Balancing cognitive control mode in a dual cue version of the AX Continuous Performance Task

Increasing cognitive load to provoke reactive control mode and locus coeruleus - noradrenergic activation

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Project assignment / Master thesis at the Faculty of Medicine

UNIVERSITY OF OSLO

2/10-2015

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2015

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Abstract

Background and objectives:

Cognitive control is a term used about ways of processing information and regulating behavior, and the locus coeruleus – noradrenergic (LC-NA) system is thought to have an important role in the neural network allocating mental resources. This study aimed at affecting the balance between a proactive and a reactive cognitive control mode. The hypothesis was that the participants would use a reactive control mode with increased cognitive load. The second aim of the study was to see how cognitive load affects activity in the LC-NA system, hypothesized to elicit a load dependent LC-NA activation.

Method:

Twenty students performed the AX Continuous Performance Task (CPT), a dual response task testing cognitive control. Trials switched between single and dual cue identities to manipulate cognitive load. Pupillometry was used to measure changes in pupil diameter, an indicator of LC – NA activity. Response times, error rates and pupil dilation before and after response were analyzed.

Results:

The study showed that the increased cognitive load in the dual cue conditions had an impact on the participants, with higher error rates, longer response times and increased pupil dilation after response seen on the trials with two cue identities.

Conclusions:

The experimental manipulations had an effect on the participants, but not in a distinct reactive direction. This may be due to the experimental paradigm's unintended effect on spatial orientation in the dual cue paradigm, possibly eliciting more proactive control on these trials.

Contents

Abbrivations:

AX - CPT = AX Continuous Performance Task

DMC = Dual mechanism of control

ECV = Expected value of control

EEG = Electroencephalography

LC = Locus coeruleus

LC - NA = Locus coeruleus - noradrenergic

NA = Noradrenaline

REM = Rapid eye movement

1 Introduction

1.1 Background

The current study was initiated with two areas of interest: Can a healthy young population be manipulated to use a cognitive style imitating a reduced cognitive capacity, and is it possible to accurately measure activity in the locus coeruleus – noradrenergic (LC –NA) system, thought to reflect shifts in cognitive style? These questions include several elements from neuroscience (1). There are links towards neuropsychology and neurology, as both psychiatric (2, 3) and neurological diseases (4-6) can lead to a cognitive decline causally linked to the LC - NA system. However, this was a student project set up as a pilot study on a healthy population. The assignment is meant to be an exercise in comprehensive presentation of research for medical students, and will concentrate on the normal aspects of the topics to keep it as plain as possible. The paper will seek to give an extended but focused account of theory and research on cognitive control and the LC –NA system, a thorough presentation of the methods chosen to measure the theoretical concepts, a clear overview of the results and a cautious discussion of the theoretical implications.

1.2 Theories and research on cognitive control

1.2.1 Executive functions and cognitive control

Cognitive control is a term used about three components of cognition; prioritization of information processing, regulation of behavior and monitoring of behavior (7, 8). When we are describing cognitive control, an understanding of our executive function is central, as it can be seen as the tools used for executing cognitive control.

Two of the pioneers within establishing a theoretical understanding of executive functioning are Baddeley and Hitch (9, 10). They proposed that our executive system consists of an attention control center named the central executive, assisted by two working memory components, a phonological loop for sound stimuli and a visuo-spatial sketch pad for tactile and visual information. Norman and Shallice supplemented with a model called the supervisory attentional system, suggested to assist in prioritizing between competing response schemas when needed (11). These might be pioneer models, and can be used as a framework

for understanding our executive functioning. They address two important components, attentional control and working memory capacity.

Studies suggest that the ability to control our attention is vital to a functional working memory, as we need to filter away irrelevant information before storage (12, 13). The concept of working memory capacity has been extensively researched, suggesting three to five items as a limit for our active storage capacity (14).

1.2.2 Models on cognitive control

The dual mechanism of control (DMC) model represents one direction in understanding cognitive control, described by Todd S. Braver (7). The DMC model emphasizes the ability to anticipate future events as vital for cognitive functioning. Proactive versus reactive modes of control are terms used about two processing styles, both providing a strategy for information processing and decision making

A proactive mode will seek to establish a way of top-down processing through focused attention. While performing a task, the goal representation is kept active in working memory during the maintenance period; the time from the task is presented until it is resolved. The important factor is goal maintenance, which enhances response selection when presented with an expected stimulus. Irrelevant stimuli are filtered away. This enables task-efficiency and quick reactions (15, 16).

A reactive mode will be seen as bottom-up processing, where relatively more information are processed and categorized according to the task. Theoretically it has the advantage of flexible allocation of working memory resources in the maintenance period. Besides, when the contextual information is limited or overwhelming, a reactive mode can be more effective. However, the reactivating stimuli must be strong enough to capture our attention during the maintenance period. Moreover, when the reactivating stimulus is associated with competing responses, response selection will tend to be slowed for those using a reactive mode (15, 16).

The DMC model on cognitive control have later been supplemented by the expected value of control (ECV) model (8). The ECV model seeks to unify several theories and directions in understanding the activation of executive functions. It highlights three criteria when allocating cognitive resources: expected payoff of control, the amount of control needed for payoff and the cognitive effort one must invest to have control. The model suggests that a cost – benefit

analysis is utilized when we are allocating cognitive resources, seeking to maximize the effect of our effort.

1.3 The locus coeruleus – noradrenergic (LC – NA) system

1.3.1 Anatomy of locus coeruleus and physiology of noradrenaline

Locus coeruleus (LC) is a complex of neurons situated in the dorsal upper part of the brainstem (17). Each nucleus is around 16,0 – 18,0 mm long, with a cylindrical shape (18). They are aligned vertically along the fourth ventricle and through the upper part of pons. In humans LC consists of around 10 000 – 15 000 neurons in each hemisphere (19). It is the main source of noradrenalin in the forebrain, and the only source of noradrenaline in hippocampus and neocortex (19, 20). The only major region without noradrenergic projections from LC is the basal ganglia (21).

Noradrenaline (NA) is classified as a neurotransmitter, and it is one of the main neuromodulators in the brain (22). The cellular effect is complex, but simplified it can be described as altering cellular properties in the target cell (23) and modulating synaptic transmission between neurons by changing and preparing for changes in the membrane potential. NA is released in vesicles from the axon's terminal buttons and binds to receptors in the synapse. It is thought to exert its signaling majorly through three types of G-protein coupled receptors, α1, α 2 and β (22).

The neurons in LC have been identified to fire action potentials in two distinct ways, tonic and phasic (19, 21). Tonic firing is usually set at 1-3 Hz, but can be at 10 – 15 Hz during high arousal conditions. Tonic firing is increased during waking, and absent during REM sleep (24). Phasic firing is characterized by 2-3 action potentials at 8 – 10 Hz followed by a period of rest at 300 – 700 ms. Tonic firing from neurons in LC is well correlated with synaptic NA levels up to 5 Hz (25, 26). Phasic LC stimulation gives an enhanced NA release compared to tonic LC stimulation , and reaches a plateau from around 10 Hz (26).

1.3.2 Locus coeruleus - noradrenergic activity and cognitive functioning

Variations in LC-NA activity are thought important to cognitive processing (19, 21), and have been studied in relation to working memory, response inhibition, cognitive flexibility and emotional memory (2). In his review, Berridge et al (19) outlines two primary functional qualities of the LC - NA system in the brain (27). Firstly, LC - NA activity is strongly linked with the regulation of sleep – awake - arousal states. Secondly, LC - NA activity is thought to have important modulatory functions in processing of information. NA accentuates processing and responses of relevant stimuli, and attenuates processing and responses of irrelevant stimuli. This is illustrated in studies manipulating sensory processing of taste (28) and sounds during NA stimulation (29). The quality of LC-NA in adjusting the "filter" is also thought to take place in higher cognitive processing. The phasic - tonic firing pattern of LC neurons have been associated with two different kind of attentional states (30, 31). Phasic firing is suggested to be seen during focused attention, when the individual is engaging in exploitation to optimize a specific task performance. Tonic firing is suggested to represent a state of exploration or adaptive mode, where alternative behaviors and strategies are sought.

Expanding on the role in attentional modes, the phasic firing from LC have been suggested by Sara et al to also serve as a "reset" signal for cognitive networks (32). LC-NA activity acts by interfering with the established firing patterns in the brain, in order to reorient and adapt behavior. Corbetta et al (33) have drawn on this idea, and suggested that LC-NA activity has a central role in activating a ventral attention network, meant to help in reorienting cognitive resources. They theorized that the LC-NA burst might represent the input signal for this network, and is a part of the same neural cascade as the P300 component described in electroencephalography (EEG) studies (34), thought to derive from activation of the ventral attention network.

1.4 Measuring cognitive control with the AX-Continuous Performance Task

The AX - Continuous Performance Task (CPT) is a dual response task used to study cognitive control (15, 35). In the test participants provide a response after each two-stimulus trial. A trial consists of a cue letter (e.g. A) and a probe letter (e.g. X) presented sequentially, shortly followed by a new trial, thus the name continuous performance. The participants respond as fast as possible after the probe letter. The target trial is the AX trial, being the target cue "A" followed by the target probe "X", giving the target response. The non-target trials are

classified as AY (target cue, non-target probe), BX (non-target cue, target probe) and BY (non-target cue, non-target probe), all giving the non – target response.

AX trials typically occur at a high frequency and the non-target trials at a low frequency. Many studies use a 70 – 10 – 10 – 10 distribution (35, 36), which has been shown to facilitate a proactive mode as the cue A predicts a target response for X with a probability of 0,875. The BX trial will interfere with a reactive mode, as bottom-up processing will be lured by the target probe X. Those using a proactive mode will tend to have lower error-rates and quicker response times on AX, BY and BX trials. They use the cue letter to prepare a response for the probe. In the AY trial, a proactive mode demands a level of response inhibition. This is well documented in previous studies (35-37), showing increased response time and error rate on the AY trial.

Among healthy adults, a proactive mode will be effective when AX trials are presented at a high frequency. The cost of keeping the cue letter maintained is paid off by few errors and quick responses on most trials. It is usually no difference in the response data between BX and BY trials for healthy participants, as they know that the probability for a target trial is 0 when they see the B cue (38).

A study (16) comparing healthy older adults with a control group of younger adults revealed the lure BX – effect and the reduced AY - effect in the older group, indicating a preference for reactive control mode. Their reactive mode was amplified by a distractor stimulus presented in the cue – probe interval, challenging their capacity for maintaining the cue in order to be proactive. This effect can partly be explained by working memory capacity (15). Proactive control will be favored when cognitive resources are available and can be used with a reasonable cost. By bringing up the cognitive load in the cue – probe interval, a proactive mode will be increasingly demanding. The study highlights that both experimental manipulations and group differences can be factors explaining cognitive control mode.

1.5 Measuring locus coeruleus – noradrenergic activity with pupillometry

Berridge (19) describes in his review some of the challenges with research on the LC-NA system: *"The nature of the measures used requires a relatively large effect size to conclude an impact of NE neurotransmission on a particular system/ process. In contrast, normal*

human behavior is likely highly sensitive to slight alterations in activity rate and activity patterns of neural systems which are difficult to measure with available methodology". Using pupillometry to study LC-NA is a method to meet this challenge. There have been a large amount of studies asserting the benefits of registering pupil size changes, pupillometry, to measure LC-NA activity (39). The physiological mechanism noradrenaline have on pupil size is suggested to be through two neuro – muscular pathways (40, 41). There is an initial noradrenergic inhibitory effect on the neural trajectory of Edinger – Westphal complex - parasympathetic n.oculomotorius- m. sphincter pupillae. The secondary effect is through sympathetic activation of the m. dilatator pupillae.

As described in a recent pupillometry review (42), the adult pupil range in diameter from 3 mm in a normally lighted room (43) to 7 mm in a sparsely lit room (44). So, lighting conditions can lead to over a 100 % change in pupil size. During cognitive tasks the variations in pupil size are less pronounced, with changes in diameter seen up to 0,5 mm under fixed lighting conditions (45) (46). The pupil response during cognitive tests typically has a onset 200 – 500 ms after stimulus presentation, peaks around 1000 ms later and return to baseline rapidly after stimulus offset (40, 47). Pupillometry is a practical method because it is non-invasive and cost - effective. From a scientific viewpoint, one of the advantages of pupillometry is the relative specific measure of LC-NA activity as an indicator of arousal and effort.

Some of the first studies on sensory processing and pupil size were performed in the 1960's (48), and a strong association between increased pupil diameter and working memory load / mental effort was identified (49, 50). Later there have been suggestions of pupil dilation in relation to attentional shifts (51), degree of attentional effort (46) and facilitation of behavioral responses after decision making (52).

1.6 Pupillometry during AX-CPT-studies

There have been some studies using pupillometry during the AX-CPT over the last years, describing cognitive development in early childhood (37), the effect of reward incentives on cognitive control (35, 36) and the effect of positive emotion on cognitive control (36). A firm finding has been that during the cue -probe interval, pupil dilation is greater on B - than A - trials. Chiew and Braver (36) suggest this may be due to a greater preparatory effect on the non-target trials as they have more predictive validity, or that it is a reflection of the low

frequency of B – cue trials. Since only 20 % are B-trials they deviate from the standard pattern, and represent a conflict with the established stimuli rhythm. The first interpretation seems to be supported by Sara et al ‘s theory on phasic LC – NA activity as a reorienting signal (33).

Neither of the studies mentioned have described the pupil reaction after probe onset, although response times and error rates are trial dependent and registered after probe. This calls for an analysis of pupil size changes in this period as well, and not only in the cue – probe interval.

2 Purpose of study

The purpose of the current study was to investigate if we could provoke a reactive cognitive control mode and measure the associated LC - NA activity. If we successfully increased the cognitive load, it would be more demanding to keep the cue active in working memory. The participants' responses would be affected, indicating a change in control mode. This should be seen on error – rates and response times for BX trials, reflecting vulnerability for the "false" target probe. A reactive shift should give less errors and quicker responses on the high load AY – trial. Earlier studies have shown a trial dependent effect when the control trials and experimental trials have been mixed within blocks (35). Therefore we expected the control mode to shift back to proactivity at low – cognitive load trials. The high load AX and BY trials were expected not to be affected by the experimental manipulations. The pupil data in the post – probe phase would be expected to show a similar pattern as the response data, if the method gives an accurate measure of LC-NA activity.

2.1 Hypotheses

1) Increased cognitive load in the cue – probe interval will provoke a reactive control mode on high – cognitive load trials, giving more interference in BX – trials and less interference with the AY trials compared to the low – cognitive load trials.

2) Increased cognitive load will demand cognitive resources, with increased pupil dilation as an indication of LC-NA activity as a result.

    a) Pupil dilation changes after probe presentation should correspond with the hypothesized patterns in the behavioral data

    b) Pupil dilation changes in the cue - probe interval should be increased with higher cognitive load

3 Method

3.1 Participants

Twenty participants took part in the experiment (19-28 years of age, mean age 22 years +- 2.7 years, 16 females). The participants were all students, mainly at the Faculty of Social Science, Department of Psychology at the University of Oslo who had been recruited at seminars and lectures. The experiments took place at the cognitive laboratory at the Department of Psychology from February to March 2014.

Ethical considerations and approval

The experiment was approved for by the Regional Ethical Committee for research. All participants signed a written consent, and were self-reported free of neurological, psychiatric and drug-abusing disorders. The participants were assured that their responses were confidential and anonymous. They received a gift card at 200 NOK for participating.

3.2 Equipment

Computer test room: The participants performed the computer test in a soundproof room where illumination was kept constant.

Computer screen: 24-inch BenQ XL2420T LED monitor

Software: E-prime was used for presentation of the AX - CPT.

Eye tracker: Eye pupil diameter was measured using an iView X R.E.D. Hi-Speed eye-tracking system (SensoMotoric Instruments, SMI, Teltow, Germany) at a sampling rate of 60 Hz, and data recorded using the iView X Software (SMI, Teltow, Germany)

Pupil data: Pupil data were pre-processed in R (version 3.1.1) using RStudio (version 0.98.1049), and used for graphical illustration of pupil response over time.

Response box: Serial Response Box Model 200a (Psychology Software Tools) was used to collect responses for E-prime.

Cognitive test room: After the computer test the participants completed a set of cognitive tests in a separate soundproof room.

Statistical analysis: IBM SPSS Statistics 22.0 was used for data analysis.

Chart builder: Microsoft Office Excel 2010 was used for chart building

Illustrations: Windows Paint was used for illustration of test paradigm

3.3 Experimental design

The experiment was a modified version of the AX-CPT (15), changing the standard version in mainly two ways. Firstly, 64 % of the trials were AX-trials and 12 % of the trials were respectively AY, BX and BY trials. With this distribution, the A cue gives 0,842 probability for the X probe. Secondly, a change was made in order to increase the cognitive load.

- In the pre-cue / baseline period a black fixation mark "+" would be seen in the middle of a blue screen for 700 ms.

- Then two cue stimuli, instead of one, were presented on each side of the fixation cross simultaneously from 700 – 1000 ms. The cues were the identical in the single cue condition, but different in the dual cue condition. This was meant to demand more cognitive resources, as two identities would be kept active in the cue – probe interval.

- The cue – probe interval lasted from 1000 to 3700 ms with the fixation mark remaining in the middle of the screen.

- The probe was then presented at one side of the fixation mark from 3700 – 4000 ms, determining which of the cues having validity for response selection.

- After the probe the fixation mark remained from 4000 - 6200 ms, allowing for pupil size to return to baseline.

- Finally a 500 ms feedback slide appeared. The feedback slide was unchanged from the post – probe slide on correct responses, but on incorrect responses the fixation cross turned red and a sound was presented.

- Between each trial there was a 100 ms inter-trial interval

The experiment consisted of two blocks of 200 trials, counterbalanced in order. Of the total of 400 trials, 256 of them were AX trials, 48 AY trials, 48 BX trials and 48 BY trials. Half of each trial type was dual cue trials. The single cue trials were included as a control paradigm.. The trials were distributed in blocks using a stratified randomization, to make sure the dual and single trials were mixed in each block and that the AX-trials were evenly presented throughout. Besides the targets A and X, the stimuli used as B were B, C, E, F, J, L, M, R, S, T,U and V. The stimuli used as Y were M, N, Q, T and U.

The participants answered with a response box, pressing the key to the right for AX trials and the key to the left for the non - target trials. They were instructed to respond "as fast as possible without making mistakes" after the probe.

3.3.1 Illustration of AX-CPT paradigm

Figure 1 – 3 illustrate how the test appeared on the computer screen. Note that single cue and dual cue trials were mixed across the two blocks, and that the location of the cues and probes were counterbalanced.

Figure 1: Examples of single A cue- trials, AX at top and AY at the bottom

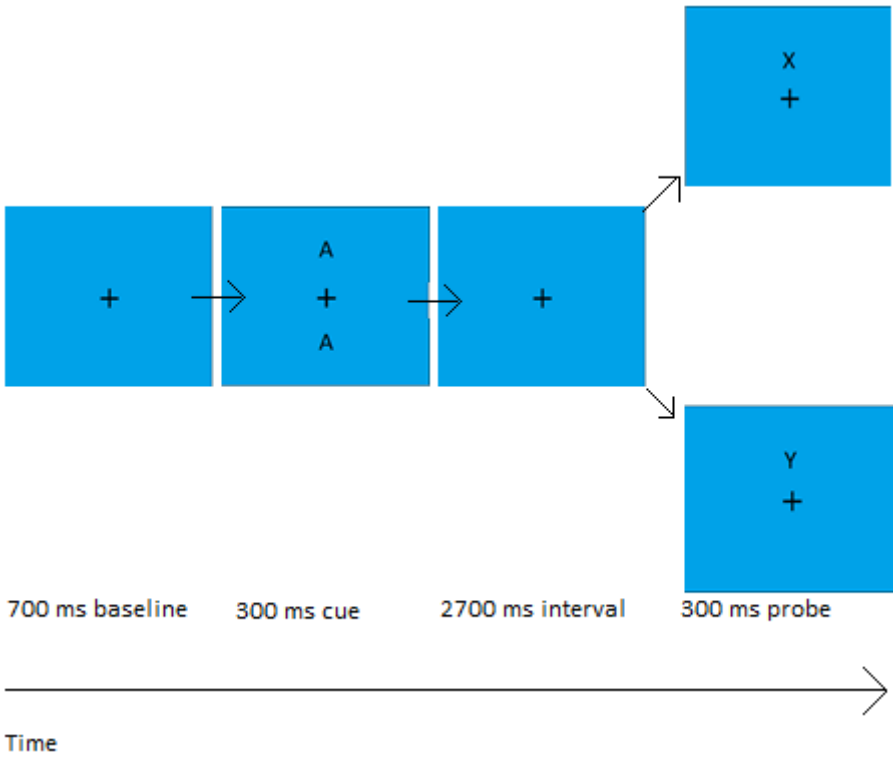


Figure 2: Examples of single B cue – trials, BX at the top and BY at the bottom

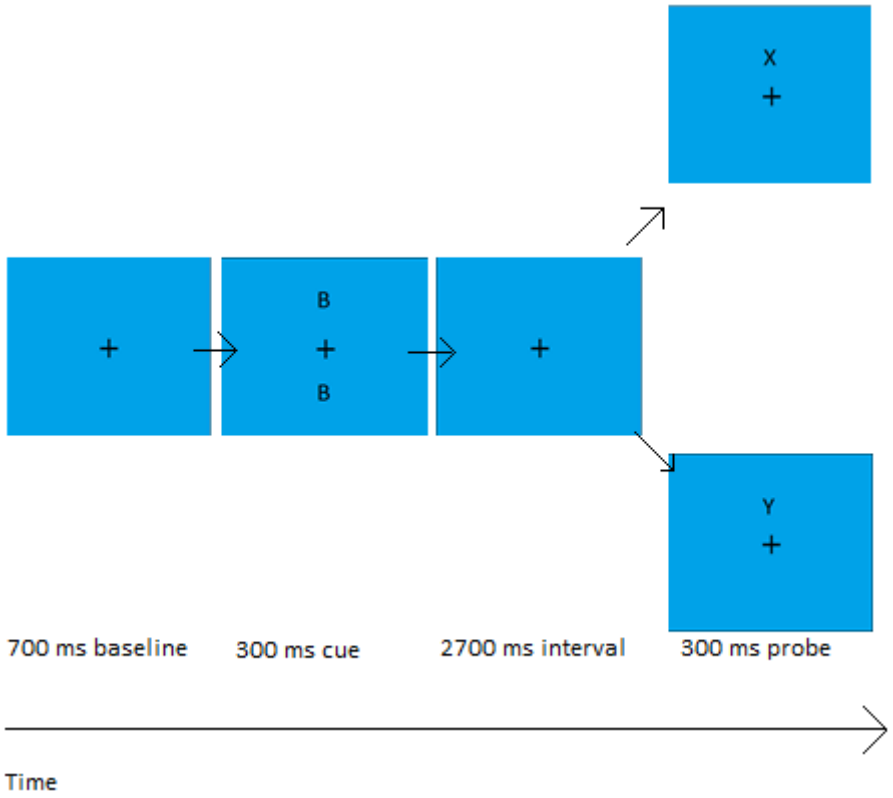
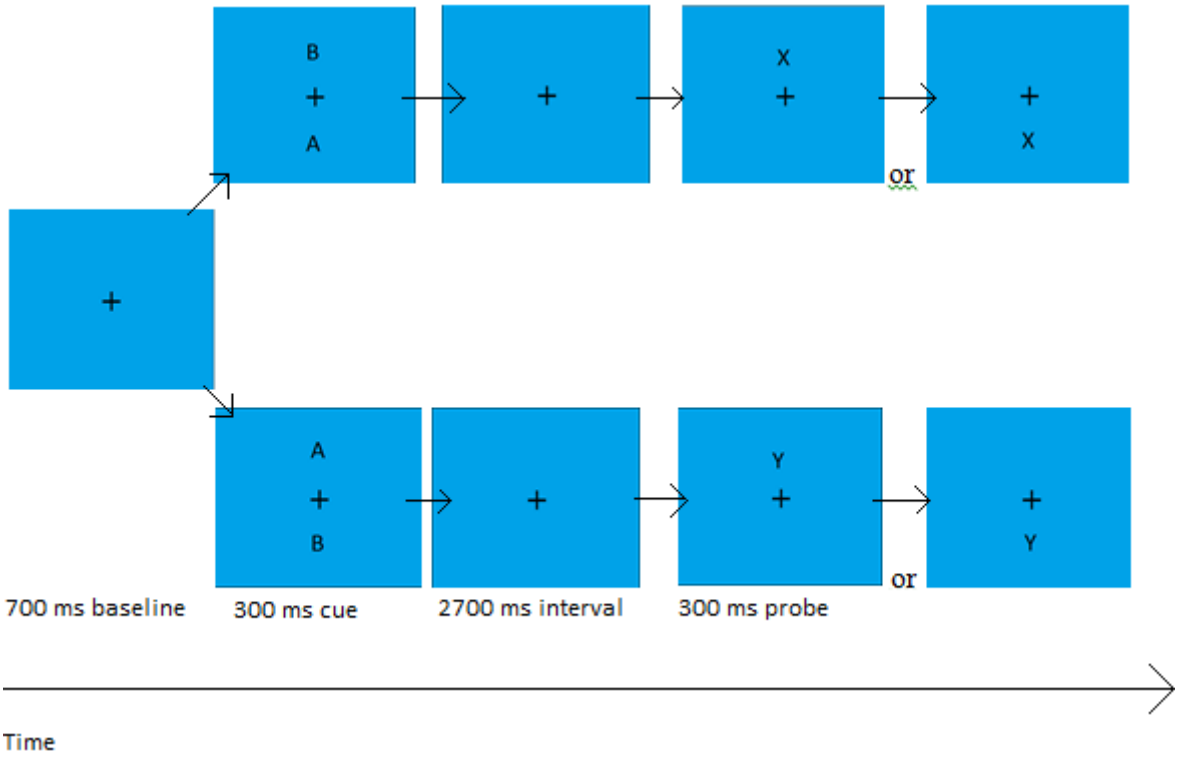


Figure 3: Examples of dual cue trials. At the top are the dual BX trial (left) and the dual AX trial (right), at the bottom are the dual AY trial (left) and the dual BY trial (right)



3.4 Test procedures

The experiment started with the participants answering a questionnaire with inclusion and exclusion criteria. They received written and oral instruction of the AX-CPT with examples of the different trial types, performed nine test trials on paper and performed 20 test trials (13 AX, 2 AY, 4 BX, 2 BY) at the computer under supervision, identical to the test itself. They were placed in a chair without head support in a distance from the screen optimal to the eye-tracker. They were instructed to limit their head movement during the test. The eye tracker was calibrated with a 9-point fixation procedure with the precision of horizontal – vertical gaze estimate aimed at being below 0,5 mm.

The participants performed each experimental block alone in the test room. The 200 trials were presented continuously, except of three mandatory pauses after 50, 100 and 150 trials at around 20 seconds. For each 50 trial block the participants would sit with their eyes fixed at the computer screen for around 6 minutes while responding. They were instructed not to leave the test chair due to eye- tracker calibration in the short breaks, but they could drink water and eat some snack. After 200 trials the participants could have a longer break if needed, before re-calibrating the eye-tracker and engaging with the last 200 trials in the same manner as in the first part. Test time at the computer was approximately 45 minutes, not included the time for instructions, calibration and breaks.

After the computer test the participants were taken to another room to perform a set of cognitive tests (see appendix). The first two tests were the Stroop – test and the Letter Number Span test from WAIS III. Then two Ravens Progressive Matrices tests were performed sitting alone, first 12 matrices without time limit and then 36 matrices with 40 minutes time limit. The three first tests would normally take about 15 to 20 minutes. The total time of the whole experiment was around 2 hours and 15 minutes.

3.5 Data preprocessing and analysis

Of the 20 participants, all were included in the data analysis. Four dependent variables were registered for analysis: Error rate, response time, pupil size change after probe and pupil size change in the cue – probe interval.

Error rate: All incorrect responses were included, meaning both trials without a registered response and trials with erroneous response.

Response time: Only correct responses between 200 ms and 1300 ms after the probe presentation were registered for analysis in ePrime.

Pupil data: Pupil data were filtered on ePrime. Only trials with correct responses between 200 ms and 1300 ms after probe presentation were included in the pupil data analysis.

- Baseline values were calculated as mean pupil size during the 0 - 700 ms baseline period.
- Pupil response values after probe presentation were analyzed from 4000 – 6000 ms.
- Pupil response values in the cue – probe interval were analyzed from 1000 – 3500 ms.

Data analysis:

- Error rates, response times, pupil size changes after probe and pupil size change in the cue – probe interval were analyzed separately as dependent variables with a repeated measures analysis of variance.
- For the first three ANOVA's we conducted a 4 x 2 ANOVA with two within – subjects factors: The factor *trial condition* with four levels (AX, AY, BX and BY) and the factor *cognitive load* with two levels (single cue – dual cue).
- For the analysis of pupil response in the cue – probe interval we conducted an ANOVA with *cue condition* as a within - subjects factor with three levels: single A – cue, single B – cue and dual cue.

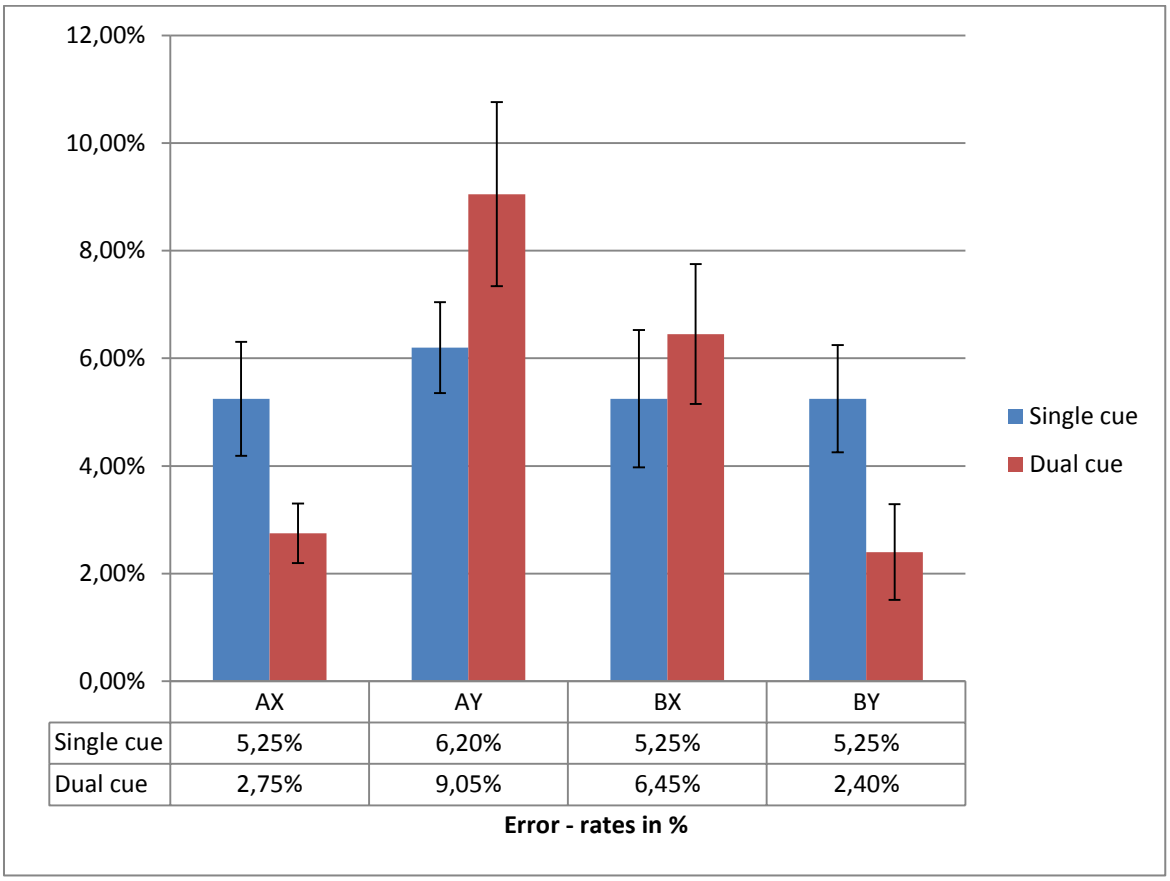
Hypothesis testing: Paired samples T – test were conducted to test the specific hypotheses against the null hypothesis.

Neuropsychological data: An overview of the frequency data from the neuropsychological tests is included in appendix.

4 Results

4.1 Error rate variance

Figure 4: Error-rates in percent



	AX	AY	BX	BY
Single cue	5,25%	6,20%	5,25%	5,25%
Dual cue	2,75%	9,05%	6,45%	2,40%

Error - rates in %

A 4 x 2 repeated – measures analysis of variance (ANOVA) was conducted for the group's error – rates.

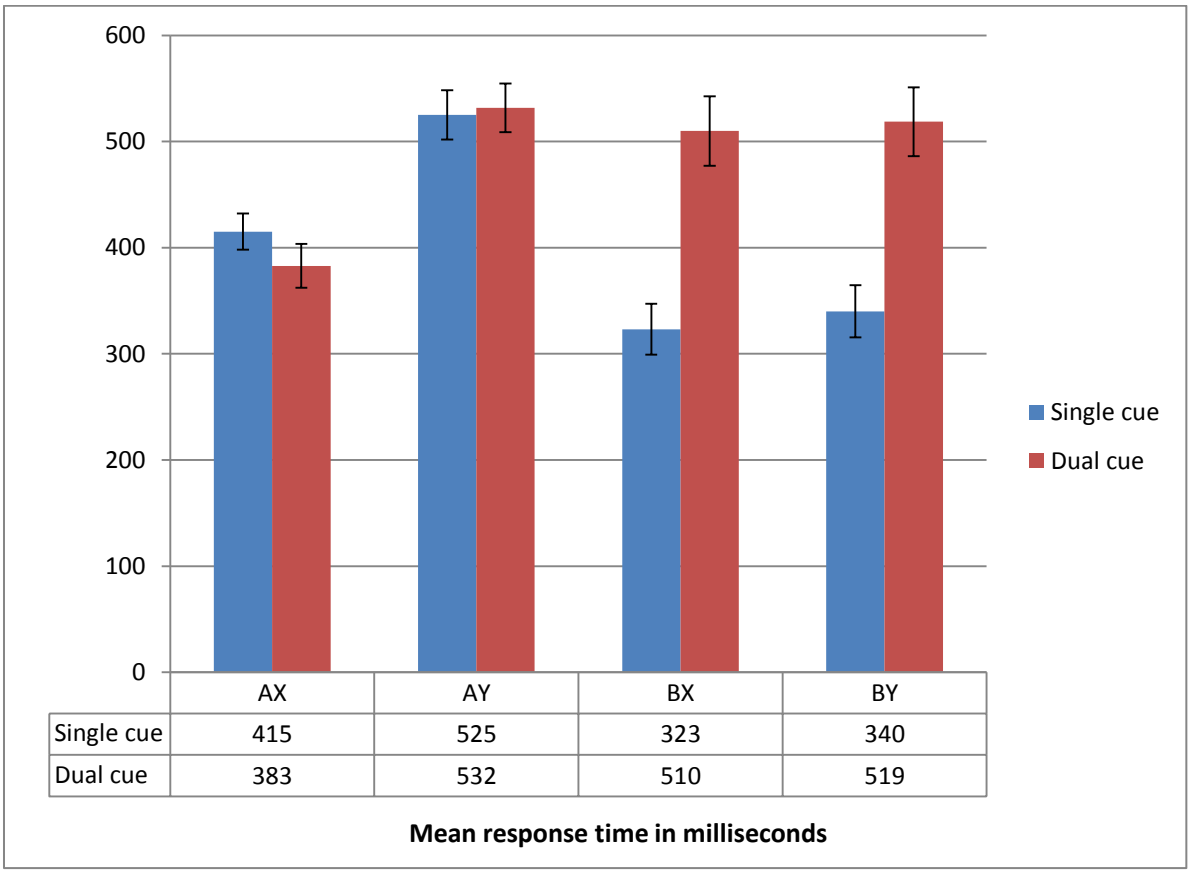
For the main effect of trial condition, the ANOVA indicate a significant effect on error rates, $F(3, 57) = 6, 78$, $p = 0{,}001$, $\eta^2 = 0{,}263$. This effect was caused by increased error rates in AY and BX trials.

For the main effect of increased cognitive load (the single – dual cue manipulation), there was no significant effect on variance in error rates, $F(1, 19) = 0{,}389$, $p = 0{,}540$, $\eta^2 = 0{,}020$.

Looking at the interaction of trial condition and single – dual cue manipulation, there was a significant effect on error rates, F (3, 57) = 6, 00, p = 0,001, η^2 = 0,240. This effect was seen in the dual AX and BY trials, with lower error rates than in the single cue paradigm, while the dual AY condition had a higher error rate than in the single cue condition.

4.2 Response time variance

Figure 5: Response times in milliseconds.



	AX	AY	BX	BY
Single cue	415	525	323	340
Dual cue	383	532	510	519

Mean response time in milliseconds

A 4 x 2 repeated – measures analysis of variance (ANOVA) was conducted for the group's response times.

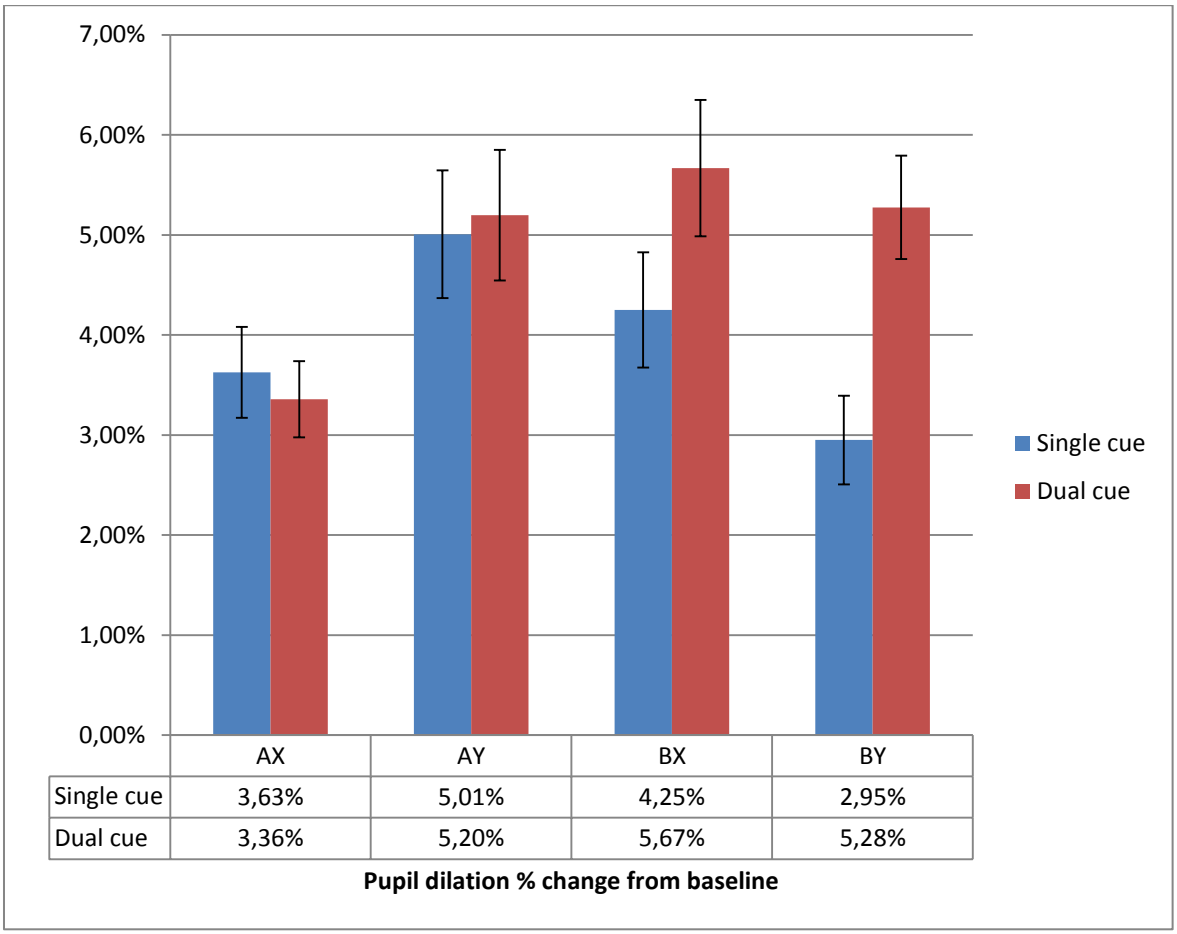
The main effect of trial condition showed a significant effect on response time, F (3, 57) = 48,20, p < 0,01, η^2 = 0,717. This effect was seen with increased response time in AY trial especially, and in the BY trial compared to the AX trial as well.

The main effect of single – dual manipulation had a significant effect on response time, F (1, 19) = 48, 47, p < 0, 01, η^2 = 0,718. This effect was seen with increased response time in the dual cue paradigm compared to the single cue paradigm.

The interaction of trial condition and single – dual manipulation showed a significant effect on response times, F (3, 57) = 82, 04, p < 0,001, η^2 = 0,812. This effect was seen as the dual BX and BY trials had increased response time compared to the single cue paradigm.

4.3 Pupil size variance

Figure 6: Percent change in pupil dilation from baseline to after probe presentation



	AX	AY	BX	BY
Single cue	3,63%	5,01%	4,25%	2,95%
Dual cue	3,36%	5,20%	5,67%	5,28%

Pupil dilation % change from baseline

4.3.1 Pupil dilation after probe

A 4 x 2 repeated – measures analysis of variance (ANOVA) was conducted for the group's pupil dilation after probe presentation.

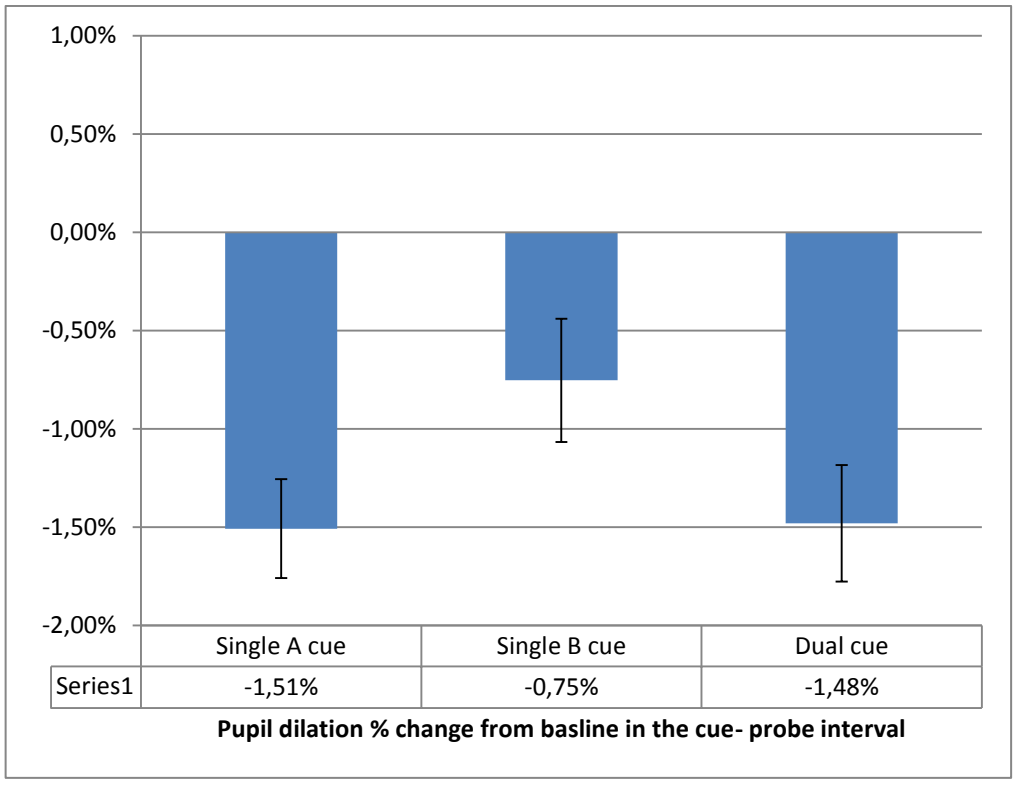
The main effect of trial condition showed a significant effect on pupil dilation, F (3, 57) = 12, 46, p < 0,001, η^2= 0, 396. This was caused by increased pupil dilation in the AY, BX and BY trials compared to the AX trial.

The main effect of single – dual manipulation showed a significant effect on pupil dilation, F (1, 19) = 16, 71, p = 0,001, η^2= 0, 468. This was caused by increased pupil dilation in the dual cue paradigm.

The interaction of trial condition and single – dual manipulation showed a significant effect, F (3, 57) = 8, 01, p = 0,001, η^2= 0,297. This interaction was seen in the BX and BY trials, with increased pupil dilation in the dual cue paradigm compared to the single cue paradigm, while the variance in AX and AY trial was relatively unaffected by the single – dual manipulation.

4.3.2 Pupil size change in the cue – probe interval

Figure 7: Percent change in pupil size from baseline to the cue – probe interval



A repeated measures analysis of variance (ANOVA) was conducted for the group's pupil size change in the cue – probe interval with cue condition as a within – subjects factor with three levels.

The main effect of cue condition showed a significant effect on pupil size change, F (2, 38) = 8,60, p = 0,001, η^2= 0,312, The effect was caused by less constriction of the pupils in the single B – cue condition.

Figure 8: Graph of pupil size change over time in all conditions (0,01 = 1 %)

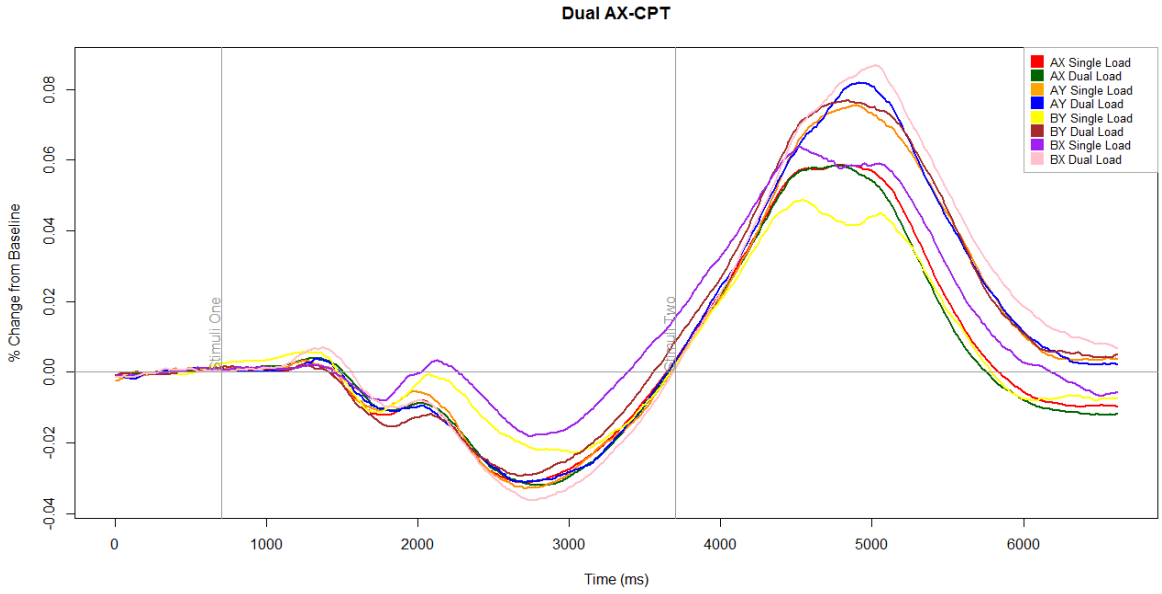
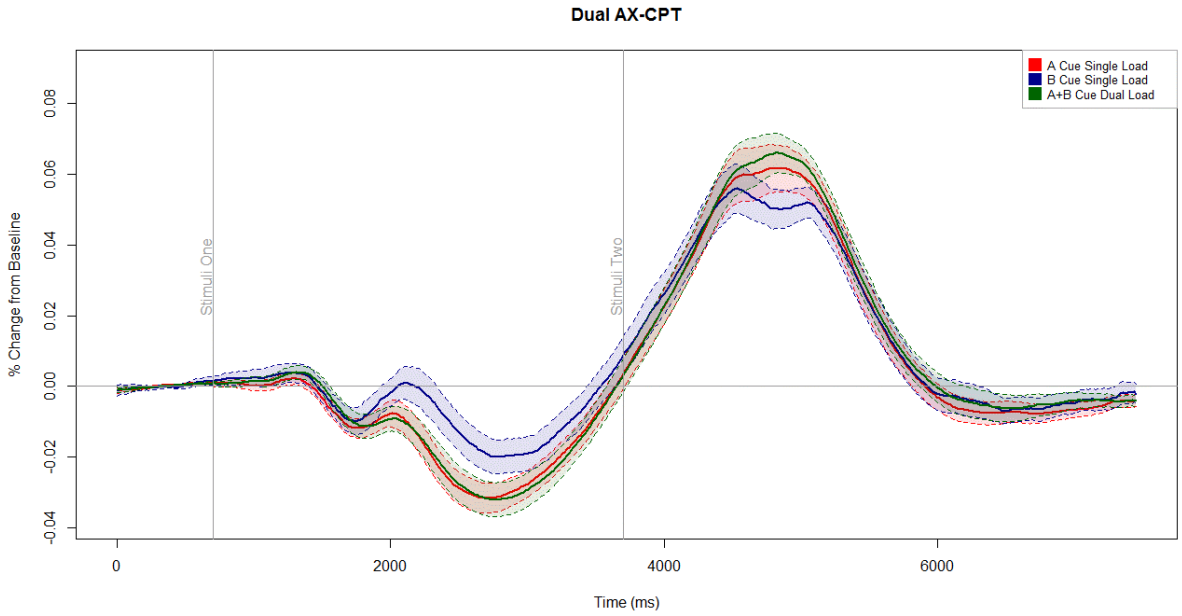


Figure 9: Graph of pupil size change over time in the cue – conditions (0,01 = 1 %)



4.4 Testing the hypotheses with paired samples T - tests

Hypothesis 1:

There will be increased response time and error rate in the dual BX trial compared to the single BX trial, and decreased response time and error rate in the dual AY trial compared to the single AY trial.

- Testing the error rates in the BX trials, there was not a significant increase in error rates from the single cue (M = 5, 25 % SD = 5, 7 %) to the dual cue (M = 6, 45 % SD = 5, 81 %) condition, t (19) = - 1, 189, p = 0,249.

- Testing the response times in the BX trials, there was a significant increase from the single cue (M = 323, 2 ms SD = 106.6 ms) to the dual cue (M = 509,9 ms SD = 146,6 ms) condition, t (19) = - 8,359, p < 0, 001.

- Testing the error rates in the AY trials, there was not a significant decrease from the single cue (M = 6,2 % SD = 3,78 %) to the dual cue (M = 9,05 %, SD = 7,6 %) condition, t (19) = - 1, 762 p = 0, 094.

- Testing the response times in the AY trial, there was not a significant decrease from the single cue (M = 525, 1 ms SD = 103,8 ms) to the dual cue (531, 8 ms SD = 102,4 ms) condition, t (19) = - 0,065, p = 525.

Hypothesis 2:

a) After the probe presentation there will be increased pupil dilation in the dual BX trial compared to the single BX trial, and a decrease in pupil dilation from the single AY trial to the dual AY trial

- Testing pupil dilation in the BX trials, there was a significant increase in pupil size from the single cue (M = 4, 25 % SD = 2, 58 %) to the dual cue (M = 5, 67 % SD = 3, 04 %) condition, t (19) = - 3, 210 p = 0,005.

- Testing pupil dilation in the AY trials, there was not a significant decrease in pupil size from the single cue (M = 5, 01 % SD = 2, 85 %) to the dual cue (M =5,20 % SD = 2,92 %) condition, t (19) = - 0,490 p = 0,630.

b) There will be increased pupil dilation in in the cue – probe interval in the dual cue condition compared to the single A cue condition

- Testing pupil dilation in the cue – probe interval, there was not a significant increase in pupil dilation from the single A cue condition (M = - 1, 51 SD = 1, 13 %) to the dual cue condition (M = - 1, 48 % SD = 1, 33 %), t(19) = -0,172 p = 0,864. For all three conditions there was a net reduction in pupil size in the cue – probe interval compared to baseline.

5 Discussion

The current study indicates that the increased cognitive load in the dual cue condition did have an impact on both the behavioral data and the pupil data, but not in a reactive direction. The dual cue condition gave an effect on the two trials challenging cognitive control mode, the AY - and BX – trial. Both trials had increased error – rates, response times and pupil dilation in the dual cue paradigm. The effect was partially seen on the dual BY – trial as well. The effect on the dual AY trial was in opposite of the hypothesis, and the effect on the dual BY trials was unintended.

Starting with discussing the single cue condition, it was included as a control paradigm and was expected to have the same response data patterns as a standard AX – CPT with only one cue. The results showed that the error-rates in the single cue condition did not have significant variance between the trial conditions. This is an uncommon finding in the standard AX-CPT paradigm, although the trend was an increased error - rate on the AY - trial. The response time on AY - trial was significantly increased compared to the other trials. This is a classical finding in a standard AX-CPT. The response time in the B – cue trials were faster than in the A – cue trials, also a normal finding among healthy participants. The changed distribution of trials, 64 – 12 – 12 – 12, was not analyzed as a controlled intervention, but did not seem to affect the participants cognitive control mode drastically.

Looking at the pupil dilation in the single cue condition, the results correspond to the response times. The pupils were relatively more dilated in the AY trial compared to the other trials, thought to reflect the increased effort needed to inhibit the prepotent target response with activation of the LC – NA system. There was also a non-significant increase in pupil dilation in the BX condition, possibly reflecting recruitment of control due to irrelevant retrieval of the X target identity. The single trial condition seems to replicate the behavioral data results from the standard AX-CPT, apart from the non-significant variance in error – rates. The pupil response data seem to correspond with the behavioral data, supporting the use of pupillometry to measure LC – NA activity.

In the dual cue condition, the hypothesis was that the paradigm would result in a load dependent reactive control shift. As described in the method section, the dual BX trial had an A and a B cue, and then the X probe presented at the same location as the B cue. We expected this trial to have increased response time and error rate compared to the single BX trial, and

possibly increased pupil dilation as an indicator of LC-NA activity. The dual BY trial also had an A and a B cue, but now followed by a Y probe at the same side as the B cue. We did not expect this condition to differ from the single BY trial in behavioral data or pupil data. On the dual AY – trial, we did not expect the standard interference with a proactive mode. If the manipulation gave a load dependent tuning towards reactivity, the dual AY – trial should have lower response time and error rate than in the single AY - trial.

The data on the dual cue condition showed a less coherent pattern than expected. The error rates were lower in the dual B – cue conditions, while the response time and pupil dilation were at the same level for the dual BX and BY - trial, as well as in the dual AY - trial. The dual AY – trial results seems to indicate increased proactivity compared to the single AY – trial, opposite of our hypothesis. As mentioned, the manipulations in the dual cue condition were meant to affect the BX – trial with more interference and the AY – trial with less interference as an indicator of reactivity, without interacting with the BY – trial.

There are some explanations for the dual cue condition's effect on the AY, BX and BY trials. The interference on the dual B cue – trials could be interpreted as an effect of invalid spatial cueing, described by Posner (53). In the dual cue condition there would always be A - and B - cue. Only the A – cue is relevant when preparing a target response, and 64% of the dual cue trials were target trials. The participants possibly chose not to "pay" attention to the B – cue line, as it had less relevance when forced to choose between the cues. Therefore, the dual cue condition gave an invalid spatial cueing effect on B - cue trials, demanding reorientation from the A – cue location to respond. This could explain the discrepancy between error rates and response times in the dual B- cue trials. The paradigm did not trigger more incorrect responses but did demand some processing time to reorient and respond. This would be in line with Corbetta et al's (33) theory on phasic LC – NA activity as a reorientation signal to activate a ventral attention network, demonstrated by the increased pupil dilation on the "invalid" spatial cues.

As for the dual AY – trial, the cue was valid in terms of location of the probe, but this possibly provoked another effect. The standard proactive interference on AY – trials might have been amplified by the spatial cueing. The condition demanded even more inhibition of the prepotent response when the Y probe was presented at the spatially expected location of the target probe X, as seen with increased error rate from the single cue to the dual cue condition. Instead of less interference with the AY – trial, the dual cue condition gave

enhanced cue maintenance. The results indicate that the effect of the AY trial is very solid across different manipulations, and it is difficult to neutralize in a population of healthy young adults.

In the cue – probe interval the pupils had a net constriction, instead of dilation as reported from other studies by Chiew and Braver (35, 36). There was however a larger pupil diameter in the single B –cue than in the single A- cue condition, partly replicating Chiew and Braver's results. The dual cue condition had a similar change in pupil size as the single A - cue condition, rejecting the hypothesis of cognitive load increasing pupil dilation in the cue – probe interval. The results from the present study might support Chiew and Braver's (36) interpretation of the pupil response in the maintenance period on B – cue trials as a reflection of greater predictive value. They suggested that the pupil dilation is a response to activation of a proactive control process. Single B - cue trials were the only ones disabling the possibility of a target response after cue presentation, eliciting an early activation of the LC – NA system to reorient. If this is correct, the increased cognitive load in the dual cue trials did not engage the same cognitive resources and LC – NA activation in the cue – probe interval as the proactive control shift in single B – cue trials.

An interesting finding from the experiment is the effect of spatial cueing in the dual cue condition, as the cue letters were presented at different locations simultaneously. This provoked an unintended spatial focus. A possible interpretation of the experimental manipulation's effect on cognitive control is that the paradigm enhanced the participant's proactive mode instead of their reactive mode. Their proactivity strategy was a combination of target cue identity maintenance and target cue location maintenance in the dual – cue trials, while the single – cue trials only needed target cue identity maintenance. This possibly demanded more response inhibition for all the non – target trials in the dual cue condition, as a result of their focused attention and proactive control mode. The study was meant to provoke a reactive cognitive control shift among healthy young adults. Possibly some of the elements from the experimental design could be used in enhancing proactivity among populations with reduced cognitive functioning.

5.1 Limitations and strengths

The results of this study must be seen in light of some limitations. This thesis is based on an experiment using a routine task. The task demands a steady level of attention from the

participants to provoke an effect from the different conditions. Time spent on a task is described as giving both negative and positive effects, depending on the type of task (54). Being a routine task with 400 trials, the experimental manipulations are possibly affected by time a negative manner, making it more demanding to allocate cognitive resources and possibly reducing the LC – NA activation. This is not controlled for in the data analysis, but was targeted when setting up the experiment with short breaks at every 50th trial.

A limitation in the analysis of the response times and pupil data is the inclusion criteria, since only correct response trials are included. This might be reasonable, as erroneous responses are known to activate frontal networks associated with attentional control (55), possibly also interacting with the LC – NA system (56). However, the analysis is of two separate sets of trials, the incorrect trials with the error – rates and the correct trials with response times and pupil dilation. A possible problem is that the dependent variables are not analyzed from the same set of trials, implicating theoretical limitations when we are comparing the data and expecting them to correlate as a result of cognitive control mode. Furthermore, there may be a loss of effect size in the analysis the response time data and pupil data when the incorrect trials are not included.

The strengths of the study are the systematic nature of the experiment, enabling control of unwanted factors. The AX – CPT is a popular experimental design, so previous studies using the method make up a solid empirical basis for comparing results. This provides a foundation for interpreting the results, and understanding unexpected effects from the experiment.

6 Conclusion

In spite of possible limitations, the results of this study add knowledge about the specific effect of the cue – manipulations and the pupil dilation after response. The experimental paradigm had an opposite effect on response time and pupil dilation in the dual AY – trial and an unexpected effect at the same measures in the dual BY-trial, thought to be a result of spatial cueing. There are areas of improvement regarding future studies using pupillometry. One of them is gathering a solid empirical basis about the pattern of the pupil response, and which time segments to focus on, e.g. maintenance interval versus response phase. The present study shows correspondence between behavioral data and pupil data in the response phase. Further knowledge would help developing more sensitive and specific analysis of the pupil response, and give insight about the role of LC – NA activation in cognitive functioning.

Acknowledgement

This study has been carried out at the Faculty of Medicine and in cooperation with the Faculty of Social Science, Department of Psychology of the University of Oslo. I am particularly grateful to my supervisor Thomas Espeseth. His comments and suggestions related to the experiments, statistics and presentation have been greatly appreciated. Special thanks to Thomas Hagen at the Department of Psychology, who was of vital importance at the cognitive laboratory in helping me planning and executing the experiment and preprocessing the data.

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Appendix

Figure 10: Stroop inhibition task. Participants were told to read the color of the letters instead of the name of the color written

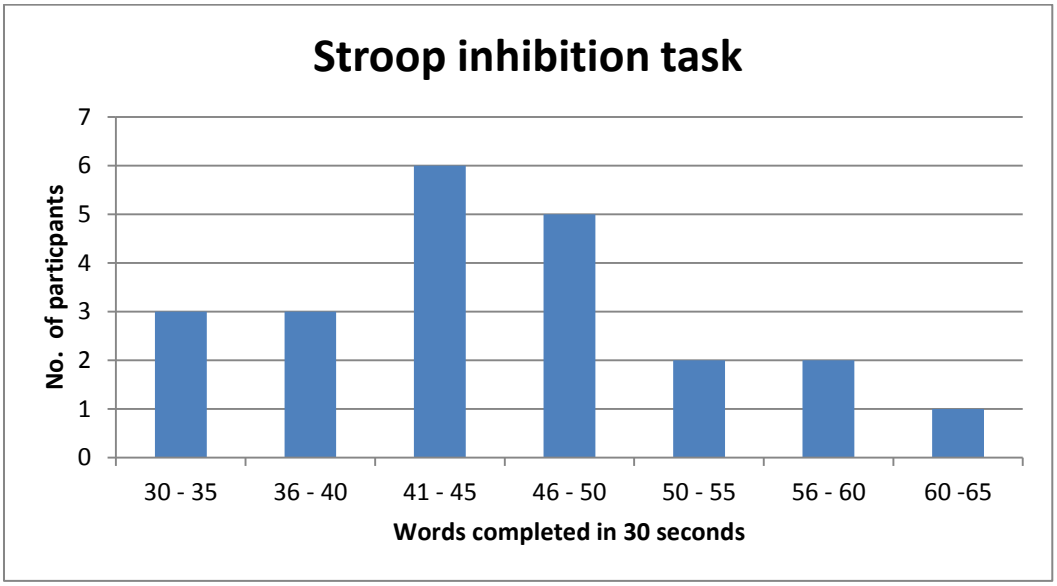


Figure 11: Letter – number span. Letters and number s were read - out in random order; the participants were told to read them back in alphabetical and chronological order.

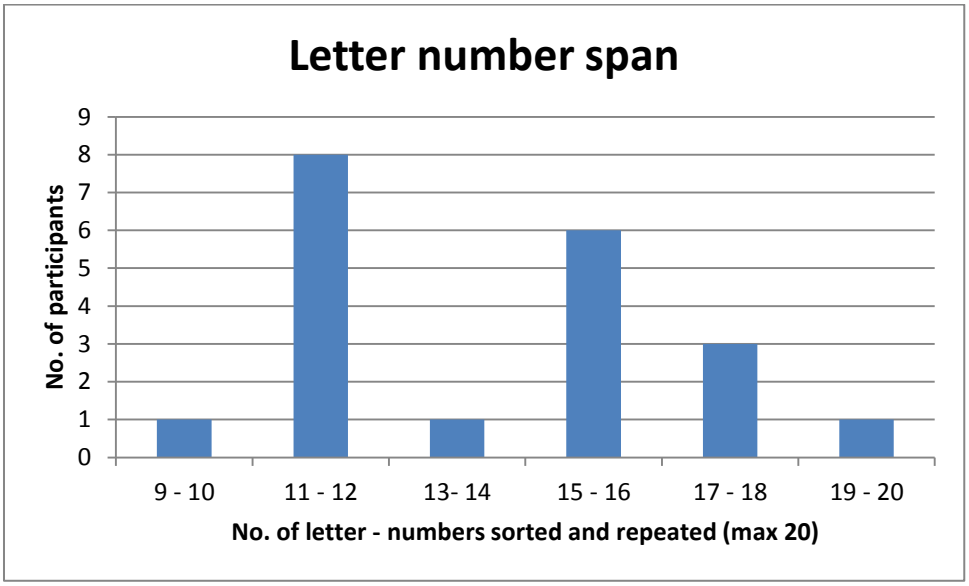
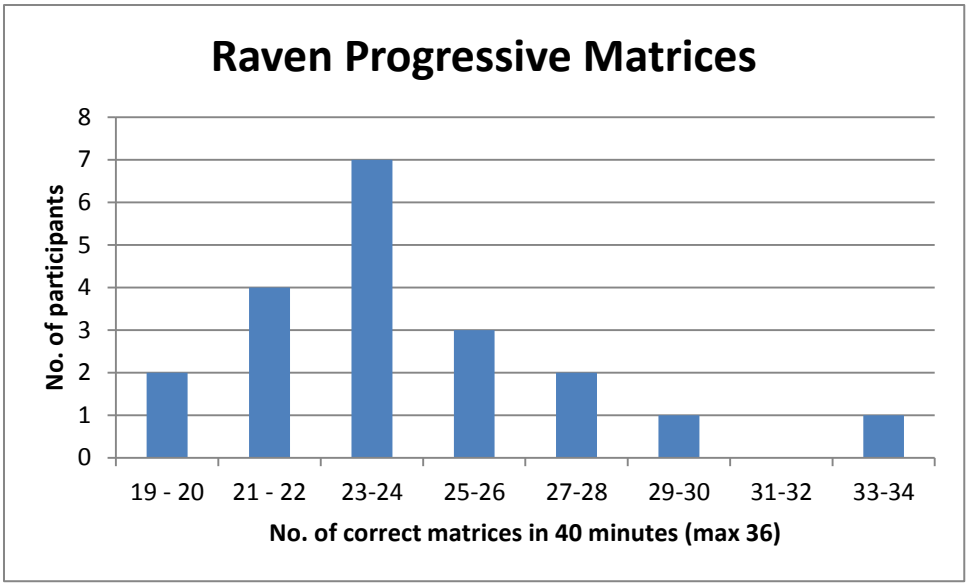


Figure 12: Ravens Progressive Matrices. Each task consists of nine matrices in a logical pattern, but one part is missing. The participants are told to choose on out of the eights alternatives that fits the pattern. The difficulty progresses with each matrix.


Raven Progressive Matrices
No. of participants
8
7
6
5
4
3
2
1
0
19 - 20
21 - 22
23-24
25-26
27-28
29-30
31-32
33-34
No. of correct matrices in 40 minutes (max 36)