your study and interpret results within the context of them. This emphasizes the importance of a robust research design.



Another way related to ERPs is to look at brain activity using microstates. It assumes that instead of potentials such as P300 the brain activation can be divided into states (below, colored segments numbered 1-6) that represent one processing stage each. It assumes that these states represent different parts of stimulus processing e.g., early perceptual processing, cognitive evaluation, or grammar processing. It is reasonable to assume that the truth of how the brain processes information is more complex than both microstates and ERPs but it is helpful to have several tools in our toolbox to understand something as complex as functional brain networks. Below is an example of a microstate analysis (Brunet, Murray & Michel, 2011). You can see that the analysis automatically separates the brain activation into differently colored sections (bottom) that are all determined to reflect a corresponding brain state. To have the computer decide a set of microstates can sometimes be a less arbitrary way of approaching brain states in cortical processing than to decide which peak is P1 or P2. In the example below we can compare if the six brain states differ if we manipulate an experimental value e.g., if we attend or not.



Summary

ERPs is a powerful method to see brain activity with a close to perfect temporal resolution, but with a relatively poor spatial resolution. It enables us the exact timing and the stages of functional brain activity. This is represented by many potentials which all represent different types of brain activity. Early ERPs are generally more consistent while later ones become increasingly paradigm specific. Thus, ERPs should always be interpreted within their paradigm and while taking existing literature into account. There are several reasons why later ERPs become less consistent. The first one is that the ERPs represent the workings of 86 billion neurons and accordingly we would expect a broad variety of activation both within and between individuals. Secondly, since ERPs are time locked to 0 ms, the further away potentials are the larger their variability will be. Hence, we see that while the earlier potentials are sharper, the later potentials are broader and more elongated. All these aspects are important to understand when evaluating ERPs. Cognizantly applied, ERPs is a powerful tool that will only increase in importance for understanding human brain function.

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Of Interest…

Consciousness has been debated by philosophers for 1000s of years. Recent developments of brain imaging technologies have enabled us to answer some of these questions better than ever before. It has at least enabled us to gain new types of evidence that give us more perspective. Benjamin Libet was a pioneer in the experimental study of consciousness, initiation of action, and free will. Most famously he invented what became known as Libet's clock. Libet's clock is a task that shows that people start to make decisions before they actually decide to do so. It involves looking at a spinning dot on a clock's surface and deciding when to press a button. Several types of results sprung from this task: one measure that showed when participants pressed the button and another measure when they indicated on the spinning clock exactly when they thought that they had decided to press the button. In addition, Libet recorded EEG to observe when this decision arose in the brain. He found profound temporal delays between these recordings which generated much debate about free will. He found an approximately two thousand millisecond delay between the first appearance of motor preparation to press the button and the act of pressing it. By observing the EEG signal he could note that the brain activity actually started several seconds before the other signals. The EEG motor signal would start gradually and ramp up until the decision to act. Some philosophers saw this as a subconscious buildup of electrical activity within the brain while others suggested that consciousness does not have to predate the button press for the activity to be conscious. Instead, the buildup of EEG activity could be part of the process of engaging in a task consciously and that these subconscious processes in the brain are the true initiator of volitional acts.