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# PRE-PRINT PUBLICATION

## **Commentary title: Improving the Integrative Memory Model by integrating the temporal dynamics of memory**

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**Target Article:** An Integrative Memory model of recollection and familiarity to understand memory deficits

**Authors of the target article:** Christine Bastin, Gabriel Besson, Jessica Simon, Emma Delhayé, Marie Geurten, Sylvie Willems, & Eric Salmon

## **Abstract**

Despite highlighting the role of the attribution system and proposing a coherent large-scale architecture of declarative memory, the integrative memory model would be more “integrative” if the temporal dynamics of the interactions between its components was clarified. This is necessary to make predictions in patients with brain injury and hypothesize dissociations.

“Integrative” is a major asset and is highly relevant to qualify the model presented by Bastin et al. in the target article. Integration is inseparable from multimodality and multidimensionality: the integrative memory model postulates that the systems processing representations, relations, and attributions are linked inside a coherent “architecture” allowing emergent properties. Within this context, one of the major advances proposed by the integrative memory model is the integration and the clarification of the role of the attribution system, which is thought to depend mostly on the prefrontal cortex. In contrast, most previous models of memory were centered on the temporal lobes and Papez circuit.

Some of the aspects of the temporal dynamics of memory that are currently not fully described in the model are: time perception during memory (Eichenbaum 2017a); time sequences that distinguish temporally distinct episodes and stimuli (Ekstrom & Ranganath 2018; Ranganath & Hsieh 2016); projection in the future (Addis & Schacter 2012); and the time scale for building memories at the cellular level (Kukushkin & Carew 2017). However, in this commentary we want to focus on another aspect of temporal dynamics that is essential to validate to clarify the architecture of the integrative memory model. Because the integrative memory model, as its name implies, integrates different components, it is crucial to specify what kind of relation they entertain. This information is also missing from the present model. The authors have devoted a large portion of the target article to describing the general architecture of the components, leaving little space to discuss exactly how they relate. (We think that their model could have been dubbed the interaction memory model just as well as the integration memory model.)

Yet, although not fully specified, the integrative memory model is already based on a few assumptions regarding its temporal dynamics. For example, in line with many previous studies, familiarity is supposed to be rapid. The model also assumes that memory “emerges from hierarchically organized representations distributed throughout the brain” (target article,

sect. 5.3, para. 1; emphasis added), which suggests a precise order in which the different components are activated. In contrast, most arrows connecting the different components of the model are bidirectional, perhaps due to the lack of knowledge about the connectivity between the components. However, the very presence of these arrows suggests structural and functional connections that have to be characterized.

Using behavioral reaction times for various memory tasks, it is possible to get an idea of the latency of the activation of some of these systems and such latencies can be used as upper time constraints. For example, behavioral paradigms based on time constraints can be used to precisely assess the speed of familiarity (Besson et al. 2012). Recording brain activity using surface EEG (electroencephalography) or MEG (magnetoencephalography), possibly with source reconstruction, or combined EEG-fMRI (functional magnetic resonance imaging) recordings (Hoppstädter et al. 2015) provides a more refined idea of the activation latencies of each component of the model. Intracranial EEG is spatially more precise and reveals, for example, a striking delay between the activity of the perirhinal cortex and the hippocampus that should be taken into account in models of memory (Barbeau et al. 2008; Trautner et al. 2004). Methodological advances even allow comparison of the neuronal activity of different medial temporal lobe regions involved in memory (Mormann et al. 2008). Moreover, it is also possible to calculate the strength of functional interactions between brain regions, as well as causality and synchrony indices, using various approaches such as fMRI (Staresina et al. 2013), intracranial EEG (Krieg et al. 2017; Kubota et al. 2013; Steinvorth et al. 2010), and thorough analyses of neuronal activity (Staresina et al. 2019).

In parallel, validating these dynamics in clinical situations is necessary. Alzheimer's disease – inducing slowly increasing damages to many brain areas involved in both the representation and attribution systems of the integrative memory model – is a pertinent example chosen by the authors. However, it is insufficient to test the model's dynamics. Experiential memory

phenomena such as déjà-vu (an erroneous feeling of familiarity) or reminiscences (memories including a mental content and recollection) allow testing of the model on another time scale (Curot et al. 2017). These phenomena are highly transient – hundreds of milliseconds to a few seconds. This is the real-time scale of familiarity feelings, recollection, ecphory, and mental imagery. They become all the more valuable when they are induced by electrical brain stimulations, since these stimulations also allow inferring the directionality and latency of connectivity (David et al. 2013; Trebault et al. 2018). For example, the absence of any subjective experience after electrical brain stimulations of the posterior cingulate cortex is mentioned in the target article, suggesting that the posterior cingulate cortex is not involved in representations (Balestrini et al. 2015; Foster & Parvizi 2017). In fact, it also suggests that the posterior cingulate cortex cannot be an entry point in the integrative memory model.

Using such approaches, it would be possible to get an idea of how the model may work effectively. It would also be possible to start making precise predictions about the consequences of injury to specific components of the integrative memory model in neuropsychological populations. Dissociations could be hypothesized and tested. As an important novel aspect of the integrative memory model is the attribution system, it appears particularly relevant to assess more specifically the relations between this system and the entity and context core systems. It is likely that clarifying the dynamics of these relationships will help to reveal novel findings regarding a variety of neuropsychological syndromes. A positive aspect of new neurocognitive models is that their details can be refined, compared to observations, and tested in new experiments, thereby opening new avenues for research. Let's go.

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