SUMMARY

We can see, interpret, reason and act. These processes all have their origin in the brain and are dependent on information encoded in neurons. However, we do not know in what language or code information in the brain is present. The question “how can we decode information from the brain?” is one of the big remaining questions in neuroscience. In this dissertation, I try to approach this question from several angles. To do this, I use behavioral experiments, electrophysiology and optogenetics. Electrophysiology is the study of the electrical activity of neurons, while optogenetics is a technique that is used to manipulate electrical activity of tissues. In Chapter 1, I introduce the techniques, concepts and brain regions that I will discuss in subsequent chapters in the search for the language of the brain.

We know that neurons use electrical signals to encode information. Therefore, electrophysiological techniques are essential to understand the code of the brain. Using electrodes, an amplifier and a speaker, the electrical activity of a neuron can be made audible. The first time I heard the spiking of a neuron, I fell in love with this technique, juxtasomal recordings. In Chapter 2, I describe how the technique can be applied to record neurons in living, awake rats. During a juxtasomal recording, a small glass pipette with a microscopically small tip is placed close to the neuronal cell membrane, allowing recording of currents over the neuronal membrane. The awake state of the rat allows us to record spiking during behavior. This means that we can study the encoding of behavior or sensation on single-neuron level. At the end of a recording session, the neuron can be filled with a dye, allowing us to study the relationship between form, function and behavior.

To translate between information in- and outside of the brain, we need to know what information we expect to find in neurons. For that goal, only recording electrical activity of neurons is not sufficient. We also need to form expectations on what information is being encoded in the electrical activity. In sensory brain regions, predictions can be made relatively easily; we expect information on the visual world in visual cortex and we expect touch information in somatosensory cortex. However, for brain regions that do not receive direct input from sensory systems these predictions are a lot more difficult, since information is pre-processed and expected inputs are harder to define. For rats, whiskers are the most important sensory system to navigate the world. We know relatively well how whisker movement and touch is encoded in whisker somatosensory cortex and we know that the posterior parietal cortex (PPC) plays a role during further processing of this information. Until now, we did not know how PPC plays her role in this process. In Chapter 3, I show that PPC neurons encode touch information for rows of whiskers and that these rows have the same order on the cortical surface as on the rat’s snout. Furthermore, I show that the upper and lower PPC neuronal layers encode information on whisker movement and that whisker touch is encoded in the upper layer.
One neuronal encoding scheme is formed by increases of neuronal spiking frequency (the number of spikes per unit of time). It has long been assumed that this is the only or main encoding scheme. In the last 10-15 years, however, it has become clear that in sensory brain regions the time between two spikes can also play an important role for further processing of information. When spikes occur in fast succession, a so-called burst, calcium can flow into the neuron and result in intracellular changes of information encoding. This process is very important when multiple separate information streams need to be combined. In Chapter 4, I therefore study the occurrence of similar processes in neurons of the executive brain regions, mPFC. I show that neurons in layer 2/3 of mPFC need faster bursts than those in layer 5 for intracellular calcium increase. Furthermore, I show that L5 neurons of awake rats generate more bursts than L2/3 neurons.

mPFC plays an important role in attention behavior and we know that mPFC neurons use spiking frequency increases to encode attentional processes. The hypothesis is that each anatomical division of mPFC has its own role during attention behavior. In Chapter 5, I used optogenetics during distinct phases of an attentional task to silence either the dorsal or the ventral mPFC division. I show that vmPFC activity during the end of the attention phase is essential for optimal attention behavior and that silencing vmPFC during this phase leads to reduced accuracy and increased impulsivity. In contrast, silencing dmPFC during this phase does not negatively impact attention behavior. However, silencing dmPFC during the full attention phase disrupts accuracy in the task. Surprisingly, silencing vmPFC during the full attention phase increases accuracy in the attention task. This means that spiking frequency increases of dorsal and ventral mPFC contain distinct information and thus that the language of the brain can differ even within a brain region.

The mPFC is not only involved in attentional processes, but also plays a role in motivation, impulse control and short-term memory. To study the neuronal code for these processes, I developed a behavioral task for rats. During this task, rats are trained to use their whiskers to discriminate the location of a movable pole and lick a sensor to earn a water reward when the pole is close to the face. To link neuronal activity to behavior, I recorded the activity of mPFC neurons while the rat is performing the task. In Chapter 6, I describe neurons that encode the task with increasing or decreasing spiking frequency, as well as neurons that do not seem to be involved. Changes in spiking rate are not only the result of motor output (licking), but also relate to the context, e.g. whether they are linked to (expectation of) reward. This shows that spiking frequency in mPFC encodes context. Furthermore, I show that spiking frequency of a subset of mPFC neurons predict whether the rat will learn from mistakes, showing a code for short-term memory. Finally, I show that low spiking frequencies can lead to mistakes when the task is easy, which I interpret as a code for impulse control.

Research does not exist in a void. Therefore, in Chapter 7, I highlight links between the chapters and I place the results in perspective with existing scientific literature. Furthermore, I formulate expectations about the functioning of cortex and provide some suggestions for future research.