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Eye-Movement Correlates of Pattern Separation in a Mnemonic Similarity Task Modified with Naturalistic Scenes

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“A human being is a part of the whole called by us ‘Universe,’ a part limited in time and space. He experiences himself, his thoughts, and feelings as something separated from the rest—a kind of optical delusion of his consciousness. This delusion is a kind of prison for us, restricting us to our personal desires and to affection for a few persons nearest to us. Our task must be to free ourselves from this prison by widening our circle of compassion to embrace all living creatures and the whole of nature in its beauty.” (Walter Sullivan, “The Einstein Papers: A Man of Many Parts,” The New York Times, March 29, 1972.)”

from *How to Change Your Mind: What the New Science of Psychedelics Teaches Us About Consciousness, Dying, Addiction, Depression, and Transcendence*

by Michael Pollan

Abstract

Pattern separation is one of the central operations of episodic memory. Tasks that evaluate the pattern separation usually base their assessments on the behavioral recall of simple objects or words and are far from real-life experiences and daily memory performance. Thus, typical tasks that assess pattern separation lack ecological validity. To address this issue, we designed a mnemonic memory test by creating naturalistic visual stimuli consisting of objects in contexts. Such stimuli are particularly beneficial for eye-tracking assessment in unrestricted viewing. Eye movements provide in-depth information about how memory is formed and retrieved compared to the usual behavioral assessment. We presented participants with images of everyday scenes while recording their eye movements, and then tested their recognition memory in a spatial discrimination test. A novel multi-dimensional scanpath similarity analysis was used to unfold the role of scanpath overlap between encoding and retrieval. We found that fixation duration and fixation number predict indexes related to pattern separation at encoding but not retrieval. Lure correct rejections had fewer fixations and higher fixation durations at retrieval compared to other combinations of conditions (lure, target) and responses (correct, incorrect). Position scanpath replay supported correct recognition. Moreover, we observed that higher perceived stress was associated with impaired lure discrimination ability and increased overgeneralization. Overall, our study showed a high sensitivity of the combination of naturalistic viewing tasks and eye tracking to memory performance, which may help assess and diagnose cognitive impairment.

Keywords: Scanpath Similarity, Mnemonic Similarity Task, Episodic Memory, Lure Discrimination, MultiMatch, Real-World Visual Search, Encoding, Retrieval

Eye-Movement Correlates of Pattern Separation in a Mnemonic Similarity Task Modified with Naturalistic Scenes

The first time we walk into a friend's kitchen, it takes a while to scan the room and to spot the paper towels sitting on the countertop. Examining a new and complex environment takes time and requires our attentional processes and active visual scanning with eye movements to construct episodic memory representations. By the time you enter the same kitchen more times or have experience scanning a scene, the process of searching becomes faster and more efficient, as you know where the paper towels and various other objects sit straight away. This example displays how visual search can evolve with increased experience of the task or scene. The second time we enter the kitchen, we may notice a change in location if the location of the paper towels and water boiler is switched. This example demonstrates our pattern separation ability, which is a process of episodic memory that helps us distinguish and tell the difference between experiences that share highly similar features (A, Å), by minimizing the overlap between the representation of these experiences in the brain (Hunsaker & Kesner, 2013). Conversely, we may remember details of our friend's kitchen when we are shown a photograph only capturing one corner. This is an example of the pattern completion process, in which a previously formed representation is restored in full of parts (Treves & Rolls, 1992).

Pattern completion and pattern separation are two crucial components of episodic memory that are opposite processes. Maintaining a balance between recovering memories based on partial information and keeping similar events apart is necessary. Although both calculations appear to depend on the hippocampus, they are also seemingly implemented by different subfields (Bonnici et al., 2012). Various tasks that assess pattern separation ability establish that re-exposing individuals to the same or similar stimuli and assessing their ability to detect a similar event correctly is a good indicator of memory performance and hippocampal integrity throughout the lifespan while being sensitive to changes in memory (Laczó et al., 2021; Stark et al., 2013). Since the hippocampus is one of the primary areas that is affected by aging and especially abnormal aging conditions such as Alzheimer's, studies also claim that pattern separation tasks are promising for early assessment of conditions that impair memory by placing high demand on the hippocampus and pattern separation ability (Laczó et al., 2021; Stark et al., 2013). Reduced ability to pattern separate, in other words, to minimize interference between related and similar events, has not only been associated with old age (Bettio, Rajendran & Gil, 2017) but also psychiatric conditions that impair cognition (i.e., schizophrenia, depression, and anxiety) (Petrik, Lagace & Eisch, 2012). However, it has not yet been explored if less severe conditions such as perceived stress levels can cause significant reductions in the ability to pattern separate; more research is needed regarding the possibility of such a relationship.

A recent review by Liu et al., 2021 drew attention to the emerging potential of eye tracking (ET) as it has high accuracy in detecting cognitive impairment. How scanpaths, fixations, and saccades come into play objectively reflects memory and pattern separation, in contrast to commonly used behavioral assessments that are not as reliable or reflective of the underlying processes. The review also underlined that this field is still very new and that more research is needed to determine the best protocols to implement ET to detect these cognitive impairments. Tracing gaze can capture relevant memory processes as they unfold over space and time, adding a new dimension to simple behavioral response paradigms. Thus, combining ET with pattern separation tasks is crucial and worth exploring to improve future assessment and diagnostic techniques of conditions impairing cognition (Liu et al., 2021).

In this study, we aimed to tackle the gap in the literature by creating a new paradigm to test pattern separation capacity, through modifying existing behavioral mnemonic discrimination paradigms. This was done by 1-) designing naturalistic scene stimuli using The Sims 4 platform to allow for an ecologically valid test suitable for free viewing. 2-) Adding a component of objective measurement to pattern separation studies by analyzing gaze patterns to capture memory processes as they unfold during memory formation and retrieval and the overlap between them. 3-) Exploring if perceived stress level can negatively impact pattern separation ability, like clinically diagnosed conditions related to stress (Lissek, 2012). Considering that significant efforts have been undertaken over the last decade to identify the role of eye-tracking in predicting and diagnosing memory conditions, such as dementia and other cognitive disorders (Liu et al., 2021; Readman et al., 2021), it is crucial to address the aims of this study.

Theoretical Background

Episodic Memory

Despite scientists' hypothesis that there were multiple forms of memory (James,1890), it was not until the 20th century that scientists could find evidence for distinctive memory functions through biological and psychological processes (Squire, 2009). A compelling memory research case was the patient H.M, whose medial temporal lobe (MTL) was surgically removed to treat severe epilepsy (Squire, 2009). He was later presented with an inability to remember factual information along with his personal experiences, yet he was able to learn a mirror-tracing task. Memory theorists hypothesized, considering these and related data, that the MTL, which consists of the structures of the hippocampus, amygdala, and parahippocampal structures, plays a crucial role in explicit long-term memory but not in short-term memory or procedural/implicit learning (Camina & Güell, 2017). Long-term memory was classified into two broad categories, namely explicit and implicit. Implicit memory is the information we remember unconsciously, such as riding a bike or reading.

On the other hand, explicit or conscious memory consists of information related to the facts we know about the world (semantic memory) and our memory for our life events and experiences (episodic memory). Episodic memory is a crucial aspect of cognition that allows us to recall the past to improve future judgments. It contains information regarding where, when, what, and why an event happened, allowing us to travel back in time mentally (Brewer,1986; Clayton & Dickinson, 1998; Rubin & Umanath, 2015).

Memory Consolidation- Encoding, Storage, and Retrieval

The three distinct but interconnected processes of information encoding, storage, and retrieval can be used to break down the consolidation of episodic memories further. Consolidation is the process in which a short-term memory trace is transformed into long-term memory through protein synthesis and synaptic potentiation (Dudai, 2004). An increase in the signals that pass from a certain synapse can be termed potentiation and is required for learning and memory (Bramham & Messaoudi, 2005). The repetition of stimuli can strengthen the synaptic pathways, thus helping memory consolidation. Encoding is the first stage of consolidation, in which sensory input is transformed into a neuronal representation that can be stored in the form of memory. While retrieval is the process in which we access encoded and stored information after some time by reactivating the previous synaptic pathways (Bramham & Messaoudi, 2005).

The encoding and retrieval mechanisms of episodic memory were shown to be distinct. In example, there have been case reports of acute amnesia sufferers not being able to retrieve certain events, but they retrieve details encoded during the amnesia after recovery. This shows that encoding and retrieval are disconnected in some forms of amnesia, leaving patients able to record current events but unable to recollect past events while experiencing amnesia (Fukatsu, Yamadori, & Fujii, 1998). Even though various studies point to differences between encoding and retrieval, some memory theories and neuropsychological evidence state that many parallels exist between the two. According to one theory, a match between encoding and retrieval is crucial for effective memory function according to Craik (1983). Thus, information retrieval is essentially an attempt to recapitulate processes initially engaged in the perception and idea of an event. Additionally, neuropsychologists have claimed that the same brain circuits involved in an event's initial perceptual processing (encoding) are also involved in the event's storage and retrieval (Damasio, 1989; Squire, 1992).

Complimentary Processes of Pattern Separation and Pattern Completion

An important function of the hippocampus in episodic memory is its capacity to quickly store non-overlapping representations of similar events and recover them from memory in response to parts of the representation. Computational models describe these processes that contribute to our visual search and memory as pattern separation and pattern completion, respectively (Marr, 1971; Norman & O'Reilly, 2003; Yassa & Stark, 2011). Memory representations of sensory/perceptual stimuli in any domain, such as visual, olfactory, auditory, tactile, and somatosensory, are included in the attributes that can undergo pattern separation and completion (Hunsaker and Kesner, 2013). A study by Laczó et al., 2021, underlines that spatial pattern separation tasks are more sensitive than object pattern separation tasks for addressing the pathology of MCI and Alzheimer's. Pattern separation relies predominantly on the hippocampus dentate gyrus (DG) to reduce interference among highly related/similar inputs by creating non-overlapping neuronal representations, whereas pattern completion accesses previously stored information given partial or degraded cues or parts of the encoded event (Madar, Ewell & Jones, 2017; Marr, 1971; Treves

& Rolls, 1992). It has been argued that pattern separation is a process that occurs during encoding, while pattern completion takes place during retrieval. The overlap between potentially comparable incoming activity patterns is reduced during encoding (pattern separation), and these representations can then be recovered at retrieval, also if partial forms of the original input pattern are shown (pattern completion) (Lie et al., 2016; Marr, 1971).

A recent study aiming to understand if these are behaviorally separable processes hasn't found a correlation between measures of pattern completion and pattern separation, further supporting the idea that the two are different properties of complex episodic memory; they are likely complementary (Ngo et al., 2020). One view state that failing to make a mnemonic distinction between similar events may result from catastrophic interference (CI), where the newly encoded information replaces similar previously stored information (Norman & O'Reilly, 2003). CI is a trade-off between the processes of separation and completion (O'Reilly & McClelland,1994). Resultantly, pattern completion where separation needs to be present will cause errors in recognition of similarities due to using partial information to recall preexisting mnemonic representations. Measuring the incorrect identification of lure (similar) objects as old is a common approach used in behavioral research to determine pattern completion or overgeneralization (Yassa et al., 2011). There is inadequate evidence to suggest that such a fault in recognition indicates pattern completion. A possible reason can be inadequate encoding (i.e., too few fixations), that result in pattern completion. Behavioral tasks as the standard MST does not reveal the underlying processes of faulty pattern separation, in other words pattern completion. Resultantly, supporting objective evidence, such as from eye movement analyses or brain imaging, is necessary to reveal the underlying processes. It is observed that lures enhance interference between the neuronal representations of memories and increase the need for pattern separation (Stark et al., 2013). In the current study, we will examine behavioral and eye-movement correlates of correct mnemonic discrimination of lures.

Pattern Separation in the Brain

The medial temporal lobe (MTL), which includes the hippocampus and surrounding cortical areas, is key in episodic memory and memory consolidation (McGaugh, 2000; Squire et al., 2004). The contextual binding theory explains the necessity of the hippocampus in episodic memory formation and storing by stating its crucial role for multiple binding objects and contextual detail of a scene (Yonelinas, 2013). According to this theory, the hippocampus receives information from multiple regions; the amygdala for emotional valence; the parahippocampal cortex for spatial information through the dorsal 'where' stream; the perirhinal cortex, and the ventral 'what' stream. Information from these structures is later bound in a complex and high-resolution manner in the hippocampus to make up individual episodic event representations. The hippocampus compares these representations to each other and continuous incoming perceptual and visual input (Olsen et al., 2012). According to computational models of the hippocampus, representations arriving from the entorhinal cortex (EC) are distributed in overlapping forms (Bonnici et al., 2012). These can be pattern separated in a robust and domain-independent manner by the dentate gyrus (DG), which then projects this signal into the hippocampal CA3 region. CA3 is thought to project to CA1 for pattern completion (Bonnici et al., 2012). Pattern separation and completion mechanisms are not viewed as binarily different but rather as various tuning function characteristics influencing the perceptual input (Yassa & Stark, 2011).

Adult neurogenesis is the process through which new neurons are created throughout life, and one of the two brain regions known to be capable of this process is the DG (Ming & Song, 2011). Multiple studies on rodents indicate that neurogenesis in the DG is critical for accurate pattern separation. Young granule cells in the DG appear essential for pattern separation (Sahay et al., 2011; Tronel et al., 2010) and participate in encoding new information (Aimone, Deng & Gage, 2010). As a result, animals with disrupted neurogenesis have disturbance in differentiating between visual stimuli and smells (Liu et al., 2012; Winocur et al., 2012). Overall, an adequate level of pattern separation ability relies on continuous neurogenesis in the DG of the hippocampus (Bonnici et al., 2012).

Stress and Pattern Separation

At the same time, pattern separation skills and neurogenesis in the DG are important for regulating moods. Reduced neurogenesis in the DG has been linked to depression (Petrik, Lagace & Eisch, 2012), stress (Cameron & Gould, 1994) as well as aging, during which, in a human's life, it is much more common to have disorders of mood regulation (Bettio, Rajendran & Gil, 2017). It has been proposed that defective pattern separation might partially explain psychiatric problems (Sahay et al., 2011). According to studies, effective memory functioning requires precisely the correct amount of pattern separation activity.

An excessive pattern separation may prevent the completion of patterns and cause a preoccupation with irrelevant details, as is the case, for instance, with autism spectrum disorder (Sahay et al., 2011). On the other hand, inadequate pattern separation may contribute to the overgeneralization of danger cues or fear found in anxiety disorders (Kheirbek, Klemenhagen, Sahay, & Hen, 2012; Sahay et al., 2011). Individuals with anxiety disorders, posttraumatic stress disorders, and panic disorders have this general fear conditioning (Lissek, 2012). Thus, exaggerated neurogenesis-related alterations in the hippocampus and DG have been linked to psychopathological disorders.

While some studies show that even acute stress may impair the negative regulation of the HPA axis, some studies find no relation (Besnard & Sahay, 2015; Hill, Sahay & Hen, 2015). It is not yet observed if less severe stress-related conditions may impair pattern separation ability as does more serious conditions like PTSD and anxiety. Thus, the relationship between higher perceived stress levels and pattern separation and completion is an interesting topic to explore.

Eye Movements Role in Memory and Pattern Separation

The oculomotor system may be a unique effector system to reveal the construction and expression of memory since it has an evolutionary history with the hippocampus and has formed a complex network of structural and functional connections with the hippocampus (Murray, Wise & Graham, 2016). The world around us is highly complex and filled with detail. Thus, based on extrinsic and intrinsic signals, visual elements fight for our attention multiple instances each second; the winner determines which item will be chosen for fixation and additional processing in the brain and determines what we remember (Cerf, Frady & Koch, 2009; Itti & Koch, 2000). As a result, memory as well as pattern separation and completion processes, to a large degree, depend on how we visually act upon the world.

Some famous selective attention models, such as the saliency map model that predict eye movements by relying solely on salient visual variables, such as color, manage to do so more than chance level (Itti & Koch, 2000). It is agreed upon that viewing is not purely bottom-up as in the example of the saliency map model, or top-down (i.e., getting a certain instruction before viewing), but a combination of exogenous and endogenous factors that combine in determining where we look. From a top-down perspective, studies have shown that visual biases, such as the inclination to focus on faces and text (Cerf, Frady & Koch, 2009) and previous information (the knowledge that a fish does not belong in a flowerpot), are also useful in developing models of viewing and predicting eye-movements (Torralba et al., 2006). Eye tracking can reveal the use of various distinctive strategies that may be selected in their regulation of gaze in line with task objectives, and it provides a tool to examine the type of information continuously processed.

Encoding

Eye movements come to play as sequences of fixations and saccades, aiding the alternate encoding and selection of relevant input components since humans cannot encode the totality of the visual world at once (Damiano & Walther, 2019). Fixations are brief moments spent looking at a point, while saccades are the rapid motions between fixations. Through this sequence repeating serially, we manage to encode visual samples that when summed, make up the whole experience as a memory representation by connecting several details of the episodic event (Damiano & Walther, 2019). The success of retrieval or memory is related to visual sampling quality during encoding. Accordingly, behavioral research demonstrates that identification accuracy is much higher for pictures encoded in free viewing conditions than limited viewing situations (Chan et al., 2011; Henderson & Hayes, 2018). Additionally, identification accuracy is highly associated with the number of visual samplings, such as the average number of fixations, for pictures encoded under free viewing (Olsen et al., 2016).

Interestingly, this relationship between the amount of visual sampling and subsequent recognition does not exist in amnesia cases, where a severe and persistent memory deficit develops due to damage to the hippocampus and its extended system (Olsen et al., 2016). A naturalistic mnemonic similarity task has established that fixations during encoding are predictive of lure discrimination performance (Rollins, Khuu & Lodi, 2019). Participants had more fixations for trials where they correctly identified a change in a lure condition compared to falsely identifying lure conditions. These case study results imply that encoding-related eye movements facilitate the collection and fusion of visual data into a coherent memory representation, especially for healthy young people. Gaze behavior at encoding is crucial for forming long-term episodic memories and pattern separation success (Liu et al., 2016).

Recent research by Molitor et al. (2014) examined young adults' eye movements as they completed the MST's continuous recognition version. Incorrect responses to lures, or trials characterized by failed mnemonic discrimination, were linked to fewer fixations during the initial presentation or encoding than trials with successful mnemonic discrimination. Overall, studies reveal that deficiencies in mnemonic discrimination may be partially explained by gaze behavior at encoding.

Retrieval

A much more limited body of research implies that eye movements may also reflect and be influenced by the contents of memory at retrieval, despite the well-established importance of eye movements in memory encoding. For instance, several studies have demonstrated that humans examine repeated images less thoroughly, with fewer fixations at fewer regions, than novel images (Althoff & Cohen, 1999; Wynn, Buchsbaum & Ryan, 2020), and other studies have demonstrated that during retrieval, eye movements are disproportionately drawn to areas of a stimulus that either reveal a prior knowledge association or that have changed since viewing it previously (Bridge, Cohen & Voss, 2017; Hannula & Ranganath, 2009). Incorrectly identifying lures as previously seen stimuli is believed to result from the retrieval-based pattern completion process (Norman & O'Reilly, 2003). However, there is no clear consensus on whether to blame retrieval-based pattern completion or inadequate encoding of investigated stimuli for failed mnemonic discrimination. By comparing eye movements made during the initial presentation of items to eye movements made during the later presentation of item repetitions and similar lures, Molitor et al. (2014) investigated the source of incorrectly identifying a lure as old, believed to reflect pattern completion, and found that both encoding, and retrieval stages played a role in successful remembering. Mnemonic discrimination ability is not process pure regarding pattern separation and completion, and the processes seem to happen simultaneously.

Encoding-Retrieval Scanpath Similarity

The memory quality cannot be reduced solely on encoding success or retrieval processes. Scanpath replay findings instead support the notion that replaying eye movements in the retrieval phase as they were at encoding helps to rebuild related and task-relevant mnemonic information into a spatiotemporal context (Johansson et al., 2022). Further claiming that eye movements are reinstated between encoding and retrieval and that oculomotor activity replay plays a functional role in successful remembering. By examining the possible differences and similarities in gaze patterns between encoding and recall/recognition, we can extract important information about the memory process with the potential to diagnose specific functions such as pattern completion and separation. For example, Olsen et al. (2014) found a significant relationship between memory for relative, but not absolute, item placements and eye movement reinstatement/similarity throughout the study and test phases of a recording of abstract visual objects. Indicating that the type and level of eye movement reinstatements is highly dependent on the task demands, and we need to explore eye movement reinstatement concerning our paradigm without being able to make extensive assumptions based on previous literature that did not employ our exact spatial discrimination task.

Scanpath Theory and Scanpath Similarity

The scanpath theory postulates that retrieval-related eye movements reflect memory and significantly contribute to its support by reinstating the encoding scanpath. Hebb was the first to observe that eye movements have a functional role in memory retrieval even when the retrieval is imagined (Hebb 1968). A sensory-motor memory trail known as a scanpath contains information on the characteristics of an image/scene as well as the associated series of fixations and alternating saccades (Noton & Stark, 1971). According to this scanpath theory, when the encoding scanpath is repeated in the event of repeated viewing, memory retrieval is enhanced by comparing provided input with stored memory traces. Although the scanpath theory has many plausible explanations, it proposes that the similarity level between the scanpaths during encoding and retrieval should predict memory performance.

During a pure recall memory task with scenes, Johansson et al., (2022) revealed that shape replay is more commonly employed by participants when reconstructing scenes where spatial relationships are foreseeable, while direction replay was more important during reconstruction scenes where the relation between elements was arbitrary. Multi-Match Analysis was utilized to examine the scanpath similarity, a vector-based algorithm created through the Matlab toolbox by Dewhursts and colleagues (2012). Ultimately, the multi-dimensional analysis provided extra information by showing how different domains of similarity in scanpaths contributed differently to a viewing strategy based on the mnemonic content of images and the task demands.

Mnemonic Similarity Task

The Mnemonic Similarity Task (MST) was designed in 2007 as a modified object recognition memory task that assesses participants' capacity for behavioral pattern separation, an indicator of hippocampal integrity (Stark et al., 2013). The MST is thought to place a high demand on pattern separation and the hippocampus. It is the most utilized task to assess pattern separation that has specificity for the DG (Stark et al., 2013). Although several versions have been created in the original MST (for a comprehensive review, refer to Stark, Kirwan & Stark, 2019), participants serially view visual object stimuli in the encoding phase. An incidental encoding approach is commonly employed in MST paradigms, aiming to ensure that the subjects do not rely on the semantic rules of the encoded image to remember it for the subsequent retrieval phase (Zhou & Crystal, 2011). Later in the retrieval phase, they indicate whether they have seen each item before (Stark et al., 2013; Stark et al., 2019). In the test phase, one-third of the pictures are exact duplicates of the study phase images (targets- 'old'), one-third of the photos are brand-new, previously unseen images (foils- 'new'), and one-third of the images are perceptually similar but not the same as the study phase images (lures- 'similar').

Successful pattern separation or mnemonic discrimination is assumed to be the correct rejection of a lure as "similar" (mnemonic discrimination), which corresponds with DG/CA3 activity and status (Stark, Kirwan & Stark, 2019). MST tasks often evaluate memory on the same day, and versions of MST often involve word (Ly et al., 2013), object (Stark et al., 2013), or scene (Leal et al., 2019) stimuli and display similar results for all. While these versions mentioned above use well-controlled stimuli, they frequently lack the contextual information seen in realistic situations. Some exceptions that made use of scene stimuli exist, a study by Aldi et al. (2018) created an MST with scene stimuli but the changes in the lure condition were not localized and the domain of change differed (i.e., wall color changed in one lure and all the cars on the street disappeared in another lure). Another study by Leal et al. (2019) used videos in the encoding phase. It later used static scenes captured from those videos or similar but completely different static images that resemble the video in the retrieval phase. However, these types of changes are not fit for our gaze behavior analysis goals. To our knowledge, no version of MST was created until now that would fit our goal of free-viewing eye movement analysis that had more local and domain-specific changes, leading us to create a novel paradigm with naturalistic scenes.

The Present Study

This study aims to observe whether gaze behavior (fixation numbers and durations) predicts the common behavioral indexes related to pattern separation (Stark, Kirwan & Stark 2019). To replicate the previous findings showing that increased sampling with fixations at encoding and retrieval supports successful retrieval (Molitor et al., 2014; Rollins, Khuu & Lodi, 2019), we investigated the fixation number and duration in memory formation and manifestation in our task. Different predictions made for eye movements at encoding and retrieval were made due to the specific demands and instructions of the task at hand since memorizing an image at encoding would call for different strategies compared to searching for changes at retrieval.

The scanpath overlap between encoding and retrieval plays a functional role in successful retrieval and indicates memory performance without behavioral responses (Johansson et al., 2022). We investigated which of the domains of scanpath similarity (see Table 1) is relevant to our naturalistic viewing task. We presumed position similarity would be most relevant due to spatial changes we employed as lures.

Lastly, we investigated if the perceived stress level of the participants during the last month correlates with the pattern separation success. There has not been any direct study, to our knowledge, that examines the effect of perceived stress level, without the presence of a severe stress-related disorder, on pattern separation ability. This research question was explorative and was not based on previous findings in the field of pattern separation. Nevertheless, we expect that the lure discrimination index would be inversely related to stress, and the overgeneralization index would positively correlate with stress.

Hypotheses

The goals of this research yielded the formulation of four hypotheses regarding gaze behavior in encoding, retrieval, and the overlap between these two memory stages. The goals also include exploring the relationship between perceived levels of stress and pattern separation:

H1: Encoding stage:

i. The number and duration of fixations at encoding will predict lure discrimination indexes (Pr, LDIsimilar, OI) in a naturalistic mnemonic similarity task.

ii. Fixation numbers and durations at encoding will be higher for correctly identified lures.

H2: Retrieval Stage:

i. The number and duration of fixations during retrieval will be predictive of lure discrimination indexes (Pr, LDIsimilar, OI) in a naturalistic mnemonic similarity task.

ii. Fixation numbers will be lower and fixation durations will be higher for correct responses, more so for lures.

H3: Scanpath Similarity/Overlap between Encoding and Retrieval:

i. Correctly identifying a lure will present with less similar scanpaths and the MultiMatch analysis will show the sensitive features of the scanpath patterns (i.e., position and shape (Table 1).

H4: Higher perceived stress will be associated with decreased ability to separate patterns and increased overgeneralization.

Methods

Participants

Twenty-seven healthy adults participated in this experiment. One participant was removed due to extensive data loss and one other participant was removed due to chance level performance on the task overall as well as the subsets of the task. In total, 25 participants´ data were included for data analyses (14 female, 11 male), with an average age of 22.8 years (SD = 4.31). Participants were recruited amongst students at Lund University, the researcher's connections, and social media posts (i.e., Facebook). Inclusion criteria were normal or corrected to normal vision and age. Pattern separation tasks are sensitive to age, our study included the youngest age range (18–35 years old) described by Stark et al. (2013). Participants were not granted any compensation for participating in the experiment.

Materials

The stimuli presented in the study and test phase consisted of images created for this experiment, using The Sims 4 video game, developed by Maxis and published by Electronic Arts. The Sims 4 game offers character creation and comprehensive tools for building indoor and outdoor objects and worlds. In total, 96 image pairs were created, with the pair of each image being the lure and consisting of a switch in the locations of two objects. Forty-eight image pairs comprised indoor scenery, and forty-eight were outdoor scenes. Other forty-eight images were created as single foils; these images did not have pairs. Among the foils, half were indoor, and the other half were outdoor scenes. By ensuring equal indoor and outdoor stimuli, we wanted to avoid differences resulting from the fact that people visually explore indoor and outdoor stimuli differently (Zangrossi et al., 2021). For counterbalancing, the image pairs were divided into three groups. Image pairs were placed in the three groups so that each image was shown as a target and a lure, to ensure there were no image biases resulting from the content creation and differences in similarity levels between images. So that if one participant saw an image repeating as a target another person saw that image´s pair as a lure at the test. The experiment was programmed and presented to participants on the PsychoPy software (version 26) (Peirce et al., 2019). The randomization of images was obtained through a Python code that generated different excel sheets for each participant that generated copies of the three groups that were counterbalanced.

Perceived Stress Scale- PSS-10

The Perceived Stress Scale (PSS) is a well-known tool for measuring stress (Cohen, Kamarck & Mermelstein, 1983). Although it was created in 1983, the instrument continues to be a popular option for assisting us in comprehending how various circumstances impact our moods and our perception of stress, as it is a quick and effective assessment tool. Analyses of the psychometric properties of this task indicated the reliability of the PSS-10, at a Cronbach's alpha score of >.70, in over 12 different studies. In our study, Cronbach's alpha showed a reliability score of .62. Regarding the small sample size, our study was relatively reliable. PSS-10 repeatedly correlated positively with anxiety and depression (Lee, 2012). This scale asks about emotions and ideas from the last month and requires rating these based on how frequently they have been experienced (see Appendix B). Ten questions on this scale are rated from the alternatives: 0 - never, 1 - almost never, 2 - sometimes, 3 - fairly often, and 4 - very often. Higher scores on the PSS indicate higher perceived stress, with individual values on the scale ranging from 0 to 40. Low stress is regarded as scores between 0 and 13; moderate stress scores between 14 and 26, while scores between 27 and 40 indicate high stress.

Task Design- Naturalistic MST

The novel MST paradigm was created as an explicit memory test that was broken up into blocks with study (encoding), distractor, and test (retrieval) phases in each block (see Figure 1). The study images comprised indoor or outdoor scenes and several objects in a context congruent with real life (see Figure 1.1). Considering that the standard version of MST used single objects without context, it would highly restrict the viewing to use that version in combination with the eye-tracking analysis. Hence, we created a new MST paradigm consisting of semantically congruent objects in a context that allows for free viewing. We designed scenes featuring commonplace daily living scenery (i.e., a kitchen counter or a garden) without emotional valence (i.e., a burning house car crash).

A recent review by Liu et al., 2016 emphasized the importance for researchers to use the attribute model to account for specific attributes in the task design while exploring ways to increase the validity of pattern separation tasks. Our stimuli´s lure scenes only had spatial changes, making it possible to reach conclusions about a specific domain's effect on pattern separation or gaze behavior.

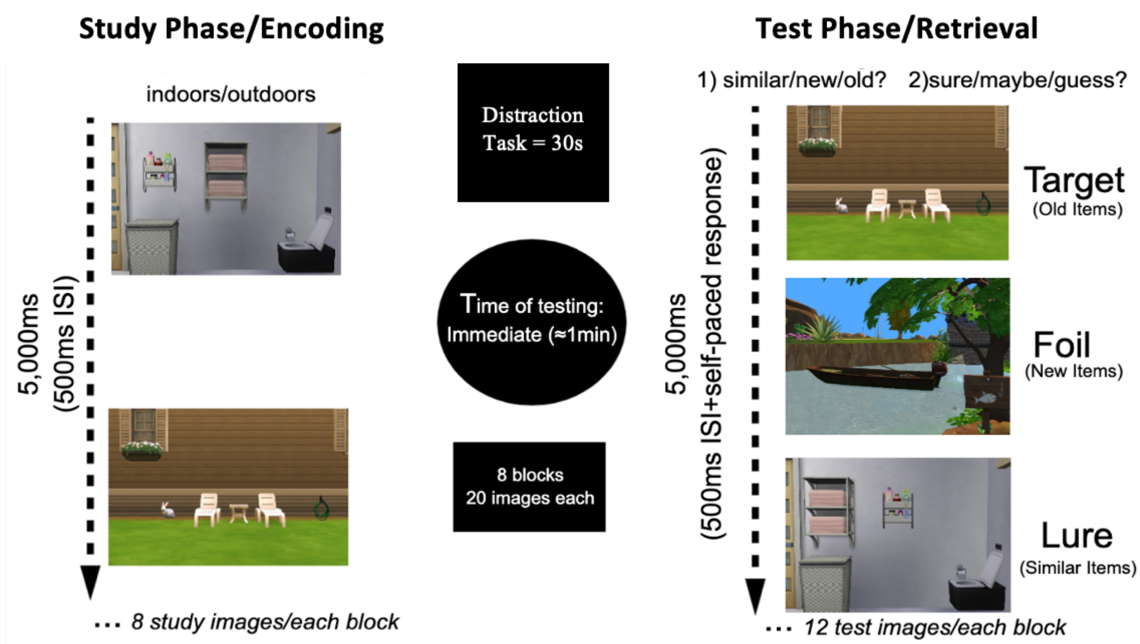
To develop a more ecologically valid memory task that incorporates the complexity of everyday experiences it is important to stick to one class of visuals to decrease noise in data, such as not using human faces in a task consistently, since human faces are processed differently than objects and words in the brain (Tsao & Livingstone, 2008). Consequently, we only used objects and did not include human faces or words in our stimuli.

In our paradigm, we did not employ an incidental encoding approach but informed participants that they would need to remember the images beforehand. We controlled for this by keeping semantic information in the scenes intact while creating lures (i.e., a fork could not move to the floor but could move elsewhere on the dinner table), so the participants could not rely on meaning to memorize the scenes. Plus, the MST´s that employ incidental encoding do not benefit from this entirely since, after only a few trials, participants grasp that the task requires them to remember the presented stimuli for the test phase.

Additionally, the mnemonic similarity rates of the classic MST's lures range from high to low similarity. To account for any bias caused by different levels of similarity of our newly created images that were not investigated for the similarity rate before, we adopted a counterbalancing method of having three sets of stimuli. These three sets of scenes are randomized and presented to participants so that each image is shown as a target and a lure for different participants an equal number of times. This way, we aimed to avoid any image biases resulting from different levels of similarity between images.

Figure 1

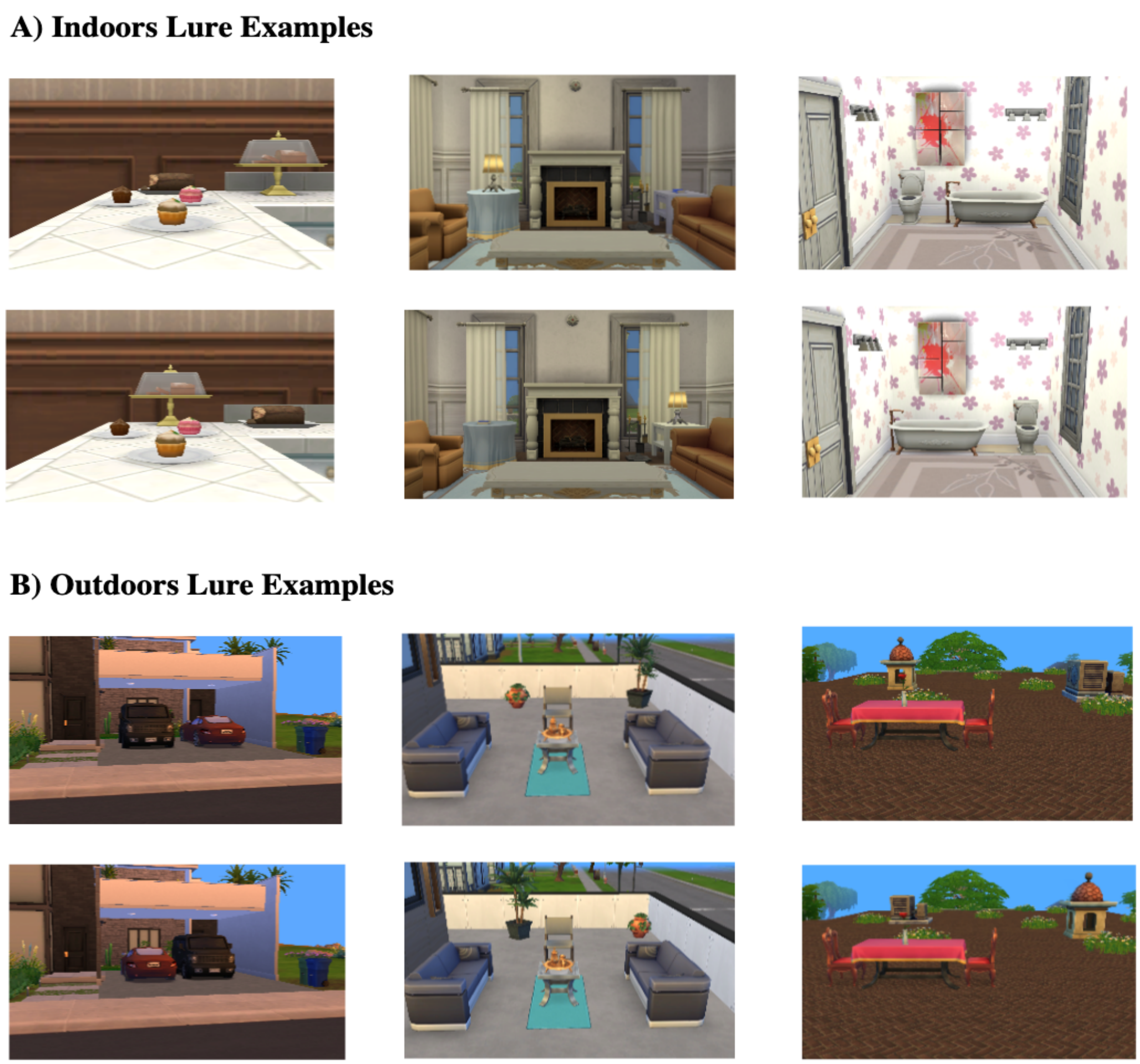
The Procedure of the Naturalistic Mnemonic Similarity Task



Note. Naturalistic mnemonic similarity task adapted for eye-tracking analysis. Participants are shown 5-sec scenes during encoding, for which there are equal numbers of indoor and outdoor stimuli. Participants are later tested on their memory for scenes (test scenes shown for 5 sec) immediately (~1-2 mins). Scenes at the retrieval phase are either the same scenes as the encoding scenes (targets), similar but not the same as the encoding scenes (lures), or not shown during any of the encoding scenes (foils); ISI = inter-stimulus interval.

Figure 1.1

Examples of Indoor and Outdoor Lure items



Note. Examples of lure scenes from the paradigm Naturalistic Mnemonic Similarity Task, created based on spatial discrimination for this study. The first rows of the A and B sections depict the study phase images; the second rows contain the lures of the subsequent row.

Procedure

First, the participants were informed that they would partake in a psychology experiment assessing memory performance by completing a behavioral memory test while an eye-tracker traces their eyes. The information above was provided in the form of informed consent (see Appendix A) and orally. Participants were first asked to sign the informed consent form and complete a demographic questionnaire (see Appendix 7). The experiment was conducted at a computer lab consisting of multiple computers connected to eye trackers. Participants entered the experiment with a maximum of 4 people. Distractions were prevented by providing a silent environment and enclosing the area around the computers to form a booth for each person.

Participants completed an eye-tracking system calibration scheme, followed by a calibration validation. Before the MST task started, participants were engaged in a practice task in line with recommendations to reduce novelty and practice effect by familiarizing individuals with the environment, task, and equipment (Lie et al., 2016). This practice task consisted of one block that exemplifies the following task that will consist of multiple blocks. The images used at practice were not shown again in the actual task, and the performance was not included in the analyses. Only during the practice block did participants get feedback as ´correct or incorrect after each response they gave.

The MST task consisted of 8 blocks, and each block of the task included 8 study and 12 test images. Participants were exposed to visual stimuli for the first time during the study phase trials. Participants were consecutively shown images in this study/encoding phase that lasted for 5000ms. There was an ISI screen of 500ms between each image. Later, a 30-second distraction screen between the study and test phases followed. During the distraction task, participants were shown a number generated for each person randomly on the screen (i.e., 450). They were asked to subtract seven from this number and continuously subtract seven from each result they got.

Later, 12 test images were presented, which were either 1- an old image they saw at the study, 2- a similar image to what they saw at the study, and 3- a completely new image they did not see at the study. Test images lasted for 5000ms with an ISI screen of 500ms between each. Each image was followed by a forced-choice question asking if they had seen the image before. The possible answers were 'old,' 'similar', and 'new.' Followed by a question asking how sure they are of the answer they gave previously, with three confidence levels being; 'sure,' maybe,' and 'guess.' The answers were given via the keyboard keys '"right, down, left" arrows. Upon finalization of the experiment, participants filled out the perceived stress questionnaire. The experiment took approximately 35 minutes, together with all preparations and the filled questionnaires.

The study's pilot with 27 participants revealed that, for the study phase, 5000 ms image presentations followed by a 500 ms ITI enable performance above chance level and prevent ceiling effects. The results of the pilot showed acceptable overall memory scores (%76). The pilot participants were aimed to be included in the study but later had to be removed due to data loss resulting from technical issues.

Apparatus

The eye-tracking technology was supplied by Lund University's Humanities Laboratory in Lund, Sweden. The default calibration in Titta (Niehorster et al., 2019) was applied to the Tobii Pro Spectrum, consisting of five calibration points and four validation points before the experiment. Re-calibrations were carried out if the visual assessment of the validation data showed significant variations in one or more validation points. Stimuli were exhibited on a 19-

inch screen with a resolution of 1600 x 1200 pixels, and the software handled and recorded the temporal parameters of the stimulus display. Eye movements were recorded on the Tobii Pro Spectrum (firmware version 1.7.6) remote eye tracking system (Tobii Technology, Sweden) at a 600 Hz temporal solution. Stimuli were displayed on the 1920 x 1080-pixel (52.8 x 29.7 cm) EIZO FlexScan EV2451 native Tobii Pro Spectrum screen. Participants were placed at a 62 cm distance from the monitor, and we arranged their chairs and tables such that their eyes were, on average, in the middle of the Tobii Pro Spectrum's headbox. The EyeLink chin and forehead rests were used to support the heads of the participants and to make sure they returned to the same position each time without needing further calibrations at each trial.

MultiMatch

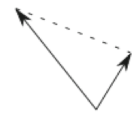
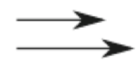
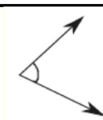
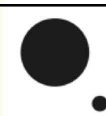
Multi-Match Analysis was used for assessing our third hypothesis, which looks into the scanpath similarity of participants between the encoding and retrieval stages of each trial/image (Dewhurst et al., 2012; Foulsham et al., 2012; Jarodzka, Holmqvist, & Nyström, 2010). The theoretical aspect of MultiMatch was proposed by Jarodzka, Holmqvist, and Nyström (2010), and Dewhursts et al. (2012) built it as a Matlab toolbox. The MultiMatch is a multi-dimensional similarity computing method for scanpaths that uses a vector-based process. In a two-dimensional space, the approach depicts scanpaths as geometrical vectors. Any given scanpath is a vector series, with the saccades represented by vectors and the saccades´ beginning and finishing points representing fixations. Compared to alternative scanpath comparison approaches, the MultiMatch method is advantageous due to its multi-dimensional analysis technique that uses five different metrics for assessing scanpath similarity (see Table 1), each capturing a different aspect of scanpath similarity.

Scanpath Similarity Analysis

To find out if observers employ a similar viewing path when they come across the same picture again, a scanpath similarity analysis was carried out. Five aspects of scanpath similarity were measured by comparing scanpaths using the MultiMatch approach (Dewhurst et al., 2012). We expected that correct identification of a lure item would result in less similar scanpaths between encoding and retrieval. Scanpaths were compared between the study and test phases for the target and lure images for each participant's trial. We calculated three different scanpath similarity scores of the target and lure pair that all corresponded to similarity measures between study and test phases for the five MultiMatch dimensions (Vector, Position, Direction, Length, and Duration). The first one was non-baselined similarity scores, which is the absolute value we got from the MultiMatch toolbox when we compared the scanpaths during the study of a specific image with the scanpath during tests of the same image or the similar one. The next one was the random measures, which was obtained by comparing the scanpath during the test with all other images during the study, except the one at hand - which corresponds to a measure of finding similarity by chance within this study and was important for eliminating the chance level similarities that can be found within this study. We calculated the final and third baselined similarity scores by subtracting the random similarity scores from the baselined similarity scores. Before the analyses, we reasoned that position similarity could be the most relevant measure to examine for our study as it compares the scanpaths concerning the order of fixation locations, and our study is a spatial discrimination task.

Table 1

MultiMatch´s scanpath comparison dimensions, taken from Dewhurst et al., 2012

Shape / Vector	Difference in the shape of the saccade vectors ($ui - vj$).	
Length	Difference in length/amplitude of two saccade vectors ($\|ui - vj\|$).	
Direction	Difference in angle between two saccade vectors.	
Position	Difference in position between aligned fixations using Euclidean distance.	
Fixation duration	Difference in fixation duration between aligned fixations.	

Statistical Analysis

The study employed a within--subject design, with the independent variables relating to condition (novel scenes, repeated scenes & similar scenes) and response accuracy (correct, incorrect) at retrieval. The dependent measures were two levels and consisted of behavioral measures (number of correct responses, Indexes of pattern separation) and eye movement data (fixation duration, number of fixations, scanpath similarity scores). The specific variables used for different analyses are presented later in the corresponding results section. We presented our results in three folds at a participant level (1-encoding stage, 2-retrieval stage, and 3- overlap between encoding and retrieval/scanpath similarity). Each dependent measure's normality was examined using the Shapiro-Wilk test separately. Levene's test or Greenhouse-Geisser for repeated measurements data were used to determine whether the variance in the data was homogeneous. IBM SPSS statistics (version 26) was used to test behavioral measurements and to analyze repeated measure ANOVAs, linear regressions, and two-way MANCOVA. P-values were reported as significant in case they were smaller or equal to .05 for all tests. MultiMatch (Dewhurst et al.,2012) method was used to perform scanpath similarity analysis in Matlab (The MathWorks, Sherborn, MA).

Lure discrimination index, or LDIsimilar is calculated by subtracting the possibility of falsely identifying a new (foil) event as similar from the possibility of correctly identifying a similar (lure) event as similar: p("Similar "|Lure) – p("Similar "|Foil) (Stark, Kirwan & Stark 2019). In the literature, there are some other indexes of lure discrimination. Additionally, two different LDIs were computed and named based on their distinctive properties: LDIold (Loiotile & Courtney, 2015), which stands for p("Old" | Target) - p("Old" | Lure), and LDInew (Cunningham et al., 2018), which stands for p("Similar" or "New" | Lure) - p("Similar" or "New" | Target). We calculated "corrected recognition," Pr, for target hits [p("Old" | Target) - p("Old" | Foil)]. Lastly, we calculated an "Overgeneralization Index" (OI) to measure the complimentary, but erroneous in this case, behavioral completion: p("Old" | Lure) - p ("Old" | Foil) (Yassa et al., 2011).

Results

Behavioral Data

No correlations existed between age and memory performance or the common indexes for assessing pattern separation (LDIsimilar, LDIold, LDInew, OI, Pr), showing that we successfully controlled for age effects with our selection criteria. Overall, participants did well on the task, correctly identifying 77.48% of targets and 66.52% of lures. The overall memory performance on the paradigm designed for this study was 80.72%. Information relating to the statistics of the important variables for this study is in Table 2. The proportions of responses (old, similar, new) to different test image conditions (target, lure, foil) can be found in Table 3.

Table 2

Descriptive Statistics of the Participants´ Demographic and Behavioral Data

	Mean	Minimum	Maximum	Standard Deviation
Age	22.80	18.00	34.00	4.31
Memory Performance	80.72%	59.00%	92.00%	6.50%
Perceived Stress Score	15.92	7.00	25.00	4.42
LDIsimilar	66.52%	38.00%	91.00%	13.33%
LDIold	52.12%	19.00%	81.00%	15.12%
LDInew	51.92%	10.00%	78.00%	15.97%
Pr	77.48%	41.00%	94.00%	11.69%
OI	25.36%	3.00%	47.00%	11.93%

Table 3

The proportion of Responses given to Different Test Conditions

Test Image Condition - Response	Minimum	Maximum	Mean	Standard Deviation
Foil - New	84.00%	100.00%	96.00%	4.06%
Foil - Old	0.00%	9.00%	2.40%	2.72%
Foil - Similar	0.00%	9.00%	1.56%	2.62%
Lure - New	0.00%	19.00%	3.88%	5.97%
Lure - Old	6.00%	56.00%	27.76%	12.45%
Lure - Similar	44.00%	91.00%	68.08%	12.65%
Target - New	0.00%	15.00%	3.44%	4.53%
Target - Old	47.00%	97.00%	79.88%	11.69%
Target - Similar	3.00%	38.00%	16.60%	10.70%

Note. The correct response to a Foil condition is New, the correct response to a Lure condition is Similar, and the correct response to a Target condition is Old.

Important Bivariate Associations Among Indexes and Gaze Behavior

Among the participants, the percentage of behavioral overgeneralization index (OI) was strongly and negatively correlated with the main measure of lure discrimination (LDIsimilar), r(23) = -..83, p< .001. LDIold and LDIsimilar were found to be strongly positively correlated, r(23) = .79, p < .001. The variables LDIsimilar and LDInew were strongly correlated, r(23) = .79, p < .001. LDIold and LDInew were found to be positively correlated, r(23) = .99, p < .001. The variables Target Recognition index (Pr) and LDInew were correlated, r(23) = .55, p = .005. Plus, The variables Target Recognition index (Pr) and LDIold correlated, r(23) = .54, p = .005. See Figure 4.

Encoding

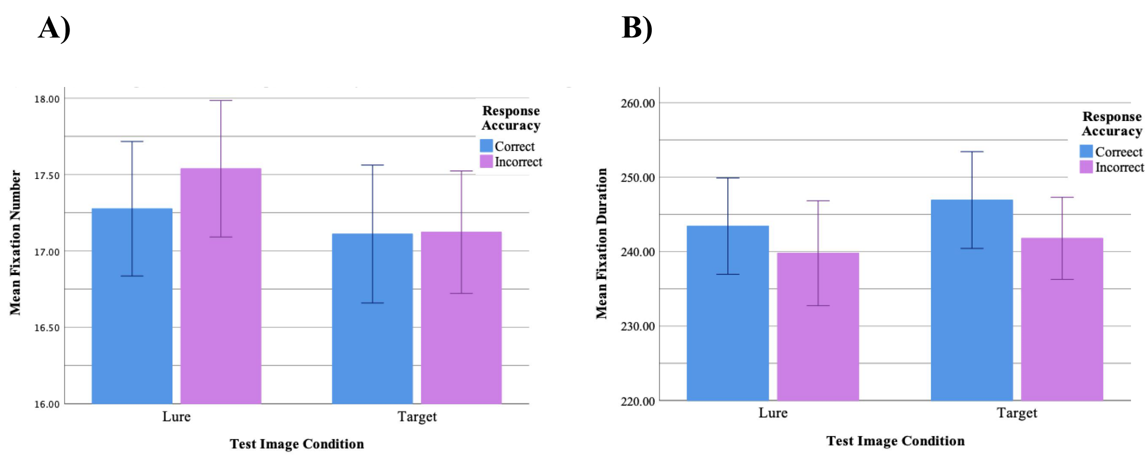
To examine if gaze behavior at encoding predicts correct pattern separation and image condition, we measured the fixation numbers and fixation durations at the study phase of a mnemonic similarity task (MST) consisting of naturalistic scene stimuli. A repeated measures ANOVA with the factors of image condition (target, lure) and response accuracy (correct, incorrect) was applied to fixation durations and the number of fixations at the study. Shapiro Wilks´s test was not significant (p>. 05), revealing that our distributions were normally distributed.

The first repeated measures ANOVA yielded that the main effect of image condition on fixation numbers was significant (F(1, 24) =4.8, p =.038). However, the main effect of response accuracy on fixation numbers was not significant (F(1, 24) = 1.1, p =.3). There was no interaction between image condition and response accuracy (F(1, 24) =1.7, p =.211). See figure 2(A) for a visualization of the results.

The second repeated measures ANOVA, revealed that the main effect of condition on fixation durations was not significant ($F(1, 24) = 1.6$, $p = .2$), the effect of response on fixation durations was also not significant ($F(1, 24) = 3.5$, $p = .1$). There was no interaction effect between condition and response on fixation duration ($F(1, 24) = 13.9$, $p = .7$). See figure 2(B) for a visualization of the results.

Figure 2

Gaze behavior as a Function of Response Accuracy and Test Image Type at Study



Note. Mean fixation numbers (A) and mean fixation durations (B) as a function of condition (target, lure) and response accuracy (correct, incorrect) at the Encoding/Study Phase. Error bars are set at +/-1 SE (standard error).

Three multiple linear regression analyses were carried out to test if the two predictors; mean fixation number and duration at encoding, predict the three indexes relevant to pattern separation in our study (LDIsimilar, Pr, OI).

In predicting LDIsimilar, the overall regression was significant. ($R2 = .349$, $F(2,22) = 5.9$, $p = .009$). The predictors' fixation number and duration were taken for similar items only. The fixation number significantly predicted LDIsimilar ($\beta = .873$, $p = .007$). Fixation duration was also found significantly predicted LDIsimilar ($\beta = .998$, $p = .002$).

The next regression for predicting PR (corrected recognition) was also significant ($R2= .519$, $F(2,22) = 4.1$, $p = .032$). It was found that fixation numbers at encoding significantly predicted PR ($\beta = .816$, $p =.014$). Fixation durations at encoding also significantly predict PR ($\beta = .838$, $p = .012$).

The next regression was conducted to predict OI (Overgeneralization Index), and it was statistically significant ($R2= .544$, $F(2,22) = 4.6$, $p = .021$). Fixation numbers at encoding were marginally significant in predicting OI ($\beta = -.627$, $p = .051$). Fixation durations at encoding significantly predicted OI ($\beta = -.907$, $p = .007$).

Retrieval

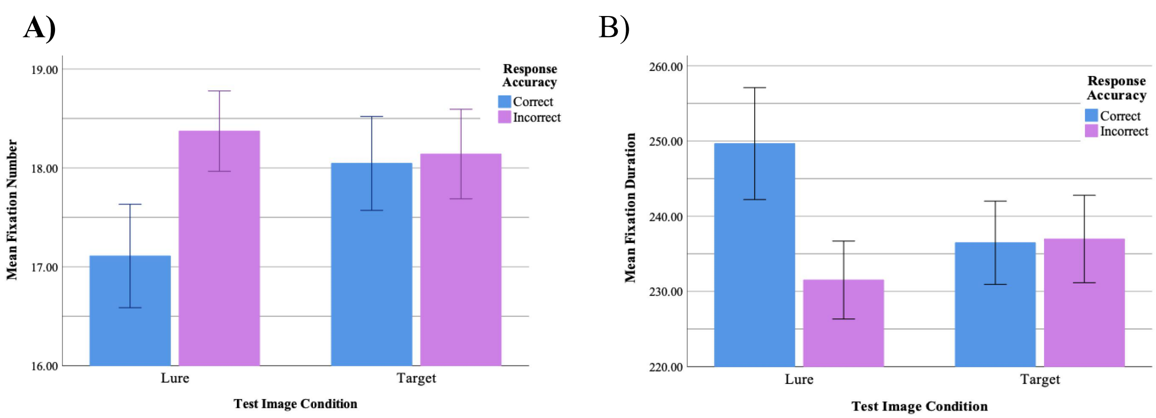
We wanted to know if visual performance at the retrieval stage differs based on correct or incorrect recognition of old and similar images. To test this, we measured the fixation numbers and fixation durations at the test stage of the MST. A repeated measures ANOVA with the factors of image condition (target, lure) and response accuracy (correct, incorrect) was applied to fixation durations and the number of fixations at retrieval. Image condition and response accuracy are the independent variables for both rmANOVA.

The first repeated measures ANOVA yielded that the main effect of image condition on fixation numbers was significant ($F(1, 24) = 8.4$, $p =.008$), as well as the main effect of response accuracy on fixation numbers at retrieval ($F(1, 24) = 12.7$, $p =.002$). The interaction of image condition and response accuracy was also significant ($F(1, 24) = 9.9$, $p =.004$). Post hoc comparisons using the Tukey HSD test indicated that the mean fixation number for correctly rejecting lures ($M = 17.1$, $SD = 0.86$) was significantly lower than incorrectly responding to a lure trial ($M =18.4$, $SD = 0.84$, $p <.001$) as well as correctly ($M =18$, $SD = 0.86$, $p =.008$) or incorrectly responding to target images (*M* =18.1, *SD* = 0.86, p =.003). Refer to Figure 3 (A) for a visualization of the results.

The second repeated measures ANOVA revealed that the main effect of the image condition on fixation durations was not significant ($F(1, 24) = 4.1$, $p = .055$). However, the effect of response accuracy on fixation durations was significant ($F(1, 24) = 9.6$, $p = .005$). See Figure 3 (B) for a visualization of the results. We also found an interaction effect between condition and response accuracy on fixation duration ($F(1, 24) = 10.2$, $p = .004$). Post hoc comparisons using the Tukey HSD test indicated that the mean fixation durations for correctly rejecting lures (*M* = 249.7, *SD* = 212.4) were significantly higher than incorrectly responding to a lure trial (*M* =231.5, *SD* = 212.4, p =.001) as well as correctly (*M* = 236.5, *SD* = 212.4, p =.019) or incorrectly responding to target scenes (*M* =237, *SD* = 212.4, p =.03).

Figure 3.

Gaze Behavior as a Function of Response Accuracy and Test Image Type at Test



Note. Mean fixation numbers (A) and mean fixation durations (B) as a function of condition (target, lure) and response accuracy (correct, incorrect) at the Retrieval/Test Phase. Error bars are set at +/-1 SE.

We wanted to see if mean fixation number and duration at retrieval predict the five indexes relevant to pattern separation in our study (LDIsimilar, Pr, OI). In order to test this, three multiple linear regression analyses were carried out.

The first regression showed that the model was not significant in predicting LDIsimilar ($R2 = .167$, $F(2,22) = 2.2$, $p = .134$). Only fixation numbers and durations for lure items were included in this analysis. It was found that the fixation number was not significant in predicting LDIsimilar ($\beta = .607$, $p = .168$). Fixation duration was also not significant in predicting LDIsimilar at retrieval ($\beta = .840$, $p = .061$).

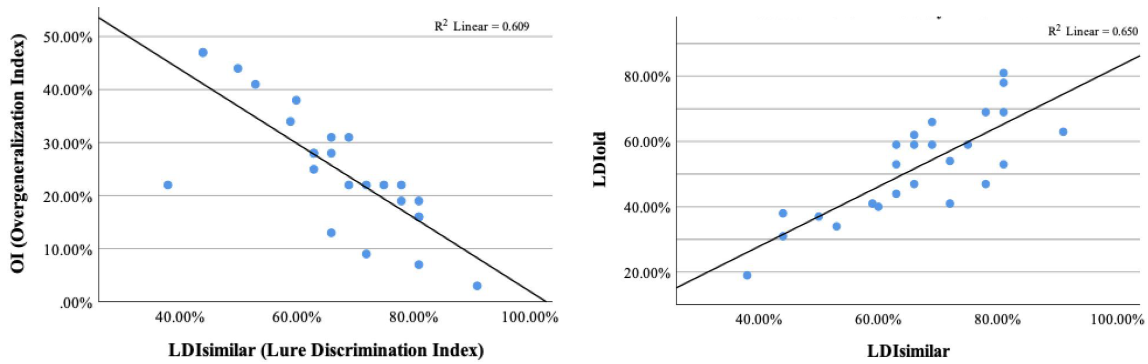
The following regression for predicting PR (corrected recognition) was not significant ($R2 = .001$, $F(2,22) = 0.0$, $p = .991$). Only fixation numbers and durations for target items were included in this analysis. It was found that fixation numbers at retrieval were not significant in predicting PR ($\beta = .067$, $p = .896$). Fixation duration at retrieval as a predictor was also non-significant ($\beta = .065$, $p = .898$).

The final regression was conducted to predict OI (Overgeneralization Index), and the overall model was statistically non-significant ($R2 = .221$, $F(2,22) = 3.1$, $p = .064$). Only fixation numbers and durations for lure items were included in this analysis. Fixation numbers at retrieval were not significant in predicting OI ($\beta = -.647$, $p = .130$). However, fixation durations at retrieval significantly predicted OI ($\beta = -.941$, $p = .032$).

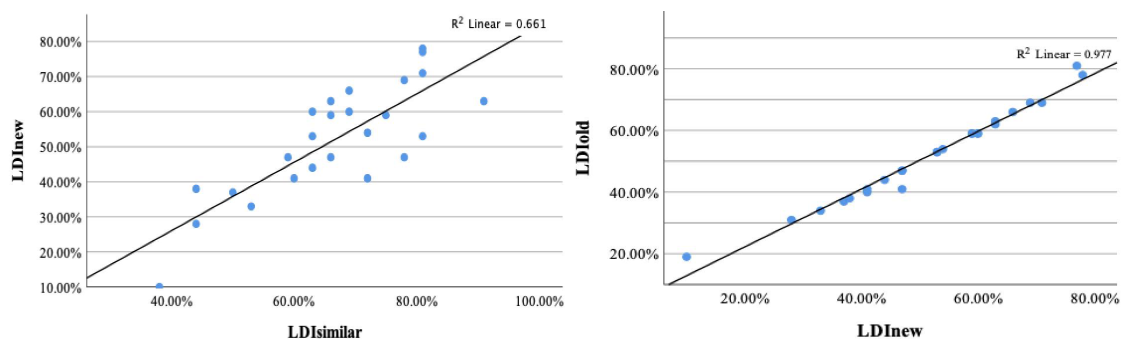
Figure 4

Scatterplots of the Correlations Between Indexes Related to Pattern Separation

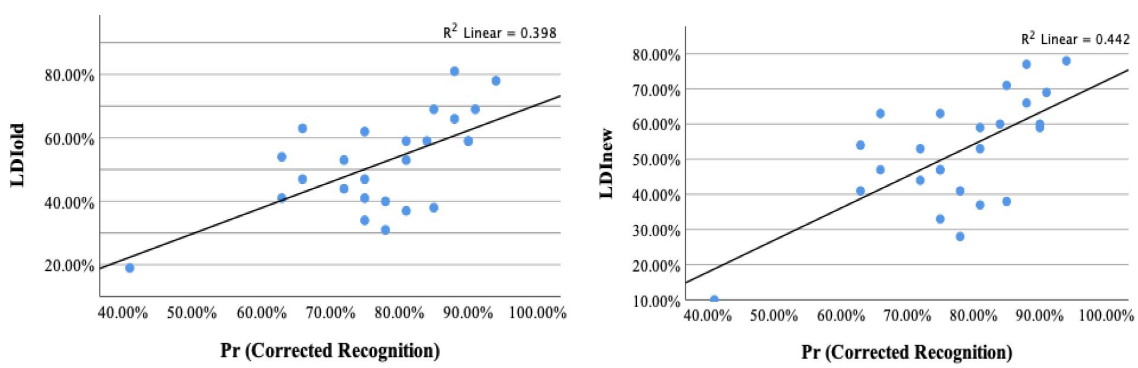
A) LDIsimilar´s correlations with OI and LDIold



B) LDInew´s correlations with LDIsimilar and LDIold



C) PR´s correlations with LDInew and LDIold



Note. Bivariate correlations between the index of lure discrimination (LDIsimilar) and alternatives of it (LDInew/old), overgeneralization (OI) and target recognition (PR). Out of all the combinations of indexes only the significant associations have been depicted in the figure.

Scanpath Similarity

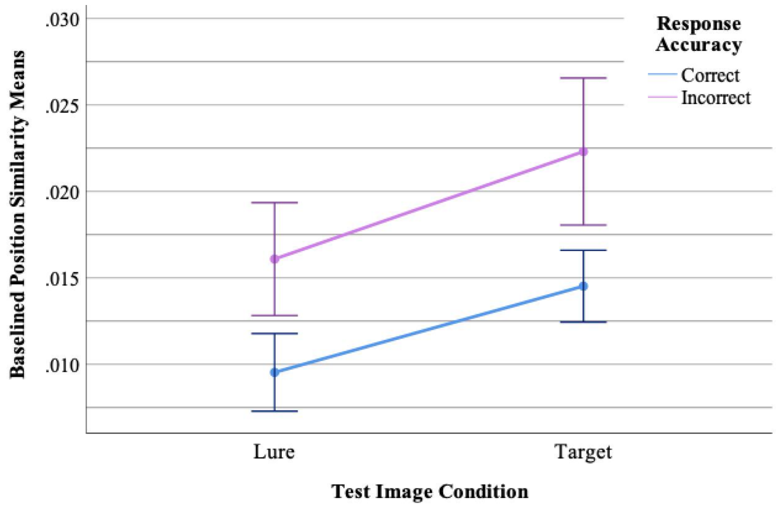
Two two-way MANCOVA´s were performed to analyze the effect of our independent variables 1-) response accuracy (correct, incorrect) and 2-) test condition (old, similar) on the five independent variables, which are the five dimensions of scanpath similarity (duration, length, position, vector, direction). These two independent variables were employed in both MANCOVA´s. However, the dependent variables were non-baselined scores of the similarity scores for the first and baselined similarity scores for the second. Confidence ratings were included as covariates for both two-way MANCOVA's to control for the forced choice design of our paradigm.

The first two-way MANCOVA revealed that there was a statistically significant main effect of response on similarity scores ($p = .043$). The between-subject analyses showed that the position domain of scanpath similarity between encoding and retrieval was significantly affected by response accuracy. The main effect of the test image condition on scanpath similarity between encoding and retrieval was not significant ($p = .354$). There was no interaction between the two independent variables for scanpath similarity ($F(1, 1581) = .244$, $p = .943$).

The second two-way MANCOVA that took baselined similarity scores as independent variables indicated that neither response ($p=.240$) nor test condition ($p=.565$) or the interaction of the two ($F(1, 1581) = .244$, $p= .640$) was significant. The between-subject analyses, again, revealed that the position similarity as a function of response accuracy (correct, incorrect) was significant (see Figure 6 for a visualization of the effect).

Figure 6

The Effect of Test Condition and Response Accuracy on Position Similarity of Scanpaths

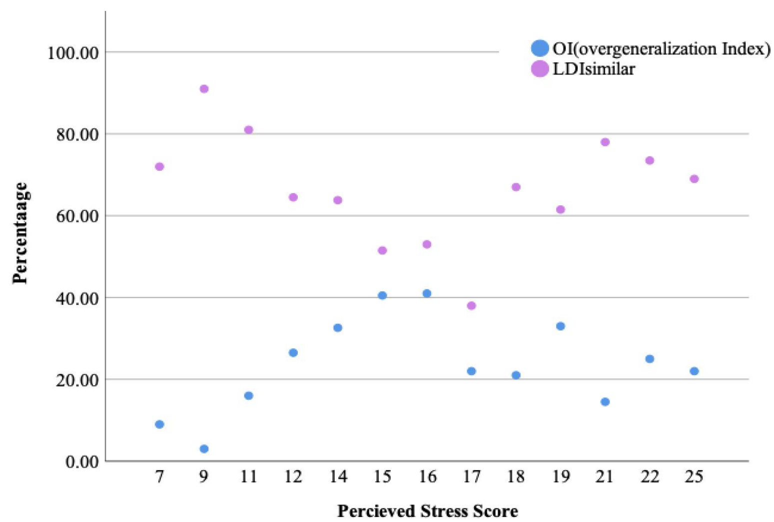


Note. Baseline Position Similarity between Encoding and Retrieval Stages of the MST task as a function of test image condition (old, similar) and response accuracy (incorrect, correct). The confidence covariate is set at= 1.78. Error bars are set at +/-1 SE.

Next, we wanted to explore the relationship of perceived stress with the indexes related to pattern separation capacity. The stress levels of ``low, moderate, high" were re-coded as "1,2,3", respectively. A Pearson product-moment correlation coefficient was computed to assess the relationship between common indexes of pattern separation (LDIsimilar/old/new, PR, OI) and the rating of perceived stress levels in the past month. There was a moderately strong, positive correlation between the Overgeneralization Index and the perceived stress level, r = .442, N = 25; plus, the relationship was significant (p = .027). The negative correlation between LDIsimilar and stress was marginally significant, r = -.393, N = 25, (p = .052). Pr, the index of target recognition, r = -.017, N = 25, did not significantly correlate with perceived stress (p = .934). The alternative measures of lure discrimination did not correlate with perceived stress levels. LDIold ($r = -.362$, $N = 25$, ($p = .075$)) and LDInew`s ($r = -.368$, $N = 25$, ($p = .070$)) correlation with stress was not significant. (See Figure 7 for a visualization of the effect)

Figure 7

The Relationship of The Index of Overgeneralization and Lure Discrimination with Stress



Note. The maximum score of stress was 25 in our study, corresponding to medium stress. There were no participants to represent a high level of perceived stress in our study.

Discussion

The current study's findings offer exciting new proof for the importance of eye movements in detecting pattern separation and the mechanisms by which eye movements and scanpath overlap play a role in visuospatial memory. To the best of our knowledge, this is the first study examining pattern separation´s reflection on eye movements in a free viewing condition with an MST task modified with naturalistic scene stimuli sticking to one domain of change in the lure condition: spatial change. The usage of contexts allowed participants to encode information in a context rather than in a context-independent scene, objects, or words, as it is most employed in MST tasks (Stark, Kirwan & Stark, 2019). With this in mind, the current study aimed to develop a more ecologically valid memory task using everyday kinds of scenes created in Sims 4 that might better delve into hippocampus function and episodic memory performance. We also added a layer of multidimensional analyses of scanpath similarities to discover the relationship between scanpath overlap and pattern separation in depth based on the task demands of this study. Finally, we wanted to explore if perceived stress could also impair pattern separation as more severe conditions related to stress, such as PTSD, as the first study to observe this relationship directly.

Fixations at Encoding and Retrieval in Predicting Indexes Related to Pattern Separation

It was long suspected that a greater quantity of sampling at encoding enables high visual acuity inspection of a larger portion of the study image/stimuli (Hollingworth & Henderson, 2002). A growing pile of research supports this notion that the sampling quality at encoding helps the learning and maintenance of mnemonic representations (Hannula et al., 2009; Henderson et al., 2005; Johansson & Johansson, 2013; Olsen et al., 2014; Olsen et al., 2016). Our results were in line with these findings by showing that the number of fixations at encoding predicted the index of lure discrimination. Specifically, the mean number of fixations and fixation duration encoding predicted LDIsimilar. The corrected recognition (PR) index was also significantly predicted by fixation number and duration at encoding. Finally, the index of overgeneralization (OI), which, for our study refers to a measure of faulty pattern completion, was also significantly predicted by fixation number and duration at encoding. This finding challenges the idea that describes overgeneralization as a process that takes place at retrieval and pattern separation at encoding and support the contemporary take on these two processes that imply, they are not mutually exclusive (Lie et al., 2016) and that both completion and separation can take place at the same time predicted with gaze behavior at encoding. On the other hand, retrieval-related fixation numbers and durations did not predict the indexes in question. Although only fixation durations at retrieval significantly predicted overgeneralization. Another study by Damiano and Walther (2019) showed that memory performance could only be predicted from gaze patterns at encoding but not retrieval and this finding was repeated in our spatial discrimination study.

Gaze Behaviors Relation to Image Condition and Response Accuracy

Out of possible responses (old, similar, new) to different conditions of test images (target, lure, foil), we were especially interested in how people react to lure trials and what proportion of people correctly classify them as "Similar" instead of "Old", which indicates successful pattern separation. We hypothesized that lure correct rejections at encoding would have higher fixation numbers and durations in our study, yet this relationship was not observed. It might be so that the regressions that predicted the lure discrimination index were more sensitive than this analysis and it is not necessarily evidence against encoding differences. Olsen et al. (2014) observed a similar disconnection between fixation numbers and durations at encoding with accurate memory performance. It may be that encoding gaze behavior may promote memory for objects, as in previous work, but not for spatial relations, as tested here and by Olsen et al. (2014).

Next, we reasoned, based on our task demands, in case participants do not detect a change at retrieval, they would keep on serially searching since they are instructed to find changes. Conversely, if they detect a change correctly at a lure condition, they will likely fixate on the location of the change and probably stop searching as they reach the goal of the task. Hence, we hypothesized that fixation numbers will be lower for correctly identifying lures while fixation durations will be higher. Our results were in line with this hypothesis, revealing that when lure items were correctly rejected the number of fixations significantly decreased and the duration of fixations significantly increased. For old items, fixation numbers were significantly higher than lure items, possibly because the visual search continues without any change detection. Lure correct rejections (identifying a lure correctly) were associated with fewer fixations than any other condition, specifically, falsely responding to a lure and identifying a target correctly or incorrectly. These findings were for the most part due to the specific goals and design of our study. Yet it is evident that by using a spatial discrimination task we can infer retrieval success through eye movement correlates. Further proving that it is possible to capture relevant information in gaze behavior with respect to mnemonic discrimination.

Gaze Replay Between Encoding and Retrieval

Gaze reinstatement between encoding and retrieval has been shown to have a functional role in accurate memory performance Johansson et al., (2022). Multi-dimensional analyses of the scanpath replay, such as Multi-Match. is a state-of-the-art method to assess different domains of scanpath replay that may be relevant to the different task goals. We revealed that position replay supported response accuracy in our study. The position dimension of scanpath similarity is based on absolute spatial coordinates. It represents a similarity measure of fixation order through temporally aligning fixations (Dewhurst et al., 2012). We have predicted beforehand that position will play a possible supportive role in our spatial discrimination task. Figure 6 gives a more in-depth idea of position replay showing that incorrect responses are related to higher position scanpath. The direction of the relationship indicates that targets have higher position replay than lures, although not significantly. This finding is reasonable and helps us understand the task at hand, further proving how scanpaths can reveal memory performance this time regarding overlap between encoding and retrieval.

The Effect of Stress on Search Performance

We sought to explore if individual variations in how stress is perceived in the last month are linked to search performance or pattern separation ability. We found that increased stress made it harder to identify lures and increased overgeneralization. In line with our results, previous research repeatedly showed that more severe conditions of stress, such as PTSD and anxiety, may be due to the overgeneralization of fear resulting from too little pattern separation ability (Kheirbek, Sahay & Hen, 2012; Lissek, 2012). A study by Nitschke et al., (2020) supports our results by showing that acute psychosocial stress impairs mnemonic discrimination processes on an unnatural object MST task. Our study further strengthened the role of psychiatric conditions in memory and added that non-clinical stress is a detrimental factor visible in a naturalistic spatial pattern separation task. This effect and the reliability of the PSS-10 scale in our study might be stronger when testing a population with higher stress levels. There were no examples of high stress among our participants, which made it hard to judge how pattern separation ability would be affected in relation to high stress. We could use the scatter plot of the correlation between behavioral measures of pattern separation and overgeneralization with stress to investigate the relationship we found in more detail (Figure 6). The non-linear arrangement of index percentages may indicate that a certain stress towards the medium stress level may even be beneficial for pattern separation. This interpretation is backed up by the hormesis hypothesis, which claims that stress can improve functioning as it goes from low to moderate but this effect is reversed once a threshold is passed (Oshri, Carvalho & Liu, 2022). Conversely, Shelton and Kirwan (2013) raised the notion that hypoactive pattern separation may be uniquely associated with depression rather than other factors, including self-reported stress, and sleep disturbances. Our study's findings contrast this notion by showing evidence that perceived stress could impair pattern separation ability. It has been shown that spatial pattern separation tasks are more sensitive to cognitive changes than object pattern separation tasks. Thus, it may be interesting to see if this relationship exists between recognition of objects and stress as well. Overall, the results revealed an interesting interplay between acute stress and mnemonic discrimination at a naturalistic recognition task that was not explored before. Further research with greater sample sizes and varying ages may be worthwhile to understand how visuospatial abilities are related to perceived stress further.

Limitations

Our paradigm has some notable limitations. First, during initial piloting, we were unable to collect any subjective judgments of mnemonic similarity ratings of our targets and lures due to a lack of resources and time. As a result, unlike some other versions of MST, our stimulus material has not been empirically evaluated for similarity levels of stimuli. Several factors prevent the study from being completely representative of the general population; we have not evaluated homogeneity by measuring an independent sample, the young age of study participants, and the dominance of an affiliation to a higher-level education institution. Nevertheless, participants from many cultural backgrounds could be included in the study, which adds to the generalizability of the findings. It is valuable to establish the link between pattern separation and gaze behavior in a multi-national sample, which is one way this study adds to research. On another note, The Sims 4 has several paid downloadable content expansion packs up to date. However, only the objects that belong to the base game have been used to create the scenes for this study due to a lack of resources. This caused limited objects to be available while creating scenes, and some objects had to show up in different scenes again which may have resulted in unwanted pattern completion. Ideally, future research can get more content and make sure every object shows up once in the stimuli. The setup of Molitor et al. (2014), like our study, was different from most other MST tasks since our experiments allowed participants to respond only after the image was presented for a set duration. While the fixed amount of time makes the analysis of fixation numbers easier, it limits the interpretation of the results because the time left during the task after the discrimination has been made may have influenced performance on the task.

Future Research and Possible Implications

A replication of this study with a bigger sample size from different populations than students can provide more information about the concepts explored. Plus, our paradigm can be improved by purchasing extension packages of the Sims to ensure no single object appears more than once between scenes. It could be an additional idea to calculate similarity scores for each scene instead of counterbalancing the stimuli and to observe if the results are comparable with the current study. Future research can further build on this paradigm by making a version of this paradigm for older adults that is relatively less complicated to prevent exceeding their cognitive resources. Nevertheless, while the overall number/duration of fixations in the complete scenes are important measures, as in this study, these measures in the areas where the critical objects were displayed, also known as areas of interest (AOI), would be relevant to look at and may strengthen the results of this study. Overall, The MST can be a promising tool in current efforts to develop an eye-tracking paradigm that can predict and diagnose Alzheimer's and similar conditions that result in cognitive decline (for a comprehensive overview, see Leal et al., 2019).

Conditions of Cognitive Decline

It is well known that the areas of the brain that are critical in AD continuum pathology are the same areas that are crucial for pattern separation (Laczó et al., 2012). According to Stark et al. (2013), the behavioral pattern separation task has the potential to be used to detect minor cognitive impairments associated with aging since it is a sensitive test for detecting early memory deterioration (Stark et al., 2013). Our study extended this finding by adding a layer of objective measurement. It improved the pattern separation task stimuli to be more representative of episodic memory, possibly making a more sensitive tool to detect cognitive impairment. Thus, it can be sensible to assign this task to different age groups, including older adults and people at various stages of the Alzheimer´s continuum, to see if the task can accurately place them into healthy, mild cognitive impairment and Alzheimer's for example. Also, by using the naturalistic pattern separation task on people who are at risk for stress, it may be possible to start providing these people with early help. Besnard & Sahay (2015) proposed that the treatment of anxiety disorders will benefit from medicinal or environmental influences that promote neurogenesis that supports pattern separation. Critically, older adults may also benefit from therapeutic and ecological approaches that increase neurogenesis since they show a tendency to overgeneralize (Wynn, Buchsbaum & Ryan, 2020). There are multiple ways in which people with cognitive impairment could promote neurogenesis, such as physical activity (Creer et al., 2010) and long-term antidepressant use (Taupin, 2006). Another unconventional method was psychedelic mushrooms; it was observed that mushrooms resulted in neurogenesis in the hippocampus and the extinction of fear conditioning in an animal study (Catlow et al., 2013). These methods should be considered in efforts to improve treatment and diagnostic methods for a crucial function of episodic memory, pattern separation.

Conclusion

The present study replicated and redesigned the mnemonic similarity task to fit eye-tracking analysis on a non-patient population by designing naturalistic stimuli that allows for free viewing and objective measurement of memory, through eye tracking. The results strengthen the influence of scanpath similarity and eye-movement patterns on memory performance from previous research. The spatial discrimination paradigm developed here, revealed that the combination of realistic viewing tasks with eye tracking was highly sensitive to memory function, which may be helpful in testing and diagnosing cognitive impairment in clinical settings. Possibly at one's home too, if in the future when eye tracking equipment becomes more accessible and tasks that assess cognitive impairment become user friendly and simplified. Treatments and activities that promote neurogenesis are promising in improving pattern separation functioning and the problems that come with too much or too little separation of fears for people suffering from psychiatric disorders or stress.

Ethics

Prior to taking part, participants provided signed, informed consent as well as verbal information. All procedures were carried out in compliance with the World Medical Association's Code of Ethics (Declaration of Helsinki) and the Swedish Act for the Ethical Review of Research Involving Humans (2003:460). The current study does not require a formal ethical evaluation by the Swedish Ethical Review Authority, as determined by Swedish authorities and stipulated in the Swedish Act concerning the Ethical Review of Research Involving Humans (2003:460), for the following reasons: It does not: (1) deal with personally identifiable information; (2) utilize techniques that require physical involvement; (3) run the risk of causing mental or bodily harm; (4) research biological samples acquired from a living or dead person that can be traced back to that person.

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Appendix A

Written Informed Consent Form

LUNDS UNIVERSITET

Permission to use data from Ecem Dilmaç's Master thesis project

I hereby agree that my test material may be used in research on cognition and memory. This includes various types of statistical and quantitative analyses, as well as the publication of articles, books or at scientific conferences and seminars.

Finally, I also give my permission for the data material to be used in teaching about cognition and memory.

By signing this document, I consent that I have been informed:

- that it is voluntary to participate and that I can withdraw at any time
- about the purpose of the recordings
- that my data is treated anonymously in all analyses and reporting
- in what form my data is saved
- that I have the right to contact Ecem Dilmaç and have my data removed from the study
- that I can contact Ecem Dilmaç to get further information about the experiment

____

Name and Surname

___________________________ ___________________________

Date and city Signature

Ecem Dilmaç, ecemdilmac18@gmail.com

Appendix B

Perceived Stress Scale- PSS-10

For each question choose from the following alternatives:
0 - never 1 - almost never 2 - sometimes 3 - fairly often 4 - very often

________ 1. In the last month, how often have you been upset because of something that happened unexpectedly?

________ 2. In the last month, how often have you felt that you were unable to control the important things in your life?

________ 3. In the last month, how often have you felt nervous and stressed?

________ 4. In the last month, how often have you felt confident about your ability to handle your personal problems?

________ 5. In the last month, how often have you felt that things were going your way?

________ 6. In the last month, how often have you found that you could not cope with all the things that you had to do?

________ 7. In the last month, how often have you been able to control irritations in your life?

________ 8. In the last month, how often have you felt that you were on top of things?

________ 9. In the last month, how often have you been angered because of things that happened that were outside of your control?

________ 10. In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?

Appendix C
Demographics Questions

DEMOGRAPHICS QUESTIONNAIRE

1. How old are you? ____________ Years

2. What is your gender?
☐ Male
☐ Female
☐ Other
☐ Prefer to not say

3. Please enter your highest educational qualification.
☐ No degree
☐ High school diploma
☐ Intermediate school leaving certificate or intermediate qualification for a technical college
☐ Bachelor's Degree
☐ Master´s Degree
☐ Post-Graduate Degree
☐ PhD
☐ Other, ________________

4. What subject are you studying/did you study?
☐ Humanities
☐ Computer science
☐ Engineering
☐ Art and cultural studies
☐ Mathematics and natural sciences
☐ Media/ design
☐ Educational science
☐ Medicine
☐ Psychology
☐ Law
☐ Social Sciences
☐ Linguistics
☐ Economics
☐ Other: _______________

5. What is your main occupation at the moment? (e.g. student assistant, commercial employee, geriatric nurse)?
☐ ______________________________
☐ Not Working