Inferring human intentions from the brain data

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Summary

The human brain is a massively complex organ composed of approximately a hundred billion densely interconnected, interacting neural cells. The neurons are not wired randomly - instead, they are organized in local functional assemblies. It is believed that the complex patterns of dynamic electric discharges across the neural tissue are responsible for emergence of high cognitive function, conscious perception and voluntary action. The brain's capacity to exercise free will, or internally generated free choice, has long been investigated by philosophers, psychologists and neuroscientists. Rather than assuming a causal power of conscious will, the neuroscience of volition is based on the premise that "mental states rest on brain processes", and hence by measuring spatial and temporal correlates of volition in carefully controlled experiments we can infer about their underlying mind processes, including concepts as intriguing as "free will", "agency" and "consciousness". Recent developments in electrophysiology and neuroimaging methods allow for increasingly more accurate estimation of spatial and temporal characteristics of decision processes.

The work presented in this thesis is intended to contribute to our understanding of the dynamics of voluntary decision processes about prospective action. In the two presented studies we probe different types of decisions and compare them in terms of behavioral and EEG characteristics. We show that decision processes are manifested by complex, broadband modulation of brain oscillatory patterns, primarily in Alpha(8-12Hz) and Beta (16-30Hz) ranges. Our results suggest that decisions about whether to act or not, what type of action to perform, and about the timing of the action have distinct dynamic representations, and thus are to some extent mediated by different neural components. Furthermore, free action can be partially explained by low level behavioral preferences, especially

in contexts where no explicit incentive favors one action over an other.

Apart from the investigation of volition, considerable part of the work presented in this thesis is dedicated to experiment design methodology and efficient EEG processing methods. We have developed a dedicated, flexible Virtual Reality Environment (VRE) platform, suitable for investigation of volition and action preparation processes with range of modalities, including electroencephalography (EEG), functional magnetic resonance (fMRI), eye-tracking (ET) and behavioral measures. By providing ecologically valid, semi-realistic experience we aimed at reinforcing the natural decision processes and minimize the problem of random-sequence generation and fatigue in participants undergoing highly repeatable cognitive experiments. Other methodological contributions presented in the thesis are related to efficient, automatized and highly data-preserving methods for processing of EEG data, based on minimal number of arbitrarily selected parameters.

Preface

This thesis was prepared at Department of Applied Mathematics and Computer Science, Technical University of Denmark (DTU Compute) and partly at Danish Research Centre for Magnetic Resonance, Copenhagen University Hospital (DRCMR) in fulfillment of the requirements for acquiring a Ph.D. degree in Engineering. The project was partly funded by Lundbeck Foundation research grant provided to Hartwig R. Siebner (DRCMR) and partly by DTU compute. My principal supervisor was Professor Ole Winther from DTU Compute. My co-supervisors were Professor Hartwig R. Siebner from DRCMR and Professor Lars Kai Hansen from DTU Compute.
The thesis treats about brain and its capacity to exercise voluntary action. In series of experiments involving Electroencephalography (EEG) and Virtual Environment (VR) we investigate electrical signatures and behavioral correlates of human free action.
The thesis consists of summary report, including detailed chapters on methodology and literature review, and collection of three journal papers (in preparation for submission).

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Konrad Stanek

Publication List

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This work could not have been done, not even started, without Professor Hartwig R. Siebner, head of research in Danish Research Center for Magnetic Resonance (DRCMR). His determination, versatility and encyclopedic knowledge of brain physiology and anatomy were indispensable. Thanks to his scientific curiosity of the brain function, combined with myriads of research initiatives, I got a chance to embark on this challenging journey through stormy waters of neuroscience of free-will, the experience both utmost challenging and unforgettable.

I bow my head to Professor Lars Kai Hansen for his extraordinary open-mindedness and scientific insights. I value highly every motivating conversation we had about brain, cognition and future of neuroscience. Importantly, it is largely due to his efforts that the fruitful collaboration between DTU and DRCMR was established.

Most of the design principles, experimental ideas and efforts throughout this project I shared with my invaluable colleague and friend Steffen Angstmann. We went together through good and bad, easy and hard, discouraging and delightful. I awe you a lot, Steffen.

I learned so much from Leo Tomasevic, it was a true pleasure to discuss with him pecularities of electrophysiology and future of electroencephalography. There are hardly any topics within this domain which we haven't discuss at least once - thank you for sharing the "EEG-geekiness", Leo.

A lot of problems that I encountered on the way were resolved with the great help of Kristoffer Madsen, probably "the most wanted" scientist in DRCMR. His experience and willingness to share his rich knowledge are truly unique.

Last but not least - I could not be more happy for all those fantastic People around me in the last years, who kept me going, even when I doubted - Jocelin, Sankhya, Martin, Silvia, Stig, Marta, Mario... there are more names. Thank you Friends for your patience, support, and love.

Abbreviations and Acronyms

α, β, γ Alpha, Beta, Gamma band respectively

CFC Cross-Frequency Coupling

CNV Contingent Negativity Variation

FFT Fast-Fourier Transform

EEG ElectroEncephalography

MEG MagnetoEncephalography

ECoG ElectroCorticography

EMG ElectroMyography

EOG ElectroOculography

EPSP Excitatory Post-Synaptic Potential

ERD Event Related Desynchronization

ERP Event Related Potential

ERS Event Related Synchronization

ERSP Event Related Spectral Perturbation

IPSP Inhibitory Post-Synaptic Potential

LERD Lateralized Event Related Desynchronization

LRP Lateralized Readiness Potential

MR Magnetic Resonance

MRI Magnetic Resonance Imaging

NIBS Non-Invasive Brain Stimulation

fMRI functional Magnetic Resonance Imaging

sMRI structural Magnetic Resonance Imaging

PAC Phase-Amplitude Coupling

PET Positron Emission Tomography

PFC Prefrontal Cortex

dlPFC Dorsolateral Prefrontal Cortex

PMC Primary Motor Cortex

RCZ Rostral Cingulate Zone

RP Readiness Potential

S1 The first stimulus (warning Precue) in delayed response Go/Nogo tasks

S2 The second stimulus (imperative Cue) in delayed response Go/Nogo tasks

SMA Supplementary Motor Area

preSMA Presupplementary Motor Area

SPM Statistical Parametric Mapping

TF Time-Frequency

TMS Transcranial Magnetic Stimulation

VR Virtual Reality Environment (in context of this thesis, the acronym "VR" will refer to our specific design, unless stated differently)

WWW What-When-Whether model of voluntary action

Contents

Chapter 1

Introduction

The following thesis will discuss the brain and its function. Although the word "fascinating" has limited usage in science, yet it is exactly the word that comes to mind when reflecting upon the immensely complex machinery of human brain, composed of 100.000.000.000 densely interconnected, interacting and constantly adapting neural cells. Those cells have different morphological structure (Fig.1.1), and are not wired randomly - instead, they are organized in local functional assemblies. The brain is a rather compact organ of jelly-consistency, composed of two symmetric hemispheres of a mango fruit size. And yet it is responsible for every conscious thought and feeling we experience. Every smell or taste, vivid colorful memory, feeling of affection or paralyzing fear, sensation of gentle breeze, or a pleasing view of a rainbow - all those qualities exist nowhere else but inside the complex circuitry of the brain, or rather, within myriads of intricate patterns of dynamic electric discharges across the neural tissue.

Considering that brain constitutes the seat of mind, medium for thinking, and the matter of any conscious experience, it is notable how self-aware, self-fascinated and self-curious the brain is about its own structure and function. And even more - its ability to self-reflect. One of the most puzzling properties of the brain is a capacity to exercise a voluntary action - to freely choose between alternatives and act according to its own "will". The problem of volition and free will has been troubling philosophers for centuries, and neuroscientists for decades. What does it mean "to intend"? Does the free-will exist or is it

simply a retrospective illusion created by brain in order to justify unconsciously determined actions and create the feeling of agency? In either case, where is the "will" circuitry located in the brain, and how is it manifested by brain dynamic oscillations?

Neither neuroscience nor neurophilosophy have provided the final answers to the "hard problem" of free will. Neither is it a purpose of this thesis. Instead, we post a range of related, more pragmatic questions. How can voluntary action be characterized by brain oscillatory activity? Can it be measured with non-invasive methods, and if so - can it be predicted? Can decision processes be disentangled from other related cognitive processes, such as attention, memory, mental imagery? Or perhaps those subprocesses constitute integral part of deciding what to do, when to do it, and whether to do it or not? With this thesis, we try to contribute to the growing domain of studies conducted in attempt to pursue the answers to those questions.

The recent developments in non-invasive neuroimaging technologies and advanced data processing enable us to revisit some of those important problems and bring us a step closer towards understanding of brain function. Through the lenses of electroencephalography (EEG) and magnetic resonance imaging (MRI), we can "zoom into" the physiological and morphological structure of the brain, and importantly, observe and appreciate its complex, non-linear, dynamic behavior. Carefully designed experimental paradigms allow us to associate behavioral measures with their corresponding electrophysiological responses, and thus learn about oscillatory nature of the brain, its functional connectivity, and precise timing of cognitive processes. By coregistering those dynamic data with structural magnetic resonance images (sMRI), segmenting out layers of skull, white and gray matter of the cortex, and modeling electromagnetic fields we can infer about spatial localization of those processes. Combining these information allows us to investigate the nature of voluntary actions and decisions in terms of their spatio-temporal characteristics and plausible pathways of information flow. Since those processes can be partially explained by, or at least related to, other cognitive processes, it is essential to evaluate the results in light of the existing literature on brain oscillations, decision making, attention and motor planning.

1.1 Brain in numbers

A brain of typical adult human weights $1.3 - 1.4kg$, corresponding to approximately 2% of body weight, yet it consumes up to 20% of total energy intake. It is composed of 100 billion neurons, and approximately the same number of

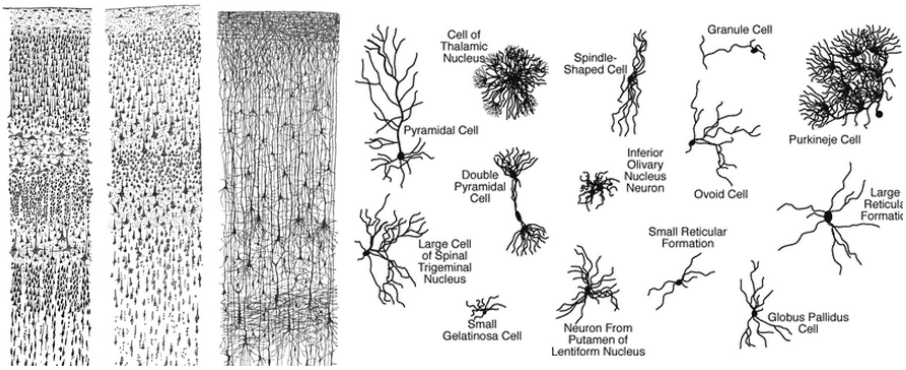

Figure 1.1: The neurons in the cortex are aligned in distinct layers. Axonal projections of pyramidal cells tend to extend perpendicular to the cortical sheath (left). Morphology of neurons differs largely - their size, shape end extension of dendritic tree depend on cell function and location in the brain (right). The drawings are adapted from pioneering works of Santiago Ramon y Cajal, Nobel price laureate and father of modern neuroscience [18].

supportive glial cells. Nearly 25% of the neurons are concentrated within thin folded sheath surrounding inner structures, the neocortex, where most of the sensorimotor function and higher cognition resides. The surface of the cortex is estimated to $2.500cm^2$ while the thickness is only $1.5-4mm$. The brain is organized into two largely independent hemispheres, interconnected by dense bunch of 250 million fibers (corpus callosum). The brain is highly plastic and constantly reconfiguring its wiring. The number of synaptic connections between neurons is estimated to 10^{14}. Also the number of functionally intact neurons is rapidly changing throughout the life span. Starting with growth of 250.000 neurons/minute in early embryonic development, the number of neurons stabilizes in the early childhood and decays through adulthood with average of 85.000 cells per day. A basic computational unit of a brain is a neuron, a cell weighing 10^{-6} gram and measuring less than 100 microns in diameter (Fig.1.1). An active membrane allows it to propagate signals, action potential, along its long axons with speed up to 120 meters/second. Neurons perform their computations by "weighing" the excitatory and inhibitory inputs received primarily through synaptic connections. Typically, each cell has 1000-10.000 synapses.

1.2 Brain, mind and volition

The problem of brain-mind dualism is one of the most persistent mysteries in human sciences. It is not trivial, perhaps not even feasible, to explain the relation between the subjective, consistent perception of "self" and the complex chain

of biochemical interactions representing it. Historically, Descartes assumed that the interface between mind and brain lies within pineal gland - a unique, tiny structure in the brain which is not bilaterally symmetrical but positioned right in the middle. Human intentions would thus originate in the "matter of soul", and through pineal gland effectuate chain of biological processes leading to bodily action. Nowadays the general consensus in science is that consciousness and volition are indeed the emergent products of complex biochemical and electrical processes within the brain matter. This approach does not invalidate the concept of "free will" and volition, however it affects the way it should be defined, understood, and scientifically investigated.

Within such framework, voluntary action can be understood as an informed, intelligent response to current sensory representation of environmental context. The response is an outcome of a balanced weighing between the predictable patterns derived from past experience and the evolutionary need for unknown exploratory behavior. The experience of volition, or commonsensical "free will" could be then explained as a unique ability to perceive and appreciate these preparatory brain processes and the selection between alternative options, which must precede any physical or mental action. In this sense, experience of volition would be closely link to introspective attention. Some theories go further suggesting that the "free-will" is a retrospective perception of a consistency between a forethought and the sensory feedback. In that sense, the role of "free will" would be a reflective narration, or confabulation, in order to causally bind the events in the stream of consciousness and hence make sense of the dynamic complexity of the environment.

Important implication of rejection of dualistic explanation of "free will", is that although it might be tempting to pursue the true origin of voluntary action, such as particular neuron or neural group, it is conceptually not feasible. The problem would be comparable to determining a single water molecule that initiates a massive oceanic wave. Brain activity is expressed through complex, multi-scale, recurrent neuronal interactions, where every action potential or synaptic current has its own cause. It is within those interacting loops where the evidence for voluntary action gradually accumulates, at certain point reaching the levels sufficient for the conscious perception of volition to emerge. Activation of those loops can be detected, observed and quantified with neuroimaging methods and electroencephalography, just as an oceanic wave can be measured with buoys or satellite images.

The neurophilosophy of volition is a vast and exciting domain. However it lies far beyond the scope of this thesis. For extensive overview of topics related to volition and free will, combining insights from neurophilosophy and neuroscience, the reader is encouraged to the books of Baer et al [8] and Nadel et al [112], as well as review articles [45, 47, 136] tackling the current state-of-art in

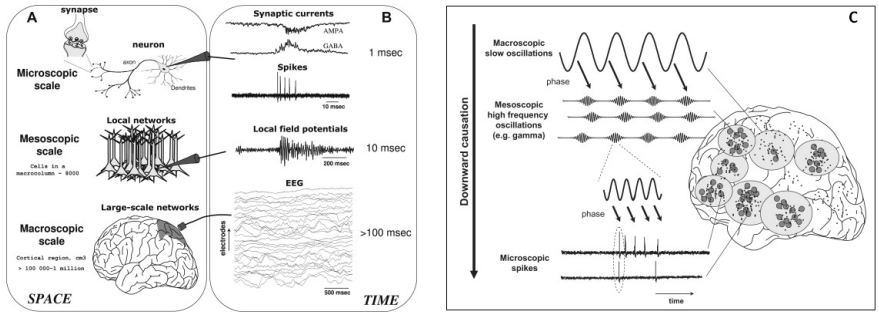

Figure 1.2: The brain circuitry has a multi-level architecture spanning over multiple spatial (A) and temporal (B) scales. Different recording modalities, such intracellular recordings, local field potentials or EEG can capture the dynamics on each scale. Typically, an EEG electrode records from scalp area of a square centimeter, including up to a million of underlying neural cells. This reflects synchronous post-synaptic activity in hundreds of cortical columns. (C) Hierarchical organization of brain communication. Processes on different scales causally influence each other. Macroscopic networks oscillate with lower frequencies and their phase can influence power of the more focal, fast oscillations. This process that can contribute to functional binding of distributed neural assemblies and support large scale information integration. (figure adapted from Le Van Quyen [78], with permission from Elsevier)

empirical approaches to neuroscientific study of "free will".

1.3 EEG and brain dynamics

The main medium for communication in the brain is a minuscule electrical signal, an action potential (or spike), propagated by neural cells across active membranes of their axons. Upon reaching synaptic junction, action potential will cause neurotransmitter to be released and transmitted to the receptors on the dendritic tree of the post-synaptic neuron. This will cause a flow of ionic currents through the membrane and if the summed dendritic currents exceed certain threshold, a new action potential will be generated at the post-synaptic neuron. By this mechanism information can be transmitted through neural networks and thousands of neurons are organized into local, functional, synchronously oscillating assemblies. Those assemblies can be selectively recruited into larger distributed cortical networks responsible for cognition, perception and sensorimotor function. The cerebral cortex has a complex, multi-scale organization, where each level operates with distinct spatial and temporal constraints. The electroencephalography (EEG) is a convenient technique operating on the most macroscopic level, capturing coordinated simultaneous activity of millions of neural cells (Fig.1.2).

EEG is a noninvasive technology to record fast changes of electric activity in the brain with surface electrodes. The oscillations are measured as a potential difference between pairs of electrodes. Most of the current EEG systems contain between 32 and 256 electrodes covering entire scalp, usually one or two of them are designated as reference channels. Different methods are used to improve the interface (reduce resistance) between skin and electrodes, with gel-based passive/active systems being the most popular in laboratory setting.

The neural cells in the cortex are not placed randomly, but have horizontal (layers I-VI) and vertical (cortical columns) organization. Scalp recorded EEG signals reflect primarily the summed excitatory (EPSP) and inhibitory (IPSP) post-synaptic potentials at vertically aligned dendritic trees of pyramidal cells of layer V. When a neural assembly is jointly recruited to a functional task, the coherence of EPSP/IPSP patterns increases locally, sometimes to the levels sufficient to be detected by surface EEG sensors. The second important component of EEG signal originates from macroscopic, summed ionic currents flowing from neural source to EEG sensors through brain tissue, the phenomenon known as volume conduction. The vast part of information contents of brain electric activity never reaches the surface, due to partial cancellation of local signals and due to attenuation of signals on brain-skull-electrode interfaces. Notably, the amplitudes recorded by EEG do not exceed $50\mu V$, which is 3 orders of magnitude lower than neuronal membrane potential ($70mV$).

For successful application of EEG methodology in neuroscientific research, it is important to appreciate its relative strengths and limitations. The strongest limitation is a poor spatial resolution. As discussed above, each EEG electrode covers the cortical area of 1cm^2 corresponding to approximately a million of neural cells. Considering however the volume conduction of electric fields through biological tissue, each electrode captures in fact an overlapping activity from multiple distal sources, amounting jointly for hundreds of millions of functionally-organized cells. Furthermore, EEG represents a two-dimensional surface projection of brain oscillations, which emerged in complex three-dimensional brain structure. This poses further challenges (inverse problem) on disentangling the superficial and deep sources of activity, and thus reconstructing the original source. Finally, the changes of conductivity between cortex, cerebrospinal fluid (CSF), skull, skin and electrodes, which are subject specific, also contribute to spatial blurring and mixing of the signals recorded by neighboring electrodes.

Some of those shortcomings are however circumvented by the fundamental advantage of EEG - its high temporal resolution. Typically signals are recorded with sampling rates 512Hz-5kHz, and can reliably resolve brain oscillations in ranges 0.01-100Hz (higher frequencies are attenuated due to volume conduction problem). High temporal precision, combined with high-density electrode montage covering entire skull, can be thus used to extract some spatial information.

Subtle, time-sensitive modulation of instantaneous phase and amplitude distribution over scalp can be used to infer about connectivity and directionality of information flow in the brain. Combined with structural information from magnetic resonance and conductivity modeling, multi-channel temporal signals can be used to reconstruct the estimated true sources.

Furthermore, in many scientific and clinical applications of EEG, the spatial location of the effect is not the main priority. Sometimes, the location estimate is known from other modalities, such as fMRI. Scientists and clinicians are then interested in temporal characteristics of the signal - when the effect of interest emerges and how long it lasts, what is its oscillatory nature, can it be predicted, and can it be affected by sensory, experimental manipulation. EEG is indispensable for tackling this kind of problems. It is completely non-invasive and thus not restricted to animal studies or clinical patient studies (ECoG, LFP). It is much faster than magnetic resonance imaging (MRI) and thus provides complementary temporal information. Although slightly less sensitive than MEG, EEG is considerably cheaper, and can be used both in laboratory setting as well as outside.

1.4 MRI and brain structure

Structural magnetic resonance imaging (sMRI) a common modality in neuroscience and clinics to obtained detailed images of inner structure of brain and body. MRI uses a sequences of powerful magnetic pulses (over 10.000 times stronger than Earth magnetic field) to realign and perturb hydrogen nuclei of water molecules, present in different densities in different types of tissue. Upon returning to their "low energy" state, the nuclei release energy, which is measured by receiver coils. The relaxation time is however dependent on the type of tissue (gray matter, white matter, skull, etc). This information is used by advanced signal processing methods to reconstruct a precise 3D structure of the inner brain tissue. Modulation of parameters of the sequence of pulses will determine the types of tissue to be enhanced and suppressed on the resulting images. MRI can reconstruct spatial shape of gray matter (cell bodies), white matter (fibers, axons), cerebrospinal fluid and skull, with precision of approximately $1mm$. Such images are often used for clinical assessment of volumetric abnormalities and diagnosis of diseases. In context of EEG, structural MR images can be further processed to extract precise 3D head models (forward modeling) and reconstruct spatial sources of fast encephalographic signals (inverse modeling).

1.5 Virtual Environments in neuroscience

The vast majority of neuroscientific studies are based on very simple visual or auditory stimuli, usually presented in forms of pictograms, simple animations, or sequences of beeps. Obviously, such simplification facilitates strict experimental control and helps to isolate the task-relevant brain activity. On the other hand, in the natural environment humans are constantly exposed to rich multisensory stimulation. Phenomena such as attentional selection, task switching and social context may profoundly influence the information flow in the brain. While performing neuroscientific experiments in natural environment is complicated (events and context can not be precisely manipulated) or even not feasible (most of the imaging techniques require large and non-portable recording apparatus, i.e. fMRI, MEG), the virtual environments constitute a promising alternative. Virtual environments can ensure exact control of experimental condition, sequence, randomization and stimuli type and timing, while at the same time providing more natural, ecologically valid experience to participants. Although posing some challenges on data analysis and interpretation of potential findings, the obtained results might be more generalizable to real-life scenarios and thus help better to understand human brain processes outside the laboratory environment.

However, virtual environments seem to be strongly underrated in cognitive neuroscience and neuroimaging research. Out of 92.000 of published studies employing EEG and fMRI, only 230 involved virtual environment (0.25%), and those usually refer to specific applications only, primarily within the field of brain-computer interfacing (BCI). Some interesting examples are related to control of a wheelchair on simulated streets by tetraplegic patients [80], simulated walking [128] and control of virtual car [170], assessment of driver cognitive performance [86], perception of "spatial presence" [68], and oscillations during maze navigation [61].

A considerable part of this thesis is dedicated to design of specialized Virtual Environment (VR) for neuroscientific studies. Motivation, design considerations, and application of VR to experimental studies of voluntary action will be discussed in further Chapters.

1.6 Objectives of the thesis

The main purpose of this thesis is to investigate the nature of human voluntary action. By applying range of analytical methods to high-resolution multi-

channel EEG data acquired in carefully design experiments, we intend to describe the EEG signatures and the role of known neurophysiological oscillations (theta, alpha, gamma) in voluntary action. In particular, we pursue differences in electrical responses in respect to different types of decisions, such as "whether" to perform an action or not, "what" kind of action to perform, and "when" to perform an action.

Second goal of this thesis was to design and construct enhanced experimental platform for cognitive studies based on Virtual Environment. By doing so, we intended to increase ecologic validity of the experiments, enhance natural decision taking processes, while maintaining rigorous experimental control over the timing and the nature of experiment. The platform has been used in range of voluntary action experiments involving EEG, fMRI, Eye-tracking and behavioral data acquisition, some of which will be discussed in the following Chapters.

1.7 Structure of the thesis

This Introduction (**Chapter 1**) is followed by a comprehensive literature review (**Chapter 2**), elaborating on several domains of neuroscience relevant to the work presented later, in particular the studies of volition and motor preparation, insights into functional role of brain oscillations and EEG methodologies relevant to studies of higher cognitive function. Afterwards, **Chapter 3** focuses on the methodology, including devices and apparatus, software, experimental designs, and data analysis. The two main studies of voluntary decision which constitute the fundamental part of this thesis are summarized in **Chapters 4 and 5**, while **Appendix A and B** contain respective journal manuscripts (in preparation). **Chapter 6** discusses in detail the design and motivation for our Virtual Environment and summarizes the jornal manuscript attached in **Appendix C**. The final **Chapter 7** concludes and summarizes the thesis and presents our further research pursuits. **Appendix D** describes in detail the automatized EEG data processing toolbox that was developed during the work on this thesis. Case studies and application to our datasets will be discussed, which highlights important aspects of early processing of EEG data. **Appendix E** summarizes the conference contributions.

Chapter 2

Literature review

In the following, I shall review the literature related to the subject of the thesis. In particular I will present the scientific approaches to tackle the problem of volition with different brain imaging methods and discuss the studies investigating neuroanatomical sources of free action. However the main focus will remain around the temporal and spectral correlates of voluntary processes in terms of brain oscillations, which are the most relevant for the work presented in the further chapters.

2.1 Neuroscience and free will

The problem of volition and free-will have been troubling philosophers for centuries and neuroscientists for decades. And as the problem remains unsolved, the developments in neuroimaging and electrophysiology enables us to identify certain types of electrical responses and particular anatomical areas in the brain which correlate with voluntary decisions. These findings cast more light on the complex nature of volition, and allow us to construct more precise theoretical models. The models can support our understanding of certain aspects of volition and decision taking, such as temporal constraints, role of conscious awareness, predictability of outcome, preferential biases, differences between internally generated versus externally triggered actions. Probably the most

widespread premise for the neuroscience of volition is that the "mental states rest on brain processes", and hence by analysis of controlled experimental brain data we can learn about their underlying mind processes, including concepts as intriguing as "free will", "agency" and "consciousness".

There have been many attempts of address the problem of volition with use of EEG, functional magnetic resonance (fMRI) and noninvasibe brain stimulation (NIBS) methods, such as transcranial magnetic stimulation (TMS). It should be also stated here that many (if not majority) of the studies do not attempt to directly tackle the "hard problem" of free-will, but instead try to find and describe the functional and electrophysiological correlates of voluntary decisions and internally driven actions. It is important to bear in mind that those correlates may account for entire chain of causally related processes involved in, or related to, voluntary decisions [45] and thus may capture more than mere, isolated act of "free choice". It is reasonable to assume that certain processes may constitute an integral part of the rather widely understood notion of "intention formation", for example the processes like: self-monitoring and introspective attention to action selection [74, 76], knowledge-system access and memory processes [56, 64] related to options evaluation, or processes of forward modeling and sensory prediction [105]. One could also argue, and this is generally the stand I take throughout this thesis, that attempts to isolate neural substrate of volition from other essential mental processes (such as introspective attention to the process of exercising free-will) would be, even conceptually, inappropriate. Investigating volition should therefore focus on observing causal chains of relevant neural processes, characterized by specific brain circuitry and electrophysiological characteristics (i.e. oscillations).

In general, there are several different approaches to probe volition. The majority of studies focus on voluntarily initiated, free-paced movements, where participants decide on timing (and sometimes the type of action). Other studies focus on voluntary selection of actions or goals, usually a free choice between two movement alternatives. In order to relate the physiological responses to mental states, some studies rely additionally on the participant's subjective reports, such as the perceived time and the intensity of the "urge" to move.

2.1.1 Models of volition

Important contributions, and the current state-of-art on the intersection between decision neuroscience, psychology and philosophy, come from the theoretical and empirical works of Brass and Haggard [13, 45], who proposed a model of voluntary action (WWW-model) composed of three fundamental decisions: "Whether" to commit to an action, "When" to initiate an action (action tim-

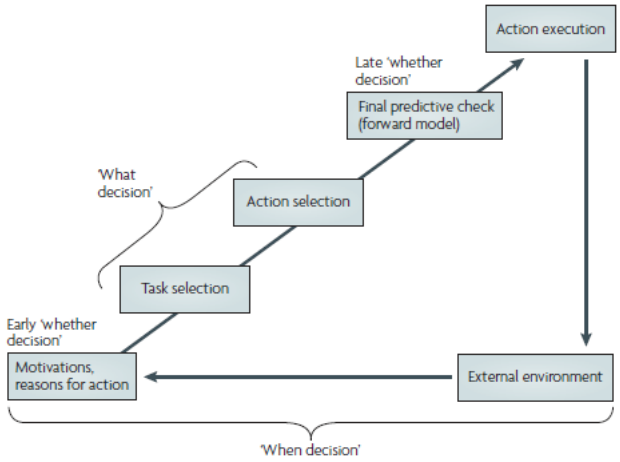

Figure 2.1: Fundamental components of volition: decisions "whether" to commit to an action, "when" to initiate an action (action timing), and "what" type of action to perform (action/goal selection). Reproduced, with permission, from Haggard et al [45].

ing), and "What" type of action to perform (action/goal selection), see Fig.2.1. The "whether" decision can be further divided into early and late components [72], the former to decide whether to engage in action, while the latter reflecting final predictive check or ability to inhibit preprepared action. Kuhn at al [72] in fMRI focused on "late whether", and suggested that intentional non-action is a mode of action and recruits similar neural resources as intentional action, and thus "early whether" component can be closely related or equivalent to "what" decision. For detailed presentation of the model and in-depth discussion in context of volition and free will, the reader is encouraged to read the extensive review [45].

The validity of WWW-model is supported by a line of evidence from fMRI studies, showing that different components of voluntary decisions recruit partially distinct neuronal networks [13, 49, 72, 141]. The pre-SMA and bilateral dorsal premotor areas are selectively active in action selection ($What$) while the timing adjustment ($When$) is mediated by network consisting of superior pre-SMA, insula, putamen and cerebellum. On the other hand, some other areas are common to both types of decisions, i.e. dorsolateral prefrontal cortex (DLPFC) and intraparietal sulcus (IPS). The $Whether$ type of decision is mediated by areas of the dorso-medio-frontal cortex (dFMC) and rostral cingulate zone (RCZ), located more anterior than pre-SMA [13, 72].

The Whether/What/When model (WWW-model) was an inspiration for the second of the two studies presented in this thesis (Chapter 5), while the first

study (Chapter 4) focuses on Whether-type of decision, i.e. internal choice between acting or withholding the action.

2.1.2 Electrophysiology of volition

The pioneering work in the field of neuroscience of volition can be attributed to Benjamin Libet, who in his famous "Libet's clock" studies [85] showed that the electrical cortical activity (readiness potential, RP) precedes not only the initiation of voluntary action, but also the subjective feeling of "will" to initiate the action, by as much as 350ms on average. Those results casted doubt on whether the voluntary action is initiated consciously, or rather prepared by brain circuitry before the conscious awareness is informed. In other words, the study presented first empirical challenge to the notion of "free-will" in its common sense. Libet proposed an alternative explanation, namely, that "free-will" can be manifested through "free won't", i.e. the ability to consciously and voluntarily veto the unconsciously initiated choice, and thus abandon the implementation of related motor program before the execution [84]. Libet's experiments inspired a lot of follow-up studies, which elaborated on the original findings. For instance, [46] showed that lateralized readiness potentials (LRP) precede awareness of directionality in free choice between left and right index finger. Recent study using Libet's paradigm and involving single-cell recordings from patients undergoing epileptic surgery, showed that firing patterns of as little as 256 neurons from preSMA area is sufficient to predict the intention to move, up to 1 second before the "urge" is reported by patients [36]. The interpretation of Libet's results in context of volition and free-will was repeatedly addressed by attacks of skepticism [8, 58, 112]. First of all, estimation of exact timing might be unreliable and dependent on participants attentional split between the internal decision processes and the clock face they needed to observe in order to report the timing. Secondly, it was speculated that the recorded data, in particular RP deflection, could represent the combined cognitive processes related to obeying and fulfilling the experiment instructions, while the true act of volition could have happened only at the moment when participants agreed to participate in the study. There is also a larger empirical study that failed to observe correlations between onsets of either RP or LRP to the reported time of "will", and thus claimed that RP and LRP represent processes independent of will and consciousness [144]. Another study [138], although not directly confronting Libet's claims, has shown that magnitude of RP deflection depended on participant's prior belief in the notion of "free-will". This suggests that RP, at least partially, reflects other cognitive processes such as attention, performance-monitoring, or commitment to the task.

Slow potentials proved to be a valuable method to investigate free-paced vol-

untary action, however not a unique one. Brain oscillations have been shown to play a central role in cognitive function of the brain, in particular attention, information encoding and temporal binding of distributed brain areas into functional assemblies [17, 64, 90, 119]. It is thus very plausible that neural processes of volition are expressed by broadband oscillations. Indeed, high-frequency Gamma (>40Hz) oscillations were reported to be involved in range of sequential processes related to preferential, voluntary decision making [44]. Alpha (8-13Hz) and Beta (16-30Hz) oscillations have been well studied in context of action preparation [30, 127, 157] but it remains unclear whether they distinguish internally-generated from externally-cued actions [27]. The topic of brain oscillations will be expanded in further sections of this chapter.

2.1.3 Delayed response tasks in context of volition

Delayed response reaction time tasks are typically based on two, usually visual, stimuli - early S1 and late S2, followed by appropriate motor response [30, 34, 37]. The early S1 (precue) can deliver complete or incomplete information about the action to be prepared, and S2 can be either congruent (Go signal) or incongruent (No-go signal or alternative Go) to the S1. By experimental manipulation of information contents of S1 and S2 and observing the modulation of brain signals in the interval between S1 and S2, a lot has been inferred about brain preparation of action and early/late inhibition of action. Two prevalent phenomena are contingent negative variation (CNV) and spectral desynchronization ERD in alpha and beta ranges. CNV is a slow negative potential reflecting active buildup of attentional resources and sensory expectations about upcoming stimulus [34, 155, 165]. It is known that CNV is larger in Go condition than in NoGo condition [32, 147], can be lateralized if response type is known [73], and correlates with reaction times [97]. Preparatory effects other than CNV were also observed in terms of event-related desynchronization (ERD) in Alpha [27, 32] and in Beta rhythms [30].

A lot of research was done regarding CNV and ERD phenomena especially in the context of externally triggered actions and inhibition (cued Go/NoGo tasks) [33, 34, 37, 147], however only few studies examined whether CNV and ERD are dependent on the mode of action selection (internally driven or externally triggered) [27, 159]. Although most of those studies did not include a component of free decision, they are indeed informative in context of volition. It is reasonable to assume that once the voluntary decision had been made and intention about action had been formed, the further action preparation mechanisms should be identical to those of externally-cued context (after informative S1). Indeed this is what we observe in our Study 1. It implies that phenomena such as timing and magnitude of CNV and ERD, as well as their interpretation as attentional

expectation and motor preparation, remain intact regardless of the mode of action selection.

It should be also noted here that the readiness potential (RP) in the Libet sense, and the CNV do not reflect exactly the same neural processes, despite their apparent similarity. While the former manifests a self-paced, unconsciously initiated voluntary action, the latter corresponds to conscious expectation or preparation for the external stimulus or externally triggered action. On the other hand, in the context of attention both RP and CNV could reflect gradual process of allocating attentional resources to the action preparation, regardless its nature. In the context of voluntary decisions with delayed response (i.e. studies presented in this thesis, also [27], and prospective memory tasks [142]), CNV may occur in several ways. Firstly, CNV deflection following decision but preceding the imperative stimulus is expected, along with contralateral RP preceding action, regardless whether decision was internally generated (voluntary), or externally cued. Secondly, CNV deflection can also precede the decision itself.

2.1.4 Internally-generated vs externally-cued actions

In a quest to discover the "holy grail" of volition, a lot of work has been done to compare two fundamental modes of action selection - internally-generated and externally-cued actions - in experiments involving fMRI [22, 24], PET [26, 52], EMG [115] and EEG [27, 156, 166] modalities. This approach, although not always aiming directly at the problem of volition, can inform about relevant behavioral and electrophysiological differences, as well as neuroanatomical locations mediating internally-generated and externally-triggered actions.

The first mode is referred to as internally-generated actions or voluntary actions. In common sense, these are the actions where the "free will" can be exercised. More strictly, the information regarding action is generated internally, by deliberate and conscious decision process. This information determines time and type of the action, for instance free choice of when to tap a finger, or which sequence to tap. The second mode is referred to as externally-cued action (other terms used are stimulus-driven action, or externally-triggered action). These are sensory-guided actions, determined by specifics of external event or environment, such as visual stimulus. The most explicit case of this category are spinal reflexes, such as knee jerk or Achilles reflex, which do not involve cortical processing. More casual examples of externally-triggered actions can be found in reaction-time experiments, where participants are instructed to immediately perform particular action in response to given stimulus, or in object grasping tasks.

It is important to note that this distinction is by no means exact or mutually exclusive. In practice, almost every action (with exception of spinal reflexes) will involve to certain extent both intentional and externally-guided components of action selection [166], and as such will to certain extent activate both pathways [22], [109] in coordinated manner. Every externally-guided action, with exception of spinal reflexes, must take into account information about certain intentional states (for instance intention to follow experiment instructions regarding pressing left of right finger following visual stimulus flash, or more striking example - the famous Milgram's obedience experiment [106] - where participants applied painful electric shocks to innocent person following verbal instructions of experimenter). Similarly, every internally-generated action requires some stimulus guidance, or information from environment, in planning and executing the intended action (for instance, intentional action of crossing the street will be guided by visual/auditory stimuli such as traffic lights or noise of approaching truck). One could argue that internally-driven actions are just a particularly complex, intricate version of stimulus-driven actions, which involve contextual processing and account for memory, proprioceptive and emotional states rather than simple sensory processing.

However, there is a lot of evidence from neuroimaging and animal studies that the internal and external modes of action selection are mediated by distinct cortical networks [22, 26, 52, 76, 120], the former mediated by more rostral brain areas (prefrontal cortex, preSMA) while the later is more caudally located (sensory parietal areas and lateral premotor cortex). Neuroanatomical coordinates will be discussed in more detail in the next section. Apart from spatial differences, these two modes of action selection have different temporal characteristics [156, 159, 166].

According to some models of cognitive control [146], the stimulus-driven loops may control behavior as long as stimuli provide sufficient information for the routine, behavioral schemas. In case the stimuli are ambivalent, or if the need for exploratory behavior emerges [21, 23], the volitional, internally-driven system overtakes control. Another interesting findings were reported by Goldberg et al [39], who demonstrated in fMRI study that internally-generated, voluntary actions have a common neural substrate with the "intrinsic" network, which is responsible for endogenous mental processes such as emotional introspection and self-judgment. Thus there might be a biophysiologically dictated connection between phenomenal concepts of "free will" and "the self".

2.1.5 Neuroanatomy of volition

A number of neuroanatomical areas have been related to different aspects of volition, owing to wide range of neuroimaging and animal studies, and clinical cases of neurological disorders of volition.

Depending on whether an action is internally-generated or stimulus-driven, it is mediated by one of the two distinct cortical networks [24, 45, 120, 139]. The first network, corresponding to volition-related pathway, consists of supplementary motor area (preSMA), which receives inputs from basal ganglia and several areas of prefrontal cortex, primarily orbitofrontal cortex, anterior cingulate cortex (ACC), rostral cingulate zone (RCZ) and dorsolateral prefrontal cortex (DLPFC). The second network, corresponding to sensory-guided and stimulus-driven actions, starts in early sensory areas (i.e. visual cortex in case of visually-guided action), followed by higher-level sensory integration areas in parietal cortex, which project to lateral premotor areas. Both pathways however terminate in primary motor cortex (M1) which is the final stage before the efferent motor command is propagated down the spinal tract to the muscle terminals [120]. The schematic representation of the networks involved in voluntary action is depicted by Fig.2.2.

Several studies show that preSMA plays a central role in voluntary action [74, 111, 153]. Firstly, the readiness potentials preceding voluntary action and intention, like those observed in original Libet's clock experiment and the follow-up studies, have been source localized at preSMA [168]. Secondly, fMRI studies consistently report that BOLD responses in preSMA area are stronger [52, 74], their timing is earlier [22] and the duration longer [156] in voluntary actions as compared to externally-cued actions. Finally, electrical stimulation of cortical surface at preSMA region at patients undergoing epilepsy surgery, causes feeling of "urge" to move [35], while stronger stimulation initiates actual movement. However, several lines of evidence suggest that despite preSMA's critical role to volition and its correlation with subjective feeling of "urge", it is not necessarily the very first component in the causal chain of neural processes corresponding to voluntary action. Important inputs to preSMA are provided by prefrontal cortex and basal ganglia.

Dorsolateral prefrontal cortex (DLPFC) and anterior cingulate cortex (ACC) were shown to be involved in conscious and intended motor action, reflecting the internal generation and motor planning [22, 52, 151]. It was suggested that there is no single dedicated "will center" within DLPFC, but instead exact activation patterns depend on the type of the willed action to be performed [50]. Rostral cingulate zone (RCZ) at the median wall of prefrontal cortex is also relevant to volition [24, 109]. In a fMRI study Mueller et al [109] observed that

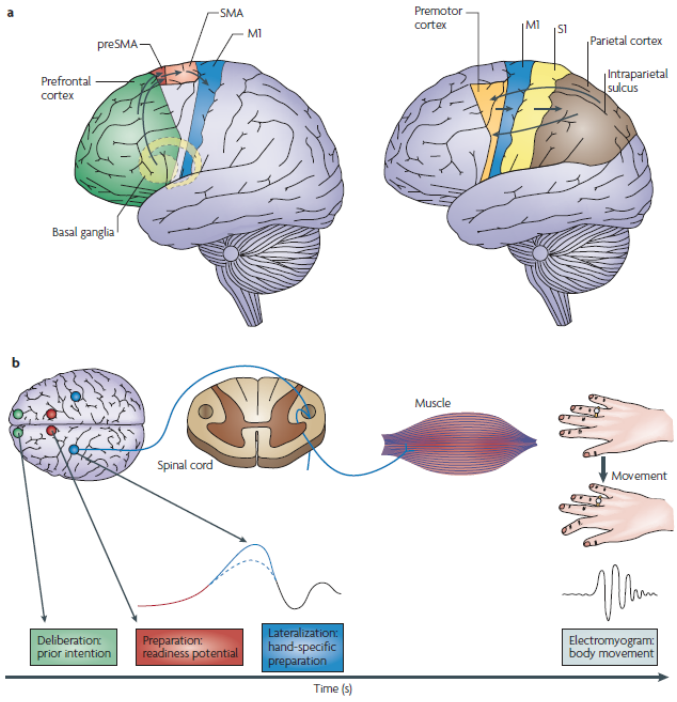

Figure 2.2: (A) Cortical networks involved in voluntary (top left) and externally guided (top right) actions. The voluntary network consisting primarily of basal ganglia, prefrontal areas and preSMA, while external action network consists of early and integration parietal areas and lateral premotor areas. Both networks converge at primary motor cortex from where the motor command is sent down to the muscle through cortico-spinal tracts (bottom). The two networks are by no means exclusive, and many typical actions will involve to certain extend both the prefrontal and parietal circuitry. (B) Readiness potentials recorded at scalp before the action are originating from preSMA area. It is plausible that early intentions and early strategic planning is mediated by frontopolar areas, before action preparation is initiated in preSMA. (Reproduced, with permission, from Haggard et al [45]).

significant BOLD contrasts occurred only in RCZ (but not in preSMA), when comparing internal/external modes of action selection. RCZ can be also critical in voluntary inhibition, or free decision not to act [72]. In the latter study, the authors reported no difference in activation of RC in voluntary decision between acting or abstaining from action, which suggests that voluntary non-acting is a mode of action in terms of its neural implementation. In the analogous context to that of Libet's experiments, however using fMRI modality, [148] reported that BOLD activity, predicting the laterality of voluntary left/right index finger movement, starts to build up in frontopolar cortex as early as 8 seconds before conscious awareness of 'will'. The activity then spread to parietal areas (precuneus, posterior cingulate) and preSMA, finally reaching contralateral primary motor area (M1). Interestingly, the BOLD trace of early preconscious intention

in prefrontal cortex is not limited to motor tasks, but expands over abstract decisions [149]. On the other side, it was suggested that DLPFC activation in free action context may be more related to increased attentional demand to action selection process, rather than actual generation of those actions [76]. This supports the hypothesis that attention might be a critical component of the intention formation process (and related subjective feeling of 'urge'). While the former is mediated by DLPFC, the latter is represented by increased activity in preSMA area.

Basal ganglia is the second volition-relevant component, which projects strongly to preSMA [2]. It has been shown with local-field potential(LFP) recordings, that oscillations in subthalamic nucleaus (functional part of basal ganglia) predict voluntary hand movements by more than 1 second [91], which is earlier than the onsets of readiness potentials originating from preSMA [85, 168]. Functional imaging studies suggest that basal ganglia is activated stronger in self-initiated than externally-cued movements [22].

In summary, the most relevant neuroanatomical areas in context of volition and free-action are: distributed areas of prefrontal cortex (DLPFC, AAC, RCZ), preSMA and SMA, and basal ganglia, while lateral premotor areas and parietal cortex (precuneus, intraparietal sulcus, posterior cingulate) have been mostly linked to externally-guided actions. Primary motor cortex is the final area where those two distinct pathways converge. Finally, it is important to note that this distinction is by no means exact or mutually exclusive. In practice, almost every motor task (with exception of reflexes) will involve to certain extent both intentional and externally-guided components of action selection [166], and as such will to certain extent activate both pathways [22, 109] in coordinated fashion.

Furthermore, internally-generated decisions regarding the "willed" actions are mediated by different neural components depending on the type of response [50], and the type of voluntary decision [13, 49, 141]. In particular, the "what", "whether" and "when" components of voluntary decision (as discussed earlier) seem to be represented by partially distinct neural processes. Investigation of dynamic aspects of this difference (measured with EEG) is the main motivation for our Study 2 (Chapter 5).

2.1.6 Brain stimulation and volition

Other insights to neural pathways mediating the voluntary action come from noninvasive brain stimulation (NIBS) methods such as transcranial magnetic stimulation (TMS), or from clinical methods, primarily electrical stimulation

of brain surface during awake surgery of patients undergoing treatment of intractable epilepsy. Stimulation of primary motor cortex initiates involuntary motor response, however patients do not have the subjective feeling of neither urge, intention nor ownership of that action [122]. The effect is different if the presupplementary motor area (preSMA) is targeted. Sufficiently strong stimulation initiates the motor response, however this time patients report that they indeed planned the movement, or felt the urge to move [35]. The feeling of "urge" remains even if stimulation is too week to cause an overt response. Other studies applying TMS stimulation to the same area showed that the subject voluntary action and the feeling of agency can be biased, or tricked, by properly timed stimulation [12] and that the perceived onset of intention can be manipulated by stimulation applied shortly after the voluntary movement execution [75]. The latter study suggests that feeling of intention may, to certain extent, depend on the brain activity after the action has been executed, which renders the intention closer to retrospective perception rather than causal mechanism.

2.1.7 Neurological disorders of volition

Another source of knowledge regarding the nature of voluntary action are the clinical studies of the patients with certain disorders of control, inhibition or initiation of free action. On the other hand, understanding the dynamics and anatomy of volition is essential for development of effective therapeutic interventions and treatments methods.

The well studied examples include "utilization behavior" following frontal lobe damage (especially preSMA area), where patients compulsively reach for and use the objects in their surrounding [82] and alien/anarchic hand syndromes, where patients do not have the feeling of agency or ownership of the movement of one of their limbs, usually due to disruption of connection between primary motor and premotor areas. Both those neuropsychological conditions suggest that preSMA plays an important role in voluntary selective inhibition of actions which are irrelevant or unjustified [111, 153]. Another disorders of volition include obsessive-compulsive disorder and Tourette syndrome [135], where patients are usually aware of "urge" and tension building before the tic onset. Prolonged inhibition of tic is mentally exhausting, and thus it is not straightforward to determine whether tics are voluntary or involuntary. This suggests that, in certain contexts, an intentional inhibition of action can be equivalent to, or even more resource demanding, than voluntary action. Another explicit dysfunction of "will" system is observed in conditions of aboulia and akinetic mutism [10, 98], usually effect of lesions to basal ganglia or prefrontal cortex. Patients display inability to initiate spontaneous action or make a choice, and

lack of drive and motivation. This condition explicitly suggests the existence of a biological, mechanistic representation of the concept of "free will", and indicates that volition as such should be quantified on continuous scale (level of volition) rather than binary scale (presence or absence of volition).

2.2 Brain oscillations

Due to its micro- and macroscopic structure, abundant in recurrent feedback loops on multiple scales, brain can be understood as a complex system of weakly coupled oscillating systems. Neural oscillations are the critical phenomenon bridging the gap between spiking neurons and behavior [16]. Regardless if in idle resting-state, during demanding cognitive task or integration of multi-sensory information, the distant cortical areas as well as local neural assemblies are integrated into functional task-specific workspaces by means of oscillations [16, 90]. Depending on the nature of the task, its complexity, and the connectivity structure of the mediating neural resources, different compositions of frequencies (or rhythms) will be observed at electrophysiological recordings, ranging from slow Delta(.5-2Hz), Theta(3-7Hz) and Alpha(8-13Hz), up to faster Beta(16-30Hz), low Gamma(30-60Hz) and high Gamma(70-200Hz) oscillations. Often, although not exclusively, the central oscillatory frequency will depend on the scale of the underlying neuronal network, thus the fastest oscillations will reflect activity in local, function-specific networks, while slower oscillations will play role in functional integration of distributed cortical resources [19]. Information routing via cortico-cortical and thalamo-cortical networks is performed by mechanisms of excitation and inhibition providing temporal windows for coherent execution of relevant tasks [17, 90].

A growing number of studies involving EEG, MEG and ECoG, as well as intracranial recordings from animals and humans, have linked the oscillatory phenomena to various cognitive, sensory and motor functions. It is important to emphasize though, that there is no one-to-one relation between a given oscillatory frequency and particular cognitive processes. Instead, the similar oscillations (in terms of their spectral extension), such as Alpha, can be involved in very different tasks in different brain areas at different times.

Modulation of power in low frequency bands (Theta-Alpha, 3-12Hz) had been linked to central executive function [20, 63], working-memory [56] and attention [64]. Increased theta oscillations in parietal areas relates to episodic memory encoding [65] and retrieval of items [66], while frontal theta power correlates positively with working memory load [56], and negatively with default mode network [143]. Interaction of theta, alpha and gamma rhythms may constitute a

fundamental mechanism for information encoding and coordinated information flow in brain [19, 88, 119].

The role of alpha oscillations (8-13Hz) has been broadly studied in various contexts, in particular its relation to attention [64] and memory [53, 62], perception [7], and motor preparation [27]. Alpha oscillations are often interpreted as manifestation of brain's "idling" mode [131], because its power tends to increase in resting state, drowsiness, during closed eyes intervals, and with decreasing task demand. However, it is currently believed that role of Alpha oscillations is wider than simple idle rhythm. W. Klimesch proposed inhibition-timing hypothesis [67], according to which alpha synchronization may represent top-down inhibitory control, while alpha desynchronization reflects gradual release of inhibition over the task-relevant areas. Given that Alpha guides the attention, allows semantic orientation and access to knowledge base, it may be considered as the rhythm reflecting the most fundamental cognitive processes [64]. Other studies employing cross-frequency analysis show that alpha-gamma coupling may be relevant for visual information coding [118] and integration of distributed networks into functional units [119]. In general, alpha power is suppressed along with growing need for cognitive processing, attentional resources allocation, or task complexity. In the context of this thesis, the role of alpha in attention and self introspection is of particular interest, as it might suggest the alpha oscillations involvement in the process of conscious, voluntary action.

The particular role is assigned to Alpha/Mu (8-13Hz) and Beta (16-24Hz) oscillations, which are recognized as main rhythms of motor function [6, 30, 55, 70, 71, 124, 131, 132] both if movement is generated as response to stimulus or free-paced. Broadband reduction of power in range from Theta(3-6Hz) to Gamma(>40Hz) is observed during preparation to externally-cued action in delayed response Go-NoGo tasks [37, 40], and as such can reflect global preactivation of sensorimotor cortices and attentional orienting. Desynchronization of Alpha and Beta rhythms is stronger in Go than in NoGo condition [5], and lateralized if the pre-cue carries information about laterality of requested action [30]. Moreover, Alpha and Beta oscillations are modulated by motor imagery [103] and may correlate with activation of mirror neuron system during action observation [110], either of which can be reflected in decision processes. Beta bursts are also relevant to externally [71, 169] and internally [164] generated inhibition of action, and prefrontal Beta oscillations may reflect behavioral rule selection [54].

Oscillations in higher frequency have broad significance in cognition and sensorimotor function, and can also be relevant to volition and free action. It has been shown that distinct gamma modulation over different cortical areas encode subsequent stages of preferential choices and free decisions [44]. Many studies showed involvement of gamma in planning and execution of motor function

[37, 127, 130]. Gamma oscillations are also relevant for memory and attention [57], and were suggested to mediate the attentionally modulated functional communication between prefrontal and visual cortex [41]. It plays role in memory consolidation in sleep [79]. Gamma rhythms are critical in perception and multi-modal feature binding to create coherent representations of objects and concepts [4, 31]. Transient synchronization in gamma band was suggested to be a correlate of conscious visual perception [31, 93, 104].

Furthermore, converging evidence suggests that oscillations in low and high frequencies are coupled and the coupling may reflect a fundamental mechanism for establishing functional workspaces of distributed brain areas [19, 78]. Notably, neuronal workspaces recruiting widely distributed brain areas may be responsible for emergence of higher cognitive function of consciousness [25]. It has been shown in different studies that bursts of fast Gamma oscillations tend to occur preferentially on certain phases of slower Theta and Alpha waves [88], and the degree of coupling can be task-dependent [162, 163]. Task and stimulus dependent modulation of phase-amplitude coupling (PAC) supports the hypothesis of phase-dependent coding of information in brain [87, 88, 167].

While the most of research efforts focus on well-established physiological bands ranging from Delta to Gamma (1-100Hz) it is important to note that additional information might be contained beyond those spectra [161]. Those are often referred to as infra-slow (0.01-0.5Hz) and ultra-high (100-600Hz) oscillations. EEG sleep studies [102, 161] show that slow cortical oscillations (<1Hz) play an important role in modulating cortical excitability during sleep, organizing and timing other rhythms characteristic for sleep such as slow waves and spindles. Those slow oscillations seem to have prefrontal origin and promote toward posterior areas in a form of slow traveling wave [102]. Amplitudes of faster oscillations are modulated by phase of ultra-slow wave [161]. Ultra-slow oscillations are not limited to sleep states and were reported to affect fundamental aspects of cognition in awake state, such as perception and ability to detect stimuli [108], and thus influence behavioral performance. In resting state, there is evidence that electrophysiological activity is weakly coupled with other slow peripheral physiological rhythms such as respiration, cardiac rhythm, and blood-oxygenation levels [126], operating on range of 0.01-0.1 Hz, which corresponds to a cycle of several seconds up to over a minute. On the other extremity, attempts are made to measure ultra-fast oscillations with surface and epidural EEG [113]. For example, fast wavelet responses to peripheral nerve stimulations, measured with epidural EEG over primary sensory cortex at frequencies up to 600Hz, were shown to correlate precisely with the timing of neuronal spike discharges [9]. The study elegantly demonstrates that macroscopically observed oscillations may directly reflect the very fine cellular phenomena.

In summary, a lot of converging evidence points at the central role of neuronal

oscillations in the functioning of the brain [17, 31, 60, 63, 90]. A specific coding of information, as well as dynamic organization of neuronal assemblies into functional workspaces is realized by means of complex, multi-scale interaction of networks oscillating in broadband frequencies ranging from 0.01 to 600Hz [79, 90]. Investigating those oscillations, their interactions and behavioral/cognitive correlates seem to be a crucial aspect to understand the brain dynamics. In particular, spectral contents of brain oscillations can be informative in context of voluntary action.

2.3 EEG methods

In this section I review selection of literature related to EEG/MEG analysis. It should be noted though that in the last two decades, along increase of computational power, and availability of high-resolution multichannel EEG systems, the number of methodological approaches exploded. Thus I will limit in this brief review to those methods that either (1) are used in further analysis steps, or (2) are a well-established standard in the field and thus must be mentioned here. Furthermore, for more details regarding methods used in this work, the reader is encouraged to proceed to Chapter 3.

The first EEG traces were recorded in 1929 by Hans Berger. Although already at that time one could appreciate the oscillatory nature of brain signals, it quickly became obvious that the subtle electrical correlates of behavior are invisible in background activity, further obscured by environmental noise. Almost a decade later, Hallowell Davis proposed simple averaging approach, where multiple repetitions of the same neurocognitive experiment recorded and averaged together, with premise of canceling out irrelevant activity while preserving task-relevant signal. This approach, known as Event Related Potential (ERP) remained almost unchanged until today, and has become one of the most widely used method in clinical and academic neurophysiology. In recent decades, with the advancement of EEG recording equipment and processing power of computers, the ERPs are computed with considerably higher temporal and spatial (multi-channel) resolution. For detailed review of basic ERP methodology, guidelines and recommendations, the reader is encouraged to classic book of Steven Luck [92] and consensus guidelines [133].

The advancement of EEG analysis and visualization came with introduction of open-source tools such as EEGLAB [28] and FieldTrip [117], enabling researchers to visualize multivariate spectral and temporal data and its topographic distribution [59]. Very significant contributions to EEG analysis were made by Scott Makeig and his group, who introduced Independent Component

Analysis (ICA) to the domain of multichannel EEG data [95]. ICA decomposes data into set of maximally temporally independent components, each characterized by particular topographic distribution [116]. Given its spatial and temporal characteristic, components can be classified as either artifactual (muscular, cardiac, oculo-motor origin) or as representing a genuine, independent neural source. Another valuable contribution of Makeig's group is extension of the notion of ERP into so called ERP-image - a method of looking at a raster plot of time-aligned, sorted, smoothed individual trials. ERP-image provides valuable insights into dynamics of brain response and correlations with external stimuli/responses, information that would be (at least partially) lost in simple ERP averaging process [59].

The limitation of ERP approach is that it is only capable to capture the brain responses that are phase-locked to the stimulus (evoked response). In order to measure oscillatory responses to stimulus that very in phase (induced response), G. Pfurtscheller proposed to compute power of band-pass filtered signals prior to averaging, thus obtaining measures of event-related synchronization (ERS) or desynchronization (ERD) [129]. In case of Alpha and Beta frequencies, it has been suggested that ERD reflects the enhanced cortical activity, while ERS corresponds to suppressed activity, or cortical "idling" [125].

The time-frequency (TF) analysis is a direct extension of ERD/ERS methodology to account for spectral power changes over multiple spectral bands and temporal windows. The time-frequency decomposition results in a map of power modulation on the time-frequency space, and can be used to infer about involvement and interaction of different oscillations at different time intervals. Different methods have been proposed to perform TF analysis, the most commonly used are windowed Fourier transform [38], Morlet wavelet decomposition and Hilbert transform [79]. In general, selection of decomposition method and its parameters aims at finding an optimal trade-off between temporal and spectral resolution. Although some methods might be more appropriate for particular task, it has been shown that with adjusted decomposition parameters they yield very comparable results [14, 79]. For review of TFA methods we redirect readers to [140], and for practical considerations to online documentation and tutorials of Fieldtrip toolbox [117].

Wide range of spectral analysis methods can be applied to measured electrophysiological signals depending on the nature of the investigated phenomena. Each method provides specific, complementary type of information. Apart from power estimates, an instantaneous phase of signal in frequency bands of interest can be measured, which can be used to compute cross-site phase coherences [114, 150] or phase-diversity [160] of oscillations recorded across multiple sites. Those measures can inform about local synchrony and interregional connectivity. Phase information can also inform about degree of phase-locking to stimu-

lus/event (inter-trial phase coherence (ITPC) [28] or phase locking factor (PLF) [154], see [140] for review. Furthermore, combined information about instantaneous phase and amplitude can be used to compute phase-amplitude coupling (PAC) [158] between slow and fast oscillations, and can indirectly inform about functional interaction between local and global networks [19, 78, 87, 162, 163].

In context of multi-channel EEG/MEG analysis, one of the nontrivial problems researches must face is the problem of selection of appropriate statistical test. Unless there is a strong a-priori hypothesis about spatial and temporal location of the effect, all points need to be tested (i.e. 128channels x 200 time samples) which often yields vast number of multiple comparisons. Considering high spatial and temporal correlation (between neighboring channels and neighboring points in time or spectrum), standard correction methods such as Bonferoni or False-Discovery Rate are too conservative and result in excessive number of false negatives (type 2 error, accepting null hypothesis while in reality it should be rejected). Another common problem with standard statistical approaches (ANOVA, Student t-tests) is their assumption of normally distributed statistical variable - the assumption that is often violated in case of multi-subject, electrophysiological data. To account for those two problem, nonparametric statistical tests based on cluster-mass permutation tests were proposed [100], where all the test statistics are grouped into multi-dimensional clusters based on their spatial, temporal and spectral adjacency. Permutation tests follow on the cluster level. The method can be used for testing ERP and time-frequency contrasts, as well as connectivity and coherence [101]. See Maris and Oostenveld [100, 101] for in-depth discussion of the strengths and limitations of the method and its formal validity.

For more elaborated review of methods for spectral and temporal analysis of EEG signals see [43, 96, 140, 158], and [43, 100] for detailed discussion of statistical methodology. Practical aspects as well as case examples of ERP and TF analysis and cluster-mass permutation tests will be presented in Chapter 3, Methods for EEG data analysis.

Chapter 3

Materials and Methods

In this Chapter technical aspects of the thesis will be in focus. I will start from a brief description of the hardware apparatus employed for empirical data acquisition in Study 1 and Study 2, i.e. EEG, Eye-tracking system and structural MR imaging. Following that, the software implementations of experimental designs (visual stimulation) will be discussed, in particular PsychoPy based design for the Study 1, and a dedicated Virtual Reality Environment designed for the Study 2. Finally, the aspects of scientific computing and data analysis will be presented: algorithmic solutions to automatized pre-processing of EEG datasets, data cleaning, ERP and time-frequency analysis, and statistical comparisons. Individual head modeling and source reconstruction will be briefly discussed.

3.1 Brain measurement apparatus

3.1.1 High-resolution EEG

The EEG data presented in the following chapters of this thesis were acquired with Biosemi Active Two system, with 128 active, low-impedance Ag-AgCl electrodes.

The pre-amplified signal from each active electrode were sent to low noise DC coupled post-amplifier (Biosemi AD-box), with a first order anti-aliasing filter, followed by Delta-Sigma modulator (oversampling rate of 64), and decimation filter with a steep 5th order response and 24-bit output. The digital outputs of 128 AD converters were digitally multiplexed and sent to the acquisition computer via optical fiber in uncompressed form.

Apart from 128 EEG channels, two additional, vendor-specific electrodes labeled GND and CLS were positioned in the proximity of central Cz location and served as grounding and hardware reference. Another two auxiliary surface Ag-AgCl electrodes were used as primary reference channels at bilateral mastoids. Electromyographic (EMG) signals from the left and right index fingers were recorded with surface bipolar Ag-AgCl electrodes positioned at the first dorsal interosseous muscle. Electrooculography (EOG) signals were recorded with two bipolar surface Ag-AgCl electrodes positioned lateral to the outer canti of the right eye (hEOG) and below the right eye at the cheekbone (vEOG).

All data were amplified and digitized at sample rate of 512Hz. Immediately after recording, all data were re-referenced to average mastoids signal. External visual stimuli (PsychoPy in Study 1 and Virtual Environment in Study 2) and button-press responses were synchronized with EEG signals via parallel port triggering, with maximum delay times below 1ms. The same triggering system was used to synchronize environmental events with EEG and Eye-Tracking system (the latter only in Study 2).

The brief overview of the equipment and is presented at figure 3.1, and the specification of Biosemi ActiveTwo system is provided in Appendix F.

3.1.2 Eye-Tracking system

For the purpose of synchronous recording of eye movement, we applied the integrated RED250 system from SMI SensoMotoric Instruments. The RED250 system is contact free, based on remote infra-red camera, capable of tracking eye gaze position and pupil diameter changes, while correcting for head movements.

The eye-tracking data was recorded in Study 2, involving virtual environment task. SMI calibration was performed as the last step before commencing each experimental sesion, i.e. immediately after EEG montage preparation, when the participants is in his required position in relation to the screen and keyboard, as described in the previous section. The calibration procedure is guided by the vendor's acquisition software and requires that participants repeatedly fixate the gaze on subsequent calibration points on the screen, until the standard

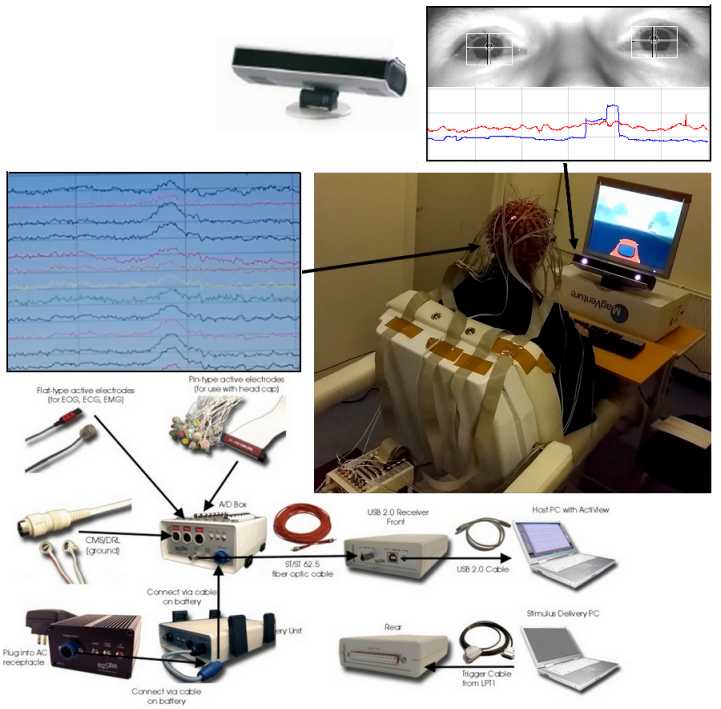

Figure 3.1: Biosemi ActiveTwo EEG system and SMI SensoMotoric RED250 eye-tracking system - components and hardware configuration.

deviation of the estimate is below certain thresholds. Additional manual check was performed in which participants continuously tracked the mouse cursor moved randomly by the experimenter.

The eye-tracking data were digitized and stored at 120Hz. Importantly, all the triggers (generated both by virtual environment and participants button presses), were recorded simultaneously by the SMI and EEG acquisition computers. This allowed for subsequent synchronization of EEG and eye-tracking data samples with precision <1ms. The main measures derived from the data are: event-related changes in gaze position and pupil diameter, as well as condition-dependent changes in fixation distribution and saccade parameters.

The brief overview of the equipment and configuration used is presented at Fig.3.1, and the specification of the SMI eye-tracking system is provided in Appendix F.

3.1.3 Structural MRI and coregistration

In Study 2, additionally to EEG data, structural magnetic resonance images (MRI T1) were acquired for each of the participants, before the first experiment session. The images were acquired with prospect of follow-up analysis based on subject-specific source localization of the brain oscillations. Anatomical imaging was done using Philips 3T scanner, with a T1 weighted Magnetization Prepared Rapid Acquisition Gradient Echo sequence (TR = 6 s, TE = 2.7 s, acquisition matrix = 288x288, field of view =245x245x208 mm^3, flip angle = 8^o, voxel size = 0.85x0.85x0.85 mm3). The exemplary three-dimensional image of the brain of one of the participants is presented at Fig.3.8 (top panel). To facilitate subsequent integration of EEG data with structural MR information, the exact locations of each EEG electrode in 3D space were recorded with Localite Neuro-Navigation system, and co-registered with 3D brain images by an iterative surface matching procedure performed with SPM software [89].

3.2 Experimental designs

3.2.1 Study 1: PsychoPy based design

In Study 1, we investigated the nature and the neural correlates of voluntary decisions to act or to inhibit the action, along with related motor and cognitive processes. The details of the study and the experimental design are presented in Chapter 4 (Manuscript 1).

In short, the experimental design was based on PsychoPy platform. The PsychoPy is a popular, open-source, Python-based tool for designing experiments, primarily used by neuroscientists and experimental psychologists [121]. It supports presentation of visual/auditory stimuli, randomization of trials, and recording behavioral data, such as reaction times. The Study 1 was based on sequence of carefully timed and pseudo-randomized visual stimuli, that triggered certain cognitive and motor responses (Fig. 3.2). The sequence and timing of the onsets of visual stimuli were synchronized with electroencephalographic signals by means of hardware triggering (see Section 3.1.1).

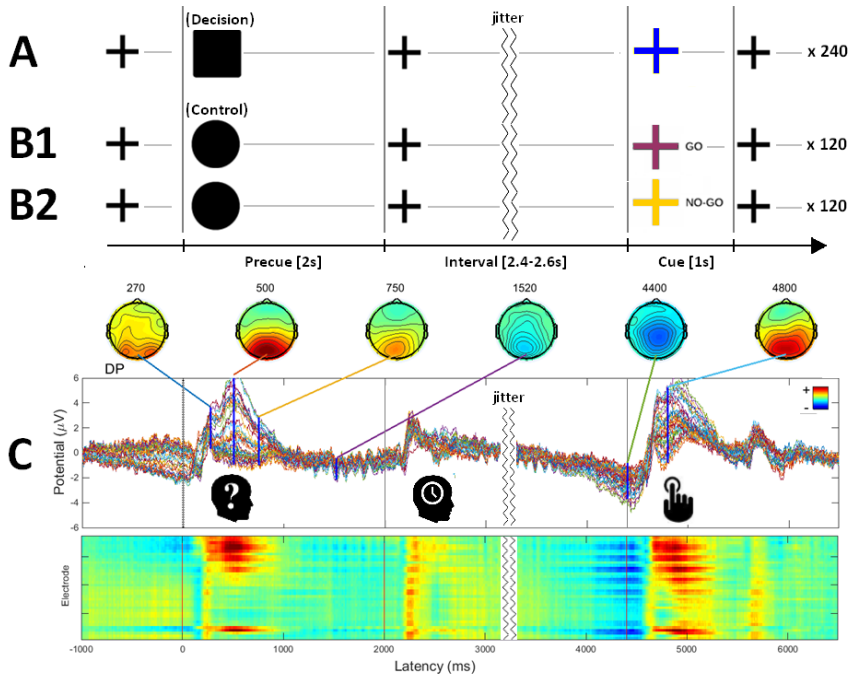

Figure 3.2: Study 1 design: Participants freely decide whether to press a button or not, and execute the action few seconds later. The experimental design and averaged EEG responses are presented. **(A)** Visual stimuli (PsychoPy based) in voluntary decision trials. Participants take fast decision during of Precue interval of 2 seconds duration, maintain decision in memory during Retention interval of 2.4-2.6 seconds, perform internally-generated action (press or no-press) immediately after colored Cue. **(B)** Visual stimuli in Control trials. Participants relax and passively wait during Precue and Retention interval. Depending on the color of Cue, they press or do not press the button. **(C)** Multi-channel envelope of grand ERPs - averaged brain responses corresponding to 'Decision-Press' trials. Each time point (latency) can be represented as 2D topographic distribution of potentials (panel C top). Alternative, common visualization is a two-dimensional color-coded raster plot of ERPs in [channel x time] space (panel C bottom). For a detailed description of the experiment and the results see Chapter 4.

3.2.2 Study 2: Virtual Reality Environment (VR) design

In Study 2, we investigated the nature and EEG correlates of different types of voluntary decisions. We designed and implemented a Virtual Reality Environment (VR), simulation of a car driving, which replaced the standard pictogram-based visual stimuli. The main motivation for VR was to provide ecologically valid, semi-realistic experience, more entertaining and less tedious for participants, and thus enhancing the natural brain processes while minimizing the problem of random-sequence generation. The motivation and design considerations are presented in Chapter 6 (Manuscript 3), while the application of the VR in the EEG study of voluntary action is discussed in Chapter 5 (Manuscript 2).

In short, the VR environment was designed in a modular way separating experimental logic from the details of implementation and visualization aspects. The experimenter can used standard tools, such as Matlab to construct the experiment. The definitions are passed via XML markup language to C# based game generator. The final simulation and visualizations are handled by Unity3D platform. The VR can be used for wide range of cognitive tasks. A particular task can be defined by (1) specifying instructions given to participants, (2) specifying pseudo-randomized sequence of conditions and trials, and (3) adjusting visual stimuli. The latter encompasses a number of parameters, most importantly road shapes, cross-road configuration, visibility, and the car and the camera dynamics.

We exploited the VR environment in range of studies of voluntary action involving EEG, Eye-tracking and fMRI modalities. In the Study 2 presented in this thesis the participants played multiple repeated car simulation games. Occasionally, during 2 second long intervals while passing through a tunnel, the participants were taking free decisions regarding subsequent actions, such as:

- "What" to do (left/right turn),
- "When" to do (first/second turn),
- "Whether" to turn or not.

The voluntary decisions were subsequently investigated in terms of the modulation of scalp recorded signals, i.e. event-related potentional(ERP) and spectral modulation of power in time-frequency domain (Fig. 3.3). The VR was sending triggers denoting game events and participant actions to EEG and ET apparatus by means of hardware triggering, which facilitated synchronization of brain responses with complex VR-based visual stimulation. The general scheme of VR

platform and experimental data flow are presented in Fig. 6.1, and described in detail in Chapter 6.

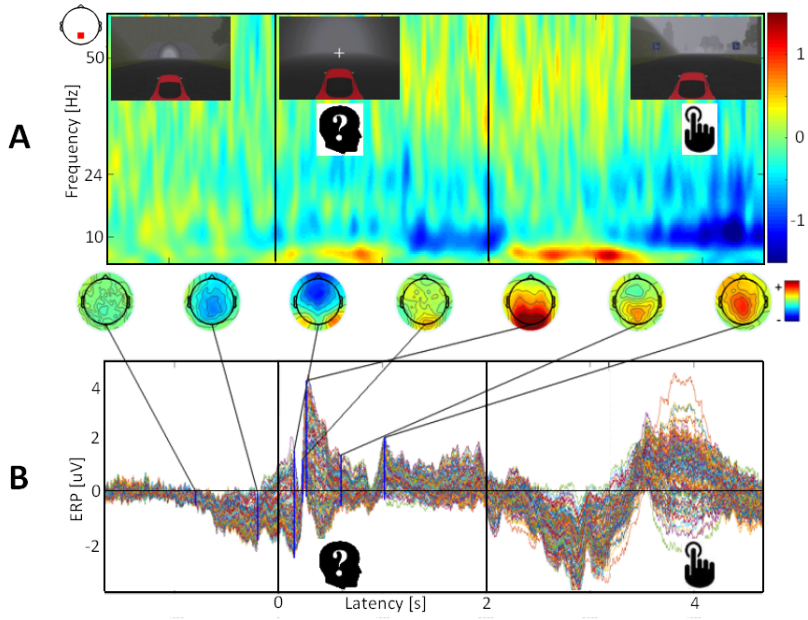

Figure 3.3: Study 2 design: Participants play repeated car simulation games. Every time in a tunnel, they take voluntary decisions about prospective action of turning a car into one of the side-roads. **Inset panels:** screen view before, inside and after the tunnel. Corresponding brain responses, preprocessed and trial averaged, are presented. **Panel A:** Time-frequency contrast between 'Whether'-decision trials and Control trials, time-locked to the tunnel onset (decision interval), measured at centro-parietal electrode (Pz). **Panel B:** ERP envelope from 128 electrodes, corresponding to Whether decision trials, time-locked to the tunnel onset (decision interval). For a detailed description of the experiment and the results see Chapter 5.

3.3 Scientific computing and data analysis

Most of the EEG methods and computations presented in this thesis were performed in Matlab environment. Data processing and analysis was implemented as a pipeline scripts combining in-house methods with open-source toolboxes such as EEGLAB [28] primarily for basic preprocessing and ICA decomposition and visualizations, Fieldtrip [117] primarily for statistics, SPM [89] for EEG/MRI corregistration, forward/inverse modeling and source localization, EYE-EEG toolbox [1] for eye-tracking data analysis, and others. Computations applied to the multi-subject and multi-session data were automatized for

the purpose of reproducibility, and parallelized with Matlab Parallel Computing toolbox. Appendix D presents details of automatized methods for efficient, robust data cleaning based on minimal number of subjective parameters. The exact methods of data analysis are described in Section 3.4, while particular analytic choices are introduced in methods sections of Study 1 (Chapter 4) and Study 2 (Chaper 5).

3.4 Methods for EEG data analysis

3.4.1 EEG preprocessing pipeline

All the data in study Study 1 and Study 2 was processed in automatized fashion, to avoid subjective biases as well as to generate fully reproducible results. We developed a set of in-house scripts using the EEGLAB data structure, and combined in-house, EEGLAB and Fieldtrip preprocessing and visualization functions, to perform all the cleaning steps from the early data import, referencing, filtering, downsampling, epoch extraction, through automatized cleaning and evaluation of results, up to application of cluster-mass permutation tests in temporal and time-frequency domain.

All the presented EEG data were referenced to average mastoids. We applied only minimal filtering (0.2-120Hz) to avoid distortion of spectral information. The 50Hz line noise was cleaned with sine regression method (CleanLine toolbox [11]), rather than notch filtering.

All datasets were cleaned automatically with respect to absolute thresholds, cross-channel correlations, and high-frequency noise. In particular, we have developed a toolbox for automatized, robust data cleaning, based on minimal number of arbitrary parameters. The toolbox and its application are presented in detail in Appendix D.

3.4.2 GFP analysis

The Global Field Potential (GFP) was first proposed by Lehmann and Skrandies [81]. It is a powerful and compact metric to characterize electrophysiological responses of the brain, yet surprisingly often omitted in interpreting EEG/MEEG studies. Mathematically, GFP is defined as a standard deviation of averaged brain responses (such as ERP), computed across N average-referenced channels. GFP effectively reduces the dimensionality of the data from NxM to

1xM, where N is the number of channels and M number of time samples in the interval of interest. As such, GFP can be interpreted as a global measure of brain responses, or alternatively - as a measure of "hilliness" of topographic distribution of scalp potentials. As discussed in [81], the peaks of GFP wave correlate with periods of relatively stable topographic distribution of potentials (low standard deviation between successive topographic maps), while low GFP values relate with higher topographic maps variance. The primary limitation of GFP is that it by definition discards information about spatial location of effect. On the other hand, it is sensitive and efficient to infer temporal characteristics of brain responses, i.e. onset/offset of activity, latency of peak of evoked responses, global magnitude and duration of effect. Furthermore, GFP can be applied as a preliminary step to detect intervals of interest, while the detailed multichannel analysis of spatial distribution can follow afterwards. A considerable advantage of GFP is its property of being reference-free, and thus unbiased to the selection of reference channels. Finally, dealing with a single GFP timeseries rather than N ERP timeseries reduces the problem of multiple comparison inherent to statistical tests of multichannel EEG data, and hence may render more accurate statistical results in applications where the timing, rather than spatial distribution, is the primary target of investigation.

3.4.3 Event Related Potentials (ERP)

The concept and meaning of ERP analysis were discussed in Chapter 2. The main premise of the ERP analysis is based on the additive noise model, according to which the process of averaging together the signals from multiple repetitions of experimental condition will lead to cancellation of random, non-phase locked noise, while preserving task-relevant, phase-locked brain activations. The latter is referred to as evoked response, as opposed to induced oscillatory response (discussed later).

To investigate evoked activity in Study 1 and 2 such as decision related ERP and slow potentials preceding action (contingent negativity variation, CNV), the epochs of interest were extracted from cleaned datasets, which accounted for 2 second long intervals in which participants were taking voluntary decisions. The trial data were normalized by subtracting the average amplitude over the prestimulus intervals (baseline correction). Finally, the trials corresponding to different conditions were averaged separately. This resulted in two dimensional datasets [*channel* x *time*] for each condition. Those datasets were subsequently submitted to cluster-mass permutation tests to find significant regions (clusters) in time and space, which differed between conditions. The example of statistical ERP analysis of data from Study 1 is presented in the Fig. 3.4.

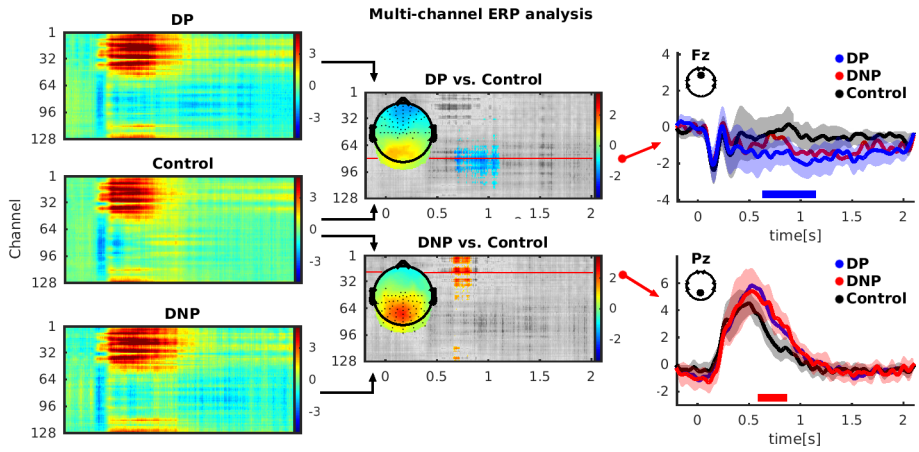

Figure 3.4: Exemplary results of ERP analysis and visualizations (dataset from Study 1). Trials belonging to decision-press (DP), decision-no-press (DNP) were compared to control condition (middle panels). The conditions were subtracted and cluster-mass permutation tests were applied to identify the regions (clusters) in space and time differentiating decision conditions from control (middle panel, colored patches). Post-hoc visualizations highlight the exact spatial (inset topomaps) and temporal (right panels) extension of the significant clusters, for a selected time interval or an electrode respectively. For a detailed description of the experiment and the results see Chapter 4.

In the work presented in this thesis, a raster plot visualization of multi-channel ERPs will be extensively used, where amplitude of the ERP are represented as color-coded pixels on the [*channel* x *time*] plane (Fig. 3.4, left panels). The advantage of this visualization is that it represents the complete spatio-temporal information, where two-dimensional spatial information is encapsulated on the ordinate axis, while temporal is maintained on the abscissa axis. The raster plots are also convenient to visualize spatio-temporal extension of statistically significant clusters differentiating two experimental conditions (Fig. 3.4, middle panels).

For more precise spatial information, such as distribution of signals (usually averaged over given time interval) over topographically aligned channels, topographic map visualizations will be used (Fig.3.4, middle panel inset maps). For detailed temporal information, such as a time course and confidence intervals of the ERP at the given scalp channel, typical ERP plots will be employed (Fig.3.4, right panels).

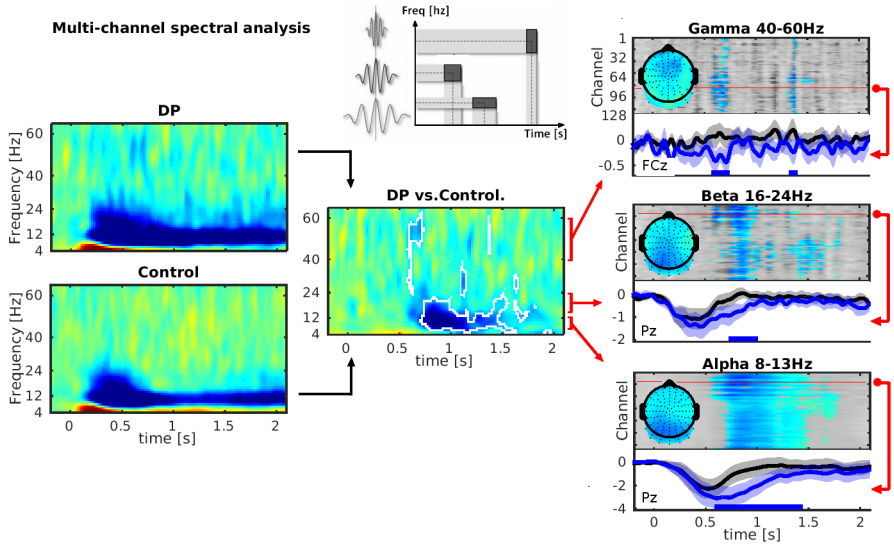

Figure 3.5: Exemplary results of time-frequency analysis (dataset from Study 1). Morlet wavelet decomposition is performed for each channel and trial, followed by averaging the trials belonging to distinct conditions, in this case decision-press (DP) condition and control condition (left panels). The conditions are subtracted from each other and cluster-mass permutation tests are applied to identify the regions (clusters) in time/spectrum/topographic location which are specific to decision condition only (middle panel). Post-hoc visualizations highlight the exact temporal and spatial extension of the significant clusters (right panels). For a detailed description of the experiment and the results see Chapter 4.

3.4.4 Spectral analysis

The concept and role of brain oscillations were discussed in Chapter 2. Here, I will briefly describe the methods to compute the spectral contents of EEG signal as a function of time, i.e. time-frequency (TF) decomposition. The result of the TF analysis is an estimate of signal power, averaged across the trials, at any given point on time-frequency plane. The time-frequency analysis is sensitive to signal modulation that is not phase-locked to the stimulus, and thus would partially or completely disappear in the process of ERP averaging. These not-phase-locked oscillations are often referred to as induced response.

The modulation of signal power is often quantified as a relative change in relation to arbitrary selected baseline (usually the pre-stimulus interval), and thus is expressed as percentage of change [%] or decibels on logarithmic scale [dB]. The relative power change is referred to as the event-related spectral perturbation (ERSP) [94] when related to entire broadband spectrum, or as the event-related desynchronization/synchronization (ERD/ERS) [123, 125, 129] when the signal

is extracted from a narrow band of interest.

There are several well-established methods of spectral analysis. The most straightforward method is to perform narrow band-pass filtering followed by squaring the amplitude values to estimate the signal power as a function of time [129]. The drawback of this method is that exact frequency bands need to be predetermined. The method is useful for testing particular hypothesis or limiting inferences to known physiological frequency bands, such as Theta(3-7Hz), Alpha(8-13Hz), Beta(16-30Hz) and Gamma(40-80Hz), however it does not show the entire spectral band or interactions between different oscillations. On the other hand, the Fourier transform can show the exact power amplitude across entire spectrum, however lacks the temporal resolution. Solution to this is to apply a successive Fourier transforms to overlapping chunks of data defined by windowing function. In this way both temporal and spectral information is preserved, and the width of the window determines the trade-off between temporal/spectral precision [38].

To further optimize time-frequency decomposition, the window width can be adjusted as a function of frequency, with larger windows for the low, and narrower for the high frequencies. The wavelet transform is a useful method in this case, which is computed as the inner product between complex wavelet function and the original signal. The wavelet function can be defined differently depending on the characteristics of the signal, but in case of physiological signals like EEG the Morlet wavelet family is the most commonly used [79], which is based on the complex exponential function bounded by Gaussian envelope. The mother wavelet is progressively scaled along frequency axis to provide increasing temporal precision for higher frequency oscillations (and hence decreasing spectral precision (see scheme at the top middle panel of the Fig. 3.5). The Morlet wavelet decomposition is well suited for exploratory analysis of broad spectral changes without a priori assumptions, and thus was extensively used in Study 1 (Chapter 4) and Study 2 (Chapter 5). Although different methods were proposed for TF analysis, and some might be more appropriate for particular task, it has been shown that with adjusted decomposition parameters they yield very comparable results [14, 79]. For further review of TF methods we redirect readers to [79, 140].

The typical procedure (as applied in Study 1 and 2) was the following. The epochs of interests were extracted, which accounted for 2 second long intervals in which participants were taking voluntary decisions. For each channel, and each epoch, the TF information was computed at the frequency ranges 4-80Hz with a step of 1Hz. Time window varied from 750ms at the lowest frequency (3 wavelet cycles) to 190ms at the highest (15 wavelet cycles). The temporal resolution of decomposition was set to 64 samples/seconds. The time-frequency maps were baseline corrected for 500ms directly preceding Precue onset, and

converted to logarithmic scale to express ERS/ERD in Decibel units [dB]. The TF maps corresponding to each condition were averaged together. Thus the final epoch-averaged time-frequency data for each condition and participant had 3 dimensions [*channel* x *frequency* x *time*] (i.e. in Study 1 the size for decision period was [128 x 77 x 148]). This three-dimensional time-frequency information was used for statistical comparisons (nonparametric cluster-mass permutation tests), for extraction of event-related spectral power modulation (ERS and ERD) in particular frequency bands of interest, such as Theta(4-7Hz), Alpha(8-13Hz), Beta(16-24Hz) and Gamma(40-60Hz), and for evaluation of topographic distribution of ERS/ERD patterns. The scheme is depicted by Fig.3.5 and discussed in detail in Study 1 (Chapter 4) and Study 2 (Chapter 5).

3.4.5 Statistical comparisons

The most of the statistical tests performed in our Study 1 and Study 2 were based on large units of comparison, such as two-dimensional multi-channel ERPs or three-dimensional multi-channel time-frequency maps. Such tests are unbiased and take into consideration all the available data, without a priori assumptions or constraints, and thus are perfectly suited for explorative analysis. On the other hand, the number of points being compared is massive, reaching up to 10^6 in [*channel* x *frequency* x *time*] domain. Standard methods for correction for multiple comparisons, such as Bonferoni correction, are overly conservative for these type of comparisons and would result with large number of false negative estimates. The reason for this is that Bonferoni correction assumes independency of multiple tests being performed, while EEG data is highly correlated in time (due to high-resolution acquisition), in spectrum (due to inherent smoothing in time-frequency decomposition) and in space (due to volume conduction and signal dispersion on brain-skull-skin interfaces).

Thus for the most of the statistical comparisons we employed the repeated measures, two-tailed cluster-mass permutation tests [15, 99], as implemented in Fieldtrip toolbox [117]. The tests were performed on (1) one-dimensional GFP traces, (2) two-dimensional, averaged, multi-channel ERP amplitudes and (3) three-dimensional, averaged, multi-channel time-frequency maps. In all cases, family-wise alpha level was set to 0.05. All 128 electrodes and all time points corresponding to the relevant decision processes were included. In case of TF data, entire spectrum from 4-80Hz was used in the main comparisons, while in more specific tests the spectrum was constrained to low (4-30Hz) or high (40-60Hz) band. The electrodes within distance of less than 5cm of one another were considered spatial neighbors, yielding in average 7.8 neighbors per electrode. For each comparison, repeated measures t-tests were computed using the original data and 1000 random within-participant permutations. For each permutation,

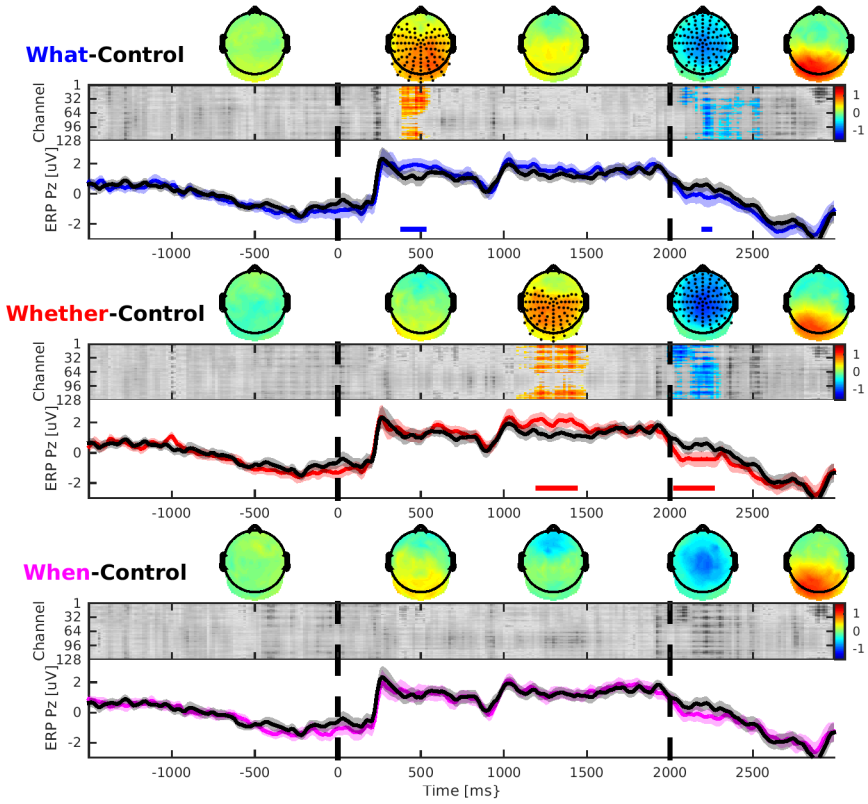

Figure 3.6: Example of application of nonparameteric cluster-mass permutation tests to handle massive number of multiple comparisons, while accounting for spatial, temporal and spectral correlation of multi-channel ERPs. The results are taken from Study 2. The three different conditions corresponding to What, Whether, When and Control conditions were submitted to the cluster-mass permutation tests. Significant positive clusters ($p<0.05$, corrected) were found in What and Whether conditions but not in When condition. The temporal and spatial extension of the clusters is denoted by color-coded patch on raster plot, and dotted electrodes on the topomaps above. Spatially robust, positive ERP components occur in different latencies, which may suggest distinct neural processes mediating those two types of decisions. For a detailed description of the experiment and the results see Chapter 5.

all t-scores corresponding to uncorrected p-values lower or equal to 0.05 were combined into clusters. The mass of each cluster was computed as the sum of the t-scores within that cluster. The highest cluster mass in each of the tests was used to estimate the distribution of null hypothesis.

With this type of statistical tests we could account for all the available data, without any a-priori constraints to either temporal or spatial extension of po-

tential effects. Thus we minimized the need for subjective choices, while maintaining weak control of the family-wise alpha level (i.e., correcting for very large number of multiple comparisons). Cluster-mass permutation tests have been shown to perform well in exploratory studies and in case of broadly distributed ERP/ERSP effects [42, 99] by accounting for high temporal, spectral and spatial correlations inherent to high resolution EEG data, which is their fundamental advantage.

The exemplary result of cluster-mass permutation test applied to data from our VR study is presented at Fig. 3.6. Decisions $What$, $Whether$ and $When$ are compared to $Control$ condition in the entire [128 $channels$ x 288 $time\ samples$] space. Significant positive clusters can be observed at early ($What$) and late ($Whether$) latencies, which indicate spatially robust positive ERP components.

Apart from cluster-mass permutation tests, other statistical tests were used selectively in certain contexts. For the post-hoc assessments of the effect, simple Student's t-tests were employed. Furthermore, to evaluate relations between EEG measures and behavioral measures (RT), we used Pearson product-moment correlation coefficients and R-square metrics.

3.4.6 Coregistration of EEG with Eye-Tracking data

The Eye-tracking (ET) data [137], recorded simultaneously with EEG, has multiple advantages. Firstly, using the two modalities can provide complementary information about the investigated cognitive/perceptual phenomena [29, 145]. Secondly, saccade dynamics extracted from ET data can be used for efficient EEG correction for oculo-motor artifacts [134]. Finally it can be used as a validation and assessment of participants performance while undergoing EEG experiment.

For example, in context of our Study 2 using VR, EEG and ET, the eye-tracking information was used to validate that subjects obeyed the instructions and fixated while in the tunnels (Fig. 3.7, top panels). Secondly, ET revealed some interesting cognitive phenomena. The pupil dilation was considerably higher during voluntary decision trials than control trials (Fig. 3.7, bottom panel). Secondly, lateral saccadic movements in the direction of intended turn preceded the turn by over 2-3 seconds (Fig. 3.7, middle panel).

The raw eye-tracking data consists of multiple time series describing parameters such as instantaneous horizontal/vertical gaze position, pupil dilation, head position, etc. The first step of the analysis of ET data was to coregister those with the EEG time-series. The process is straightforward since the ET data regis-

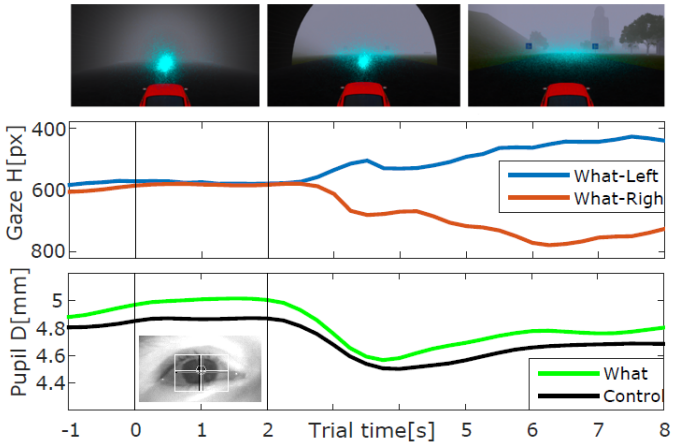

Figure 3.7: Application of eye-tracking modality to study of voluntary action in Virtual Environment. **Top panels:** distribution of fixation positions in the tunnel(decision interval), at the tunnel exit, and before the action. **Middle panels:** Time-course of average fixation position in the What condition (left/right turn choice). Short after decision interval, participants start to gaze in the direction of intended turn. **Bottom panels:** Pupil dilates in the in the decision trials. The effect might be due to voluntary decision processes or due to general attentional and mental engagement.

ters the same trigger markers as EEG data (triggers are send to both devices by stimulation platform, in this case - our Virtual Environment). For several sessions, where the trigger information was lost due to hardware problems, we restored EEG-ET synchrony by in-house scripting exploiting the unique eye-blink patterns. Each eye-blink are registered as massive potential changes on EEG side, and transient signal losses on ET side. As a result, of above steps, we obtained eye-tracking time-series aligned to EEG time-series, and encoded them as additional channels in EEG file structure.

The second step of ET analysis is to convert the high-resolution, continuous ET time-series into more interpretable sequences of oculomotor events, such as saccades (rapid, often subconscious changes of gaze position) and fixations (prolonged gaze position, usually at least 80ms). The conversion is performed by thresholding the velocity of gaze time series, and results in generating of a long sequence of events (fixation and saccade onsets) aligned with EEG data. For this step, the EYE-EEG plugin [1] was used.

At this stage, various types of analysis can be performed, such as fixation distribution in given latencies, time-courses of gaze position or pupil dilation, etc. Some exemplary ET data related to our VR study is presented in the Fig.3.7.

3.4.7 Corregistration of EEG with structural MR images

In Study 2, additionally to EEG data, structural magnetic resonance images (MRI T1) were acquired for each of the participants, before the first experiment session. The images were acquired, preprocessed and coregistered with EEG data with prospect of follow-up statistical analysis based on subject-specific source estimations of the brain oscillations. The preprocessing of the structural data and its corregistration with dynamic EEG data are presented below. However, since the rest of the thesis will focus primarily on the sensor-level inferences and statistics, I only briefly present the steps needed for EEG/sMRI corregistration, followed by subject-specific head modeling, and finally examples of source localization of brain oscillations related to voluntary decisions.

The anatomical imaging was done using Philips 3T scanner, with a T1 weighted Magnetization Prepared Rapid Acquisition Gradient Echo sequence (TR = 6 s, TE = 2.7 s, acquisition matrix = 288x288, field of view =245x245x208 mm^3, flip angle = 8^o, voxel size = 0.85x0.85x0.85 mm3). The exemplary three-dimensional image of the brain of one of the participants is presented at Fig.3.8.

For each subject the acquired image was segmented to extract distinct head tissues, in particular scalp, skull, gray matter (cortical sheath), white matter (brain fibers), cerebro-spinal fluid. Separated tissue images were subsequently used to reconstruct three dimensional tissue surfaces, in form of meshes consisting of 8192 triangles. Since different tissues have distinct electrical conductivity, their shape and interfaces affect volume currents distribution. The proper segmentation and surface reconstruction procedure is essential for subsequent forward head modeling and inverse modeling of cerebral sources. The segmentation was performed with SPM software [89], which optimizes the process by bias correction, spatial gaussian filtering and voxel labeling based on probabilistic tissue maps [3]. The exemplary segmentation results and surface mesh reconstruction are presented at Fig.3.8.

To facilitate subsequent integration of EEG data with structural MR information, the exact locations of each EEG electrode in 3D space were recorded with Localite Neuro-Navigation system, and co-registered with 3D brain images by an iterative surface matching procedure performed with SPM software [89]. The procedure minimizes the summed square of the distances between electrode positions and the surface of scalp tissue extracted in segmentation step as described earlier. As a result, the information about each electrode position in relation to the underlying cortical tissue is recorded for future analysis. The combined structural information, coregistered electrode locations and dynamical EEG information can be then used to construct precise, subject and session-specific forward models (projection of arbitrary 3D brain source onto 2D scalp surface)

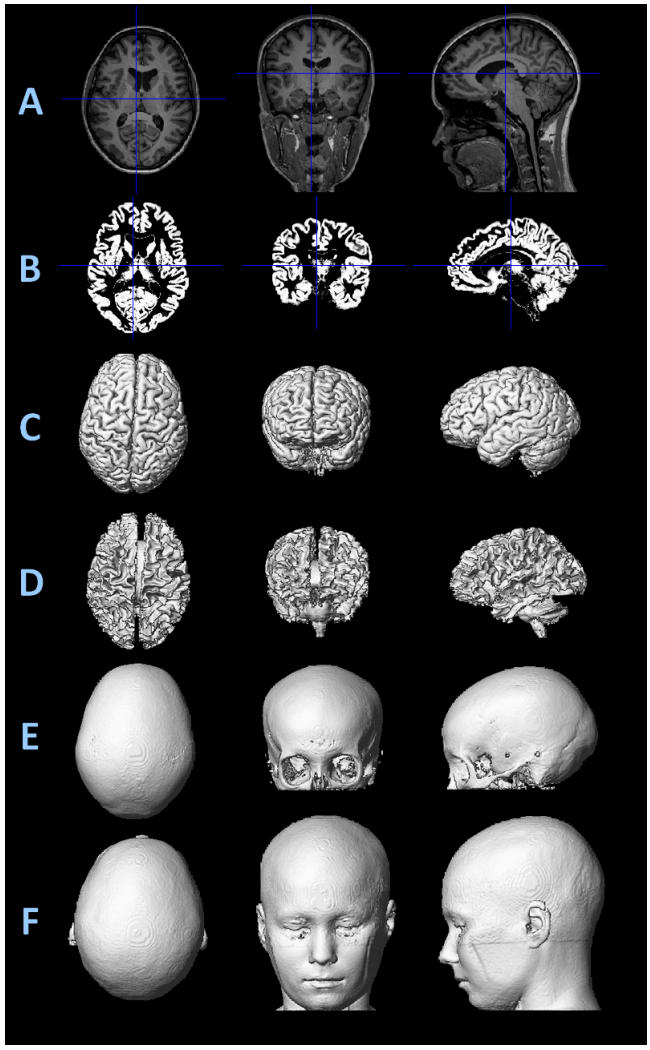

Figure 3.8: Segmentation of brain tissue and reconstruction of surfaces are the preliminary steps to compute forward and inverse head models. The exemplary procedure for one of the participants in Study 2 is presented. **(A)** T1-weighted, three-dimensional anatomical image of the whole brain, on sagittal, coronal and axial planes respectively. **(B)** Gray matter (cortical sheath) isolated in segmentation process. The segmented, three-dimensional images are used for surface reconstruction of the cortex **(C)**, white matter **(D)**, outer skull **(E)** and scalp **(F)**, for each participant independently.

and to compute inverse solutions (projection of observed 2D scalp distribution onto anatomically constrained 3D space of brain tissue). The Fig.3.9 illustrates an exemplary electrode coregistration results and 4-shell forward model construction based on anatomical participant-specific constraints.

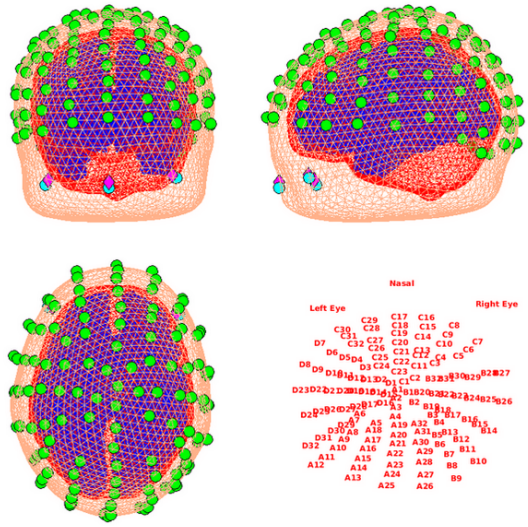

Figure 3.9: The electrode relative locations in space were measured with Localite Neuro-Navigation system. The iterative surface matching procedure (SPM toolbox) was used to align the electrodes and fiducial points with the scalp surface extracted from T1-weighted anatomical images. The combined spatial information about surfaces and electrodes can be used to construct multi-shell, boundary-element (BEM) forward models projecting activation of arbitrary brain source onto channel space. Inverse models can be computed, often based on probabilistic bayesian inference, to provide estimated projection of given current distribution in channel space onto three-dimensional brain volume (ill-posed problem).

Finally, the individual head models can be used to reconstruct neuro-anatomically constrained sources of the brain activity. Each reconstruction is based on a relevant topographic activation map, constructed from the activation of all electrodes (for instance Alpha power) averaged over a certain time interval. The normalization of subject-specific source estimates to the MNI space allows to represent the across-subject source localization results in a standardized coordinate system and perform statistical comparisons in voxel space. The Fig.3.10 presents estimated sources of Alpha and Beta oscillations from Study 2, representing the voluntary decision of whether to turn the car or not. The probabilistic, distributed source estimation methods were used, based on smooth Loreta priors and constrained to cortical tissue volume, as implemented in SPM toolbox [89].

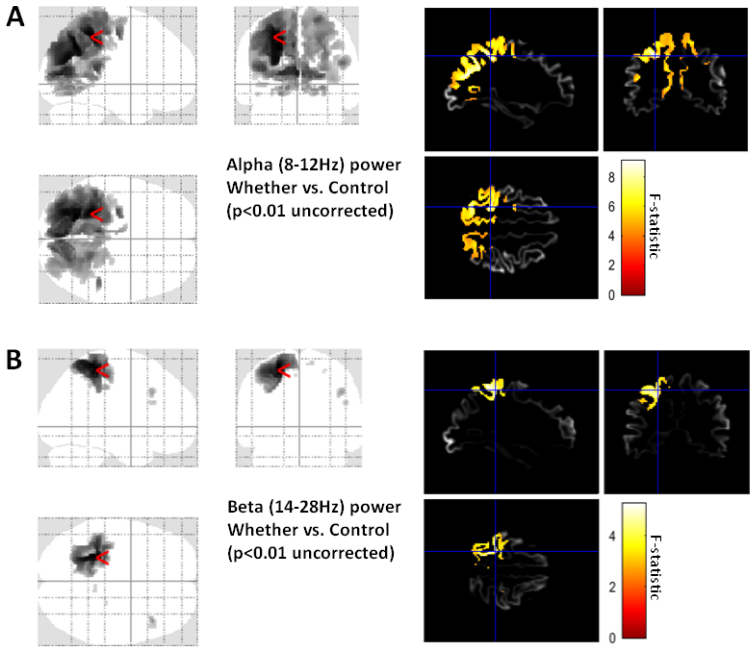

Figure 3.10: Source reconstruction of Alpha (panel A) and Beta (panel B) oscillations characterizing voluntary decision of whether to turn a car or not (Study 2). The statistical inference was performed after normalizing individual subject source estimates to standardized MNI space. Individual source estimations were based on the probabilistic bayesian inference with smooth Loreta priors, constrained to cortical tissue extracted in segmentation step, as implemented in SPM toolbox.

3.4.8 Cross-frequency coupling

As mentioned in the previous chapter, converging evidence from electrophysiological studies suggest that oscillations in low and high frequencies are functionally coupled (cross-frequency coupling, CFC), and that dynamics of the CFC may reflect a fundamental mechanism for establishing functional workspaces of distributed brain areas [19, 78, 163], communication between local and global networks [78] and possibly for functions of consciousness [25]. Bursts of fast Gamma oscillations tend to occur preferentially on certain phases of slower Theta and Alpha waves [88], often in a task-dependant manner [162, 163]. Brain oscillations at different frequencies can interact in various ways, one of them being the phase-amplitude (PAC) coupling, where the amplitude of high-frequency oscillations is modulated by the phase of low-frequency oscillations. Analysis of PAC can provide a complementary information to the time-frequency analysis. The majority of PAC examples in literature is based on intracranial recordings,

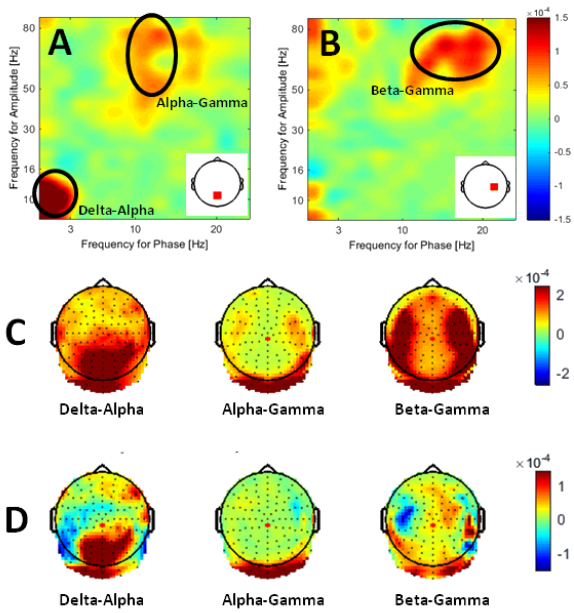

Figure 3.11: Phase-amplitude coupling (PAC) was evaluated for "'Whether" type of decisions from the Study 2. PAC was assessed by computing the Modulation Index (MI) for all 128 channels and all frequency pairs from the range 1-24Hz (frequency for phase) and 6-80Hz (frequency for amplitude) for the 2 seconds long epochs encompassing voluntary decisions. **Panel A:** Comodulogram (for occipital midline electrode, Oz) is computationally expensive to compute however efficiently scans for PAC interactions between any frequency pairs within band of interest. Delta-Alpha and Alpha-Gamma coupling is clearly visible at occipital area. **Panel B:** Comodulogram for right motor area electrode (C4). Beta-Gamma coupling is dominating. **Panel C:** Topographic distribution of MI for Delta-Alpha, Alpha-Gamma and Beta-Gamma pairs in "Whether" decision condition is non-random and covers parietal, occipital and bilateral motor areas respectively. **Panel D:** Topographic distribution of difference of MI between "Whether" and "Control" conditions. The positive and negative values reflect that PAC is task modulated.

ECoG and LFP. Evaluation of PAC is not easy with EEG modality because the estimates of the amplitude of high frequency signal are less reliable.

However, we applied PAC analysis to decision conditions from the Study 2 and consistently observed interactions for three pairs of frequencies - Delta-Alpha, Alpha-Gamma and Beta-Gamma (Fig. 3.11). We assessed the PAC for all the 128 channels and all frequency pairs from the range 1-24Hz (frequency for phase) and 6-80Hz (frequency for amplitude) for the 2 seconds long epochs encompassing voluntary decisions. The method proposed by Tort et al [158] was used, which consists of extracting instantaneous phase of low-frequency oscillatory signal and instantaneous amplitude of high-frequency oscillatory signal

(by means of Hilbert tranform of narrow band filtered signal), followed by calculation of Modulation index (MI). The MI measures the distance between two distributions and calculates how much the amplitude distribution over phase bins deviates from the uniform distribution. Our preliminary results suggest that PAC was consistently found between three pairs of frequencies (Fig. 3.11, panels A and B), had non-random topographic distribution covering parietal, occipital and bilateral motor areas (Fig. 3.11, panel C), and to certain extent was task modulated (Fig. 3.11, panel D). Further analysis is needed however to assess the statistical power of those estimates.

Chapter 4

Study 1: Brain rhythms of voluntary action and intentional inhibition.

The nature of voluntary action has been investigated in contexts of subjective free will ([46, 85, 112]), internally and externally generated actions [27, 120, 166], neuroanatomy of volition circuitry [39, 45, 52, 153]. Most of the studies however focus on free-paced voluntary action (so called intention-in-action), which has certain limitations. Furthermore, very few studies exploit fully the time frequency analysis to infer about broadband brain oscillations reflecting decision processes.

In the Study 1 (Manuscript 1, reprinted in Appendix A), we investigated the EEG signature of voluntary decision about future action. We deliberately introduced delay between a decision and its resulting action, in attempt to disentangle those two processes. We show that both decisions "to act" and decisions "not to act" share some common neural processes probably related to introspective attention and options selection, manifested by a prolonged modulation of the Alpha and Beta oscillations. However, those two decisions differ by other neural processes, presumably related to motor preparation and manifested by modulation of Gamma rhythms and contralateral components of Alpha and Beta. After voluntary decision "to act", the further preparation for voluntary action is in-

distinguishable from a preparation for externally-cued action, and is reflected by early contingent negative variation (CNV), lateralization of Alpha (αLERD) and broadband power desynchronization (ERD). However, those preparation processes are abandoned in case of voluntary decision "not to act".

We also found that the magnitude of αERD in free decision interval was positively correlated with reaction times in Decision condition but not in Control condition, i.e. participants with the most emphasized αERD tended to respond faster, even though the decision interval (and thus the peak of the αLERD) preceded the action by interval of several seconds. On the other hand, the magnitude of CNV deflection was positively correlated with reaction times only in Control condition, but not in Decision condition. Indeed, in the Control trials it was the visual stimulus, rather than the internal decision, that guided the action or inhibition, and thus the stronger CNV might reflect the capacity to perceive and categorize the informative stimulus and generate quick response accordingly.

In summary, we suggest that Alpha and Beta oscillations play an important role in voluntary decision about prospective action, and may represent the cognitive processes inherently associated with internal action selection and action inhibition. The ability to understand and detect the oscillatory activities in different frequency bands will not only help to comprehend the processes of volition, but can also support the work towards designing enhanced, intention-driven BCI systems in the foreseeable future.

Chapter 5

Study 2: EEG signature of voluntary decisions in Virtual Reality Environment.

The capacity to perform a voluntary action and freely choose action parameters is one of the fundamental qualities of human nature. It has been proposed that decision about voluntary action has distinct, complementary components, such as decisions "what" to do, "when" to do, and "whether" to do or not [13, 45]. Those components have different functional role and can be mediated by distinct neural substrates [45, 49].

In Study 2 involving EEG and Virtual Reality Environment (Manuscript 2, reprinted in Appendix B), we investigated temporal and spectral differences between different types of voluntary decisions. In attempt to enhance the natural decision processes in the brain and reduce random sequence generation, we replaced pictogram-based task with a simulated car driving in a dedicated Virtual Reality Environment (VR).

We show that, similarly like in Study 1, voluntary decisions are manifested by prolonged alpha and beta power modulation. However the magnitude and timing of EEG signatures differs in distinct types of decisions. *Whether* decisions have the strongest manifestation in broadband power desynchronization

extending up to gamma range, while *What* decisions are represented by earlier positive ERP deflection. The *When* decisions had the weakest spectro-temporal representation and did not differ statistically from the control condition.

Furthermore, we observed that voluntary actions are subconsciously biased by low-level behavioral preferences, such as the preference to the "first" over the "second", the "right" over the "left" and "acting" over "not acting". This regularity can explain a part of the entropy of the "free will"-driven behavior, at least in the contexts where random or exploratory behavior is probed, and no direct rewards are associated with alternative choices.

Chapter 6

Virtual Reality Environment for scientific study of cognition

In a large part of our empirical studies we decided to use a dedicated car driving simulation, the Virtual Reality Environment (VR), in place of standard, pictogram-based visual stimuli. The application of the VR in neuroscientific study of voluntary action was presented in Manuscript 2 (reprinted in Appendix B), while the details of the VR design and applicability to neuroimaging studies in general are discussed in Manuscript 3 (reprinted in Appendix C). Below, I briefly discuss the general motivation, design features and construction of the VR platform.

6.1 Motivation

The motivation for VR comes from the following rationale. Primarily, by providing ecologically valid, semi-realistic experience we aimed at reinforcing the natural decision processes and minimize the problem of random-sequence generation [51]. Secondly, the game environment promotes active participation of

subjects in multiple repetitions of the task and reduces the undesired influence of fatigue and/or boredom. Thirdly, the car driving paradigm is a suitable and naturally appealing setup for the purpose of the study of voluntary action, i.e. investigating the nature of intention formation and the differences between *Whether*, *What* and *When* types of voluntary decision [13].

6.2 Requirements

A virtual environment (or a gaming environment in general) in context of neuroscientific experimentation must fulfill certain criteria. First of all it needs to be capable of synchronization with specialized equipment with millisecond-range precision, so that the brain signals from EEG and fMRI, and eye-tracking information, can be correlated with environmental events. Secondly, it needs to accept alternative inputs (specialized input devices in MR scanner, or neurofeedback control signal in BCI setting). The platform must be highly flexible to allow the experimental manipulation, such as carefully planned timing and type of events, randomization of conditions, specification of visual aspects of scenery such as brightness, visibility, distribution of distractors. Finally, in context of our study, it was crucial to minimize the unnecessary, task-irrelevant motor activity. In particular, we wanted the car to automatically follow the curvature of the road, while participants intervention was only required when they intended to turn at a cross-road. This enabled us to focus on volition related motor and cognitive processes, while minimizing the task-irrelevant, confounding motor activity which would be otherwise needed to sustain the car on the road. Since it was not possible to find off-the-shelf product meeting the above requirements, we have designed our own dedicated VR environment.

6.3 Design and implementation

Our primary goal was to implement the VR environment in a flexible fashion, to facilitate its potential application to different experimental settings, such as studies of volition, attention, brain-computer interfacing (BCI), etc., and with different modalities (EEG, fMRI, Eye-tracking), thus rendering it useful for potential future follow-up studies. So far, the VR design was used to perform series of studies investigating voluntary action, using EEG (presented in this thesis in Chapter 5) and in parallel studies involving fMRI imaging (in preparation). Besides, we have adapted and tested the VR in real-time BCI context, where the classified EEG/EOG signals (such as occipital alpha power, or horizontal eye

movements) were used as a control signal to interact with environment (turn the car, reduce speed, etc).

The graphical part and physics of the car simulation were implemented in Unity3D platform, backed by C# and JavaScript programming languages. The experimental design is specified by set of Matlab based scripts. Notably, the game logic, graphical scenery and the car behavior, are all governed by precise specification provided by the experimenter.

The main VR features, relevant to our studies but also the neuroscientific experimental approaches in general, are listed below.

Modularity and Configurability The entire game logic (experiment design) is entirely defined by external XML files, which are read and effectuated by the game engine at the start of each block. The configuration files are provided by experimenter, and specify the following aspects of the experiment: number and sequence of trials, the exact shape of the roads, position and type of the crossroads, size of the scene and thus duration of the trial, speed profile of the car, instructions displayed at the beginning of each block.

Alternative inputs The game does not read keyboard input directly, but instead reads control signals from input text file. The text file in turn can be updated by any arbitrary input device with help of supportive external scripts (i.e. fMRI compatible touchpad). In particular, the file can be updated by BCI classifier thus rendering VR suitable to run in brain-interface closed-loop.

'Smart' roads The road is constructed from the set of invisible control points specified by experimenter. This serves several purposes: (1) the road is generated automatically by spline interpolation between points, (2) every control point can cause certain event, such as car turning at the cross-road or car changing speed, (3) car can automatically follow road curvature, (4) the points of interest (such as cross-road or tunnel entry) can send hardware trigger to external devices.

Auto-pilot mode The invisible control points on the road allow automatic adjustment of car orientation to be tangent the road curvature at each time point, making the car automatically follow the road. This reduces motor activity of the participant only to requested situations, such as turning at the crossroad. Secondly, the car can automatically turn to specified cross-roads, which is important for Control condition (discussed later).

Synchronization Any event in the game, such as car reaching a certain control point on the road or participant pressing a button, can cause immediate execution of external executable script. In particular, this mechanism is used to send hardware triggers (via parallel port) to data acquisition equipment (through Biosemi synch-box to EEG and Eye-tracking acquisition computers).

Time-sensitive event logging Apart from hardware triggers, the game generates regular, equally time-spaced status logs and stores them in text file. The information stored is time stamp since the beginning, car position, orientation, speed, current block and trial.

Visual features Most of the environment features and their graphical appearance are configurable, such as fog density, height of mountains, camera position, textures, types and positions of distractor objects such as trees or buildings, etc.

Trial-to-trial teleport Participants have the feeling of continuous, uninterrupted navigation through sceneries, separated by tunnels. In practice, each scenery is an identifiable, trackable, counterbalanced, pseudo-randomized trial. The smooth transition is realized by teleporting the car (while surrounded by dense fog in the tunnel) from trial n to n+1 upon reaching the final control.

6.4 Experimental setup - VR, EEG and ET

The block diagram of VR design and synchronization with multi-modal EEG and eye-tracking data is presented in the Fig. 6.1. Set of Matlab scripts specifies experimental design details, in particular it defines the trials and pseudo-randomizes them, specifies instructions displayed to participant, determines exact shape of the roads and positions of the crossroads. For each block of the experiment, one Unity3D game is compiled, based on the specified experimental design. Thus the exact contents and timing of each game is a priori determined to meet requirements of the repetition based, cognitive experiment.

During the experiments, fast electroencephalographic data from participants scalp were recorded with 128-channel Biosemi ActiveTwo system, along with EMG and EOG signals, as detailed in 3.1.1. Simultaneously, eye-tracking data were acquired with SMI system. The synchronization between the VR, EEG and ET is achieved through hardware triggering, namely every relevant event

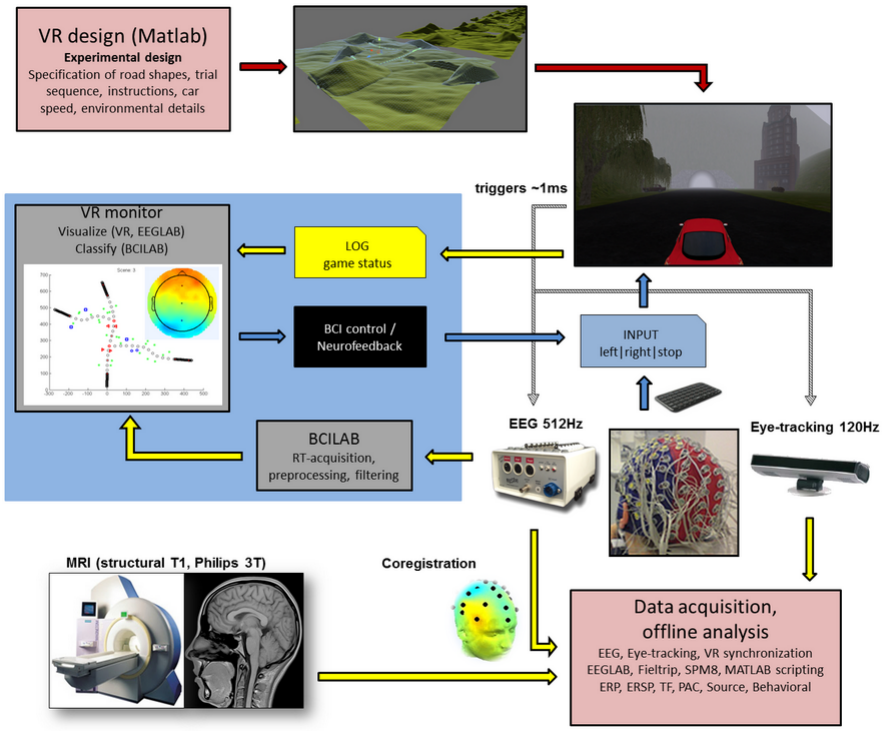

Figure 6.1: VR design and synchronization with multi-modal data. A set of Matlab scripts specifies experimental design, i.e. sequence and timing of trials, shape of roads, position of crossroads, etc (top). For each block of experiment, one Unity3D game is compiled, based on the specified experimental design (top-right). During the cognitive experiment, fast encephalographic data from participants scalp and eye-tracking data are acquired (mid-right), which are synchronized with the game events by hardware triggering. Prior to the main experiment, structural MR images of participant brain are recorded with Philips 3T scanner (bottom-left). EEG signals can then coregistered offline with structural MR images by means of 3D electrode position measurements (Localite NeuroNavigation system). The blue shaded area (mid-left) demonstrates VR used in real-time, closed-loop mode (BCI). The VR-monitor application loads and preprocesses EEG data and the game status logs. The real-time visualizations are generated, and optionally - a control signal brain data can be computed (i.e. Alpha oscillatory power) and supplied as input to the game.

in VR game executes external script communicating with Biosemi SynchBox through parallel port.

The optional BCI operation mode of VR is presented as shaded blue area at Fig. 3.1.1. The signals are recorded in real-time with support of low-level functions of BCILAB toolbox, providing real-time data acquisition and buffering. After a minimal preprocessing (filtering and thresholding), the data are presented by VR-monitor Matlab-based application in either raw or band-filtered form, along

with status information from the game (position of the car on the road, trial number, etc). Based on real-time EEG signals, simple threshold measures can be defined (i.e. topographic laterality, or averaged power of selected channels) to generate control signal, which in turn can be delivered back to VR game (closed-loop), through input file. This functionality can serve as a BCI control signal (steering the car), or as a neurofeedback (information provided to participant through VR messaging).

Moreover, some other relevant data, are recorded independently before and after the main experiment. These include structural MR images of participants brains with 3T Philips scanner, and spatial coordinates of electrodes in relation to scalp recorded with Localite NeuroNavigation systems. Combining those with multivariate EEG timeseries is performed offline, and can significantly improve the precision of source localization and spatial normalization of signals.

6.5 Modular construction of Virtual Reality for neuroimaging research.

The VR was constructed with the purpose of extensibility and adaptability to wide range of neuroscientific experiments. One of the main design goals was to achieve modular structure by separation of the implementation layers from experiment design layer. In Manuscript 3 (reprinted in Appendix C), we discuss this concept along with design challenges and benefits of virtual environments in neuroscientific research. Exemplary data from fMRI and EEG recordings in VR setup is also presented.

Chapter 7

Conclusions

7.1 Discussion and conclusions

The work presented in this thesis is a selection of results, problems and accomplishments from the last four years of my research, aiming at measurement of EEG signatures of human intentions, voluntary decisions and free actions. During the process I managed to find answers to some of the initially posed questions, while, on the other hand, many further ideas and research prospects emerged, which I will discuss in the further section. It is important to emphasize here, that the results presented here are only a very modest contribution to the growing and evolving field of the neuroscience of volition.

Considerable part of the efforts focused on methodologies of EEG signal processing and of complex stimulus presentation in alternative experimental designs (VR platform). The former resulted in development of methods for automatic data preprocessing and efficient artifact cleaning, which is highly data-preserving and based on minimal number of arbitrary parameters (see Appendix D). Secondly, number of supportive tools were developed (combining in-house methods with the functionality of EEGLAB, Fieldtrip, SPM toolboxes) to perform efficient time-frequency and phase-amplitude coupling analysis, cross-modal integration of EEG with sMRI and ET, visualizations of multi-dimensional statistical analysis of the EEG data.

The latter resulted in development of a dedicated Virtual Reality (VR) car simulation with the purpose to provide a natural platform for neuroscientific studies of cognition in semi-realistic, yet strictly controllable, experimental environment. The main motivation was to reinforce the natural cognitive processes and minimize the problem of random-sequence generation and promote active participation in the highly repeatable cognitive tasks. Our goal was to design the VR platform in a modular and customizable way, separating experimental design layer from the implementation and graphical representation. In this way, the VR after moderate modification can be used to pursue many experimental questions related to volition, perception, attention, action preparation and others. In particular, the car driving paradigm was a suitable and naturally appealing setup for the purpose of our studies of voluntary action. As such we have successfully applied it to the range of empirical studies using EEG (see Chapter 5), fMRI (see Chapter 6, details reported elsewhere) and Eye-tracking (see Chapter 3). The closed-loop setup for the purpose of BCI studies was also tested (see Chapter 6). The details of the modular structure of VR and discussion of rationale and feasibility of Virtual Reality environments in neuroscience are presented in Chapter 6 and Appendix C.

The main part of the work was dedicated to electrophysiological correlates (measured with EEG) of voluntary decisions about prospective actions. In both Study 1 and Study 2 we imposed a time interval separating decision processes from subsequent action execution, in attempt to disentangle the intention formation from the respective motor implementation. Study 1 was based on standard pictogram-based design (PsychoPy platform), while the Study 2 employed the rich, constantly changing visual stimulation (VR platform).

The Study 1 investigated EEG signatures of the neural processes related to voluntary decisions "to act" or "not to act" in context where respective motor response are postponed in time. The results suggest that the occurrence of voluntary decisions can be detected by scalp recordings, and distinct spatio-temporo-spectral patterns can distinguish between early intention "to act" or "not to act". The decision is manifested by prolonged, global desynchronization of Alpha and Beta oscillations, dominating in parietal areas. Only in decisions "to act", the Alpha and Beta desynchronization was significantly lateralized, and assisted by brief modulation of Gamma oscillations. The Alpha oscillations seem to reflect the chain processes related to conscious decision, while its spatial distribution can suggest possible involvement of motor preparation/imagery processes related to a prospective action. The action preparation, as assessed by CNV and broadband desynchronization, is abandoned in case of voluntary decision "not to act". However, the action preparation remains unchanged regardless if subject voluntarily decided "to act" or merely expects an external guidance. For detailed description of the study results see Chapter 4.

In the Study 2 we investigated three types of voluntary decisions (What, When, Whether), their spectral signature and the possibility to detect and distinguish those decisions from EEG scalp recordings. The Study 2 was also a feasibility study for the VR platform in context of neuroscientific study of higher cognitive function. The voluntary decisions were manifested by prolonged Alpha and Beta power modulation (effect similar as reported in the Study 1). However the magnitude and timing of EEG signatures differed in distinct types of decisions. "Whether" decisions were manifested by the strongest and most prolonged Alpha ERD, assisted by significantly higher Gamma power. The "What" decisions were represented by the early positive ERP, while the "Whether" decisions by the late positive ERP deflection. The "When" decisions had the weakest spectro-temporal representation and did not differ statistically from the control condition. Furthermore, we observed that voluntary actions are subconsciously biased by low-level behavioral preferences, such as the preference to the "first" over the "second", the "right" over the "left" and "acting" over "not acting". The latter was also observed in the Study 1. This regularity can partially explain the entropy of the "free will"-driven behavior, at least in the contexts where random or exploratory behavior is probed, and no direct rewards are associated with alternative choices. For detailed discussion of the Study 2 see Chapter 5.

In summary, our main findings suggest that decision processes are detectable by EEG scalp recordings. Furthermore, different types of decisions (What, When, Whether) have partially different temporal and spectral representation, which goes in line with other fMRI studies showing involvement of distinct neural pathways in different types of decisions. Alpha, Beta, and Gamma oscillations seem to play important role in voluntary decision and intention formation. The dominating Alpha desynchronization in decision interval may reflect at least two categories of neural processes - motor-related preparation/inhibition of action, and cognitive components related to conscious act of volition and introspective attention to that act.

7.2 Future work

The work presented in this thesis certainly has not exhaustively exploited all possible analytical approaches nor the potential of the rich multi-modal data that we collected in the Study 2. In the following, I will highlight several other methodological approaches and preliminary results obtained in context of the Study 2, which will be tentatively elaborated on and published in the course of my future research.

EEG and MRI In the Study 2, we have acquired the structural T1-weighted MR images of all the participants (3T Philiphs scanner), and spatial positions of electrodes in each session (Localite Nuero-Navigation system). We have preprocessed the data to segment out different brain tissues and compute subject-specific head models. In preliminary attempts, we obtained anatomically plausible Bayesian source estimates of decision related Alpha/Beta brain oscillations in the parietal cortex and motor areas. The procedure is briefly highlighted in Chapter 3, however further work is needed for concluding and reporting the source localization results. This approach can help to relate our findings to other studies based on fMRI and PET modalities, as well as improve signal-to-noise ratio by accounting for subject and session specific variability. Furthermore, in the series of parallel studies involving fMRI and VR (reported elsewhere, in preparation) we have found multiple brain regions being active in What, When and Whether decisions, in particular the prefrontal cortex and the preSMA region. In Bayesian framework, the statistically significant voxels in fMRI contrasts can be used to form anatomically constrained priors to the probabilistic EEG source modeling, and thus further enhance precision and interpretability of the source estimates.

EEG and ET In the Study 2, we have acquired eye-tracking activity, including gaze position and pupil dimension. We have preprocessed and coregistered the ET time series with the EEG activity, and with the VR events (as discussed briefly in Chapter 3). The information was used for validation that subjects obeyed the eye-fixation instructions, however the potential of the dataset is considerably larger. The statistical analysis of the saccadic activity and pupil dillation in relation to cognitive processes of voluntary decision deserves a further investigation and tentatively an independent report. Our preliminary results reveal that horizontal eye saccades predict early the direction of the intended turn, and that decision processes are reflected by on average 3-4% pupil dilation.

Cross-frequency coupling The considerable part of the EEG analysis performed in Study 1 and Study 2 was focused on broad-band time-frequency analysis. We observed the selective modulation of oscillations in Alpha, Beta and Gamma ranges. Thus a natural, data-justified, next step is to investigate interactions between those different frequencies. One of the common methods to evaluate this interaction, exploited mostly in ECoG and LFP recordings, is the phase-amplitude coupling (PAC). A growing number of studies suggest that Theta-Gamma and Alpha-Gamma coupling is relevant to cognitive function and may constitute fundamental mechanism for information coding and dynamic formation of functional workspaces in the brain. Our preliminary PAC results from the Study 2 (discussed briefly in Chapter 3), suggest that: (1) PAC can be reliably

detected by scalp EEG, (2) PAC is topographically organized for different frequency pairs, (3) PAC is task-modulated and thus plausibly can be applied as an alternative method of further investigation of voluntary decision.

Real-time decision decoding In both Study 1 and Study 2 the off-line analysis showed that the patterns of modulation of the brain oscillations were not identical for different types of conscious voluntary decisions and their outcomes. It would be of utmost interest to quantitatively evaluate the feasibility and accuracy of single-trial classification of those decision processes. Future work along this path could aim at designing enhanced, intention-driven BCI systems in place of current systems which are based on less-natural processes such as imagery, visual or auditory attention. With this prospect in mind, we have designed and tested our VR platform in the closed-loop BCI mode, which can support future experimental attempts to tackle the real-time classification of natural decision processes.

7.3 Final word

The neuroscience of volition is a challenging and uneasy domain of human sciences. The effects being pursued are rather subtle in their nature, subjective, context specific, and often intermingled with other cognitive processes. It is nontrivial, and perhaps not even feasible, to isolate the mere act of volition from other neural processes such as introspective attention and self-monitoring. Yet understanding of the phenomena of voluntary action is the key to understand a fundamental aspect of a human nature - the capacity to exert a "free action". As such it can profoundly affect the fields of psychology, psychiatry, legal system, nature of social phenomena, and many others.

With the work presented in this thesis, we only contribute a single drop of insights into the ocean of research focused on this fascinating subject. I believe it is essential for the science to tackle and to probe the mystery of human "free action" from all possible angles, including neuroimaging of the anatomical sources, observation of the fast electrophysiological characteristics and the behavioral correlates, developing diverse experimental paradigms, constructing physiological and conceptual models of volition. The emerging field of neurophilosophy can help to build plausible theories and interpretations, combining the rapidly growing database of neuroscientific insights with the centuries of experiences from psychology, psychiatry and philosophy fields. The mechanistic understanding of the neurophysiological processes involved in internal action generation at some points need to address subjective nature of conscious perception of "self" and

"will" - only then can we claim that the problem of volition was fully resolved. Otherwise, it remains rather disputable if "internally-generated action" is equivalent to "free action", and if the fact of an action being generated by internal processes, disregarding conscious perception of "will", categorizes this action as "freely willed".

Every human being understands, deeply and intuitively, the quality of being "free". Nevertheless, the pure definition of this term in the context of brain, mind and consciousness is not trivial. Perhaps one day we will be able to understand the strict meaning of this term sufficiently enough to pass this unique insight to a human-invented machine. Perhaps not.

Appendix A

Manuscript 1: Brain rhythms in voluntary action and intentional inhibition

Brain rhythms in voluntary action and intentional inhibition.

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Abstract

The nature of volition and free-will has long been investigated by neuroscientists and philosophers of mind. One of the most critical aspects of free human behavior is a voluntary decision of "whether" to commit to an action or not. It has been suggested that decisions not-to-act are by no means passive but involve similar neural components as decisions to act. In this EEG study we investigate spectral signatures of intention 'to act' and 'not to act' in early stages of voluntary decision formation, as well as compare their differential activations in later stages of response preparation. In particular, based on multi-channel time-frequency analysis we found that desynchronization patterns in alpha and beta band distinguish decision processes from passive expectation, while lateralization of alpha and power modulation of gamma discriminates between decisions 'to act' and 'not to act'. We discuss the role of broadband oscillations in intention formation and preparation of voluntary motor response, and suggest that the alpha and gamma oscillations may play important role for early neural processes governing human free action.

Keywords:
voluntary action, intention formation, motor preparation, alpha oscillations, presupplementary motor area (preSMA), electroencephalography(EEG)

1. Introduction

One of the most critical aspects of free human behavior is a voluntary decision of "whether" to commit to an action or not [32, 48, 91].

The nature of free voluntary action, and its relation to widely understood concept of “free will”, has been debated by philosophers of mind for centuries.

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The famous study of Libet's clock [53] directed attention of neuroscientific community to the problem of volition. The study showed that readiness potentials (RP) recorded with scalp EEG precede not only the action, but also the conscious awareness of the will to perform that action, which challenged the notion of "free will" and human freedom. The original findings of B.Libet were targeted by skeptical critic [7, 63], but also reproduced and elaborated by other groups. For instance, Haggard et al [34] showed that lateralized readiness potentials (LRP) precede awareness of directionality in free choice between left and right index finger, while Fried et al [25] reproduced Libet's paradigm showing that firing rates of single neurons in presupplementary motor area (preSMA) predicts awareness of volition up to 1 second. It has been also proposed that "free will" might be manifested by the ability to consciously inhibit unconsciously initiated action, which can be conceptualized as "free won't" [52].

Notably, all neuroimaging studies of volition are purely correlational, and none has proved a causal, executive function of a particular brain area which could be labeled as the origin of intention formation. Considering complex, recurrent nature of brain circuitry, even the mere idea of existence of such true origin is conceptually difficult. Any activity within neural assembly, dendritic current or action potential has its own biophysiological cause. It is rather within neural loops, constantly updated by current and past contexts, where the actions are originated. Those loops may include parietal cortex, basal ganglia and prefrontal areas with preSMA [32]. Thus more tangible understanding of volition is to consider it as a capacity of an individual to allocate attentional resources to the action-selection processes performed constantly in the brain, along with the capacity to make the meaning of action and its causes, and thus to assume ownership/agency over the outcome of resulting action [77]. "Free will" is not a specific cognitive property or ability, nor has it a causal power. It is rather an outcome of chain of causal events in the brain, and as such should not be studied in isolation - perhaps processes such as introspective attention, conflict processing, knowledge access constitute its intrinsic and necessary part.

Regardless whether neuroscience can or cannot provide the final answers to the hard problem of direction of causality between consciousness and action, i.e. existence of commonsensical "free will", it may certainly address related pragmatic problems - such as determining which neural substrates are involved in free action selection [36, 48, 69], what micro- and macro-scale electrical signatures correlate with voluntary processes [25, 30, 53, 91], which neural resources are distinct and which are common to different types of free decisions [9, 35, 81], can disorders of volition [8, 57, 76] be addressed with systematic therapeutic methods, and finally - are the processes of intentional action detectable and discriminable for brain-computer interfacing (BCI) purposes [51, 86]. Along those lines, a lot of work has been done to compare two fundamental modes of action selection - internally-generated and externally-cued actions - in experiments involving fMRI [15, 16], PET [17, 36], EMG [64] and EEG [18, 88, 93] modalities. It has been shown that the two modes of action selection have different temporal characteristics [88, 90, 93] and involve distinct neural pathways [15, 17, 36, 50]. The volition-related network consists of supplementary motor area (preSMA),

which receive inputs from basal ganglia and prefrontal cortices (ACC, RCZ, DLPFC). The second network, corresponding to sensory-guided and stimulus-driven actions, starts in early sensory areas, followed by higher-level sensory integration areas in parietal cortex, which project to lateral premotor areas. Both pathways terminate in primary motor cortex (M1) which is the final stage before the efferent motor command is propagated down the spinal tract to muscle terminals [68]. It is important to note that this distinction is by no means exact or mutually exclusive. In practice, almost every action (with exception of spinal reflexes) will involve to certain extent both intentional and externally-guided components of action selection [93], and as such will to certain extent activate both pathways [15], [61] in coordinated manner. For completeness, it should be mentioned that the role of sensory areas and their connections to premotor areas in voluntary action should not be underrated. The match between predicted effect of motor command (prospective prediction) and the afferent sensory feedback (retrospective check) might be critical for the emergence of the feeling of agency [33] and perhaps for the experience of conscious will itself [94].

Brass and Haggard [9, 32] proposed a conceptual framework explaining a voluntary action as a composition of 'what', 'when' and 'whether' components, each describing different aspect of intended action . Those components account for type, timing, and initiation/inhibition of action respectively, and may have different neural representation and electrophysiological dynamics [9, 35, 48, 81]. The 'whether' component can be further divided into 'early' (decision to engage into action preparation or not), and 'late' (final validation and capacity to inhibit preprepared action). In context of this study, the time course of the 'early whether' component is investigated, which corresponds to intention formation regarding engaging or disengaging from action preparation. It has been suggested that intentional non-action is a mode of action and recruits similar neural resources as intentional action [48]. Thus 'early whether' can correspond to a choice between equivalent alternative options, and in this sense resembles the 'what' type of decision.

Growing evidence from empirical and theoretical studies indicate that cortical oscillations and cross-frequency interactions may constitute the fundamental mechanism of neural computation and effective integration of information across multiple spatiotemporal scales [12, 13, 54, 55]. Different brain rhythms and interactions between them have been associated to perception, cognition and sensorimotor function [2, 13, 41]. Thus it is very plausible that brain oscillations and selective modulation of spectral power (ERD/ERS) are the fundamental mechanisms underlying certain aspects of voluntary decisions, which motivated the methodological choices in our data analysis.

Alpha/Mu (8-13Hz) and Beta (16-24Hz) oscillations are recognized as main rhythms of motor function [5, 20, 46, 47, 70, 74, 75], both if movement is generated as response to stimulus or free-paced. Broadband reduction of power in range from Theta(3-6Hz) to Gamma(>40Hz) is observed during preparation to externally-cued action in delayed response Go-NoGo tasks [26, 27], and as such can reflect global preactivation of sensorimotor cortices and attentional orient-

ing. Desynchronization of Alpha and Beta rhythms is stronger in Go than in NoGo condition [4], and can be lateralized if precue carries sufficient information about parameters of the requested action [20]. Moreover, Alpha and Beta oscillations are modulated by motor imagery [59] and may correlate with activation of mirror neuron system during action observation [62], either of which can be reflected in decision processes. Beta bursts are also relevant to externally [47, 95] and internally [91] generated inhibition of action.

Apart from its relevance to motor function, the modulation of power in low frequency bands (Theta-Alpha,3-12Hz) had been linked to central executive function [14, 41], working-memory load [38] and attention [42]. Role of Alpha oscillations seem to be much broader than simple idle rhythm. W.Klimesch proposed inhibition-timing hypothesis [45], according to which Alpha synchronization may represent top-down inhibitory control, while Alpha desynchronization reflects gradual release of inhibition over the task-relevant areas. Given that alpha guides the attention, correlates with behavioral performance and allows memory and knowledge base access, it may be considered as a rhythm reflecting the most fundamental cognitive processes [42].

Oscillations in higher frequency bands can also be relevant to volition and free action. It has been shown that distinct gamma modulation over different cortical areas encode subsequent stages of preferential choices and free decisions [30]. Gamma is also relevant for memory and attention [39] and for execution of motor function [71, 73].

In context of motor preparation and attentional expectation of upcoming stimulus, variations of delayed response Go/NoGo tasks are commonly employed [20, 24, 26]. In such tasks participants receive a warning stimulus (S1), followed by delayed imperative stimulus (S2). A slowly accumulating negativity preceding the imperative stimulus usually by 0.5-3 seconds can be observed at central and frontal EEG channels, which is known as contingent negative variation (CNV) [87, 92]. Despite its apparent similarity to readiness potential (RP) [53], CNV reflects distinct phenomena. While RP is related to motor preparation and can occur without external stimuli [53, 89], CNV is related to attention and expectancy of upcoming imperative stimulus and is present even if overt motor response is not required [80]. Usually however, the late part of CNV will contain both lateralized RP and stimulus preceding negativity [10], where the amplitude of the former depends on parameters of the motor response while the latter on expected informativeness of stimulus. In context of externally-cued response preparation, late CNV is larger in Go than NoGo condition [22, 85] and correlates positively with reaction times.

While large number of studies elaborated on CNV and ERD effects related to response preparation in externally-cued mode of action selection, there is surprisingly few reports of the oscillatory signatures of internally-generated, voluntary actions, and those are confined primarily to Alpha/Beta bands [18, 90].

Therefore, our primary goal is to evaluate the broadband spectral contents of voluntary decisions 'to act' and 'not to act'. Given the wide functional meaning and rich cognitive associations of oscillations in theta-gamma range reported in

literature (as discussed earlier), it is very plausible that interplay between those broadband oscillations might have critical role in effectuating and synchronizing the neural processes of voluntary decisions, as well as subsequent processes of action preparation and inhibition.

We propose a paradigm in which intended actions are separated from voluntary decision by jittered interval of several seconds. We evaluate broadband neural oscillations in the early stages of decision (formation of intention about future action) and in later stages of action preparation (effectuating or inhibiting action), and compare the modulation of signal to idle control condition, in which participants do not generate internal decision but act according to external cue. The motivation for such paradigm is twofolds. Firstly, in daily situations it is common that voluntary decision about action does not result in instantaneous implementation of the respective motor command, but often in formation of intention to perform a given action in future, where the delay can range from seconds to days. Secondly, other paradigms which involve a free-paced voluntary action, and thus do not specify the exact timing of decision, face at least two main challenges. In case of voluntary decision to act, the neural processes of action selection and intention formation may be confounded by immediately following processes of action preparation and motor implementation. Secondly, in case of voluntary decision not to act, there is no overt response and thus it is difficult to localize in time the onset of neural processes corresponding to intentional non-acting, or inhibition. It is impossible to determine whether the lack of action results from explicit conscious decision "not to act" or perhaps from the passiveness and lack of decision process at all. Our paradigm resolves those two major issues by (1) time-locking decision and action to visual cues (precue and cue respectively), and (2) imposing jittered interval of several seconds between decision (intention formation) and action (motor preparation and execution).

Since we expect broadband patterns of modulation in time-frequency domain to differ decisions from baseline, as well as decisions 'to act' from decisions 'not to act', we include in statistical analyses the entire frequency spectrum ranging Theta to Gamma band (4-65Hz). Additionally, we are also interested in action preparation that follows voluntary decision - in particular, whether ERD and CNV are modulated by mode of action selection (internally-generated vs. externally-cued), whether ERD and CNV are suppressed in case of intentional non-action and whether ERD and CNV correlate with reaction times. We also expect motor related readiness potentials (RP) to coexist with CNV, which can be verified by lateralization of RP and ERD. Notably, our Control condition resembles closely a delayed response Go/NoGo task with informative S2 cue, commonly used in studies of externally-cued action.

2. Methods

Participants Sixteen healthy adult participants (ten females) were recruited for the study. The mean age was 33.8 (std=7.3). All participants were in-

formed about the purpose of the study and signed informed consent, in accordance with ethical requirements of the local committee.

Data acquisition EEG data was acquired with Biosemi ActiveTwo system with 128 active electrodes. Two reference electrodes were positioned on left and right mastoids. Electromyographic (EMG) signal from the right index finger was recorded with surface bipolar electrodes positioned at the first dorsal interosseous muscle. All data were amplified and digitized at sample rate of 512Hz. Visual stimuli and button-press responses were synchronized with EEG signals via parallel port triggering in Python/Psychopy environment.

Task Participants were comfortably seated in front of the screen, with both wrists resting on the keyboard. The 15-inch LCD screen was positioned at the distance of 60cm from participant eyes. Stimuli width and height were set to 3cm.

Each participant performed 480 repetitions split into 8 blocks of 60 trials. To minimize fatigue and increase commitment to the task, participants could freely decide upon duration of the break between the blocks. The sequence of trials (conditions) was fully randomized within blocks. Participants were instructed to fixate gaze on the fixation cross (or corresponding symbol of identical dimensions) and avoid unnecessary movements, including eye blinks.

The scheme of the task is presented at Fig.1. In free-decision trials, the fixation cross was replaced by circle/square to indicate a Precue-interval of 2 seconds, where participants were freely choosing whether they intend to press the button or abstain from doing so. Participants were asked to take an independent decision each time and avoid pre-planning or changing mind. After 2 seconds the circle/square was replaced back by fixation cross, to indicate a Retention-interval of jittered duration of 2.4-2.6 seconds, where participants were supposed to keep their decision in mind and wait. Finally, fixation cross altered color to indicate Cue-interval of 1 second, where participants had to press or not-press the button, depending on their earlier decision. Right index finger response was used. The next trial started after jittered interval of 2.4-2.6 seconds.

In control trials, durations of all stimuli and intervals were identical. However, during Precue-intervals participants were not making decisions, but instead relaxing and passively waiting. During the Cue-interval, the color of fixation cross indicated whether the participants should press the button or not.

The assignment of a symbol (circle of square) to the Precue-interval (decision or control), and the color (blue, yellow, magenta) to the cue interval, was fixed for each participant and counter-balanced across participants. Subjects were asked to carefully memorize the meaning of symbols/colors and perform a short training session before the experiment started. Furthermore, they were asked a set of control questions between the blocks, to ensure they remembered instructions.

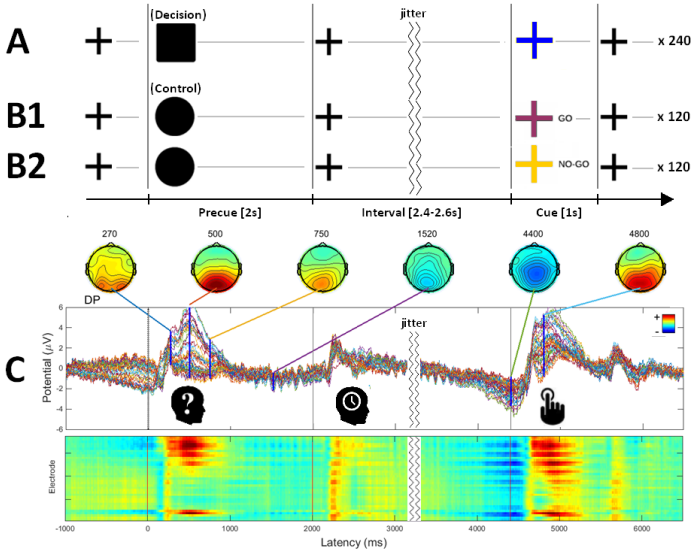

Figure 1: Experimental design and averaged EEG responses in Study 1. **(A)** Visual stimuli in voluntary decision trials. Participants make decision during of Precue interval of 2 seconds duration, maintain decision in memory during Retention interval of 2.4-2.6 seconds, perform internally-generated action (press or no-press) immediately after colored Cue. **(B)** Visual stimuli in Control trials. Participants relax and passively wait during Precue and Retention interval. Depending on the color of Cue, they press or do not press the button. **(C)** Multi-channel envelope of grand ERPs - averaged brain responses corresponding to 'Decision-Press' trials. Each time point (latency) can be represented as 2D topographic distribution of potentials (panel C top). Alternative, convenient visualization is a two-dimensional color-coded raster plot of ERPs at (channel x time) space (panel C bottom).

EEG data preprocessing The EEG data were referenced to averaged mastoids signals and bandpass-filtered at 0.2-100Hz and downsampled to 256Hz. The relatively low value of high-pass (0.2Hz cut-off) was used to account for low-frequency components of CNV traces. The long trials were extracted from -1000ms before the Precue onset until 6500ms after the Precue onset, thus covering the entire period of task-relevant events, including decisions, retention, action preparation and execution. The baseline of 1000ms preceding the Precue interval was subtracted from each trial. Short jitter intervals (0-200ms) were removed at the midpoint of the retention interval (3200ms). Noisy channels were interpolated and the remaining noisy epochs were cleaned by thresholding (moving window 500ms, threshold 120uV). Infomax ICA was computed on the precleaned datasets [66]. ICA components corresponding to eye blinks, eye movements and and general discontinuity were removed from data (EEGLAB [19] and ADJUST [60] toolboxes). Final visual inspection

was performed to ensure that no noisy epochs remained. In total, on average 37 epochs (out of 480) were removed, 5.6 channels (out of 128) interpolated, and ICA components accounting for 58.1% of total variance were corrected for, most of those related to eye-blinks and eye-movements.

ERP/CNV analysis To investigate evoked activity such as ERP and slow potentials of CNV, the trials corresponding to DP, DNP, CP and CNP conditions were averaged separately. Subsequently, the intervals of interest were extracted. The first interval of -200-2100ms, time-locked to the Precue interval accounted for ERPs related to decision task, including visual and cognitive components. The second interval of -2000-1500s, time-locked to the Cue-interval, accounted primarily for the CNV negativity related to action preparation and Cue expectation, as well as motor related ERPs after the Cue onset. Considering the sampling rate of 256Hz, the final epoch-averaged data for each condition and participant had a size of [128x590] for decision interval and [128x896] for action preparation interval, in [channel x time] space. Critically, both intervals were based on precisely the same data cleaning procedure and the same baseline.

Time-Frequency analysis To investigate induced activity and event-related changes in spectral power we applied Morlet wavelets to decompose channel data into time frequency (TF) representation. The TF information was computed for each channel and epoch at the frequency range 4-65Hz with a step of 1Hz. Time window varied from 750ms at the lowest frequency (3 wavelet cycles) to 300ms at the highest (20 wavelet cycles). The temporal resolution of decomposition was set to 64 samples/seconds. The decomposition was performed on the entire trials of -1000-6000ms, time-locked to the Precue interval, after the cleaning procedure and jitter correction (as detailed above). The time-frequency maps were baseline corrected for 500ms directly preceding Precue onset. Subsequently, the intervals of interest were extracted: -200-2100ms time-locked to the Precue interval (decision related), and -1100-1000ms time-locked to the Cue-interval (action preparation and execution). Thus the final epoch-averaged time-frequency data for each condition and participant had size of [128x62x148] for decision interval and [128x62x138] for action preparation interval, in [channel x frequency x time] space. The three-dimensional time-frequency information was used for statistical comparisons (nonparametric cluster-mass permutation tests), and for extraction of event-related spectral power perturbation (ERSP) for visualization purposes, in theta(4-7Hz), alpha(8-13Hz), beta(16-24Hz) and gamma(40-60Hz) bands.

Lateralization in time-frequency domain (LTF) was assessed by subtracting time-frequency maps of right central, centro-frontal and centro-parietal electrodes from their left counterparts:

$$LTF = (TF_{FC3} + TF_{C3} + TF_{CP3})/3 - (TF_{FC4} + TF_{C4} + TF_{CP4})/3$$

The same time interval of -200-2100ms was used, while the spectral band was set to 4-30Hz, to account for entire low-frequency range. Thus a unit of

comparison had dimension of [27x148] in [frequency x time] space.

Statistcal tests In all performed statistical tests, the multi-channel data series from Decision and Control conditions were submitted to repeated measures, two-tailed cluster-mass permutation tests [11, 58], as implemented in Fieldtrip toolbox [1]. The tests were performed both on the averaged, multi-channel signal amplitudes (ERP/CNV effects) and on the averaged, multi-channel time-frequency maps (spectral effects). Family-wise alpha level was set to 0.05. All 128 electrodes and all time points corresponding to the Pre-cue interval and the Cue interval were included in the tests. In each of the statistical tests, a unit of comparison was two-dimensional [channel x time] (for ERP/CNV), two-dimensional [frequency x time] (for spectral laterality) or three-dimensional three-dimensional [channel x frequency x time] (for TF data). In case of TF data, entire spectrum from 4-65Hz was used in the main comparisons, while in more specific tests the spectrum was constrained to low (4-30Hz) or high (40-60Hz) band (as detailed in Results sections). The electrodes within distance of less than 5cm of one another were considered spatial neighbors, yielding in average 7.8 neighbors per electrode. For each comparison, repeated measures t-tests were computed using the original data and 1000 random within-participant permutations. For each permutation, all t-scores corresponding to uncorrected p-values lower or equal to 0.05 were combined into clusters. The mass of each cluster was computed as the sum of the t-scores within that cluster. The highest cluster mass in each of the tests was used to estimate the distribution of null hypothesis.

This type of statistical tests allowed us to account for all the available data, without any a-priori constraints to either temporal or spatial extension of potential effects. Thus we minimized the need for subjective choices, while maintaining weak control of the family-wise alpha level (i.e., correcting for very large number of multiple comparisons). Cluster-mass permutation tests have been shown to perform well in exploratory studies and in case of broadly distributed ERP/ERSP effects [29, 58] by accounting for high temporal, spectral and spatial correlations inherent to high resolution EEG data, which is their fundamental advantage.

Furthermore, to evaluate relations between EEG measures (CNV, Alpha power) and behavioral measures (RT), we used Pearson product-moment correlation coefficients and R-square metrics. Finally, simple Student's t-tests were used occasionally for post-hoc assessment of ERP and laterality measures.

Correlational analysis To investigate correlation between behavior and EEG data, we first computed individual mean reaction times (one value per subject). Then we extracted the maximum negativity of CNV in the 2 seconds interval preceding action, and maximum desynchronization of Alpha power within the 2 seconds of decision interval (128 values per subject, one for each channel). Those two metrics were chosen based on the results of prior EEG analysis which suggested that CNV and αERD play important role in action preparation and voluntary decision, respectively. Finally, for each channel

we computed Pearson correlation coefficients (and R^2 values of linear fit) between reaction times and CNV/Alpha scores. Apart from reporting p-values and correlation coeffcients, we present topographic distributions of most predictive electrodes, as well as CNV/Alpha traces of slow and fast responders obtained by median split.

3. Results

The following notation will be used to denote different types of trials: **Decision** (voluntary decision trials), **Control** (control trials), **DP** (voluntary decision to press), **DNP** (voluntary decision not to press), **CP** (control with press), **CNP** (control without press).

Behavioral data The mean reaction time (RT) in Decision trials was 422ms (std=57ms). The mean RT in Control trials was 523ms (std=69ms). The RTs in Decision trials were faster than in Control trials ($p<0.001$) in average by 101ms. This regularity was observed for every participant. Detailed distribution of reaction times in DP and CP conditions is presented at Fig.8, bottom panels.

In Decision trials, all subjects displayed preference to DP over DNP. The mean asymmetry equaled 61% (std=7.3%), indicating that participants chose to press the button on average in 61% of their decisions, and intentionally abandon action in remaining 39% of decisions.

ERP analysis - Decision interval The nonparameteric cluster-mass permutation tests were performed on the multichannel ERP traces from 128 channels and covering the time interval -200-2100ms (Decision interval). Contrasting DP and DNP conditions against Control condition revealed two types of ERP effects, a posterior positive and a prolonged frontal negative components, present in both DP and DNP conditions. However their magnitude was not equal. The posterior positive component only reached significance in DNP condition ($p=0.03$), but not in DP condition ($p=0.18$). The post-hoc analysis of cluster suggests it extends over 70 posterior electrodes over the interval of 620-840ms. The frontal negative component only reached significance in DP condition ($p=0.02$), but not in DP condition ($p=0.24$). The post-hoc analysis of the cluster suggests it extends over 61 frontal and fronto-central electrodes over the interval of 650-1100ms. Direct comparison of DP against DNP condition did not yield significant differences ($p=0.18$), probably due to insufficient statistical power resulting from choice asymmetry between DP and DNP conditions (participants decided to press the button in on average 61% of trials while abstain from pressing in only 39% of trials).

The spatial and temporal extension of the ERP differences between DP, DNP and Control conditions are presented at Fig.2.

Time-Frequency analysis in Decision interval Statistical comparison of DP and Control conditions with cluster-mass permutation tests revealed two significant, negative clusters. The first cluster ($p<0.01$) was prolonged in time (490-1850ms), prevalent in Alpha (8-13Hz) but extending to Beta range (16-24Hz).

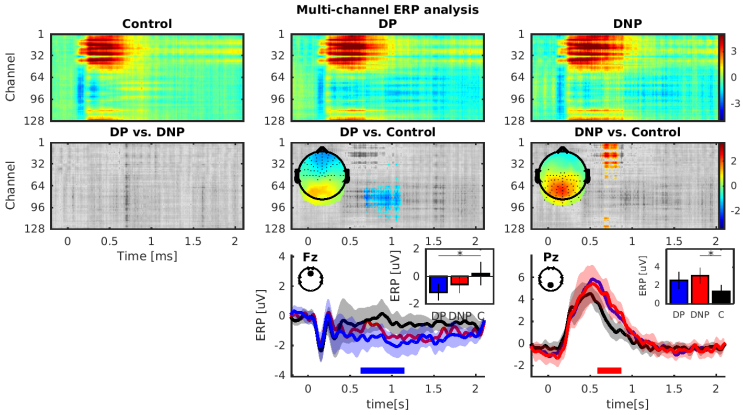

Figure 2: Event related potentials time-locked to the onset of Decision interval. **Top panels:** all the ERPs in *[channel x time]* space corresponding to Control, DP and DNP conditions. **Middle panels:** ERP differences of DP-DNP, DP-Control and DNP-Control. Statistically significant regions (cluster-mass permutation tests) are color-coded, while remaining points are shaded. Although both DP and DNP displayed larger posterior positivity and anterior negativity than Control, only DP reached significance in frontal regions, while DNP in posterior regions. **Bottom panels:** The time course with 95% confidence intervals of the ERPs for the representative channels (Fz and Pz). The inset topomaps show the spatial distribution of the significant clusters, while the inset bar-charts their average activation in the significant interval for DP(blue), DNP(red) and Control(black).

The cluster extended over all 128 channels, however αERD dominated in posterior and centro-posterior areas. The second negative cluster (p=0.035) lasted shorter (500-720ms) and dominated in Gamma band (45-60Hz). The modulation of Gamma power was strongest over frontal and fronto-central channels (Fig.3, middle column).

Statistical comparison of DNP and Control conditions revealed only one significant negative cluster ($p<0.01$), similar in its extension to the Alpha cluster of the DP-Control contrast. It was prolonged in time (560-1830ms), spread over Alpha (8-13Hz) and Beta ranges (16-24Hz), extended over 128 channels with αERD dominating over posterior and centro-posterior channels. There were no other significant clusters, in particular not in Gamma band (Fig.3, right column).

The direct comparison of DP and DNP in entire [channel x frequency x time] space did not reach significant effects. As mentioned before, statistical power of this comparison is reduced by considerable choice asymmetry (61% DP, 39% DNP). Therefore, to test difference in Gamma band between DP and DNP conditions we constrained the region of interest spectrally to 40-60Hz range and temporally to 500-1000ms interval, while still accounting for all 128 channels. The choice can be justified by the following three rationale: (1) the interval corresponds to ERP effects, (2) the interval corresponds to the onset of ERD in Alpha/Beta bands, and ERD reaching its peak values, (3) the spectral band

accounts for gamma effects observed in DP-Control statistical tests (notably, independent test). The statistical test showed that DP condition differed from DNP condition in Gamma band (p=0.03). The negative cluster spread over entire 40-60Hz band and time interval 660-740ms (Fig.3, left column).
Similarly, to compare Alpha/Beta band activity between DP and DNP conditions, we constrained region of interest spectrally to 4-20Hz and temporally to 500-2000ms. Although αERD seemed considerably stronger and prolonged in DNP condition, the difference did not reach significance (p=0.58).
In summary, both DP and DNP were characterized by broadband desynchronization of oscillatory power predominantly in Alpha and Beta range (8-24Hz). DP condition differed significantly in Gamma band (40-60Hz) from DNP and Control conditions, in time interval coinciding with ERP effects and onset of Alpha/Beta ERD. Detailed contrasts and statistical results are presented at Fig.3.

Lateralization in Decision interval In order to test whether the brain oscillatory activity is lateralized in Decision interval, we computed lateralized time-frequency maps (LTF), as detailed in Methods section. The same time interval of -200-2100ms was used, while spectral band was set to 4-30Hz to account for entire low-frequency range.
The desynchronization in Alpha/Beta range (8-16Hz) was stronger at the contralateral (left) electrodes, in all conditions. However, the duration and magnitude of lateralized desynchronization (LERD) was the strongest and most prolonged in DP condition (Fig.4). The DP condition differed significantly from DNP (p=0.039) and from Control condition (p=0.029), with LERD lasting 500ms longer. There were no significant differences between DNP and Control conditions (p=0.45).

Action preparation/inhibition In this section we evaluate brain activations directly preceding the action. The ERP differences were assessed by means of cluster mass permutation tests on all channels from the interval -2000-1500ms time-locked to the onset of the Cue. The slow negative potential (CNV) was present in DP, CP and CNP conditions and we found no significant difference between those conditions in the interval preceding action. However, CNV was nearly completely abandoned in DNP condition. Significant negative cluster was found in DP-DNP comparison (p<0.005, -280-350ms) and significant positive cluster in DNP-CNP comparison (p<0.005, -450-320ms). Clusters extended over all channels but dominated in central region. For detailed distribution of effect see Fig.5.
Similarly, spectral lateralization was evaluated by cluster-mass permutation tests on time-frequency maps of difference between left and right channels. Similarly as in case of CNV deflection, contralateral desynchronization in Alpha range was observed in DP, CP and CNP conditions, however it is abandoned in DNP condition. Significant negative clusters were found in DP-DNP comparison (p=0.03, -700-370ms) and significant positive cluster in DNP-CNP comparison (p<0.005, -1140 - -310ms). For detailed distribution of the effect see Fig.6.

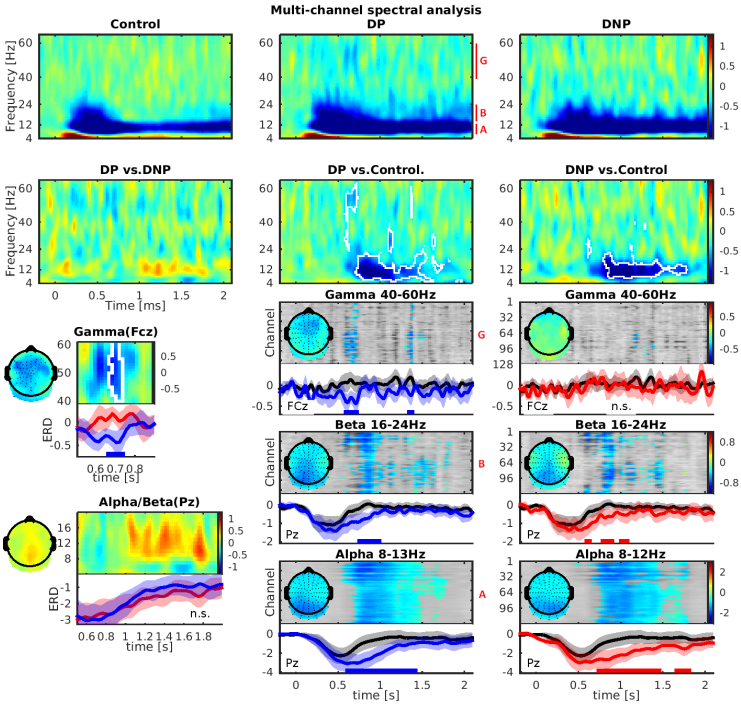

Figure 3: Voluntary decisions are characterized by broad-band modulation of power (ERD), dominating in Alpha and Beta range (8-24Hz). **Top panels:** Morlet wavelet time-frequency decomposition of Control, DP and DNP conditions. **Middle panels:** the differences DP-DNP, DP-Control and DNP-Control are presented in left, middle and right columns respectively, with statistically significant regions marked by white lines. Cluster-mass permutation tests were performed in entire *(channel x time x frequency)* space. **Lower panels:** modulation of power over all electrodes in frequency bands of interest, with the significant regions color-coded. The inset topomaps show averaged spatial distribution of ERD effect over the interval of 700-1000ms. The colored traces present the time-courses of signal power with 95% confidence intervals, in the selected frequency bands, for representative channels (Pz, FCz).

Spectral signature of action preparation was evaluated by cluster-mass permutation tests in period -1000-1000ms and entire broadband frequency range 4-65Hz. Short before the Cue stimulus, stronger broadband responses were observed in DP, CP and CNP conditions than in DNP condition, in particular lateralized Beta and Gamma desynchronization. Significant negative clusters were found in DP-DNP comparison (p=0.01) and significant positive cluster in DNP-CNP comparison (p=0.024).

In particular, the difference in Theta band (4-7Hz) was prevalent in comparison of DP and DNP conditions. The negative cluster (p=0.01) spread over frontal

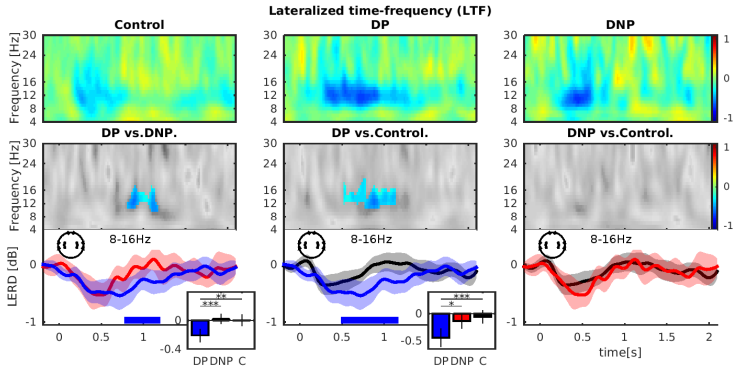

Figure 4: Power modulation in Decision interval is most lateralized during decisions to act (DP). **Top panels:** the time-frequency lateralization maps were computed by subtracting averaged time-frequency maps of selected right channels from their corresponding left channels. **Middle panels:** Cluster-mass permutation tests revealed that DP condition differed from DNP and Control with stronger contralateral desynchronization, but there was no difference between DNP and Control. The non-significant regions are shaded. The significant cluster extended over high alpha and beta range (10-24Hz). **Bottom panels:** time course of lateralized alpha/beta desynchronization (LERD) in DP(blue), DNP(red) and Control(black) conditions, with 95% confidence intervals. The inset bar charts show the mean magnitudes of LERD in the significant regions.

and fronto-central channels. The Theta power increased in DNP (ERS) and decreased in DP condition (ERD) in the interval preceding action by over 1000ms. Importantly, we did not find any significant spectral differences between preparation to voluntary action (DP condition) and preparation for externally-cued action (CP and CNP), neither in distribution of ERD/ERS patterns nor in lateralization. The only difference observed between DP and CP conditions occurred at the final stage of CNV deflection, where CNV peaks were on average more negative in CP condition (positive cluster, p=0.036, 40-290ms, posterior channels). For detailed distribution of spectral effect see Fig.7.

Action execution/inhibition As the motor execution is not the primary goal of this study, we limit here to rather general observations. Motor potentials were considerably higher in CP than in DP condition ($p<0.005$). Both DP and DNP conditions displayed prolonged positivity after the Cue onset, although the latter represented intentional inhibition rather than action. Positivity was stronger in DP condition ($p<0.005$) mostly observed over central and parietal areas (Fig.5) Characteristic contralateral Beta rebound was observed in DP and Control conditions, but not in DNP.

EEG-RT correlations In externally cued condition (CP), we found no correlations between αERD and RT. However, the CNV negativity was positively correlated with RT (subjects with more negative CNV deflection responded faster). The effect was robust and statistically significant at 71 (out of 128)

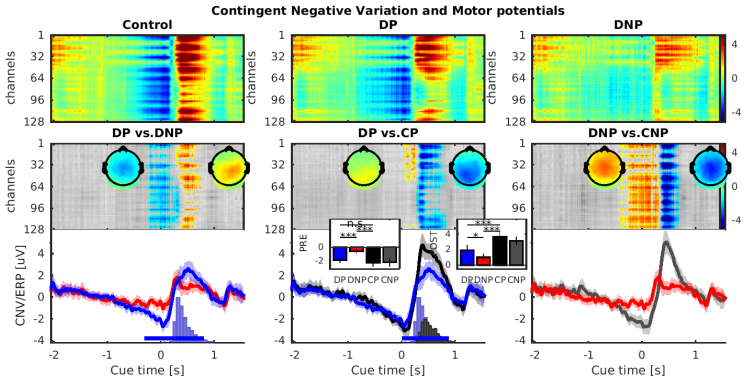

Figure 5: Preparation to action is manifested by slowly accumulating, prolonged ERP negativity (contingent negative variation, CNV), lateralized desynchronization (Fig.6) and broad-band power modulation (Fig.**??**). **Top panels:** multi-channel ERP/CNV traces, time-locked to the onset of the Cue stimulus (t=0, Action call). **Middle panels:** statistical evaluation (cluster-mass permutation tests) of three main contrasts: DP-DNP, CP-CNP and DP-CP, in (channel x time) space. Insignificant regions are faded out. The inset topomaps represent spatial distribution of activity in 500ms before(left) and after(right) action, while the bar charts illustrate the average ERP amplitude in those intervals, for each condition separately. **Bottom panels:** channel-averaged ERP/CNV traces with 95% confidence intervals and the histograms of reaction times overplotted at the lower edge. Notably, the action preparation (as indexed by CNV) is largely abandoned in DNP condition, while preparation for voluntary action (DP) seems equivalent to preparation for unknown, externally-cued action (CP or CNP).

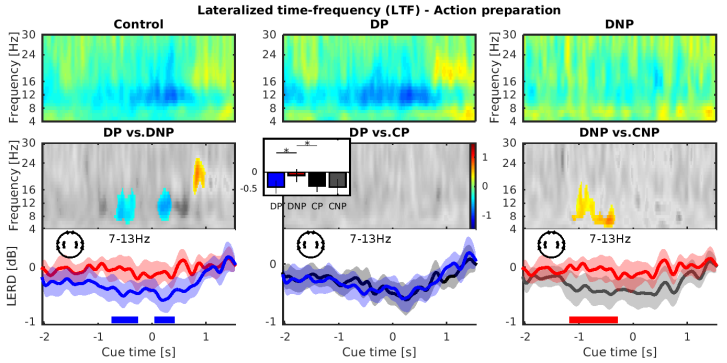

Figure 6: The Alpha/Beta power modulation is lateralized in preparation for freely intended actions (DP) and for unknwon, externally-cued actions (CP and CNP). However there was no lateralization in case of the intentional inhibition (DNP). **Top panels:** Time-frequency lateralization maps (top panels) were computed by subtracting averaged time-frequency maps of selected right channels from their corresponding left channels. Lateralization in Alpha can be observed followed by characteristic post-movement Beta rebound in Control and DP conditions. **Middle panels:** statistical evaluation (cluster-mass permutation tests) of three main contrasts: DP-DNP, CP-CNP and DP-CP, in [frequency x time] space. The non-significant regions are shaded. **Bottom panels:** time course of lateralized Alpha desynchronization (LERD) in DP(blue), DNP(red) and Control(black) conditions, with 95% confidence intervals. The inset bar charts show the mean magnitudes of LERD in the period of 1 second preceding action.

electrodes, primarily distributed over central and frontal regions. For representative Cz channel, the correlation was 0.62 (p=0.01). In voluntary decision condition (DP), the effect was reverse. We found no correlations between CNV and RT, but αERD correlated robustly with RT at 64 (out of 128) electrodes, primarily distributed over posterior and contralateral regions. For representative Pz channel, the correlation was 0.63 (p=0.009). The correlation plots, scalp distributions of predictive channels, and CNV/Alpha traces of fast and slow responders are presented at Fig.8.

4. Discussion

4.1. Temporal and spectral signature of voluntary decisions

To our knowledge, the spectral contents of voluntary decision about prospective action has not been systematically studied. Other reports focused primarily on intention-in-action, where spectral effects might be due to motor preparation for action directly following decision [91], or were constrained to particular band of interest such as Alpha and Beta [18, 90]. One of aims of this study was to evaluate a complete, time-frequency signature of voluntary decision (when contrasted with a baseline Control condition), and thus assess the duration, the magnitude and the frequency contents of the decision processes.

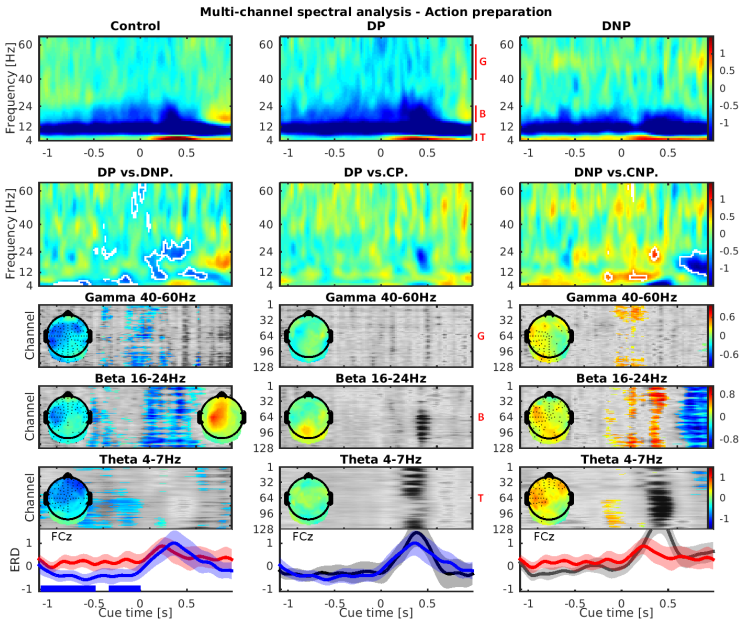

Figure 7: Broadband modulation of power (ERD) is stronger in preparation for voluntary action (DP) than in voluntary inhibition (DNP), during the retention interval preceding Cue stimulus (Action call). Preparation for voluntary action (DP) does not differ from preparation for unknown externally-cued action (CP and CNP). **Top panels:** Morlet wavelet time-frequency decomposition of Control, DP and DNP conditions. **Middle panels:** the differences DP-DNP, DP-CP and DNP-CNP are presented in left, middle and right columns respectively, with statistically significant regions marked by white lines. Cluster-mass permutation tests were performed in entire [channel x time x frequency] space. **Lower panels:** modulation of power over all electrodes in frequency bands of interest, with the significant regions color-coded. The inset topomaps show averaged spatial distribution of ERD effect over the interval of 500ms preceding the action. The colored traces present the time-courses of signal power with 95% confidence intervals, in the selected frequency bands for a representative channel (FCz).

The dominating effect obtained by contrasting Decision conditions with Control condition was reflected by global, prolonged Alpha and Beta ERD lasting nearly 1500ms, before returning towards the baseline. The effect spread over entire scalp, but the effect size was largest over parietal and centro-parietal regions. Interestingly, a strong Alpha/Beta ERD was very similar in its duration and magnitude for DP and DNP conditions, that is, regardless if decision resulted in action or inhibition of action. Although visual inspection suggests slightly longer duration of αERD in DNP condition, the effect did not reach statistical significance, even after constraining region of interest (Fig.3, bottom). Secondly, we found also spectral signatures specific to DP condition

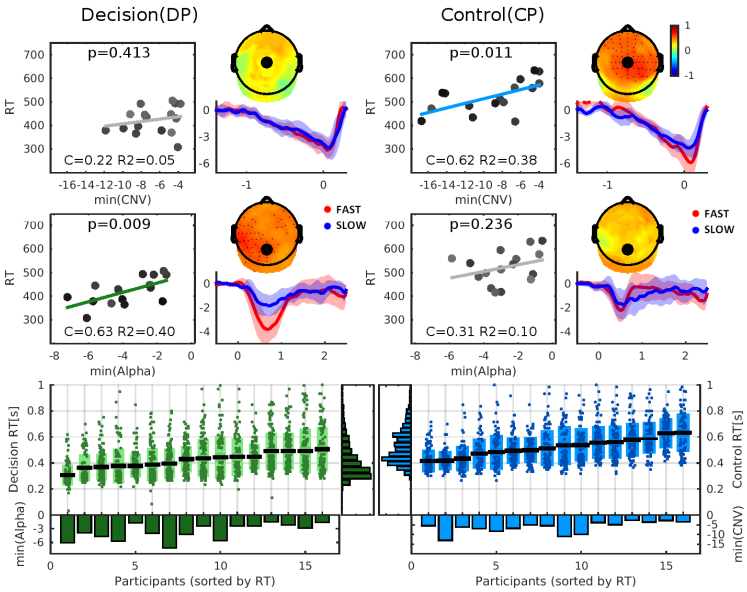

Figure 8: Correlations between behavioral and electrophysiological measures depend on the mode of action selection. **Top panels:** in externally-cued condition (CP) the reaction times correlated with maximum negativity of CNV, but not with maximum αERD. Conversely, in decision condition (DP) the reaction times correlated with maximum αERD, but not maximum CNV. The inset topomaps show the R^2 score of the linear fit of all scalp channels ($p<0.05$, marked with black dots), showing that the CNV-RT and Alpha-RT correlations are robust and spreads over wide regions. The inset traces show grand average responses of fast(red) and slow(blue) participants as divided by median split, in respective EEG measure, i.e. CNV and αERD respectively. **Bottom left panel:** individual mean reaction times in DP aligned with correlated mean αERD. **Bottom right panel:** individual mean reaction times in CP aligned with correlated mean CNV amplitudes.

only. In particular, lateralization of Alpha power was considerably more prolonged (>1000ms), with desynchronization dominating on the side contralateral to movement (left hemisphere) (Fig.4). Furthermore we observed brief, but statistically significant desynchronization of Gamma power, only in DP condition, which coincided in time with onset of alpha ERD.

The fact that strong contrasts were observed between Decision conditions and Control, as well as between DP and DNP conditions, constitute a promising phenomenon in context of brain-computer interfacing (BCI). Further studies are needed to investigate whether the specific signatures of DP and DNP can be used for single-trial classification, which would be a significant step towards designing natural intention-driven BCI systems.

4.2. Broadband oscillations and their role in intention formation

The knowledge of exact temporal, spectral and spatial extension of the decision effects in DP and DNP conditions can inform about complex nature of voluntary decisions and its inherent neural processes. Modulation of Alpha/Beta band in our task might reflect at least two distinct aspects of neural processing. The first may relate to involvement of motor system while the other represents cognitive and attentional processes.

First of all we observed widespread, prolonged and bilateral Alpha desynchronization in both DP and DNP conditions (Fig.3), even though the latter does not result in overt motor response. The fact that ERD occurred in both DP and DNP conditions (Fig.3), suggests that it may reflect cognitive processes (rather than motor preparation), which are present independently of decision outcome. Those processes may be related to attention [42] towards internal action selection [49], self-monitoring, or mental effort related to selection between two alternative future plans (action or no action).

It is very plausible, that decreased Alpha power may correlate with allocation of introspective attentional resources to the neural processes of action selection. Alpha band has been already linked to attentional processes [42, 90]. Even if the attentional needs are different depending on the outcome (action or non-action), they should be similar at least in the early stages of decision, before sufficient evidence is accumulated for one of the options for the intention to be formed. Such function of Alpha would explain close resemblance of αERD in parietal areas in both conditions. In fact, it can be arguably suggested that the introspective attention is not only a mere cognitive add-on to volition, but rather an intrinsic and indispensable component of any conscious, internally-generated, voluntary choice. Under such assumption, modulation of Alpha can be interpreted not only as a correlate of introspective attention, but also as an indirect electrophysiological correlate of the early processes of intention formation.

Secondly, we observed that Alpha/Beta lateralization was present briefly in all conditions, but it was significantly prolonged only in DP condition. This may suggests that DP condition contains additional component related to early preparation of motor program, or to mental imagery of the motor plan. Contralateral Alpha was repeatedly shown to be related to motor preparation [20, 74, 89] and Beta rhythms to motor imagery [59] and action selection [90].

Thus, Alpha and Beta oscillations may play more than one role in voluntary decision. Indeed, there is a converging evidence in literature that Alpha oscillations are not representing a particular neural process, but represent very different processes relevant to cognition and sensorimotor function. The functional meaning of Alpha modulation will depend primarily on the task and context, but also the exact frequency specifics, and recording site [4, 6, 28, 31, 37, 41, 42]. The peak Alpha frequencies can vary across subjects [3] and within-subject, where it tends to shift towards higher frequencies as a function of cognitive load and channel location [31, 67].

There are only few studies directly linking Alpha oscillations with volition

and free action. Deiber et al [18] contrasted Alpha oscillations in delayed response task between "free" condition (where after precue subjects could freely decide between left or right hand), "full" condition (where precue indicated the left or right hand response) and "none"condition (where precue was not informative, and the cue indicated type of response). They concluded that Alpha oscillations are only related to strategy of motor preparation, but do not resolve the mode of action selection (internal decision or external cue). However their task was different than ours. Participants were choosing between the type of response, rather than between acting or not acting, and thus the overt response was always present. Tremblay et al [90] investigated the role of Alpha and Beta oscillations in internally-generated and externally-cued actions of either finger movement or speech production. They suggested that mode of action affects ERD patterns and the Alpha oscillations are more related to attentional processes, while the Beta band reflects action selection and execution processes.

4.3. Active nature of voluntary non-action

Our results suggest that conscious decision not to act (DNP) is not passive, but to certain extent involves the same neural processes as decision to act (DP), which is manifested by closely resembling pattern of Alpha/Beta desynchronization and ERP modulation in DP and DNP (Fig. 3 and Fig. 2). If the opposite was true, we would expect that any decision related mental processing is abandoned, and thus cortical activation (indexed by the Alpha/Beta ERD) would be considerably reduced to the levels observed in Control condition. This was however not the case, and ERD pattern in DNP was approximately equally large and prolonged as in DP. Hence, although DNP does not produce an overt motor response, certain brain processes remain active and result in modulation of scalp EEG signals. Those processes may correspond to attention to action selection, conflict monitoring, or mental imagery of the action to be inhibited - processes inherently linked to decision independent of the final outcome. Our results are closely in line with fMRI findings reported by Kuhn et al [48], where they found that rostral cingulate zone (RCZ) was equally activated regardless of decision outcome. Furthermore, by contrasting decision to act with decision not to act, they found difference only in contralateral motor cortex. This supports our lateralized ERD in alpha band, which is present only in DP but not in DNP.

4.4. Inhibition in voluntary decision

During voluntary decision intervals, we observed prolonged frontal ERP negativity, which was present regardless of the final decision outcome (although statistically significant only in Go decisions). The negativity lasted approximately from 500ms to 2000ms (Fig. 2, bottom left). The onset of negativity coincided with onsets of desynchronization in a broad spectrum including Alpha, Beta and Gamma bands (Fig. 7). Notably, γERD was strongest at the frontal channels and its short temporal occurence coincided with the onset of ERP negativity. A possible function role of those modulations is active inhibition [23, 91]. Since we observed both the negativity and ERD in both Go

and NoGo decisions, they can be explained by at least two plausible inhibitory mechanisms: (1) intentional and permanent inhibition of action in NoGo trials, and (2) sustained but temporary inhibition of prepared action in the Go trials, while awaiting for the imperative Cue stimulus. In literature, the frontal negativity was repeatedly linked to inhibition processes. In Go/NoGo paradigms involving monkeys, Sasaki et al [82] reported negative potentials over frontal lobes related to inhibition of the movement. Filipovic et al [23] suggested that early negative components of ERP (N1 complex) might reflect inhibitory nature of NoGo decision. Several other studies showed that electrical stimulation of prefrontal cortex in monkeys [83] inhibits or delays the prepared Go action, and TMS stimulation of dorsal premotor cortex in humans interferes with action selection process [79, 84]. In most of those studies the inhibition-related activity was observed in early period of approximately 100-200ms after stimulus, and was related to immediate motor response. In context of our study however, the effect is much more dispersed in time, which can be explained by the fact that decision processes (intention formation) need to occur before the inhibition takes place, i.e. before implementation of the motor inhibition processes in NoGo trials, and before implementation of temporary inhibition of motor response in Go trials. The timing of this internal decision processes might be longer than the timing of external cue processing in Go/NoGo tasks, thus rendering inhibition-related negativity in our task delayed and prolonged. Secondly, inhibition in our Decision interval is related to future action rather than to immediate motor preparation. Walsh et al [91] in their study observed Beta power increase when participants in the last moment freely abandoned voluntarily initiated actions. Similarly, in externally cued Go/NoGo task the pre-movement Beta rebound was significant only in NoGo condition [95]. Indeed we observed that although βERD is significant in both our Go and NoGo trials, it is less widespread and weaker in the NoGo condition (so absolute Beta power is higher) than in Go condition (Fig. 7), which may correspond to similar inhibitory effect to that reported by Walsh et al [91].

4.5. Preparatory processes after voluntary decision

We have observed slow negativity potential (contingent negative variation, CNV) preceding Cue stimulus in the Control condition, when response was not known, and in DP condition, where the response was predetermined by earlier decision. However, CNV was abandoned in DNP condition, where the response was voluntarily inhibited (see Fig. 5) (since no action was planned, obviously there was no behavioral benefit in either motor preparation for action or sensory preparation for Go stimulus).

Importantly, CNV did not differ between DP and Control conditions, which implies that after a decision 'to act' had been made, the late preparatory activity for internally generated action is identical to the preparation for an externally cued, unknown action. Thus the findings from the domain of studies investigating action preparation in context of externally-cued, delayed-response tasks [20, 24, 26, 85] can be generalized onto internally generated actions, in contexts where the decision explicitly precedes the action itself.

In context of motor preparation and attentional expectation of upcoming stimulus, variations of delayed response Go/NoGo tasks are commonly employed [20, 24, 26]. In such tasks participants receive a warning stimulus (S1), followed by delayed imperative stimulus (S2). A slowly accumulating negativity preceding the imperative stimulus usually by 0.5-3 seconds can be observed at central and frontal EEG channels, which is known as contingent negative variation (CNV) [87, 92]. Despite its apparent similarity to readiness potential (RP) [53], CNV reflects distinct phenomena. While RP is related to motor preparation and can occur without external stimuli [53, 89], CNV is related to attention and expectancy of upcoming imperative stimulus and is present even if overt motor response is not required [80]. Usually however, the late part of CNV will contain both lateralized RP and stimulus preceding negativity [10], where the amplitude of the former depends on parameters of the motor response and the latter on expected informativeness of stimulus. In context of externally-cued response preparation, late CNV is larger in Go than NoGo condition [22, 85] and correlates positively with reaction times.

Increased Theta oscillations has been shown to be relevant to episodic memory [43] and memory storage and retrieval [21, 44]. The frontal Theta power correlates with working memory load [38]. We observed that Theta power was higher in our DNP condition, where the action was intentionally inhibited, than in DP and Control conditions (Fig. 7). The Theta modulation commenced approximately 1 second before the imperative Cue stimulus, and dominated at centrofrontal and frontal areas. It may suggest that intentional non-action, which was less frequent choice than intentional action (participants freely chose 'to act' on average in 61% of trials), involved more actively the working-memory encoding and retrieval. It is plausible that participants focused on remembering to inhibit the default action (up-regulation of theta oscillations), while at the same time contributing less attentional resources to the expectation of upcoming 'Go' cue (reduced CNV negativity). Sustained Theta modulation could be interpreted as a trace of active inhibition, or retrieval of information about the inhibition from the working-memory. Beta oscillations were higher in DNP condition than in DP conditions in the interval directly preceding Cue stimulus, which can indicate intentional late inhibition of action. As such, our late Beta modulation could correspond to P. Haggard's late component of "whether" decision [32], and would closely correspond to inhibition-related Beta modulation reported by [91], where subjects were internally generating free-paced movements and, in some of the trials, intentionally inhibiting them in the last moment before execution. A similar Beta increase effect was reported in context of externally cued NoGo stimulus [95] There is also another plausible explanation of reduced Beta and Gamma oscillations in DP condition, in the interval directly preceding action. Several studies have shown broadband reduction of power during expectation for imperative stimulus in delayed response tasks [26, 27]. Such a global decrease of oscillatory activity is believed to increase cortical excitability and thus facilitate processing of the target stimulus and related actions. Thus it is reasonable that we observe such a broadband desynchronization in our DP trials (where motor action is predetermined by earlier decision and stimulus contents

is effectively a "Go" signal) and in Control trials (where motor action might or might not occur depending on stimulus contents), but not in DNP (where action is intentionally abandoned in earlier decision, and stimulus contents is irrelevant). Finally, it is known that both free-paced and externally-cued movements are preceded by lateralized Alpha/Beta ERD, followed by bilateral ERD during movement initiation and Beta rebound shortly after [40, 65, 72, 75, 89]. Those motor related components can account for the lateralized Beta ERD preceding action and contralateral Beta ERS following action in our DP and CP condition, but not in DNP (Fig.7 and Fig.6).

In summary, although we observed numerous differences between voluntary action and voluntary non-action in the action preparation interval (CNV, broadband lateralized ERD, post-movement Beta ERS), we found no differences between preparation for voluntary action (DP condition) and preparation for unspecific externally-cued action (CP condition). This indicates that action preparatory processes following voluntary decision "to act" are completely equivalent to preparation for externally-cued action. On the other hand, voluntary decision "not to act" results in withdrawal from motor preparation, yet preserves the trace of active inhibition in form of prolonged, increased Theta power.

4.6. Behavioral results and EEG/RT correlations

For every participant, we observed an approximately 100ms faster reaction time in DP condition than CP condition. This is not unexpected finding, considering that in Decision conditions response was predetermined by participant's prior choice, while in Control condition participants needed to map the response (press or do not press the button) to the color of imperative stimulus, which required additional semantic processing and thus resulted in increased RTs. The difference is similar to analogous reported in Deiber et al [18]. The absolute reaction times in our DP and CP conditions are only slightly larger to those reported in other studies [18, 26], in conditions with informative S1 or S2 respectively. The larger reaction times could be due to considerably longer interval between Precue and Cue in our study (4.4-4.6s) and more explicit distinction between preparation, retention and action. Furthermore, the shorter reaction times in DP condition as compared to CP constitute a fine validation of the paradigm, by confirming that participants indeed had made their decision prior to the imperative Cue.

Interestingly, for every participants we observed behavioral biases in voluntary Decision condition, with clear preference 'to act' over 'not to act'. The average asymmetry of choice was 61%, with minimum of 51% and maximum of 74%. In another study (in preparation) we observed similar low-level behavioral biases in spatial choices (preference to 'right' over 'left') and temporal domain choices (preference to 'earlier' over 'later'). Importantly, those biases are emerging entirely from participants free binary choices, and are not influenced by experimenter's feedback or instructions. The participants are merely instructed to take new, independent, binary decisions in every trial, and avoid planning ahead. Participants remain unaware of the regular bias governing their

choice. Thus, it seems that a certain fraction of variance in human voluntary action can be explained by low-level behavioral preferences.

In order to investigate potential relations between main EEG effects and behavioral measures, we performed correlational analysis between αERD, CNV and reaction times.

Correlations between CNV deflection and RTs were already investigated in literature [22, 56], however results were not always converging (for a review see Smith et al [85]). In our study we found that only in the externally-cued CP condition, the significant CNV-RT correlations were observed. In CP condition participants needed to process the semantic meaning of Cue stimulus to determine whether the action is required or not. The effect was robust and spanned over nearly all central and fronto-central channels. The fastest responding participants had more negative deflection of CNV (Fig. 8, top panels). Interestingly, CNV did not correlate with RT in internally-driven DP condition, where participants action was already determined by their prior voluntary decision. Those results suggest, that CNV magnitude affects primarily the efficiency of sensory processing of informative Cue stimulus and response mapping, rather than efficient implementation of motor response [78]. If the opposite was the case, we would expect CNV-RT correlation to occur regardless of the mode of action selection (DP or CP).

Secondly, we were interested whether the maximum desynchronization of Alpha power in the Decision interval min(αERD), which is the dominating effect discriminating voluntary decision trials from control trials, affects the reaction times. We found that only in DP condition αERD was correlated with RTs, and the effect was robust over majority of parietal and central contralateral channels (Fig. 8, middle panels). In externally-cued CP condition, no significant correlations between αERD and RT were found. There are several plausible explanations of this effect. Firstly, αERD might represent efficient encoding of preplanned motor program for the future use. This hypothesis is further supported by contralateral distribution of correlating channels. Secondly, αERD could reflect a general level of arousal and thus the commitment of individuals to their internally-selected actions, which by reducing the entropy of action outcome may lead to shorter reaction times. Finally, αERD can be also relevant to efficient encoding of planned action in working-memory system, which would then facilitate the retrieval and implementation of motor command after the onset of imperative Cue stimulus. Increased Theta and Alpha power was previously shown to correlate with working-memory load [21, 38]. Although the load imposed by our task on working-memory system is not large (a binary decision between action or non-action), it is important to note that participants performed the task repeatedly in 480 trials. Thus certain level of encoding efficiency is obviously necessary to avoid confusing the current trial decision from multitude of similar simple choices performed earlier.

5. Conclusions

We investigated EEG signatures of the neural processes related to voluntary decisions "to act" or "not to act" in context where respective motor response are postponed in time. Our results suggest that the occurrence of voluntary decisions can be detected by scalp recordings, and distinct spatio-temporo-spectral patterns can distinguish between early intention "to act" or "not to act".

The statistical analysis of broad time-frequency spectrum and event-related modulation suggest the following chain of neural events. The decision is manifested by prolonged, global desynchronization of Alpha and Beta oscillations, dominating in parietal areas. Only in decisions "to act", the Alpha and Beta desynchronization becomes significantly lateralized, and this process is assisted by brief modulation of Gamma oscillations. The role of Alpha seem to be a critical biomarker of ongoing processes related to conscious decision, while its spatial distribution can suggest a presence of the motor preparation/imagery processes related to a prospective action.

In the retention interval the EEG modulation differs depending on whether participant decided "to act" or "not to act". In case of decision "to act", motor preparation processes start along with attentional expectation of the imperative stimulus, which is manifested by slowly increasing CNV broadband, lateralized desynchronization from Alpha to Gamma band, in the last moments preceding action. The latter processes may reflect global increase of cortical excitability preceding intended motor command. Finally, the action implementation is manifested by desynchronization in Alpha/Beta bands, followed by contralateral Beta rebound.

In case of decision "not to act", Theta band oscillations are considerably increased, which seem to encode the trace of active inhibition, or memory trace of the inhibition requirement. Increased Theta is accompanied by nearly abandoned CNV negativity and lack of spectral desynchronization, which suggests decrease of the expectation for imperative stimuli (no action needed, thus no behavioral benefit in preparing for perception and action), and ceased preparation of motor program. Also the absence of of the Beta rebound suggests early, rather than late, abandonment of action preparation.

In brief, modulation of Alpha, Beta and Gamma oscillations seem critical to voluntary decision processes including intention formation regarding prospective action, while slower oscillations in Theta and slow accumulating negativity (CNV) manifest retention of decision in working-memory and preparation of respective, intended motor action or inhibition.

Dominating Alpha ERD in decision interval might reflect at least two categories of neural processes: (1) motor-related preparation/inhibition of action (manifested by lateral αERD and fronto-central γERD), and (2) cognitive components related to conscious act of volition and introspective attention to that act (manifested by global, bilateral, prolonged αERD).

References

[1] Fieldtrip toolbox [www.ru.nl/neuroimaging/fieldtrip].

[2] E. Başar, C. Başar-Eroglu, S. Karakaş, and M. Schürmann. Brain oscillations in perception and memory. *International Journal of Psychophysiology*, 35(2-3):95–124, mar 2000.

[3] E. Başar, M. Schürmann, C. Başar-Eroglu, and S. Karakaş. Alpha oscillations in brain functioning: an integrative theory. *International journal of psychophysiology : official journal of the International Organization of Psychophysiology*, 26(1-3):5–29, jun 1997.

[4] C. Babiloni, A. Brancucci, L. Arendt-Nielsen, F. Babiloni, P. Capotosto, F. Carducci, F. Cincotti, L. Romano, A. C. N. Chen, and P. M. Rossini. Alpha event-related desynchronization preceding a go/no-go task: a high-resolution EEG study. *Neuropsychology*, 18(4):719–728, 2004.

[5] C. Babiloni, F. Carducci, F. Cincotti, P. M. Rossini, C. Neuper, G. Pfurtscheller, and F. Babiloni. Human movement-related potentials vs desynchronization of EEG alpha rhythm: a high-resolution EEG study. *NeuroImage*, 10(6):658–65, dec 1999.

[6] C. Babiloni, F. Vecchio, A. Bultrini, G. Luca Romani, and P. M. Rossini. Pre- and poststimulus alpha rhythms are related to conscious visual perception: a high-resolution EEG study. *Cerebral cortex (New York, N.Y. : 1991)*, 16(12):1690–700, dec 2006.

[7] J. Baer, J. C. Kaufman, and R. F. Baumeister. Are We Free?: Psychology and Free Will. *Are We Free?: Psychology and Free Will*, pages 1–367, 2008.

[8] G. Berrios and M. Gili. Will and its disorders: a conceptual history. *History of Psychiatry*, 6(21):087–104, mar 1995.

[9] M. Brass and P. Haggard. The What, When, Whether Model of Intentional Action. *The Neuroscientist*, 14(4):319–325, aug 2008.

[10] C. Brunia. Movement and stimulus preceding negativity. *Biological Psychology*, 26(1-3):165–178, jun 1988.

[11] E. T. Bullmore, J. Suckling, S. Overmeyer, S. Rabe-Hesketh, E. Taylor, and M. J. Brammer. Global, voxel, and cluster tests, by theory and permutation, for a difference between two groups of structural MR images of the brain. *IEEE transactions on medical imaging*, 18(1):32–42, sep 1999.

[12] G. Buzsáki and B. O. Watson. Brain rhythms and neural syntax: implications for efficient coding of cognitive content and neuropsychiatric disease. *Dialogues in clinical neuroscience*, 14(4):345–67, dec 2012.

[13] R. T. Canolty and R. T. Knight. The functional role of cross-frequency coupling. *Trends in cognitive sciences*, 14(11):506–15, nov 2010.

[14] J. F. Cavanagh and M. J. Frank. Frontal theta as a mechanism for cognitive control. *Trends in cognitive sciences*, 18(8):414–21, aug 2014.

[15] R. Cunnington, C. Windischberger, L. Deecke, and E. Moser. The preparation and execution of self-initiated and externally-triggered movement: a study of event-related fMRI. *NeuroImage*, 15(2):373–85, feb 2002.

[16] F. Debaere, N. Wenderoth, S. Sunaert, P. Van Hecke, and S. P. Swinnen. Internal vs external generation of movements: differential neural pathways involved in bimanual coordination performed in the presence or absence of augmented visual feedback. *NeuroImage*, 19(3):764–76, jul 2003.

[17] M. P. Deiber, R. E. Passingham, J. G. Colebatch, K. J. Friston, P. D. Nixon, and R. S. J. Frackowiak. Cortical areas and the selection of movement: a study with positron emission tomography. *Experimental Brain Research*, 84(2):393–402, jan 1991.

[18] M.-P. Deiber, E. Sallard, C. Ludwig, C. Ghezzi, J. Barral, and V. Ibañez. EEG alpha activity reflects motor preparation rather than the mode of action selection. *Frontiers in Integrative Neuroscience*, 6:59, jan 2012.

[19] A. Delorme and S. Makeig. EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *Journal of neuroscience methods*, 134(1):9–21, mar 2004.

[20] L. M. Doyle, K. Yarrow, and P. Brown. Lateralization of event-related beta desynchronization in the EEG during pre-cued reaction time tasks. *Clinical Neurophysiology*, 116(8):1879–1888, aug 2005.

[21] E. Düzel, W. D. Penny, and N. Burgess. Brain oscillations and memory. *Current opinion in neurobiology*, 20(2):143–9, apr 2010.

[22] S. Filipović, M. Jahanshahi, and J. Rothwell. Uncoupling of contingent negative variation and alpha band event-related desynchronization in a go/no-go task. *Clinical Neurophysiology*, 112(7):1307–1315, jul 2001.

[23] S. R. Filipović, M. Jahanshahi, and J. C. Rothwell. Cortical potentials related to decision-making: comparison of two types of go/no-go decision. *Neuroreport*, 10(17):3583–3587, nov 1999.

[24] S. R. Filipović, M. Jahanshahi, J. C. Rothwell, S. R. Filipovic, M. Jahanshahi, and J. C. Rothwell. Cortical potentials related to the nogo decision. *Exp Brain Res*, 132(3):411–415, apr 2000.

[25] I. Fried, R. Mukamel, and G. Kreiman. Internally generated preactivation of single neurons in human medial frontal cortex predicts volition. *Neuron*, 69(3):548–62, feb 2011.

[26] I. Funderud, M. Lindgren, M. Løvstad, T. Endestad, B. Voytek, R. T. Knight, and A. K. Solbakk. Differential Go/NoGo activity in both contingent negative variation and spectral power. *PLoS ONE*, 7(10):e48504, 2012.

[27] C. M. Gómez, E. Vaquero, D. López-Mendoza, J. González-Rosa, and M. Vázquez-Marrufo. Reduction of EEG power during expectancy periods in humans. *Acta neurobiologiae experimentalis*, 64(2):143–51, jan 2004.

[28] I. C. Gould, A. C. Nobre, V. Wyart, and M. F. S. Rushworth. Effects of decision variables and intraparietal stimulation on sensorimotor oscillatory activity in the human brain. *The Journal of neuroscience : the official journal of the Society for Neuroscience*, 32(40):13805–18, oct 2012.

[29] D. M. Groppe, T. P. Urbach, and M. Kutas. Mass univariate analysis of event-related brain potentials/fields I: A critical tutorial review. *Psychophysiology*, 48(12):1711–1725, dec 2011.

[30] A. G. Guggisberg, S. S. Dalal, A. M. Findlay, and S. S. Nagarajan. High-frequency oscillations in distributed neural networks reveal the dynamics of human decision making. *Frontiers in human neuroscience*, 1:14, jan 2007.

[31] S. Haegens, H. Cousijn, G. Wallis, P. J. Harrison, and A. C. Nobre. Inter- and intra-individual variability in alpha peak frequency. *NeuroImage*, 92:46–55, may 2014.

[32] P. Haggard. Human volition: towards a neuroscience of will. *Nature reviews. Neuroscience*, 9(12):934–46, dec 2008.

[33] P. Haggard and V. Chambon. Sense of agency. *Current biology : CB*, 22(10):R390–2, may 2012.

[34] P. Haggard and M. Eimer. On the relation between brain potentials and the awareness of voluntary movements. *Experimental Brain Research*, 126(1):128–133, apr 1999.

[35] F. Hoffstaedter, C. Grefkes, K. Zilles, and S. B. Eickhoff. The "what" and "when" of self-initiated movements. *Cerebral cortex (New York, N.Y. : 1991)*, 23(3):520–30, mar 2013.

[36] I. H. Jenkins. Self-initiated versus externally triggered movements: II. The effect of movement predictability on regional cerebral blood flow. *Brain*, 123(6):1216–1228, jun 2000.

[37] O. Jensen. Oscillations in the Alpha Band (9-12 Hz) Increase with Memory Load during Retention in a Short-term Memory Task. *Cerebral Cortex*, 12(8):877–882, aug 2002.

[38] O. Jensen and C. D. Tesche. Frontal theta activity in humans increases with memory load in a working memory task. *European Journal of Neuroscience*, 15(8):1395–1399, apr 2002.

[39] X. Jia and A. Kohn. Gamma rhythms in the brain. *PLoS Biology*, 9(4):e1001045, apr 2011.

[40] J. Kaiser, N. Birbaumer, and W. Lutzenberger. Event-related beta desynchronization indicates timing of response selection in a delayed-response paradigm in humans. *Neuroscience Letters*, 312(3):149–152, oct 2001.

[41] W. Klimesch. EEG alpha and theta oscillations reflect cognitive and memory performance: a review and analysis. *Brain Research Reviews*, 29(2-3):169–195, 1999.

[42] W. Klimesch. α-band oscillations, attention, and controlled access to stored information. *Trends in cognitive sciences*, 16(12):606–17, dec 2012.

[43] W. Klimesch, M. Doppelmayr, H. Russegger, and T. Pachinger. Theta band power in the human scalp EEG and the encoding of new information. *Neuroreport*, 7(7):1235–40, may 1996.

[44] W. Klimesch, S. Hanslmayr, P. Sauseng, W. Gruber, C. J. Brozinsky, N. E. A. Kroll, A. P. Yonelinas, and M. Doppelmayr. Oscillatory EEG correlates of episodic trace decay. *Cerebral cortex (New York, N.Y. : 1991)*, 16(2):280–90, feb 2006.

[45] W. Klimesch, P. Sauseng, and S. Hanslmayr. EEG alpha oscillations: The inhibition–timing hypothesis. *Brain Research Reviews*, 53(1):63–88, 2007.

[46] R. Kristeva-Feige, C. Fritsch, J. Timmer, and C.-H. Lücking. Effects of attention and precision of exerted force on beta range EEG-EMG synchronization during a maintained motor contraction task. *Clinical Neurophysiology*, 113(1):124–131, jan 2002.

[47] A. A. Kühn, D. Williams, A. Kupsch, P. Limousin, M. Hariz, G.-H. Schneider, K. Yarrow, and P. Brown. Event-related beta desynchronization in human subthalamic nucleus correlates with motor performance. *Brain : a journal of neurology*, 127(Pt 4):735–46, apr 2004.

[48] S. Kühn and M. Brass. When doing nothing is an option: The neural correlates of deciding whether to act or not. *NeuroImage*, 46(4):1187–1193, jul 2009.

[49] H. C. Lau, R. D. Rogers, P. Haggard, and R. E. Passingham. Attention to intention. *Science (New York, N.Y.)*, 303(5661):1208–10, feb 2004.

[50] H. C. Lau, R. D. Rogers, N. Ramnani, and R. E. Passingham. Willed action and attention to the selection of action. *NeuroImage*, 21(4):1407–1415, 2004.

[51] Lew. Detection of self-paced reaching. 2012.

[52] B. Libet. *Neurophysiology of Consciousness*. Birkhäuser Boston, Boston, MA, 1993.

[53] B. Libet, C. A. Gleason, E. W. Wright, and D. K. Pearl. Time of conscious intention to act in relation to onset of cerebral activity (readiness-potential). *Brain*, 106(3):623–642, sep 1983.

[54] J. E. Lisman and O. Jensen. The θ-γ neural code. *Neuron*, 77(6):1002–16, mar 2013.

[55] F. Lopes da Silva. EEG and MEG: relevance to neuroscience. *Neuron*, 80(5):1112–28, dec 2013.

[56] H. Mantanus, M. Timsit-Berthier, A. Gerono, and R. von Frenckell. A correlation study of contingent negative variation, reaction time, and EEG power spectrum in control and psychopathological populations. *Biological psychology*, 13:227–37, dec 1981.

[57] R. S. Marin and P. A. Wilkosz. Disorders of Diminished Motivation Focus on Clinical Practice and Research. *J Head Trauma Rehabil*, 20(4):377–388, jan 2005.

[58] E. Maris. Statistical testing in electrophysiological studies. *Psychophysiology*, 49(4):549–65, apr 2012.

[59] D. J. McFarland, L. A. Miner, T. M. Vaughan, and J. R. Wolpaw. Mu and Beta Rhythm Topographies During Motor Imagery and Actual Movements. *Brain Topography*, 12(3):177–186, 2000.

[60] A. Mognon, J. Jovicich, L. Bruzzone, and M. Buiatti. ADJUST: An automatic EEG artifact detector based on the joint use of spatial and temporal features. *Psychophysiology*, 48(2):229–40, feb 2011.

[61] V. A. Mueller, M. Brass, F. Waszak, and W. Prinz. The role of the preSMA and the rostral cingulate zone in internally selected actions. *NeuroImage*, 37(4):1354–61, oct 2007.

[62] S. D. Muthukumaraswamy and B. W. Johnson. Primary motor cortex activation during action observation revealed by wavelet analysis of the EEG. *Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology*, 115(8):1760–6, aug 2004.

[63] L. Nadel and W. Sinnott-Armstrong. Conscious Will and Responsibility: A Tribute to Benjamin Libet. *Conscious Will and Responsibility: A Tribute to Benjamin Libet*, pages 1–288, 2010.

[64] S. S. Obhi and P. Haggard. Internally generated and externally triggered actions are physically distinct and independently controlled. *Experimental Brain Research*, 156(4):518–523, jun 2004.

[65] S. Ohara, A. Ikeda, T. Kunieda, S. Yazawa, K. Baba, T. Nagamine, W. Taki, N. Hashimoto, T. Mihara, and H. Shibasaki. Movement-related change of electrocorticographic activity in human supplementary motor area proper. *Brain: a journal of neurology*, 123:1203–15, 2000.

[66] J. Onton, M. Westerfield, J. Townsend, and S. Makeig. Imaging human EEG dynamics using independent component analysis. *Neuroscience and biobehavioral reviews*, 30(6):808–22, jan 2006.

[67] M. Osaka. Peak Alpha Frequency of EEG during a Mental Task: Task Difficulty and Hemispheric Differences. *Psychophysiology*, 21(1):101–105, jan 1984.

[68] R. E. Passingham. Two cortical systems for directing movement. *Ciba Foundation symposium*, 132:151–64, jan 1987.

[69] B. Pesaran, M. J. Nelson, and R. A. Andersen. Free choice activates a decision circuit between frontal and parietal cortex. *Nature*, 453(7193):406–9, may 2008.

[70] G. Pfurtscheller. Central beta rhythm during sensorimotor activities in man. *Electroencephalography and Clinical Neurophysiology*, 51(3):253–264, mar 1981.

[71] G. Pfurtscheller, B. Graimann, J. E. Huggins, S. P. Levine, and L. A. Schuh. Spatiotemporal patterns of beta desynchronization and gamma synchronization in corticographic data during self-paced movement. *Clinical Neurophysiology*, 114(7):1226–1236, jul 2003.

[72] G. Pfurtscheller and F. Lopes da Silva. Event-related EEG/MEG synchronization and desynchronization: basic principles. *Clinical Neurophysiology*, 110(11):1842–1857, nov 1999.

[73] G. Pfurtscheller and C. Neuper. Simultaneous EEG 10 Hz desynchronization and 40 Hz synchronization during finger movements. *Neuroreport*, 3(12):1057–60, dec 1992.

[74] G. Pfurtscheller, A. Stancák, and C. Neuper. Event-related synchronization (ERS) in the alpha band — an electrophysiological correlate of cortical idling: A review. *International Journal of Psychophysiology*, 24(1-2):39–46, nov 1996.

[75] G. Pfurtscheller, A. Stancák, and C. Neuper. Post-movement beta synchronization. A correlate of an idling motor area? *Electroencephalography and Clinical Neurophysiology*, 98(4):281–293, apr 1996.

[76] H. S. Prado, M. C. Rosario, J. Lee, A. G. Hounie, R. G. Shavitt, and E. C. Miguel. Sensory phenomena in Obsessive-Compulsive Disorder and tic disorders: a review of the literature. *CNS Spectrums*, 13(5):425–432, may 2008.

[77] Z. H. Rappaport. The neuroscientific foundations of free will. *Advances and technical standards in neurosurgery*, 37(37):3–23, jan 2011.

[78] C. Rebert and J. Tecce. A summary of of CNV and reaction time. *EEG Clin. Neurophysiol. Suppl.*, pages 173–178, 1973.

[79] T. Ro, A. Henik, L. Machado, and R. D. Rafal. Transcranial magnetic stimulation of the prefrontal cortex delays contralateral endogenous saccades. *Journal of cognitive neuroscience*, 9(4):433–40, jul 1997.

[80] D. S. Ruchkin, S. Sutton, D. Mahaffey, and J. Glaser. Terminal CNV in the absence of motor response. *Electroencephalography and Clinical Neurophysiology*, 63(5):445–463, may 1986.

[81] K. Sakai. What and when: Parallel and convergent processing in motor control. *Journal of Neuroscience*, 20(7):2691 – 2700, 2000.

[82] K. Sasaki and H. Gemba. Electrical activity in the prefrontal cortex specific to no-go reaction of conditioned hand movement with colour discrimination in the monkey. *Experimental Brain Research*, 64(3):603–606, nov 1986.

[83] K. Sasaki, H. Gemba, and T. Tsujimoto. Suppression of visually initiated hand movement by stimulation of the prefrontal cortex in the monkey. *Brain Research*, 495(1):100–107, aug 1989.

[84] N. Schluter. Temporary interference in human lateral premotor cortex suggests dominance for the selection of movements. A study using transcranial magnetic stimulation. *Brain*, 121(5):785–799, may 1998.

[85] J. L. Smith, S. J. Johnstone, and R. J. Barry. Effects of pre-stimulus processing on subsequent events in a warned Go/NoGo paradigm: Response preparation, execution and inhibition. *International Journal of Psychophysiology*, 61(2):121–133, aug 2006.

[86] C. S. Soon, M. Brass, H.-J. Heinze, and J.-D. Haynes. Unconscious determinants of free decisions in the human brain. *Nature neuroscience*, 11(5):543–5, 2008.

[87] J. J. Tecce. Contingent negative variation (CNV) and psychological processes in man. *Psychological Bulletin*, 77(2):73–108, 1972.

[88] G. Thut, C.-A. Hauert, P. Viviani, S. Morand, L. Spinelli, O. Blanke, T. Landis, and C. Michel. Internally driven vs. externally cued movement selection: a study on the timing of brain activity. *Cognitive Brain Research*, 9(3):261–269, jun 2000.

[89] C. Toro, G. Deuschl, R. Thatcher, S. Sato, C. Kufta, and M. Hallett. Event-related desynchronization and movement-related cortical potentials on the ECoG and EEG. *Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section*, 93(5):380–389, oct 1994.

[90] P. Tremblay, D. M. Shiller, and V. L. Gracco. On the time-course and frequency selectivity of the EEG for different modes of response selection: evidence from speech production and keyboard pressing. *Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology*, 119(1):88–99, jan 2008.

[91] E. Walsh, S. Kühn, M. Brass, D. Wenke, and P. Haggard. EEG activations during intentional inhibition of voluntary action: an electrophysiological correlate of self-control? *Neuropsychologia*, 48(2):619–26, jan 2010.

[92] W. G. Walter. Slow potential waves in the human brain associated with expectancy, attention and decision. *Archiv fur Psychiatrie und Nervenkrankheiten Vereinigt mit Zeitschrift fur die Gesamte Neurologie und Psychiatrie*, 206(3):309–322, 1964.

[93] F. Waszak, E. Wascher, P. Keller, I. Koch, G. Aschersleben, D. a. Rosenbaum, and W. Prinz. Intention-based and stimulus-based mechanisms in action selection. *Experimental Brain Research*, 162(3):346–356, apr 2005.

[94] D. M. Wegner and T. Wheatley. Apparent mental causation. Sources of the experience of will., 1999.

[95] Y. Zhang, Y. Chen, S. L. Bressler, and M. Ding. Response preparation and inhibition: the role of the cortical sensorimotor beta rhythm. *Neuroscience*, 156(1):238–46, sep 2008.

Appendix B

Manuscript 2: EEG signatures of voluntary decisions in Virtual Reality Environment.

EEG signature of voluntary decisions in Virtual Reality Environment.

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Abstract

The nature of volition and free-will has long been investigated by neuroscientists and philosophers of mind. Decisions about future actions are not always unitary, but instead may tackle particular aspect of the prospective action, such as timing, type of response or choice of whether to commit to an action or withstand. Growing evidence from neuroimaging studies suggests that different types of decisions may involve distinct neural substrates. In this EEG study we focus on temporal and spectral characteristics of three different types of voluntary decisions, in a paradigm involving continuous driving of a simulated car through a virtual environment. We show that voluntary decisions are manifested by broadband Alpha-Gamma desynchronization patterns, however the timing, magnitude and spectral contents of the modulation is not identical. Furthermore we show that human free choice is consistently biased by low-level behavioral preferences, which can explain part of the variance of "free action" outcome.

Keywords:
voluntary action, virtual environment, intention formation, alpha oscillations, presupplementary motor area (preSMA), electroencephalography(EEG)

1. Introduction

Understanding of the nature of human "free action" has a profound significance not only from the philosophical standpoint [5, 56], but also in domains such as legal system and responsibility [56], clinical practice and treatment of disorders of volition [8, 45, 67] and cognitive neuroscience [26, 47, 68].

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Rather than assuming a causal power of conscious will, the modern neuroscience of volition is based on the premise that "mental states rest on brain processes", and hence by measuring spatial and temporal correlates of volition in strictly controlled experiments we can infer about their underlying mind processes, including concepts as intriguing as "free will" and "consciousness". Although subjective report from the participants is often of interest (such as the perceived time of "urge" to move), it can be often circumvented by the experimental design. With this EEG study we intend to contribute to the current understanding of the dynamics of the processes involved in voluntary decisions about prospective actions, in a paradigm where the participants drive simulated car through a Virtual Reality (VR) environment and repeatedly take free choices regarding further route, in explicitly marked time intervals.

A lot of research efforts has been made to identify the neural circuitry involved in voluntary action. Two fundamental modes of action selection are often compared in the literature - the internally-generated and externally-cued actions, in experiments involving fMRI [14, 15], PET [16, 31], EMG [57] and EEG [17, 74, 78] modalities. One could argue that the internally-generated actions are just a particularly intricate version of the externally-cued actions, where decision is determined not only by neural representation of the early sensory inputs but also by the representation of prioprioceptive-, memory- and emotional states. However, it was repeatedly showed that the two modes of action selection have different temporal characteristics [74, 76, 78] and involve distinct neural pathways [14, 16, 31, 43]. The volition-related network consists of supplementary motor area (preSMA), prefrontal cortices (ACC, RCZ, DLPFC) and basal ganglia. The second network, corresponding to sensory-guided and stimulus-driven actions, starts in early sensory areas, followed by parietal cortex and sensory integration areas, projecting then to the lateral premotor areas. Both pathways terminate in primary motor cortex (M1) which is the final stage before the efferent motor command is sent down the spinal tract to the muscle terminals [61]. Regardless this distinction, in practice it is not always possible to categorize an action as entirely external or internal. Internally-generated actions will often require sensory guidance, while externally-cued actions will need a voluntary component for initiation (or disinhibition) of the motor preparation and execution. Thus the distinction is not exact nor mutually exclusive and in practice almost every action (with exception of spinal reflexes) will involve to certain extent both mechanisms [78] and as such may activate both pathways [14, 54] in coordinated manner. Finally, the role of sensory areas and its connections to the premotor areas might be relevant for voluntary action. The formation of forward models of intended action [52], as well as matching the predicted effect of motor command (prospective prediction) to the afferent sensory feedback (retrospective check) might be critical for the emergence of the feeling of agency [27] and perhaps for the experience of the volition and conscious will [79].

Brass and Haggard [9, 26] proposed a conceptual framework explaining a voluntary action as a composition of $What$, $When$ and $Whether$ components, each describing different aspect of intended action . Those components account

for the type, timing, and initiation/inhibition of the action respectively. The *Whether* component can be further divided into the "early" and the "late" components [26], where the former reflects decision to engage into action preparation or not, while the latter corresponds to the final validation and to the capacity to inhibit the preprepared action. Importantly, it has been shown in several fMRI studies that the three components may recruit partially distinct functional networks and have different neuronal realization [9, 29, 42, 71]. This suggests that electrophysiological dynamics, measured as the timing and spectral content of EEG responses, should also differ for *What*, *When* and *Whether* decisions. Validation of this hypothesis is one of the motivations for our study.

The nature of voluntary action has been repeatedly probed with EEG, and electrophysiological recordings in general, mostly in the context of free-paced action. In that context the slow, negative readiness potentials (RP) are known to precede not only the action itself but also the conscious awareness of the intention to act [28, 46, 47]. However, there are only few studies investigating spectral contents of voluntary decisions, and those are confined either to one particular type of decision or to arbitrary frequency bands. The voluntary inhibition has been shown to be reflected by Beta power modulation [77] and high-frequency Gamma (>40Hz) oscillations were reported to be involved in range of sequential processes related to preferential, voluntary decision making [24]. Alpha (8-13Hz) and Beta (16-30Hz) oscillations have been well studied in context of externally cued action preparation [19, 63, 75] but it remains unclear whether they distinguish internally-generated from externally-cued actions [17, 76]. To our knowledge, there are no reports of detailed comparison of different decision components in temporal and time-frequency domains.

Cortical oscillations and cross-frequency interactions may reflect the fundamental mechanisms of neural computation and effective integration of information across multiple spatiotemporal scales [11, 12, 48, 49]. Different brain rhythms and interactions between them have been associated to perception, cognition and sensorimotor function [1, 12, 36]. Modulation of Theta(3-7Hz) and Alpha (8-13Hz) rhythms was linked to central executive function [13, 36], working-memory load [33] and attention [37]. Alpha synchronization may represent top-down inhibitory control, while Alpha desynchronization reflects gradual release of inhibition over the task-relevant areas [39]. Given that alpha guides the attention, correlates with behavioral performance and allows memory and knowledge base access, it may be considered as a rhythm reflecting the most fundamental cognitive processes [37]. Besides its cognitive role, Alpha/Mu (8-13Hz) along with Beta (16-24Hz) oscillations are also recognized as main rhythms of motor function [3, 19, 40, 41, 62, 65, 66], both if movement is generated as response to stimulus or free-paced. Broadband reduction of power in range from Theta(3-6Hz) to Gamma(>40Hz) is observed during preparation to externally-cued action in delayed response Go-NoGo tasks [20, 21], and as such can reflect global preactivation of sensorimotor cortices and attentional orienting. Desynchronization of Alpha and Beta rhythms is stronger in Go than in NoGo condition [2], and can be lateralized if precue carries sufficient information about parameters of the requested action [19]. Moreover, Alpha and Beta

oscillations are modulated by motor imagery [51] and may correlate with activation of mirror neuron system during action observation [55], either of which can be reflected in decision processes. Beta bursts are also relevant to externally [41, 81] and internally [77] generated inhibition of action. Oscillations in higher frequency bands can also be relevant to volition and free action. It has been shown that distinct gamma modulation over different cortical areas encode subsequent stages of preferential choices and free decisions [24]. Gamma play role in execution of motor function [63, 64] and is relevant for memory and attention [34]. Considering the broad involvement of neural oscillations in realization of the cognition and motor function, it is very plausible that brain oscillations and selective modulation of spectral power (ERD/ERS) are the fundamental mechanisms underlying certain aspects of voluntary decisions, which motivated the methodological choices in our study.

In this EEG study we investigate voluntary decisions in a paradigm involving maneuvering a simulated car through a landscape of a dedicated Virtual Reality (VR) environment. By replacing the standard pictogram-based with the VR platform we intended to provide a natural, semi-realistic experience and thus reinforce the natural decision processes, while minimize the problems of monotony, fatigue and random-sequence generation [30]. Furthermore, a car driving paradigm is a suitable and naturally appealing setup for the purpose of investigating the differences between distinct components of voluntary decision.

We are interested in comparing three types of voluntary decisions about prospective action, along the taxonomy proposed by Brass and Haggard [9], i.e. *What* to do (left or right side-road), *When* to act (first or second side-road) and *Whether* to act (turn or no turn). Notably, our *Whether* condition corresponds to "early Whether" discussed above. On the other hand, our *When* condition is externally paced and involves a decision about timing of a future action. In this sense, our *When* condition involves selection between two temporal options, similarly like *What* condition involves selection between two spatial options. Thus our *When* condition differs subtly from the *When* component discussed by Brass and Haggard [9], where *When* decision is free-paced and initiates action in internally determined time moment. Furthermore it is important to emphasize that there was no reward nor incentive in our paradigm to favor one choice over another.

In our paradigm, the time intervals for decisions are determined and precede the motor execution by jittered intervals of approximately 4-10 seconds. The motivation for such paradigm is twofolds. Firstly, in daily situations it is common that voluntary decision about action does not result in instantaneous implementation of the respective motor command, but often in formation of intention to perform a given action in future, where the delay can range from seconds to days. Secondly, other paradigms which involve a free-paced voluntary action, and thus do not specify the exact timing of decision, face at least two main challenges. Firstly, the neural processes of action selection and intention formation may be confounded by immediately following processes of action preparation and motor implementation. Secondly, in case of voluntary decision not to act, there is no overt response and thus it is difficult to localize in time

the onset of neural processes corresponding to intentional non-acting, or inhibition. Our paradigm resolves those two major issues by (1) time-locking decision to visual cues (car crossing through a tunnel), and (2) imposing jittered interval of several seconds between decision (intention formation) and action (motor preparation and execution).

We expect that, given the broad functional and cognitive meaning of neural oscillations in Theta-Gamma range reported in literature (as discussed earlier), it is very plausible that interplay between those broadband oscillations might also play a critical role in effectuating and synchronizing the neural processes of voluntary decisions. Thus we expect selective modulation of oscillatory power to be present in the intervals corresponding to voluntary decisions. Secondly, given growing evidence from other studies indicating that different types of voluntary decisions are mediated by partially distinct neural pathways [9, 29, 71], we expect the dynamic brain responses to differ accordingly across *What*, *When* and *Whether* decisions, in terms of the timing and the spectral contents of the EEG response.

2. Methods

Participants Fifteen healthy adult student were recruited for the study (7 females) and each participated in three experimental sessions on three different days. The mean age was 24.7 (std=2.3). All participants were informed about the purpose of the study and signed an informed consent, in accordance with ethical requirements of the local committee.

Experiment All the participants took part in three experimental sessions on three different days. Each session consisted of multiple blocks in which participants were instructed to take various voluntary decisions in respect to driving a car through a virtual environment. The EEG, EMG and ET data was acquired simultaneously. Before the first session, structural T1-weighted MR image of the participants head was acquired. After each session, the electrode positions were measured with Localite Neuro-Navigation system. Finally, the participants filled a short questionnaire related to their performance and experience from the experiment. The scheme is presented in the Fig. 2, while the details of the task and experimental design are discussed in detail below.

Virtual environment We have designed and implemented a dedicated Virtual Reality (VR) environment for neuroscientific studies of cognition. The platform was designed in a modular fashion, separating the experimental design (Matlab based, XML specification of experiment) from the implementation and visualization layers (C#, JavaScript and Unity3D engine), and as such can be easily adapted to studies of volition, action preparation, attention, etc. Furthermore, the VR has been tested in experiments involving EEG, Eye-tracking and fMRI modalities, as well as closed-loop BCI mode. While the feasibility assessment and the detailed description of the VR are reported elsewhere (in preparation), below we will describe its adaptation to the current

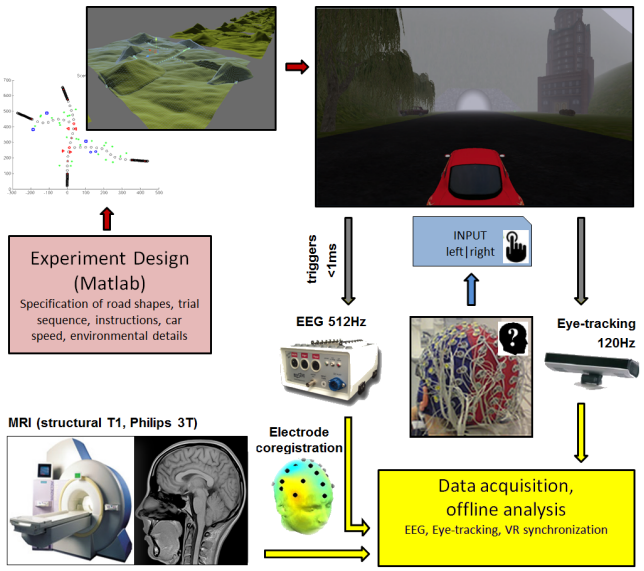

Figure 1: Virtual Reality (VR) design and synchronization with multi-modal data. A set of Matlab scripts specifies experimental design, i.e. sequence and timing of trials, shape of roads, position of crossroads, etc (top left). For each block of experiment, one Unity3D game is compiled, based on the specified experimental design (top right). During the cognitive experiment, fast encephalographic data from participants scalp and eye-tracking data are acquired (mid-right), which are synchronized with the game events by hardware triggering. Prior to the main experiment, structural MR images of participant brain are recorded with Philips 3T scanner (bottom left). EEG signals can then coregistered offline with structural MR images by means of 3D electrode position measurements (Localite Neuro-Navigation system).

study of voluntary decisions. The Fig. 1 presents an overall block diagram of the VR platform and the data flow scheme, while the Fig. 3 illustrates the experimental setup and trial structure.

Task A session consists of multiple VR games (blocks) with breaks in between. In each of the games the participant continuously drives a simulated car through subsequent sceneries (trials) which are connected by tunnels. In every tunnel the participant takes decisions regarding her action in the next scenery (for instance, decision between turning into the left or into the right side road). After leaving the tunnel, the participant turns into the appropriate side road, following her earlier decision. Importantly, the car follows the roads automatically and the participant input (button press) is only required when she intends to turn into a side-road.

Conditions Every game (block) is randomly assigned one of the four conditions, three of which correspond to different types of voluntary decisions and

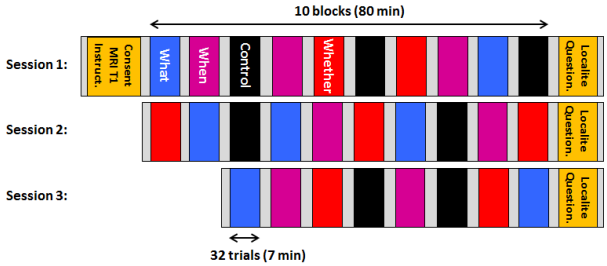

Figure 2: The participants took part in three sessions on three different days, each session was composed of 10, 10 and 8 blocks respectively. The conditions (types of decision to be taken) were assigned pseudo-randomly to the blocks. The first session was preceded by structural T1-weighted MR image acquisition. Each session was followed by electrode position measurements and a short questionnaire. Exemplary sequence of blocks for one of the participants is presented.

one to the control condition, where no decision is taken:

What Voluntary decision about *What* action to perform. In the tunnel, participant decides between left or right side-road, without knowing which side road would occur first (spatial decision)

When Voluntary decision about *When* to act. In the tunnel, participant decides between first or second side-road, without knowing if it will be left or right turn (temporal decision).

Whether Voluntary decision about *Whether* to act or not. In the tunnel, participant decides between turning into the first side road (action) or passively driving straight (no overt action).

Control No voluntary decisions. Participant passively observes the car, which automatically and randomly turns into side roads or drives straight.

Decision Voluntary decision in general, any of *What*, *When* or *Whether* conditions.

Block design and randomization The experiment has a block design, where each block corresponds to one of the conditions specified above. Each participant performed 3 sessions on different days, consisting of 10, 10 and 8 blocks respectively. Each block contained 32 trials (repetitions) of particular condition (see Fig. 2). Thus, in total 840 trials were acquired from each participant (210 trials per condition). Critically, we have automatically generated precisely 210 possible template layouts of the VR environment. Each of those templates corresponds to one trial and is used exactly once in each experimental condition. The trials are assigned to blocks in random order. The order of blocks (conditions) is also randomized (see Fig. 2, colored blocks). In this way we excluded the possibility of hidden biases imposed by rich visual stimulation, when comparing conditions in later analysis. Trials lasted approximately 13 seconds, blocks 7 minutes, and entire session approximately 80min. Participants could freely decide upon duration of the breaks between the blocks.

Trial structure Every trial (one of 210 possible templates) starts with a tunnel. Following the tunnel, open-air scenery shows up with a gently curved road leading to another tunnel (see Fig. 3, top panels). Along the road, there are two side roads, one leading to the left and one leading to the right. Their order is randomized. Side roads are marked by two symmetrically place road signs indicating turn possibility. Each of the side roads leads to another tunnel. Regardless which of the three routes participant chooses (left, right or straight), after reaching the ending tunnel the car will be transparently relocated to the entry tunnel of the subsequent trial (Fig. 3, top-middle panel). As a result, the sequence of trials (sceneries) if fully determined by experimental design, even though participants have subjective feeling of 'continuous navigation' through the environment. Duration of trials ($13.5 \pm 1.0s$), as well as onsets of the first ($5.5 \pm 0.04s$) and the second ($9.4 \pm 0.06s$) side roads are jittered by experimental manipulation and the physics of the car. However, the average duration of trial is equal regardless which route is taken, that is, participant gets no time benefit in taking one choice over another.

Tunnel - voluntary decision interval The critical point in the study is the construct of the tunnel. The tunnels mark the time interval when the actual decision processes are taking place regarding voluntary action. In tunnels, participants are supposed to stabilize their gaze on the fixation cross (as opposed to the rest of the game, where they can freely move their eyes). Furthermore, the visual field is stable and strongly constrained by dark, dense fog (Fig. 3, top-right panel). The onset and the midpoint of a tunnel are marked by two horizontal white lines on the road surface. Participants are instructed to take decision (specific to current condition, as explained earlier), as soon as the car crosses the first white line, marking the entry of the tunnel. Decision should be accomplished within $1.95 \pm 0.025s$, which is indicated by the second white line inside the tunnel.

Scenery - voluntary action interval After subsequent $1.2 \pm 0.025s$ the car leaves the tunnel. Depending on the earlier decision, participants awaits for the appropriate side road and executes the proper action (turn or not). The action is executed by pressing a key with left or right index finger within the natural interval of -2s to -0.5s before approaching the respective side road.

Instructions The main guidelines and instructions were given before starting the experiment. The participants were informed about the goal of the study, structure of the VR environment and details of the task. In particular, it was emphasized that decisions should be quick, spontaneous and independent in each tunnel. Participants should avoid pre-deciding, planning ahead and changing their mind after decision has been made. They should fixate gaze on the fixation cross while driving through the tunnels.

Before commencing the experiment, the participants performed short training session to get accustomed with the task, timing and the environment. Moreover, after each session, participants filled a simple control questionnaire ensuring they obeyed and understood the instructions.

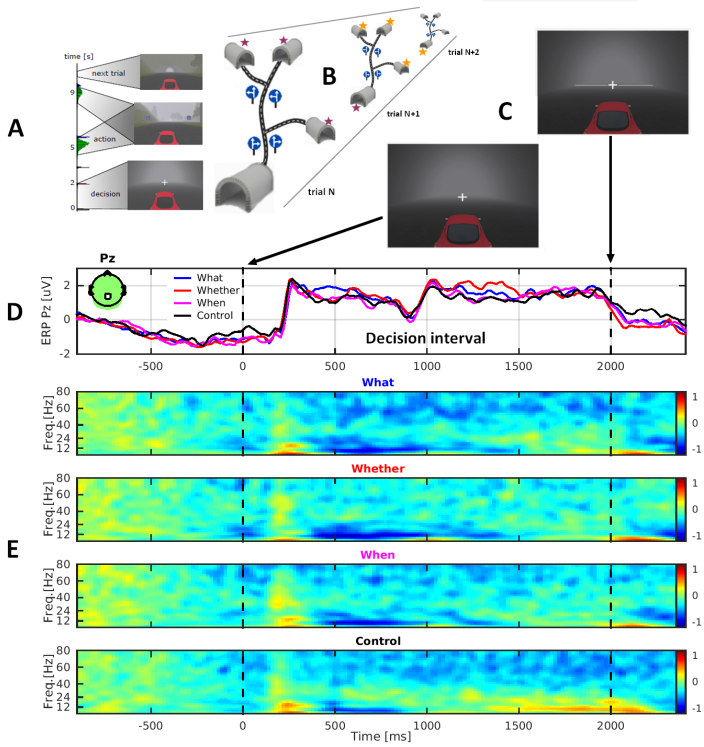

Figure 3: Experimental design and data analysis overview. **Panel A:** In each trial the participants take voluntary decisions while passing through a tunnel and perform the respective action a few seconds later, upon approaching the appropriate side road. **Panel B:** Each trial starts with the tunnel and has two side-roads denoted by symmetrically positioned road signs. The side-roads terminate with tunnels leading to the same destination trial. The participants have a feeling of continuous navigation through the environment, however the sequence of trials is experimentally controlled. **Panel C:** The decision interval of duration of 2 seconds is delimited by the tunnel entry and the moment when fixation cross crosses the white line on the road. **Panels D and E:** The decision interval (characterized by stable, foggy visual field) is submitted to the statistical tests presented further. The event-related potentials (ERP, panel D) and time-frequency maps (TF, panel E) specific to distinct Decisions and the Control condition will be compared to determine the EEG signatures of voluntary decisions. Pre-tunnel intervals will be used as a baseline, as specified later.

Critically, the experimental conditions differed only in terms of instructions presented visually to participants at the beginning of each block. The specific condition-related instructions informed which type of decision participant is supposed to repeatedly take in the course of the subsequent 32 trials. Participants were also reminded to take independent, spontaneous decisions, avoid

pre-deciding, planning ahead and changing their mind after decision had been made.

Data acquisition EEG data was acquired with Biosemi ActiveTwo system with 128 active electrodes. Two reference electrodes were positioned on left and right mastoids. Electromyographic (EMG) signals from the left and right index fingers were recorded with surface bipolar electrodes positioned at the first dorsal interosseous muscles. All data were amplified and digitized at sample rate of 512Hz. Continuous stream of visual stimulation (virtual environment) and button-press responses were synchronized with EEG signals via parallel port triggering. Apart from EEG data, the eye-tracking (ET) data was acquired with SMI Red system with sampling rate of 120Hz, and synchronized with EEG signals by the same hardware triggering mechanism. Additionally, the structural T1-weighted magnetic resonance images (sMRI) were acquired before the first session for each of the subjects. Positions of Biosemi electrodes were measured with Localite Neuro-Navigation system and coregisterred with anatomical images. The ET and sMRI data will be presented elsewhere (in preparation), while in this article we focus on EEG and behavioral results only. The scheme of the hardware configuration and the experimental data flow is presented at Fig.1.

EEG data preprocessing One participant was excluded from further analysis, as due to medical reasons he could not participate in MR acquisition which was a part of data acquisition protocol. The EEG data from the remaining 14 participants (42 sessions) were referenced to averaged mastoids reference channels, bandpass-filtered at 0.2-100Hz and downsampled to 256Hz. Long trials were extracted from 2.0 second before till 13.0 seconds after the Tunnel onsets, thus covering the entire interval of task-relevant events including decision, retention, action preparation and execution. The average amplitude of the baseline from -2000ms to -1000ms preceding the Tunnel onset was subtracted from each trial. The interval from -1000ms to 0ms was not included in baseline calculation to avoid inclusion of the confounding slow negative potential (CNV) preceding the Tunnel onset (Fig. 3 and Fig. 5).

Noisy channels were interpolated and the remaining noisy epochs were cleaned by thresholding (moving window 500ms, threshold 120uV). Infomax ICA was computed on the precleaned datasets [58]. ICA components corresponding to eye blinks, eye movements and local noise were removed from data (EEGLAB [18] and ADJUST [53] toolboxes). Final visual inspection was performed to ensure that no noisy epochs remained. In total, on average 17.6 epochs (out of 300) were removed from each session dataset, and 4.2 channels (out of 128) were interpolated. ICA components accounting for 59.8% of total variance were corrected for, most of those related to eye-blinks and eye-movements.
Depending on the block type (decision What, *When* or*Whether*) and participants choice (Left or Right, First or Second, Turn or NoTurn), each trials was labeled accordingly, so that different contrasts can be analyzed in subsequent analysis.

Event-related potential (ERP) analysis To investigate evoked activity, all the single trials corresponding to different decision/outcome were averaged separately. Then, for the purpose of comparing decision related activity, the interval from -1500ms to 3000ms, time-locked to the Tunnel onset was extracted. The interval accounted for both visual components and cognitive components related to voluntary decision. The ERP data was downsampled to 64Hz for the purpose of statistical comparisons, thus the final epoch-averaged data for each condition and participant had the size of (128 *channels* x 288 *time samples*). These data were submitted to further statistical tests (as discussed later), and used for visualization of temporal (ERP traces) and spatial (ERP topomaps) distribution of EEG activity.

Time-Frequency(TF) analysis To investigate induced activity and event-related changes in spectral power we used Morlet wavelets to decompose channel data into time frequency (TF) representation. The TF information was computed for each channel and epoch at the frequency range 4-80Hz with a step of 2Hz. Time window varied from 750ms at the lowest frequency (3 wavelet cycles) to 190ms at the highest (15 wavelet cycles). The temporal resolution of decomposition was set to 50 samples/seconds. The decomposition was performed after the cleaning procedure, on the trial subintervals directly surrounding the decision interval, i.e. from -1500ms to 3000ms, time-locked to the Tunnel onset. The time-frequency maps were baseline corrected for the interval from -1000ms to -500ms directly preceding the Tunnel onset. The final epoch-averaged time-frequency data for each condition and participant had size of [128 *channels* x 38 *frequency bands* x 158 *time samples*). The three-dimensional time-frequency information were subsequently submitted to nonparametric cluster-mass permutation tests, in order to evaluate statistically significant regions of desynchronization (ERD) or synchronization (ERS) of cortical oscillations. The TF data were also used for visualization of event-related spectral power perturbation (ERSP) in physiologically meaningful frequency bands, in particular the Alpha (8-13Hz), Beta (16-30Hz) and Gamma (50-80Hz) ranges.

Statistcal tests In all performed statistical tests, the multi-channel data series from Decision and Control conditions were submitted to repeated measures, two-tailed cluster-mass permutation tests [10, 50], as implemented in Fieldtrip toolbox [59]. The tests were performed on (1) two-dimensional, averaged, multi-channel ERP amplitudes and (2) three-dimensional, averaged, multi-channel time-frequency maps. In all cases, family-wise alpha level was set to 0.05. All 128 electrodes and all the time points corresponding to the intervals of interest (as described above) were included in the tests. In case of TF data, entire spectrum from 4-80Hz was used in the comparisons. The electrodes within distance of less than 5cm of one another were considered spatial neighbors, yielding in average 7.8 neighbors per electrode. For each comparison, repeated measures t-tests were computed using the original data and 1000 random within-participant permutations. For each permutation, all t-scores corresponding to uncorrected p-values lower or equal to 0.05 were combined

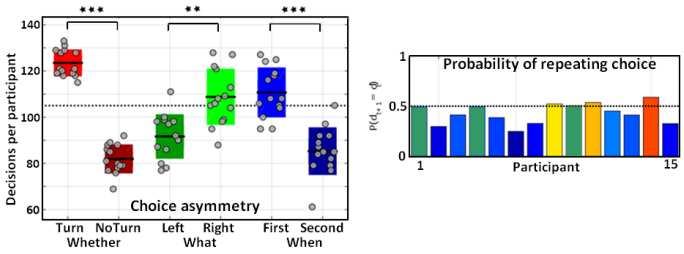

Figure 4: Behavioral biases in voluntary decision. **Left panel:** Number of choices in$Whether$(red), $What$(green) and $When$(blue) condition. Mean values (solid line), standard deviations (shaded area), and individual participant scores (gray dots) are presented. All participants displayed behavioral preferences to the Right turn over the Left, to the First side road over the Second, and to the Turn choice over the No-turn choice. **Right panel:** Probability of participant repeating her previous binary choice. Considerable bias to flip the choice can be observed for the majority or participants.

into clusters. The mass of each cluster was computed as the sum of the t-scores within that cluster. The highest cluster mass in each of the tests was used to estimate the distribution of null hypothesis.

This type of statistical tests allowed us to account for all the available data, without any a-priori constraints to either temporal or spatial extension of potential effects. Thus we minimized the need for subjective choices, while maintaining weak control of the family-wise alpha level (i.e., correcting for very large number of multiple comparisons). Cluster-mass permutation tests have been shown to perform well in exploratory studies and in case of broadly distributed ERP/ERSP effects [23, 50] by accounting for high temporal, spectral and spatial correlations inherent to high resolution EEG data, which is their fundamental advantage.

3. Results

The following notation will be used to denote experimental conditions (different types of decisions and the intentional outcomes):

What 'what' type of decision, free choice between left and right sideroad

When 'when' type of decision, free choice between first and second sideroad

Whether 'whether' type of decision, free choice between turning or not turning

Control control condition, participants are passive and do not make any choices

.

Behavioral data - choice asymmetry In all decision conditions, considerable asymmetry of choice was observed. The results are generated based on all

single-trial choices. In total 8820 were performed, 2940 for each decision type, 210 by each participant. Number of omission errors was negligible (<1%).

In the *Whether* condition, the participants preference to turn rather than abstain from turning (p<0.001). The mean asymmetry was 60.1% (std=2.8%), meaning that on average participants chose to turn in 60.1% and abstain from turning in 39.9% of trials. The most biased participant had asymmetry of 65.2%, while the least biased 55.6%.

In the *What* condition the participants displayed a preference to turn right rather than left (p=0.009). The mean asymmetry was 54.2% (std=5.1%). The most biased participant had asymmetry of 62.4%, while the least biased 44.2%.

In the *When* condition, the participants displayed a preference to turn into the first side road rather than into the second (p<0.001). The mean asymmetry was 56.5% (std=4.4%). The most biased participant had asymmetry of 63.9%, while the least biased 47.5%.

Detailed asymmetry results are presented in the Fig. 4, left panel.

Behavioral analysis - choice predictability Predictability of the choice on trial-to-trial basis was modeled with a simple, first-order Markov process. The model estimated a probability of participant repeating her last binary choice (for instance, probability of choosing left turn if the previous choice was also toward left, in *What* decision condition). The value of 0.5 corresponds to ideal randomly generated sequence, values below 0.5 indicate that participant had tendency to flip the choice (e.g. left-right-left-right-...), while values above 0.5 indicate that participant had tendency to repeat the previous action (e.g. left-left-left-left-...).

On average, probability of participant repeating her choice was 0.43 (std=0.10). Only one of the participants had considerably reverse tendency (0.59), and five others were close to 0.5 value. Remaining eight participants had a strong tendency to flip their choice. The most extreme individual score was 0.25, indicating that mere observation of choice sequence of that participant would allow to correctly predict her next trial choice with 75% chance of success.

Individual predictability values are presented in the Fig. 4, right panel.

ERP results The spatial and temporal extension of the ERP differences between *What*, *When*, *Whether* and Control conditions are presented in the Fig. 5.

The nonparametric cluster permutation tests were performed on the multichannel ERP traces from 128 channels and covering the time interval from -1500ms to 3000ms, where the subinterval of 0ms to 2000ms corresponds to the Decision interval.

The comparison of *What* with *Control* revealed an early positive ERP effect (p=0.04). The post-hoc inspection of the cluster suggests the effect occur in the time interval from 380ms to 550ms, and was widespread over 113 out of 128 electrodes (Fig. 5, top panel). The amplitude was highest at the central

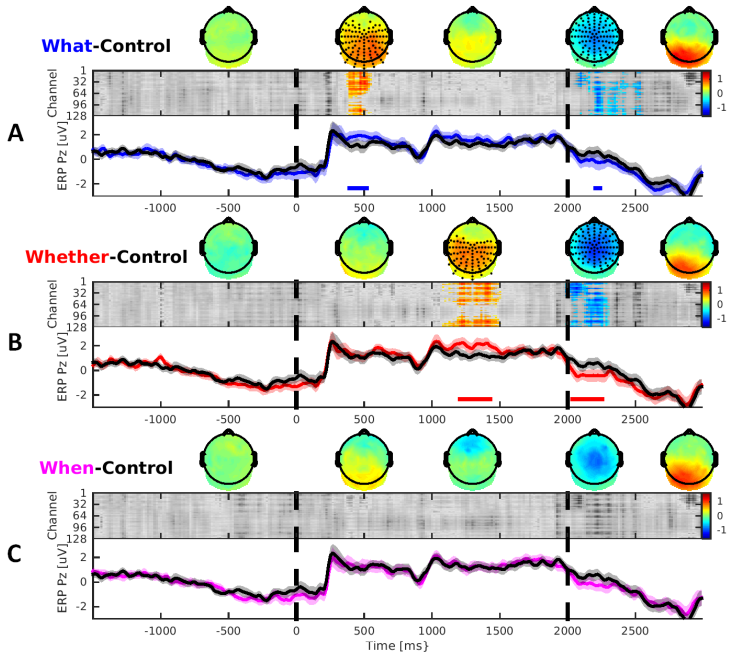

Figure 5: The ERP signatures of different decision types, obtained by subtracting the grand ERPs of the Control trials from the grand ERPs of the Decision trials, i.e. *What* (panel A, blue trace), *Whether* (panel B, red trace) and *When* (panel C, magenta trace). Each panel contains topographic distributions of potentials in the selected time-intervals (-500ms, 500ms, 1300ms, 2200ms, 2800ms) with significant electrodes marked by dots, a raster plot of all ERPs in *channel* x *time* space with non-significant regions faded out (cluster-mass permutation tests), and an ERP trace of Decision and Control conditions with shading representing 95% confidence intervals. Vertical dashed line denote decision interval (between the tunnel entry and the white line on the road). Notably, the posterior positive ERP effect occurs later in *Whether* than in *What* decisions, while *When* decisions did not display significant effect at all.

and the parietal areas. ERP activity at this time interval was not observed neither in *Whether* nor in *When* conditions.

The comparison of *Whether* with *Control* revealed considerably later positive ERP effect (p=0.005). The post-hoc inspection of the cluster suggests the effect was occured in the time interval from 1100ms to 1500ms, and spread over 112 posterior electrodes. The amplitude and spatial extension was similar to the *What-Control* effect however it was more prolonged (Fig. 5, middle panel). There was no significant ERP activity at this time interval neither in *What* nor in *When* conditions. The comparison of *When* with *Control* did not reveal

significant clusters. The ERP traces of the *When* condition behaved similarly to ERP traces of the *Control* condition (Fig. 5, bottom panel).

In direct comparisons of different types of decisions, only the contrast the *Whether* - *When* yielded significant positive cluster (p=0.002), which closely corresponded to the *Whether* - *Control* effect described above. In the comparison of the *What* condition with the *Whether* conditions, one positive cluster and one negative cluster were close to significance thresholds (p=0.075 and p=0.09 respectively). Those clusters corresponded to the early *What* and the late *Whether* effects described earlier.

Finally, the *What* and *Whether* decisions displayed a negative deflection of ERP immediately following the Decision interval (corresponding to the car crossing the white line in the tunnel). The significant, negative clusters (p=0.03 and p=0.017 respectively) spread over majority of the channels with the strongest effect at the central channels. The *When* decision had similar tendency, however the cluster was not significant (p=0.11).

Time-Frequency results Details of time-frequency differences and statistical results are presented in the Fig. 6, while the time-frequency decomposition results for individual conditions are illustrated in the Fig. 3, panel E.

The nonparametric cluster permutation tests were performed on the multichannel ERP traces from 128 channels and covering the broad spectrum 4-80Hz and the time interval from -1000ms to 2200ms, where the subinterval of 0ms to 2000ms corresponds to the Decision interval.

The time-frequency decomposition shows that all Decision conditions as well as the *Control* condition displayed broadband desynchronization starting approximately 500ms before the Tunnel (Fig. 3, panel E). However, the statistical comparisons indicated that the magnitude and spectral extension of the modulation was not identical across the different conditions.

Statistical comparison of the *What* and *Control* conditions revealed a a significant negative cluster (p=0.022). The cluster was prolonged in time 500-2200ms, dominated in Alpha (8-13Hz) range but briefly extended to Beta (16-30Hz) frequencies. The cluster reflects widespread Alpha and Beta ERD, dominating in the parietal region and stronger on the contralateral side (Fig. 6, panel A).

A similar negative cluster (p=0.024) was found in comparison of *Whether* and *Control* conditions. The cluster spanned over Alpha and Beta frequencies, however the Alpha ERD started earlier (-50-2200ms) and was more bilateral than in *What* condition. The second significant cluster (p=0.014) was positive and extended over Gamma (50-80Hz) range in the time interval 500-2050ms. The cluster corresponds to Gamma ERS, which was observed only in *Whether* condition (Fig. 6, panel B). A similar cluster differentiated *Whether* and *What* conditions in direct comparison (p=0.029) (Fig. 6, panel D).

In comparison of *When* and *Control* condition, a similar Alpha ERD was observed, however due to lower magnitude and spatial extension the cluster

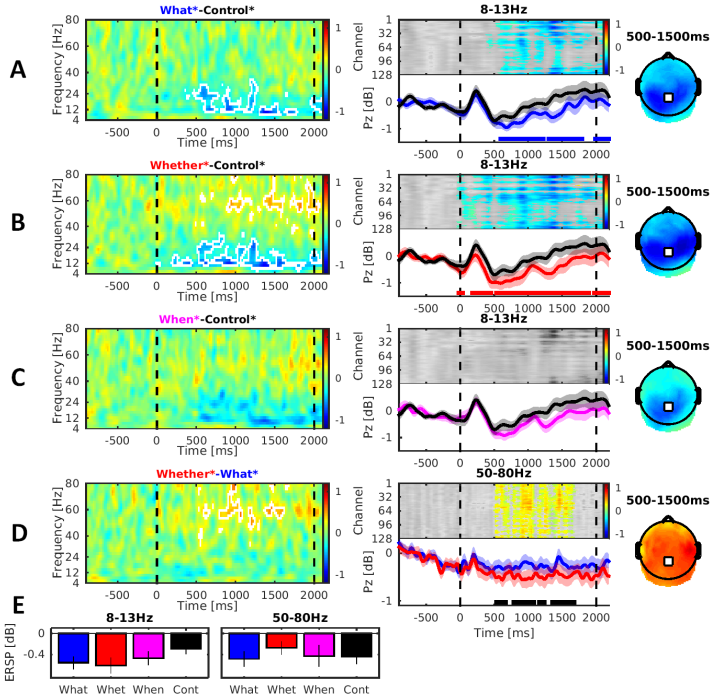

Figure 6: Time-frequency contrasts were computed for each possible pair of Decision and *Control* conditions. Three-dimensional data units in [*channel* x *frequency* x *time*] space were submitted to the cluster-mass permutation tests to determine spatio-spectro-temporal regions differentiating the conditions. The significant contrasts ($p<0.05$, corrected) at the representative centro-pariatel channel Pz are presented on the left panels. The exact extensions of the significant clusters are denoted by white lines. The middle panels present Alpha(8-13Hz) power desynchronization (αERD) at the multi-channel raster view (with non-significant regions faded out) and the traces of αERD for the representative Pz channel in different conditions. Topographic maps at the right panel indicate mostly parietal locus of the αERD. All Decisions are reflected by considerable Alpha and Beta modulation when compared with *Control* condition, although for the *When* condition the magnitude and spatial extension is not sufficient to reach cluster-level significance. The *Whether* condition is the only one with significantly reduced Gamma(50-80Hz) ERD. A widespread Gamma modulation differentiates the *Whether* decisions from the *What* decisions in direct comparison. The Alpha and Gamma power, averaged over all the channels and the time interval of 500-1500ms, are presented at the bottom bar plots.

slightly missed the significance thresholds ($p=0.057$) (Fig. 6, panel C).

4. Discussion

Behavioral results Interestingly, for every participants we observed substantial behavioral biases. Those biases were not participant specific, but gener-

alized over entire sample. Importantly, there was no behavioral benefit nor reward associated with choices, and the sequence of trials was also not affected by previous-trial choice. All except one participants displayed preference to "right" turn over "left" turn (54.2% assymetry on average). This can be justified by right-handedness, however we did not perform handedness assessment to validate this claim. The second plausible explanation is that participants are unconsciously biased towards the more routine behaviors. In the countries with right-hand traffic regulation, the right turns are more frequent and usually collision-safe. Even stronger preference biases were observed towards "turn" over "no turn" (60.1% on average) and "turn first" over "turn second" (56.5% on average). This tendency can be explained by individual impulsivity tendency. Regardless the exact psychological mechanisms behind the observed phenomena, it is notable that the unconscious behavioral biases can explain considerable part of a "free will"-driven action, especially in contexts were there are no explicit benefits associated with particular choice, or if the behavior is intentionally exploratory.

Importantly, those biases are emerging entirely from participants free binary choices, and are not influenced by experimenter's feedback or instructions. The participants are merely instructed to take new, independent, binary decisions in every trial, and avoid planning ahead. Participants remain unaware of the regular bias governing their choice. Thus, it seems that a certain fraction of variance in human voluntary action can be explained by low-level behavioral preferences.

Spectral modulation of Alpha, Beta and Gamma We have observed that prolonged Alpha and Beta desynchronization characterized all types of voluntary decisions, including *What* (p=0.022), *Whether* (p=0.024) and *When* (p=0.057, close to significance level). The reduction of Alpha power was prolonged for nearly 2 seconds of decision interval and covered almost entire scalp, although it was most emphasized at parietal channels (Fig. 6). The increased Gamma power was only observed in *Whether* condition (p=0.014), and the effect was strongest in central and parietal areas.

The Alpha and Beta band modulation in our task may reflect two distinct aspects of neural processing. The first possibility is related to involvement of motor system by either preactivation of the motor command [3, 17, 19] or imagery of the prospective action [51]. In case of *Whether* and *When* conditions the laterality of the response is not known a priori, thus it is possible that both options are equally preactivated. The second plausible function of the Alpha oscillations can be related to the joint activity of the early neural cognitive processes involved in internally-generated action selection. Those cognitive components could reflect a valuation of alternative options, conscious perception of the action selection and general mental effort related to a free choice. Decreased Alpha power may correlate with allocation of introspective attentional resources to the neural processes of action selection. Alpha band has been already linked to attentional processes [37, 76]. The allocation of attentional resources is presumably required for all types of conscious, voluntary

decisions, which would explain the occurence of the αERD in all the conditions. On the other hand, different types of decision may require a varying degree of the mental effort and attentional resources, which would explain differences in the magnitude of the αERD. It can be arguably suggested that the introspective attention is not a cognitive confound of volition, but rather an intrinsic and indispensable component of any conscious, internally-generated, voluntary choice. Under such assumption, modulation of Alpha can be interpreted not only as a correlate of introspective attention, but also as an indirect electrophysiological correlate of the early processes of intention formation.

The prolonged duration of the αERD may indicate that the decision is a relatively long process in which alternative actions and their outcomes are progressively valued and the evidence for either of them is accumulated. In this sense, decisions would be closely related to resolving a conflict between two competing options [69, 70]. The conflict monitoring is mediated by preSMA and rostral cingulate zone (RCZ) areas of the fronto-median cortical wall [69, 70]. Alternatively, prolonged αERD can reflect the processes following the voluntary decision, such as active attention to the selected option or the process of encoding of the decision outcome in the working memory. Indeed, reduction of Alpha band power was demonstrated during encoding of words in working memory [38].

In fact, it is plausible that the widespread αERD can be attributed not to a single process, but rather to multiple overlapping processes relevant to voluntary decisions. The evidence from the literature indicates that Alpha frequency oscillations multiple roles in cognition and sensorimotor integration. The functional meaning of Alpha depends primarily on the task and context, but also the exact frequency specifics and the recording site [2, 4, 22, 25, 32, 36, 37, 60].

We also observed increased Gamma power, but only in the *Whether* condition (Fig. 6). In fact, the *Whether* condition was the only one in which the participant had an option to consciously and voluntarily refrain from executing any action, i.e. decide not to act. The other two conditions always resulted in an action (turn into one of the side-roads). Thus it is possible that increased Gamma reflects active inhibition of an action, or conflict between options "to act" and "not to act". Indeed, synchronous activity of the cortical inhibitory interneuron networks is often manifested by gamma band oscillations [7].

The study of Yuval-Greenberg et al. [80] rose concerns that most of the Gamma band activity observed in EEG and MEG studies may reflect micro-saccadic eye activity rather than true brain sources. Although we cannot exclude this possibility with absolute certainty, we consider it unlikely in case of our study. Firstly, because statistically significant Gamma modulation was observed only in one of the conditions and not in the others, which would imply that saccadic activity was present only in *Whether* condition. Secondly, the *Whether* condition was identical to the other conditions in terms of visual stimulation and timing. Thirdly, the oculo-motor artifacts were handled in preprocessing steps and corrected for by rejection of respective ICA components.

Distinct EEG patterns in What, When and Whether decisions Our results suggest that all three components of voluntary decisions have distinct temporal and spectral representations. As discussed earlier, the magnitude and duration of the αERD differed between the conditions, and only *Whether* condition was characterized by Gamma ERS (Fig. 6). Furthermore, the *What* condition had significant, positive, early ERP component (p=0.04), while the *Whether* had a significant, late, positive ERP component (p=0.005). The *When* decision did not differ from the *Control* in terms of ERP (Fig. 5).

The differences in the oscillatory dynamics which we observed are not unexpected, considering the converging evidence from fMRI studies that different types of voluntary decisions recruit partially distinct neuronal networks [9, 29, 42, 71]. The pre-SMA and bilateral dorsal premotor areas are selectively active in action selection (*What*) while the timing adjustment (*When*) is mediated by network consisting of superior pre-SMA, insula, putamen and cerebellum. On the other hand, some other areas are common to both types of decisions, i.e. dorsolateral prefrontal cortex (DLPFC) and intraparietal sulcus (IPS). The *Whether* type of decision is mediated by areas of the dorso-mediofrontal cortex (dFMC) and rostral cingulate zone (RCZ), located more anterior than pre-SMA [9, 42]. Given that those areas only partially overlap, it is highly expected that the very nature of the respective neuronal functions differs as well, and so do the temporal constraints and the resource requirements. This can explain statistically significant differences in the ERP and ERD/ERS observed in our data.

Interestingly, we have not observed ERP effect in the *When* condition, and the corresponding αERD effect was considerably weaker than in the other conditions and in fact did not reach the significance levels (p=0.057). One of the possible explanation is that the *When* condition in our paradigm is externally determined in time and tackles the choice of the timing of the future action, whereas the *When* condition as defined by Brass and Haggard model is free-paced, or "internally determined" in time and tackles the initiation of internal action. As such, our *When* condition involves selection between two competing temporal options, similarly like *What* condition involves selection between two competing spatial options. It is plausible that the temporal options are more abstract and thus have more subtle neuronal representation than the spatial options, where the neuronal substrate is clearly defined (action preparation for the left or right index finger movement).

It is also possible, that despite the best attempts we have not managed to completely disentangle the pure *What*, *When* and *Whether* components of voluntary action. If that would be the case, one of our conditions could implicitly activate more than one of the decision components. For instance, assuming that participants make their choices based on the prospective memory system [72] and thus mentally visualize their next action based on the recent history of their choices, it is possible that *Whether* and *When* conditions would implicitly involve the *What* component in form of the envisioned assumption about direction of the turn.

Finally, it is also possible that each of the conditions involves a conflict resolution between two competing, alternative options [69, 70]. The differences in EEG responses could then be attributed to distinct neuronal representation of the competing options in different conditions (spatial left/right, temporal first/second, inhibitory turn/no-turn).

Detection and classification of decision process Our results suggest that the voluntary decision processes regardless of their final outcome can be detected by scalp recordings, even though the actual motor execution is deliberately postponed in time by interval of several seconds. Furthermore, the patterns of modulation of the brain oscillations were not identical for different types of the conscious voluntary decisions.

In context of free-paced initiation of movement (the *When* component according to Brass and Haggard [9]), Soon et al. [73] demonstrated in fMRI study that in certain circumstances the intention to move can be predicted as early as 10 seconds before it enters conscious awareness. In another study using online EEG Bai et al. [6] reported successful prediction of intention to move on average 0.6 seconds before the movement onset, based on Alpha and Beta power shift and slow readiness potentials.

Considering that we observed a robust modulation of EEG signals for all components of voluntary decision, the question arises if those distinct components can be detected and classified on single trial basis, in the context where the actual motor action is postponed in time. Further studies along this line are needed to assess feasibility of such classification, which could lead to constructing enhanced, non-invasive, intention-driven BCI systems.

5. Conclusions

We applied a dedicated, ecologically-valid Virtual Reality environment to the neuroscientific study of voluntary decisions, in order to provide a rich, continuous visual stimulation resembling natural life scenarios. By doing so we intended to enhance the natural decision processes and minimize the problems of fatigue and random sequence generation [30].

We found that the three fundamental types of voluntary decision about prospective action (*What*, *When* and *Whether* components [9]) differ in their temporal signature and broadband spectral modulation. The *Whether* decisions have the strongest spectral response and involve Gamma band modulation, possibly due to involvement of inhibitory mechanisms. The *When* decisions display the weakest EEG response, perhaps due to less explicitly defined neuronal representation of the abstract concepts related to time domain.

Regardless of the type of decision, we observed a significant power desynchronization, particularly prolonged in Alpha(8-13Hz) range, lasting for approximately 2 seconds. It has been repeatedly demonstrated that low frequency oscillations play fundamental role in attention, memory, functional integration and executive function ([35, 37, 44, 49]). Our results suggest that Alpha and Beta

oscillations may also play a critical role in voluntary decision formation. The role of those oscillations can be twofolds: (1) preactivation of motor command and (2) representation of higher cognitive components such as introspective attention, option valuation and mental imagery of the intended choice.

The rich spectral representation of voluntary action is a promising finding in relation to BCI research. The tentative next step is to quantitatively assess a feasibility of single-trial, online detection of decision processes with prospect of constructing enhanced, intention-driven BCI systems. Also further investigation is needed to localize sources of the EEG signatures and thus relate our findings more precisely to the fMRI literature [9, 26, 29, 71].

References

[1] E. Başar, C. Başar-Eroglu, S. Karakaş, and M. Schürmann. Brain oscillations in perception and memory. *International Journal of Psychophysiology*, 35(2-3):95–124, mar 2000.

[2] C. Babiloni, A. Brancucci, L. Arendt-Nielsen, F. Babiloni, P. Capotosto, F. Carducci, F. Cincotti, L. Romano, A. C. N. Chen, and P. M. Rossini. Alpha event-related desynchronization preceding a go/no-go task: a high-resolution EEG study. *Neuropsychology*, 18(4):719–728, 2004.

[3] C. Babiloni, F. Carducci, F. Cincotti, P. M. Rossini, C. Neuper, G. Pfurtscheller, and F. Babiloni. Human movement-related potentials vs desynchronization of EEG alpha rhythm: a high-resolution EEG study. *NeuroImage*, 10(6):658–65, dec 1999.

[4] C. Babiloni, F. Vecchio, A. Bultrini, G. Luca Romani, and P. M. Rossini. Pre- and poststimulus alpha rhythms are related to conscious visual perception: a high-resolution EEG study. *Cerebral cortex (New York, N.Y. : 1991)*, 16(12):1690–700, dec 2006.

[5] J. Baer, J. C. Kaufman, and R. F. Baumeister. Are We Free?: Psychology and Free Will. *Are We Free?: Psychology and Free Will*, pages 1–367, 2008.

[6] O. Bai, V. Rathi, P. Lin, D. Huang, H. Battapady, D. Y. Fei, L. Schneider, E. Houdayer, X. Chen, and M. Hallett. Prediction of human voluntary movement before it occurs. *Clinical Neurophysiology*, 122(2):364–372, feb 2011.

[7] M. Bartos, I. Vida, and P. Jonas. Synaptic mechanisms of synchronized gamma oscillations in inhibitory interneuron networks. *Nature reviews. Neuroscience*, 8(1):45–56, jan 2007.

[8] G. Berrios and M. Gili. Will and its disorders: a conceptual history. *History of Psychiatry*, 6(21):087–104, mar 1995.

[9] M. Brass and P. Haggard. The What, When, Whether Model of Intentional Action. *The Neuroscientist*, 14(4):319–325, aug 2008.

[10] E. T. Bullmore, J. Suckling, S. Overmeyer, S. Rabe-Hesketh, E. Taylor, and M. J. Brammer. Global, voxel, and cluster tests, by theory and permutation, for a difference between two groups of structural MR images of the brain. *IEEE transactions on medical imaging*, 18(1):32–42, sep 1999.

[11] G. Buzsáki and B. O. Watson. Brain rhythms and neural syntax: implications for efficient coding of cognitive content and neuropsychiatric disease. *Dialogues in clinical neuroscience*, 14(4):345–67, dec 2012.

[12] R. T. Canolty and R. T. Knight. The functional role of cross-frequency coupling. *Trends in cognitive sciences*, 14(11):506–15, nov 2010.

[13] J. F. Cavanagh and M. J. Frank. Frontal theta as a mechanism for cognitive control. *Trends in cognitive sciences*, 18(8):414–21, aug 2014.

[14] R. Cunnington, C. Windischberger, L. Deecke, and E. Moser. The preparation and execution of self-initiated and externally-triggered movement: a study of event-related fMRI. *NeuroImage*, 15(2):373–85, feb 2002.

[15] F. Debaere, N. Wenderoth, S. Sunaert, P. Van Hecke, and S. P. Swinnen. Internal vs external generation of movements: differential neural pathways involved in bimanual coordination performed in the presence or absence of augmented visual feedback. *NeuroImage*, 19(3):764–76, jul 2003.

[16] M. P. Deiber, R. E. Passingham, J. G. Colebatch, K. J. Friston, P. D. Nixon, and R. S. J. Frackowiak. Cortical areas and the selection of movement: a study with positron emission tomography. *Experimental Brain Research*, 84(2):393–402, jan 1991.

[17] M.-P. Deiber, E. Sallard, C. Ludwig, C. Ghezzi, J. Barral, and V. Ibañez. EEG alpha activity reflects motor preparation rather than the mode of action selection. *Frontiers in Integrative Neuroscience*, 6:59, jan 2012.

[18] A. Delorme and S. Makeig. EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *Journal of neuroscience methods*, 134(1):9–21, mar 2004.

[19] L. M. Doyle, K. Yarrow, and P. Brown. Lateralization of event-related beta desynchronization in the EEG during pre-cued reaction time tasks. *Clinical Neurophysiology*, 116(8):1879–1888, aug 2005.

[20] I. Funderud, M. Lindgren, M. Løvstad, T. Endestad, B. Voytek, R. T. Knight, and A. K. Solbakk. Differential Go/NoGo activity in both contingent negative variation and spectral power. *PLoS ONE*, 7(10):e48504, 2012.

[21] C. M. Gómez, E. Vaquero, D. López-Mendoza, J. González-Rosa, and M. Vázquez-Marrufo. Reduction of EEG power during expectancy periods in humans. *Acta neurobiologiae experimentalis*, 64(2):143–51, jan 2004.

[22] I. C. Gould, A. C. Nobre, V. Wyart, and M. F. S. Rushworth. Effects of decision variables and intraparietal stimulation on sensorimotor oscillatory activity in the human brain. *The Journal of neuroscience : the official journal of the Society for Neuroscience*, 32(40):13805–18, oct 2012.

[23] D. M. Groppe, T. P. Urbach, and M. Kutas. Mass univariate analysis of event-related brain potentials/fields I: A critical tutorial review. *Psychophysiology*, 48(12):1711–1725, dec 2011.

[24] A. G. Guggisberg, S. S. Dalal, A. M. Findlay, and S. S. Nagarajan. High-frequency oscillations in distributed neural networks reveal the dynamics of human decision making. *Frontiers in human neuroscience*, 1:14, jan 2007.

[25] S. Haegens, H. Cousijn, G. Wallis, P. J. Harrison, and A. C. Nobre. Inter- and intra-individual variability in alpha peak frequency. *NeuroImage*, 92:46–55, may 2014.

[26] P. Haggard. Human volition: towards a neuroscience of will. *Nature reviews. Neuroscience*, 9(12):934–46, dec 2008.

[27] P. Haggard and V. Chambon. Sense of agency. *Current biology : CB*, 22(10):R390–2, may 2012.

[28] P. Haggard and M. Eimer. On the relation between brain potentials and the awareness of voluntary movements. *Experimental Brain Research*, 126(1):128–133, apr 1999.

[29] F. Hoffstaedter, C. Grefkes, K. Zilles, and S. B. Eickhoff. The "what" and "when" of self-initiated movements. *Cerebral cortex (New York, N.Y. : 1991)*, 23(3):520–30, mar 2013.

[30] M. Jahanshahi and G. Dirnberger. The left dorsolateral prefrontal cortex and random generation of responses: Studies with transcranial magnetic stimulation. *Neuropsychologia*, 37(2):181–190, 1998.

[31] I. H. Jenkins. Self-initiated versus externally triggered movements: II. The effect of movement predictability on regional cerebral blood flow. *Brain*, 123(6):1216–1228, jun 2000.

[32] O. Jensen. Oscillations in the Alpha Band (9-12 Hz) Increase with Memory Load during Retention in a Short-term Memory Task. *Cerebral Cortex*, 12(8):877–882, aug 2002.

[33] O. Jensen and C. D. Tesche. Frontal theta activity in humans increases with memory load in a working memory task. *European Journal of Neuroscience*, 15(8):1395–1399, apr 2002.

[34] X. Jia and A. Kohn. Gamma rhythms in the brain. *PLoS Biology*, 9(4):e1001045, apr 2011.

[35] W. Klimesch. EEG-alpha rhythms and memory processes. *International Journal of Psychophysiology*, 26(1-3):319–340, 1997.

[36] W. Klimesch. EEG alpha and theta oscillations reflect cognitive and memory performance: a review and analysis. *Brain Research Reviews*, 29(2-3):169–195, 1999.

[37] W. Klimesch. α-band oscillations, attention, and controlled access to stored information. *Trends in cognitive sciences*, 16(12):606–17, dec 2012.

[38] W. Klimesch, M. Doppelmayr, H. Russegger, and T. Pachinger. Theta band power in the human scalp EEG and the encoding of new information. *Neuroreport*, 7(7):1235–40, may 1996.

[39] W. Klimesch, P. Sauseng, and S. Hanslmayr. EEG alpha oscillations: The inhibition–timing hypothesis. *Brain Research Reviews*, 53(1):63–88, 2007.

[40] R. Kristeva-Feige, C. Fritsch, J. Timmer, and C.-H. Lücking. Effects of attention and precision of exerted force on beta range EEG-EMG synchronization during a maintained motor contraction task. *Clinical Neurophysiology*, 113(1):124–131, jan 2002.

[41] A. A. Kühn, D. Williams, A. Kupsch, P. Limousin, M. Hariz, G.-H. Schneider, K. Yarrow, and P. Brown. Event-related beta desynchronization in human subthalamic nucleus correlates with motor performance. *Brain : a journal of neurology*, 127(Pt 4):735–46, apr 2004.

[42] S. Kühn and M. Brass. When doing nothing is an option: The neural correlates of deciding whether to act or not. *NeuroImage*, 46(4):1187–1193, jul 2009.

[43] H. C. Lau, R. D. Rogers, N. Ramnani, and R. E. Passingham. Willed action and attention to the selection of action. *NeuroImage*, 21(4):1407–1415, 2004.

[44] M. Le Van Quyen, J. Foucher, J. Lachaux, E. Rodriguez, A. Lutz, J. Martinerie, and F. J. Varela. Comparison of Hilbert transform and wavelet methods for the analysis of neuronal synchrony. *Journal of neuroscience methods*, 111(2):83–98, oct 2001.

[45] F. Lhermitte. 'Utilization behaviour' and its relation to lesions of the frontal lobes. *Brain*, 106(2):237–255, jun 1983.

[46] B. Libet. *Neurophysiology of Consciousness*. Birkhäuser Boston, Boston, MA, 1993.

[47] B. Libet, C. A. Gleason, E. W. Wright, and D. K. Pearl. Time of conscious intention to act in relation to onset of cerebral activity (readiness-potential). *Brain*, 106(3):623–642, sep 1983.

[48] J. E. Lisman and O. Jensen. The θ-γ neural code. *Neuron*, 77(6):1002–16, mar 2013.

[49] F. Lopes da Silva. EEG and MEG: relevance to neuroscience. *Neuron*, 80(5):1112–28, dec 2013.

[50] E. Maris. Statistical testing in electrophysiological studies. *Psychophysiology*, 49(4):549–65, apr 2012.

[51] D. J. McFarland, L. A. Miner, T. M. Vaughan, and J. R. Wolpaw. Mu and Beta Rhythm Topographies During Motor Imagery and Actual Movements. *Brain Topography*, 12(3):177–186, 2000.

[52] R. C. Miall and D. M. Wolpert. Forward models for physiological motor control, 1996.

[53] A. Mognon, J. Jovicich, L. Bruzzone, and M. Buiatti. ADJUST: An automatic EEG artifact detector based on the joint use of spatial and temporal features. *Psychophysiology*, 48(2):229–40, feb 2011.

[54] V. A. Mueller, M. Brass, F. Waszak, and W. Prinz. The role of the preSMA and the rostral cingulate zone in internally selected actions. *NeuroImage*, 37(4):1354–61, oct 2007.

[55] S. D. Muthukumaraswamy and B. W. Johnson. Primary motor cortex activation during action observation revealed by wavelet analysis of the EEG. *Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology*, 115(8):1760–6, aug 2004.

[56] L. Nadel and W. Sinnott-Armstrong. Conscious Will and Responsibility: A Tribute to Benjamin Libet. *Conscious Will and Responsibility: A Tribute to Benjamin Libet*, pages 1–288, 2010.

[57] S. S. Obhi and P. Haggard. Internally generated and externally triggered actions are physically distinct and independently controlled. *Experimental Brain Research*, 156(4):518–523, jun 2004.

[58] J. Onton, M. Westerfield, J. Townsend, and S. Makeig. Imaging human EEG dynamics using independent component analysis. *Neuroscience and biobehavioral reviews*, 30(6):808–22, jan 2006.

[59] R. Oostenveld, P. Fries, E. Maris, and J. M. Schoffelen. FieldTrip: Open source software for advanced analysis of MEG, EEG, and invasive electrophysiological data. *Computational Intelligence and Neuroscience*, 2011, 2011.

[60] M. Osaka. Peak Alpha Frequency of EEG during a Mental Task: Task Difficulty and Hemispheric Differences. *Psychophysiology*, 21(1):101–105, jan 1984.

[61] R. E. Passingham. Two cortical systems for directing movement. *Ciba Foundation symposium*, 132:151–64, jan 1987.

[62] G. Pfurtscheller. Central beta rhythm during sensorimotor activities in man. *Electroencephalography and Clinical Neurophysiology*, 51(3):253–264, mar 1981.

[63] G. Pfurtscheller, B. Graimann, J. E. Huggins, S. P. Levine, and L. A. Schuh. Spatiotemporal patterns of beta desynchronization and gamma synchronization in corticographic data during self-paced movement. *Clinical Neurophysiology*, 114(7):1226–1236, jul 2003.

[64] G. Pfurtscheller and C. Neuper. Simultaneous EEG 10 Hz desynchronization and 40 Hz synchronization during finger movements. *Neuroreport*, 3(12):1057–60, dec 1992.

[65] G. Pfurtscheller, A. Stancák, and C. Neuper. Event-related synchronization (ERS) in the alpha band — an electrophysiological correlate of cortical idling: A review. *International Journal of Psychophysiology*, 24(1-2):39–46, nov 1996.

[66] G. Pfurtscheller, A. Stancák, and C. Neuper. Post-movement beta synchronization. A correlate of an idling motor area? *Electroencephalography and Clinical Neurophysiology*, 98(4):281–293, apr 1996.

[67] H. S. Prado, M. C. Rosario, J. Lee, A. G. Hounie, R. G. Shavitt, and E. C. Miguel. Sensory phenomena in Obsessive-Compulsive Disorder and tic disorders: a review of the literature. *CNS Spectrums*, 13(5):425–432, may 2008.

[68] Z. H. Rappaport. The neuroscientific foundations of free will. *Advances and technical standards in neurosurgery*, 37(37):3–23, jan 2011.

[69] K. R. Ridderinkhof, M. Ullsperger, and E. A. Crone. The Role of the Medial Frontal Cortex in Cognitive Control. *Science (New York, N.Y.)*, 306(5695):443–447, oct 2004.

[70] M. F. S. Rushworth, M. E. Walton, S. W. Kennerley, and D. M. Bannerman. Action sets and decisions in the medial frontal cortex. *Trends in Cognitive Sciences*, 8(9):410–417, sep 2004.

[71] K. Sakai. What and when: Parallel and convergent processing in motor control. *Journal of Neuroscience*, 20(7):2691 – 2700, 2000.

[72] D. L. Schacter, D. R. Addis, and R. L. Buckner. Remembering the past to imagine the future: the prospective brain. *Nature reviews. Neuroscience*, 8(9):657–61, sep 2007.

[73] C. S. Soon, M. Brass, H.-J. Heinze, and J.-D. Haynes. Unconscious determinants of free decisions in the human brain. *Nature neuroscience*, 11(5):543–5, 2008.

[74] G. Thut, C.-A. Hauert, P. Viviani, S. Morand, L. Spinelli, O. Blanke, T. Landis, and C. Michel. Internally driven vs. externally cued movement selection: a study on the timing of brain activity. *Cognitive Brain Research*, 9(3):261–269, jun 2000.

[75] C. Toro, G. Deuschl, R. Thatcher, S. Sato, C. Kufta, and M. Hallett. Event-related desynchronization and movement-related cortical potentials on the ECoG and EEG. *Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section*, 93(5):380–389, oct 1994.

[76] P. Tremblay, D. M. Shiller, and V. L. Gracco. On the time-course and frequency selectivity of the EEG for different modes of response selection: evidence from speech production and keyboard pressing. *Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology*, 119(1):88–99, jan 2008.

[77] E. Walsh, S. Kühn, M. Brass, D. Wenke, and P. Haggard. EEG activations during intentional inhibition of voluntary action: an electrophysiological correlate of self-control? *Neuropsychologia*, 48(2):619–26, jan 2010.

[78] F. Waszak, E. Wascher, P. Keller, I. Koch, G. Aschersleben, D. a. Rosenbaum, and W. Prinz. Intention-based and stimulus-based mechanisms in action selection. *Experimental Brain Research*, 162(3):346–356, apr 2005.

[79] D. M. Wegner and T. Wheatley. Apparent mental causation. Sources of the experience of will., 1999.

[80] S. Yuval-Greenberg, O. Tomer, A. S. Keren, I. Nelken, and L. Y. Deouell. Transient Induced Gamma-Band Response in EEG as a Manifestation of Miniature Saccades. *Neuron*, 58(3):429–441, 2008.

[81] Y. Zhang, Y. Chen, S. L. Bressler, and M. Ding. Response preparation and inhibition: the role of the cortical sensorimotor beta rhythm. *Neuroscience*, 156(1):238–46, sep 2008.

Appendix C

Manuscript 3: Modular construction of Virtual Reality for neuroimaging research.

MODULAR CONSTRUCTION OF VIRTUAL REALITY FOR NEUROIMAGING RESEARCH

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Highlights:

- We developed a framework to combine virtual reality with neuroimaging experiments
- This framework integrates classic experimental principles like jitter, randomisation and trial based design
- Parametric manipulation of experimental factors is provided by parametric changes in the VR itself.
- The framework allows for researchers to keep a high level of control over their experimental specification while visualization aspects can be outsourced to software developers.
- The required experimental infrastructure does not differ from a standard neuroimaging experiment.

Keywords: Virtual Reality, fMRI, EEG, navigation, voluntary

Abstract

We constructed a framework for generation of Virtual Reality (VR) which was suited for neuroimaging experiments and provides a car driving experience. The VR generation hereby followed the principle to allow for specification of the experiment in a way common to neuroscience. Design features of standard neuroimaging experiments, for instance randomisation, jittering or factorial, trial-based design were transferred to the VR. Yet, we took care of creating a seamless experience for the user which disguises these design principles to a higher extent as a standard design would do.

VR construction is based on a layered software architecture and strongly relies on the principle of modularity. In a first step, the layout is specified in 2D in the form of XML documents. In a second step XML documents are processed further to 3D scenes via procedural landscape generation and in the third step they are linked together and an executable is created which can be run on a standard PC. Input / Output is integrated flexibly via different subroutines and a communication protocol relying on text files, so that every hardware, especially custom made, can be used. Due to the separation into experimental logic and visualization researchers without a background in software engineering are able to design, control and change their experiment whereas visualisation can be developed in a separate manner.

We provide some imaging results to show principal usability of the design, as well as some behavioural and questionnaire data to show how subjects received the VR.

INTRODUCTION

Functional Magnetic Resonance Imaging has provided invaluable insights into how the human brain works, both in healthy volunteers and in patients. It's field of application has broadened from research in cognitive neuroscience to clinical applications (Matthews et al., 2006) and continues to expand into fields like marketing research or brain computer interfaces (Reimannke et al., 2011; Sitaram et al., 2009). Behavioural paradigms, however, which are presented to subjects in the scanner via screen and headphones, have widely remained the same. They mostly involve static stimuli, following a certain study specific logic with a certain degree of jitter. Such stimuli are relatively easy to construct, relatively easy to present and, what might be even more important, relatively easy to optimize towards specific aspects - like for instance contrast - while other aspects of the stimulus space - like for instance saturation - can be controlled accordingly. Mechanisms underlying their presentation are well-studied and they can be closely related to psychological concepts like stimulus – response theory (Guthrie, 1935; Hull, 1943; Thorndike, 1898) and psychophysics (Gescheider, 1997). Statistical theory provides powerful methods for their analysis like signal detection theory or linear regressions (Aiken et al., 2003; Green et al., 1966).

Yet, these are rarely the kind of stimuli which we experience in our daily lives and research in many topics might suffer from missing ecological validity. Such topics involve more complex tasks, for instance decision making where a high number of variables potentially have to be taken into account (Heekeren et al., 2003; Sanfey et al., 2003), emotions where interaction with other acting agents and memory might be a decisive factor (Dolcos et al., 2004; Dolcos et al. 2005; Murty et al., 2012), consciousness and many others. Here, research might benefit a lot from studying human subjects in their natural habitat. Use of an fMRI scanner in the outer world however is not to expect in the near future as these machines are extremely bulky and with the development of scanners with higher field strengths machines rather get bigger than smaller. Thus, the scanner cannot be brought into the real world but the real world must be simulated in the scanner. For these purposes the use of Virtual Reality (VR) technique has been proven very successful (Maguire, 2012; Spiers & Maguire., 2004; Spiers & Maguire, 2007). VRs provide a high level of experienced reality, an immersive feeling and high ecological validity. In fact, they can be optimized towards certain aspects in the same way as simple stimuli and for instance be constructed with parametrical regularity. Moreover, social situations can be recreated in an identical manner and thus become comparable across subjects, a scenario which never occurs in real life as interaction always contaminates a social situation (observer-effects, experimenter effects).

Yet, compared to the number of neuroimaging studies that have been published the overall number of studies employing VR is very small (Table 1). On average, only a few out of 1000 neuroimaging studies employed a VR paradigm and of these few some are literature reviews, purely methodological studies

or investigations that reused existing paradigms. We see two main reasons as to why this potentially extremely useful technique is so underrepresented.

Table1: Number of studies employing Virtual Reality in EEG/fMRI compared to the total number of studies (data taken from an abstract-title PubMed search 02/05/2016 with the keywords VR/Virtual Reality and EEG/Electroencephalography or fMRI/functional Magnetic Resonance Imaging).

	Neuroimaging & VR	Neuroimaging only	Relative Frequency [%]
fMRI	127	30555	0.4
EEG	103	61862	0.15

First, almost every one of the published articles introducing a new VR paradigm stresses the complexity, thus costs, which is inherent in this approach. This complexity is present on all steps of the experiment, both in designing an experiment, constructing the stimuli, in presenting a subject with the experiment and in analysing the data. Reasons are both technical ones and the high number of dimensions involved. As it is so expensive to introduce a new paradigm a number of studies have used pre-existing stimuli like movies or commercially available games (Maguire, 2012). That however diminishes experimental power.

Second, we believe that it is a problem for many researchers that they do not have the full control over their experimental design. Whereas many Neuroscientists are trained users of (script)-languages like MATLAB (The MathWorks Inc. Natick MA) or Python (Python Software Foundation, www.python.org) not very many have a background in software engineering and are familiar with the construction of VR. That means, that control over experimental stimuli has to be outsourced, a scenario that might be unpopular for researchers and allows only a limited number of flexibility. Importantly, parametric changes in a VR paralleling parametric modulations, which are a powerful tool for fMRI experiments, seem almost impossible to communicate to third-party providers. Complete solutions on the other hand, for instance (Mueller et al., 2012) lack this aspect of manipulating the VR in a parametric manner and might be too constrained.

A solution for these two problems must be able to break down complexity in a way that leaves control over important aspects to the scientists. We here report our development of a Virtual Reality framework that tries to overcome the aforementioned problems and implements such a solution. This is mostly achieved by relying on a layered software architecture which allows for specification of an experiment in a way typical for imaging research. The framework was developed in the context of a VR to be used for investigation of voluntary action decisions with EEG and fMRI. Whereas the neurobiological results of those experiments are reported elsewhere we here describe the very framework and show some data to validate our points.

MATERIALS AND METHODS

Construction principles / design aim

In order to investigate voluntary action decisions, we aimed for creating a landscape of roads and tunnels through which the participant would drive with a car in a first or third person perspective. In the tunnel periods participants were supposed to voluntarily decide a side road which to turn down to. The decision period and the subsequent motor action are spaced out by some seconds to account for the sluggishness of the BOLD signal (Glover, 2011) which is the signal measured in fMRI. Our design tried to incorporate several aspects which we considered crucial for a VR – Neuroimaging approach. Firstly, in order to be able to relate our results to the existing literature and ensure comparability with previous findings we deemed it crucial to have a structure which reflects the usual setup of trials or blocks. This structure is common for factorial designs, and allows for comparing the manipulation of different aspects/factors. Importantly, this is also the experimental structure which is assumed by many analysis software packages (e.g. SPM for fMRI). Generating an experiment in that framework will make data analysis easier as existing analysis tools can be used.

However, we wanted to disguise this trial based setup as much as possible and instead create a seamless user experience. Following current software development paradigms, we aimed for separating content (i.e. the experimental structure and logic) and visualization as much as possible. This allows for independent manipulation and to outsource some development tasks, for instance to software firms. As an important practical aspect we considered usability of standard hardware, i.e. the standard computer and trigger setup present at our imaging site.

As the experimental logic in itself to a huge extent reflects a two-dimensional version of the experiment we refer to it as the 2D skeleton. For the remainder of this article we will be rather specific in describing our current VR. It should be obvious, however, that the general framework is easily translatable to any type of virtual reality approach. At some occasions we'll point general applicability for all types of problems out.

2D XML skeleton

Our 2D skeleton contained the crucial aspects of the basic shape of our road layout and the experimental logic, i.e. the main specification of the experiment. The skeleton was divided into **four** parts: the **layout/shape** information which described the static road network, information about **dynamic events** along the road network, e.g. whether the car should turn by itself in a control trial, information about **objects** in a scene, for instance about road signs or distractor events and **link information**, i.e. how to transition from one scene to the next.

In order to describe the shape of the road we used cubic splines. These are piecewise polynomials which can be used to interpolate between sets of points. Splines create organic shapes and trajectories and are widely used in computer graphics, game design and animation. Their shape is defined by a set of control

points and by constraining them in a certain way several splines can be aligned smoothly. We randomized control points positions according to some predefined logic. In this way we obtained jittering in our road layout. Dynamic event information was specified in units of the underlying road shape. For this purpose, we defined what we called *waypoints* along the shape of the road. Each waypoint had some information assigned which would specify for instance the position of the waypoint on the road, whether to turn (in a control trial), whether to show an image or a text string (for instance for debugging) and more. Object information was specified in absolute scene coordinates and link information basically contained the scene numbers.

We stored the respective information in document object models (DOM) and saved them as XML files (Extensible Markup Language, W3C, www.w3.org/XML/). That seemed appropriate for our purpose for various reasons. First, the format is simple, widely usable, both human and machine readable, descriptive and can be generated in many different ways, both with a simple text editor but also with a programming language (we used MATLAB here). Second, by providing XML schema definition (XSD), the interface between our 2D skeleton and subsequent processing steps can be clearly defined. Third, the tree-structure of an XML file made it easy to translate the trial-structure of a neuroimaging experiment to the DOM. Each trial had its own entry in each DOM which contained all the information for that respective trial and they can be easily interlinked. Finally, in case we needed to specify more information about other aspects, we simply could have created additional files, specialized to the respective aspect of interest and following the same tree-structure. In this way we achieved a considerable breakdown of complexity.

3D object files

In a next step, the shape information of the 2D skeleton was extended to the third dimension. For this purpose, procedural landscape creation was used in C#. The details of this process are described in (Arslan & Jørgensen, 2012) and will be omitted here.

The resulting three-dimensional models were stored in .OBJ-files, a format to store 3D geometry which is widely accepted by graphics applications, for instance game engines. In order to provide some level of control over visualisation to researchers some of the parameters of the 2D to 3D step which had been considered important for the very experiment (e.g. the width of the tunnels) had been defined beforehand and could optionally be specified by adding a further XML file to the 2D skeleton. Note, that this requires close coordination with the party responsible for programming this step. Apart from these parameters the 3D step was however independent. The 2D to 3D step requires some more advanced graphics and programming knowledge (procedural landscape generation) and is a good candidate for outsourcing. Likewise, due to the exact specification of the underlying 2D skeleton and the XML schema definition it is a good candidate for separate development and research on the graphics side, for instance by exploiting bachelor or master projects.

3D+ experiment.exe

In a last step, the 2D skeletons (dynamic and link information) and the .OBJ files containing the 3D models were loaded into a game engine. We here used Unity (Unity Technologies, San Francisco, CA) but potentially any game engine might be used that offers adequate functionality. Purpose of a game engine is to provide the proper physics, methods for rendering and collision detection; some also contain forms of Artificial Intelligence (AI) for behaving agents which might considerably ease the creation of a social context. The use of a game engine has several advantages and has also been suggested previously (Mueller et al., 2012).

All of the trials belonging to an experiment were placed in an empty game template in an arbitrary position. Link information from the 2D skeleton was then applied to connect the trials and so to bind the single trials together to an experiment, providing a seamless user experience. Lastly, the now enriched scene was compiled to an executable file for which we used the inbuilt compilation routines provided by Unity.

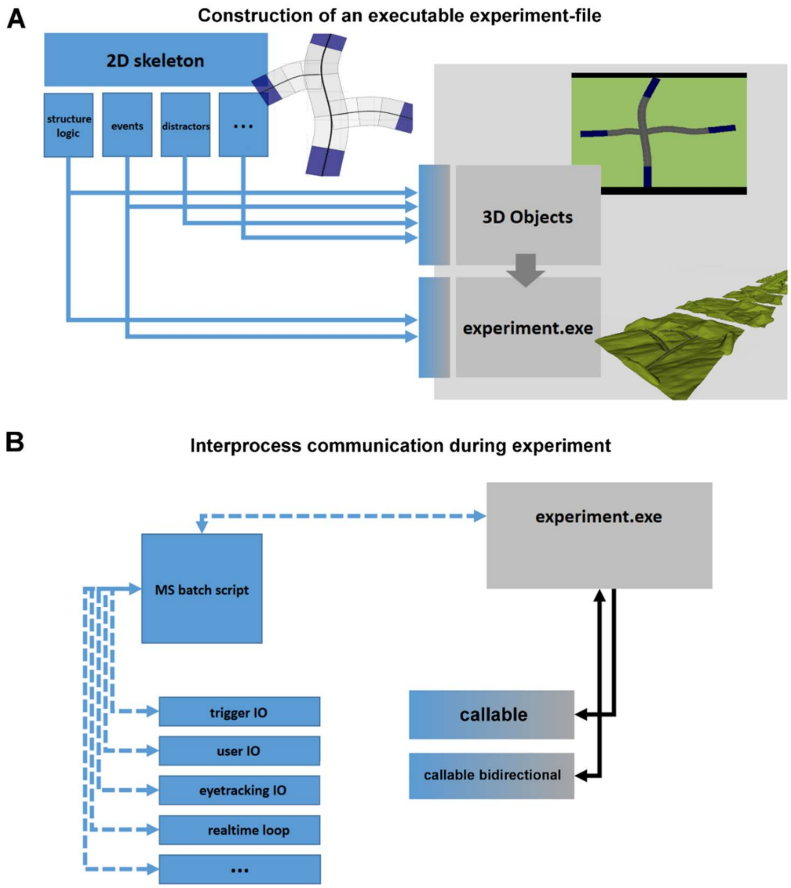

Fig. 1: A) Construction of the VR. The grey box in the upper right is connected to the rest of the experiment only through a well-defined interface and can be outsourced. Whereas in theory a separation in static and dynamic content in the 2D skeleton might be possible we found it more feasible for our purposes to have a higher number of dedicated files. For testing purposes a simple visualisation can be programmed which is only focusing on some aspects of the experiment and omits 3D objects and the game engine but instead only relies on the 2D parameters and link information.

B) Process communication while running an experiment. All the processes are bound together by a Microsoft batch script. In the main loop of the experiment.exe a placeholder for callables must exist in order to enable invoking functionality from inside the game. The logic of when to invoke what with what parameters can equally be specified in the 2D skeleton and bound into the generation of the experiment.exe as visualized in A).

Experimental infrastructure

In line with our design goal we were able to employ standard experimental hardware for our setup. To create the experiment, we used a desktop PC with 6GB RAM and a standard i5 dual core processor with 3 Ghz. Alternatively, we used a notebook with 8GB RAM and a similar processor, both running Windows 7 (Microsoft Corporation, Redmond, WA). To run the experiments, we relied on comparable machines.

We pursued a similar approach to break down complexity during the experiment as during its construction. We used small specialised programs to handle aspects like communication with the MR scanner or communication with other experimental hardware (for instance eyetracking hardware or button press devices). Thus, they were controllable by research personnel and only needed to be instantiated according to a predefined way (Fig. 1B). We used windows batch scripts in order to thread processes together and to start and finish them in the correct order. Batch files were written out by MATLAB. In this way we reduced the communication between the executable experiment files and other processes to a minimum.

For communication with the MR scanner (trigger signals) this meant that we could rely on the standard Python functions which are used at the imaging site to access the parallel port. The only change as compared to a standard fMRI experiment was that we compiled them for performance reasons. For user input we relied on a communication protocol based on text files. Separate applications would record from the hardware (in this case: custom made MR compatible mice), analyse the results and write events into a text file, which was read out by the main thread of the VR at critical time points. This solution is comparatively slow but very flexible and was deemed sufficient for our purposes. A more appropriate solution with shorter response times might be the use of sockets and pipes or shared memory. The important aspect is to synchronize with the ones programming the experiment.exe as to ensure that information is exchanged correctly and read out when needed; for us a regular update interval proved useful that also served for logging information.

Virtual Reality Experiments

We ran four different experiments with different configurations of the VR, different lengths and different ways of instructing the participants. Three of these experiments were run with fMRI, one was combined with EEG. Two were block designs with instructions being given beforehand by the experimenter whereas the other two had a fast event related setup. Here the instructions changed in every trial. Instruction change was realised by road-sign-like objects that were specified in the objects file at appropriate locations (see previous section).

Experiments were covered by an ethics approval of the regional ethics committee (project ID: H-3-2012-146) and in total 80 subjects underwent neuroimaging. The neurobiological results of our research question are shown elsewhere. In the following we will focus on presenting the results with respect to our VR.

RESULTS

Depending on the length of the experiments the files resulted in about 3GB of compiled code. We did not experience any performance issues while running the experiments and the interplay of the different modules, threaded together with batch files worked smoothly.

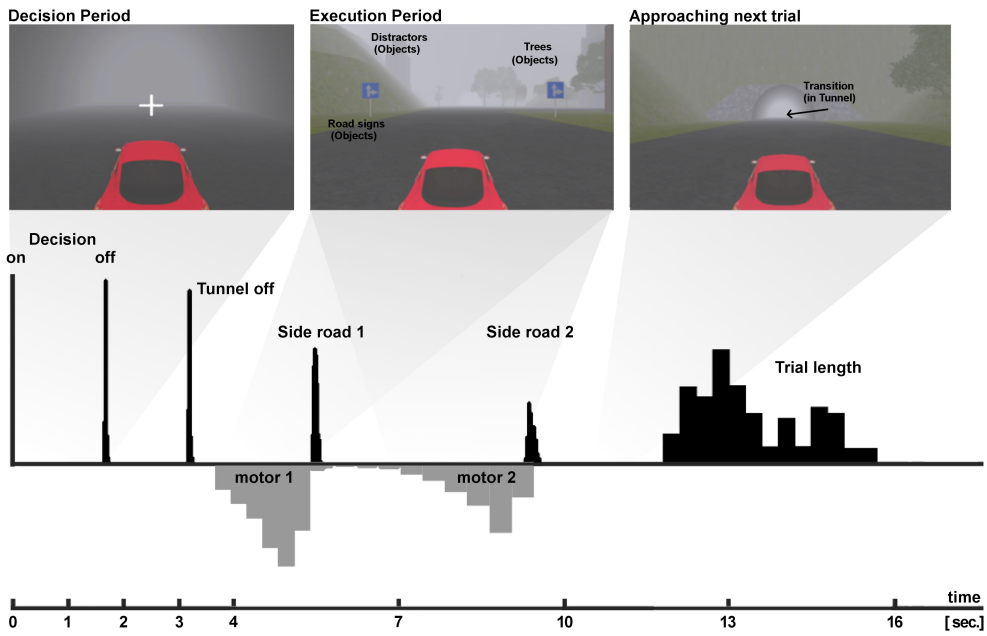

Fig 2: Screenshots and setup of the VR. Every trials starts with a decision period while the car is driving in a tunnel. Later in the trial participants are supposed to act out their decision, involving turning down into the first or the second side road. As visible in the histograms on the timeline critical events (decision period,

position of the roads) follow a rather strict time course whereas a considerable amount of jitter is present on the overall trial length. Motor actions are depicted in grey and indicate times of button presses.

Brain Imaging

Compared to a standard fMRI experiment input in VR is embedded in an (audio-) visual stream of rich complexity. Thus, potentially many brain regions might be involved in the task. We used a navigation-like task to frame the context for our question regarding voluntary action decisions. Thus one should expect brain regions to be activated that reflect both the navigational element of the task, the voluntary component and the visual aspects. We report four contrasts in the following (Figure 3). Contrasts were calculated with SPM12 software (Statistical Parametric Mapping; Wellcome Trust Centre for Neuroimaging, London, UK; http://www.fil.ion.ucl.ac.uk/spm) and second level (group statistics) significance level was set to $p < 0.05$ (familywise error corrected for multiple comparisons).

Motor activity occurs when participants indicate the direction of their decision. Figure 3A.1 shows right-hemispheric (contralateral) motor activity when subjects use their left finger. Right finger presses resulted in a mirror inverted activity pattern (not shown here).

Figure 3A.2 reflects the main effects of the decision period where subjects had to make a voluntary decision. Amongst different other regions strong activity in pre-SMA can is observed which is expected (Brass & Haggard, 2008; Haggard, 2009; Krieghoff, Waszak, Prinz, & Brass, 2011; Kühn, Haggard, & Brass, 2009).

As reasoned above the nature of our task is navigation-like. We expected navigation related activity (Figure 3A.3) in periods when subject would make a decision which way to go next particularly in parahippocampal regions (Hugo J. Spiers & Maguire, 2007).

Eventually, to account for the presentation form (visual stream) we expected to see activity in visual areas sensitive to visual flow. Figure 3A.3 shows the result for control trials only, where motion area MT+ is activated bilaterally. Task trials containing a decision component feature the same activity in these visual areas (not depicted here).

EEG data shows task processing with high temporal resolution. Figure 3.B1 reflects the contrast between task (voluntary decision) and control. Event related synchronisation as a response to the task is observed in the theta-frequency band (4-7Hz) whereas desynchronisation, occuring predominantly in the alpha-band (8-28 Hz) indicate decision processes and preparation of motor activity. Figure 3B.2 shows event related potentials as responses to events in the VR. World events like entering the tunnel evoke visual potentials whereas the subsequent more central components probably are connected to the decision.

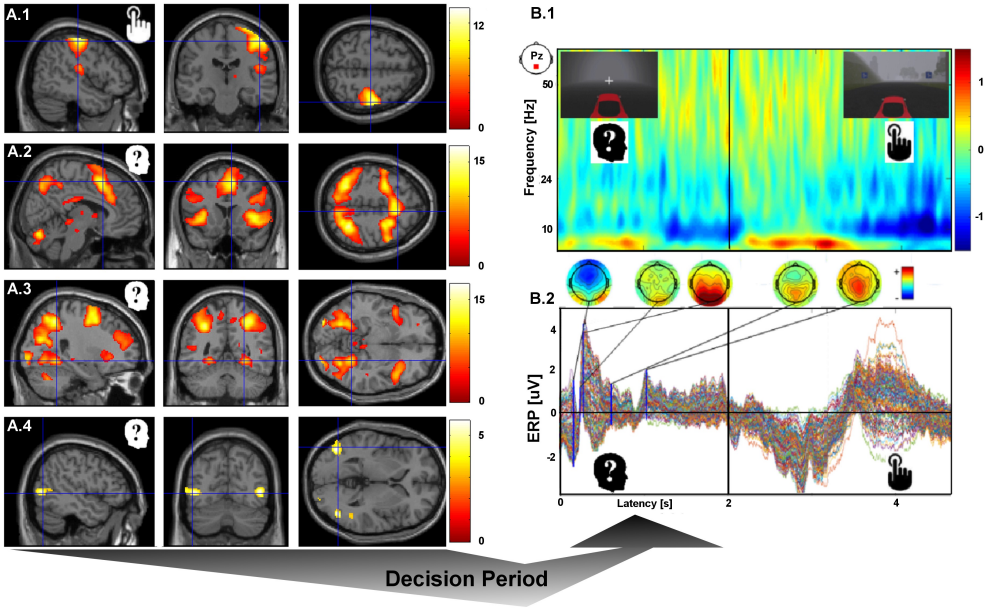

Fig 3: Brain activity as recorded while participants were performing the task. Panel A.1-A.4: Summary fMRI-statistics in a set of 23 participants. T-maps are overlaid on a standard MNI brain. Panel B.1-B.2 shows single subject EEG data, undergoing the same task.

A.1 Left button press → right motor cortex activity. The right button press contrasts (not shown here) roughly reflects mirror inverted left hemispheric activation. A.2 Period of interest (voluntary decision making). Amongst other regions of the task- positive network the pre-SMA is activated. A.3 Main effect of all tasks (all types of voluntary decisions): parahippocampal activity is expected as all conditions – due to context and the nature of the task – involve a navigational aspect. A.4 Motion area MT+ significantly activated in the control conditions when no decision is made. The same activation pattern is observed in the task

B.1 Time-frequency contrast between decision and control in the period of interest (voluntary decision). Red reflects ERS in the 4-7 Hz theta range whereas blue reflects ERD, predominantly in the alpha & beta (8-28Hz) range, related to motor preparation. B.2 Envelope of al event related potentials (ERP) on the decision condition. Dominant peaks show visual processing; following central components reflect the decision about the prospective motor action.

Behavioural data – response balance

An important aspect with respect to voluntary decision making is how balanced responses are. Do participants favour one option over another and if so, to which extent? Our paradigm offered 3 different binary decisions (choose the left or the right side road / the first or the second / turn down or drive straight ahead) which were neither encouraged nor discouraged by reward, instruction or other incentives. Table 2 shows the response distribution.

Table 2: Average behavioural balance [Choice in %] in a subset of 43 subjects. The first row depicts participants (n = 23) having undergone a blocked design, the second row participants (n = 20) that were tested with a fast, event related design. Rows 3 and 4 show the number of participants that would have to be excluded for classification purposes; in parentheses the total number of participants.

	Right / Left Binary Decision		First / Second Binary Decision		Turn / Straight Binary Decision	
Block	52	48	55	45	60	40
Fast event	56.3	43	56.3	43	54	46
Block_exclude[1]	0 (23)		1 (23)		5 (23)	
Event_exclude[1]	4 (20)		4 (20)		12 (20)	

[1] Exclusion criterion: asymmetry index more extreme than 0.3; identical with Soon et al. (2008)

Subjects self-reports

We presented a short questionnaire to a subset of participants (n = 43) and conducted a short interview after the experiment. The questionnaire was about whether the environment was perceived as being naturalistic and immersive, whether subjects estimated that they were able to time their decisions correctly and whether they stuck to their decision once it had been done or whether they changed it. Latter was important as for fMRI purposes we had a temporal delay between the making of a decision and its indication via a motor act. Whereas the principle problem of a subject being collaborative always exists one might assume that a more interesting, richer environment might encourage exploratory behaviour to a higher extent than usual. The interviews did not reveal any particularities. Questionnaire results are shown in table 2.

Table 3: Summary of self-reports of a subset of 43 subjects about their experience in the VR. Immersion has been measured on a 3-point Likert scale and is present in % here; timing and commitment have been rated on 5-point scales with values of 1 indicating correct timing / absolute commitment and 5 incorrect timing / no commitment.

	Immersive feeling [%]	Correct timing when making decision [1-5]	Commitment to the decision made [1-5]
Block	97.9	1.9	1.6
Fast event	96.7	2.1	1.3

Discussion

In the present study we developed and implemented a modular approach to generate a virtual reality environment for use in the neuroimaging environment. The cardinal design feature of our design is that separated the experimental logic from its visualisation and implementation as an actual 3D-experiment. The benefit is that neuroscientific researchers can focus on experimental design work and specify an experiment in two dimensions whereas the 3D generation can be outsourced. For testing reasons the 3D step might even be omitted, creating a simplified 2D visualisation of (sub-) aspects, suited for piloting. This visualisation can for instance be done in MATLAB, a script language familiar to many in Neuroscience. In this way the design process is kept flexible and the experiment generation process is accessible to researchers.

Previous attempts have either relied on pre-existing stimuli (e.g. Maguire et al., 2006; Maguire et al., 1998) or have been very specific in the generation of their VR resulting in a closed system (Mueller et al., 2012). Even though the framework described in the latter offered the option to design an experiment we are not aware of any study that made the VR construction and parameterisation an explicit part of the experimental design process. Depending on the research question aforementioned attempts are hence rather suited to an observational approach and do not provide the advantages an experimental studies. We figure that this is a crucial point preventing acceptance of VR as a tool in the Neuroimaging community.

Opposed to many VR neuroimaging studies which have been conducted up to date, we do not use our car driving VR to investigate an aspect like navigation, obvious to the 3D setup. Instead, our primary focus of interest, voluntary decision making, is embedded in the context (as it would be in 'real life'); by sticking to a standard trial based design we do not exploit its full power, even though we tried to disguise this aspect as good as possible. The reason is the requirement of having transition conditions between trials that are visually identical. This can be quite challenging as it limits experimental freedom and, in particular, puts heavy constraints on visualisation. Yet, in order to relate our findings to previous ones we deliberately chose this setup; we argue that in future steps one might be able to resolve the current strict separation of trials. Leaving out the transition periods will have immediate consequences for visualisation which can be tackled in different ways. So can 3D generation, i.e. creation of the .OBJ files take place after several trials of interest have been linked together; in this way bigger chunks are created. Alternatively, the transition between trials can be camouflaged by procedural landscape generation. This then probably requires a closer integration of step 2 (3D models) and step 3 (3D+ experiment). It should be kept in mind that also analysis will become more complex.

On a broader conceptual level this our use of VR mirrors a paradigm change in Neuroimaging research; previously, prevalent approaches tried to assign particular function to particular brain regions, i.e. they investigated functional specialisation and localisation. More recent attempts try to understand interrelations between different distinct units of a network, i.e. functional integration (Friston, 2002;

Sporns et al., 2004). We believe that by providing a natural framework of sufficient complexity and ecological validity a situation is created that allows for the different nodes of the brain-network to work in a more realistic manner and forward realistic input into the network. Not artificially separating stimuli into discrete isolated entities thus means creating a true basis for investigation of functional integration.

This might potentially be especially important for the investigation of voluntary decision making for which the current VR was designed. Here, the participant cannot rely on external criteria like reward maximization in order to guide behaviour. It is an open question what exactly drives a voluntary decision but probably integration of different types of information on different timescales, for example perception and autobiographic memory, will be involved. Due to the lack of external criteria and constraints response patterns can become quite unbalanced. Depending on how brain imaging data obtained in such a situation will be used this might pose a severe problem. Classification approaches for instance that try to predict behavioural outcome based on the brain state at the time of the decision suffer from unbalanced responses and might yield artificially high classification rates. Thus, an exclusion criterion for subjects whose response patterns are too unbalanced is required (Bode et al., 2011; Lages & Jaworska, 2012; Soon et al., 2008). Soon et al. (2008) for instance used as their inclusion criterion an asymmetry index not more extreme than 0.3 what reflects a 65% - 35% ratio. They had to exclude 22 of their 36 subjects as they failed to produce spontaneous decisions staying within these boundaries. As depicted in table 2 our binary decisions came on average not even close to their cut-off. On an individual basis we would have to exclude a number of subjects, yet by far not as many as they had to. Balancing of responses can in principle be enforced by instructions, however it is likely that constraints are put on a free decision process which invoke other and possibly disturbing processes like counting or other additional monitoring processes or the attempt to generate random behaviour. Therefore, it is desired that the task as such puts constraints on subject's behaviour which the participant sis not aware of and which do not interfere. This aspect our VR seems to have provided well.

An exact formal specification of the interface between logic and visualisation is required for our approach. We here used XML in combination with an adequate schema definition. All generation mechanisms that implement that schema definition can be valid generators for an experiment. This eases communication with suppliers, minimizes misunderstandings and helps to break down complexity inherent in a high-dimensional approach such as VR. The use of a mark-up language which is both human and machine readable hereby proved to be a decent choice and fulfilled its purpose well. One might speculate about future dialects of mark-up languages which are specifically derived to describe experimental setups. This might further ease the integration of machines to support and conduct experiments and present behavioural paradigms, could however also apply to areas as remote as for instance controlling robots for TMS or other experimental hardware.

An advantage of a formal specification is that it in fact already requires a lot of considerations about the possible states an experiment can take and a lot of thought work itself; usually, these considerations

are implemented in form of some code to generate a logic and at best copy-pasted to the next study. Storage and possible reuse of the logic in the way proposed can be more efficient. The XML files can easily be stored and distributed, as well as easily used for regeneration. This has a number of potential benefits.

Quite often cultural aspects of experiments are for instance not taken into account. Especially higher level cognitive and emotional processing might be more susceptible to intercultural differences. Separating experimental logic from its visualisation itself means that the very same study can be conducted with a totally different visualisation in different cultures. The same argument applies for replication studies. The progress in visualisation throughout the years has been huge and a study with a visualisation conducted 10 years ago might have lower acceptance rates when being replicated, now. Being able to update just one part of an experiment without the need for a total redesign lowers cost and workload and can for instance also be carried out as a research project at an institute researching in visualisation.

Yet, we acknowledge that it conceptually can be very challenging to separate experimental logic from its presentation. Furthermore, there will probably always be peculiarities which must be handled separately for one specific experiment. Nonetheless, even when using commercial software packages, these descriptions must be made and if a researcher wants to keep a certain level of control then it is mandatory to formalize them.

A cardinal feature of a VR is the degree of immersion it allows for. We here used standard hardware in the form of a MR–compatible computer screen. Allowing for separate manipulation of visualisation and hardware also allows for controlling the level of immersion independently. Evidence exists that the degree of immersion in VR has an effect on behaviour (Gutierrez et al., 2007) and attempts have been made to manipulate it in the neuroimaging environment (Hoffman et al., 2003). VRs as different as simple mazes (Astur et al., 2005) and cubes representing tunnels (Plank et al., 2010) have been used, as well as complex worlds (Maguire et al., 2006) and advanced VR-goggle technology (Hoffman et al., 2003). However, we are not aware of any investigation that tried to investigate degree of immersion systematically and to shed light on its neural underpinnings.

Summing these considerations up we basically argue for a separation into content and visualization, a design principle that is known in computer science as Separation of Concerns (SoC, Dijkstra, 1982). Commercial stimulus presentation software like E-Prime (Psychology Software Tools Inc, Pittsburgh, PA) or Presentation (NeuroBehavioral Systems, Albanym, CA) likewise provide this separation to a certain extent. While being suited for many experimental research questions, they rely on proprietary languages and lack the flexibility which we describe here.

The SoC principle we recommend here is probably almost always considered somehow in experimental design processes in most laboratories around the world. Our contribution is to show, that such an approach is working for a comparatively high degree of complexity and still is relatively easy to handle.

Furthermore, we show a specific way of how a reliable separation could look like. That approach proved feasible, stable and easy to handle when implementing four different but related setups. They differed in their parameterization of the roads (e.g. number of roads), length of the scenes, and their instructions, being either presented in blocks or on every trial. These changes were entirely covered by our framework and no changes in the very experiment generation process had to be undertaken. In order to manipulate the general VR layout bigger adjustments would be necessary which would involve changing the 3D objects and the experiment. Yet, due to its modular structure the biggest parts of our experiment would be reusable.

Last but not least, modular components are quite flexible and can be replaced easily. We here relied on algorithmic generation and extensive randomization to generate the particular road-shapes for the 2D skeleton. Other approaches are conceivable like for instance hand drawing shapes and generating a skeleton from them (Arslan & Jørgensen, 2014). Such techniques will further ease the use of VR technique by adding an intermediate construction layer suited to the special needs of the neuroscience community and hopefully help making this useful technique more available in the future.

Conclusions

We argue for an adequate separation of concerns by separating experimental logic from visualization and show a reliable way of how to achieve that. Employing this approach, we create a VR suited for the investigation of voluntary decision making which features good experimental characteristics. The separation we describe involves a mark-up language (XML) to store and pass information and an adequate schema definition (XSD) that formally specifies the interface between different steps of the VR generation process. Research in visualisation and neuroimaging research focusing on the paradigm aspect can be divided properly. Whereas we report the advantage of such an approach for a complex scenario, the generation of virtual reality, this principle might even turn out useful for different types of experiments, also simpler ones.

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Conflicts of interest

The authors declare that they have no conflict of interest.

References

Aiken, L. S., West, S. G., & Pitts, S. C. (2003). Multiple Linear Regression. *Handbook of Psychology*. John Wiley & Sons, Inc.

Arslan, B., & Jørgensen, P. (2012). *Car Simulation for Neurofeedback Research*. Denmarks Technical University, DTU, Asmussens Alle, Building 305, DK-2800 Kgs. Lyngby, Denmark.

Arslan, B., & Jørgensen, P. (2014). Real-time Procedural Generation [video file]. Retrieved April 26, 2016, from https://www.youtube.com/watch?v=GSh2FT_a-0s

Astur, R. S., St. Germain, S. A., Baker, E. K., Calhoun, V., Pearlson, G. D., & Constable, R. T. (2005). fMRI hippocampal activity during a virtualradial arm maze. *Applied Psychophysiology Biofeedback*, *30*(3), 307–317.

Bode, S., He, A. H., Soon, C. S., Trampel, R., Turner, R., & Haynes, J. D. (2011). Tracking the Unconscious Generation of Free Decisions Using Uitra-High Field fMRI. *PLoS ONE*, *6*(6).

Brass, M., & Haggard, P. (2008). The what, when, whether model of intentional action. *The Neuroscientist : a review journal bringing neurobiology, neurology and psychiatry*, *14*, 319–325.

Dijkstra, E. W. (1982). On the Role of Scientific Thought. *Selected Writings on Computing: A personal Perspective* (pp. 60–66).

Dolcos, F., LaBar, K. S., & Cabeza, R. (2004). Interaction between the amygdala and the medial temporal lobe memory system predicts better memory for emotional events. *Neuron*, *42*(5), 855–863.

Dolcos, F., LaBar, K. S., & Cabeza, R. (2005). Remembering one year later: role of the amygdala and the medial temporal lobe memory system in retrieving emotional memories. *Proceedings of the National Academy of Sciences of the United States of America*, *102*(7), 2626–31.

Friston, K. (2002). Functional integration and inference in the brain. *Progress in Neurobiology*, *68*(2), 113–143.

Gescheider, G. A. (1997). *Psychophysics: The Fundamentals*. *scan psychology* (Vol. 435).

Glover, G. H. (2011). Overview of functional magnetic resonance imaging. *Neurosurgery Clinics of North America*.

Green, D. G., & Swets, J. a. (1966). Signal detection theory and psychophysics. *Society*, *1*, 521.

Guthrie, E. R. (1935). *The Psychology of Learning*. *Psychology* (Vol. 44).

Gutierrez, F., Pierce, J., Vergara, V. M., Coulter, R., Saland, L., Caudell, T. P., Goldsmith, T. E., et al. (2007). The effect of degree of immersion upon learning performance in virtual reality simulations for medical education. *Studies in health technology and informatics*, *125*, 155–160.

Haggard, P. (2009). Neuroscience. The sources of human volition. *Science (New York, N.Y.)*, *324*(5928), 731–733.

Heekeren, H., & Wartenburger, I. (2003). An fMRI study of simple ethical decision-making. *Neuroreport*, *14*(9), 1215–9.

Hoffman, H. G., Ph, D., Richards, T., Ph, D., Coda, B., Richards, A., & Sharar, S. A. M. R. (2003). The Illusion of Presence in Immersive Virtual Reality during an fMRI Brain Scan, *6*(2), 127–131.

Hull, C. (1943). *Principles of Behavior*. New York: Appleton-Century Crofts.

Krieghoff, V., Waszak, F., Prinz, W., & Brass, M. (2011). Neural and behavioral correlates of intentional actions. *Neuropsychologia*, *49*(5), 767–776.

Kühn, S., Haggard, P., & Brass, M. (2009). Intentional inhibition: How the "veto-area" exerts control. *Human Brain Mapping*, *30*(9), 2834–2843.

Lages, M., & Jaworska, K. (2012). How predictable are "spontaneous decisions" and "hidden intentions"? Comparing classification results based on previous responses with multivariate pattern analysis of fMRI BOLD signals. *Frontiers in Psychology*, *3*(MAR).

Maguire, E. a, Burgess, N., Donnett, J. G., Frackowiak, R. S., Frith, C. D., & O'Keefe, J. (1998). Knowing where and getting there: a human navigation network. *Science (New York, N.Y.)*, *280*(5365), 921–924.

Maguire, E. A. (2012). Studying the freely-behaving brain with fMRI. *NeuroImage*, *62*(2), 1170–1176. Elsevier Inc.

Maguire, E. A., Nannery, R., & Spiers, H. J. (2006). Navigation around London by a taxi driver with bilateral hippocampal lesions. *Brain*, *129*(11), 2894–2907.

Matthews, P. M., Honey, G. D., & Bullmore, E. T. (2006). Applications of fMRI in translational medicine and clinical practice. *Nature reviews. Neuroscience*, *7*(9), 732–744.

Mueller, C., Luehrs, M., Baecke, S., Adolf, D., Luetzkendorf, R., Luchtmann, M., & Bernarding, J. (2012). Building virtual reality fMRI paradigms: A framework for presenting immersive virtual environments. *Journal of Neuroscience Methods*, *209*(2), 290–298. Elsevier B.V.

Murty, V. P., LaBar, K. S., & Adcock, R. a. (2012). Threat of Punishment Motivates Memory Encoding via Amygdala, Not Midbrain, Interactions with the Medial Temporal Lobe. *Journal of Neuroscience*, *32*(26), 8969–8976.

Plank, M., Onton, J., Makeig, S., Gramann, K., & Jolla, L. (2010). Human EEG Correlates of Spatial Navigation within Egocentric and Allocentric Reference Frames, 191–206.

Reimann, M., Schilke, O., Weber, B., Neuhaus, C., & Zaichkowsky, J. (2011). Functional magnetic resonance imaging in consumer research: A review and application. *Psychology & Marketing*, *28*(6), 608–637.

Sanfey, A. G., Rilling, J. K., Aronson, J. a, Nystrom, L. E., & Cohen, J. D. (2003). The neural basis of economic decision-making in the Ultimatum Game. *Science (New York, N.Y.)*, *300*(5626), 1755–1758.

Sitaram, R., Caria, A., & Birbaumer, N. (2009). Hemodynamic brain-computer interfaces for communication and rehabilitation. *Neural Networks*, *22*(9), 1320–1328.

Soon, C. S., Brass, M., Heinze, H. J., & Haynes, J. D. (2008). Unconscious determinants of free decisions in the human brain. *Nat Neurosci*, *11*(5), 543–545.

Spiers, H. J., & Maguire, E. A. (2004). A "landmark" study on the neural basis of navigation. *Nature Neuroscience*, *7*(6), 572–574.

Spiers, H. J., & Maguire, E. a. (2007). Neural substrates of driving behaviour. *NeuroImage*, *36*(1), 245–255. Elsevier Inc.

Sporns, O., Chialvo, D. R., Kaiser, M., & Hilgetag, C. C. (2004). Organization, development and function of complex brain networks. *Trends Cogn Sci*, *8*(9), 418–425.

Thorndike, E. L. (1898). Animal intelligence: An experimental study of the associative processes in animals. *Psychological Review*, *2*(4), 1–107.

Appendix D

Automatized multi-modal EEG data processing

D.1 Abstract

Manual cleaning of EEG/MEG data, based on visual observation and subjective judgment of the experimenter, is one of the most commonly reported approaches to early data processing in EEG/MEG studies, despite being the most inefficient one. Such approach suffers several serious pitfalls: (1) it is time-consuming, (2) it is not reproducible, (3) depends strongly on experimenter's experience and preferences, (4) in extreme cases may lead to emergence of spurious statistical effects (false positives) or reduction of true effects (false negatives), especially if experimenter is not blindfolded to condition/group labels in the early processing steps. Here we propose an automatized, reproducible method of EEG/MEG data processing which is fast, unbiased and based upon a minimal set of parametric criteria (absolute thresholds, spectral power thresholds, across-channel correlation). Furthermore, the method is highly data-preserving, by performing local interpolation of artifactual data selectively in [channel x trial] space. Finally, concise reports are automatically generated to allow the experimenter to evaluate the processing results globally and report them in publications.

D.2 Introduction

The vast majority of EEG/MEG studies report data cleaning in overly general, inexact manner. Statements of the kind: 'The data was visually inspected and artifactual epochs were removed from further analysis' are commonly encountered and accepted. Such approaches should be based on solid criteria, and those should be reported in detail [43]. However, a lot of potential issues may arise from a purely manual cleaning. First of all it remains unknown to the reader and to the peer reviewer which criteria were undertaken by authors to ensure high-quality, artifact-free data. The results may depend to high extent on the technical experience of the experimenter. Notably it is not unusual that 'the most tedious' work of data cleaning is often performed by least experienced members of the lab or novice students. Even if the task is performed by skilled technician it will be still subjective, with choices dependent on overall data quality, relative subject's data quality, and in worst case - on the group or condition the dataset belongs to. Finally, manual inspection effectively yields as many parameters of the cleaning procedure, as many trials and channels are in the data (or more generally equal to the number of subjective binary choices being made). As a result, the whole process is hardly reproducible, even if performed by the same experimenter. In summary, manual data cleaning may lead to hardly reproducible results and depend on skills and subjective opinion of experimenter. At worst case, it may lead to spurious emergence of false positive findings or suppression of true effects.

Automatized and semi-automatized methods may provide equal or higher quality of data cleaning, while being much faster to perform, and preserving the unbiasedness and objectiveness of data [43, 48]. A common approach is to systematically apply a certain set of rules to the dataset in order to (semi-)automatically detect and eliminate channels and epochs exceeding certain criteria. Popular toolboxes like EEGLAB [28] and Fieldtrip [117] offer some support in this task, for instance channels can be assessed by kurtosis, normality of distribution, and epochs by maximum voltages, signal slope, or spectral features. Another strategy to data cleaning is based on correction rather than elimination and use of signal processing methods to isolate artifactual components from genuine brain components. Some of the common methods are based on independent component analysis (ICA), principal component analysis (PCA), linear regression, signal space projection (SSP), for review see [43].

Although automatized approaches are considerably better than manual data cleaning some problems still remain. Firstly, usually more data is removed than it is necessary. For instance, while using a typical thresholding method a noise

in a single (or few) channels will cause the entire trial to be eliminated. Analogically, a short lasting, transient, high-frequency noise at a given channel (for example in the last few minutes of experiment) may result in sufficient change of kurtosis that the entire channel will be interpolated, instead of the noisy interval only. Also the signal processing based methods risk partial removal of brain sources, if those are temporally correlated with artifactual sources (i.e. eye-blinks). Secondly, there is little support for the experimenter to run those methods in a batch mode on all datasets and thus evaluate the global results and efficiency of the cleaning procedure. The latter is critically important especially for larger studies consisting of hundreds of datasets. The need for effective automatized data cleaning might become even more important along with the emergence of cheap, portable EEG solutions [152] and with increasing crowd-sourcing of EEG data acquisition to the outside laboratory environments [69, 83].

With the toolbox proposed in this manuscript we intend to circumvent the above limitations by providing the following functionality:

1. Rule-based, objective data cleaning
2. Efficient detection of artifactual data by thresholding:
   - Epoch Voltage
   - Sample-to-sample Voltage
   - Spectral Power in Beta/Gamma range
   - Channel Correlation
3. Support for batch processing and reporting of the global results
4. Data-preserving by means of economical, local interpolation in the 2-dimensional [channel x trial] space

D.3 Methods

The proposed approach combines several measures to efficiently detect and handle both local and global artifacts. Importantly, the method automatically cleans all experimental datasets applying only 6 predetermined parameters, as opposed to subjective manual data cleaning where effectively every binary decision is a hidden parameter (thus the number of hidden parameters would effectively equal to the summed number of trials and channels). We propose typical values for those parameters, however optimal values will obviously depend on epoch length, number of channels, EEG system, etc.

The parameters are listed below and described in detail in the further sections:

V_e Maximum allowed Epoch Voltage spread [μV]

V_{ss} Maximum allowed sample-to-sample voltage spread [μV]

S_{bg} Maximum allowed spectral power in beta-gamma range [μV^2]

C_c Minimum required correlation with neighbor channels [a.u.]

T_e Tolerance on epoch [%]

T_c Tolerance on channel [%]

The sequence of processes is following:

1. Experimenter specifies the allowed threshold values for V_e, V_{ss}, S_{bg}, C_c parameters, and tolerance parameters T_e, T_c.
2. For each dataset and for each (channel x trial) combination, the empirical values of V_e, V_{ss}, S_{bg}, C_c are computed. According to the specified thresholds and T_e and T_c tolerances, local interpolation is applied to eliminate noisy chunks of data, defined as those that exceed the threshold values.
3. Report of the cleaning is generated, one detailed report for each dataset, and one summary report for the entire experiment (as discussed below).
4. Depending on results, the experimenter might want to return to step (1) and adjust the threshold parameters
5. ICA decomposition is performed for each cleaned dataset, followed by automatized ICA classification of artifactual components based on spatio-temporal features (modified ADJUST toolbox [107] is used).
6. Report of ICA correction is generated, one detailed report for each dataset, and one summary report for the entire experiment.

Local interpolation The main approach to correcting for noisy intervals of data is a local interpolation in [channel x epoch] space. In the first step, EEG datasets of each subject/session are divided into epochs (event-based, or temporarily chunks of 1s for continuous data). For each trial and channel, the exclusion criteria are computed (Fig.D.1, left panels) as discussed

below, and compared against allowed thresholds. This step results in creating 2-dimensional mask [channel x epoch] indicating chunks of data that will need to be excluded (Fig.D.1, middle panels). At this stage, instead of interpolating the entire channels or eliminating the entire trials we allow for local interpolation of the channel data only within those epochs, where the artifactual noise was recognized. This solution preserves a lot of data which otherwise would be eliminated by standard methods. It should be noted though that too many noisy channels (10% and more) within the same epoch can render local interpolation imprecise and in that case the entire epoch should be indeed interpolated. This constraint is captured by epoch tolerance T_e and channel tolerance T_c parameters.

Epoch Voltage threshold (V_g) The global voltage threshold is the simplest measure to detect signal abnormalities. It is the difference between maximum and minimum amplitude of the signal within an epoch. Usually epochs with V_g exceeding 100μV can be considered as artifactual. The V_g measure is sensitive to detection of eye-blinks and high amplitude movement related artifacts.

Sample-to-sample Voltage threshold (V_{ss}) The sample-to-sample voltage threshold is another simple measure to detect rapid signal changes (spike- or step-alike). It is a maximum difference between to points adjacent in time. Usually epochs with V_{ss} exceeding 60μV can be considered as artifactual. The V_{ss} is sensitive to detect signal inconsistencies, high-frequency environmental noise and horizontal eye movements.

Spectral thresholds (S_{bg}) The muscular, ocular and environmental sources of noise are often expressed in high power in Beta/Gamma range (>24Hz). We estimate the single-trial power spectrum for each epoch and channel with Fast-Fourier transform, and use this measure as another criterion to detect artifacts. The spectral power measure is complementary to V_g and V_{ss} defined earlier in the sense that high-frequency noise is not necessarily high in amplitude.

Channel correlation thresholds (C_c) The criterion is based on the following rationale. EEG/MEG surface recordings are strongly affected by volume conduction and brain-skull-skin interfaces. This results in considerable spatial blurring of recorded signals, and thus - especially in case of high-density systems (64+ channels) - intrinsically high correlation between a channel and its nearest neighbors. Reduction of correlation may only occur in case of exogenous influences affecting subgroup of channels or individual channels selectively (muscular artifact, electrode movement against skin, etc). Thus reduction of channel correlation all of its neighbors below certain threshold level may be considered artifactual. This criterion is independent from absolute amplitudes and spectra, and thus

complements V_g, V_{ss} and S_{bg} measures defined earlier. Furthermore it can eliminate artifacts while preserving high-amplitude sources where needed (such as eye movements and eye-blinks). C_c is computed independently for each channel and epoch, as a minimum correlation of this channel with its 5 nearest neighboring channels, within given epoch.

Optional ICA decomposition and artifact correction ICA has been successfully used for EEG data cleaning from ocular artifacts, muscular artifacts and general discontinuities [59, 77, 96, 107]. However, successful decomposition of data into ICA components requires reasonably pre-cleaned and stationary dataset. Failure to provide this may result in artifact-oriented decomposition where most of the ICA components are attracted to artifactual, high-variance chunks of original data. Thus, to obtain the optimal results, we propose to use our thresholding method as a primary cleaning step, followed by ICA decomposition and automatized classification/elimination of artifactual ICA components. An optional third step will repeat threshold-based cleaning, however with more rigid threshold values.

Reporting and visualization We consider appropriate summarization and visualization of cleaning result a critical functionality, that allows the experimenter to assess the resulting quality of cleaned data and the impact of the cleaning method. This information can be used to re-evaluate the threshold levels and possibly re-run cleaning procedure. Several reports are generated:

Dataset cleaning details The report presents details of cleaning results for each individual dataset, including estimated values of V_{ss}, V_g, S_{bg}, C_c for each channel/epoch combination (Fig.D.1, left panels), respective exclusion masks obtained by comparing those measures with thresholds (Fig.D.1, middle panels). Finally the impact of cleaning is presented by comparing the dataset before and after the procedure, in terms of multi-channel ERP (Fig.D.1, top right panels), multi-channel Power Density (Fig.D.1, middle right panels) and Global Field Power (GFP) and its standard deviation (Fig.D.1, bottom right panels)

Global cleaning results The report presents summary effect of data cleaning applied to multiple datasets (typically all datasets of the given experiment, in this example 16 subjects dataset). The information presented is number of interpolated channels, removed trials and local interpolation points for each dataset (Fig.D.2, top left panels), global and individual ERPs before and after cleaning (Fig.D.2, right panels), global and indiviudal GFPs before and after cleaning (Fig.D.2, middle panels).

ICA correction - Dataset details The report presents details of ICA correction for each individual dataset. The components were automatically recognized as brain origin, eye-movement or general discontinuity.

The topographic maps of those three groups and their projections onto ERP space are presented at Fig.D.3, left side panels. The right panels present ERP, Spectral Density and GFP before and after the ICA correction.

ICA correction - Global results The report summaries the effect of ICA correction applied to multiple datasets (typically all datasets of the given experiment, in this example 16 subjects dataset). The components were automatically recognized as brain origin, eye-movement or general discontinuity.The number of components in each group, and the respective total variance explained by each group are summarized for each subject (Fig.D.4, top right panels), along with grand projection of each group onto channel space (Fig.D.4, lower right panels). The individual and grand GFPs and ERPs are also presented, before and after ICA correction (Fig.D.4, middle and right column panels).

D.4 Results

We have applied the toolbox to complete datasets from two EEG experiments. The first experiments accounted for 16 subjects, 480 trials of 6 seconds duration, 128 channels Biosemi system. The second experiment accounted for 42 sessions (14 subjects, 3 sessions each), 270-300 trials of 13 seconds duration, 128 channels Biosemi system. Both datasets were referenced to average mastoids, filtered in the broadband range 0.2-120Hz, downsampled to 256Hz, and epoched. No prior manual pre-cleaning was performed of any type.

In both cases the entire threshold cleaning procedure was fast (<15min), and could we easily re-iterated after adjusting cleaning parameters to particular experiment specifics and requirements. The threshold-based local interpolation cleaning was followed by ICA decomposition and automatized ICA classification of artifactual components based on spatio-temporal features (modified ADJUST toolbox [107]).

The global results for dataset 1 are presented at Fig.D.2 and Fig.D.4. On average 37.6 epochs (out of 480) were removed and 5.6 channels (out of 128) were interpolated. Additional 0.27% of data were locally interpolated. On average, 62.1 components were classified as brain origin, which accounted for 41.9% of total data variance. The remaining 9.8 components (44.2% of total variance) were classified as eye-origin, 56 as general noise (13.9% of total variance) artifactual.

Similar global results for dataset 2 are presented at Fig.D.5 and Fig.D.6. On average 17.6 epochs (out of 300) were removed and 4.2 channels (out of 128) were

interpolated. Additional 0.36% of data were locally interpolated. On average, 63.4 components were classified as brain origin, which accounted for 40.1% of total data variance. The remaining 8.9 components (51.0% of total variance) were classified as eye-origin, 55.7 as general noise (8.9% of total variance) artifactual.

The 2-step procedure resulted in clean datasets, ready for submission to statistical tests. Visual inspection did not reveal remaining residual noise or obvious artifacts that would require further intervention. Importantly, the entire procedure can be easily repeated if such need arises, for example if early processing choices need to updated (different filters, modification of epoch intervals, additional subjects available, etc.).

D.5 Summary and conclusions

Automated and unbiased data cleaning procedures are critical to obtain high-quality, reproducible, statistical results in EEG/MEG studies. We presented extendable framework that (1) efficiently detects and eliminates artifacts in objective and unbiased way, (2) preserves data by economical local interpolation procedure, and (3) is considerably faster than manual methods and can be applied in batch mode to all datasets of given experiment. The presented method limits to the minimum the number of experimenter's subjective choices, and thus reduces the risk of spurious false positive and false negative findings. Importantly, the method vastly reduces the time needed to perform the early data processing, thus allowing to focus more efforts on important aspects of statistical inferences. If applied in parallel (for example via Matlab's Parallel Processing toolbox), hundreds of datasets can be processed within minutes. Finally, if applied multiple datasets, the method will provide informative summary reports. Those reports may help to assess general data quality, impact of cleaning results, and also recognize outlying datasets to be considered for exclusion.

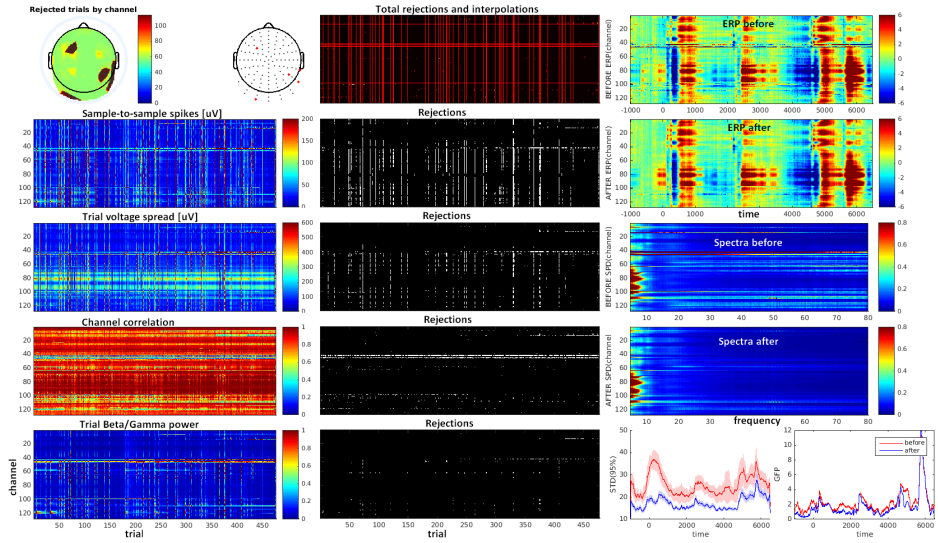

Figure D.1: The exemplary detailed report of cleaning results for a typical individual dataset. For each channel/trial pair, the 4 parameters are estimated to be subsequently compared with predefined thresholds to preserve or remove the data points (left and middle panels). Results before and after cleaning in terms of multi-channel ERP, spectral density and GFP are displayed (right panels).

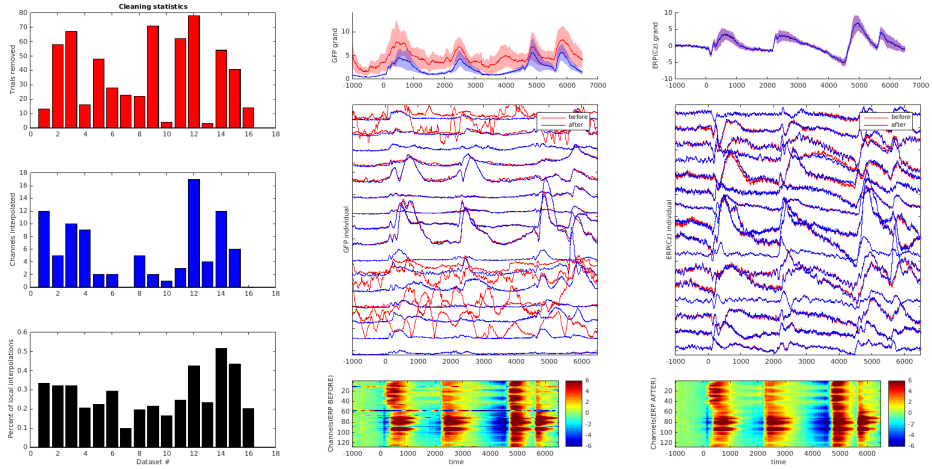

Figure D.2: The summary report of cleaning results applied to entire dataset of 16 subjects from Study 1. Number of rejected trials, interpolated channels, and percentage of local point interpolations are presented at left panels. The impact of the cleaning procedure on the individual datasets multi-channel ERPs (right panels) and GFP (middle panels), as well as grand multi-channel ERP (bottom right panels).

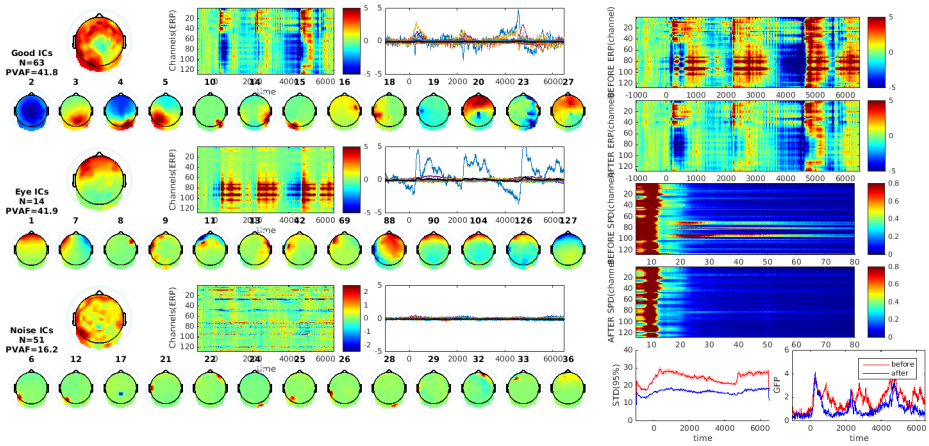

Figure D.3: The exemplary detailed report of ICA correction for a typical individual dataset.The ICA components are automatically classifed into brain/eye/noise categories based on spatial and temporal features (left panels). The impact of ICA correction on the final multi-channel ERP, spectral density and GFP is reported (right panels)

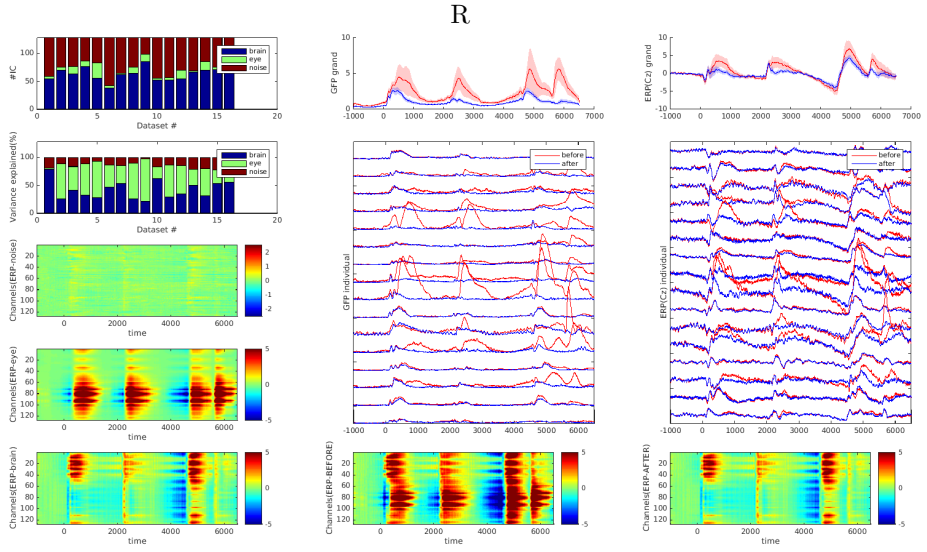

Figure D.4: The summary report of ICA correction applied to entire dataset of 16 subjects from Study 1. Number of components classified into brain/eye/noise categories (and their corresponding variances) are reported (left panels) along with the grand impact of ICA correction on the final quality of data. Summary for all sessions datasets (right panels).

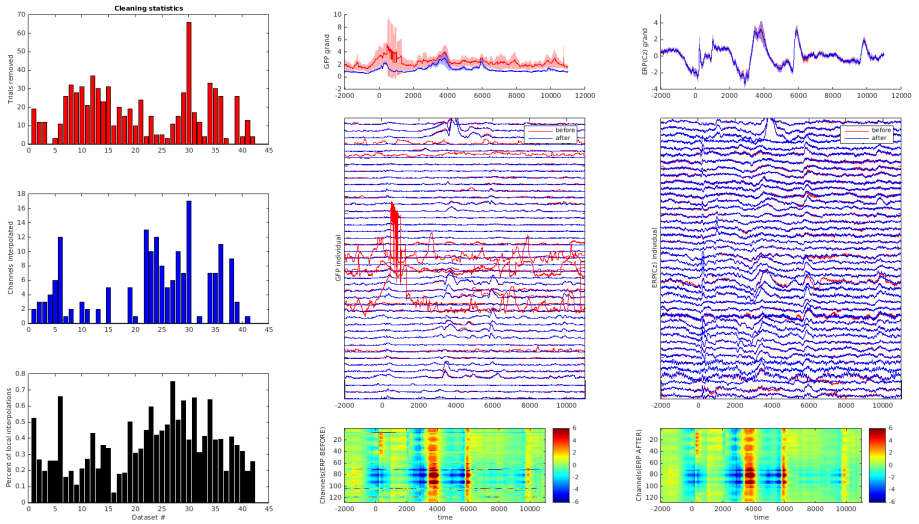

Figure D.5: The summary report of cleaning results applied to entire dataset of 45 sessions from Study 2. Number of rejected trials, interpolated channels, and percentage of local point interpolations are presented at left panels. The impact of the cleaning procedure on the individual datasets multi-channel ERPs (right panels) and GFP (middle panels), as well as grand multi-channel ERP (bottom right panels).

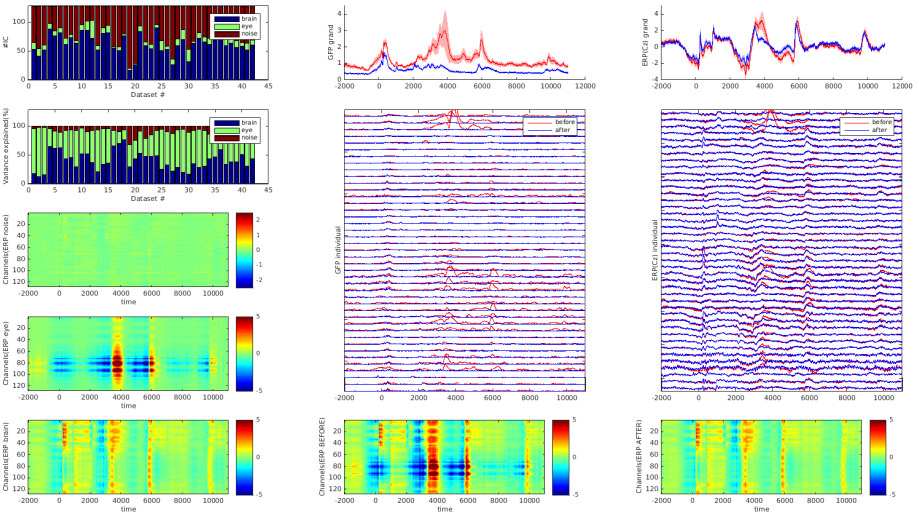

Figure D.6: The summary report of ICA correction applied to entire dataset of 45 sessions from Study 2. Number of components classified into brain/eye/noise categories (and their corresponding variances) are reported (left panels) along with the grand impact of ICA correction on the final quality of data. Summary for all sessions datasets (right panels).

Appendix E

Conferences and contributions

The appendix summarizes the conference contributions made in relation to the topics investigated in this thesis. The accepted conference abstracts, and a scaled version of a poster are attached.

E.0.1 ASSC conference 2015

Conference of Association of Scientific Study of Consciousness
Paris, France, 7th-10th July, 2015

Poster presentation:
"What, When, Whether - the electrophysiological correlates of voluntary action in virtual environment"
(the scaled copy of the poster is attached below the abstract)

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The study of (Libet 1985) gave rise to active discussion among scientists over the nature of free-will and conscious voluntary action, suggesting that, at least in certain circumstances, an intention to perform voluntary action can be predicted from prior neural activity. (Brass and Haggart 2008) proposed to distinguish three different classes of voluntary decisions: "what" type of action to perform, "when" to act, and "whether" to act or not. Those distinct decisions might involve different neural pathways and distributed anatomical regions (Haggart 2008, Brass 2013, Mueller 2007, Krieghoff 2009), including medial pFC, ACC, preSMA and SMA, PMC, and parietal cortex.

In our study we confront participants with the three classes of decisions in more natural, yet still strictly controlled experimental setup, involving navigating a car through a virtual environment. By adopting the virtual environment, rather than abstract pictogram-based stimuli, we intend to provide more natural platform for analysis of neural correlates of voluntary action, and avoid common problems such as random sequence generation behavior (Jahanshahi 1999) and lack of external validity (Haggart 2008).

Each of the 16 participants performed 840 voluntary decisions split into blocks corresponding to "what" (left/right turn), "when" (first/second crossroad), "whether" (turn or do not turn), and "control" (do not take any decisions). High-resolution EEG data was acquired with 128-channel Biosemi ActiveTwo system. Oculomotor activity was recorded with SMI eye-tracking system and synchronized with EEG signals. Furthermore, for each participant we acquired structural MR brain image (3T Philips scanner), and recorded exact electrode coordinates with Localite neuro-navigation system.

We demonstrate electrophysiological differences in activation of selected brain regions related to the three aforementioned classes of decisions, in terms of timing, spatial distribution and time-frequency modulation of lower (theta/alpha) and higher (gamma) frequency bands, time-locked to the onset of the decision intervals. This event-related modulation of EEG signals, along with subject-specific T1 images, sessionspecific electrode coordinates, and set of spatial filters are then used to reconstruct decision-relevant neuroanatomical sources distributed over prefrontal, motor and parietal cortical regions.

Abstract no.: P 157

What, When, Whether - electrophysiological correlates of voluntary action in virtual environment.

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Introduction

The nature of volition has been a subject of scientific pursuit for a long time. The famous study of (Libet 1985) gave rise to active discussion over the nature of free-will and conscious voluntary action, suggesting that, at least in certain circumstances, an intention to perform voluntary action can be predicted from prior neural activity. (Brass and Haggart 2008) proposed to distinguish three distinct classes of voluntary decisions: **"what"** type of action to perform, **"when"** to act, and **"whether"** to act or not, which might involve different neural pathways and distributed cortical regions, including medial pFC, ACC, preSMA and SMA, PMC, and parietal cortex.
In the light of **growing evidence of involvement of neural oscillations in various cognitive processes** (Klimesh et al) and **cross-frequency interactions** between those processes (Canolty at al.,2006), we hypotesize that **voluntary action may result from, or be manifested by, transient modulation of brain oscillations.** Those in turn can be investigated through surface measures such as evoked potentials (ERP), spectral perturbations (ERSP) and phase/amplitude modulation (PAC, PCF).

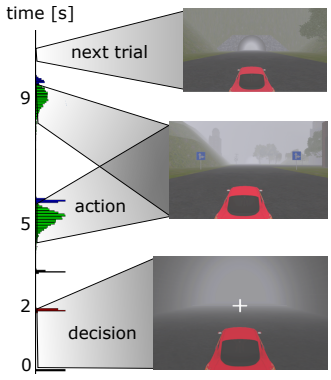
We confront participants with three classes of decisions in natural, yet still strictly controlled experimental setup, involving navigating a car through virtual environment. **We demonstrate several electroencephalographic markers that distinguished voluntary action from control condition, such as event related changes in evoked potentials and broad spectral modulation of power, ranging from theta up to gamma bands.**

Methods

15 healthy subjects participated in 3 sessions each. Dedicated Virtual Environment was designed to create quasi-natural, yet strictly controllable experimental setup Visual stimuli and pseudo-random sequence were counterbalanced to be identical in Decision and Control conditions. High-resolution EEG data was recorded with Biosemi Active2 128 channel system, Eye-tracking data with SMI system, and structural MR scans with 3T Philips.

Each participant performed 840 trials in blocks of 30, corresponding to different types of decision:
"Whether" (turn/no turn)
"What" (left/right)
"When" (first/second),
"Control" (lack of voluntary decision).

Participants were instructed to make a spontaneous decision in the tunnel (2 sec. interval), keep the decision in the memory and **execute it 3-7sec. later** upon reaching the desired cross-road, by single button press



Brain oscillations

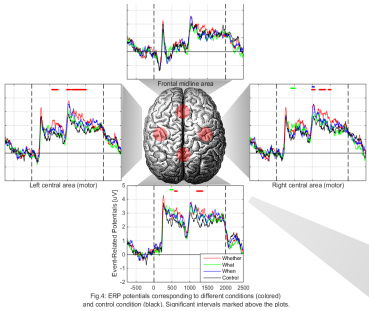


Fig.4. ERP potentials corresponding to different conditions (colored) and control condition (black). Significant intervals marked above the plots.

Data processing

The data from 42 sessions was preprocessed, labeled, cleaned for artifacts, corrected for oculo-motor artifacts (ICA approach). For the results presented here, **epochs of 3s. duration time-locked to the onset of the tunnel (decision interval)** were extracted.

Event-Related potentials

At the first step of analysis, we contrasted Event-Related potentials of **decision trials against control trials**. Fig.4 shows the representative ERPs from selected regions of interest spanning over **parietal (Pz) and frontal (Fz) midline, lateral motor area (C3 and C4)**. In the parietal and central electrodes we found statistically significant **early (500ms) and late (>1000ms) components**, particularly evident in **"whether"**-type of decisions.

Time-Frequency and ERSP analysis

We performed time-frequency analysis on all 128 channels, and extracted time series of event-related power changes (ERSP, induced activity) in the well-known physiologically relevant frequency bands. **Morlet Wavelet decomposition with variable cycles** was used, which provides good trade-off between temporal and spectral accuracy of resulting time-frequency images. Alternative approach, based on narrow-band filtering followed by Hilbert transform, yielded very comparable results.
Fig.5A presents time-frequency grand average at **parietal area (Pz) for whether-type condition (top left) and control condition (top right)**. Those images correspond to logarithm of relative change (dB scale) of power spectra after at the decision intervals. The comparison of those two (Fig.5A, bottom) yields the spectral modulation that was characteristic for voluntary decision but absent in control. The **modulation of low theta rhythms** is clearly visible (may contribute to ERP effect discussed earlier), **followed by late alpha desynchronization and intensive, transient gamma burst**.

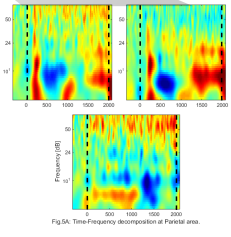


Fig.5A: Time-Frequency decomposition at Parietal area.

In order to observe this type of modulation over entire scalp surface, we analyzed time courses of the above mentioned spectral time-series and their task-control differences. To account for large number of multiple comparisons on highly correlated time-series, we performed **cluster-based permutation statistics** (FieldTrip toolbox).
The global results of those tests in **channel/freq.band/time space**, are presented on Fig.5("whether"), Fig.6("what"), Fig.7("when"). Color-coded patches correspond to significant effect of decision process (p<.05, corrected). **Modulation, and apparent interaction, of different oscillatory processes is evident especially for "whether" and "what" conditions.**

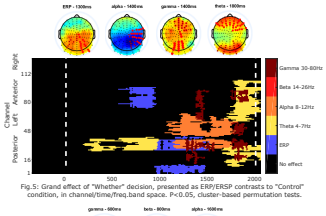


Fig.5: Grand effect of "Whether" decision, presented as ERP/ERSP contrasts to "Control" condition, in channel/time/freq.band space. P<0.05, cluster-based permutation tests.

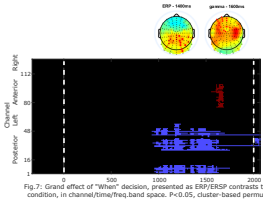


Fig.7: Grand effect of "When" decision, presented as ERP/ERSP contrasts to "Control" condition, in channel/time/freq.band space. P<0.05, cluster-based permutation tests.

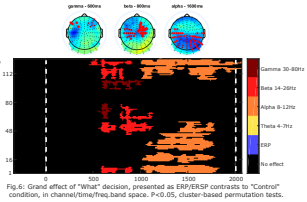


Fig.6: Grand effect of "What" decision, presented as ERP/ERSP contrasts to "Control" condition, in channel/time/freq.band space. P<0.05, cluster-based permutation tests.

Behavioral statistics

Our results indicate that human behavioral is non-random and voluntary choice is clearly biased to certain patterns, even in the absence of explicit incentive, goal, or reward. All except one participants represented bias towards "right", "first" and "turn" choices, in "what", "when" and "whether" decisions respectively (Fig [1]). It may be related to handedness, impulsivity, or result from subconscious minimization of the perceived task difficulty.

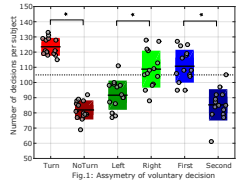


Fig.1: Assymetry of voluntary decision

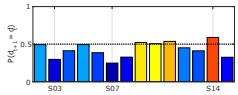
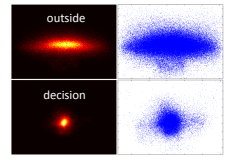


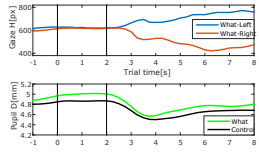
Fig.2: Probability of subject repeating her last binary choice. The value is close to 0.5 for random generator.

The outcome of the binary decision is predictable, even with as simple model as first-order Markov chain, which considers only single prior outcome to predict the following one. Nearly all participants had higher tendency to revert action (i.e. left choice after prior right), than random sequence generator would have (Fig[2])

Eye-tracking statistics

Simultaneously with EEG, 120Hz eye-tracking data was recorded, with primary goal to validate that participants followed fixation instructions and that observed EEG activation patterns are not due to systematic oculo-motor activity in decision intervals. Heatmap and gaze position densities are good metrics.





However, ET data reveals a lot of interesting behavioral information as well. On left-top figure we observe that almost immediately after decision interval, long before the cross-road is visible, participants start to gaze towards desired turn direction.
Left-bottom figure shows pupil diameter. Pupil dilation is stronger in decision condition decision trials, particularly in decision intervals.

Conclusions

Humans are poor in generating random behavior. Even in the lack of reward or explicit incentive, humans display biases to certain behavioral patterns, and tendency to create transient, local incentives.

Nature of volition can be studied in context of brain oscillation and selective modulation of power bands. Our preliminary results indicate wide range of spectral perturbations patterns (**from slow theta to gamma**) following the onset of decision intervals. It must be noted though, that along with "act of volition" per se, those oscillation may encode other supportive cognitive processes, such as spatial and motor imagery, memory system access.

The **patterns of spectral perturbations varied between different types of decision ("What", "When", "Whether").** This may support the hypothesis that they are mediated (at least partially) by different cortical pathways.

Brass, M. and P. Haggard (2008). "The what, when, whether model of intentional 3action.", Neuroscientist 1(4): 319-325.
Klimesch, W. (1999). EEG alpha and theta oscillations reflect cognitive and memory performance: A review and analysis. Brain Res. Rev.29 , 169–195.
Canolty at al (2006). "High Gamma Power Is Phase-Locked to Theta Oscillations in Human Neocortex" , Science 15 September 2006: 313 (5793), 1626-1628.

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dr. Ole Winther, Technical University of Denmark, Cognitive Systems
Lundbeck Foundation

E.0.2 PMC10 conference 2015

Progress in Motor Control 10th Conference
Budapest, Hungary, 22th-25th July, 2015

Symposium talk:
"What, When, Whether - the electrophysiological correlates and classification of voluntary action in virtual environment"

Konrad Stanek[1,2], Hartwig R. Siebner[2], Steffen Angstmann[2], Kristoffer H. Madsen[2], Ole Winther[1]
(1) Technical University of Denmark, DTU Compute, Cognitive Systems
(2) Danish Research Centre for Magnetic Resonance, Hvidovre Hospital, Denmark

The study of (Libet 1985) gave rise to active discussion among scientists over the nature of free-will and conscious voluntary action, suggesting that, at least in certain circumstances, an intention to perform voluntary action can be predicted from prior neural activity. (Brass and Haggart 2008) proposed to distinguish three different classes of voluntary decisions: "what" type of action to perform, "when" to act, and "whether" to act or not. Those distinct decisions might involve different neural pathways and distributed anatomical regions (Haggart 2008, Brass 2013, Mueller 2007, Krieghoff 2009), including medial pFC, ACC, preSMA and SMA, PMC, and parietal cortex.

In our study, we confront participants with the three classes of decisions in more natural, yet still strictly controlled experimental setup, involving navigating a car through a virtual environment. We investigate the behavioral and electrophysiological characteristics of different classes of decisions and identify the relevant neuroanatomical regions modulated between conditions. By adopting the virtual environment, rather than abstract pictogram-based stimuli, we intend to provide more natural platform for analysis of neural correlates of voluntary action, and avoid common problems such as random sequence generation behavior (Jahanshahi and Dirnberger 1999) and lack of external validity (Haggart 2008). The virtual environment ensures properly balanced randomization of trials corresponding to distinct classes of decision and synchronizes participants' behavior and environmental variables with EEG data. While navigating a simulated car, each of the 16 participants performed 840 voluntary decisions split into blocks corresponding to "what" (left/right turn), "when" (first/second crossroad), "whether" (turn or do not turn), and "control" (do not take any decisions). The decisions were time-locked to the intervals when car was passing through tunnels with stable visual field, constant luminance and visible fixation cross. Depending on prior decision, participants performed action of button

press few seconds later upon approaching an appropriate crossroad.
High-resolution EEG data was acquired with 128-channel Biosemi ActiveTwo system. Oculo-motor activity and gaze position were recorded with SMI eye-tracking system and synchronized with EEG signals.. For each participant we acquired structural MR brain image (3T Philips scanner) and recorded exact electrode coordinates with Localite neuro-navigation system.
We demonstrate electrophysiological differences in activation of neural networks distributed over cortical midline related to the three aforementioned classes of decisions, in terms of timing, spatial distribution and power modulation of lower (theta/alpha) and higher (gamma) frequency bands, time-locked to the onset of the decision intervals. This event-related modulation of EEG signals, along with subject-specific T1 images, session-specific electrode coordinates, and set of spatial filters are then used to reconstruct decision relevant neuroanatomical sources activated in prefrontal, motor and parietal cortical regions.
Furthermore, we apply spatial filtering to select the most discriminative features and apply probabilistic methods (Tipping 2001, Frolov 2011) to classify decision trials against control trials and to predict decision outcome on single-trial basis. We demonstrate above-chance prediction accuracy and discuss feasibility of using single-trial classification of voluntary decisions to build natural, intention-driven BCI systems.

E.0.3 Donders Discussions

Donders Discussions conference, Neurophilosophy session
Nijmegen, Netherlands, 5th-6th November, 2015

Neurophilosophy session talk:
"Brain oscillations and complex nature of voluntary action"

Konrad Stanek[1,2], Ole Winther[1], Steffen Angstmann[2], Kristoffer H. Madsen[2], Hartwig R. Siebner[2]
(1) Technical University of Denmark, DTU Compute, Cognitive Systems
(2) Danish Research Centre for Magnetic Resonance, Hvidovre Hospital, Denmark

The nature of volition and free will has been a subject of scientific debate for decades, especially since the famous study of (Libet 1985). Recent developments in neuroimaging technologies allow us to gradually bridge the gap between the conceptual models and neurophysiological evidence. Growing number of studies and experimental designs try to determine the anatomical sources and temporal characteristics of voluntary actions and decisions that precede them. (Brass and

Haggard 2008) proposed three main components of voluntary action: "what", "when" and "whether". Each may involve different neural pathways and cortical regions, including medial pFC, ACC, preSMA and SMA, PMC, and parietal cortex.

In our experiments participants are confronted with different types of binary, voluntary choices, both in classic pictogram-based paradigms and in more realistic designs involving navigating a simulated car through a dedicated virtual environment. Participants decide "what" to do (left/right turn), "when" to act (first/second crossroad), "whether" to act (turn or do not turn). Spectral analysis of high-resolution EEG data revealed task-modulated oscillatory activity in parieto-frontal cortical areas at wide range of spectra, starting from theta (4-7Hz) and alpha (8-12Hz) up to gamma (40-80Hz) frequencies. Furthermore, the cross-frequency interactions between those activities may indicate hierarchical organization of the underlying neuronal networks, where the phase of slow-oscillating thalamo- and cortico-cortical networks modulates the amplitude of fast, focal, task-specific assemblies. Our results suggest that voluntary decisions, even as simple as navigation-alike choices, might outcome from complex interaction of coordinated cognitive processes, such as introspective attention, working-memory, motor and spatial imagery. Each of those can be reflected by distinct spatio-temporal activity patterns, which poses considerable challenges on data analysis and interpretation.
During the talk I will highlight several promising methods for investigating subtle nature of brain oscillations, such as wavelet decomposition, cross-frequency coupling measures, and benefits of mass univariate approach for robust statistics and unbiased analysis of high-resolution EEG.

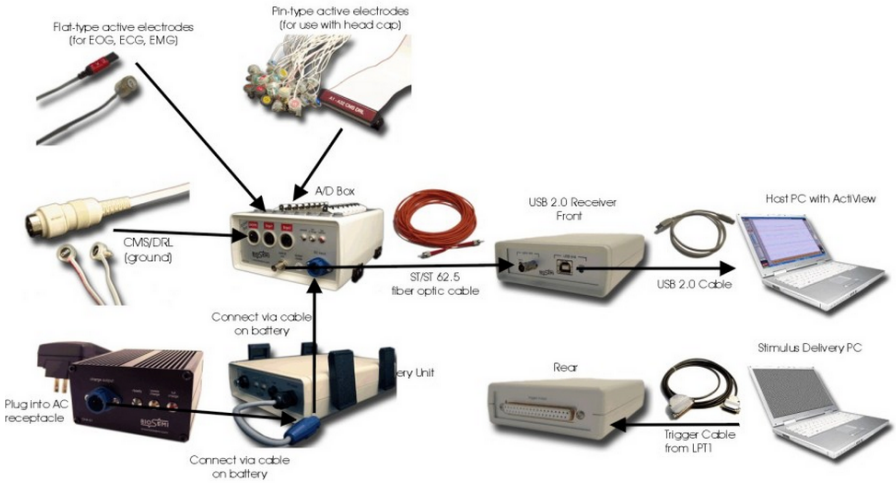
Appendix F

Specification of EEG/ET apparatus

The appendix contains the vendor specification of the devices used in the studies presented in this thesis for EEG and eye-tracking data acquisition:

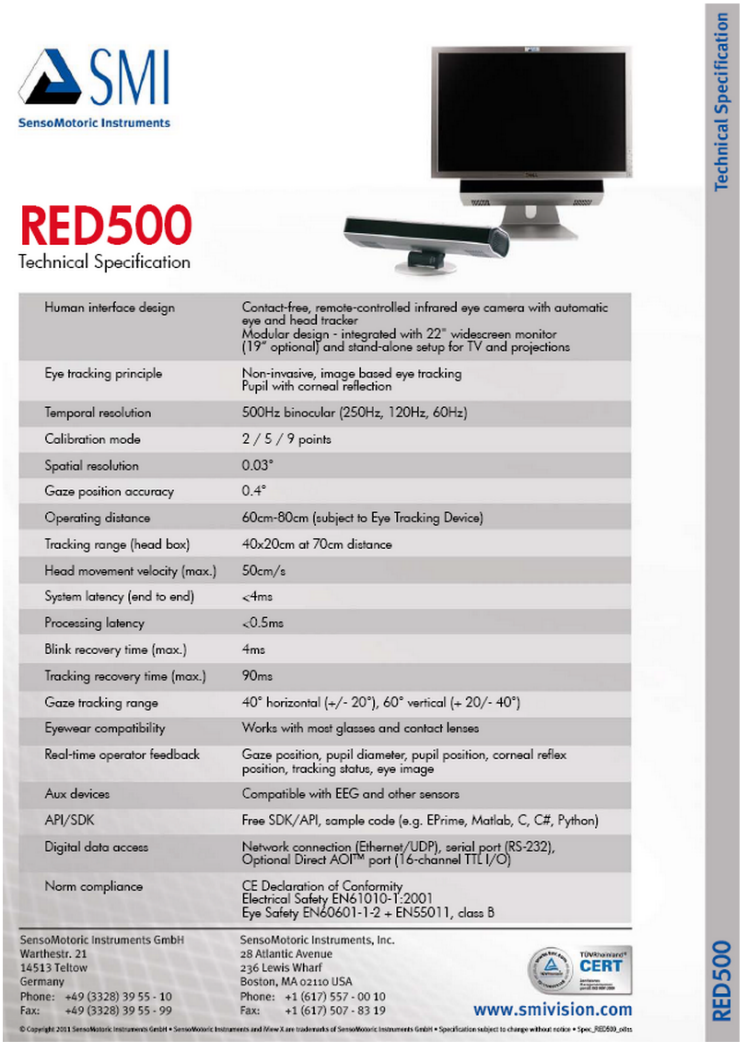
1) EEG Biosemi ActiveTwo system (Figure F.1)

2) SMI RED eye-tracking system (Figure F.2)



Sample-rate options: (sample rate is adjustable by user)	2048 Hz	4096 Hz	8192 Hz	16,384 Hz
Max. number of channels @ selected sample rate:	280	280	280	152
Bandwidth (-3dB):	DC - 400 Hz	DC - 800 Hz	DC - 1600 Hz	DC - 3200 Hz
Low-pass response	5^{th} order sinc digital filter			
High-pass response	fully DC coupled			
Digitalization:	24 bit, 4^{th} order Delta-Sigma modulator with 64x oversampling, one converter per channel			
Sampling skew:	< 10 ps			
Absolute sample rate accuracy (over temp range: 0-70 C)	0.1 Hz	0.2 Hz	0.4 Hz	0.8 Hz
Relative sample rate accuracy (jitter)	< 200 ps			
Quantization-resolution	LSB = 31.25 nV, guaranteed no missing codes			
Gain accuracy:	0,1 %			
Anti aliasing filter	fixed first order analog filter, -3dB at 3.6 kHz			
Total input noise (Z_e < 10 kOhm):, full bandwidth	0.8 uV_{RMS} (5 uV_{pk-pk})	1.0 uV_{RMS} (6 uV_{pk-pk})	1.4 uV_{RMS} (8 uV_{pk-pk})	2.0 uV_{RMS} (12 uV_{pk-pk})
1/f noise (Z_e < 1 MOhm):	1 uV_{pk-pk} @ 0.1..10Hz			
Amplifier current noise:	< 30 fA_{rms}			
Input bias current:	< 100 pA per channel			
Input impedance Active Electrode	300 MOhm @ 50 Hz (10^{12} Ohm // 11 pF)			
DC offset:	< 0.5 mV			
DC drift	< 0.5 uV per degree Celsius			
Input range	+262 mV to -262 mV			
Distortion	< 0.1 %			
Channel separation	> 100 dB			
Common Mode Rejection Ratio	> 100 dB @ 50 Hz			
Isolation Mode Rejection Ratio	> 160 dB @ 50 Hz			
Power Consumption	4 Watt @ 280 channels inversely proportional with the number of installed channels			
Battery capacity, standard battery	25 Watt-hour, 3 cell sealed lead-acid (double capacity battery is available as an option)			
Battery life on standard battery	> 5 hours @ 280 channels inversely proportional with the number of installed channels			
Battery charge time (with external fast charger):	< 3.5 hours for a 100% charge			
Leakage current, normal operation:	< 1 $uA_{rms.}$			
Leakage current, single fault	< 50 uA_{rms}			
Trigger inputs:	16 inputs on optical receiver (isolated from subject section) , TTL level			
Trigger outputs:	15 outputs on optical receiver (isolated from subject section) , TTL level			
PC interface:	USB2.0			
Size of front-end, including battery-box (H x W x D)	120 x 150 x 190 mm			
Weight of front-end, including battery-box	1.1 kg			
Warranty	3 years			

Figure F.1: Top: Biosemi ActiveTwo EEG system components overview. Bottom table: Vendor specification for biopotential measurement system, type ActiveTwo Mk2 with two-wire active electrodes.



SMI
SensoMotoric Instruments

RED500
Technical Specification

Technical Specification

Human interface design	Contact-free, remote-controlled infrared eye camera with automatic eye and head tracker Modular design - integrated with 22" widescreen monitor (19" optional) and stand-alone setup for TV and projections
Eye tracking principle	Non-invasive, image based eye tracking Pupil with corneal reflection
Temporal resolution	500Hz binocular (250Hz, 120Hz, 60Hz)
Calibration mode	2 / 5 / 9 points
Spatial resolution	0.03°
Gaze position accuracy	0.4°
Operating distance	60cm-80cm (subject to Eye Tracking Device)
Tracking range (head box)	40x20cm at 70cm distance
Head movement velocity (max.)	50cm/s
System latency (end to end)	<4ms
Processing latency	<0.5ms
Blink recovery time (max.)	4ms
Tracking recovery time (max.)	90ms
Gaze tracking range	40° horizontal (+/- 20°), 60° vertical (+ 20/- 40°)
Eyewear compatibility	Works with most glasses and contact lenses
Real-time operator feedback	Gaze position, pupil diameter, pupil position, corneal reflex position, tracking status, eye image
Aux devices	Compatible with EEG and other sensors
API/SDK	Free SDK/API, sample code (e.g. EPrime, Matlab, C, C#, Python)
Digital data access	Network connection (Ethernet/UDP), serial port (RS-232), Optional Direct AOI™ port (16-channel TTL I/O)
Norm compliance	CE Declaration of Conformity Electrical Safety EN61010-1:2001 Eye Safety EN60601-1-2 + EN55011, class B

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www.smivision.com

RED500

Figure F.2: SMI RED eye-tracking system - vendor specification.

Bibliography

[1] EYE-EEG toolbox [www2.hu-berlin.de/eyetracking-eeg].

[2] D. Akkal, R. P. Dum, and P. L. Strick. Supplementary motor area and presupplementary motor area: targets of basal ganglia and cerebellar output. *The Journal of neuroscience : the official journal of the Society for Neuroscience*, 27(40):10659–73, oct 2007.

[3] J. Ashburner and K. J. Friston. Unified segmentation. *NeuroImage*, 26(3):839–851, jul 2005.

[4] C. Başar-Eroglu, D. Strüber, M. Schürmann, M. Stadler, and E. Başar. Gamma-band responses in the brain: A short review of psychophysiological correlates and functional significance. *International Journal of Psychophysiology*, 24(1-2):101–112, 1996.

[5] C. Babiloni, A. Brancucci, L. Arendt-Nielsen, F. Babiloni, P. Capotosto, F. Carducci, F. Cincotti, L. Romano, A. C. N. Chen, and P. M. Rossini. Alpha event-related desynchronization preceding a go/no-go task: a high-resolution EEG study. *Neuropsychology*, 18(4):719–728, 2004.

[6] C. Babiloni, F. Carducci, F. Cincotti, P. M. Rossini, C. Neuper, G. Pfurtscheller, and F. Babiloni. Human movement-related potentials vs desynchronization of EEG alpha rhythm: a high-resolution EEG study. *NeuroImage*, 10(6):658–65, dec 1999.

[7] C. Babiloni, F. Vecchio, A. Bultrini, G. Luca Romani, and P. M. Rossini. Pre- and poststimulus alpha rhythms are related to conscious visual perception: a high-resolution EEG study. *Cerebral cortex (New York, N.Y. : 1991)*, 16(12):1690–700, dec 2006.

[8] J. Baer, J. C. Kaufman, and R. F. Baumeister. Are We Free?: Psychology and Free Will. *Are We Free?: Psychology and Free Will*, pages 1–367, 2008.

[9] S. N. Baker, G. Curio, and R. N. Lemon. EEG oscillations at 600 Hz are macroscopic markers for cortical spike bursts. *The Journal of physiology*, 550(Pt 2):529–34, jul 2003.

[10] G. Berrios and M. Gili. Will and its disorders: a conceptual history. *History of Psychiatry*, 6(21):087–104, mar 1995.

[11] N. Bigdely-Shamlo, T. Mullen, C. Kothe, K.-M. Su, and K. A. Robbins. The PREP pipeline: standardized preprocessing for large-scale EEG analysis. *Frontiers in Neuroinformatics*, 9, jun 2015.

[12] J. P. Brasil-Neto, A. Pascual-Leone, J. Valls-Solé, L. G. Cohen, and M. Hallett. Focal transcranial magnetic stimulation and response bias in a forced-choice task. *Journal of Neurology, Neurosurgery & Psychiatry*, 55(10):964–966, oct 1992.

[13] M. Brass and P. Haggard. The What, When, Whether Model of Intentional Action. *The Neuroscientist*, 14(4):319–325, aug 2008.

[14] A. Bruns. Fourier-, Hilbert- and wavelet-based signal analysis: are they really different approaches? *Journal of neuroscience methods*, 137(2):321–32, aug 2004.

[15] E. T. Bullmore, J. Suckling, S. Overmeyer, S. Rabe-Hesketh, E. Taylor, and M. J. Brammer. Global, voxel, and cluster tests, by theory and permutation, for a difference between two groups of structural MR images of the brain. *IEEE transactions on medical imaging*, 18(1):32–42, sep 1999.

[16] G. Buzsáki and X.-J. Wang. Mechanisms of gamma oscillations. *Annual review of neuroscience*, 35:203–25, jan 2012.

[17] G. Buzsáki and B. O. Watson. Brain rhythms and neural syntax: implications for efficient coding of cognitive content and neuropsychiatric disease. *Dialogues in clinical neuroscience*, 14(4):345–67, dec 2012.

[18] S. R. Cajal. *Comparative study of the sensory areas of the human cortex*. 1899.

[19] R. T. Canolty and R. T. Knight. The functional role of cross-frequency coupling. *Trends in cognitive sciences*, 14(11):506–15, nov 2010.

[20] J. F. Cavanagh and M. J. Frank. Frontal theta as a mechanism for cognitive control. *Trends in cognitive sciences*, 18(8):414–21, aug 2014.

[21] J. D. Cohen, S. M. McClure, and A. J. Yu. Should I stay or should I go? How the human brain manages the trade-off between exploitation and exploration. *Philosophical transactions of the Royal Society of London. Series B, Biological sciences*, 362(1481):933–42, may 2007.

[22] R. Cunnington, C. Windischberger, L. Deecke, and E. Moser. The preparation and execution of self-initiated and externally-triggered movement: a study of event-related fMRI. *NeuroImage*, 15(2):373–85, feb 2002.

[23] N. D. Daw, J. P. O'Doherty, P. Dayan, B. Seymour, and R. J. Dolan. Cortical substrates for exploratory decisions in humans. *Nature*, 441(7095):876–9, jun 2006.

[24] F. Debaere, N. Wenderoth, S. Sunaert, P. Van Hecke, and S. P. Swinnen. Internal vs external generation of movements: differential neural pathways involved in bimanual coordination performed in the presence or absence of augmented visual feedback. *NeuroImage*, 19(3):764–76, jul 2003.

[25] S. Dehaene and L. Naccache. Towards a cognitive neuroscience of consciousness: Basic evidence and a workspace framework, 2001.

[26] M. P. Deiber, R. E. Passingham, J. G. Colebatch, K. J. Friston, P. D. Nixon, and R. S. J. Frackowiak. Cortical areas and the selection of movement: a study with positron emission tomography. *Experimental Brain Research*, 84(2):393–402, jan 1991.

[27] M.-P. Deiber, E. Sallard, C. Ludwig, C. Ghezzi, J. Barral, and V. Ibañez. EEG alpha activity reflects motor preparation rather than the mode of action selection. *Frontiers in Integrative Neuroscience*, 6:59, jan 2012.

[28] A. Delorme and S. Makeig. EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *Journal of neuroscience methods*, 134(1):9–21, mar 2004.

[29] O. Dimigen, W. Sommer, A. Hohlfeld, A. M. Jacobs, and R. Kliegl. Coregistration of eye movements and EEG in natural reading: Analyses and review. *Journal of Experimental Psychology: General*, 140(4):552–572, 2011.

[30] L. M. Doyle, K. Yarrow, and P. Brown. Lateralization of event-related beta desynchronization in the EEG during pre-cued reaction time tasks. *Clinical Neurophysiology*, 116(8):1879–1888, aug 2005.

[31] A. K. Engel and W. Singer. Temporal binding and the neural correlates of sensory awareness. *Trends in Cognitive Sciences*, 5(1):16–25, jan 2001.

[32] S. Filipović, M. Jahanshahi, and J. Rothwell. Uncoupling of contingent negative variation and alpha band event-related desynchronization in a go/no-go task. *Clinical Neurophysiology*, 112(7):1307–1315, jul 2001.

[33] S. R. Filipović, M. Jahanshahi, and J. C. Rothwell. Cortical potentials related to decision-making: comparison of two types of go/no-go decision. *Neuroreport*, 10(17):3583–3587, nov 1999.

[34] S. R. Filipović, M. Jahanshahi, J. C. Rothwell, S. R. Filipovic, M. Jahanshahi, and J. C. Rothwell. Cortical potentials related to the nogo decision. *Exp Brain Res*, 132(3):411–415, apr 2000.

[35] I. Fried, A. Katz, G. McCarthy, K. J. Sass, P. Williamson, S. S. Spencer, D. D. Spencer, I. Fried, A. Katz, A. Katz, G. McCarthy, G. McCarthy, K. J. Sass, K. J. Sass, P. Williamson, P. Williamson, S. S. Spencer, S. S. Spencer, D. D. Spencer, and D. D. Spencer. Functional organization of human supplementary motor cortex studied by electrical stimulation. *Journal of Neuroscience*, 11(November):3656–3666, nov 1991.

[36] I. Fried, R. Mukamel, and G. Kreiman. Internally generated preactivation of single neurons in human medial frontal cortex predicts volition. *Neuron*, 69(3):548–62, feb 2011.

[37] I. Funderud, M. Lindgren, M. Løvstad, T. Endestad, B. Voytek, R. T. Knight, and A. K. Solbakk. Differential Go/NoGo activity in both contingent negative variation and spectral power. *PLoS ONE*, 7(10):e48504, 2012.

[38] D. Gabor. *Theory of communication*, volume 181. 2006.

[39] I. Goldberg, S. Ullman, and R. Malach. Neuronal correlates of "free will" are associated with regional specialization in the human intrinsic/default network. *Consciousness and Cognition*, 17(3):587–601, sep 2008.

[40] C. M. Gómez, E. Vaquero, D. López-Mendoza, J. González-Rosa, and M. Vázquez-Marrufo. Reduction of EEG power during expectancy periods in humans. *Acta neurobiologiae experimentalis*, 64(2):143–51, jan 2004.

[41] G. G. Gregoriou, S. J. Gotts, H. Zhou, and R. Desimone. High-frequency, long-range coupling between prefrontal and visual cortex during attention. *Science (New York, N.Y.)*, 324(5931):1207–10, may 2009.

[42] D. M. Groppe, T. P. Urbach, and M. Kutas. Mass univariate analysis of event-related brain potentials/fields I: A critical tutorial review. *Psychophysiology*, 48(12):1711–1725, dec 2011.

[43] J. Gross, S. Baillet, G. R. Barnes, R. N. Henson, A. Hillebrand, O. Jensen, K. Jerbi, V. Litvak, B. Maess, R. Oostenveld, L. Parkkonen, J. R. Taylor, V. van Wassenhove, M. Wibral, and J.-M. Schoffelen. Good practice for conducting and reporting MEG research. *NeuroImage*, 65:349–63, jan 2013.

[44] A. G. Guggisberg, S. S. Dalal, A. M. Findlay, and S. S. Nagarajan. High-frequency oscillations in distributed neural networks reveal the dynamics of human decision making. *Frontiers in human neuroscience*, 1:14, jan 2007.

[45] P. Haggard. Human volition: towards a neuroscience of will. *Nature reviews. Neuroscience*, 9(12):934–46, dec 2008.

[46] P. Haggard and M. Eimer. On the relation between brain potentials and the awareness of voluntary movements. *Experimental Brain Research*, 126(1):128–133, apr 1999.

[47] M. Hallett. Volitional control of movement: the physiology of free will. *Clinical Neurophysiology*, 2007.

[48] F. Hatz, M. Hardmeier, H. Bousleiman, S. Rüegg, C. Schindler, and P. Fuhr. Reliability of fully automated versus visually controlled pre- and post-processing of resting-state EEG. *Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology*, 126(2):268–74, feb 2015.

[49] F. Hoffstaedter, C. Grefkes, K. Zilles, and S. B. Eickhoff. The "what" and "when" of self-initiated movements. *Cerebral cortex (New York, N.Y. : 1991)*, 23(3):520–30, mar 2013.

[50] F. Hyder, E. A. Phelps, C. J. Wiggins, K. S. Labar, A. M. Blamire, and R. G. Shulman. "Willed action": a functional MRI study of the human prefrontal cortex during a sensorimotor task. *Proceedings of the National Academy of Sciences of the United States of America*, 94(13):6989–94, jun 1997.

[51] M. Jahanshahi and G. Dirnberger. The left dorsolateral prefrontal cortex and random generation of responses: Studies with transcranial magnetic stimulation. *Neuropsychologia*, 37(2):181–190, 1998.

[52] I. H. Jenkins. Self-initiated versus externally triggered movements: II. The effect of movement predictability on regional cerebral blood flow. *Brain*, 123(6):1216–1228, jun 2000.

[53] O. Jensen. Oscillations in the Alpha Band (9-12 Hz) Increase with Memory Load during Retention in a Short-term Memory Task. *Cerebral Cortex*, 12(8):877–882, aug 2002.

[54] O. Jensen and M. Bonnefond. Prefrontal alpha- and beta-band oscillations are involved in rule selection. *Trends in Cognitive Sciences*, 17(1):10–12, jan 2013.

[55] O. Jensen, P. Goel, N. Kopell, M. Pohja, R. Hari, and B. Ermentrout. On the human sensorimotor-cortex beta rhythm: Sources and modeling. *NeuroImage*, 26(2):347–355, jun 2005.

[56] O. Jensen and C. D. Tesche. Frontal theta activity in humans increases with memory load in a working memory task. *European Journal of Neuroscience*, 15(8):1395–1399, apr 2002.

[57] X. Jia and A. Kohn. Gamma rhythms in the brain. *PLoS Biology*, 9(4):e1001045, apr 2011.

[58] H.-G. Jo, T. Hinterberger, M. Wittmann, T. L. Borghardt, and S. Schmidt. Spontaneous EEG fluctuations determine the readiness potential: is preconscious brain activation a preparation process to move? *Experimental brain research*, 231(4):495–500, dec 2013.

[59] T. P. Jung, S. Makeig, M. Westerfield, J. Townsend, E. Courchesne, and T. J. Sejnowski. Analysis and visualization of single-trial event-related potentials. *Human brain mapping*, 14(3):166–85, nov 2001.

[60] M. J. Kahana. The Cognitive Correlates of Human Brain Oscillations. *J. Neurosci.*, 26(6):1669–1672, 2006.

[61] M. J. Kahana, R. Sekuler, J. B. Caplan, M. Kirschen, and J. R. Madsen. Human theta oscillations exhibit task dependence during virtual maze navigation. *Nature*, 399(6738):781–4, jun 1999.

[62] W. Klimesch. EEG-alpha rhythms and memory processes. *International Journal of Psychophysiology*, 26(1-3):319–340, 1997.

[63] W. Klimesch. EEG alpha and theta oscillations reflect cognitive and memory performance: a review and analysis. *Brain Research Reviews*, 29(2-3):169–195, 1999.

[64] W. Klimesch. α-band oscillations, attention, and controlled access to stored information. *Trends in cognitive sciences*, 16(12):606–17, dec 2012.

[65] W. Klimesch, M. Doppelmayr, H. Russegger, and T. Pachinger. Theta band power in the human scalp EEG and the encoding of new information. *Neuroreport*, 7(7):1235–40, may 1996.

[66] W. Klimesch, S. Hanslmayr, P. Sauseng, W. Gruber, C. J. Brozinsky, N. E. A. Kroll, A. P. Yonelinas, and M. Doppelmayr. Oscillatory EEG correlates of episodic trace decay. *Cerebral cortex (New York, N.Y. : 1991)*, 16(2):280–90, feb 2006.

[67] W. Klimesch, P. Sauseng, and S. Hanslmayr. EEG alpha oscillations: The inhibition–timing hypothesis. *Brain Research Reviews*, 53(1):63–88, 2007.

[68] S. E. Kober, J. Kurzmann, and C. Neuper. Cortical correlate of spatial presence in 2D and 3D interactive virtual reality: an EEG study. *International journal of psychophysiology : official journal of the International Organization of Psychophysiology*, 83(3):365–74, mar 2012.

[69] N. Kovacevic, P. Ritter, W. Tays, S. Moreno, and A. R. McIntosh. 'My Virtual Dream': Collective Neurofeedback in an Immersive Art Environment. *PloS one*, 10(7):e0130129, jan 2015.

[70] R. Kristeva-Feige, C. Fritsch, J. Timmer, and C.-H. Lücking. Effects of attention and precision of exerted force on beta range EEG-EMG synchronization during a maintained motor contraction task. *Clinical Neurophysiology*, 113(1):124–131, jan 2002.

[71] A. A. Kühn, D. Williams, A. Kupsch, P. Limousin, M. Hariz, G.-H. Schneider, K. Yarrow, and P. Brown. Event-related beta desynchronization in human subthalamic nucleus correlates with motor performance. *Brain : a journal of neurology*, 127(Pt 4):735–46, apr 2004.

[72] S. Kühn and M. Brass. When doing nothing is an option: The neural correlates of deciding whether to act or not. *NeuroImage*, 46(4):1187–1193, jul 2009.

[73] M. Kutas and E. Donchin. Preparation to respond as manifested by movement-related brain potentials. *Brain Research*, 202(1):95–115, nov 1980.

[74] H. C. Lau, R. D. Rogers, P. Haggard, and R. E. Passingham. Attention to intention. *Science (New York, N.Y.)*, 303(5661):1208–10, feb 2004.

[75] H. C. Lau, R. D. Rogers, and R. E. Passingham. Manipulating the experienced onset of intention after action execution. *Journal of cognitive neuroscience*, 19(1):81–90, jan 2007.

[76] H. C. Lau, R. D. Rogers, N. Ramnani, and R. E. Passingham. Willed action and attention to the selection of action. *NeuroImage*, 21(4):1407–1415, 2004.

[77] V. Lawhern, W. D. Hairston, and K. Robbins. DETECT: a MATLAB toolbox for event detection and identification in time series, with applications to artifact detection in EEG signals. *PloS one*, 8(4):e62944, jan 2013.

[78] M. Le Van Quyen. The brainweb of cross-scale interactions. *New Ideas in Psychology*, 29(2):57–63, aug 2011.

[79] M. Le Van Quyen, J. Foucher, J. Lachaux, E. Rodriguez, A. Lutz, J. Martinerie, and F. J. Varela. Comparison of Hilbert transform and wavelet methods for the analysis of neuronal synchrony. *Journal of neuroscience methods*, 111(2):83–98, oct 2001.

[80] R. Leeb, D. Friedman, G. R. Müller-Putz, R. Scherer, M. Slater, and G. Pfurtscheller. Self-paced (asynchronous) BCI control of a wheelchair in virtual environments: A case study with a tetraplegic. *Computational Intelligence and Neuroscience*, 2007, 2007.

[81] D. Lehmann and W. Skrandies. Reference-free identification of components of checkerboard-evoked multichannel potential fields. *Electroencephalography and clinical neurophysiology*, 48(6):609–21, jun 1980.

[82] F. Lhermitte. 'Utilization behaviour' and its relation to lesions of the frontal lobes. *Brain*, 106(2):237–255, jun 1983.

[83] L. D. Liao, C. T. Lin, K. McDowell, A. E. Wickenden, K. Gramann, T. P. Jung, L. W. Ko, and J. Y. Chang. Biosensor technologies for augmented brain-computer interfaces in the next decades, 2012.

[84] B. Libet. *Neurophysiology of Consciousness*. Birkhäuser Boston, Boston, MA, 1993.

[85] B. Libet, C. A. Gleason, E. W. Wright, and D. K. Pearl. Time of conscious intention to act in relation to onset of cerebral activity (readiness-potential). *Brain*, 106(3):623–642, sep 1983.

[86] C.-T. Lin, I.-F. Chung, L.-W. Ko, Y.-C. Chen, S.-F. Liang, and J.-R. Duann. EEG-based assessment of driver cognitive responses in a dynamic virtual-reality driving environment. *IEEE transactions on bio-medical engineering*, 54(7):1349–52, jul 2007.

[87] J. Lisman and G. Buzsaki. A Neural Coding Scheme Formed by the Combined Function of Gamma and Theta Oscillations. *Schizophrenia Bulletin*, 34(5):974–980, jul 2008.

[88] J. E. Lisman and O. Jensen. The θ-γ neural code. *Neuron*, 77(6):1002–16, mar 2013.

[89] V. Litvak, J. Mattout, S. Kiebel, C. Phillips, R. Henson, J. Kilner, G. Barnes, R. Oostenveld, J. Daunizeau, G. Flandin, W. Penny, and K. Friston. EEG and MEG data analysis in SPM8. *Computational Intelligence and Neuroscience*, 2011, 2011.

[90] F. Lopes da Silva. EEG and MEG: relevance to neuroscience. *Neuron*, 80(5):1112–28, dec 2013.

[91] C. Loukas and P. Brown. Online prediction of self-paced hand-movements from subthalamic activity using neural networks in Parkinson's disease. *Journal of neuroscience methods*, 137(2):193–205, aug 2004.

[92] S. J. Luck. An Introduction to the Event-Related Potential Technique — The MIT Press, 2005.

[93] Q. Luo, D. Mitchell, X. Cheng, K. Mondillo, D. Mccaffrey, T. Holroyd, F. Carver, R. Coppola, and J. Blair. Visual awareness, emotion, and gamma band synchronization. *Cerebral cortex (New York, N.Y. : 1991)*, 19(8):1896–904, aug 2009.

[94] S. Makeig. Auditory event-related dynamics of the EEG spectrum and effects of exposure to tones. *Electroencephalography and Clinical Neurophysiology*, 86(4):283–293, apr 1993.

[95] S. Makeig, A. J. Bell., T.-P. Jung, and T. J. Sejnowski. Independent Component Analysis of Electroencephalographic Data. *Advances in Neural Information Processing Systems*, 8:145–151, 1996.

[96] S. Makeig and J. Onton. ERP Features and EEG Dynamics. dec 2011.

[97] H. Mantanus, M. Timsit-Berthier, A. Gerono, and R. von Frenckell. A correlation study of contingent negative variation, reaction time, and EEG power spectrum in control and psychopathological populations. *Biological psychology*, 13:227–37, dec 1981.

[98] R. S. Marin and P. A. Wilkosz. Disorders of Diminished Motivation Focus on Clinical Practice and Research. *J Head Trauma Rehabil*, 20(4):377–388, jan 2005.

[99] E. Maris. Statistical testing in electrophysiological studies. *Psychophysiology*, 49(4):549–65, apr 2012.

[100] E. Maris and R. Oostenveld. Nonparametric statistical testing of EEG- and MEG-data. *Journal of neuroscience methods*, 164(1):177–90, aug 2007.

[101] E. Maris, J.-M. Schoffelen, and P. Fries. Nonparametric statistical testing of coherence differences. *Journal of neuroscience methods*, 163(1):161–75, jun 2007.

[102] M. Massimini, R. Huber, F. Ferrarelli, S. Hill, and G. Tononi. The sleep slow oscillation as a traveling wave. *The Journal of neuroscience : the official journal of the Society for Neuroscience*, 24(31):6862–70, aug 2004.

[103] D. J. McFarland, L. A. Miner, T. M. Vaughan, and J. R. Wolpaw. Mu and Beta Rhythm Topographies During Motor Imagery and Actual Movements. *Brain Topography*, 12(3):177–186, 2000.

[104] L. Melloni, C. Molina, M. Pena, D. Torres, W. Singer, and E. Rodriguez. Synchronization of neural activity across cortical areas correlates with conscious perception. *The Journal of neuroscience : the official journal of the Society for Neuroscience*, 27(11):2858–65, mar 2007.

[105] R. C. Miall and D. M. Wolpert. Forward models for physiological motor control, 1996.

[106] S. Milgram. Behavioral Study of Obedience. *Journal of abnormal psychology*, 67(4):371–378, 1963.

[107] A. Mognon, J. Jovicich, L. Bruzzone, and M. Buiatti. ADJUST: An automatic EEG artifact detector based on the joint use of spatial and temporal features. *Psychophysiology*, 48(2):229–40, feb 2011.

[108] S. Monto, S. Palva, J. Voipio, and J. M. Palva. Very slow EEG fluctuations predict the dynamics of stimulus detection and oscillation amplitudes in humans. *The Journal of neuroscience : the official journal of the Society for Neuroscience*, 28(33):8268–72, aug 2008.

[109] V. A. Mueller, M. Brass, F. Waszak, and W. Prinz. The role of the preSMA and the rostral cingulate zone in internally selected actions. *NeuroImage*, 37(4):1354–61, oct 2007.

[110] S. D. Muthukumaraswamy and B. W. Johnson. Primary motor cortex activation during action observation revealed by wavelet analysis of the EEG. *Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology*, 115(8):1760–6, aug 2004.

[111] P. Nachev, C. Kennard, and M. Husain. Functional role of the supplementary and pre-supplementary motor areas. *Nature reviews. Neuroscience*, 9(11):856–69, nov 2008.

[112] L. Nadel and W. Sinnott-Armstrong. Conscious Will and Responsibility: A Tribute to Benjamin Libet. *Conscious Will and Responsibility: A Tribute to Benjamin Libet*, pages 1–288, 2010.

[113] E. Niedermeyer. Ultrafast Frequencies and Full-Band EEG, Ultrafast EEG Activities and Their Significance. *Clinical EEG and Neuroscience*, 36(4):257–262, oct 2005.

[114] P. L. Nunez, R. Srinivasan, A. F. Westdorp, R. S. Wijesinghe, D. M. Tucker, R. B. Silberstein, and P. J. Cadusch. EEG coherency. I: Statistics, reference electrode, volume conduction, Laplacians, cortical imaging, and interpretation at multiple scales. *Electroencephalography and clinical neurophysiology*, 103(5):499–515, nov 1997.

[115] S. S. Obhi and P. Haggard. Internally generated and externally triggered actions are physically distinct and independently controlled. *Experimental Brain Research*, 156(4):518–523, jun 2004.

[116] J. Onton, M. Westerfield, J. Townsend, and S. Makeig. Imaging human EEG dynamics using independent component analysis. *Neuroscience and biobehavioral reviews*, 30(6):808–22, jan 2006.

[117] R. Oostenveld, P. Fries, E. Maris, and J. M. Schoffelen. FieldTrip: Open source software for advanced analysis of MEG, EEG, and invasive electrophysiological data. *Computational Intelligence and Neuroscience*, 2011, 2011.

[118] D. Osipova, D. Hermes, and O. Jensen. Gamma power is phase-locked to posterior alpha activity. *PloS one*, 3(12):e3990, jan 2008.

[119] J. M. Palva, S. Palva, and K. Kaila. Phase synchrony among neuronal oscillations in the human cortex. *The Journal of neuroscience : the official journal of the Society for Neuroscience*, 25(15):3962–72, apr 2005.

[120] R. E. Passingham. Two cortical systems for directing movement. *Ciba Foundation symposium*, 132:151–64, jan 1987.

[121] J. W. Peirce. PsychoPy-Psychophysics software in Python. *Journal of Neuroscience Methods*, 162(1-2):8–13, 2007.

[122] W. Penfield. The Mystery of Mind. *Princeton University Press*, 1975.

[123] G. Pfurtscheller. Graphical display and statistical evaluation of event-related desynchronization (ERD). *Electroencephalography and Clinical Neurophysiology*, 43(5):757–760, nov 1977.

[124] G. Pfurtscheller. Central beta rhythm during sensorimotor activities in man. *Electroencephalography and Clinical Neurophysiology*, 51(3):253–264, mar 1981.

[125] G. Pfurtscheller. Event-related synchronization (ERS): an electrophysiological correlate of cortical areas at rest. *Electroencephalography and Clinical Neurophysiology*, 83(1):62–69, jul 1992.

[126] G. Pfurtscheller, I. Daly, G. Bauernfeind, and G. R. Müller-Putz. Coupling between intrinsic prefrontal HbO2 and central EEG beta power oscillations in the resting brain. *PloS one*, 7(8):e43640, jan 2012.

[127] G. Pfurtscheller, B. Graimann, J. E. Huggins, S. P. Levine, and L. A. Schuh. Spatiotemporal patterns of beta desynchronization and gamma synchronization in corticographic data during self-paced movement. *Clinical Neurophysiology*, 114(7):1226–1236, jul 2003.

[128] G. Pfurtscheller, R. Leeb, C. Keinrath, D. Friedman, C. Neuper, C. Guger, and M. Slater. Walking from thought. *Brain research*, 1071(1):145–52, feb 2006.

[129] G. Pfurtscheller and F. Lopes da Silva. Event-related EEG/MEG synchronization and desynchronization: basic principles. *Clinical Neurophysiology*, 110(11):1842–1857, nov 1999.

[130] G. Pfurtscheller and C. Neuper. Simultaneous EEG 10 Hz desynchronization and 40 Hz synchronization during finger movements. *Neuroreport*, 3(12):1057–60, dec 1992.

[131] G. Pfurtscheller, A. Stancák, and C. Neuper. Event-related synchronization (ERS) in the alpha band — an electrophysiological correlate of cortical idling: A review. *International Journal of Psychophysiology*, 24(1-2):39–46, nov 1996.

[132] G. Pfurtscheller, A. Stancák, and C. Neuper. Post-movement beta synchronization. A correlate of an idling motor area? *Electroencephalography and Clinical Neurophysiology*, 98(4):281–293, apr 1996.

[133] T. W. Picton. Guidelines for using human event-related potentials to study cognition: Recording standards and publication criteria. *Psychophysiology*, 37(2):127–152, 2000.

[134] M. Plöchl, J. P. Ossandón, and P. König. Combining EEG and eye tracking: identification, characterization, and correction of eye movement artifacts in electroencephalographic data. *Frontiers in human neuroscience*, 6:278, jan 2012.

[135] H. S. Prado, M. C. Rosario, J. Lee, A. G. Hounie, R. G. Shavitt, and E. C. Miguel. Sensory phenomena in Obsessive-Compulsive Disorder and tic disorders: a review of the literature. *CNS Spectrums*, 13(5):425–432, may 2008.

[136] Z. H. Rappaport. The neuroscientific foundations of free will. *Advances and technical standards in neurosurgery*, 37(37):3–23, jan 2011.

[137] D. C. Richardson and M. J. Spivey. Eye-Tracking: Characteristics and Method, 2004.

[138] D. Rigoni, S. Kühn, G. Sartori, and M. Brass. Inducing disbelief in free will alters brain correlates of preconscious motor preparation: the brain minds whether we believe in free will or not. *Psychological science*, 22(5):613–8, may 2011.

[139] G. Rizzolatti, G. Luppino, and M. Matelli. The organization of the cortical motor system: new concepts. *Electroencephalography and clinical neurophysiology*, 106(4):283–96, apr 1998.

[140] B. J. Roach and D. H. Mathalon. Event-related EEG time-frequency analysis: an overview of measures and an analysis of early gamma band phase locking in schizophrenia. *Schizophrenia bulletin*, 34(5):907–26, sep 2008.

[141] K. Sakai. What and when: Parallel and convergent processing in motor control. *Journal of Neuroscience*, 20(7):2691 – 2700, 2000.

[142] D. L. Schacter, D. R. Addis, and R. L. Buckner. Remembering the past to imagine the future: the prospective brain. *Nature reviews. Neuroscience*, 8(9):657–61, sep 2007.

[143] R. Scheeringa, M. C. M. Bastiaansen, K. M. Petersson, R. Oostenveld, D. G. Norris, and P. Hagoort. Frontal theta EEG activity correlates negatively with the default mode network in resting state. *International journal of psychophysiology : official journal of the International Organization of Psychophysiology*, 67(3):242–51, mar 2008.

[144] A. Schlegel, P. Alexander, W. Sinnott-Armstrong, A. Roskies, P. U. Tse, and T. Wheatley. Barking up the wrong free: readiness potentials reflect processes independent of conscious will. *Experimental brain research*, 229(3):329–35, sep 2013.

[145] S. Sereno. Measuring word recognition in reading: eye movements and event-related potentials. *Trends in Cognitive Sciences*, 7(11):489–493, nov 2003.

[146] T. Shallice. From Neuropsychology to Mental Structure. Tim Shallice. Cambridge University Press, New York, 1988. xvi, 462 pp. *Science (New York, N.Y.)*, 246(4931):827–8, nov 1989.

[147] J. L. Smith, S. J. Johnstone, and R. J. Barry. Effects of pre-stimulus processing on subsequent events in a warned Go/NoGo paradigm: Response preparation, execution and inhibition. *International Journal of Psychophysiology*, 61(2):121–133, aug 2006.

[148] C. S. Soon, M. Brass, H.-J. Heinze, and J.-D. Haynes. Unconscious determinants of free decisions in the human brain. *Nature neuroscience*, 11(5):543–5, 2008.

[149] C. S. Soon, A. H. He, S. Bode, and J.-D. Haynes. Predicting free choices for abstract intentions. *Proceedings of the National Academy of Sciences of the United States of America*, 110(15):6217–22, apr 2013.

[150] P. Srinivasan, R., Winter, WR., Ding, J., Nunez. EEG and MEG cohrence: measures of functional connectivity at distinct spatial scales of neocortical dynamics. *J Neurosci Methods*, 166(1):41–52, 2008.

[151] K. M. Stephan, M. H. Thaut, G. Wunderlich, W. Schicks, B. Tian, L. Tellmann, T. Schmitz, H. Herzog, G. C. McIntosh, R. J. Seitz, and V. Hömberg. Conscious and subconscious sensorimotor synchronization–prefrontal cortex and the influence of awareness. *NeuroImage*, 15(2):345–52, feb 2002.

[152] A. Stopczynski, C. Stahlhut, M. K. Petersen, J. E. Larsen, C. F. Jensen, M. G. Ivanova, T. S. Andersen, and L. K. Hansen. Smartphones as pocketable labs: visions for mobile brain imaging and neurofeedback. *International journal of psychophysiology : official journal of the International Organization of Psychophysiology*, 91(1):54–66, jan 2014.

[153] P. Sumner, P. Nachev, P. Morris, A. M. Peters, S. R. Jackson, C. Kennard, and M. Husain. Human medial frontal cortex mediates unconscious inhibition of voluntary action. *Neuron*, 54(5):697–711, jun 2007.

[154] C. Tallon-Baudry, O. Bertrand, C. Delpuech, and J. Permier. Oscillatory gamma-band (30-70 Hz) activity induced by a visual search task in humans. *The Journal of neuroscience : the official journal of the Society for Neuroscience*, 17(2):722–34, jan 1997.

[155] J. J. Tecce. Contingent negative variation (CNV) and psychological processes in man. *Psychological Bulletin*, 77(2):73–108, 1972.

[156] G. Thut, C.-A. Hauert, P. Viviani, S. Morand, L. Spinelli, O. Blanke, T. Landis, and C. Michel. Internally driven vs. externally cued movement selection: a study on the timing of brain activity. *Cognitive Brain Research*, 9(3):261–269, jun 2000.

[157] C. Toro, G. Deuschl, R. Thatcher, S. Sato, C. Kufta, and M. Hallett. Event-related desynchronization and movement-related cortical potentials on the ECoG and EEG. *Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section*, 93(5):380–389, oct 1994.

[158] A. B. L. Tort, R. Komorowski, H. Eichenbaum, and N. Kopell. Measuring Phase-Amplitude Coupling Between Neuronal Oscillations of Different Frequencies. *Journal of Neurophysiology*, 104(2):1195–1210, aug 2010.

[159] P. Tremblay, D. M. Shiller, and V. L. Gracco. On the time-course and frequency selectivity of the EEG for different modes of response selection: evidence from speech production and keyboard pressing. *Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology*, 119(1):88–99, jan 2008.

[160] F. van Ede, S. van Pelt, P. Fries, and E. Maris. Both ongoing alpha and visually induced gamma oscillations show reliable diversity in their across-site phase-relations. *Journal of neurophysiology*, 113(5):1556–63, mar 2015.

[161] S. Vanhatalo, J. Voipio, and K. Kaila. Full-band EEG (FbEEG): an emerging standard in electroencephalography. *Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology*, 116(1):1–8, jan 2005.

[162] B. Voloh, T. A. Valiante, S. Everling, and T. Womelsdorf. Theta-gamma coordination between anterior cingulate and prefrontal cortex indexes correct attention shifts. *Proceedings of the National Academy of Sciences of the United States of America*, 112(27):8457–62, jul 2015.

[163] B. Voytek. Shifts in gamma phase–amplitude coupling frequency from theta to alpha over posterior cortex during visual tasks. *Frontiers in Human Neuroscience*, 4, oct 2010.

[164] E. Walsh, S. Kühn, M. Brass, D. Wenke, and P. Haggard. EEG activations during intentional inhibition of voluntary action: an electrophysiological correlate of self-control? *Neuropsychologia*, 48(2):619–26, jan 2010.

[165] W. G. Walter. Slow potential waves in the human brain associated with expectancy, attention and decision. *Archiv fur Psychiatrie und Nervenkrankheiten Vereinigt mit Zeitschrift fur die Gesamte Neurologie und Psychiatrie*, 206(3):309–322, 1964.

[166] F. Waszak, E. Wascher, P. Keller, I. Koch, G. Aschersleben, D. a. Rosenbaum, and W. Prinz. Intention-based and stimulus-based mechanisms in action selection. *Experimental Brain Research*, 162(3):346–356, apr 2005.

[167] A. J. Watrous, L. Deuker, J. Fell, and N. Axmacher. Phase-amplitude coupling supports phase coding in human ECoG. *eLife*, 4:e07886, jan 2015.

[168] S. Yazawa, A. Ikeda, T. Kunieda, S. Ohara, T. Mima, T. Nagamine, W. Taki, J. Kimura, T. Hori, and H. Shibasaki. Human presupplementary motor area is active before voluntary movement: subdural recording of Bereitschaftspotential from medial frontal cortex. *Experimental Brain Research*, 131(2):165–177, mar 2000.

[169] Y. Zhang, Y. Chen, S. L. Bressler, and M. Ding. Response preparation and inhibition: the role of the cortical sensorimotor beta rhythm. *Neuroscience*, 156(1):238–46, sep 2008.

[170] Q. Zhao, L. Zhang, and A. Cichocki. EEG-based asynchronous BCI control of a car in 3D virtual reality environments. *Chinese Science Bulletin*, 54(1):78–87, jan 2009.