

A pupillary measure of forgetting: Memory interference is revealed by pupil size changes at retrieval

Amanda Bjernestedt
amandabjernestedt@gmail.com

supervisors / handledare

Roger Johansson
Philip Pärnamets
Mikael Johansson

KOGM20

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Pupil size can change not only in response to light input but also to cognitive processes. Pupillometry, the study of the pupil, can provide intriguing insights into human cognition. In particular, pupil dilation is a reliable measure of cognitive load, and many studies have shown this effect in relation to various memory tasks. A robust way to study memory is through the release from proactive interference paradigm, where encoding of similar memory traces gradually cause forgetting of earlier ones. When the items presented are no longer similar to the previous, interference is resolved, presumably through mechanisms of selecting and inhibiting no longer relevant stimuli. When interference resolution occurs, there is less demand on cognitive resources. This decrease in cognitive load was hypothesized to be shown as a decrease in pupil dilation when a memory is successfully retrieved. This was investigated in a pupillometry study where pupil size was tracked throughout buildup and release of interference. No significant difference in pupil size was found at the point of cued retrieval, when participants were instructed to think of but not say aloud the words they had been shown, but there were significant differences when participants verbally uttered the retrieved words. The results reveal a relationship between inhibitory memory mechanisms and changes in pupil size, and imply that this could be a simple but sensitive measure of memory interference in future research.

1 Introduction

The mechanisms of selection and inhibition are fundamental to human cognition. Throughout the day, we constantly inhibit stimuli in order to attend to other stimuli. We move the fovea of the eye to focus on parts of our environment while other parts remain in marginal or peripheral vision, for example while reading or looking at a picture. An established method for studying selection and inhibition the Stroop task, in which names of colors (e.g. "red"), are printed either in the corresponding color or a different one (e.g. "red" is printed in either red or blue), and the task is to name the color of the word. We find it much easier to name the color which corresponds to the word than when the color and word are incongruent, because incongruent words require a conscious effort to inhibit the meaning of the word, and to focus only on the color of the ink.

Selection and inhibition of material is also fundamental to retrieval of memories. This can be illustrated with an example. Imagine going to a party where you meet a number of unfamiliar people. After shaking hands with a nine men who all have brown hair and work as librarians, it can be difficult to remember even a single name. However, when

work as librarians, it can be difficult to remember even a single name. However, when you leave the room and meet three women who are blonde and work as pilots, you will probably find it easier to remember their names simply because they are not also brown-haired librarians.

This type of memory failure is annoying but common. It can be explained by interference theory, which states that forgetting occurs when several memory traces, which are related to the memory you are searching for, compete for activation during recall. The fact or event that you try to remember is not lost, but irrelevant information gets in the way. This occurs both with items learned before the information that you want to recall, as proactive interference, or for items learned after, as retroactive interference (see Postman, 1961 and Anderson, 2003, for reviews). However, when we manage to forget those first few names we heard, we can more easily remember the names of the recent people we meet, since the earlier information is inhibited and is no longer competing for retrieval.

There are different accounts of why memory interference occurs. However, they all work on the assumption that while memory storage in the brain is infinite, the amount of attention and effort we can devote to recalling our memories is limited. Consequently, some memories are likely to be forgotten so that we can attend to others. If we were able to remember everything we have ever experienced, focusing on present events might be impossible. As annoying as forgetting can be, it is also adaptive and necessary when a sought after memory is to be properly selected.

How can these mechanisms of selection and inhibition be studied? There are several methods, ranging from purely behavioral studies to neurocognitive studies using functional magnetic resonance imaging (fMRI) or event-related potentials (ERP). Another, less used method, is to measure pupil dilation using an eye tracker. Pupillometry has proved to be a sensitive measure with high temporal resolution. The pupil responds not only to light and central nervous system activity but also to cognitive activity. The pupil has been shown to respond with dilation to processes such as mental arithmetic, language processing, and short-term and long-term memory tasks (see Beatty & Lucero-Wagoner, 2000, for a review).

Aim and scope of the thesis

There is still limited knowledge about the relationship between pupil activity and memory retrieval. Few studies have investigated whether the pupil can reveal anything about the processes that underly selection of relevant memories and inhibition of irrelevant ones. This is the general aim of the study, as well as specifically investigating this relationship in a situation of release from interference.

The connection between cognitive processes and their neural correlates is one of many areas of investigation in cognitive science, but it is arguably vital for a good understanding of human cognition. Therefore I will try to relate cognitive phenomena to models of neural function throughout this thesis.

First, I will review the relationship between the pupil and cognition within different areas, looking at findings that relate to memory selection. Next I will explain memory function, focusing on selection and inhibition at encoding and retrieval. Then, I will review the existing literature on memory and the pupil. Next follows the hypothesis, methods and results of the present study. Finally, I will discuss the results related to the presented theories and suggest how they can lead to future research.

2 Theoretical background

Pupil size changes and cognition

Light passes through the pupil of the eye onwards to the lens which focuses onto the retina, which in turn connects to the brain to create visual perception. Pupil size changes are controlled by the autonomic nervous system, with sympathetic nerve fibers controlling dilation and parasympathetic ones controlling constriction. The pupil dilates for dim light and for focusing on distant stimuli, and constricts for bright light and focusing on close objects ("Pupil", 2015).

As previously mentioned, the pupil also appears to respond to cognitive activity. Functioning as a window into the mind, the pupil reacts not only to external stimuli

functioning as a window into the mind, the pupil reacts not only to external stimuli such as intensity of light, caused by the pupillary light reflex (PLR), but also to inner states and cortical activity (Laeng, 2013). In the latter cases, pupil dilation is linked to norepinephrine release in the brain from the locus coeruleus, the so-called LC-NE complex, which is part of the autonomous nervous system (Einhäuser, Stout, Koch & Carter, 2008; Hoffing & Seitz, 2015). Although effects are small compared to PLRs (Holmqvist et al., 2011), measuring task-evoked pupillary responses can give insight into cognitive processes. Early pupillometry studies established that the pupil dilates in response to increased cognitive load, such as demanding arithmetic tasks (Hess & Polt, 1964; Beatty & Kahneman, 1966). Kahneman later argued that "much like the electricity meter outside your house or apartment, the pupils offer an index of the current rate at which mental energy is used" (2011, p. 34). In short, pupillometry provides a continuous, sensitive, real-time method for studying cognitive load during various mental tasks.

The pupil acts both as a measure of attention to and processing of incoming stimuli; in Kahneman's influential theory of attention, pupil dilation is used as the primary measure (1973). The pupil has also been shown to respond differently to stimuli of different modalities and complexity. Klingner, Tversky and Hanrahan (2011) showed that pupil dilation was greater when stimuli were presented aurally compared to visually during a variety of tasks, although the dilation patterns over time were similar. During perceptual processing of faces, the pupil responds to faces with longer response latencies compared to the PLR, possibly reflecting a higher level of perceptual processing (Conway, Jones, DeBruine, Little, & Sahraie, 2008). The pupil also has different reactions to faces depending on picture orientation and species (greater pupil constrictions to upright and inverted faces as compared to scrambled faces; greater pupil constrictions to human faces than to macaque faces) (Conway et al., 2008) as well as race (dilating more when studying faces of another race than one's own) (Goldinger, He, & Papesh, 2009). The pupil is also a measure of interest, emotion and arousal, as pupil dilation can be caused by e.g. seeing an attractive person or something scary, reactions which do not necessarily involve conscious cognition (Laeng, 2013).

The question remains why there is a connection at all between cognitive processes and change in pupil size. Why is this part of the visual system, which primarily functions to automatically regulate light input, also affected by cognition? As previously mentioned, regulation of light input allows us to clearly see stimuli under different light conditions and at different distances. This in turn allows us to focus attention on what interests us or is deemed important. It is possible that the mechanism might have evolved from a reflex to a more versatile mechanism to allow us to process more complex situations. Arousal of the sympathetic nervous system prepares us for undertaking of demanding tasks ("Human nervous system", 2015), and the pupil dilates in response to activation of this system. There remains much to be investigated about these processes, which doubtlessly can provide valuable insight into the nature of human cognition.

Pupil size changes and interference

Pupil diameter can be a measure of both the amount, e.g. number of items to keep in memory, and the intensity, e.g. increasingly challenging reasoning tasks, of the cognitive load (Beatty, 1982a). Kahneman & Beatty (1966) found that the pupil dilated in response to an STM task in which digit strings were presented and then immediately recalled. The longer the digit strings that were learned, the more the pupil dilated, only to constrict when the items were recalled or "unloaded" from memory. The fluctuations in pupil size gave a continuous measure of variations in cognitive load, on a second-by-second level.

More recent studies have shown even more time-sensitive fluctuations in pupil diameter during tasks, when cognitive control is needed to select and inhibit responses. Laeng, Ørbo, Holmlund and Miozzo (2011) let participants perform the Stroop task while recording pupil diameter and found that the pupil dilated more when the color and word were incongruent, while congruent pairs produced a smaller pupil diameter than non-color control words. Laeng et al. found these results to support pupillometry as a robust measure of "perceptual rivalry" due to semantic processing (understanding the word's meaning impedes the ability to name the color of the word when it differs from

word's meaning impedes the ability to name the color of the word when it differs from the meaning of the word). The pupil dilation in the Stroop task is due to interference from distractors, i.e. color-incongruent words.

In another study of perceptual rivalry when viewing ambiguous stimuli, Einhäuser, Stout, Koch and Carter (2008) found pupil dilation just before participants reported a "perceptual switch", i.e. when they interpreted the stimulus as something else. Since pupil dilation is linked to the LC-NE complex, which is involved in certain types of decision making (e.g. continue a task or leave and explore), Einhäuser et al. argue that pupil dilation is also a measure of other processes involving selection and inhibition, indirectly linked to this neural circuit.

Do these findings from perceptual rivalry and the cognitive control needed to resolve competition extend to the selective and inhibitive processes present during memory interference? Before we investigate this question, we need to know about how memory functions.

How do we learn and remember?

In models of memory, there are three key concepts: encoding, storage, and retrieval. In this section I will give an overview of the more established accounts of the processes behind these concepts.

Encoding refers to the process whereby experiences create so called memory traces thought to consist of synaptic connections in the brain (Purves et al., 2013, p. 245). When new information is learned and represented in memory, it can be encoded in different ways (Goldstein, 2011, pp. 170 – 178). In a conversation, the sound of a person's voice is encoded auditorily, the person's face is coded visually, and the subject of the conversation is coded semantically. The modality of encoding affects how the information is later recalled. If two memories are encoded similarly, they can interfere with each other at recall. This has been shown in studies where proactive interference (previously learned material blocking memory for new material) occurs for different types of stimulus material such as syllables (Peterson & Peterson, 1959), pictures of faces (Darling, Martin & Macrae, 2010), and words (Wickens, 1970).

New information is widely considered to be stored in short term memory (STM). According to the established model, the span of STM is limited, holding around 5- 7 items for 30 seconds at most (Goldstein, 2011, pp. 123 – 126). However, for dynamic processes such as reading, counting and problem solving, STM needs not only storage but also manipulation and transferring of information. For this, we use working memory (WM) to temporarily hold information about what we are presently attending to. In Baddeley's influential model (Baddeley, 2000), the components of WM are the phonological loop (acoustic and verbal information), the visuospatial sketchpad (visual and spatial information), and the episodic buffer (integrated information from long term memory). An additional component called the central executive directs attention to and between the other components. The neural basis of WM seems to be primarily in the prefrontal cortex, with activation in areas related to controlling of attention and holding of information.

According to Baddeley (2000), the most well-established component of WM, with evidence both from behavioral and neuroimaging studies, is the phonological loop. It consists of both a temporary store and a rehearsal system for words and sounds. The phonological loop is an important component in the experimental paradigm used in this study, which will be explained further below. For now, it is sufficient to note that memory that is held in STM can be disturbed when a person is forced to verbally repeat irrelevant sounds. Speaking interferes with rehearsal and prevents storage of the relevant information (Goldstein, 2011, p. 133). There are alternative accounts of STM/WM that focus more on function than on domain, such as one put forth by Nairne (2002). Instead of separate, finite stores that rehearse information as in Baddeley's model, he proposes that STM can best be explained by focusing on the fact that retrieval cues (see below) activate information, which gives rise to STM. This information can then be actively inhibited instead of decaying (Nairne, 2002; for a decay interpretation of STM, see Brown, 1958 and Peterson & Peterson, 1959).

Additionally, Kane, Bleckley, Conway & Engle (2001) propose that the capacity of WM greatly depends on general control of attention, which causes variations in individual capacity. This general capacity can then be paired with "domain-specific

skills” to provide a unified model of WM (Conway & Engle, 1996). Neither of these models are incompatible with interference theory, but in this thesis I am focusing on Baddeley’s model since it provides a good explanation of some key aspects of my study.

To distinguish between STM and long term memory (LTM), it can be said that information remembered for longer than about 30 seconds is stored in LTM, which has infinite storage capacity as opposed to STM. However, the distinction is not clear-cut, since the use of our memory often involves interaction of both STM and LTM. Brain imaging studies have shown that the two memory systems can activate both separate and overlapping areas while in use, implying that they may have mechanisms in common (Goldstein, 2011, pp. 149 – 155).

Although the STM/LTM distinction can be difficult to make one defining characteristic of LTM is that of an archive from which we can retrieve events from our life (episodic memory) or facts that we have learned (semantic memory). These types of memory are said to be explicit, i.e. available for conscious access, as opposed to implicit memories such as knowing how to ride a bike. The difference between episodic and semantic memory lies in the way we experience them: retrieving episodic memories can be likened to mental time travel, where we can imagine ourselves back in the situation when we experienced an event (Tulving, 1985). Episodic memory allows us to “discriminate between familiar (encountered) and novel stimuli”, and to remember detail about an event where we have previously encountered a stimulus (Badre & Wagner, 2007, p. 2890).

Meanwhile, experiencing semantic memory is knowing something, e.g. that Stockholm is the capital of Sweden, but not necessarily remembering where and when we first learned that fact (Tulving, 1985; Goldstein, 2011, pp. 157 – 159). There is also neurophysiological evidence that episodic and semantic memory are separated in the brain (Goldstein, 2011, p. 158).

Memories are stored in the brain by processes of consolidation which occurs when a memory trace is stabilized. These processes are regulated by several systems in the brain. Different brain areas process different kinds of memories, e.g. the hippocampus and episodic memory vs. the basal ganglia and procedural memory, and as we experience events storage processes in these areas are activated at a cellular level. At the same time, stress hormones are released in part of the amygdala which then interacts with other brain regions to modulate consolidation. Consolidation processes can be disrupted, e.g. by other information learned shortly after (retroactive interference) or by inhibition of the protein synthesis involved in consolidation, which makes it more difficult to recall the event (McGaugh, 2000).

When episodic memories are first stored, the involvement of the hippocampus is critical as it is believed to store a summary of the event which connects to different areas of the cortex, creating a distributed representation (Purves et al., 2013, pp. 293 – 297). As time passes, the activation of memories are believed to be gradually overtaken by neocortical areas (McGaugh, 2000).

Retrieval from long-term memory storage usually depends on a retrieval cue. Simply put, a cue is something associated with the memory, e.g. a feature that was present at encoding, and encountering the cue reactivates the associated information. This information is then held active in WM as we think about the memory. Retrieval can be either involuntary, e.g. seeing a person who was at a party and being reminded of that party, or voluntary, e.g. trying to remember the party by thinking about the house in which it took place (Purves et al., 2013, p. 284).

Retrieval of recent episodic memories are believed to be regulated by the hippocampus, while more remote ones can be accessed directly via retrieval cue from the distributed representations in cortical areas. Prefrontal regions can provide cues, help search for the correct memory trace, and evaluate the retrieved information in a monitoring process. In this process, irrelevant or inappropriate memories can be rejected, refining the recovery of the memory. These processes require continuous attention and operate quickly, usually without conscious awareness (Purves et al., 2013, pp. 300 – 304).

A successful retrieval cue causes activation of the distributed memory representation, reactivating components associated with the remembered event, a function known as pattern completion. The hippocampus is thought to assist in pattern completion, and also

in pattern separation which functions to distinguish similar patterns of neural activity. Meanwhile, components that are irrelevant and compete for attention are suppressed, “thereby favoring remembering of event details from goal-relevant knowledge domains” (Badre & Wagner, 2007, p. 2891). This cognitive control process is thought to be regulated by areas in ventrolateral and dorsolateral prefrontal cortex (VLPFC and DLPFC) (Levy, Kuhl & Wagner, 2010; Badre & Wagner, 2007). In particular, VLPFC seems to be involved in selecting the correct information from areas where the knowledge is stored (Badre & Wagner, 2007).

Going back to the question whether cognitive mechanisms used to select and inhibit certain dimensions, e.g., during a Stroop task, extend to control of memory retrieval, fMRI findings support the theory of a common mechanism (Badre, Poldrack, Paré-Blagojev, Insler, & Wagner, 2005; Badre & Wagner, 2005) as similar activation was shown during selective tasks, such as a Stroop task, and when selective retrieval was performed.

Badre et al. (2005) also propose a distinction between the processes of retrieval and selection, but argue that they share the same general cognitive control mechanism. As mentioned, VLPFC is involved in retrieving knowledge from long-term memory stores, and selecting the appropriate trace among competitors. Mid-left VLPFC is activated during generalized control processes when searching for a specific fact or event, involving selection among competitors and variations of cue-target associative strength. Meanwhile, left anterior VLPFC together with the middle temporal lobe responded to tasks involving cue-target associative strength but not competition. This occurs both for semantic and episodic memory (Badre et al., 2005; Badre & Wagner, 2007). Competition is thought to occur after items in memory have already been activated, i.e. after retrieval, after which selection between competitors is performed. From this the authors draw the conclusion that since only a certain area seems to deal with post-retrieval competition, this should be a separate neural function. Post-retrieval selection can be thought of as a top-down process, while cue-target associative strength can be an automatic, bottom-up process, as when seeing a person involuntarily reminds you of an event associated with that person. Stronger associations require less VLPFC activation and thus requires less cognitive control to retrieve the memory, while weaker associations require more cognitive control when bottom-up processes are insufficient (Badre et al., 2005).

How do we forget?

Sometimes we fail to successfully use these monitoring processes, such as selecting the target memory and inhibiting competing memories. Interference occurs as a result of several memory traces associated with the same cue, which causes forgetting.

Above I have described some of the mechanisms that allow us to create and recall memories. As mentioned earlier, there are different accounts of why and how these mechanisms fail when we forget. As Levy, Kuhl and Wagner (2010) state in a review, most likely no explanation can account for all types of forgetting. Instead they argue that “forgetting may arise from a disruption to any of the events that promote successful memory” (Levy et al., 2010, p. 136), presenting behavioral as well as neurophysiological evidence for some of these processes.

The main explanatory models relevant to the present study are retrieval competition and resolving of competition. During retrieval competition, alternative memories with an association to the cue for retrieval become activated instead of the relevant memory, essentially blocking it from recall. Interference occurs not only in human memory, but also in artificial neural networks as “catastrophic interference”, when “the process of learning a new set of patterns suddenly and completely erase[s] a networks’ knowledge of what it has already learned” (French, 1999, p. 128). Evidently, this common problem is difficult to escape even in carefully created artificial memory systems.

Interestingly, resolving this type of competition also causes forgetting. When areas such as VLPFC succeed in inhibiting competing traces, they are stopped from being recalled. If this inhibitory process is repeated, studies on retrieval induced forgetting (RIF) show that the memory traces becomes more difficult to recall in the future and conversely, easily forgotten (Anderson, Bjork & Bjork, 1994; Levy et al., 2010). This process of selective retrieval is thought to be adaptive since it can reduce future

interference (Wimber, Alink, Charest, Kriegeskorte & Anderson, 2015). Studies on stopped retrieval, or directed forgetting, where participants consciously attempt to not think of a certain memory, show similar results (Levy et al., 2010). Taken together, these results indicate that this type of forgetting occurs “due to weakening of the competitors, rather than simply strengthening of alternative representations” (Levy et al., 2010 p. 147).

While there is some controversy about the underlying mechanisms of interference, particularly by proponents of competition theory as the main cause for forgetting (see Anderson, 2003, and Storm & Levy, 2012 for reviews), the prominent theory is that forgetting primarily occurs due to failure to inhibit competing items at the retrieval stage. Consequently, when inhibition is successful, interference is resolved, as shown in many studies (Anderson, Bjork & Bjork, 1994; Badre & Wagner, 2005; Kuhl, Dudukovic, Kahn & Wagner, 2007, Wimber et al., 2008; Healy, Campbell, Hasher & Osher, 2010; Storm & Levy, 2012).

A recent fMRI study by Wimber et al. (2015), operating under this hypothesis, indicate that individual memories can be suppressed through interference resolution through pattern suppression, i.e. inhibition of the neural distributed network that the memory consists of. They observed pattern suppression of individual memories by first localizing the neural activation pattern in visual cortex of target, competitor and baseline pictures. Then, during retrieval, they measured activation of the competing item as participants were retrieving target items. Participants performed repeated recalls, and as they became more successful at retrieval and pattern completion of target items, competitor items were suppressed and pattern completion was reduced. They also found that VLPFC activation predicted these suppressions, consistent with previous findings that this area is involved in memory inhibition.

Further findings show that demands on selective and inhibitory mechanisms decrease when competing traces are suppressed during retrieval-induced forgetting (Kuhl, Dudukovic, Kahn & Wagner, 2007). When competitors were forgotten, there was reduced activity in the PFC regions anterior cingulate cortex (ACC) and right VLPFC, areas that are associated with inhibition and response conflict. ACC activity was coupled with hippocampus activity at retrieval, suggesting that ACC not only monitors competing responses, as is generally believed, in behavior but also in memory.

Together, these findings suggest that to forget irrelevant information can be a way for the brain to spare resources for remembering more important information.

Release from interference – forgetting in order to remember

Inhibition theory has been widely used to explain resolved interference within the RIF paradigm, but less so within the previously mentioned release from proactive interference (RPI) paradigm. Studying the RPI effect from the point of view of inhibition theory has the potential to shed more light on the neural processes that cause forgetting.

During release from proactive interference, an adaptive type of forgetting occurs. Going back to the party scenario, it can be very difficult to remember even a single name after shaking hands with a nine men who all have brown hair and work as librarians. According to Wickens', Reutener's and Eggemeier's (1972) theory of semantic encoding, if we perceive something as belonging to a certain category, we encode that category along with the rest of the memory. During retrieval, the category is activated along with the memory. If many items from the same category were learned at the same time, or have overlapping potential retrieval cues, they will interfere with each other. Going back to the party example in the introduction, release from interference is like leaving the room at the party and meeting new people who have other things in common, and therefore fewer overlapping potential retrieval cues.

This process can be reliably demonstrated within Wickens' RPI paradigm (1970). The procedure consists of four trials, and each trial contains an encoding phase, a distraction task of around 18 seconds, and a recall phase. The distraction task consists of verbally counting backwards in order to prevent rehearsal, or disturbing the phonological loop as interpreted with Baddeley's model of working memory, since recall would be too easy otherwise. Memory performance usually declines rapidly between trials 1 and 3, only improve considerably in trial 4. This is explained by the

fact that the items to be learned are connected by semantic category (e.g. fruits), and this connection causes items that were learned earlier to interfere with items learned later, which are then more likely to be forgotten. Retrieval of items supposedly causes activation of the general category, i.e. fruits. Release from proactive interference occurs when the category is changed, e.g. from fruits to animals. At this point, memory performance on the animal items improves, since the competing traces from the fruit category are no longer being activated.

The RPI paradigm as it was used by Wickens and collaborators (1963; 1970; 1972; 1976) builds upon a number of early studies by Brown (1958) and Peterson and Peterson (1959) that tested working memory capacity. In their experiments participants memorized combinations of three letters and recalled them after an interval of counting backwards by 3's out loud, the intervals increasing as the experiment went on, and memory performance declining along with it. Peterson & Peterson (1958) explained the declining memory performance with the theory of decay, stating that the earlier combinations were forgotten because the memory of them simply weakened with time. Keppel & Underwood (1963) reanalyzed the data of Peterson & Peterson (1958) and concluded that the effect was in fact due to proactive interference, and this is now the most established interpretation.

Wickens, Born and Allen (1963) used a modified version of the Brown-Peterson task where interference was resolved in later trials for one of the experimental groups by switching the stimulus class from letters to numbers. In 1970, Wickens introduced semantic interference into the paradigm by manipulating the attributes of the items that were to be memorized. Among other stimulus materials, he used words from categories with varying amounts of semantic attributes in common, and found that words belonging to the same semantic category created more interference than words belonging to e.g. the same grammatical category. Likewise, the biggest RPI effect was found when using different semantic categories as the explaining variable. The semantic encoding theory they later develop can account for these findings, and they are also consistent with theories of selection of domain-specific features that occurs at retrieval. According to this model, the semantic category that the searched-for item belongs to seems to be a particularly effective retrieval cue.

RPI has been found to occur reliably in healthy populations, and occasionally in populations with Alzheimer's disease, although these patients show a significantly smaller buildup of interference and consequently smaller release from the same (Multhaup, Baluta & Faust, 2003). Older, healthy people are more susceptible to proactive interference than younger people (Carretti, Mammarella & Borrella, 2012; Loosli, Rahm, Unterrainer, Weiller & Kaller, 2014) which indicates that a general inhibitory mechanism thought to decline with age is involved in dealing with interference as well.

Bäumel & Kliegl (2013) report decreased response latencies during release from PI, arguing that this meant a decrease in size of the participants' "mental search set" due to elimination of the competing items in the search process. An alternative, but compatible, explanation is that less cognitive control was needed to reduce interference at these trials. This explanation is supported by findings from Badre & Wagner (2005, 2007), who showed that left mid-VLPFC was active during resolution of PI in working memory, arguing that this is the same post-retrieval selection mechanism used to resolve competition as in brain imaging studies of item recognition (Jonides, Smith, Marshuetz, Koeppel, & Reuter-Lorenz, 1998), semantic retrieval (Badre et al., 2005) and episodic retrieval (Badre & Wagner, 2007). When the left mid-VLPFC is lesioned or disrupted by transcranial magnetic stimulation, memory performance is negatively affected (Badre & Wagner, 2007). Furthermore, people with amnesia due to lesions on left PFC do not show release from interference in RPI tasks (Moscovitch, 1982). These and other findings (see Jonides & Nee, 2006, for a review) provide compelling evidence that cognitive control during memory retrieval is responsible for resolving interference.

Memory and pupillometry

As previously mentioned, pupil responses have been linked to working memory load (e.g. Beatty & Kahneman, 1966). These fluctuations in cognitive load can be measured with a high temporal sensitivity, as phasic major pupil dilations and constrictions can be observed within milliseconds. Phasic pupil dilation is distinguished from tonic pupil

be observed within milliseconds. Phasic pupil dilation is distinguished from tonic pupil dilation: phasic movements are short, quick responses while tonic movements are slower and can be measured over a hour long durations. It is mainly phasic responses that are linked to changes in cognitive load (1982b).

In a recent study, Heitz, Schrock, Payne and Engle (2008) found that, during sentence reading and encoding of letters, individuals with a general lower WM capacity showed larger pupil dilations compared to baseline than did individuals with a higher WM capacity, suggesting that those with low WM capacity have to exert more cognitive effort during semantic tasks.

Furthermore, there are several findings linking pupil dilation to encoding and retrieval of long term memory, both episodic and semantic (see Goldinger & Papesh, 2012, for a review). Gardner, Beltramo and Krinsky (1975) found that more pupil dilation occurred at encoding and retrieval of number sequences than at rehearsal, thus showing that pupil dilation reflects not only cognitively effortful tasks in general but also processes more directly related to memory.

Headley (1980) investigated the pupil response during recall of semantic memories, as responses to questions such as “In what country is the Taj Mahal?”. When people could recall the facts, their pupils were more dilated than when they were unable to respond. This effect persisted even when their response was incorrect. Conversely, when they responded that they thought they knew the answer but could not recall it, the pupil was more dilated than when they simply responded that they did not know. However, even in the latter case the pupil still dilated as compared to baseline. This suggests that both successful retrieval, attempted retrieval and failed retrieval all engage cognitive control processes but with varying amounts of effort involved.

This pupil-retrieval effect has been shown even when retrieval is not consciously performed. Laeng et al. (2007) found that amnesiacs who were presented with previously viewed stimuli, and were asked if they remembered them, showed pupil dilation even when they did not consciously recognize the items. After other similar findings on item recognition memory in healthy participants, Võ et al. (2008) proposed the “pupil old/new effect”: pupil dilation is larger in response to presentation of words that had already been viewed, and were correctly recognized as “old”, as compared to words that were correctly recognized as “new”. They argue that this is because more cognitive effort is required to determine an item as already viewed, compared to rejecting a new item. The pupil old/new effect was replicated by Heaven & Hutton (2011), who found that it occurred even when participants were instructed to pretend they did not recognize the old items, implicating that the pupil can reveal remembering even when we try to hide it. Otero, Weekes & Hutton (2011) demonstrated the old/new effect for auditory stimuli material and for when participants falsely believed they recognized an item. To summarize, the pupil old/new effect appears to be a robust measure of retrieval in recognition memory.

In a study of pupil size during encoding (Kafkas & Montaldi, 2011), participants were shown images without instruction, and the images were thus incidentally encoded without explicit top-down processes involved. Participants were later surprise tested on these items. Pupil size at encoding predicted memory strength in this recall period: forgotten items elicited pupil constriction at encoding compared to successfully retrieved items. The authors argue that these results might be due to a “mechanism that serves to restrict the focus of internal processing”, i.e. selection, and as this mechanism operates more effectively, pupil dilation is reduced. Effective encoding then makes the items more likely to be successfully retrieved. The authors propose that this mechanism could be autonomically controlled, as reflected by pupil responses, similarly to what Einhäuser et al. (2008) argue in the aforementioned study on selection during perceptual tasks.

These findings are corroborated by Naber, Frässle, Rutishauer & Einhäuser (2013) who studied the mechanisms of successful retrieval of natural scenes. Their study differed from Kafkas & Montaldi in that they explicitly instructed their participants to encode the stimuli, and also measured pupil size at retrieval. They found that correctly remembered items elicited pupil constriction at encoding, in line with previous results, and that the pupil was more dilated at retrieval for previously viewed items than for new ones, in line with Võ et al. (2008) and Otero, Weekes & Hutton (2011). However, the results of Naber et al. differ from these studies in that they used natural scenes as stimuli, which demonstrates that these effects occur in relatively realistic situations as

stimuli, which demonstrates that these effects occur in relatively realistic situations as well.

In a recent study by Ariel & Castel (2014), participants studied and later recalled items that were assigned high or low values of importance. Participants remembered high-value items better because they devoted more mental resources selectively to those items at encoding, which corresponded to pupil dilation. While their eyes were fixated an equal amount of time on high-value and low-value items, the pupil dilated more at high-value items. The authors argue that this shows that the increase in memory strength for high-value items was not due to participants simply ignoring the low-value items. This indicates that conscious, selection of information devotes more cognitive resources for that information.

In a study of memory strength at retrieval, van Rijn, Dalenberg, Borst & Sprenger (2012) showed that memory strength elicited a decreased pupil dilation. Items were repeatedly viewed and then cued for retrieval. The items which had been repeated more, and which had shorter delays between encoding and cue presentation, had more memory strength at retrieval as shown by a higher percentage correct retrieval and shorter response times. These items also showed less pupil dilation compared to items with less memory strength. It is possible that these items required less inhibitory effort to retrieve and thus elicited less pupil dilation.

Recent results from Hoffin and Seitz (2015) further indicate a connection between norepinephrine release, pupil dilation and successful encoding and retrieval. They used a paradigm of task-irrelevant learning which studies the learning of stimuli that are not the focus of attention. Most compellingly, they found that when stimulus presentation was paired with an unexpected sound, with the purpose to cause activation the LC-NE system and induce pupil dilation, retrieval of these items were more successful than for control items. Although these results are the opposite with previous results where pupil constriction predicts subsequent memory strength, they can still be said to point to the same general mechanism: activation of the LC-NE system stimulates learning and the more effectively cognitive resources are used at encoding, the less the pupil will dilate. As was shown by van Rijn et al. (2012), this appears to also be true at retrieval.

Apart from the present study, the only study that has tracked pupil responses to memory in a release from interference task is, to my knowledge, by Engle (1975). He investigated an explanation of proactive interference which proposes that items from a new category, i.e. the first items in a series of trials or the items for which release from interference occurs, always receive the most attention and are therefore easier to recall. Using positively and negatively loaded words to create interference, and pupil diameter as a measure of attention, he found that there was no difference in pupil dilation during encoding of RPI items compared to PI items. Thus he concluded that the release effect was not a consequence of an increase of allocated attention.

All of these findings are in line with the previously mentioned findings by e.g. Badre et al. (2005) in which prefrontal activation predicts control processes in memory. It is possible that activity of the VLPFC, medial temporal lobe and LC-NE complex collaborate on the control mechanisms that regulate encoding and retrieval of memories. It is reasonable to predict that the similar mechanisms underlying release from interference and the inhibitory control that it involves. Since the pupil has been found to dilate during increased cognitive load, it would also be reasonable to predict that it would shrink in size during this decrease in load that RPI leads to. As mentioned in previous sections, pupil dilation has proven to be a reliable and sensitive measure of cognitive load, even compared to more complex methods such as ERP and fMRI.

The present study

In this study, I will investigate the mechanisms of selection and inhibition that monitor successful retrieval of target items in competition with competing items, and the effect that these processes have on pupil size change.

I predict that proactive semantic interference will build up and cause forgetting of words, culminating in trial 4. When there is a category switch in trial 4, I predict that interference will be resolved and memory performance will improve. Furthermore, I predict that when proactive interference occurs, the average pupil size will increase (i.e. pupil dilation will occur) due to increase in cognitive load. Critically, when release from proactive interference occurs this increase in pupil size will be significantly smaller due

to a decrease in cognitive load involved in recall, as compared to when proactive interference occurs, the increase in pupil size will be significantly smaller due to a decrease in cognitive load involved in recall.

- H1: Memory performance, as demonstrated by number and order of correctly recalled items, will be significantly better when release from interference is present compared to when interference is present.
- H2: The pupil will dilate during recall when interference is present.
- H3: The pupil will be significantly less dilated at recall when interference is resolved than when interference is present.

Investigating these hypotheses will shed more light on the connection between pupil dilation and the handling of memory interference. Hopefully, it can provide a reliable, temporally sensitive physiological measure of the handling of interference similarly to the pupil old/new effect for recognition memory. Additionally, if the hypotheses gain support, it will provide further evidence for the inhibition theory of interference.

3 Method

Participants

A total of 33 participants were recruited from the student population at Lund University. Two participants did not complete the experiment, and their data was excluded from the original sample. The mean age of the remaining 31 participants (15 male) was 27.3 years (SD = 8.5). All were fluent in Swedish and had normal or corrected-to-normal vision. All gave written informed consent and received a cinema voucher for their participation.

Design

The experimental paradigm for this study was an adapted version of Wickens' RPI paradigm. A within-subjects design was used, where each participant had to go through a number of trials with varying build-up of interference and release of the same. The experiment had two conditions, called PI (proactive interference) and RPI (release from proactive interference). In the PI condition, interference was created by having the participants encode 12 words from the same semantic category over four consecutive trials. These lists are divided into groups of 3 words with retrieval following each group. This procedure is then repeated in 4 trials, which together constitute a block. In the RPI condition, release from interference was created by shifting the semantic category of the 3 words presented in the fourth trial to one which had none or few attributes in common with the preceding 9 words.

For the ordering of conditions, categories and items, a unique version of the experiment was created for each participant in order to avoid order and learning effects. The order of conditions was pseudorandomized within each version, meaning that the order was random with the restriction that each condition never occurred more than three times in a row. The stimulus categories, 36 in total, were organized into three sets, A, B and C, with 12 categories in each. These sets were then organized into a Latin square. For each experiment version, one row of the Latin square was used; going back to the first after every combination had been used. The first letter of each combination denoted the set that would be used for PI, and the second and third for RPI. For example, experiment 1 used the combination ABC, and in that version the categories from set A were used in the PI blocks, set B for the first three trials in the RPI blocks, and set C in the last trial in the RPI blocks. This was done because the size of the RPI effect was assumed to vary depending on which categories followed after each other.

The internal order in which the categories appeared within each set was shuffled after every three experiment versions. This was done to ensure that a certain category would not always appear in the same place in the experiment.

The study used verbal data for the memory performance scores, meaning that the participants said the words they recalled out loud instead of writing them down. There are two benefits to verbal responses within this paradigm. A fixation point can be used

the two scenarios to verbal responses within this paradigm. A fixation point can be used during the testing phase which is the same luminance and contrast as during the encoding phase, avoiding pupil size fluctuation due to light changes. Also, the participants will be able to keep this fixation during the entire experiment, unlike with written testing which would cause pupil changes and loss of contact with the eye tracker due to eye movement towards the keyboard.

Stimuli

All items in the experiment were Swedish words. The items were taken from the Swedish semantic category norms defined by Hellerstedt, Rasmussen & Johansson (2012), a collection of words from 80 categories sorted by strength of association to the category, starting with the most typical item. The lists were produced by reading the name of a category aloud to Swedish speaking participants and letting them freely write down all the words they could think of belonging to that category. All words that were generated by five or more percent of the participants were included, and sorted by frequency and average rank order in which the word was recalled. From this, the association strength of a word to a category was determined (Hellerstedt, Rasmussen & Johansson, 2012). Material from this collection has been used previously to produce PI and RPI effects (Bjernerstedt, 2013).

432 nouns from 36 categories were selected from this collection. The first 12 words in a category list, in the order of most to least typical, constituted one block. Items 1 – 3 in the list were presented in trial 1, 4 – 6 in trial 2, and so on. The idea was that the first, more typical, items would be more strongly activated by the cue and would therefore induce the most possible interference within a block. The least typical items (items 10 – 12 from the lists) always appeared in trial 4, regardless of condition, so that the hypothesized interference would be comparable between conditions.

The categories used in the experiment were selected according to three criteria. The first was that the words should be of sufficiently neutral emotional valence, so that pupil effects due to emotion would be avoided.

The second was that the categories would have as few semantic attributes as possible in common with each other, preferably none, so that they could all be matched with each other to produce semantic RPI effects. In some cases common attributes could not be avoided, such as between "insects" and "birds" (both animals), but they were deemed to still be sufficiently semantically different to be included.

The third was that the categories should have no items in common with each other. There were some exceptions to this: the word fot (foot) appeared in both the measures of distance and body parts categories; New York appeared in both cities and American states; bil (car) appeared in both toys and modes of transportation. However, since these homonyms are not semantically identical, they were still included.

Equipment

For pupil recording, an SMI RED 250 remote eye tracker with a 250 hz sampling frequency was used, with iView X 2.7 software on a laptop. A Dell Optiplex 755 PC presented stimuli using PsychoPhysics Toolbox in MATLAB 2012b. The instructions and stimuli were shown on a 22" widescreen monitor (resolution = 1024 x 768 pixels) in black Arial 14 point font on a grey background. These colors were selected to decrease the contrast as much as possible, as well as to avoid colored stimuli, in accordance with Porter and Troscianko (2003). The memory data, in the form of verbal responses, were recorded manually by the experiment leader into an Excel sheet during the experiment, using the codes "1" for correct response and "0" for no or incorrect response. The participant was seated in an adjustable chair about 70 cm from the monitor. The desk was height adjustable and the monitor was adjustable by position and angle. For the eye tracker, a five-point calibration routine was used. Calibrations were accepted if the deviation scores were around 0.5° visual angle or less, otherwise the calibration was repeated.

Procedure

Prior to the experiment, the participants received written instructions. The instructions

included a short description of the experimental procedure, information about the voluntary nature of their participation, including their right to withdrawal, that they would get a break after the first half of the experiment and that they would receive a cinema voucher if they completed the experiment. They also received supplementary verbal instructions and were allowed to ask questions. When the experiment program was started, they again received written instructions on the screen. These included, apart from the previously explained procedure, requests to remember to always utter their responses aloud and to always keep their eyes on the screen during the experiment. Then they completed a short practice run consisting of one trial, which was not recorded, in order to familiarize the participant with the experiment.

After the practice trial, calibration of the eye tracker was performed. The monitor position and desk height were adjusted for each participant for better recording accuracy. Before recording began, participants were verbally encouraged to sit still and try not to blink too much, and were reminded to keep their eyes on the screen.

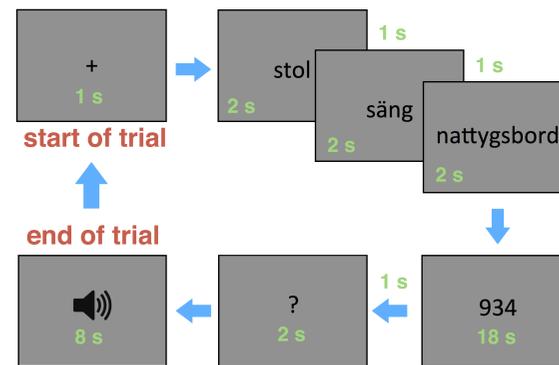


Figure 1. Overview of trial structure. Note that the time notations were not shown in the experiment.

Subsequently the first trial began (see Fig. 1 for a visualization of a trial). Presentation of a triad of words, distraction task, cue and response constituted one trial. Depending on the condition, after three trials, the word category was either changed (RPI) or remained the same (PI). Four trials constituted a block. The experiment consisted of 12 blocks in each condition, with 24 blocks in total.

Before each trial, a "+" symbol was shown for 1 second in the center of the screen, during which baseline pupil diameter was measured. It also served as a fixation point. The relatively long presentation duration was chosen in order to allow the pupil to constrict after the previous response phase, and because a stimulus shown for a shorter duration might have been perceived as a flash, causing the participant to get surprised and blink.

After the baseline stimulus, 3 items (a triad) were presented sequentially in the center of the screen, one by one. Each word was shown for 2 seconds, with a 1 second interval between words. After each triad, a distraction task was performed for 18 seconds. The task was to count backwards, verbally, by 7's from a three-digit number that was presented on screen. This was done, as in the classic Brown-Peterson procedure for testing working memory (Brown, 1958; Peterson & Peterson, 1959), to prevent the participant from rehearsing the words, thus causing them to be more likely to forget them.

After a 1 second interval began the testing phase, when participants were tested on the last three words they saw. At the beginning of the testing phase, the participant was shown a question mark ("?") for 2 seconds. This served as a memory cue where recall of the most recent items, and the possible inhibition of earlier items, was thought to occur. The participants been instructed to think about the words and prepare for response when they saw the question mark, but not say anything. This was the critical phase for the hypothetical pupil dilation. The 2 second duration of the cue was to allow a 1 second delay between the onset of cognitive load and the TEPR, in accordance with Kuchinke et al. (2007).

Following this a speaker symbol was shown for 8 seconds when participants were allowed to verbally utter the words they could recall. The time allowed for recall was the

same as in Wickens, Dalezman and Eggemeier (1976). The participants had been encouraged to utter the words in the order they saw them, and if they succeeded, they were given an extra point on their memory performance score for each trial, in addition to the one point each correctly recalled word gave. This separation of cue phase and response phase was done to avoid possible confounding effects on the pupil as a consequence of speech planning and motor activity.

After 12 blocks, the participant was able to take a break for as long as they wanted, in order to minimize fatigue effects. During this break they were offered water and candy and were once again able to ask questions (as long as the answers did not reveal the purpose of the experiment). After the break, which usually lasted for a few minutes, another nine-point calibration was performed. After this, the second half of the experiment began.

The experiment took one hour to perform, excluding instructions and break. The experiment leader was present in the same room as the participant for the entirety of the experiment but was not in the participant's line of vision. After the completed experiment, participants were debriefed about the purpose of the experiment, were allowed to ask questions, signed a consent form and received a cinema voucher.

Measures and analysis

The maximum memory performance score was four points per trial, one point for each word and one extra point if they were given in the correct order, as in Wickens et al (1976). Recalled words that did not have the same grammatical form (e.g. "the hammer" instead of "hammer") as the word that had been presented were accepted as correct responses if they retained the same general semantic meaning. Words uttered after the 8 second response phase were not counted. The remaining verbal response data was analyzed with a repeated measures 2x4 analysis of variance (ANOVA) with condition (PI vs RPI) and trial (1 vs 2 vs 3 vs 4) as factors. If an interaction effect of condition and trial was found, the difference scores between trial 3 and 4 was analyzed using post hoc pairwise comparisons.

The most prominent effect of memory interference is thought to occur during the fourth trial in the PI condition blocks. If such an effect is found during the initial memory performance analysis, the mean pupil size across participants during the recall phase of the fourth trial will be compared between conditions.

Pupil size was recorded continuously throughout the experiment. In total, there are 96 trials and thus 96 baseline and pupillary response recordings per participant. The interval of interest for the hypothesis is during the 2 second cue phase, i.e. 28 seconds into each trial. The following 8 second response phase was also measured to account for latent pupil responses.

Mean pupil dilation is the pupillary response of interest in this study, and the most commonly used pupillary response used to measure cognitive load, according to Van Gerven et al., (2004). In order to analyze the mean pupil dilation ratio across participants, the mean baseline values will be subtracted from the raw values in the intervals of interest.

Parametric statistical methods (ANOVA and t-tests) will be used to analyze the mean pupil dilation in order to determine peak responses and amplitude of change. Additionally, non-parametric tests based on permutation of the whole time-series will be performed in order to analyze the time course of pupillary change to determine when during the trial any significant differences are found. (Blair & Karinski, 1993).

Since the experiment has a within subjects design, the results for each participant will be aggregated prior to all analyses.

Data processing

All pre-analysis data processing was performed in MatLab. To begin with, the pupil recordings were converted into millimeters using a conversion factor of 3.2 pixels per millimeter.

Subsequently, correction for blinks, non-recordings and artifacts was performed in three steps. First, all instances of 0 mm pupil measurements were replaced by NaN values, including the 10 preceding samples and the 10 following samples. Second, the

data was checked for any remaining values smaller than 1 mm or larger than 9 mm, which were identified as artifacts and also replaced by NaN values. Third, a linear interpolation was performed in order to correct the data for these exclusions, applying an algorithm based on the last good data point before and first good data point after the artifact (Steinhauser, 2011). Trials where more than half of the samples had to be excluded were discarded from analysis.

Lastly, following artifact correction, the data was signal averaged and filtered, using a 10Hz low-pass filter. Applying signal averaging which averages trials together resolves background noise present in pupil data, such as CNS activity and light responses. Filtering further reduce noise and artifacts due to e.g. measurement and signal processing, increasing signal-to-noise ratio (Steinhauser, 2011).

4 Results

Behavioral data

A repeated measures ANOVA showed a significant interaction effect of condition and trial number on memory performance, $F(3, 29) = 6.07$, $p < .01$, $\eta^2 = .07$, as well as main effects of both condition, $F(1, 29) = 4.25$, $p < .01$, $\eta^2 = .01$, and trial, $F(3, 29) = 19.26$, $p < .01$, $\eta^2 = .19$. Proactive interference caused escalating forgetting within a few trials, but forgetting decreased in the fourth RPI trial as a result of release from interference. The subsiding memory performance in trials 1 to 3, and the difference between conditions regarding trial 4, are shown in Figure 2, below.

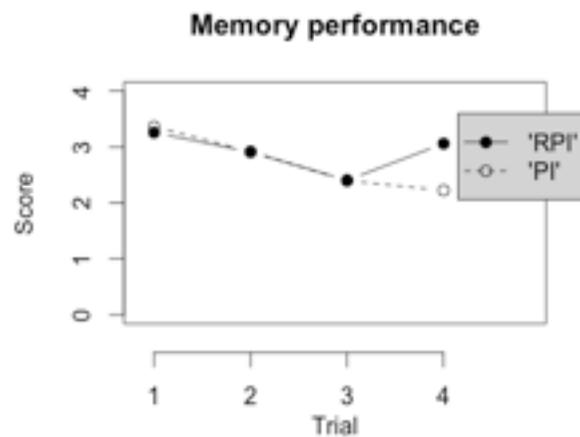


Figure 2. Average memory performance as a function of condition and trial. Black dots represent the RPI trials and white dots represent PI trials.

Post hoc Tukey tests with a 95% confidence level showed that this release from interference effect was significant: both the difference between trial 3 and trial 4 in the RPI condition (mean difference = 0.65, $p < 0.01$), and the difference between PI and RPI in trial 4 (mean difference = 0.83, $p < 0.01$). The mean score in trial 4 in the PI condition was 2.23 (SD = 0.8), and in the RPI condition 3.06 (SD = 0.7). The RPI effect, in trial 4, was shown to be large: $d = 1.14$.

Pupil data

After data processing and correction for artifacts, 9% of the original samples were excluded from analysis. Of the remaining samples, 1480 were from the PI condition and 1496 from the RPI condition. These samples were baseline averaged by subtracting the baseline sample from each trial from each sample.

During the 2 second cue phase, an ANOVA showed no significant interaction effect of condition and trial on average pupil size: $F(3, 90) = 0.99$, $p = .4$. A paired t-test of the difference between conditions during the fourth trial also showed no significance: $t(30) = 0.941$, $p = .35$, $d = 0.15$ (see Fig. 3).

A permutation test of significance, with 20,000 Monte Carlo simulations, for the cue phase in trial 4, similarly, showed no significant differences between the conditions at any time point $p = .12$ (see Fig. 4).

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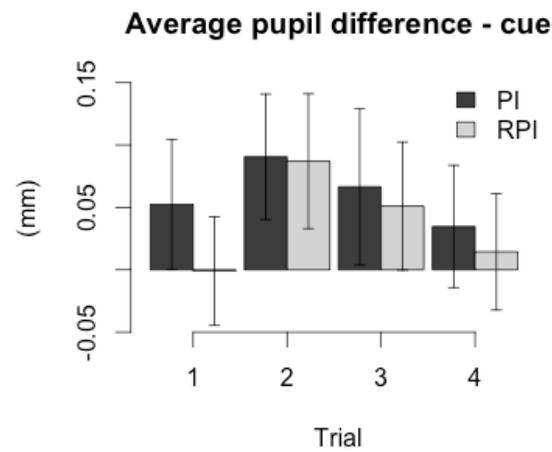


Figure 3. Bar chart showing the average difference in pupil diameter in mm during the cue phase compared to baseline, for all four trials. Black bars represent PI trials and grey bars represent RPI trials. Error bars show 95% confidence intervals.

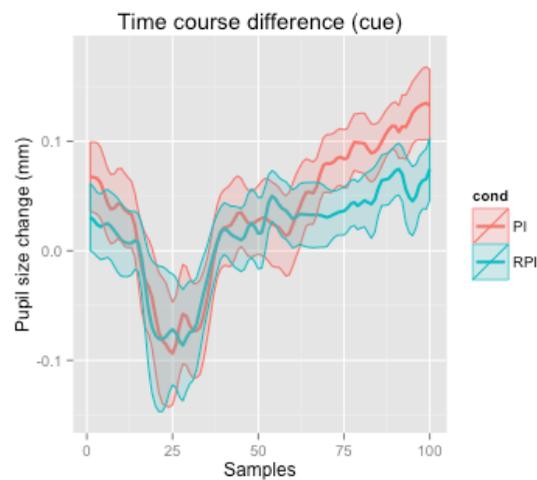
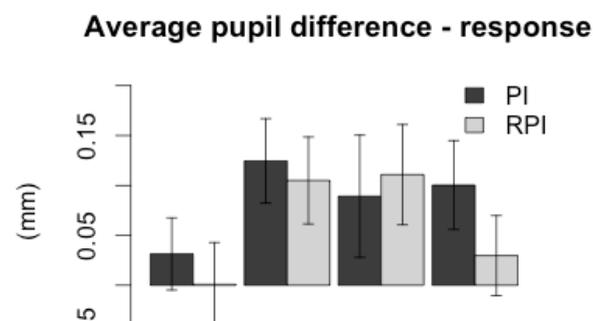


Figure 4. Time course differences in pupil size between conditions during trial 4 in the cue phase. Down sampled to 50hz. Shaded regions show standard error. No differences were found in the time course of the pupillary signals.

Regarding the 8 second verbal response phase, an ANOVA showed a significant interaction effect of condition and trial, $F(3, 90) = 2.73$, $p < .01$. A paired t-test showed that the difference in pupil size between conditions in the fourth trial was significant, $t(30) = 2.672$, $p = .01$, $d = 0.61$. Differences in all other trials were nonsignificant, all $ps > .13$. This shows that release from interference caused the pupil to dilate less during the response phase (see Fig. 5).

To investigate where the pupil difference in the response phase began, an extended time course difference analysis was performed. Thus, the analyzed interval was extended to 4 seconds after cue presentation. A permutation test of significance with 20,000 Monte Carlo simulations showed a significant pupil difference during this time period between conditions: $t(30) = 3.14$, $p = .03$. This shows that the difference in pupil dilation between interference and interference resolution was initiated at the end of the cue phase, extending and reaching significance in the response phase (see Fig. 6).



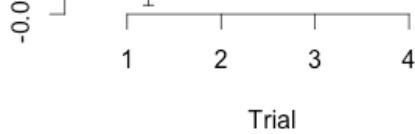


Figure 5. Average difference in pupil diameter in mm during the response phase compared to baseline, for all four trials. Black bars represent PI trials and grey bars represent RPI trials. Error bars show 95% confidence intervals.

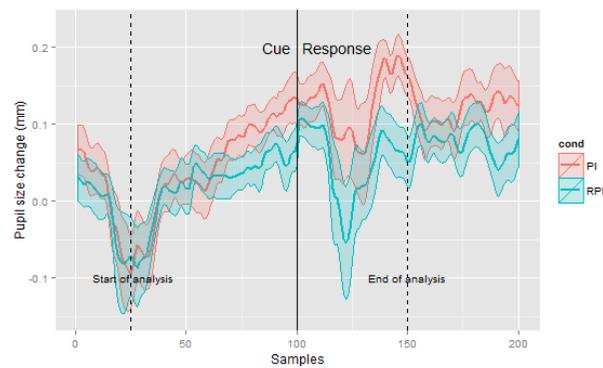


Figure 6. Time course differences in pupil size between conditions during trial 4 in the cue phase and 2 seconds into the response phase. Down sampled to 50hz. Shaded regions show standard error. A significant difference was found in the time course of the pupillary signals within this time period.

Beyond hypothesis testing, an additional exploratory analysis was performed to reveal when the largest pupil differences at retrieval occurred. Post hoc Tukey tests show that the largest pupil dilation in the cue phase for both conditions occurs in trial 2, producing a significant difference as compared to trial 4 in the cue phase ($p = .01$), and a 0.09 mm dilation from trial 1 to trial 2 in the response phase ($p < .01$).

5 Discussion

Interpretations and limitations

The results show that memory performance was predictably worsened by semantic interference, and that release from interference affected performance positively, resulting in more correctly recalled words, as hypothesized (H1). Meanwhile, there seemed to be a connection between pupil size and interference as it occurred during the verbal response phase. This caused the pupil to dilate in response to interference, as compared to pupil size at release from interference, which was less dilated. However, this effect was not present in the cue phase as hypothesized (H2, H3), even if there was a trend towards it as shown by permutation tests (see the final 250 samples of Fig. 4).

The interference effect was clearly observed in the behavioral data as a declining slope. Meanwhile, pupil diameter fluctuations showed a pattern of decreasing pupil dilation over trials, except in trial 1. This is mostly congruent with results from Engle (1975). As reported, the largest pupil dilation seems to occur in trial 2 for both conditions, and a large difference occurs between trial 1 and 2 in the response phase. There is also a difference between conditions in trial 1, with more pupil dilation in the PI condition. What could cause these patterns?

One possible explanation is that the measure of the pupil baseline size just before stimulus presentation did not actually reflect the baseline. There could be latent effects of the ongoing cognitive processes from the last retrieval phase. A recommendation for future studies is to measure the baseline at another point in the experiment, e.g. just before the distraction task, to minimize confounds.

Another possibility is a latent effect of the preceding experimental block on the beginning of the next one. The order of conditions was pseudo-randomized, and it is possible that RPI blocks were preceded by RPI blocks more often than by chance,

causing a kind of double RPI effect by shifting the category twice (i.e. a new category word was shown in trial 4 of one block, and then again in the first trial of the next block) – consequently, causing an RPI effect at the beginning of the block. This effect is rather unlikely to have occurred very often over the course of an experiment, and while the order of conditions should be more rigidly controlled in further studies in case of latent effects it is highly unlikely to fully explain the data reported here.

One other possible explanation is that the varying pupil diameters were caused by varying levels of typicality. Since the first word presented at the beginning of each block is the most typical word of its category, relatively little inhibition and selection is needed during the recall of this word. Words that are strongly associated with their category, i.e. have more cue-target associative strength, can make retrieval more automatic and less dependent on post-retrieval selection, in line with findings by Badre et al (2005). The typicality rating drops with the next word, presumably requiring more effort to recall as the first word is still strongly activated in memory and needs to be inhibited. In other words, an active selection between memory traces is required that depends more on the relative strength of the first word than the amount of competing memory traces.

The average decrease in pupil dilation in trials 3 and 4 could be due to task fatigue and faltering attention: as the task gets more difficult, participants focus less attention on the task, thus recruiting less cognitive load. It could also be that since the items to be retrieved are less typical and have a weaker association to their semantic category, they can be more easily separated from earlier items and thus require less inhibitory mechanisms.

We know pupil responses to correlate with a range of physiological and cognitive mechanisms other than memory. In future studies, a more rigidly controlled experimental environment is recommended, for example with a tower mounted eye tracker and with no experiment leader or technician present in the room. On the other hand, the remote eye tracker and relative freedom of movement for the participants probably avoided data loss and confounding effects due to fatigue.

A limitation of this study was the lack of response time data during the response phase. This made the study much less time-sensitive than it could have been, since recorded response times for words could have given a more sensitive measure of the relationship between pupillary responses and recall. Response time recording is highly recommended in similar studies.

In this study, the point of recall was limited to the 2 second cue presentation, to avoid artifacts related to speech activity. Physiologically, the memory pupil effect could have occurred within this time span. However, we do not know whether participants actually spent the cue phase trying to recall the words, or whether the actual recall took place during the verbal response phase. Response times may have been delayed as the block progresses and retrieval gets increasingly more difficult. This could explain the declining pupil dilation in the cue phase in trials 3 and 4, supposing that participants waited longer to answer during these trials.

This is also a matter of how recall is operationalized. If we allow the operationalization to expand to the response phase, it can be argued that these results indicate a strong relationship between handling of memory interference and pupil response – just not within the exact time interval that was hypothesized. Since the inhibitory mechanisms involved in interference control are thought to be cortical (Badre & Wagner, 2007), and longer pupil responses latencies have been linked to cortical processes (Barbur, Wolf & Lennie, 1998), these latent responses seem less surprising. Possibly, the same effect could be shown for the cue phase in a study with more participants. A cue that is directly linked to the items showed in a specific trial, e.g. the name of the category which the words belong to, might be used for a higher chance of activating the associated items.

An observation to take into account while interpreting these results is that the effects of PI and RPI seems to vary with age and with time of day (Hasher, Chung, May, & Foong, 2002). As this might reflect varying levels of cognitive control, it could have an effect on pupil size. Time of day and age were not controlled variables in this study, but age spread amongst participants was fairly large, and the experiments were performed at different times of the day. However, the within-subjects design of this study should control for these variables.

This study is the first to investigate pupil size change at retrieval in an interference resolution task. Only one previous study (Engle, 1975) has explored the relationship between pupil size and interference control. However, the present study differs from that study both in theoretical perspective and methodological framework. Critically, Engle studied pupil responses during encoding, not retrieval; he used various levels of emotional value in his stimulus material, which creates a possible confound of arousal on the resulting pupil responses; older equipment was used, reducing sensitivity compared to modern equipment which was used in this study. His was also a between-subjects study which is less sensitive in taking into account individual differences in working memory capacity.

The results of this study seem to be compatible with the inhibition theory of interference, with less inhibitory mechanisms needed for retrieval of RPI items, as reflected in decreased pupil dilation. Evidence for inhibition theory comes mainly from studies of retrieval-induced forgetting (Anderson, 2003), and has been shown to activate inhibitory areas using methods ranging from fMRI (e.g. Wimber et al., 2008, 2015) to ERPs (Staudigl, Hansmayr, & Bäuml, 2010; Hellerstedt & Johansson, 2014), and transcranial direct current stimulation (tDCS) (Penolazzi et al., 2014). Findings from these studies have been interpreted as strong evidence of the role of inhibitory mechanisms in memory. Meanwhile, conclusive evidence from pupillometry is yet to be found. This study is the first step to providing further support for the inhibition account by providing pupillary response results.

There are some alternative accounts to this theory of forgetting, even if they can be said to be less established compared to the overwhelming evidence of inhibition theory. The main alternative account is competition theory, which states that strengthening of competitors, e.g. by repetition, is what causes interference (Raaijmakers & Jakab, 2012). However, since no repetition of items was performed in this study, it is unlikely to explain the present results.

Using pupillometry to study these phenomena is relatively simple and non-invasive compared to other methods such as fMRI. As with other methods, is difficult to put forward claims about causation since pupillometry provides only correlates of neural activity. However, it is an effective “reporter variable” for cognitive mechanisms such as processes involved in memory and can give a greater understanding of them. We do not yet know the direct underlying neural foundation of the pupil responses to memory functions, but future studies with simultaneous recording of brain activity could elucidate this. This might also reveal a connection between prefrontal control processes and LC-NE system activation, in relation to memory retrieval. I argue that the RPI paradigm is a suitable paradigm in which to study this since it reliably evokes cognitive mechanisms of interest and has few plausible confounding variables.

In conclusion, this study replicated interference and interference resolution effects from previous studies, but found no significant connection between pupil diameter and interference resolution at the point of cued recall. During the verbal response phase, however, there was a significant difference between pupil size between conditions, with the pupil being more dilated in the interference condition. This finding has implications for the relationship between pupil size and the cognitive mechanisms that affect successful retrieval through inhibition and selection, and opens up for further investigation.

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References

- Anderson, M. C., Bjork, R. A., & Bjork, E. L. (1994). Remembering can cause forgetting: retrieval dynamics in long-term memory. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, 20(5), 1063.
- Anderson, M. C. (2003). Rethinking interference theory: Executive control and the mechanisms of forgetting. *Journal of Memory and Language*, 49(4), 415-445.
- Ariel, R., & Castel, A. D. (2014). Eyes wide open: enhanced pupil dilation when selectively studying important information. *Experimental Brain Research*, 232, 337-344.
- Baddeley, A. (2000). The episodic buffer: a new component of working memory? *Trends in cognitive sciences*, 4(11), 417-423.
- Badre, D., Poldrack, R. A., Paré-Blagoev, E. J., Insler, R. Z., & Wagner, A. D. (2005). Dissociable controlled retrieval and generalized selection mechanisms in ventrolateral prefrontal cortex. *Neuron*, 47(6), 907-918.
- Badre, D., & Wagner, A. D. (2007). Left ventrolateral prefrontal cortex and the cognitive control of memory. *Neuropsychologia*, 45(13), 2883-2901.
- Barbur, J. L., Wolf, J., & Lennie, P. (1998). Visual processing levels revealed by response latencies to changes in different visual attributes. *Proceedings of the Royal Society of London B: Biological Sciences*, 265(1412), 2321-2325.
- Beatty, J., & Kahneman, D. (1966). Pupillary changes in two memory tasks. *Psychonomic Science*, 5(10), 371-372.
- Beatty, J. (1982a). Task-evoked pupillary responses, processing load, and the structure of processing resources. *Psychological bulletin*, 91(2), 276.
- Beatty, J. (1982b). Phasic not tonic pupillary responses vary with auditory vigilance performance. *Psychophysiology*, 19(2), 167-172.
- Beatty, J., & Lucero-Wagoner, B. (2000). The pupillary system. In J. T. Cacioppo, L. G. Tassinary, and G. G. Berntson (Eds.) *Handbook of psychophysiology*, 2 (142-162). Cambridge University Press.
- Bjernerstedt, A. (2013). En händelse att minnas: kan eventsegmentering reducera proaktiv interferens?.
- Blair, R. C., & Karniski, W. (1993). An alternative method for significance testing of waveform difference potentials. *Psychophysiology*, 30, 518-524.
- Brown, J. (1958). Some tests of the decay theory of immediate memory. *Quarterly Journal of Experimental Psychology*, 10 (1), 12-21.
- Carretti, B., Mammarella, I. C., & Borella, E. (2012). Age differences in proactive interference in verbal and visuospatial working memory. *Journal of Cognitive Psychology*, 24(3), 243-255.
- Conway, A. R., & Engle, R. W. (1996). Individual differences in working memory capacity: More evidence for a general capacity theory. *Memory*, 4(6), 577-590.
- Conway, C. A., Jones, B. C., DeBruine, L. M., Little, A. C., & Sahraie, A. (2008). Transient pupil constrictions to faces are sensitive to orientation and species. *Journal of Vision*, 8(3), 17.
- Darling, S., Martin, D., & Macrae, C. N. (2010). Categorical proactive interference effects occur for faces. *European Journal of Cognitive Psychology*, 22(7), 1001-1009.
- Einhäuser, W., Stout, J., Koch, C., & Carter, O. (2008). Pupil dilation reflects perceptual selection and predicts subsequent stability in perceptual rivalry. *Proceedings of the National Academy of Sciences*, 105(5), 1704-1709.
- Gardner, R. M., Beltramo, J. S., & Krinsky, R. (1975). Pupillary changes during encoding, storage, and retrieval of information. *Perceptual and motor skills*, 41(3), 951-955.
- Goldinger, S. D., He, Y., & Papesh, M. H. (2009). Deficits in cross-race face learning: Insights from eye movements and pupillometry. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, 35(5), 1105.
- Goldinger, S. D., & Papesh, M. H. (2012). Pupil Dilation Reflects the Creation and Retrieval of Memories. *Current Directions in Psychological Science*, 21(2), 90-95.
- Goldstein, E. B. (2011). *Cognitive Psychology*. Wadsworth, Cengage Learning.
- Hasher, L., Chung, C., May, C. P., & Foong, N. (2002). Age, time of testing, and proactive interference. *Canadian Journal of Experimental Psychology/Revue canadienne de psychologie expérimentale*, 56(3), 200.
- Heuer, B., & Hyman, S. R. (2011). Keeping an eye on the truth? Pupil size changes

- Heaver, B., & Hutton, S. B. (2011). Keeping an eye on the truth? Pupil size changes associated with recognition memory. *Memory*, 19(4), 398-405.
- Heitz, R. P., Schrock, J. C., Payne, T. W., & Engle, R. W. (2008). Effects of incentive on working memory capacity: Behavioral and pupillometric data. *Psychophysiology*, 45(1), 119-129.
- Hellerstedt, R., Rasmussen, A. & Johansson, M. (2012). Swedish category norms. *Lund Psychological Reports*, 12(3).
- Hellerstedt, R., & Johansson, M. (2014). Electrophysiological correlates of competitor activation predict retrieval-induced forgetting. *Cerebral Cortex*, 24(6), 1619-1629.
- Hess, E. H., & Polt, J. M. (1964). Pupil size in relation to mental activity during simple problem-solving. *Science*, 143(3611), 1190-1192.
- Hoffing, R. C., & Seitz, A. R. (2015). Pupillometry as a Glimpse into the Neurochemical Basis of Human Memory Encoding. *Journal of cognitive neuroscience*.
- Holmqvist, K., Nyström, M., Andersson, R., Dewhurst, R., Jarodzka, H., & van de Weijer, J. (2011). *Eye Tracking. A Comprehensive Guide to Methods and Measures*. Oxford University Press.
- Human nervous system. (2015). In *Encyclopaedia Britannica*. Retrieved from <http://academic.eb.com.ludwig.lub.lu.se/EBchecked/topic/409709/human-nervous-system>
- Jonides, J., Smith, E. E., Marshuetz, C., Koeppel, R. A., & Reuter-Lorenz, P. A. (1998). Inhibition in verbal working memory revealed by brain activation. *Proceedings of the National Academy of Sciences*, 95(14), 8410-8413.
- Jonides, J., & Nee, D. E. (2006). Brain mechanisms of proactive interference in working memory. *Neuroscience*, 139(1), 181-193.
- Kane, M. J., Bleckley, M. K., Conway, A. R., & Engle, R. W. (2001). A controlled-attention view of working-memory capacity. *Journal of Experimental Psychology: General*, 130(2), 169.
- Kafkas, A., & Montaldi, D. (2011). Recognition memory strength is predicted by pupillary responses at encoding while fixation patterns distinguish recollection from familiarity. *The Quarterly Journal of Experimental Psychology*, 64(10), 1971-1989.
- Kahneman, D., & Beatty, J. (1966). Pupil diameter and load on memory. *Science*, 154(3756), 1583-1585.
- Kahneman, D. (1973). *Attention and effort*. Englewood Cliffs, NJ: Prentice-Hall.
- Kahneman, D. (2011). *Thinking, fast and slow*. New York: Farrar, Straus and Giroux.
- Keppel, G., & Underwood, B. J. (1962). Proactive inhibition in short-term retention of single items. *Journal of verbal learning and verbal behavior*, 1(3), 153-161.
- Klingner, J., Tversky, B., & Hanrahan, P. (2011). Effects of visual and verbal presentation on cognitive load in vigilance, memory, and arithmetic tasks. *Psychophysiology*, 48(3), 323-332.
- Kuchinke, L., Võ, M. L. H., Hofmann, M., & Jacobs, A. M. (2007). Pupillary responses during lexical decisions vary with word frequency but not emotional valence. *International Journal of Psychophysiology*, 65(2), 132-140.
- Kuhl, B. A., Dudovic, N. M., Kahn, I. & Wagner, A.D. (2007). Decreased demands on cognitive control reveal the neural processing benefits of forgetting. *Nature Neuroscience*, 10(7), 908-914.
- Laeng, B., Waterloo, K., Johnsen, S. H., Bakke, S. J., Låg, T., Simonsen, S. S., & Høgsæt, J. (2007). The eyes remember it: oculography and pupillometry during recollection in three amnesic patients. *Journal of cognitive neuroscience*, 19(11), 1888-1904.
- Laeng, B., Ørbo, M., Holmlund, T., & Miozzo, M. (2011). Pupillary Stroop effects. *Cognitive Processing*, 12, 13-21.
- Laeng, B. (2013, August). Pupillometry and Cognitive Processing. PowerPoint presentation at the 17th European Conference on Eye Movements, Lund, Sweden.
- Levy, B. J., Kuhl, B. A., & Wagner, A. D. (2010). The functional neuroimaging of forgetting. In S. Della Sala (Ed.) *Forgetting* (135-163). New York: Psychology Press.
- Loosli, S. V., Rahm, B., Unterrainer, J. F., Weiller, C., & Kaller, C. P. (2014). Developmental change in proactive interference across the life span: evidence from two working memory tasks. *Developmental Psychology*, 50(4), 1060-1072.
- Mathôt, S., Van der Linden, L., Grainger, J., & Vitu, F. (2013). The pupillary light response reveals the focus of covert visual attention. *PLoS ONE*, 8(10): e78168.
- Moscovitch, M. (1982). Multiple dissociation of function in the amnesic syndrome. In J.

- Moscovitch, M. (1982). Multiple dissociation of function in the amnesic syndrome. In E. S. Cermak (Ed.), *Human memory and amnesia* (pp. 337–370). Hillsdale, NJ: Erlbaum Associates.
- Multhaup, K. S., Balota, D. A., & Faust, M. E. (2003). Exploring semantic memory by investigating buildup and release of proactive interference in healthy older adults and individuals with dementia of the Alzheimer type. *Journal of the International Neuropsychological Society*, 9(6), 830 – 838.
- Naber, M., Frässle, S., Rutishauser, U., & Einhäuser, W. (2013). Pupil size signals novelty and predicts later retrieval success for declarative memories of natural scenes. *Journal of vision*, 13(2), 11.
- Nairne, J. S. (2002). Remembering over the short-term: The case against the standard model. *Annual review of psychology*, 53(1), 53-81.
- Otero, S. C., Weekes, B. S., & Hutton, S. B. (2011). Pupil size changes during recognition memory. *Psychophysiology*, 48(10), 1346-1353.
- Papesh, M. H., & Goldinger, S. D. (2012). Pupil-BLAH-metry: Cognitive effort in speech planning reflected by pupil dilation. *Attention, Perception, & Psychophysics*, 74(4), 754-765.
- Penolazzi, B., Stramaccia, D. F., Braga, M., Mondini, S., & Galfano, G. (2014). Human memory retrieval and inhibitory control in the brain: beyond correlational evidence. *The Journal of Neuroscience*, 34(19), 6606-6610.
- Peterson, L. R., & Peterson, M. J. (1959). Short-term retention of individual verbal items. *Journal of Experimental Psychology*, 58(3), 193–198.
- Porter, G., & Troscianko, T. (2003). Pupillary response to grating stimuli. *Perception*, 32.
- Postman, L. (1961). The present status of interference theory. In *Conference on Verbal Learning and Verbal Behavior, 1959, US*. McGraw-Hill Book Company.
- Purves, D., Cabeza, R., Huettel, S. A., LaBar, K. S., Platt, M. L., Woldorff, M.G. (2013). *Principles of cognitive neuroscience* (2nd ed.). Sinauer Associates.
- Pupil. (2015). In *Encyclopaedia Britannica*. Retrieved from <http://academic.eb.com.ludwig.lub.lu.se/EBchecked/topic/483706/pupil>
- Raaijmakers, J. G., & Jakab, E. (2013). Rethinking inhibition theory: On the problematic status of the inhibition theory for forgetting. *Journal of Memory and Language*, 68(2), 98-122.
- Ricker, T. J., Vergauwe, E., & Cowan, N. (2014). Decay theory of immediate memory: From Brown (1958) to today (2014). *The Quarterly Journal of Experimental Psychology*, (ahead-of-print), 1-27.
- Staudigl, T., Hanslmayr, S., & Bäuml, K. H. T. (2010). Theta oscillations reflect the dynamics of interference in episodic memory retrieval. *The Journal of neuroscience*, 30(34), 11356-11362.
- Steinhauer, S. R. (2011, September). Analysis of Pupillary Data. PowerPoint presentation at the Society for Psychophysiological Research Workshop, Boston, U.S.
- Storm, B. C., & Levy, B. J. (2012). A progress report on the inhibitory account of retrieval-induced forgetting. *Memory & Cognition*, 40(6), 827-843.
- Tulving, E. (1985). How many memory systems are there? *American Psychologist*, 40, 385 – 398.
- Van Gerven, P. W., Paas, F., Van Merriënboer, J. J., & Schmidt, H. G. (2004). Memory load and the cognitive pupillary response in aging. *Psychophysiology*, 41(2), 167-174.
- van Rijn, H., Dalenberg, J. R., Borst, J. P., & Sprenger, S. A. (2012). Pupil dilation covaries with memory strength of individual traces in a delayed response paired-associate task. *PLoS One*, 7(12), e51134.
- Võ, M. L. H., Jacobs, A. M., Kuchinke, L., Hofmann, M., Conrad, M., Schacht, A., & Hutzler, F. (2008). The coupling of emotion and cognition in the eye: Introducing the pupil old/new effect. *Psychophysiology*, 45(1), 130-140.
- Wickens, D. D., Born, D. G., & Allen, C. K. (1963). Proactive inhibition and item similarity in short-term memory. *Journal of Verbal Learning and Verbal Behavior*, 2(5), 440-445.
- Wickens, D. D. (1970). Encoding categories of words: An empirical approach to meaning. *Psychological Review*, 77(1), 1-15.
- Wickens, D. D., Reutener, D. B., & Eggemeier, F. T. (1972). Sense impression as an encoding dimension of words. *Journal of Experimental Psychology*, 96(2), 301.
- Wickens, D. D., Dalezman, R. E. & Eggemeier, F. T. (1976). Multiple encoding of word attributes in memory. *Memory & Cognition* 4(3) 307-310.

- attributes in memory. *Memory & Cognition*, 1(3), 307-316.
- Wimber, M., Bäuml, K. H., Bergström, Z., Markopoulos, G., Heinze, H. J., & Richardson-Klavehn, A. (2008). Neural markers of inhibition in human memory retrieval. *The Journal of Neuroscience*, 28(50), 13419-13427.
- Wimber, M., Alink, A., Charest, I., Kriegeskorte, N., & Anderson, M. C. (2015). Retrieval induces adaptive forgetting of competing memories via cortical pattern suppression. *Nature neuroscience*, 18(4), 582-589.
- Yi, Y., & Friedman, D. (2011). Event-related potential (ERP) measures reveal the timing of memory selection processes and proactive interference resolution in working memory. *Brain research*, 1411, 41-56.