COMENIUS UNIVERSITY IN BRATISLAVA
FACULTY OF MATHEMATICS PHYSICS AND INFORMATICS

Behavioural and electrophysiological characteristics of cognitive control

Diploma thesis

2018 **Bc. Petra Šlahorová**

COMENIUS UNIVERSITY IN BRATISLAVA
FACULTY OF MATHEMATICS, PHYSICS, AND INFORMATICS

Behavioural and electrophysiological characteristics of cognitive control

Diploma thesis

Study programme:	Cognitive Science
Field of study:	2503 Cognitive Science
Supervising department:	Department of Applied Informatics
Supervisor:	RNDr. Barbora Cimrová, PhD.

Bratislava, 2018 **Bc. Petra Šlahorová**

Univerzita Komenského v Bratislave
Fakulta matematiky, fyziky a informatiky

77940139

ZADANIE ZÁVEREČNEJ PRÁCE

Meno a priezvisko študenta: Bc. Petra Šlahorová
Študijný program: kognitívna veda (Jednoodborové štúdium, magisterský II. st., denná forma)
Študijný odbor: kognitívna veda
Typ záverečnej práce: diplomová
Jazyk záverečnej práce: anglický
Sekundárny jazyk: slovenský

Názov: Behavioural and electrophysiological characteristics of cognitive control
Behaviorálne a elektrofyziologické charakteristiky kognitívnej kontroly

Cieľ: Urobte prehľad existujúcej literatúry ohľadom kognitívnej kontroly a AX-CPT. Analyzujte získané dáta a identifikujte elektrofyziologické charakteristiky pre proaktívnu a reaktívnu kognitívnu kontrolu. Navrhnite možné spôsoby aplikácie výsledkov pre výskum klinických skupín.

Literatúra:
Braver, T. S. (2012). The variable nature of cognitive control: a dual mechanisms framework. Trends in cognitive sciences, 16(2), 106-113.
Gonthier, C., Macnamara, B. N., Chow, M., Conway, A. R., & Braver, T. S. (2016). Inducing proactive control shifts in the AX-CPT. Frontiers in Psychology, 7.
Luck, S. J., & Kappenman, E. S. (Eds.). (2011). The Oxford handbook of event-related potential components. Oxford University Press.

Anotácia: Teória duálnych mechanizmov hovorí o existencie dvoch odlišných módov – proaktívnej kontrole ako 'včasnej selekcii' a reaktívnej kontrole ako 'neskorej korekcii'. Tento model je založený na jednoduchej paradigme s oneskorenou odpoveďou, známej ako test vytrvalého výkonu (AX-CPT). Rôzne vzorky vykazujú počas tejto úlohy rozdielny výkon, reakčný čas a elektrofyziologické charakteristiky. Čiže porovnanie dvoch zdravých a troch klinických skupín v spomínaných parametroch vzhľadom na ich vek a zdravotný stav, môže priniesť zaujímavé zistenia o povahe kognitívnej kontroly.

Vedúci: RNDr. Barbora Cimrová, PhD.
Katedra: FMFI.KAI - Katedra aplikovanej informatiky
Vedúci katedry: prof. Ing. Igor Farkaš, Dr.

Dátum zadania: 22.11.2016

Dátum schválenia: 06.12.2016

prof. Ing. Igor Farkaš, Dr.
garant študijného programu

.....
študent

.....
vedúci práce

Comenius University in Bratislava
Faculty of Mathematics, Physics and Informatics

77940139

THESIS ASSIGNMENT

Name and Surname:	Bc. Petra Šlahorová
Study programme:	Cognitive Science (Single degree study, master II. deg., full time form)
Field of Study:	Cognitive Science
Type of Thesis:	Diploma Thesis
Language of Thesis:	English
Secondary language:	Slovak

Title: Behavioural and electrophysiological characteristics of cognitive control

Aim: Review the existing literature on cognitive control and AX-CPT. Analyse obtained data and identify electrophysiological characteristics for proactive and reactive cognitive control. Suggest possible uses of the results in further research with clinical groups.

Literature:
Braver, T. S. (2012). The variable nature of cognitive control: a dual mechanisms framework. Trends in cognitive sciences, 16(2), 106-113.
Gonthier, C., Macnamara, B. N., Chow, M., Conway, A. R., & Braver, T. S. (2016). Inducing proactive control shifts in the AX-CPT. Frontiers in Psychology, 7.
Luck, S. J., & Kappenman, E. S. (Eds.). (2011). The Oxford handbook of event-related potential components. Oxford University Press.

Annotation: The theory of dual mechanisms (DCM) suggests the existence of two distinct modes – proactive control as an 'early selection' and reactive control as a 'late correction'. This framework was built on a simple delayed-response paradigm known as AX-Continuous Performance Task (AX-CPT). Various samples, of which many are untested, differ in performance, reaction times and electrophysiological characteristics in the task. Therefore, a comparison of two healthy and three clinical groups in those parameters in accordance with their age and clinical condition may bring an interesting insight into the nature of cognitive control.

Supervisor:	RNDr. Barbora Cimrová, PhD.
Department:	FMFI.KAI - Department of Applied Informatics
Head of department:	prof. Ing. Igor Farkaš, Dr.
Assigned:	22.11.2016
Approved:	06.12.2016

prof. Ing. Igor Farkaš, Dr.
Guarantor of Study Programme

Student

Supervisor

DECLARATION

I hereby declare that this thesis was written solely by myself and the work contained herein is my own except where explicitly stated otherwise by reference or acknowledgement. It has not been submitted for any other degree or professional qualification.

.....

ACKNOWLEDGEMENTS

I would like to thank all the experts from Laboratory for Clinical Neuroscience at the Department of Neurology, University Medical Centre in Ljubljana, Slovenia, namely Jure Bon, MD, PhD., Ruben Perellon Alfonso and Indre Pileckyte for introducing me to the topic, collection of the data, close cooperation, and valuable advice through the entire process. Furthermore, many thanks go to my supervisor RNDr. Barbora Cimrová, PhD. for the guidance, useful comments and remarks. Last but not least, I would like to express sincere gratitude to my partner, family and friends for support, patience and unfailing encouragement through the process of writing this thesis.

ABSTRAKT

ŠLAHOROVÁ, Petra. *Behaviorálne a elektrofyziologické charakteristiky kognitívnej kontroly* [diplomová práca]. Univerzita Komenského v Bratislave. Fakulta matematiky, fyziky a informatiky; Katedra aplikovanej informatiky. Školiteľ: RNDr. Barbora Cimrová, PhD. Bratislava: FMFI UK, 2018. 53s.

Táto práca skúmala behaviorálne a elektrofyziologické charakteristiky kognitívnej kontroly v súvislosti s postupujúcim vekom a klinickým stavom. Celkový počet 90 participantov pozostával z 2 zdravých (mladí a starí) a 3 klinických skupín (pacienti v počiatočnom štádiu Parkinsonovej choroby; v neskoršom štádiu s miernym kognitívnym poškodením; a pacienti s amnestickým kognitívnym poškodením s vysokým rizikom progresu do Alzheimerovej choroby). Všetci participanti vykonali AX-Continuous Performance Task (AX-Test vytrvalého výkonu, AX-CPT), ktorý sa zvyčajne využíva k odhaleniu deficitov v spracovaní/udržiavaní kontextu a prevedení odpovede. Výsledky poukázali na zachovanú presnosť, ale pomalší výkon v úlohe vo všetkých starších skupinách. Napriek tomu, že sme identifikovali v rôznych podmienkach viacero efektov viazaných na nápovedu, cieľový podnet a interval medzi nimi, nepodarilo sa nám zachytiť signifikantné rozdiely medzi väčšinou skupín. K podrobnejšiemu vysvetleniu súvisiacich mechanizmov bude potrebný ďalší výskum na väčších vzorkách, so zameraním aj na ERP latencie.

Kľúčové slová: AX-CPT, kognitívna kontrola, kognitívne deficity

ABSTRACT

ŠLAHOROVÁ, Petra. *Behavioural and electrophysiological characteristics of cognitive control* [Diploma Thesis]. Comenius University in Bratislava. Faculty of Mathematics, Physics, and Informatics; Department of Applied Informatics. Supervisor: RNDr. Barbora Cimrová, PhD. Bratislava: FMPH UK, 2018. 53 p.

This thesis examined behavioural and electrophysiological characteristics of cognitive control in relation to advancing age and clinical condition. The total number of 90 subjects consisted of 2 healthy (young and old) and three clinical groups (patients in early stage of Parkinson‘s disease; in later stage with mild cognitive impairment; and patients with amnestic mild cognitive impairment with high risk of progression to Alzheimer‘s disease). All subjects performed AX-Continuous Performance Task (AX-CPT) which is usually applied to reveal deficits in context processing/maintenance and response execution. The results indicated preserved accuracy but slower performance in the task in all older groups. Even though we identified a number of cue-, delay-, and target-related effects across conditions we lacked to capture significant differences among most of the groups. Therefore, to provide more detailed explanation of underlying mechanisms, further research on larger samples is needed, with focus also on ERP latencies.

Keywords: AX-CPT, cognitive control, cognitive impairment

CONTENT

INTRODUCTION

My personal motivation for this thesis originates from three main sources. The topic choice was highly influenced by my psychological background combined with the later transition into more technical field of cognitive science, and the final decision was made during my stay in Ljubljana, Slovenia thanks to the collaboration with the local Laboratory for Clinical Neuroscience which have luckily lasted until today.

The main concept examined in the present study is cognitive control in the context of aging and neurodegenerative changes. Undoubtedly, intelligent behaviour is crucially dependent on cognitive processes and the ability to control their course. However, a notable decline in cognitive performance is observed throughout the life. Coupled with that, the rising standard of living leads to population aging interconnected with the higher prevalence of neurodegenerative diseases. Even though the research tradition in this field have exceeded more than three generations of experts, the exact characteristics of the most substantial human asset are still poorly understood. New studies hypothesise that subtle cognitive changes may markedly precede an emergence of actual symptoms. Therefore, the knowledge of underlying control mechanisms is of special relevance for early diagnostics and prevention of cognitive deficits as it immediately concerns more and more people.

This thesis provides a thorough theoretical basis for concept of cognitive control from interdisciplinary perspective starting with (1) an overview of existing theories and functional distinction, then proceeds with (2) related neural correlates with emphasis on event-related potentials, and closes the theoretical part with (3) a summary of state of the art regarding possible causes for cognitive control variability, in healthy and clinical populations, respectively.

In order to address the research problem, we combine a basic cognitive task with tools used in neuroscience with the aim to inspect behavioural and neurophysiological characteristics of cognitive control and compare them across multiple task-conditions, as well as, amongst healthy and clinical samples. We hope that it will add to a current knowledge and unveil future directions for unresolved issues.

A bigger picture through the lens of interdisciplinarity

As noted earlier, the topic of this thesis connects various fields and methods, namely cognitive psychology, neuroscience, descriptive and inferential statistics, basic programming and clinical practise. Interdisciplinarity is an inevitable aspect of this work which is even multiplied given the fact that it is being elaborated under the international Cognitive Science programme (MEi:CogSci).

Cognitive science is a scientific field which combines methodology and knowledge from psychology, philosophy, linguistics, education, neurobiology, and computer science, studying the structure and function of human mind. It attempts to promote cross-disciplinary cooperation to integrate existing concepts, methods, and data; and enable an emergence of thoughts through constructive expert discussion. Compared to isolated knowledge, we believe that such a coherent approach, not only in research area but also in medical practise, technological fields, or even everyday life may be the right way to a better, open-minded society.

1 COGNITIVE CONTROL

Automatic versus cognitive processes

The vast majority of processes that occur in the brain are automatic, performed without sustained attention, voluntary control or even without conscious awareness. Breathing, heartbeat, even speaking and listening have traditionally been viewed as automatic actions (Clark, 1999). For example, once someone learns to read fluently it is almost impossible to look at the written text and not to see the meaning. Those processes are more effective and can be carried out in parallel as distinct from cognitive processes execution of which is constrained by limited capacity of resources. Strangely enough, neither the nature of the resource, nor the reason for the limitation has yet been identified (Carter, Kofler, Forster, & McCullough, 2015). Despite that the literature provided numerous suggestions of possible causes for the limitation, such as: metabolic (Kennedy and Scholey, 2000), structural (Egner, 2017), functional/computational (Botvinick, Cohen, 2014), or temporal (Gazzaley and Rosen, 2016), none can fully explain the issue.

Another major concern regarding controlled versus automatic processing is the relationship between those two. The first distinction treated the two as a dichotomy, separate mechanisms, which was soon criticised (Kahneman and Treisman, 1984). Posner and Snyder and Davidson (1980) provided evidence using a Stroop task that processes considered automatic may sometimes rely on attention and control, hence they seem to depend on the context in which they are executed. On the other hand, many controlled processes may become faster, less effortful and in the end automatic with practice if the association between stimuli and responses remains fixed (Schneider and Shiffrin, 1977).

Taken together, the current approach interprets controlled and automatic processes as the opposite ends of a single continuum, and the exact position on it, given a particular task, is a function of both learning and the context in which it takes place. The advantages of automatic processes like high speed of execution, effortlessness or resistance to interference are counterbalanced (despite the striking constraints) with notable flexibility of cognitive processes in terms of diverse behaviours it supports (Egner, 2017).

Origins of the concept and previous theories.

Consequently, more difficult situations when automatic responses might lead to an error, require cognitive control (Brown, 2013). Cognitive control is a set of processes that plays an important role in higher cognitive functioning, however, it is difficult to define. Admittedly, it is one of the most distinguishing characteristics of human behaviour. The simplest definition describes it as the ability to flexibly adapt behaviour to demands of specific task, favouring the task-relevant goal-oriented information over other competing ones (Botvinick et al., 2001).

The concept has started to form in 1950s when Donald Broadbent (1953) hypothesized about the existence of selective attention. The term "cognitive control" was put in use later, in 1975 by psychologist Michael Posner and gained a central role in cognitive psychology soon after. But still, after more than 65 years of progress the exact mechanisms by which it arises are unknown. Throughout the time, a number of theoretical models and theories has been proposed (see Atkinson, Shiffrin, 1968; Norman, Shallice, 1986; Posner, Snyder, Solso, 2004) to characterise the function of cognitive control.

Early symbolic models, which were based on production system architectures, such as the Adaptive Character of Thought (ACT-R) model (Anderson, 1983) inspired by the work of Newell assume that the control is centralised over the direct flow of information from sensory input, through memory, to motor output. Those unitary models rely on representations stored in declarative memory and suppose that complex cognition originates from interaction of procedural and declarative memory (Anderson, 1983).

Besides that, Alan Baddeley and Graham Hitch (1974) argued that there must be some supervisory component which manipulates the information stored in short-term memory rather than simple passive retention of information. Based on that they created a working memory model with central executive who drives the system as its commander. It laid a ground for a tremendous research branch of "executive functioning". In fact, it was a very fuzzy term since many authors added various components to this concept, ranging from one to many. Executive functioning and cognitive control are treated as synonyms nowadays. The basic cognitive processes may still differ from publication to publication and consist of components, or rather functions such as attentional control, task switching, monitoring and updating of representations in working memory, inhibitory control of dominant responses and so on (Goldstein, Naglieri, 2014).

Later attempts to simulate the behaviour of humans or animals aimed on neurobiologically plausible mechanisms and led to striking rise of neural networks models (e.g. Cohen, Servan-Schreiber, and McClelland, 1992). The leading theory in this field, the guided activation theory (GAT), proposed that representations are activated and manipulated in the prefrontal cortex (PFC) from where control is exerted and guided along other pathways. The models built on GAT repeatedly confirmed this fundamental claim. They usually implement tasks such as the Wisconsin Card Sorting Test or the Stroop task which are sensitive to PFC damage (Miller, Cohen, 2001).

Alternative approach explores cognitive control in terms of cognitive cost during the performance of a task. These theories are known as economic or "cost/benefit" (Christie, Schrater, 2015). Solomon (1948) proposed that individuals follow a rule of least mental effort when achieving a goal to minimize the costs stemming from extensive utilization of attention and working memory. Some authors (Kool at al., 2010) consider it a fundamental principle of cognition.

A similar view or rather extension of the cognitive cost approach, is elaborated in normative theory (also referred to as rational analysis or the ideal observer method) (Deneve, Latham, Pouget, 1991; Tanner, Swets, 1954), which seeks to identify the optimal computation for a function of interest. This notion pursues to find an "objective function" able to explain which tasks or goals should be followed at a given time or how the task should be accomplished optimally with minimal costs. The specific branch of normative theory which studies satisfactory decision-making under constraints is called bounded rationality (Simon, 1955).

To sum it up, majority of current theories agree that the key mechanisms underlying the cognitive control are (1) activation of representations, (2) inhibition of irrelevant stimuli, and (3) implementation of relevant behaviour to achieve a desired goal.

Apart from all the previously mentioned theories, we decided to choose the one introduced in the following subchapter.

1.1 Dual mechanisms of cognitive control

The most widely used theory nowadays regarding utilization of cognitive control seems to be Braver's theory of dual mechanisms (DMC) (Braver, Gray, Burgess, 2007). It was initially proposed to study cognitive aging deficits and later elaborated for many other research areas. The central hypothesis of this framework suggests the existence of two distinctly operating modes – proactive control as a form of 'early selection' and reactive control as 'late correction' (Braver, 2012).

Proactive control

The proactive control is a prospective mode which helps to prepare the cognitive system to respond in a particular way. It is an active, sustained maintenance of a goal-relevant information, before the interference occurs. This strategy is most effective when anticipated events are frequent, with short retention intervals. The main advantage is a continual adjustment of plans and behaviours and the predictive use of context available to influence processing (Botvinick et al., 2001). However, attention span and working memory capacity are limited, so proactive control becomes impractical when the delay of interference is too long, due to continual goal maintenance which makes it resource consuming.

Reactive control

In contrast, the reactive control is engaged only if needed, triggered by specific event, by activation of long-term memory pathways or through episodic information retrieval. It is a bottom-up strategy, goal representations are activated or retrieved when interference is detected. Therefore, it is more computationally efficient, without high demands on working memory or attention, although the disadvantage is the repeated reactivation of the goal (Braver, 2012).

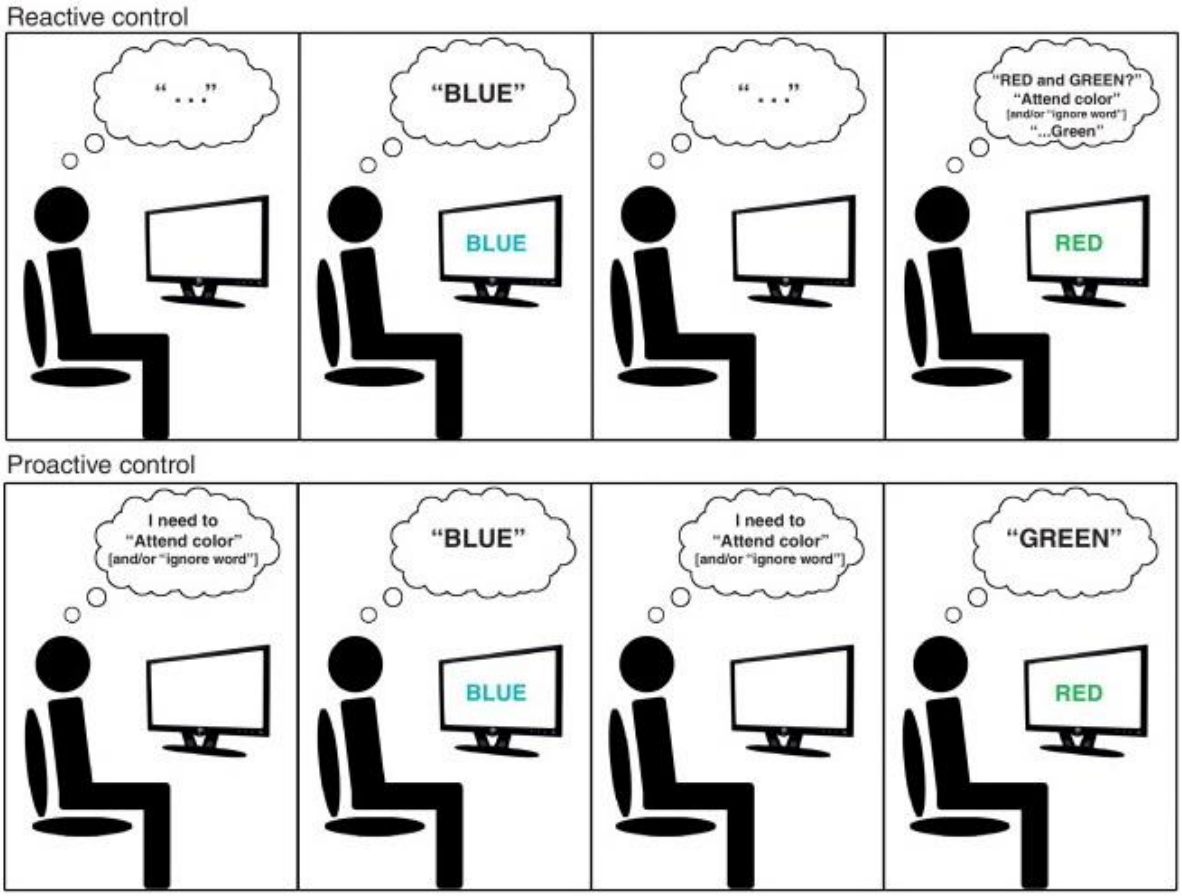

Figure 1: *Illustration of use of proactive versus reactive control strategy in the Stroop task. Reactive control reactivates the goal when target stimuli is presented while proactive control maintains the goal information throughout the entire task (Braver, 2012).*

1.2 AX-CPT paradigm

Braver with colleagues (2007) built his theory on a simple delayed-response paradigm known as the AX-Continuous Performance Task (shortly AX-CPT) which is widely used in cognitive control studies nowadays. Besides examination of particular cognitive control strategy, it has many other research applications such as study of goal maintenance, context processing, sustained attention or limitations of working memory (Marcora, Staiano, Manning, 2009).

Origins of the task date back in 1950's when Rosvold with colleagues (1956) came up with a simple, yet sophisticated tool to measure behavioural disturbances and decrements in information processing. In the AX-CPT various letters are alternately presented on a computer screen. Subjects are instructed to respond by pressing a target-button whenever

the letter A (a cue) is followed by the letter X (a probe) and non-target button or refrain from action otherwise. A combination of four types of trials might occur:

- AX trial, which was previously mentioned and is considered a target trial;
- BX trial, when any letter other than A is followed by X;
- AY trial, when any letter other than X succeeds the letter A;
- BY trial, when a letter other than X succeeds a letter other than Y (Barch, Braver, 2005).

Incorrect responses that occur in AX and AY trials are usually marked as errors due to proactive control, while BX and BY trials evoke reactive control errors. Trials starting with A-cue carry contextual information that produces expectancies necessary for proactive control engagement, however with negative effect on performance in AY trials. On the other hand, BX trials trigger undesired tendency to respond to X which requires to be overridden by reactive control, since this strategy is activated only in response to a critical stimulus (Cooper et al., 2017).

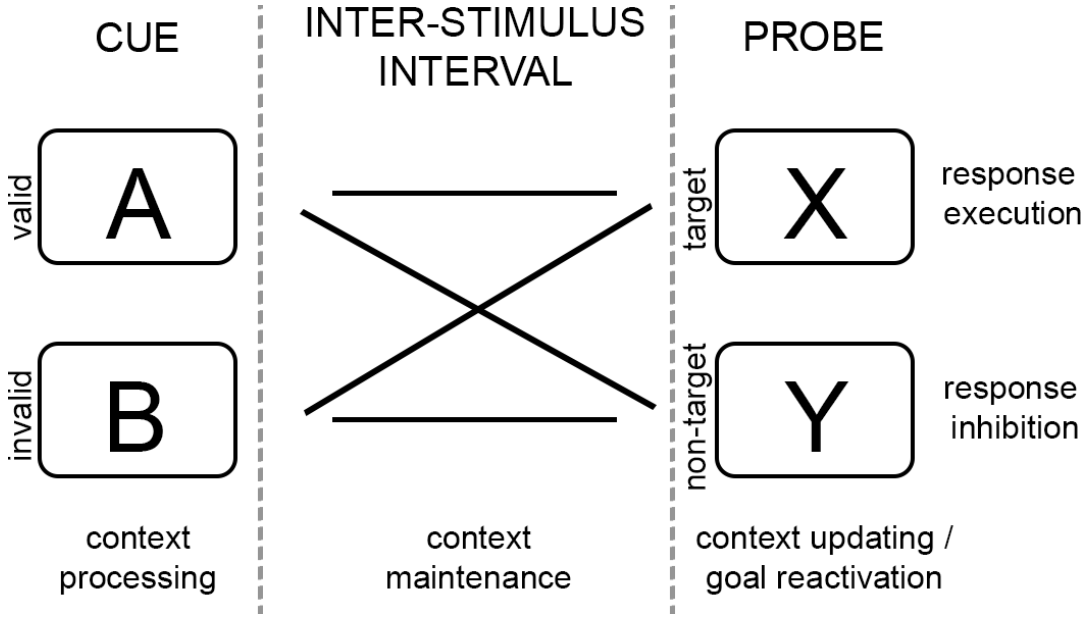

Figure 2: *Our illustration of AX-CPT scheme summarising all fundamental information about the task.*

Many variations of the task have been provided, such as modifications of inter-stimulus interval length, trial type proportions, including strategy training or no-go trials. Those manipulations can elicit intra-individual changes or reveal cognitive deficits of specific groups (Braver, 2012). The third chapter is dedicated to a more detailed description of the outlined cognitive control variability.

2 NEURAL CORRELATES OF COGNITIVE CONTROL

Behavioural measures may bring an important asset while studying cognition, nonetheless, they merely reflect the overt outcome and more covert information processing stays hidden. That is where searching for neural correlates of cognition and actual brain processes employed during task performance comes to play.

2.1 Brain areas underlying cognitive control

Substantial evidence has supported the notion that the prefrontal cortex (PFC), with its specialized processing capabilities and extensive connectivity with other brain regions, represents a key structure for both modes of cognitive control. It is responsible for active maintenance of contexts, rules, goals, even in the case of distractions and allows to bias processing in other neural systems in accordance with the desired goal (Botvinick, Braver, 2015). Furthermore, PFC neurons remain active not only during a cue presentation but also afterwards until the objective is fulfilled. In comparison, there are other brain regions capable of delayed response execution, although these are much more prone to distractions (Cole, Braver, Meiran, 2017).

One of the most characteristic functions of PFC is its plasticity and flexibility. Besides manipulation of existing representations, PFC constantly adds new ones and updates them. Moreover, when particular feature is important for accomplishment of some task, the sensitivity of neurons towards this feature may increase, and vice versa. On the other hand, damage of PFC tissue is connected to decline in behavioural flexibility (Braver et al., 2009).

Prefrontal area is often divided into three main sub-regions, each with its specific function: (1) the *lateral* consisting of dorsolateral (DLPFC) and ventrolateral part (VLPFC), (2) the *medial* consisting of anterior cingulate cortex (ACC) and the medial prefrontal cortex (MPFC), and (3) the *orbitofrontal* (OFC) further divided into medial, ventral, lateral, and frontopolar sections (Kropotov, 2010). For illustration see Figure 3.

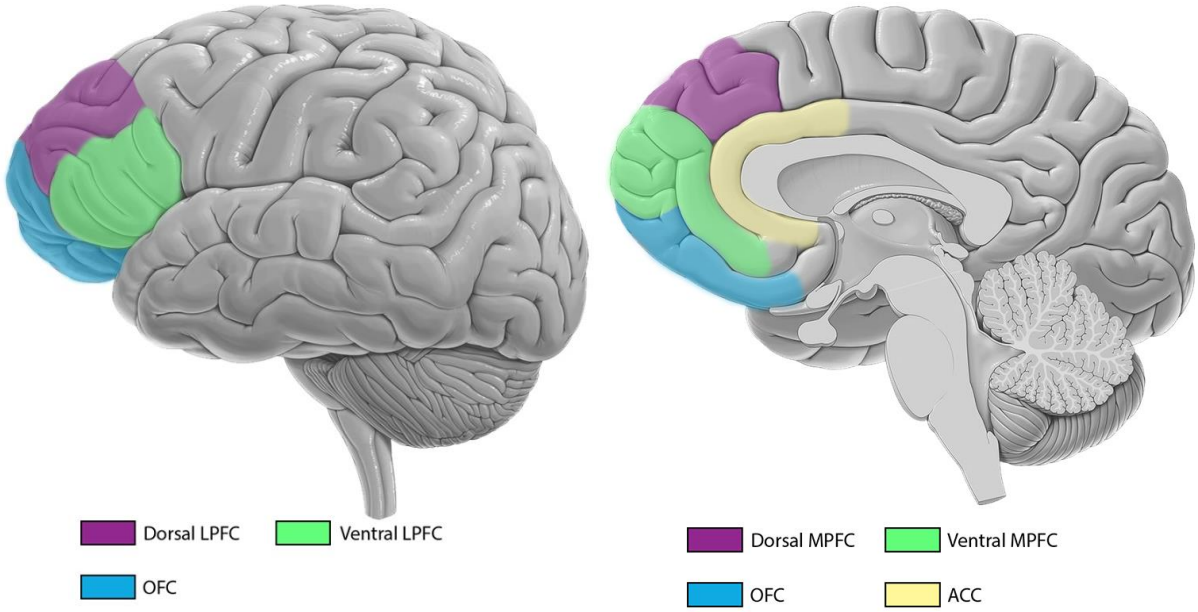

Figure 3: *Lateral (left image) and medial view (right image) of the brain areas associated with cognitive control (Kenhub, 2018). LPFC = lateral prefrontal cortex, MFPC = medial prefrontal cortex, OFC = orbitofrontal cortex, ACC = anterior cingulate cortex.*

Scientifically described temporal dynamics and localization of brain activity was shown to be in accordance with DMC framework. Increased activity in lateral region, reflecting goal maintenance, was confirmed to be associated with sustained anticipation and preparation for upcoming events and with proactive control. The study of motivational characteristics of cognitive control (Savine, Braver, 2010) pointed out that activity in left DLPFC is increased on trials demanding high accuracy and speed relative to low-incentive trials.

On the contrary, the activation profile of reactive control is slightly different, and it encompasses also wider frontoparietal network accompanied with other brain regions. Reactive control is characterised by a short burst of activity in lateral PFC, which manifests reactivation of goal due to the detection of interference (Braver et al., 2009). The MFC area, and especially ACC, supplements the function of lateral PFC. ACC is involved in performance monitoring and detection of conflicting information processing and serves as a bottom-up regulator of attention. Thus, the role of ACC resides in comparing actual performance with set goals in order to signal lateral PFC to optimize behaviour (Ridderinkhof et al., 2004), and its activity is greater during high-conflicting trials (Botvinick et al., 1999). Apart from MFC, associative connections prove to be an alternative

source of goal reactivation that directs the information through posterior cortical areas (Braver et al., 2009).

Neuroimaging studies have reliably confirmed the association between prefrontal areas and cognitive control mechanisms. Furthermore, recent findings have shown that control is implemented by a larger set of distributed brain regions. Coupled with that, prior theories are moving towards a broader view that suggests important roles of lateral and medial frontal, and parietal regions in exerting control.

Many fMRI studies tried to explain the frontal – parietal relationship and underlying mechanisms. To give an example, Dosenbach with colleagues (2008) suggested a dual-networks architecture of top down control consisting of (1) fronto-parietal and (2) cingulo-opercular network.

The cluster analysis of the fMRI data indicated that these systems run distinct types of sustained activity – the first system is adaptive, it initiates and adjusts control, while the second is stable, maintaining sustained attention over the entire task (Dosenbach et al., 2008) (see Figure 4). We believe that this model describes the same control modes as DMS framework and extends previous knowledge of neural correlates of cognitive control, even though the authors use different terminology for similar processes.

2.2 EEG studies and ERP components

EEG studies examining cognitive control mainly focus on two topics: neural oscillations and event-related potentials (ERPs). Regarding neural oscillations, AX-CPT seems to modulate activity in alpha (lower 8-10 Hz, upper 10-13 Hz) and beta (13-30 Hz) bands, while gamma (>30 Hz) band is not affected. Increases in alpha are associated with active suppression of irrelevant information when attention or preparation is required. Beta is the characteristic frequency band of the motor cortex and its power decreases prior to movement onset (Cooper et al., 2015). Bickel et al. (2012) found broad parieto-occipital event-related desynchronization (ERD) in the alpha band throughout the cue evaluation period and modulation of beta power in fronto-central regions reflecting motor preparation. Cooper with colleagues (2015) confirmed that reactive control is associated with fronto-parietal theta connectivity. The proactive control is also associated with theta band oscillatory synchronization but in a different fronto-parietal network.

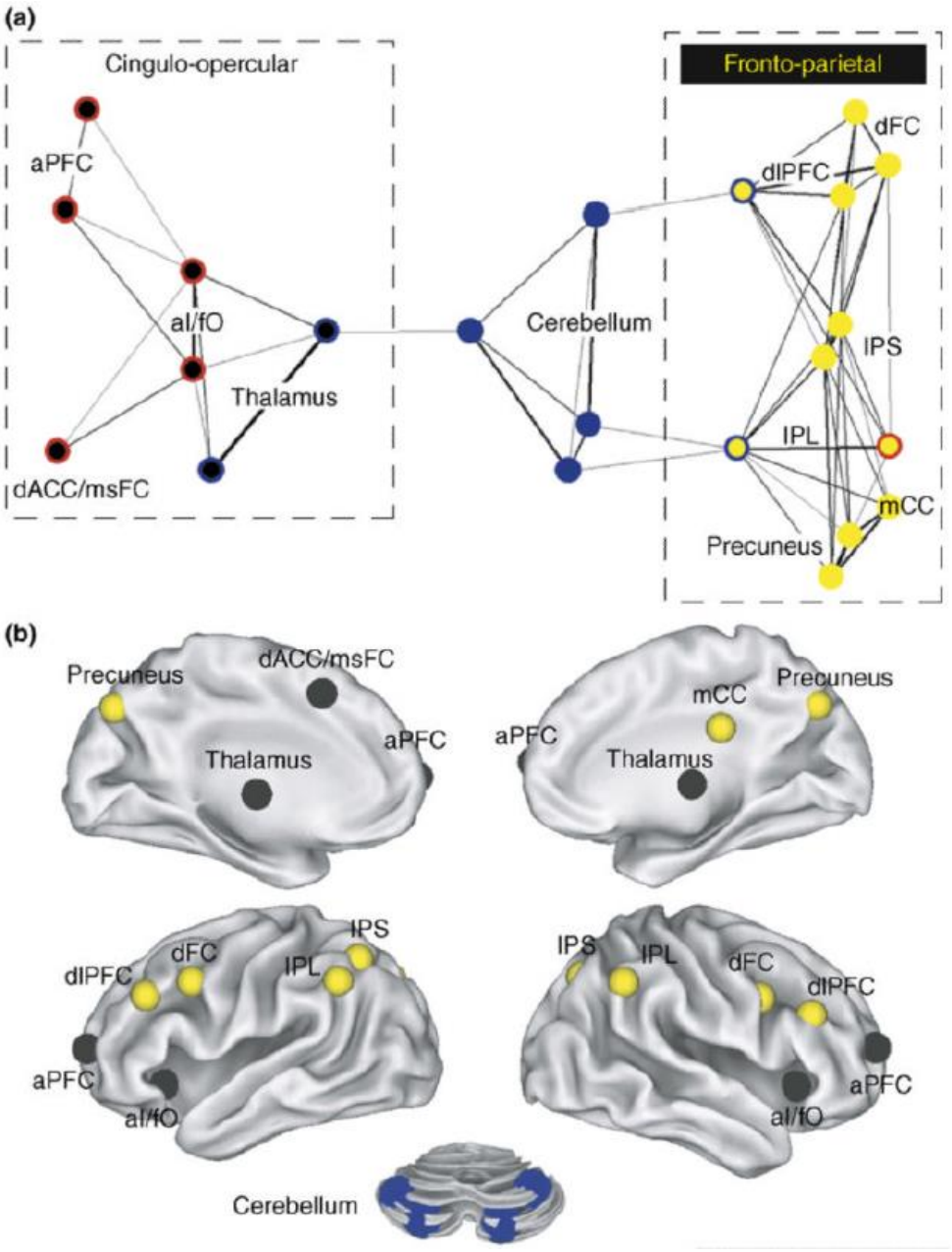

Figure 4: *Dual-network architecture according to Dosenbach et al. (2008). (a) Connection space of control brain regions, those who share more connections are closer, connections with thicker lines are stronger. The colour of the node indicates the affiliation to specific network (black represents cingulo-opercular; blue is cerebellar; and yellow is fronto-parietal). The outer colour manifests the predominant type of control signal (red is context-maintenance, blue is error-related, and yellow is cue-related). (b) Control networks shown on a surface of the human brain (gray nodes represent cingulo-operculat network, yellow fronto-parietal, and blue colour stands for cerebellar regions).*

Event-related potentials (ERPs) are of higher relevance for current study as their analysis provides a deeper understanding primarily of preparatory and inhibitory processes occurring during the cue – probe interval and after target onset (Dias, Foxe, Javitt, 2003). Previous research revealed several related components which are discussed in the following section.

The amplitude of N2 is believed to be associated with conflict processing in cognitive control and demonstrates the competition between task-relevant and task-irrelevant inputs. The neural generator of N2 likely lies in the medial PFC, more specifically in the anterior cingulate cortex (ACC) (Qi et al., 2014; Schmid et al., 2015).

Similarly, the part of studies concentrates on P3 component which reflects the discrimination between stimuli. Gratton (et al., 1990) observed that the amplitude of the parietal P3 elicited by the cue is proportional to the amount of obtained information about upcoming stimulus. Similar increase in P3 amplitude is apparent after cue presentation during AX-CPT and it is hypothesised to reflect attention.

Further, the contingent negative variation (CNV), which is considered the firstly discovered cognitive ERP component (Walter et al., 1964), can be observed during the period between cue and probe and it is typically measured at the fronto-parietal electrode sites. When this phase is lengthened to several seconds, division into two components is visible: (1) so called O-wave that is an early negative wave representing fixation on the cue and (2) subsequent E-wave reflecting response preparation or sometimes termed as readiness potential/Bereitschaftpotential (Kononowicz, Penney, 2016).

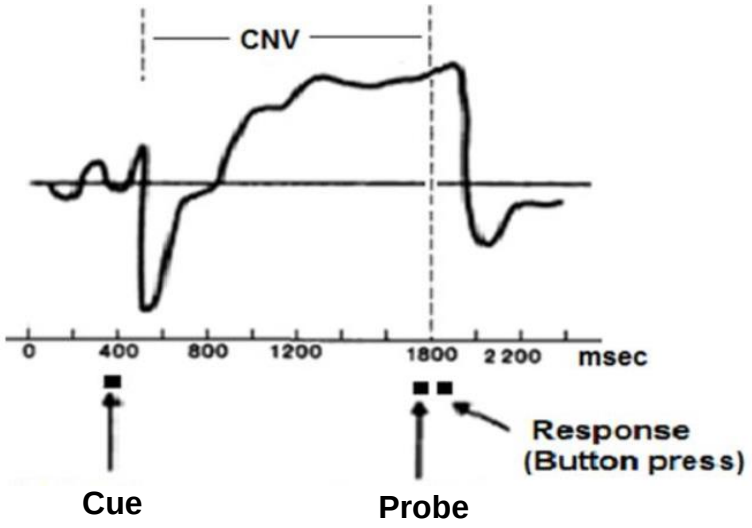

Figure 5: *A typical course of CNV with O-wave negativity at the beginning and E-wave prior to probe (Walter et al., 1964).*

2.3 Dopaminergic system

If we dig deeper into electro-chemical substrates of cognitive control, PFC activity is closely related to dopaminergic (DA) system. The system is known for neuromodulation of the synaptic plasticity at the cellular level from where it can contribute to influencing global network structure (Luna et al., 2015).

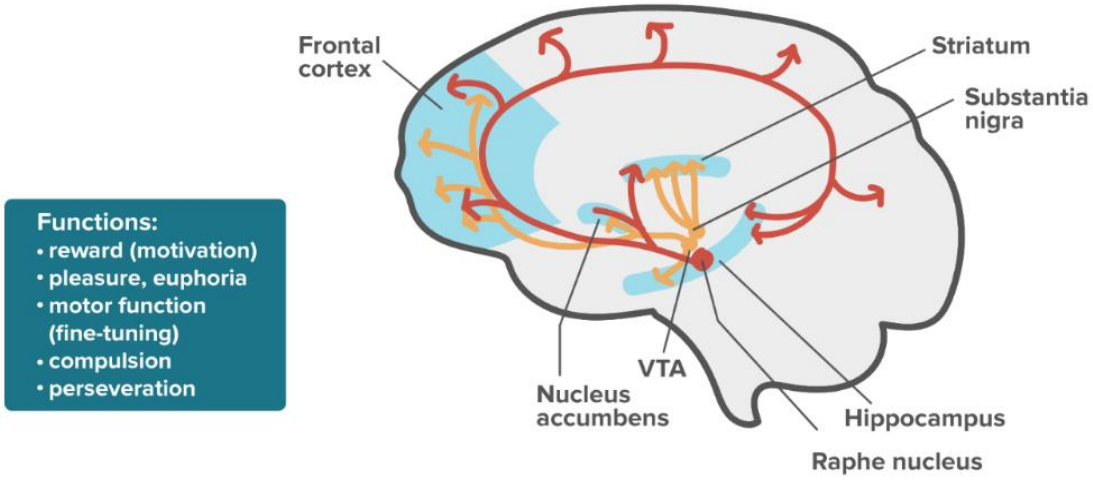

Figure 6: *Dopamine pathways starting in brain stem and branching toward PFC (Dopamine pathways, n.d.).*

Some authors hypothesise (e.g. Cools, D'Esposito, 2011) that presentation of context information is linked to a phasic change in DA system, whereas reactive control is not accompanied by any gating signal mediated by DA system. The latter results only in transient activation of PFC and requires strong enough stimuli to trigger spreading activation (Braver et al., 2009).

3 VARIABILITY OF COGNITIVE CONTROL

A central assumption of the DMC framework is that situational factors can lead to a change in cognitive control strategy (Braver, 2012). Many studies had tested this hypothesis (e.g. Gonthier et al., 2016) and showed that experimental manipulations can have strong influences on the deployment of cognitive control strategy. Examples of these factors are arousal level, time of preparation, motivation, expected working memory load and so on (Braver, Barch, Cohen, 2000).

However, participants do not differ only intra-individually. There are numerous factors such as working memory capacity (Braver, Gray, Burgess, 2007), fluid intelligence (Burgess, Braver, 2010), several personality and affect-related traits that seem to cause inter-individual variability (Chiew, Braver, 2014).

In addition, the use of proactive vs. reactive control varies amongst different developmental populations and between healthy and clinical groups. Previous experiments revealed that these control mode differences result in both, distinct brain activation profiles and behavioural performance characteristics (Conway, Jarrold, 2008).

In the text below, we provide an overview of latest experimental findings and a categorization of various factors affecting cognitive control fitted into Braver's (2012) three-level distinction of cognitive control variability framework. As there are numerous factors influencing variability of cognitive control, we focus particularly on those related to our research aim, such as age-related variability, differences due to task manipulations and deficits in people with different stages of Alzheimer's and Parkinson's disease-related pathology.

3.1 Intra-individual variability

Intrinsic variability may be a core component when it comes to explanation of the temporal dynamics of control processes (Braver, 2012). Even similar tasks might, due to subtle changes, result in a different choice of cognitive control strategy and therefore in significantly different outcomes. Such differences are usually induced by using various task manipulations, but performance can vary even without any task intervention due to circadian rhythms and choice of multiple daytime measurements (Anderson et al., 2014).

Strategy training and No-Go trials

Gonthier with his colleagues (2016) demonstrated in three slightly different experiments that young healthy individuals can be systematically biased toward and away from utilization of proactive control, specifically it can be increased via strategy training and decreased by including no-go trials. The *strategy training* used in a study was a special preparation consisting of 60 practice trials where participants were asked to mentally prepare for a target response whenever they saw an A cue. A message "Remember to use the strategy" appeared on a computer screen in every inter-trial interval. It was used in the first experiment and resulted in better performance on AX trials, shorter reaction times on BX trials and decreased performance on AY trials compared to a baseline condition. It is worth noting that the training is not applicable to participants with a high baseline level of proactive control as they show no significant changes.

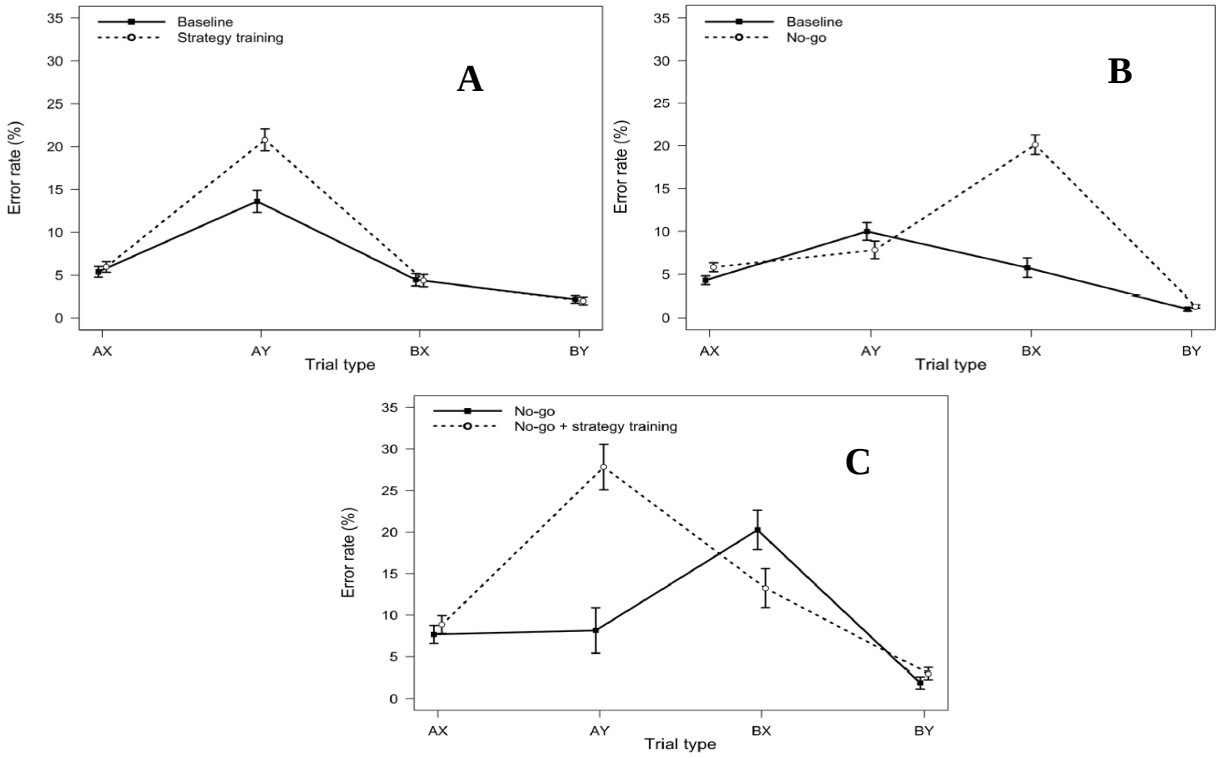

Figure 7: *Average error rates in the AX-CPT from the set of experiments conducted by Gonthier et al. (2016). (A) baseline condition and strategy training, (B) baseline condition and no-go, (C) no-go and combination of no-go + strategy training.*

On the contrary, *no-go trials*, used in the second experiment in addition to four usual trial types, served as a method to reduce proactive control. Rather than a letter, the probe was a digit and participants were required not to respond at all whenever a letter was

followed by a digit, while they should respond also to AY, BX, BY trials with a non-target button. It resulted in worse BX performance and improved AY performance. The third experiment was a combination of both methods and extended the results of previous two by lowering the interference and thus the error rate on BX trials (Gonthier at al., 2016). Graphs from the original study are displayed below (Figure 7).

Task proportions

Apart from trial modification, the frequency of occurrence of a certain trial type can also dramatically change cognitive control strategy. The most widely used ratio of AX-CPT is the AX-70, which represents 70% of AX trials and 10% of each other trial type. Empirical data as well as computational stimulations suggested that proactive strategy produces optimal performance under this task condition (Braver, Gray, Burgess, 2007). In this way, A-cue is highly predictive of a response to a probe, therefore the proportions of AX and AY trials matter and change the entire context. In addition, AX-10 version (also referred as BX-70) seems to be characterised with equally predictive power of A-cue, although higher predictive strength of B-cue towards non-target response. Alternatively, AX-40 version, with its equal probability of AX and AY trial occurrence, induces non-consistent response strategy and a need to switch control modes during the entire task (Redick, Engle, 2011).

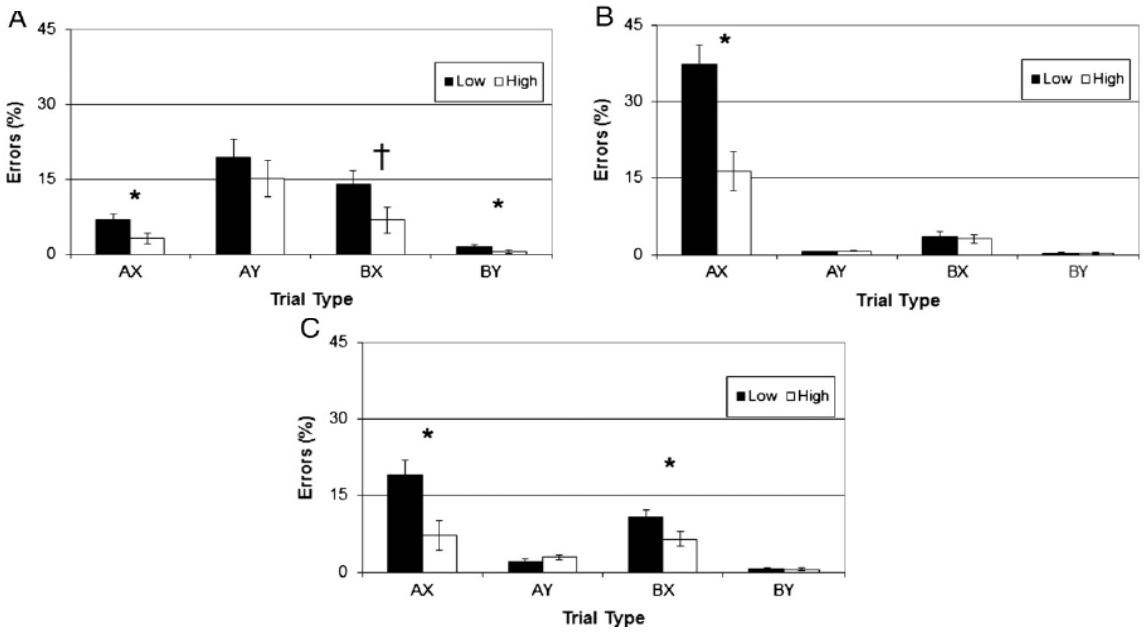

Figure 8: *Average error rates according to a version of the AX-CPT: (A) AX-70, (B) BX-70, and (C) AX-40. There are two bars for each trial type, each representing different sample – black stands for individuals with low WMC and white for individuals with high WMC (Redick, 2014).*

Redick (2014) employed all those three versions of the task in his study, even though the central issue addressed here was to examine anticipation and response preparation in high- and low-working memory capacity (WMC) individuals. As illustrated in Table 8, the performance of 2 samples significantly differed in each task condition.

In addition, Dias, Foxe and Javitt (2003) conducted a study in which participants performed three different versions of the AX-CPT (AX-70, AY-70, and BX-70). The author inspected specific ERP compounds in different time windows: cue-related positivity known as P300, delay-related negativity similar to CNV, and target-related positivity, again with characteristics of P300. The results indicated that activity after presentation of A-cue was significantly higher in BX-70 than in other versions of the task, suggesting high expectancy of a response. On the contrary, the highest potentials after B-cue presentation were under AX-70 condition (Fig. x). Likewise, activity during delay and after target presentation differed across versions and conditions (Dias, Foxe, Javitt, 2003). Another study (Adrover-Roig, Barceló, 2010) showed that inter-individual differences are more indicative in context-processing and response preparation related to cue presentation and delay, while task execution is more influenced by age and between-subject differences.

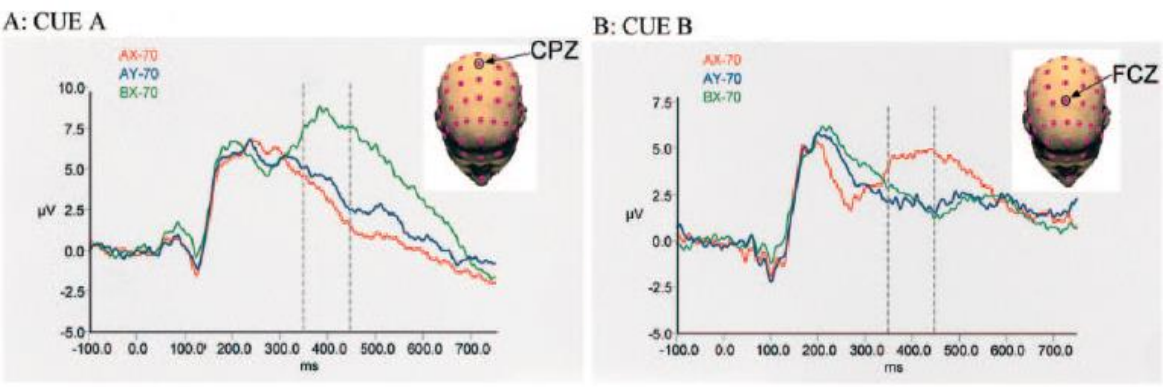

Figure 9: *Comparison of the potentials (A) after A-cue presentation and (B) B-cue presentation amongst AX-70 (70% of AX trials, 10% of AY, BX, BY, respectively), AY-70 (70% of AY trials), and BX-70 version (70% of BX trials). The area bounded by the broken lines represents time window 325-425 ms after cue presentation (Dias, Foxe, Javitt, 2003).*

Inter-stimulus interval

A number of studies demonstrated (e.g. Braver et al. 2005) that manipulation with the delay length between the cue and probe may impact AX and BX performance, especially in clinical groups. It enables examination of the ability to maintain context information over a certain time period as well as the ability to update context. Redick and Engle (2011)

observed impairments in AX-CPT performance in group of low-WMC individuals compared to high-WMC individuals which confirmed that various delay lengths put different demands on working memory.

3.2 Inter-individual variability

Factors involved in inter-individual variability are, for instance, working memory capacity, fluid intelligence but also many personality factors and affect-related traits like reward or threat sensitivity, and anxiety level which are usually perceived as "noncognitive" (Braver, 2012).

As was suggested in previous subchapter, there are considerable individual differences in working memory capacity indicating that individuals with high WMC are more prone to use proactive control strategy than individuals with low WMC. Moreover, they make significantly less AX errors (see Figure 8) which reflects their higher efficacy of goal maintenance (Redick, 2014).

Fluid intelligence (gF) is thought to be positively correlated with cognitive control as it employs similar areas of the PFC. The relationship is stronger under conditions of high interference and individuals with above average gF show higher delay-related activation in PFC (Gray, Chabris, Braver, 2003).

Many prior studies demonstrated complex interactions between affect and cognitive control (e.g. Schmid et al., 2015). To be specific, anxiety is accompanied with a reduction in active goal maintenance caused by extensive thinking about potential threats and focus on task-unrelated worries and rumination (Fales et al., 2008). Study of Shmid and colleagues (2015) uncovered that individuals with higher social anxiety use reactive control processes more than low social anxiety subjects.

3.3 Between-group variability

Variability of cognitive control is observed across different populations. In general, young healthy adults serve as a control group and demonstrate higher tendency towards proactive control compared to other developmental samples or clinical patients (Braver, 2012). Recent findings suggested that there might be also sex differences, particularly in adolescent age, however the exact nature of those contrasts is still unknown (Vijayakumar et al., 2014).

Age-related variability

The proportions to which individuals engage proactive or reactive control change throughout the life. Cognitive control abilities are closely connected to the structural maturation of underlying brain regions in young children and adolescents (Vijayakumar et al., 2014).

Tendency to use proactive control in group of young children (Luna et al., 2010) or older adults (Van Gerven, Hurks, Adam, 2017) is reduced compared to young adults (Kopp, 2014). In spite of the fact that proactive control posits age-related decline (suggested by significantly slower response time), the largely untested prediction is that reactive control may be spared with age as the number of errors in BX trials stays relatively low (Bugg, 2014). A deeper understanding of the process was provided by fMRI studies showing more detailed interactions between groups (Carter et al., 1998). Both, an under-recruitment as well as over-recruitment of certain brain areas can be seen in group of older adults in order to compensate for aging deficits. Specifically, Paxton et al. (2008) found a reduced delay-related activation in the dorsolateral PFC in group of old adults (66-83 years) compared to young adults (aged 18-31) across two delay conditions (Figure 10).

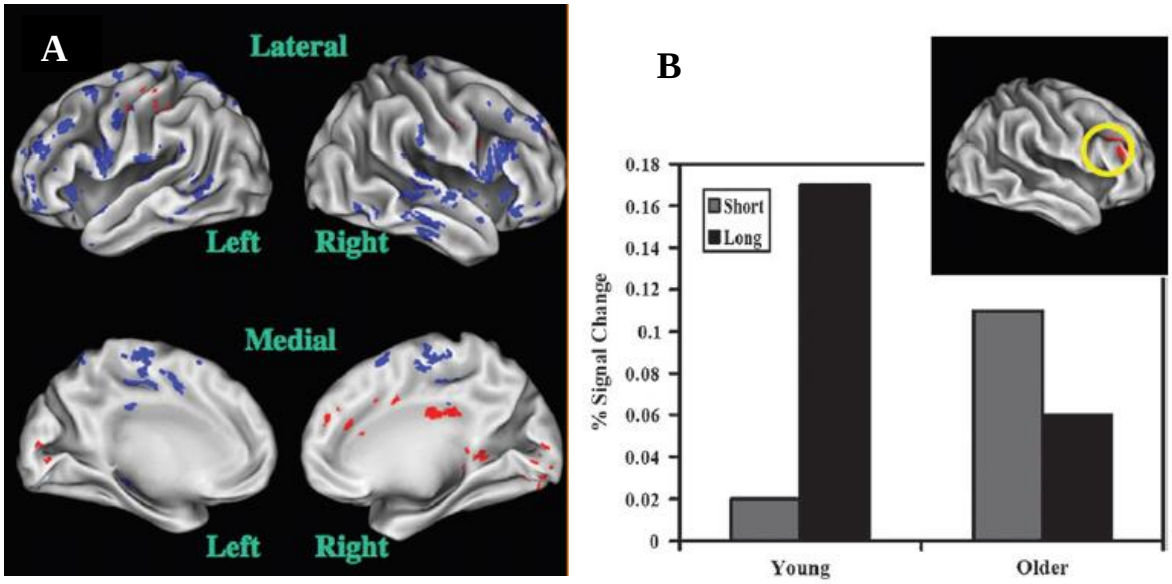

Figure 10: *(A) Brain areas showing age differences in activation during task. Red colour reflects regions where young group demonstrated greater blood oxygen level-dependent (BOLD) response, while regions with greater BOLD response in older group as compared with younger adults are blue. (B) Signal change in right DLPFC in short (1s) and long delay (5s) (Paxton et al., 2008).*

Variability in clinical groups

Studies conducted on a variety of clinical populations, such us people suffering from depression (Vanderhasselt et al., 2014), ADHD (Hoogman et al., 2017), individuals with Alzheimer's dementia (Braver et al., 2005), or schizophrenic patients (Matzke et al., 2017) revealed stable pattern of results – a decrease in proactive control strategy. On the other hand, some samples show abnormalities in both control modes (Javitt, Kantrovitz, Martinez, 2018).

Many studies (Barch et al., 2003) have found no or just small differences in cognitive control tasks between patients with various psychotic and affective disorders. However, there is a moderate evidence suggesting that despite similar character of impairments, schizophrenic patients manifest more severe declines. There is an ongoing discussion about the existence of a continuum of symptoms and diagnoses rather than categorical distinction of disorders that are usually strictly defined in diagnostic practice (Smucny et al., 2017).

We believe that similar continuum-like trend might be found in neurodegenerative diseases which are characterised by the progressive loss of neuronal structure and function resulting in dementia. Alzheimer's and Parkinson's disease stand among the most common types of neurodegeneration, even though they originate in different brain areas – one exhibits predominantly cortical, while the other subcortical involvement in the beginning of cognitive decline (Aarsland, Cummings, Larsen, 2001). There is another type of cognitive decline that points to an intermediate state between normal aging and dementia called mild cognitive impairment (MCI) which affects circa 22% of US population above 70 (Gure et al., 2013). Particularly amnestic MCI (aMCI) represents MCI subtype with high risk of progression to Alzheimer's disease. Comparisons to healthy groups revealed that aMCI individuals perform poorer in cognitive tasks (Figure 11) and posit deficits in inhibitory

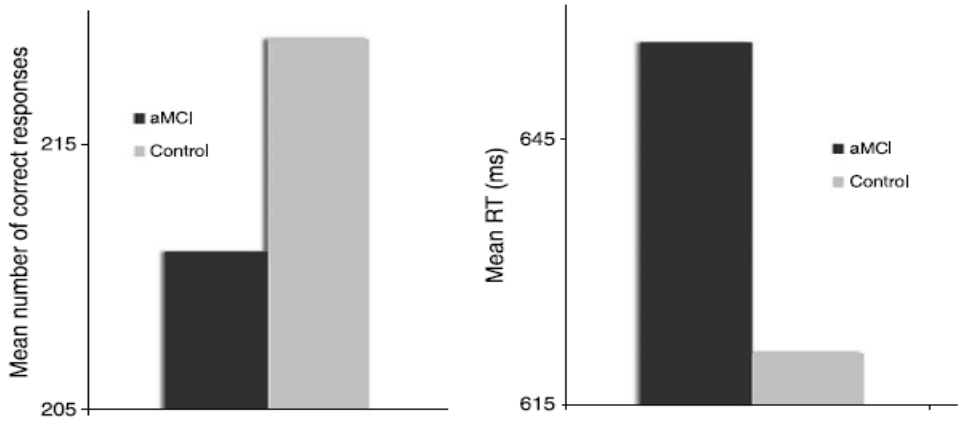

Figure 11: *Performance results (correct responses and RTs) from Cid-Fernández, Lindín, Díaz, 2014. Comparison of healthy group (Control) and subjects with amnestic MCI (aMCI).*

control, suggested by lower ERP amplitudes in N2 component (Cid-Fernández, Lindín, Díaz, 2014). Similarly, other authors (Olichney et al., 2011) revealed several cognitive ERP abnormalities in Alzheimer's disease and aMCI, specifically in P300 and N400 component and consider it important biomarkers of synaptic dysfunction.

Braver with colleagues (2005) aimed to compare cognitive control of young healthy adults (YH, aged 18-24) with two healthy aging groups (Y-OH, aged 66-75 and O-OH, 76-92 respectively) and patients with dementia of Alzheimer's type (DAT, aged 76-92) using AX-CPT and two delay length conditions (1s and 5s). Results indicated that OH show deficits in context processing compared to YH group, group of the O-OH show additional deficits in context maintenance, and DAT group demonstrated generalised decline with even greater deficits than all the other groups in both abilities and delays (Figure 12).

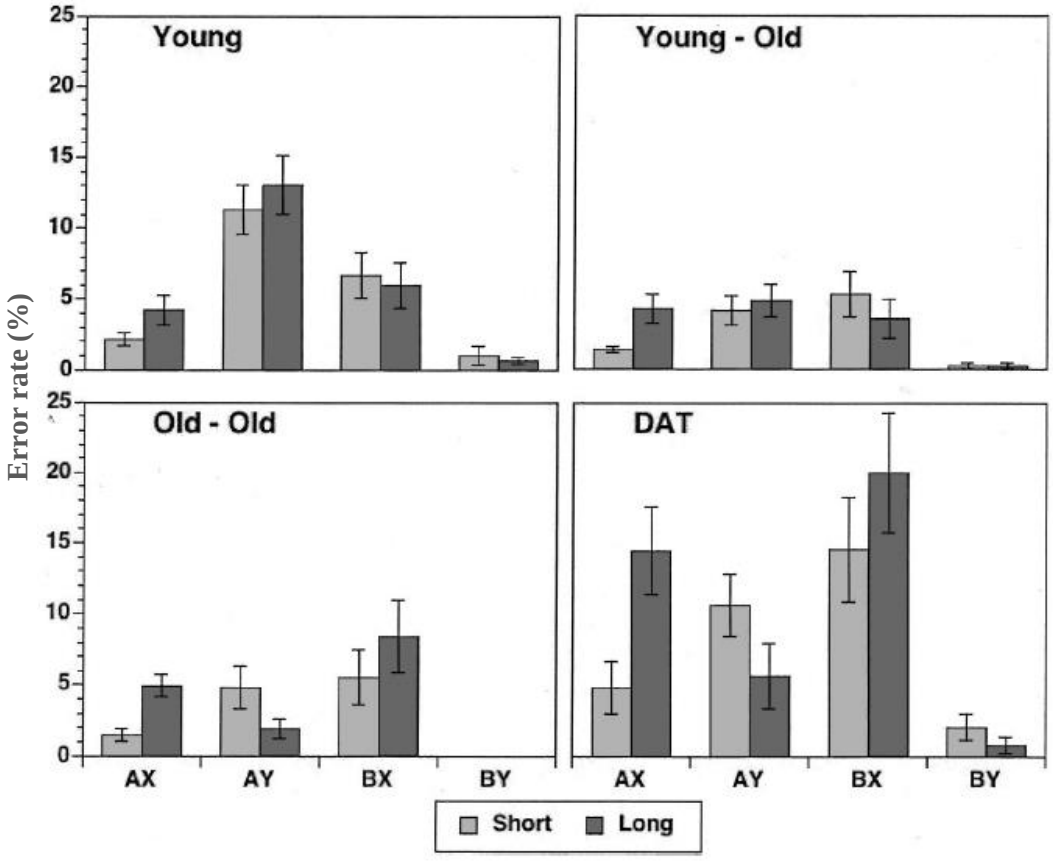

Figure 12: *The graphs display performance of 4 groups (young healthy adults, old healthy adults, the oldest healthy adults and dementia of Alzheimer's type) with error-rates (%) on the vertical axes and trial types on the horizontal axes from AX-CPT with two conditions (short delay for 1s and long delay for 5s) (Braver et al., 2005).*

Next, Moustafa, Sherman and Frank (2008) compared medicated and non-medicated Parkinson diseased (PD) patients and found that different dopamine levels in PD result in

distinct cognitive deficit profiles. In particular, non-medicated patients were unable to update new information, whereas medicated patients had problems with ignoring task-irrelevant information. In this context, it is worthwhile to consider that Parkinson diseased (PD) patients might be an interesting asset to cognitive control research since one of the main aspects of this condition is the loss of dopaminergic neurons which play an important role in modulating control. Even though, PD individuals are often examined in terms of motor performance and control (Herz et al., 2014), little attention has been devoted to their performance in AX-CPT and regarding the DMC framework.

4 RESEARCH AIM

The aim of this thesis is to study behavioural and electrophysiological characteristics of cognitive control modes, respectively proactive and reactive, in context of AX-Continuous Performance Task (AX-CPT). Our empirical study is divided into two sections: behavioural and electrophysiological investigation. Firstly, behavioural analysis will include within-subject and between-group comparisons of performance in terms of error-rates and reaction times (RTs) amongst given healthy and clinical groups (namely young healthy adults, older healthy adults, Parkinson's patients in early stage of disease, Parkinson's patients with mild cognitive impairment, and patients with amnestic mild cognitive impairment with high risk of Alzheimer's disease). Secondly, we will investigate event-related potentials associated with cue-, delay- and target-effects and compare the mean amplitudes at specific time windows among groups and across task trials, blocks and delay types.

Our goal is to extend the existing knowledge and provide more detailed description of aging effects and neurodegenerative changes in cognitive control. This effort might bring a better understanding of control processes and infer possible indicators of future development of neurodegenerative diseases.

4.1 Research questions and hypotheses

The main and the broadest research question, encompassing the whole research problem is:

> ***Q:*** *Are there any significant within-subject differences in behavioural and electrophysiological characteristics in the AX-CPT due to task manipulations; and between-group differences due to aging and neurodegenerative process?*

According to the point of view, the main issue can be split into two parts – (1) behavioural and (2) electrophysiological.

Previous research has shown that task manipulations (such as delay length and trial proportions) may influence the choice of cognitive control strategy. Moreover, older age and various clinical conditions go hand in hand with the decline in cognitive performance, reaction time, and transition towards more reactive control strategy (e.g. Braver, 2005). Yet,

the character and trigger of those changes is still unknown. In order to address this issue, we formulated the following research questions and hypotheses:

Q_1: Are there any within-subject or between-group differences in our *behavioural* data?

H1: We expect generally higher error rates and RTs in trials with longer delay, especially in clinical groups.

H_2: We expect more errors on BX and AY trials in AX-70 block than in BX-70; and more AX errors in BX-70 block than in AX-70.

H_3: We expect higher RTs on AY and BX trials in AX-70 block than in BX-70; and on AX trials in BX-70 block.

H_4: We expect generally higher RTs in all elderly (healthy and clinical) groups compared to young healthy adults.

Q_2: Do electrophysiological data characteristics differ with regards to cue-, delay-, or target-related effects?

H_1: We expect significant differences in mean amplitudes of chosen time windows in AX-70 and BX-70 condition after cue presentation, during the delay, and after target presentation.

H_2: We expect significant differences in mean CNV amplitude in short and long delay.

H_3: We expect significant differences in mean P300 amplitude after cue A and cue B presentation.

H_4: We expect significant differences in mean P300 amplitude after target presentation in AX and AY trials.

H_5: We expect significantly different mean amplitudes in chosen time windows among groups.

Since there is no universal ERP measure that could differentiate between proactive and reactive cognitive control, we plan to inspect the proactive-reactive relationship based on the pattern of results, similarly as in Dias, Foxe, Javitt (2003), who analysed ERP components in specific time windows to capture different cue and target effects. Even though the author concluded that control modes changes are not always in accordance with observed brain activity, we expect that there might be some electrophysiological differences amongst clinical groups based on the distinct origins (cortical vs. subcortical) of deficits in Parkinson's and Alzheimer's disease (Aarsland, Cummings, Larsen, 2001). Previous

research that detected ERP abnormalities in clinical samples (Olichney et al., 2011) supports this prediction.

4.2 Participants

A total sample of participants who took place in the whole experiment was 90 subjects (M = 58.44 years, 50 females, 40 males) divided into five groups, two healthy (young and old adults) and three clinical (patients in early stage of Parkinson‘s disease; in later stage with mild cognitive impairment; and patients with amnestic mild cognitive impairment with high risk of progression to Alzheimer‘s disease). The participants were distributed into clinical groups after series of diagnostic sessions with experienced professionals at the University medical centre in Ljubljana, Slovenia. A detailed description of each group with corresponding demographic data can be seen in Table 1 below.

	GROUPS	NUMBER	AGE RANGE	AVERAGE AGE	STANDARD DEVIATION	GENDER
HEALTHY	Young adults	30	19 - 28	22.57	1.74	14 F / 16 M
HEALTHY	Older adults	14	55 - 78	66.92	7.03	10 F / 4 M
CLINICAL	Parkinson's disease	14	59 - 76	65.5	5.47	4 F / 10 M
CLINICAL	Parkinson's disease with cognitive impairment	13	57 - 77	67.85	6.54	7 F / 6 M
CLINICAL	Mild cognitive impairment	19	54 - 82	69.37	7.54	15 F / 4 M

Table 1: *Demographic data of participants separately for each research sample.*

As we encountered few technical problems during the measurements, the number of subjects slightly differs in some analyses as the data had been missing, lost, or disrupted. We describe it in more detail in Data pre-processing and Results.

4.3 Task

The AX-CPT was constructed based on the Braver‘s (2009) version of the task and implemented using E-prime software (Schneider, Eschman, Zuccolotto, 2002). Each trial started with a cue presentation (letter A or B) in the centre of the screen for 300 ms followed

by the inter-stimulus interval. There were two types of intervals – (1) short delay lasting 1500 ms and (2) long delay lasting 4000 ms. The subsequent probe (letter X or Y) was also presented for 300 ms. The participants had 2000 ms of response time, since the beginning of the probe followed by 1000 ms of an inter-trial interval. Subjects were instructed to press a button whenever they observed an A cue followed by X, otherwise they should refrain from answering as there was no non-target button. It was recorded as a wrong answer when no answer was given on AX trial.

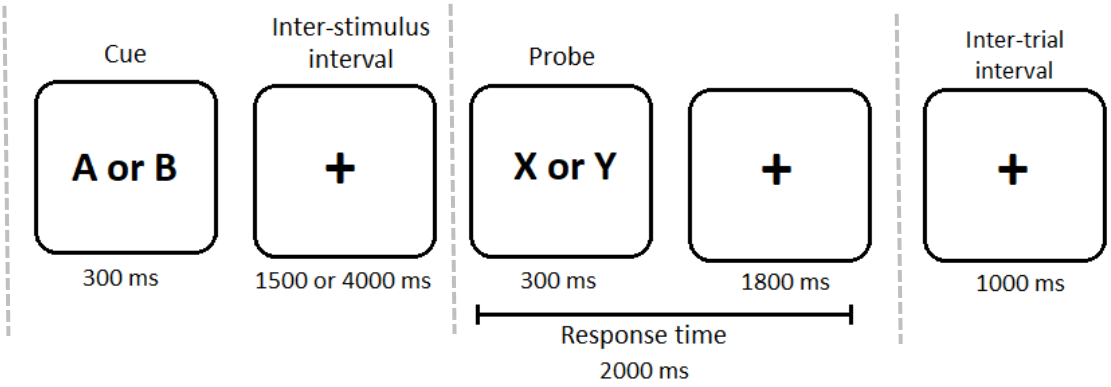

Figure 13: *The AX-CPT scheme used in present study.*

Two types of blocks with different proportions of each trial type were used in the study. We labeled them as AX-70 and BX-70. The AX-70 block consisted of 70% of the AX trials and 10% of AY, BX and BY trial type, respectively. The proportions of the BX-70 block were 70% of BX trials and 10% of each of the other trial types. One block comprised of 50 short-delay and 50 long-delay trials and altogether, 6 blocks were used (3 blocks of AX-70 and 3 blocks of BX-70). The presentation of trials within each block was in random order. The purpose of task manipulations (short/long delay and AX-70/BX-70 condition) was to challenge different control mechanisms and reveal specific ERP components.

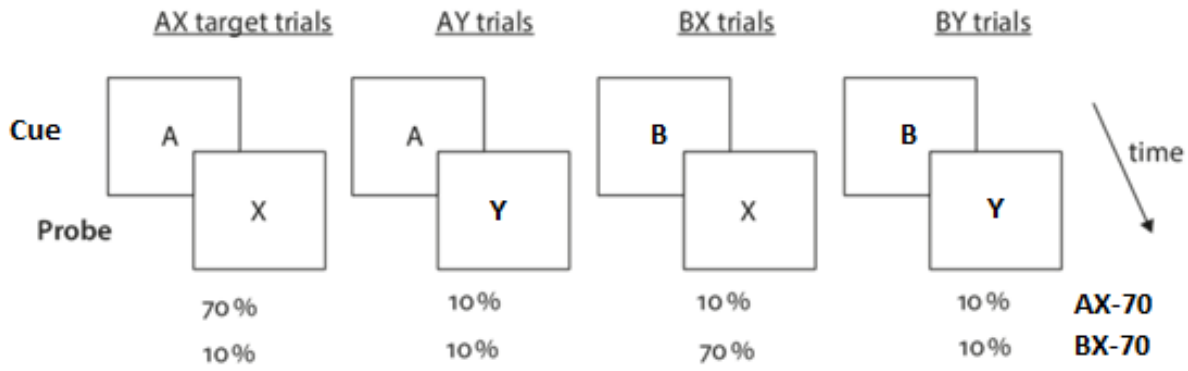

Figure 14: *Proportions of trials within AX-70 and BX-70 block used in present study.*

4.4 Procedure and data collection

Our study is a part of a bigger ongoing project that is being held at the Laboratory for Clinical Neuroscience at the Department of Neurology, University Medical Centre in Ljubljana, Slovenia. The data was collected during two-year period, from 2012 to 2013. All subjects participated voluntarily and signed informed consent. Clinical subjects were long-term clients of the clinic and their diagnosis was identified after several thorough diagnostic evaluations by experienced professionals.

Each subject was tested individually, seated on a comfortable chair in an acoustically attenuated room with light on. Prior to the actual task, participant's head was scrubbed using an abrasive gel to remove skin dirt, then EEG cap was placed and SuperVisc gel was applied to enable continual contact between head and electrodes. We employed standard international 10-20 system using 32 active Ag/AgCl electrodes system actiCAP (Brain Products GmBH, Germany) (Figure 15). AFz electrode served as a reference and ground electrode was located on the scalp. Data was recorded with sampling frequency at 500Hz, amplified using BrainAmp, with a built-in low-pass filter at 0.016 Hz. Individual impedances were kept below 5kΩ.

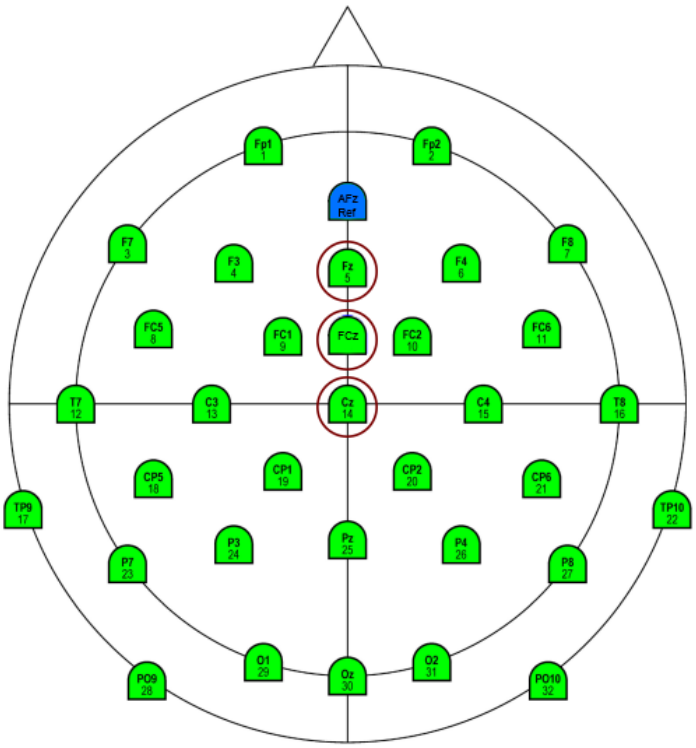

Figure 15: A layout of the standard 32-channel actiCAP arrangement from Brain Products GmBH, Germany. Electrodes important for our analysis are circled (Fz, FCz, Cz).

After setting all up, an experimenter explained the task and instructed participants to perform it as quickly, and at the same time, as accurately as possible. The stimuli were presented on a computer screen located 80 cm from them. The response accuracy and reaction times were recorded automatically by the software. EEG recording was synchronised with behavioural data and markers were set on cue and probe onset and button press (response). Before the actual task, subjects underwent a practice session to ensure above chance performance in the subsequent task.

4.5 Data pre-processing

Behavioural data pre-processing

For purposes of behavioural analysis, reaction times and error rates were extracted from the E-prime session logs. Percentages from raw numbers of incorrect hits were calculated. To control for outliers and extreme values, we tried three different approaches due to fact that performance of clinical subjects varies even within the same group and it is complicated to decide whether these deviations result from an experimental error or another factor associated with the disease.

(1) The first and the simplest method was to use all original data.

(2) The second approach was winsorization (Dixon, Yuen, 1974). According to this method, extreme values were replaced with the lowest/largest number that was not an outlier.

(3) The last option was exclusion of participants. We excluded 5 participants with significantly poorer performance in target-trials.

During the analyses, the same set of statistical tests was run on each dataset to observe and compare how extreme values affect our data. Based on the applied approach, markedly different results were observed in error-rates and slightly different results in delay-effect analysis. Since error-rates were significantly higher in some participants and their results bordered with random response (e.g. 50 incorrect answers out of 105) or might have represented poor understanding of the task (e.g. 30 and more incorrect answers out of 105), we decided to exclude 5 subjects from the analysis. Even after exclusion of those outermost individuals, winsorized data still produced results different from both, original and censored data and those contrasts were not uniform suggesting that winsorization may in this case entail questionable intervention to the data.

EEG data pre-processing

A standard EEG pre-processing procedure used at the laboratory (Repovš, 2010) was performed. The signal was first parsed into epochs based on markers in EEGLAB, an open source MATLAB toolbox for EEG analysis (Delorme, Makeig, 2004). Epochs with large artefacts (e.g. movement artefacts) were removed by visual inspection, blinks and other eye movement artefacts were rejected through a version of Independent component analysis (AMICA) in EEGLAB. Channels with continual noise were rejected before ICA and missing channels later interpolated. Afterwards, the epochs were averaged. Five main sets of event-related potentials (ERPs) were obtained off-line, three related to the cue and the following delay period, other two related directly to the target response. For purposes of illustration, grand average images were constructed. We used separate EEGLab toolbox, called ERPLab (Lopez-Calderon, Luck, 2014) to extract the ERPs.

First cue-related ERP measure represents the ERP amplitude 450-550ms after cue A presentation at the Pz electrode site, in blocks AX-70 and BX-70. Data from 1.5s and 4s delay were joined since participants did not know right after the cue which delay will occur. Second cue-related ERP measure was associated with B cue presentation, joined for both delays, extracted from Cz electrode from time window 350-450 ms after B cue for YHC and from Fz electrode signal and 450-550 ms time window for all other groups. Exact time windows and electrodes for each measure had been chosen based on Dias (2003) and visual inspection of topographies of grand average images.

Unlike in cue- and target-related period, increase in negative direction was observed during the delay, known as contingent negative variation, reflecting expectancy of target stimuli. For shorter delay, Cz location was used based on grand average topography from time window 880-990ms after delay start. Longer delay was analysed during the 2000-2200ms time window.

First target-related ERP measure expresses the ERP amplitude 275-375 ms after the target presentation in AX sequence. Those measures were calculated separately for shorter and longer delay in Cz electrode location. Second target-related measure was gained from 325-425 ms time window, after the AY sequence, again separately for 1.5s and 4s delay in FCz electrode location.

5 RESUTLS

The results of behavioural and electrophysiological analysis are presented in two separate sections. We used following abbreviations to refer to a specific group:

- *YHC*: young healthy controls;
- *OHC*: old healthy controls;
- *PAR*: subjects in early stage of Parkinson's disease without related cognitive impairment;
- *PCI*: subjects diagnosed with Parkinson's disease with mild cognitive impairment;
- *MCI*: subjects diagnosed with amnestic mild cognitive impairment with high risk of progression to Alzheimer's disease.

5.1 Behavioural results

Error rates

To determine whether there are any significant differences in error rates among groups regarding the trial, block and delay type, we used 5x4x2x2 mixed within-subject, between-group ANOVA (group x trial x block x delay).

Compered to original dataset, 5 participants were excluded due to missing data in one of the blocks. Additionally, 5 participants (2 OHC, 1 PAR, and 2 PCI) with extremely poor performances were excluded to avoid false shift of results in any direction, leaving a total number of 80 subjects. A standard level of significance was set ($\alpha < .05$). Since the Mauchly's Test of Sphericity showed that the sphericity had been violated [$\chi 2(5) = 123.26$, $p < .001$], Greenhouse-Geisser correction ($\varepsilon = 0.65$) was applied on degrees of freedom.

The results are shown on Figure 16. The main effect of *trial type* (AX, AY, BX, BY) was significant [$F(1.95, 146.38) = 44.93$, $p < .001$, $\eta_p^2 = .375$]. Subsequent pairwise comparisons showed that performance in AX-CPT task significantly differed among all trial types ($p \leq .003$) (Table 2). Similarly, main effect of *block* [$F(1, 75) = 10.09$, $p = .002$, $\eta_p^2 = .119$] was significant with more errors in AX-70 (.039 vs. 0.28, MD -0.010), while delay length [$F(1, 75) = 0.146$, $p = .704$, $\eta_p^2 = .002$] by itself was not significant, contradicting what was expected. Between-subject factor of group was not significant [$F(4,75)= 1.54$, $p = .199$, $\eta_p^2 = .076$].

On the other side, *delay length* differed in interaction with *group* [F(4, 75)= 2.69, p = .037, $\eta_p^2 = .126$] or *block* [F(1, 75)= 7.59, p = .007, $\eta_p^2 = .092$].

	AX	AY	BX	BY
AX		-3.5**	2.9%***	4%***
AY	3.5%**		6.4%***	7.5%***
BX	2.9%***	-6.4%***		1.1%***
BY	-4%***	-7.5%***	-1.1%***	

*** p = 0.000
** p < 0.01
* p < 0.05

Table 2: *Pairwise comparisons showing the percentage of difference in error rates between each trial type (horizontal minus vertical) with asterisk sign denoting significance.*

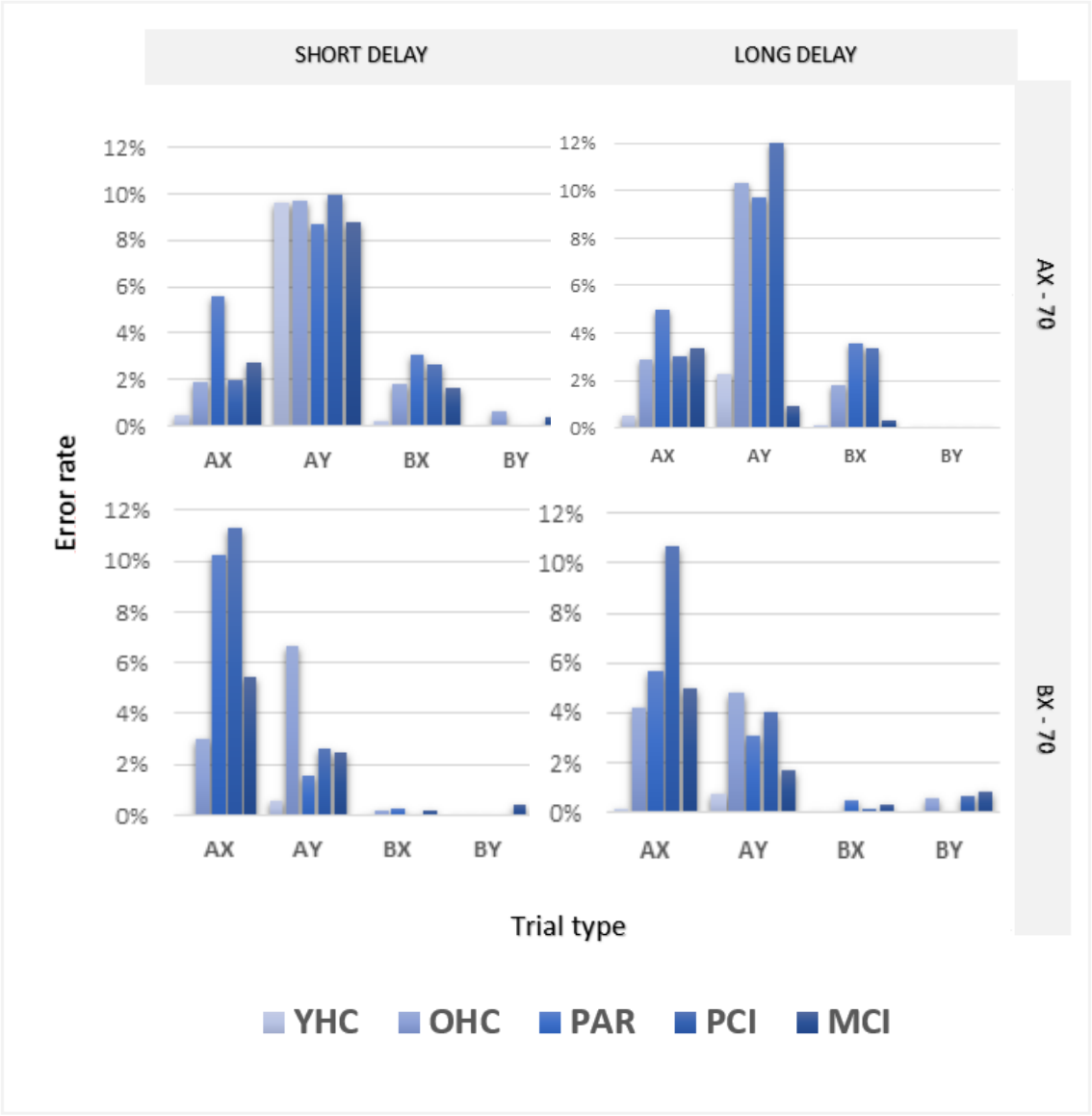

Figure 16: *Mean error rate displayed for each group (separate colour coded bars) and condition (short/long delay = columns, AX-70/BX-70 version = rows).*

Other two-way interactions proved to be significant between *trial type and group* [F(7.81, 146.37)= 2.54, p = .014, $\eta_p^2 = .119$] indicating that performance in particular trial differed among groups; and between *trial and block type* [F(1.98, 148.53)= 38.2, p < .001, $\eta_p^2 = .337$], showing that performance pattern in particular trials in AX-70 and BX-70 blocks differed. Multiple comparisons have shown that YHC performed significantly better in AX trial as compared to PAR (MD = -6.1%, p = .014) and PCI group (MD = -6.2%, p= = .026). Performance in other trials did not significantly differ among groups.

Also three-way interaction was detected among *trial, block and group* [F(6.05, 113.37)= 3.87, p < .001, $\eta_p^2 = .171$]. Post hoc comparisons revealed significant mean differences among groups on AX and BX trials in AX-70 condition and on AX, AY, and BX trials in BX-70 condition. All these significant comparisons are listed in Table 3.

All other interactions were non-significant [$F \leq 2.96$, $p \geq .066$, $\eta_p^2 \leq .094$].

Condition	Compared groups	MD	Sig.
AX trial: AX-70 block	YHC - PAR	-4.8%	.000***
	YHC - MCI	-3%	.026*
BX trial: AX-70 block	YHC - PAR	-2.8%	.036*
AX trial: BX-70 block	YHC - PCI	-10.4%	.006**
AY trial: BX-70 block	OHC - PAR	-6.5%	.025*
BX trial: BX-70 block	YHC - MCI	-0.9%	.037*

Table 3: *Post hoc between-group comparisons of mean error-rates with respect to trial type and block. Only significant comparisons are presented.*

Reaction times

Reaction times (RTs) were measured only during the target trials (AX) as there was no non-target button, and only from trials where participants responded correctly. Two participants were excluded due to technical problems and loss of data (N = 83).

Group	Delay (s)	AX-70 block	BX-70 block
YHC	1.5	381.6 (12.9)	390.4 (32.2)
	4	354.8 (44.4)	374.2 (34.9)
OHC	1.5	485.6 (67.8)	494.1 (74.2)
	4	475.3 (69.6)	518.4 (71.7)
PAR	1.5	488.4 (82.5)	493.4 (57.3)
	4	484.5 (68.9)	529.6 (66.9)
PCI	1.5	491 (115.1)	495.1 (99.7)
	4	493.5 (95.7)	534.7 (81.2)
MCI	1.5	540.2 (74.8)	560.3 (104.3)
	4	554.4 (90.4)	606.4 (105.2)

Table 4: *Descriptive statistics of RTs (ms) with respect to each group, delay length and block.*

Likewise, we used mixed design ANOVA, in this case with 3 factors 5x2x2 (group x block x delay). We found significant main effect of *block* [F(1,78) = 19.92, p < .001], main effect of *delay* [F(1,78) = 19.92, p < .001], and significant main effect of *group* [F(4,78) = 28.84, p < .001], indicating that mean RTs differed in blocks, delays and amongst groups, respectively. To be specific, mean RTs were significantly higher in BX-70 blocks (MD = 24.73 ms, p < .001); and in longer delay (MD = 10.57 ms, p = .010) (Figure 17). Since some of the group variances were unequal, we used Dunnett T3 procedure which is considered a conservative method able to determine mean differences even when group sizes and variances deviate (Shingala et al., 2015). Post hoc tests revealed that group of YHC significantly differed from all other groups (Table 5). Groups of elderly participants did not significantly differ from each other.

	YHC	OHC	PAR	PCI	MCI
YHC		-118.1***	-123.7***	-128.3*	-190.1***
OHC	118.1***		-5.6	-10.2	-72
PAR	123.7***	5.6		-4.6	-66.4
PCI	128.3*	10.2	4.6		-61.7
MCI	190.1***	-72	66.4	61.7	

*** p = 0.000
** p < 0.01
* p < 0.05

Table 5: *Multiple comparisons of mean RTs amongst groups. Values represent mean difference (vertical value minus horizontal) with asterisk sign denoting significance level.*

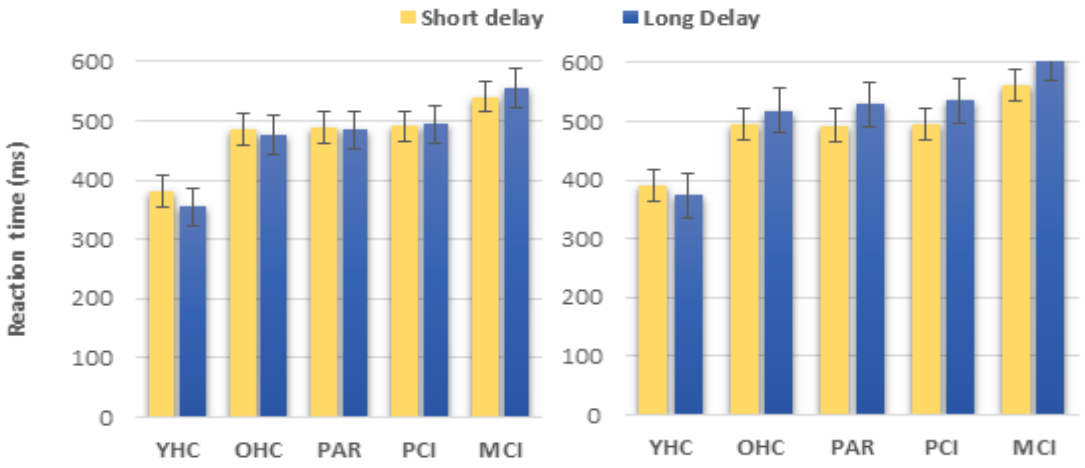

Figure 17: *Illustration of mean RTs with respect to group, block and delay type.*

Next, observed two-way interaction between *delay type and group* [F(4,78) = 8.13, p < .001] pointed out that groups were affected differently by the delay length – mean RT were higher in longer delay in all groups (OHC, PAR, PCI, MCI) except YHC group which expressed contrasting pattern. *Block by delay* interaction also proved to be above the level

of significance [F(1,78) = 31.22, p < .001], specifically RTs in AX-70 condition was significantly higher [t(82) = 2.328, p = .022)] in shorter delay (M = 460.9 ms, SD = 90.5) than in longer delay (M = 452.5 ms, SD = 103.8); while in BX-70 condition reversed pattern appeared with significantly higher RTs [t(82) = -2.967, p = .004)] in longer delay (M = 489 ms, SD = 116.1) than in short delay (M = 471 ms, SD = 97.5).

5.2 Electrophysiological analysis

All time windows and electrode sites for ERP analysis were chosen based on the similar study (Dias, Foxe, Javitt, 2003), except one location (Cz instead of FCz in delay-effects analysis) since in that case, it seemed to be more appropriate according to our grand average topography. Detailed description of particular electrode locations and time windows can be seen earlier in EEG pre-processing section.

Cue effects

To explore cue effects, two mixed design ANOVA analyses were performed (5x2: group x block). Data were analysed altogether for both delay lengths, as participants did not know right after the cue presentation which delay took place.

Firstly, we measured A-cue effects at the 450-550ms time window after A-cue presentation. An example of grand average image is displayed bellow (Figure 18):

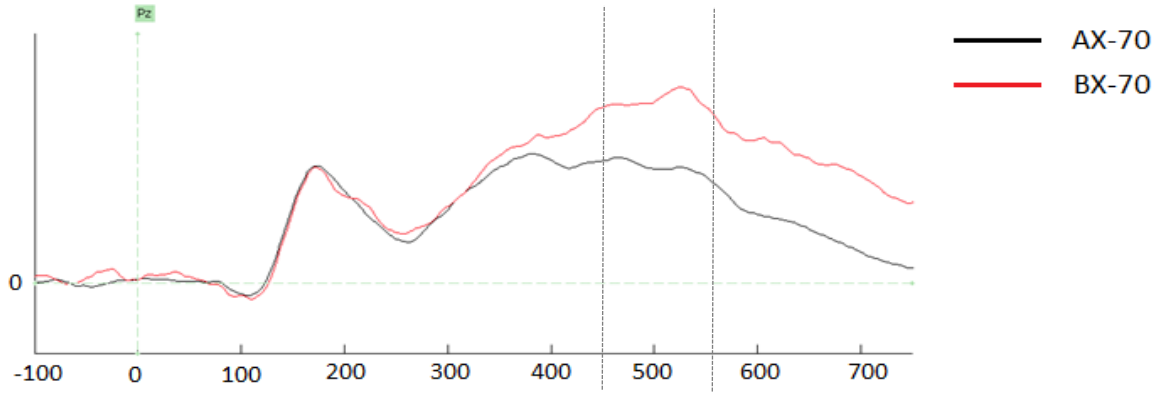

Figure 18: *Grand average ERP image from all groups illustrating activity after A-cue presentation. There are separate lines for each block type. Time window 450-550 ms is marked with broken lines.*

The main effect of *block* was significant [F(1, 82) = 41.04, p < .001], with higher mean amplitudes in BX-70 (M = 3.344 µV) than in AX-70 condition (M = 2.135 µV). Neither the

main effect of group [F(4, 82) = 0.292, p = .883], nor the block by group interaction [F(4, 82) = 1.6, p = .182] reached the level of significance.

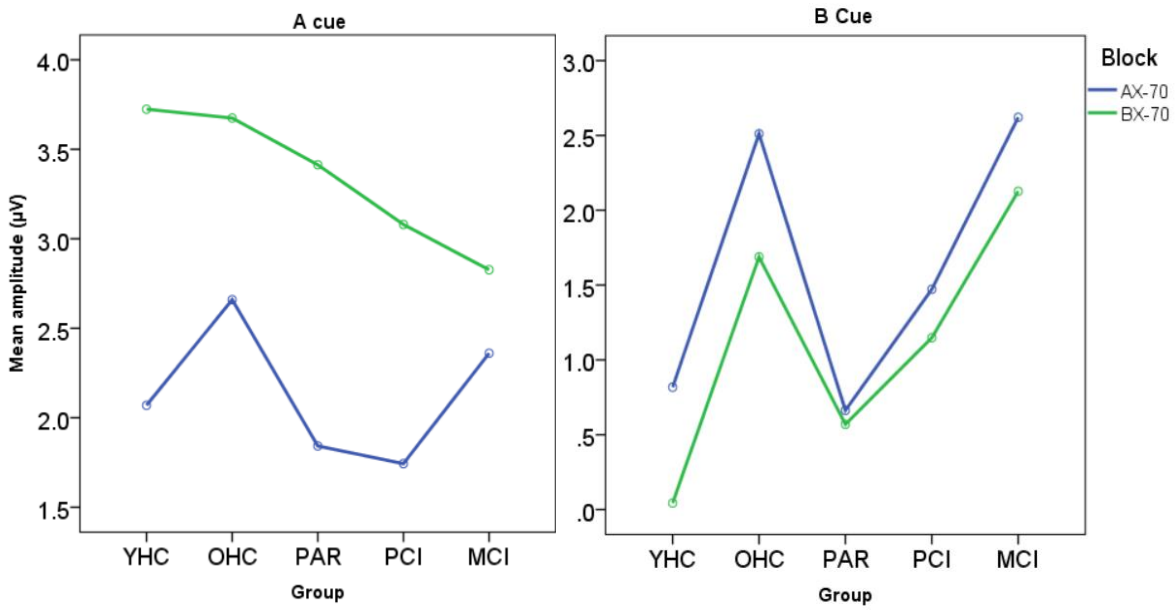

Figure 19: *The graphs display mean P300 amplitude from the period 450-550 ms after A-cue presentation (on the left) and B-cue presentation (on the right).*

Similar pattern was observed in results associated with time window between 350-450ms after B-cue presentation. We found that mean amplitudes in AX-70 and BX-70 *block* significantly differed [F(1,82) = 12.9, p = .001], although in opposite manner than in A-cue period, with higher means in AX-70 condition (M = 1.617 µV) compared to BX-70 (M = 1.115 µV). Block by group interaction was non-significant [F(4,82) = .98, p = .423].

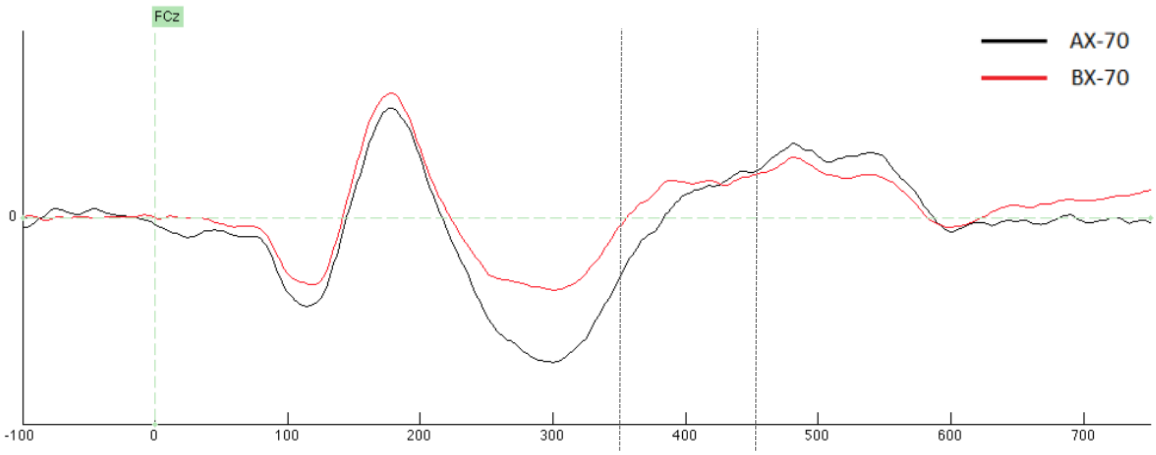

Figure 20: *Grand average ERP image from all groups plotting the activity after B-cue presentation. There are separate lines for each block type. Time window 350-450 ms is marked with two broken lines.*

Additionally, we detected significant *group* differences [F(4,82) = 6.13, p < .001], specifically in YHC versus OHC (p = .041), YHC versus MCI (p = .003), and PAR versus MCI (p = .009). Table with Dunnett T3 post hoc results is below (Table 6).

	YHC	OHC	PAR	PCI	MCI
YHC		-1.669*	-0.186	-0.879	-1.944**
OHC	1.669*		1.483	0.79	-0.275
PAR	0.186	-1.483		-0.694	-1.758**
PCI	0.879	-0.79	0.694		-1.064
MCI	1.944**	0.275	1.758**	1.064	

*** p = 0.000
** p < 0.01
* p < 0.05

Table 6: *Multiple comparisons of mean P300 amplitude amongst groups. Values represent mean difference (vertical value minus horizontal) with asterisk sign denoting significance level.*

Delay effects

To examine delay-effects, mixed design ANOVA (5x2: group x cue) was performed separately for each delay type (1.5s or 4s) and block (AX-70 or BX-70).

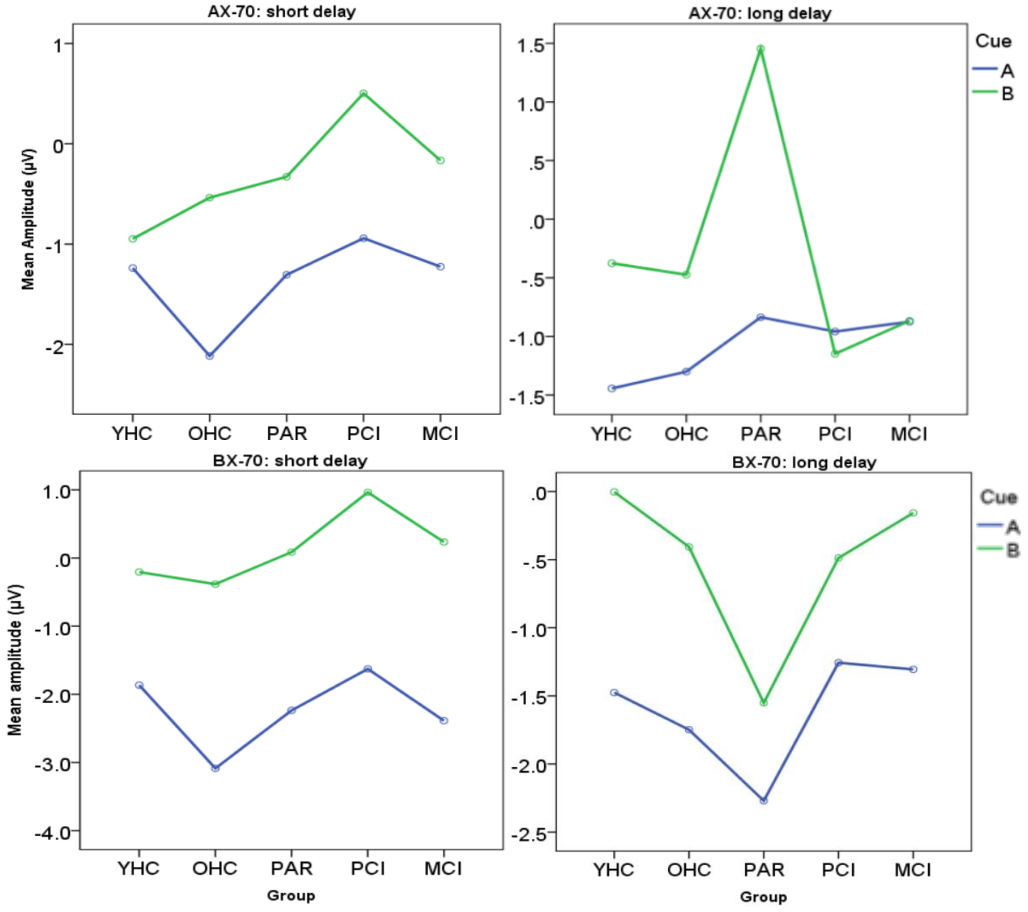

Figure 21: *The graphs display mean CNV amplitudes from the delay period: time window 880-980ms from the delay start for short delay and 2000-2200 ms for long delay.*

The results revealed significant main effect of *cue* in all conditions [F ≥ 10.03, p ≤ .002] (Table 7), whereas *cue by group* interaction was significant only in AX-70 block with longer delay [F(4,81) = 2.817, p = .030].

Block	Delay (s)	MD	F	Sig.
AX-70	1.5	-1.07	31.91	.000***
	4	-0.801	10.03	.002**
BX-70	1.5	-2.379	98.53	.000***
	4	-1.09	20.24	.000***

*** p = 0.000
** p < 0.01
* p < 0.05

Table 7: *Results from ANOVA showing significant main effects of cue separately for each block and delay length. MD = mean difference between A cue minus B cue.*

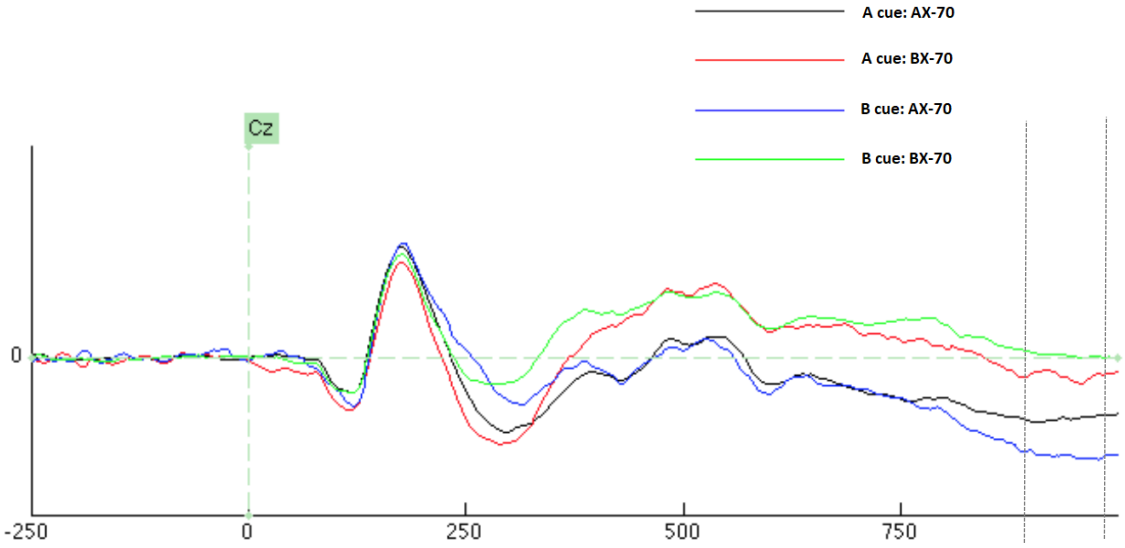

Figure 22: *Grand average ERP image from all groups plotting the activity during short delay. There are separate lines for each block type and cue (see the legend). Broken lines mark our period of interest, 890-990 ms from delay start.*

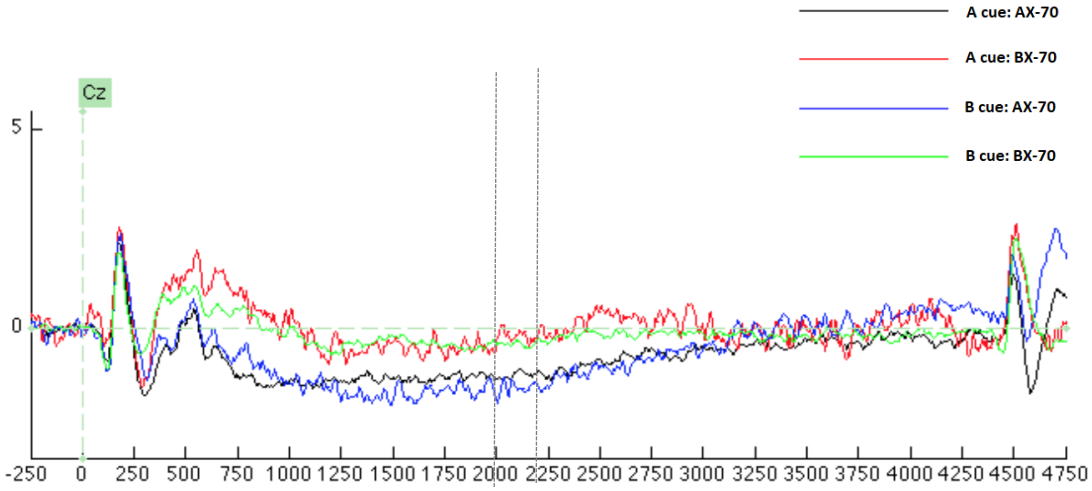

Figure 23: *Grand average ERP image from all groups plotting the activity during long delay. There are separate lines for each block type and cue. Broken lines mark period 2000-2200 ms from delay start.*

Target effects

Target effects were examined through a mixed design ANOVA (5x2x2: group x delay), separately for the AX and AY sequence. Analysis of target effects in AX trials detected significant main effect of *block* [F(1, 82) = 91.2, p < .001], specifically potentials were higher and generally positive in BX-70 (M = 1.181) while mostly negative in AX-70 (M = -0.495). Further, two significant interactions were found: *delay by group* [F(4, 82) = 4.59, p = .002] and *block by delay* [F(1, 82) = 18.76, p < .001]. Pairwise comparisons showed significant differences (p < .001) between both pairs (short delay: AX-70 versus BX-70; long delay: AX-70 versus BX-70). In general, groups did not significantly differed [F(4, 82) = 2.203, p = .076], although YHC and PCI group differed in longer delay condition (MD = 3.398, p =.007), which can be seen in Figure 24.

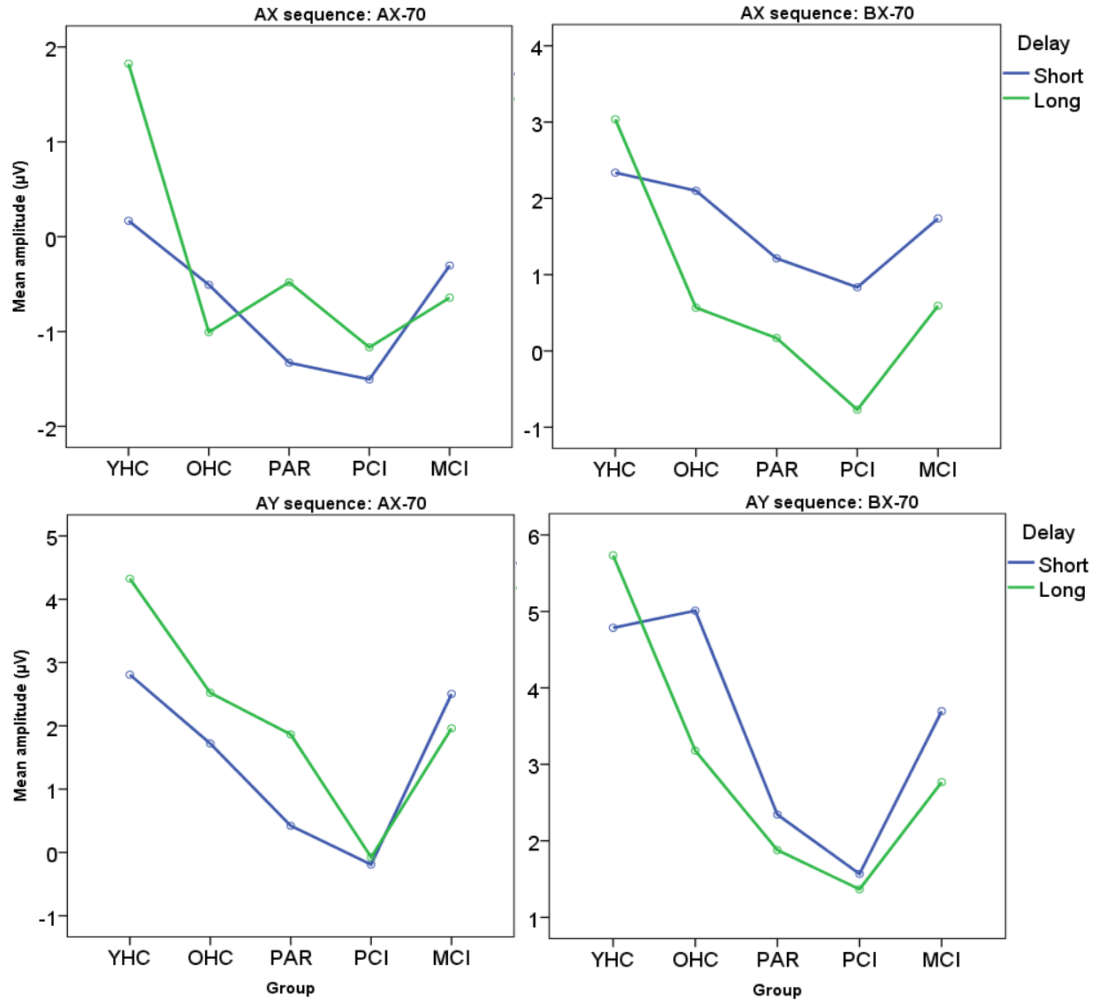

Figure 24: *The graphs display mean P300 amplitude from the period after target presentation: time window 275-375 ms for AX sequence and 325-425 ms for AY sequence.*

When considering target effects on AY trials, mean amplitudes between *blocks* significantly differed [F(1, 82) = 41.88, p < .001], and subsequent pairwise comparisons showed that potentials were almost two times higher in BX-70 block (M = 3.233) compared to AX-70 block (M = 1.786). The significant main effect of *group* [F(4, 82) = 2.96, p < .025] was confirmed only between YHC and PCI group (MD = 3.745, p = 0.039). The main effect of delay [F(1, 82) = 0.090, p = .746] did not play an important role per se, though the interaction between *block and delay* proved to be significant [F(1, 82) = 8.81., p = .004], where AX-70 condition demonstrated opposite pattern of activity compared to BX-70.

Finally, comparisons of mean amplitudes in AX and AY sequence regardless the condition uncovered significantly higher activity (p < .001) following the target presentation in AY sequence (M = 2.509) compared to AX (M = 0.343), most visible in YHC versus PCI group (MD = 3.119, p = .027) (Figure 25).

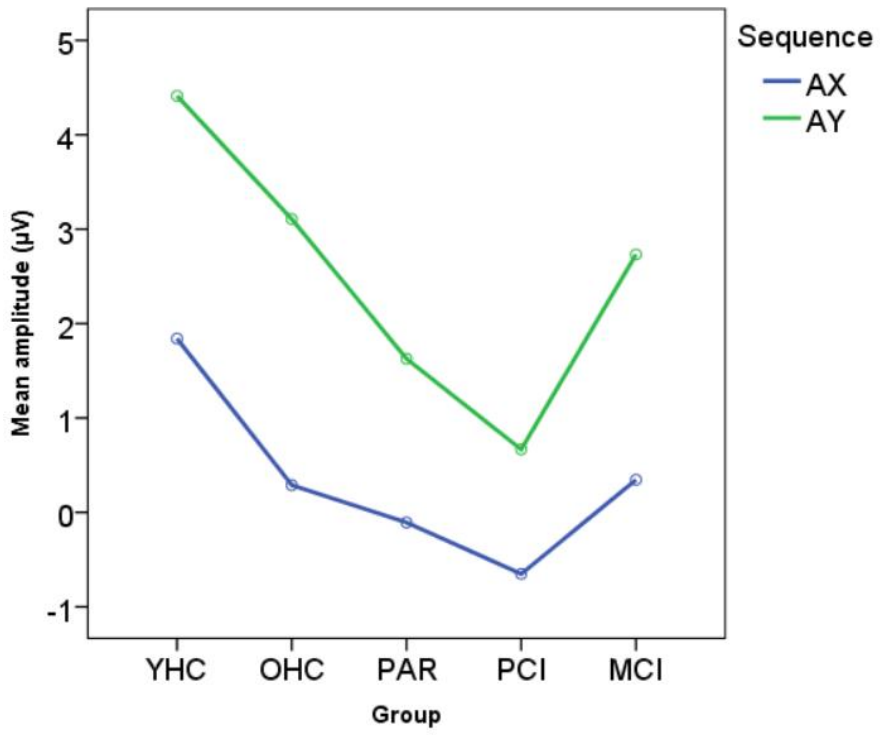

Figure 25: *Mean P300 amplitudes related to target presentation separately for each group and for AX and AY sequence.*

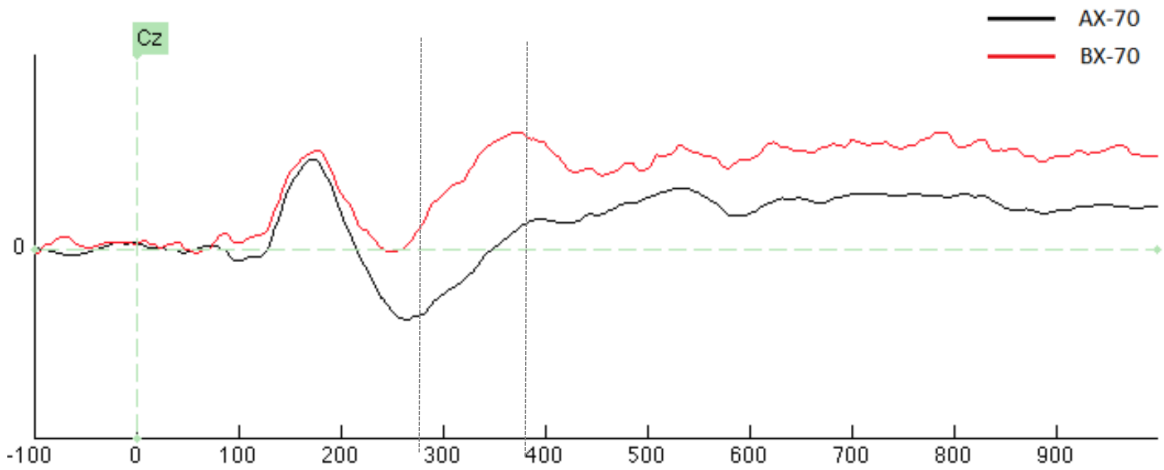

Figure 26: *Grand average ERP image from all groups plotting the activity after target presentation in AX sequence. There are separate lines for each block type. Time window 275-375 ms is marked with two broken lines.*

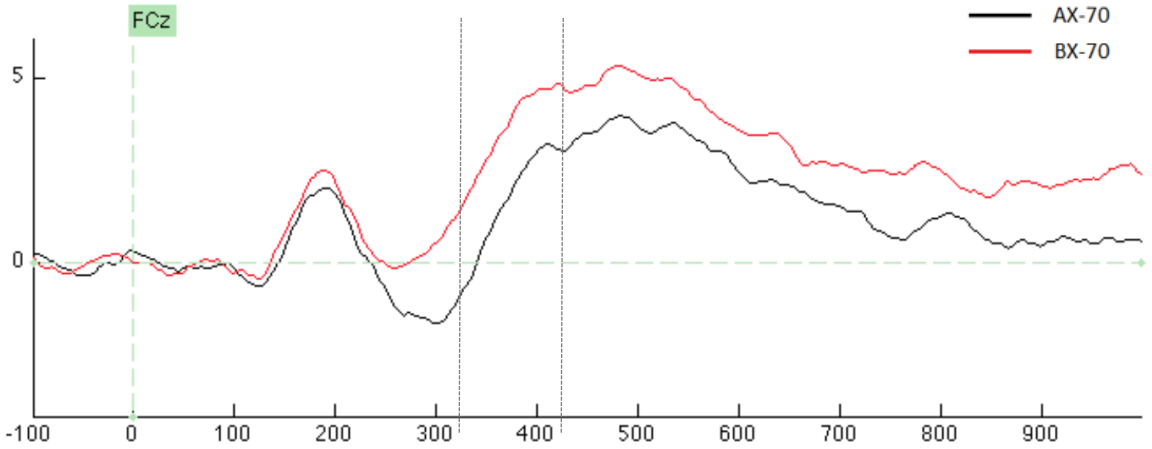

Figure 27: *Grand average ERP image from all groups plotting the activity after target presentation in AY sequence. There are separate lines for each block type. Time window 325-425 ms is marked with two broken lines.*

DISCUSSION

The results of this thesis provided further insights into behavioural and electrophysiological characteristics of cognitive control processes in relation to advancing age and neurodegenerative changes in context-processing. We both replicated and extended previous research on this topic. Our primary findings indicated that:

(1) in comparison to young healthy individuals, performance of healthy and pathological aging groups is not generally worse, only slower;

(2) specific cognitive control strategy is not always accompanied with the same brain activation profile;

(3) cue, delay, and target effects share some similar characteristics regarding the AX-CPT version – generally higher mean amplitudes observed in BX-70 throughout the task.

We will discuss our findings in more detail in the following text.

Error rates and reaction times

In terms of behavioural analysis, our findings were only partially consistent with previous research (Bugg, 2014; Redick, Engle 2011). We confirmed that overall error rate on AY and BX trials was higher in AX-70 condition as compared to BX-70. Performance on BX trial considerably indicates the extent to which individual uses context information from the cue to prepare or inhibit response (Redick, 2014). Since the probability of target trial presentation in AX-70 is high (70%), the tendency to prepare response is more prominent and otherwise better performance of healthy adults is decreased due to utilization of proactive control strategy. Surprisingly, the number of AY errors was greater than the number of BX errors even in the older group and clinical samples and in general no significant differences in performance were found. Such a pattern may occur due to delay effects which might improve BX performance at longer delays or due to successful use of compensatory mechanisms (Paxton et al., 2008). On the contrary, certain deviations in performance were identified when particular condition was examined. AX trials were more problematic in BX-70 condition, especially for older individuals and clinical groups, indicating that their ability to process context information from the A-cue was decreased. In this condition, we observed slightly, even though not significantly, higher AX error rates in both groups of patients with Parkinson's disease, supposedly pointing out to more severe

context-processing deficits in those groups. However, to examine this hypothesis, bigger sample is needed.

Regarding the delay length, no significant differences in error-rates were found as opposed to other studies (Cohen et al., 1999; Braver, 2005), which can possibly be a consequence of different choice of inter-stimulus length. This issue is further addressed in limitations. On the other hand, reaction times measured on AX trials significantly differed, both between AX-CPT versions and delays. Again, YHC scored much higher than other groups reflecting faster and more confident response pattern in younger age.

To sum it up, we successfully answered our first research question which had interrogated whether there are any differences in error rates and RTs considering the task modification, age, and clinical condition. We fully confirmed three hypotheses (H_2, H_3, H_4), and one partially (H_1).

ERPs: Cue-, delay-, and target-related effects

We observed that regardless the age or clinical state, subjects reacted differently to presentation of A and B cue. Moreover, all groups exhibited reversed pattern of P300 amplitude in A cue (significantly higher activity in BX-70 condition) as opposed to B cue (subtly higher activity in AX-70 than in BX-70 condition). Even though A cue presentation has not yielded any remarkable group differences, contrasts were apparent after B cue presentation – the cue which brings clear information about the need for response inhibition after subsequent probe. The B cue-related activity in OHC and MCI group was significantly higher than in YHC, showing that young adults utilize different strategies from those two groups. The existence of differences is in line with previous findings (Paxton et al., 2008; Kopp et al., 2014), however the context-processing pattern in our results contrasted what they had observed. We failed to confirm overall neural under-recruitment in cue processing reflecting diminished use of proactive control (Kopp et al., 2014). One plausible explanation is that the size of our sample was insufficient to describe the control strategy. Alternatively, some authors have suggested that the higher the change in strategy is, the stronger ERP amplitude appears (Dias, Foxe, Javitt, 2003). Thus, it seems that it is more difficult for OHC and MCI group to switch to inhibition plan after B-cue presentation. Surprisingly, other two clinical groups (PAR, PCI) did not encounter similar difficulties with B-cue processing suggesting the better use of compensatory mechanisms or presence of other unknown factors influencing the P300 amplitude.

Delay period revealed negative potentials similar to contingent negative variation (CNV), which is usually observed in two-step tasks between the cue and probe presentation (Walter et al., 1964). Observed gradual increase in negativity throughout the delay period was significantly higher when trial started with A-cue which supported the view from Dias, Foxe and Javitt (2003), and this larger amplitude (in negative direction) reflected motor preparation for the response. The delay length affected all groups equally, showing no differences between groups. Next, our findings provided strong evidence that different blocks produced changes in preparatory processes. Indeed, they were more evident in BX-70 condition even though the probability of response was lower, that is to say, also other processes than motor preparation were involved. Interestingly, activity of all groups except PAR was very similar, contradicting the notion that aging and clinical groups exhibit changes in neuronal activity during the delay period (Paxton et al., 2008). Conversely, few authors have suggested (Braver et al., 2005) that context maintenance may be independent of other deficits associated with older age and clinical condition such as context representation and updating. Therefore, we believe that, in some samples, cue- and target-related differences may be accompanied with less notable delay-effects. Further, if B-cue presentation preceded longer inter-stimulus interval, reversed pattern of activity was found in AX-70 and BX-70 condition in PAR group – a positive activity in AX-70 indicating no preparatory processes and generally higher negative activity in BX-70 as compared to other groups. It is difficult to say if the differences in context maintenance occur due to Parkinson's disease-related changes or whether their origin lies elsewhere. Alternatively, we assume that onset of preparatory processes may start sooner or later in different groups, which might explain not only contrasting pattern of AX-70 versus BX-70 activity in PAR group but also the lack of variability among other groups and young healthy adults.

Regarding target-effects, previous research has suggested that B-cue trials, which signalise response inhibition, do not evoke any task-related differences in P300 potentials after target presentation, while probes following cue A have a strong effect on the subsequent neural activity (Dias, Foxe, Javitt, 2003). To extend previous work we focused only on the latter. Our results successfully confirmed that target-related activity in chosen time window was generally higher in AY sequence than in AX, manifesting the strong need to inhibit prepared response due to presentation of non-target probe. Next, our findings supported the view that BX-70 version of AX-CPT evokes generally higher neural activity than AX-70 which is in accordance with results from other authors (Dias, Foxe, Javitt,

2003). Higher target-related activity in young healthy adults was observed across all conditions but reached the level of significance only in comparison to PCI group. This result contradicted preliminary suggestions (Kopp et al., 2014) that aging and clinical groups exhibit stronger goal reactivation associated with increased neural activity in the target-locked ERPs. The authors hypothesise about recruitment of additional regions or inefficient use of resources (Dias, Foxe, Javitt, 2003; Kopp et al., 2014). The unexpected results found in older groups might be partially explained with later latency of target-related activity. There are few studies confirming similar forward shift in P3 activity in elderly (Adrover-Roig, Barceló, 2010). However, it seems improbable that few tens of milliseconds might have had such a strong effect and produced opposite results. On this basis, we hypothesize about disturbed reactive control in PCI group and partial dissociation of cognitive control modes as compared to single-continuum idea. Similar preliminary findings of distinct character and operation of cognitive control modes was recently suggested by Gonthier and his colleagues (2016).

Taken together, the answers to our second research question related to electrophysiological characteristics of cognitive control, were not as satisfactory and clear as those from behavioural data. Even though we fully confirmed three hypotheses (H_1, H_3, H_4) and one partially (H_5), the direction of our results was reversed in some cases, and the underlying mechanisms causing those differences are still unknown.

5.3 Limitations

As noted earlier, the delay length was not set ideally. Most of the prior studies employed shorter delay lasting 1s or less and longer delay lasting 4s or longer (Braver, 2005), therefore we hypothesise that additional 500ms in short inter-stimulus interval might have attenuated some effects.

Further, the total number of study participants was not high enough to provide adequately strong evidence for many effects which were only outlined in our work. Coupled with that, the group of young healthy adults was twice as large as most of other groups, allowing space for undesired discrepancies in results. Similar alternations might have been induced by the presence of extreme values and outliers in our data. Even though we used various compensatory procedures to correct the data, it has not produced satisfactory results and artificial shift in results was observed. This problem may be reduced, again, by

including more participants to observe fuller spectrum of information and get closer to the normal distribution.

Last but not least, the time that passed since the data collection, has complicated the data analysis and generally, formation of this thesis. Unfortunately, not all original data was available and a lot of additional information about participants and problems related to data collection was difficult to find and assemble/or lost.

Admittedly, our research design was very complex for purposes of current thesis and due to formal content limitations as well as associated time limitations, we were unable to deliver a complete analysis including calculations of behavioural indices and subsequent examination of correlation between behavioural and electrophysiological data, or even further, time-frequency domain analysis, which might had brought additional interesting insights.

CONCLUSION

Cognitive control as a main feature of intelligent behaviour is one of the most studied terms in cognitive psychology and since the late 20th century, it gains more and more popularity in neuroscience, cognitive science and other related fields. This thesis provided overview of theoretical background as well as of current research related to cognitive control in context of advancing age and clinical condition. Despite the long history of the concept, many issues have been unresolved and required further scientific attention.

Our findings suggest that cognitive control does not necessarily reduce with age or clinical condition, and thanks to rich plasticity of the brain and many compensatory mechanisms, the deficits might be reflected only in slower response. Since the manifestation of cognitive decline stays hidden, it is very difficult to unveil those changes. AX-Continuous Performance task proved to be a powerful tool to capture various characteristics of cognitive control, starting with context processing, through context maintenance until response execution or inhibition. Indeed, it has easily detected intra-individual changes caused by task modification, and the difference between young healthy adults and other elderly or clinical groups. However, its evidential value in search for specific deficits among various elderly and clinical groups seems to be questionable as even those groups passed the task with relatively low number of errors and their performance exhibited little or no differences. Despite that, few contrasts between results of individuals with Parkinson's disease and other elderly groups (healthy old adults, individuals with amnestic mild cognitive impairment) indicated that distinct origins of deficits (cortical versus subcortical) may produce different activation profiles.

On the other hand, the lack of between-group differences might have rooted elsewhere than in use of not enough sensitive tool. It is difficult to compare old groups and detect significant changes between them as all those groups exhibit some deficits and they become more severe with advancing age even in healthy adults. Furthermore, many diseases (also Parkinson´s disease) manifests sub-clinically long before the diagnosis is set. Therefore, some of the individuals included in the elderly healthy group might have already exhibited changes in performance more typical for early stage of some disease and that might have altered overall results of the group.

To conclude, our research has built upon existing behavioural and neuroimaging findings and showed certain limitations and unresolved issues that need to be addressed in future investigations. The valuable asset of this thesis is the complex insight into cognitive control from different perspectives and the endeavour to study untested samples. Even though, a full description of mechanisms underlying proactive and reactive cognitive control is beyond the scope of this thesis, we would like to continue the collaboration with the Laboratory for Clinical Neuroscience at the Department of Neurology in Ljubljana and finish more complex analyses in the future. Apart from that, we provide few suggestions for future research. Firstly, more sensitive tools and bigger samples are needed. Furthermore, stronger focus on ERP latencies is required to identify not only the extent to which the control is affected but also how and in which direction those changes occur in time and in specific sample. Last but not least, full explanation of main causes for decline demands identification of additional factors associated with cognitive control. It is worth considering that those factors may lay far beyond context-processing mechanisms and may be of completely different character (e.g. affective or motivational).

REFERENCES

Aarsland, D., Cummings, J. L., & Larsen, J. P. (2001). Neuropsychiatric differences between Parkinson's disease with dementia and Alzheimer's disease. *International journal of geriatric psychiatry*, 16(2), 184-191.

Adrover-Roig, D., & Barceló, F. (2010). Individual differences in aging and cognitive control modulate the neural indexes of context updating and maintenance during task switching. *Cortex*, 46(4), 434-450.

Allport, A. (1993). Attention and control: Have we been asking the wrong questions? A critical review of twenty-five years. *Attention and performance XIV: Synergies in experimental psychology, artificial intelligence, and cognitive neuroscience*, 183-218.

Anderson, J. A., Campbell, K. L., Amer, T., Grady, C. L., & Hasher, L. (2014). Timing is everything: Age differences in the cognitive control network are modulated by time of day. *Psychology and aging*, 29(3), 648.

Anderson, J. R. (1983). A spreading activation theory of memory. *Journal of verbal learning and verbal behavior*, 22(3), 261-295.

Atkinson, R. C., & Shiffrin, R. M. (1968). Human memory: A proposed system and its control processes. *Psychology of learning and motivation*, 2, 89-195.

Baddeley, A. D., & Hitch, G. (1974). Working memory. *Psychology of learning and motivation*, 8, 47-89.

Barch, D. M., Carter, C. S., MacDonald III, A. W., Braver, T. S., & Cohen, J. D. (2003). Context-processing deficits in schizophrenia: diagnostic specificity, 4-week course, and relationships to clinical symptoms. *Journal of abnormal psychology*, 112(1), 132.

Barch, D.M. and Braver, T.S. (2005). Cognitive Control and Schizophrenia: Psychological and Neural Mechanisms (Chapter 6, pp. 122 - 159). In *Cognitive Limitations in Aging and Psychopathology.* Engle, R.W., Sedek, G., von Hecker, U., and McIntosh, D.N. (Eds.) Cambridge University Press.

Bickel, S., Dias, E. C., Epstein, M. L., & Javitt, D. C. (2012). Expectancy-related modulations of neural oscillations in continuous performance tasks. *Neuroimage*, 62(3), 1867-1876.

Botvinick, M. M., & Cohen, J. D. (2014). The computational and neural basis of cognitive control: charted territory and new frontiers. *Cognitive science*, 38(6), 1249-1285.

Botvinick, M. M., Braver, T. S., Barch, D. M., Carter, C. S., & Cohen, J. D. (2001). Conflict monitoring and cognitive control. *Psychological review*, 108(3), 624.

Botvinick, M., & Braver, T. (2015). Motivation and cognitive control: from behavior to neural mechanism. *Annual Review of Psychology*, 66.

Botvinick, M., Nystrom, L. E., Fissell, K., Carter, C. S., & Cohen, J. D. (1999). Conflict monitoring versus selection-for-action in anterior cingulate cortex. *Nature*, 402(6758), 179-181.

Brain Products GmBH (n.d.). *actiCAP 32ch Standard-2*, Munich, Germany. Retrieved December 10, 2017 from: http://www.brainproducts.com/files/public/downloads/actiCAP-32-channel-Standard-2_1201.pdf

Braver, T. S. (2012). The variable nature of cognitive control: a dual mechanisms framework. *Trends in cognitive sciences*, 16(2), 106-113.

Braver, T. S., Gray, J. R., & Burgess, G. C. (2007). Explaining the many varieties of working memory variation: Dual mechanisms of cognitive control. *Variation in working memory*, 76-106.

Braver, T. S., Paxton, J. L., Locke, H. S., & Barch, D. M. (2009). Flexible neural mechanisms of cognitive control within human prefrontal cortex. *Proceedings of the National Academy of Sciences*, 106(18), 7351-7356.

Broadbent, D. E. (1953). Noise, paced performance and vigilance tasks. *British Journal of Psychology*, 44(4), 295-303.

Brown, J. W. (2013). Beyond conflict monitoring: Cognitive control and the neural basis of thinking before you act. *Current directions in psychological science*, 22(3), 179-185.

Bugg, J. M. (2014). Evidence for the sparing of reactive cognitive control with age. *Psychology and Aging*, 29(1), 115.

Burgess, G. C., & Braver, T. S. (2010). Neural mechanisms of interference control in working memory: effects of interference expectancy and fluid intelligence. *PloS one*, 5(9), e12861.

Carter, C. S., Braver, T. S., Barch, D. M., Botvinick, M. M., Noll, D., & Cohen, J. D. (1998). Anterior cingulate cortex, error detection, and the online monitoring of performance. *Science*, 280(5364), 747-749.

Carter, E. C., Kofler, L. M., Forster, D. E., & McCullough, M. E. (2015). A series of meta-analytic tests of the depletion effect: self-control does not seem to rely on a limited resource. *Journal of Experimental Psychology: General*, 144, 796-815.

Chiew, K. S., & Braver, T. S. (2014). Dissociable influences of reward motivation and positive emotion on cognitive control. *Cognitive, Affective, & Behavioral Neuroscience*, 14(2), 509-529.

Christie, S. T., & Schrater, P. (2015). Cognitive cost as dynamic allocation of energetic resources. *Frontiers in neuroscience*, 9.

Cid-Fernández, S., Lindín, M., & Diaz, F. (2014). Effects of amnestic mild cognitive impairment on N2 and P3 Go/NoGo ERP components. *Journal of Alzheimer's Disease*, 38(2), 295-306.

Clark, H. H. (1996). *Using language*. Cambridge university press.

Cohen, J. D., Servan-Schreiber, D., & McClelland, J. L. (1992). A parallel distributed processing approach to automaticity. *The American journal of psychology*, 239-269.

Cole, M. W., Braver, T. S., & Meiran, N. (2017). The task novelty paradox: Flexible control of inflexible neural pathways during rapid instructed task learning. *Neuroscience & Biobehavioral Reviews*, 81(A), 4-15.

Conway, A., Jarrold, C., & Kane, M. (Eds.). (2008). *Variation in working memory*. Oxford University Press.

Cools, R., & D'Esposito, M. (2011). Inverted-U–shaped dopamine actions on human working memory and cognitive control. *Biological psychiatry*, 69(12), e113-e125.

Cooper, P. S., Wong, A. S., Fulham, W. R., Thienel, R., Mansfield, E., Michie, P. T., & Karayanidis, F. (2015). Theta frontoparietal connectivity associated with proactive and reactive cognitive control processes. *NeuroImage*, 108, 354-363.

Cooper, S. R., Gonthier, C., Barch, D. M., & Braver, T. S. (2017). The role of psychometrics in individual differences research in cognition: A case study of the AX-CPT. *Frontiers in psychology*, 8, 1482.

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

Deneve, S., Latham, P. E., & Pouget, A. (1999). Reading population codes: a neural implementation of ideal observers. *Nature neuroscience*, 2(8), 740-745.

Dias, E. C., Foxe, J. J., & Javitt, D. C. (2003). Changing plans: a high density electrical mapping study of cortical control. *Cerebral Cortex*, 13(7), 701-715.

Dixon, W. J., & Yuen, K. K. (1974). Trimming and winsorization: *A review*. *Statistische Hefte*, 15(2-3), 157-170.

Dopamine pathways, (n.d.). [Digital image]. Retrieved December 15, 2017 from: https://ka-perseus-images.s3.amazonaws.com/619bf914c2946a4629d70c8c561933efd1e95a2b.svg

Dosenbach, N. U., Fair, D. A., Cohen, A. L., Schlaggar, B. L., & Petersen, S. E. (2008). A dual-networks architecture of top-down control. *Trends in cognitive sciences*, 12(3), 99-105.

Egner, T. (Ed.). (2017). *The Wiley Handbook of Cognitive Control*. John Wiley & Sons.

Fales, C. L., Barch, D. M., Burgess, G. C., Schaefer, A., Mennin, D. S., Gray, J. R., & Braver, T. S. (2008). Anxiety and cognitive efficiency: differential modulation of transient and sustained neural activity during a working memory task. *Cognitive, affective, & behavioral neuroscience*, 8(3), 239-253.

Gazzaley, A., & Rosen, L. D. (2016). *The Distracted Mind: Ancient Brains in a High-Tech World*. MIT Press.

Goldstein, S., & Naglieri, J. A. (Eds.). (2013). *Handbook of executive functioning*. Springer Science & Business Media.

Gonthier, C., Macnamara, B. N., Chow, M., Conway, A. R., & Braver, T. S. (2016). Inducing proactive control shifts in the AX-CPT. *Frontiers in Psychology*, 7.

Gratton, G., Bosco, C. M., Kramer, A. F., Coles, M. G., Wickens, C. D., & Donchin, E. (1990). Event-related brain potentials as indices of information extraction and response priming. *Electroencephalography and clinical neurophysiology*, 75(5), 419-432.

Gray, J. R., Chabris, C. F., & Braver, T. S. (2003). Neural mechanisms of general fluid intelligence. *Nature neuroscience*, 6(3), 316-322.

Gure, T. R., Langa, K. M., Fisher, G. G., Piette, J. D., & Plassman, B. L. (2013). Functional limitations in older adults who have cognitive impairment without dementia. *Journal of geriatric psychiatry and neurology*, 26(2), 78-85.

Herz, D. M., Eickhoff, S. B., Løkkegaard, A., & Siebner, H. R. (2014). Functional neuroimaging of motor control in parkinson's disease: A meta-analysis. *Human brain mapping*, 35(7), 3227-3237.

Hoogman, M., Bralten, J., Hibar, D. P., Mennes, M., Zwiers, M. P., Schweren, L. S., ... & de Zeeuw, P. (2017). Subcortical brain volume differences in participants with attention deficit hyperactivity disorder in children and adults: a cross-sectional mega-analysis. *The Lancet Psychiatry*, 4(4), 310-319.

Javitt, D. C., Lee, M., Kantrowitz, J. T., & Martinez, A. (2018). Mismatch negativity as a biomarker of theta band oscillatory dysfunction in schizophrenia. *Schizophrenia research*, 191, 51-60.

Kahneman, D., & Treisman, A. (1984). Changing views of attention and automaticity. *Varieties of attention*, 1, 29-61.

Kenhub (2018). *Medial and lateral view of the brain* [Digital image]. Retrieved December 29, 2017 from: https://www.kenhub.com

Kennedy, D. O., & Scholey, A. B. (2000). Glucose administration, heart rate and cognitive performance: effects of increasing mental effort. *Psychopharmacology*, 149(1), 63-71.

Kononowicz, T. W., & Penney, T. B. (2016). The contingent negative variation (CNV): timing isn't everything. *Current Opinion in Behavioral Sciences*, 8, 231-237.

Kool, W., McGuire, J. T., Rosen, Z. B., & Botvinick, M. M. (2010). Decision making and the avoidance of cognitive demand. *Journal of Experimental Psychology: General*, 139(4), 665.

Kopp, B., Lange, F., Howe, J., & Wessel, K. (2014). Age-related changes in neural recruitment for cognitive control. *Brain and cognition*, 85, 209-219.

Kropotov, J. D. (2010). *Quantitative EEG, event-related potentials and neurotherapy*. Academic Press.

Lopez-Calderon, J., & Luck, S. J. (2014). ERPLAB: an open-source toolbox for the analysis of event-related potentials. *Frontiers in human neuroscience*, 8.

Luna, B., Padmanabhan, A., & O'Hearn, K. (2010). What has fMRI told us about the development of cognitive control through adolescence?. *Brain and cognition*, 72(1), 101-113.

Marcora, S. M., Staiano, W., & Manning, V. (2009). Mental fatigue impairs physical performance in humans. *Journal of applied physiology*, 106(3), 857-864.

Matzke, D., Hughes, M., Badcock, J. C., Michie, P., & Heathcote, A. (2017). Failures of cognitive control or attention? The case of stop-signal deficits in schizophrenia. Attention, Perception, & Psychophysics, 79(4), 1078-1086.

Miller, E. K., & Cohen, J. D. (2001). An integrative theory of prefrontal cortex function. *Annual review of neuroscience*, 24(1), 167-202.

Moustafa, A. A., Sherman, S. J., & Frank, M. J. (2008). A dopaminergic basis for working memory, learning and attentional shifting in Parkinsonism. *Neuropsychologia*, 46(13), 3144-3156.

Norman, D. A., & Shallice, T. (1986). *Attention to action*. In Consciousness and self-regulation (pp. 1-18). Springer US.

Olichney, J., Pak, J., Salmon, D., Yang, J. C., Gahagan, T., Nowacki, R., ... & Iragui-Madoz, V. (2011). *ERP Studies of Preclinical Alzheimer's Disease: P600 Abnormalities Are Common in Elderly Persons Who Later Develop MCI or AD Pathology*. In Neurology (Vol. 76, No. 9, pp. A233-A233). Philadelphia, USA: Lippincott Williams & Wilkins.

Paxton, J. L., Barch, D. M., Racine, C. A., & Braver, T. S. (2007). Cognitive control, goal maintenance, and prefrontal function in healthy aging. *Cerebral cortex*, 18(5), 1010-1028.

Posner, M. I. (1975). Psychobiology of attention. *Handbook of psychobiology*, 441-480.

Posner, M. I., Snyder, C. R., & Davidson, B. J. (1980). Attention and the detection of signals. *Journal of experimental psychology*: General, 109(2), 160.

Posner, M. I., Snyder, C. R., & Solso, R. L. (2004). Attention and cognitive control. *Cognitive psychology: Key readings*, 205.

Qi, S., Zeng, Q., Luo, Y., Duan, H., Ding, C., Hu, W., & Li, H. (2014). Impact of working memory load on cognitive control in trait anxiety: an ERP study. *PloS one*, 9(11), e111791.

Redick, T. S. (2014). Cognitive control in context: Working memory capacity and proactive control. *Acta psychologica*, 145, 1-9.

Redick, T. S., & Engle, R. W. (2011). Integrating working memory capacity and context-processing views of cognitive control. *The Quarterly Journal of Experimental Psychology*, 64(6), 1048-1055.

Repovs, G. (2010, January). Dealing with noise in EEG recording and data analysis. In *Informatica Medica Slovenica* (Vol. 15, No. 1, pp. 18-25).

Ridderinkhof, K. R., Ullsperger, M., Crone, E. A., & Nieuwenhuis, S. (2004). The role of the medial frontal cortex in cognitive control. *science*, 306(5695), 443-447.

Rosvold, H. E., Mirsky, A. F., Sarason, I., Bransome Jr, E. D., & Beck, L. H. (1956). A continuous performance test of brain damage. *Journal of consulting psychology*, 20(5), 343.

Savine, A. C., & Braver, T. S. (2010). Motivated cognitive control: reward incentives modulate preparatory neural activity during task-switching. Journal of Nuroscience, 30 (31), 10294-10305.

Schmid, P. C., Kleiman, T., & Amodio, D. M. (2015). Neural mechanisms of proactive and reactive cognitive control in social anxiety. *cortex*, 70, 137-145.

Schneider, W., Eschman, A., & Zuccolotto, A. (2002). *E-Prime: User's guide.* Psychology Software Incorporated.

Scudder, M. R., Drollette, E. S., Pontifex, M. B., & Hillman, C. H. (2012). Neuroelectric indices of goal maintenance following a single bout of physical activity. *Biological psychology*, 89(2), 528-531.

Shiffrin, R. M., & Schneider, W. (1977). Controlled and automatic human information processing: II. Perceptual learning, automatic attending and a general theory. *Psychological review*, 84(2), 127.

Shingala, M. C., & Rajyaguru, A. (2015). Comparison of post hoc tests for unequal variance. *International Journal of New Technologies in Science and Engineering*, 2(5), 22-33.

Simon, H. A. (1955). A behavioral model of rational choice. *The quarterly journal of economics*, 69(1), 99-118.

Smucny, J., Lesh, T. A., Newton, K., Niendam, T. A., Ragland, J. D., & Carter, C. S. (2017). Levels of Cognitive Control: A Functional Magnetic Resonance Imaging-Based Test of an RDoC Domain Across Bipolar Disorder and Schizophrenia. *Neuropsychopharmacology*.

Solomon, R. L. (1948). The influence of work on behavior. *Psychological Bulletin*, 45(1), 1.

Tanner Jr, W. P., & Swets, J. A. (1954). A decision-making theory of visual detection. *Psychological review*, 61(6), 401.

Van Gerven, P. W., Hurks, P. P., & Adam, J. J. (2017). Both facilitatory and inhibitory impairments underlie age-related differences of proactive cognitive control across the adult lifespan. *Acta psychologica*, 179, 78-88.

Vanderhasselt, M. A., De Raedt, R., De Paepe, A., Aarts, K., Otte, G., Van Dorpe, J., & Pourtois, G. (2014). Abnormal proactive and reactive cognitive control during conflict processing in major depression. *Journal of abnormal psychology*, 123(1), 68.

Vijayakumar, N., Whittle, S., Yücel, M., Dennison, M., Simmons, J., & Allen, N. B. (2014). Prefrontal structural correlates of cognitive control during adolescent development: a 4-year longitudinal study. *Journal of cognitive neuroscience*, 26(5), 1118-1130.

Walter, W. G., Cooper, R., Aldridge, V. J., McCallum, W. C., & Winter, A. L. (1964). Contingent negative variation: an electric sign of sensori-motor association and expectancy in the human brain. *Nature*, 203(4943), 380-384.