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Tangled up in Confounds: Unravelling the Controversial Roles of MTL-Structures in Familiarity and Recollection

Opinion

Recognition memory is commonly divided into 'knowing that you encountered something before' (familiarity) and 'remembering specific, accompanying details' (recollection). To date, no consensus has been reached concerning the neuronal correlates of familiarity and recollection within the medial temporal lobe, nor the methodological validity to investigate this. Specifically, a dual-process model and a multi-attribute hypothesis compete portraying the role of the hippocampus in solely recollection or both recollection and familiarity, while neither one provides conclusive arguments. The current paper aims at evaluating the reasoning within this controversy and brings up a novel perspective as well as consequent research suggestions. More specific, it is argued that if the hippocampus is involved in processing of multi-attributional stimuli, studies using multi-attributional stimuli should conclude a role of the hippocampus in both recollection and familiarity (instead of single-attributional), which implies the opposite of what is proposed in current theories. For future aims, it is important to identify an experimental distinction between familiarity and recollection before valid research can proceed.

Keywords: familiarity, recollection, medial temporal lobe, hippocampus.

To the curious mind, familiarity describes the oppressive, at times distressing, sensation of knowing without full preservation. Recollection, however, awakens a sense of relief through remembering the accompanying connections.

The author.

INTRODUCTION

Our ability to judge whether we already encountered something, an object, a face, a concept or a sound is what we entitle as recognition. Recognition memory is generally divided into the two distinct concepts of familiarity and recollection. Familiarity reflects a global measure of quantitative memory strength and can be described by means of signal detection theory-approaches (Elfman, Parks, & Yonelinas, 2008). Recollection, in contrast, refers to a threshold retrieval process of qualitative information about a specific episode; for example where or when an event took place (Yonelinas, Aly, Wang, & Koen, 2010). Currently, a longstanding debate is continuing about the exact nature of these two concepts, as well as their origin within the brain (Rugg & Vilberg, 2013; Sauvage, Fortin, Owens, Yonelinas, & Eichenbaum, 2008; Yonelinas, 1994; Yonelinas et al., 2010; Squire, Wixted, & Clark, 2007; Wixted & Squire, 2011). More specifically, no consensus has been reached regarding the role of the hippocampus or other medial temporal lobe (MTL) structures, such as entorhinal (ERC) and perirhinal cortices (PRC) in familiarity and recollection.

The current paper aims at elaborating on the current state of science within this field from a global and objective perspective while two opposing views are elucidated and

evaluated. Consequently, the author proposes an alternative viewpoint and leaves the reader with some directions for future research. All contributions are aimed at implementation of the most recent data by means of PubMed, PsychINFO and MEDLINE databases.

The controversy

Dual-process theories of recognition memory have been influential in the past. A model that is extensively used in this context is the 'dual-process signal detection model' (DPSD) proposed by Yonelinas (1994), which advocates an association- forming and retrieving role of the hippocampus supporting recollection, and establishes familiarity as a by-product of repeated neural processing outside the hippocampus (i.e. ERC, PRC) (Rugg & Vilberg, 2013; Wolk, Dunfee, Dickerson, Aizenstein, & DeKosky, 2011). Scientific evidence is derived from cases of selective hippocampal damage and hypoxia which report selective disruptions in recollection, whereas both familiarity and recollection were found to be diminished in patients with hippocampal and surrounding MTL-lesions (Adlam, Malloy, Mishkin, & Vargha-Khadem, 2009; Holdstock et al., 2008; Yonelinas et al., 2002). An interesting dissociation appeared when it was shown that ERC-volume decreases were correlated with familiarity, but not recollection (Wolk et al., 2011). Notably, a study published in 2017 concluded that age-related impairments in recollection, but not familiarity, are specifically associated with reduced hippocampal structural integrity (Schoemaker et al., 2017). Furthermore, McCullough and his team proclaimed that

hippocampal-dependent recollection functioned best under moderate stress conditions whereas cortically-based familiarity improved with higher levels of stress (McCullough, Ritchey, Ranganath, & Yonelinas, 2015).

As an opposing view, Wixted and Squire (W&S) (Smith, Wixted, & Squire, 2011; Squire et al., 2007; Wixted & Squire, 2011) argued that an essential confound underlies the recollection function allocated to the hippocampus. Namely, all conclusions are drawn upon the assumption that confidence and accuracy are high whenever recollection occurs. More specific, participants are often asked to rate their level of confidence about a recognition-decision on a 6-point scale (1=Sure Old – 6= Sure New), or to clarify whether they based their response on familiarity or recollection ('Know' or 'Remember'). Using these subjective methods, studies integrated 'remember & high-confidence (6)' responses as recollection, and 'know & lower confidence (1-5)' responses as familiarity in their designs. However, W&S argue that recollection is a continuum of memory confidence instead of limited to just the highest level. This seems to be applicable to Remember/Know-judgements and source-memory tests, indicating that recollection is - like familiarity - a scale of confidence. Subsequently, assessing the confidence is an inappropriate measure to distinguish the two concepts (Mickes, Wais, & Wixted, 2009). Hence, using such measure leads to a false dissociation between familiarity and recollection.

Even more compelling is the scientific data they brought to the table fitting their hypothesis; "the hippocampus is involved in recollection **and** familiarity", based on the functional organization of the MTL instead of on subjective distinctions and judgement-

confidence (Buffalo, Bellgowan, & Martin, 2006). Ultimately, what W&S assign as a unique function to the hippocampus is its ability to combine a wide variety of attributes associated with a particular experience to form an integrated memory trace, facilitating not solely recollection but familiarity likewise. The hippocampus is thought combine different attributes of a stimulus (spatial, tactile, olfactory, temporal, emotional, etc.), which may involve both types of recognition memory, compared to involvement of the PRC in single-attributional stimuli (Jenkins, Amin, Pearce, Brown, & Aggleton, 2004; Wan, Aggleton, & Brown, 1999). However, no human studies were reported which explicitly tested this proposal, and some broader findings were contradictory (i.e. PRC involved in recollection (Carr, Viskontas, Engel, & Knowlton, 2010)). Nevertheless, a recent finding in favour of a hippocampal role in recollection and familiarity originates from Merkow and colleagues, 2015 (2015), who used high-frequency activity (HFA) during an item-recognition memory task to show that hippocampal HPA predicted individual differences in both recollection and familiarity measures as well as overall memory performance. Taken together, the multi-attribute function of the hippocampus as proposed by W&S is supported as well as invalidated by current findings.

In *Figure 1* the two opposing stands are depicted, although simplified, in accordance with their corresponding ideas about familiarity, recollection and anatomical underpinnings (Wixted & Squire, 2011; Yonelinas et al., 2010).

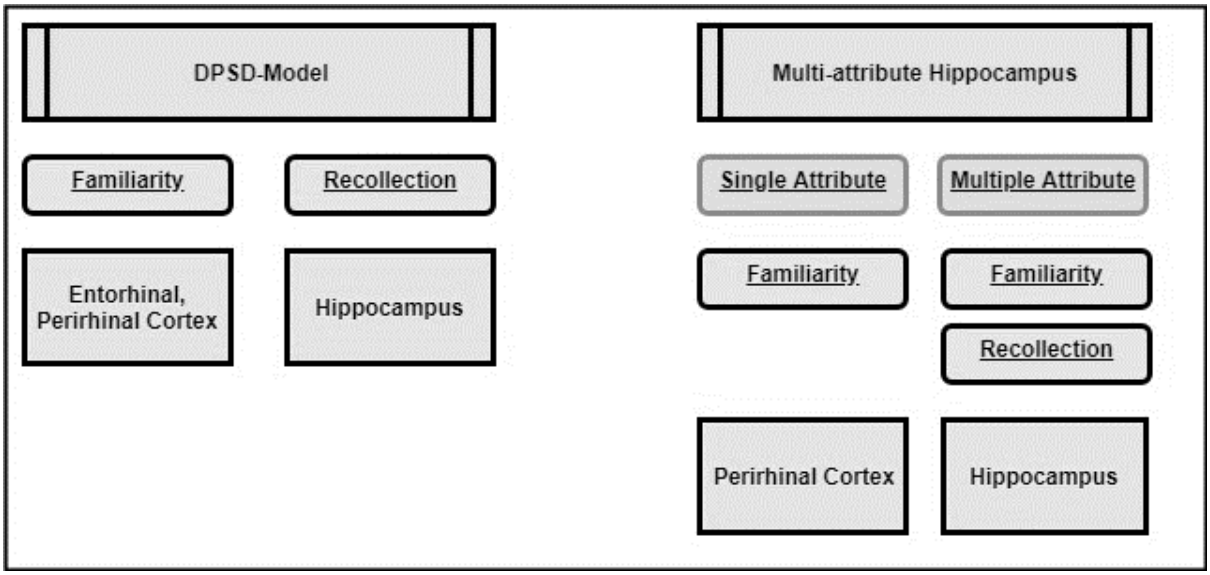

Figure 1. A dual-process model (left) versus the multi-attributional proposal of hippocampal function (right) about familiarity and recollection in the MTL

Various objecting arguments were given against the multi-attribute hypothesis, of which two interesting notes can be taken. Firstly, Montaldi and Mayes (2011) declared that hardly any studies exist that successfully avoided the 'confidence-confound', which makes the claims misleading. Truly, when rummaging current evidence, it appears to be the case that although many results point in W&S' direction of a single hippocampal function in familiarity and recollection, no study completely matches their proposal. Secondly, Diana and Ranganath (2011) stressed recollection as a prerequisite for high confidence, which makes it an emergent property of recollection, not a confound. Yet, using a handful of logical reasoning, it should be underlined that 'if P (recollection) then Q (high confidence)' does not imply 'if Q then P', equalling no necessity of recollection after high confidence and an invalid argument.

So, as a clarifying sum-up which is neither exhaustive nor sufficient, one could conclude a disagreement about the interpretation of recognition memory tests and subsequently about hippocampal function in terms of recollection and familiarity. While trying to form a corroborated opinion about the topic at hand, it becomes evident that the matter encloses a very complex problem requiring a stepwise revision.

Reconsideration

When diving into publications and research data, it can be observed that there is a slight majority favouring the DPSD-model. However, according to W&S, a confounder might be involved in this. More specific, using single- or multi-attribute stimuli may lead to different conclusions regarding neuronal structures underlying recollection and familiarity. Analysing the experimental stimuli used in various research designs, it appeared to be the case – indeed - that when a multi-attributional stimulus is used (e.g. faces & emotions or odours & media), the authors eventually concluded that recollection is linked to hippocampal function while familiarity is associated with other MTL-structures (Kafkas et al., 2017; McCullough et al., 2015; Sauvage et al., 2008; Schoemaker et al., 2017). In contrast, using single-attribute-stimuli resulted in conclusions favouring a hippocampal role in both recognition processes (Dede, Wixted, Hopkins, & Squire, 2013; Merkow et al., 2015), which ultimately comes down to the hypothesis and argumentations made by W&S (Wixted & Squire, 2011). However, rethinking this, the used logic features a remarkable inconsistency, as depicted in the following section:

- If W&S propose that the hippocampus is involved in processing of multi-attributional stimuli, which can involve both recollection and familiarity,
- and the PRC is involved when single-attribute-stimuli are presented, which involves mainly familiarity,
- then how does this explain the misinterpretation of multi-attributional stimuli causing dual-process findings (i.e. PRC = familiarity, hippocampus = recollection)? – *Figure 2.*

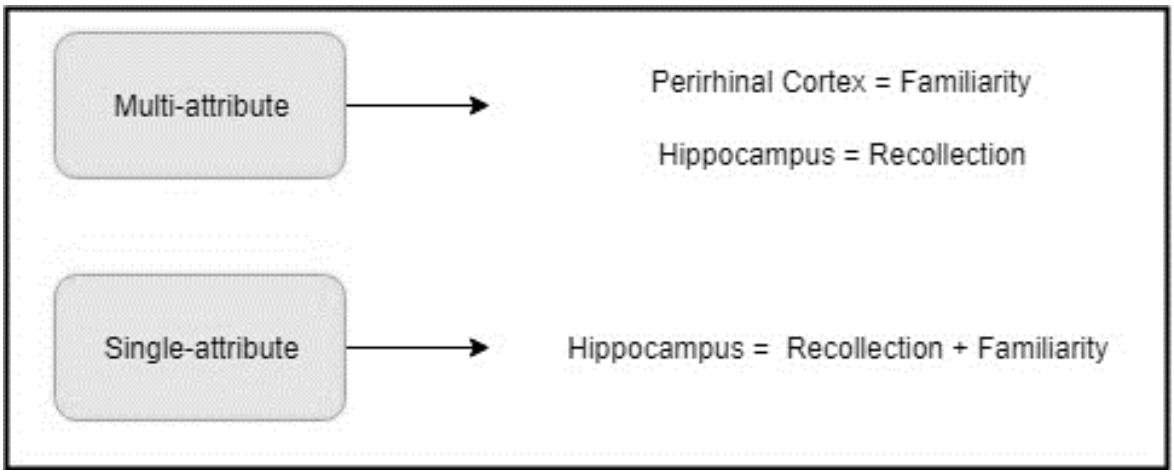

Figure 2. Graphical representation of the multi-attribute hypothesis argumentation claiming that studies using multi-attributional stimuli find dual-process evidence, while single-attributional stimuli lead to conclusions about hippocampal function in both recollection and familiarity.

Alternatives. Although the multi-attribute hypothesis is appealing, it does not comprise a perfectly valid art of reasoning. Therefore, an alternative is proposed (*Figure 3*). Would it not be more solid to argue that, if the hippocampus is involved in processing of multi-attributional stimuli, studies using multi-attributional stimuli would conclude a role of the hippocampus in both recollection and familiarity (instead of single-attributional)? This would mean quite the opposite of what is proposed above (Difference between

Figures 2 and 3). Based on the anatomical location of the hippocampus (i.e. ultimate recipient of convergent projections from (among others) PRC and ERC), W&S could be right about hippocampal involvement in processing multi-attributional stimuli. However, research should then find a hippocampal contribution in both forms of recognition memory when a stimulus has multiple attributes, compared to no hippocampal commitment in single-attributional processes.

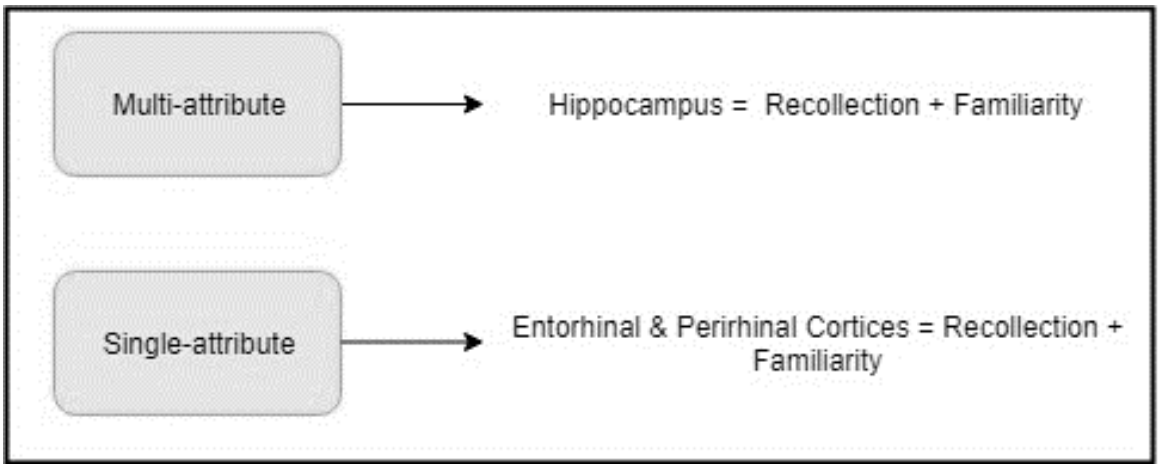

Figure 3. Graphical representation of the alternative argumentation suggesting that if the hippocampus is involved in processing of multi-attributional stimuli, studies using multi-attributional stimuli should conclude a role of the hippocampus in both recollection and familiarity, compared to no hippocampal commitment in single-attributional processes.

Methodological matters

For human approaches, all methods should be compared in regards to their neuroimaging-based activity-patterns of MTL-structures or single-neuron recordings (Gelbard-Sagiv, Mukamel, Harel, Malach, & Fried, 2008). It would be best to use faces as experimental stimuli, since these are the most convenient for incorporating single- and

multiple attributes. Besides, previous research showed that hippocampal lesions do not interrupt face memory (Bird & Burgess, 2008). Neutral faces (single-attribute) and emotional faces (multi-attribute) would be presented in separate conditions, both examining recollection and familiarity (controlling for confidence and accuracy). Subsequently, it would be of interest to observe whether hippocampal activity comes at play whenever a face is associated with an emotion, compared to sole PRC-activity in case of neutral faces, and how this relates to familiarity and recollection. Likewise, in neurophysiological animal studies measuring c-Fos levels, a paradigm with 2D objects (no spatial attributes) and odours could be used to create a comparison between single and multi-attributional stimuli, using repetition suppression[1] as an estimate of familiarity (Brown & Aggleton, 2001; Jenkins et al., 2004; Wirth et al., 2003), and pair-recall activity[2] for recollection (Yanike, Wirth, Smith, Brown, & Suzuki, 2009). Certainly, the amygdala (MTL) cannot be excluded from the debate and should be considered in terms of emotional significance during familiarity and recollection memory (Phelps, 2004).

CONCLUSION

Overall, the alternative hypothesis elucidated throughout the current paper asserts the presumption that empirical studies should support a hippocampal role in both recollection and familiarity, on condition that the hippocampus is involved in processing

[1] A phenomenon where increased firing rate signals novelty and diminishes with familiarity
[2] Responding of a neuron to a paired associate in addition to the initial preferred stimulus

multi-attributional stimuli. This alternative hypothesis identifies an inconsistency in present theories within this field and forms an attempt to regenerate the line of thought. In the end, the question persists how familiarity and recollection can be distinguished experimentally, and it can be concluded that studies should initially focus on the methodological contradictions. A clear dissociation must be made and agreed on first, before research can continue with the identification of neuronal substrates. Otherwise, the controversy will be maintained, and we will remain tangled up in confounding matters.

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