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## Memory in Contemporary Biomedicine: Cross-Disciplinary Scenarios

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### ABSTRACT

#### **Memory in contemporary biomedicine: cross-disciplinary scenarios**

Although it is true that past thinkers developed relevant taxonomies of the phenomenon of memory at the behavioral level, only in the last century has our scientific understanding of the underlying brain mechanisms of memory progressed remarkably. New acquisitions include that memory is not just a functional or physiological process, but a structural or anatomical one as well, that conceiving of memory as merely cognitive or centered on cognition is misleading, or that memory does not require any consciousness or intentionality. On the applicative side, recent technological advances offered opportunities of modifying memory with biological means, and detecting more effectively whether someone is remembering or lying. The current issue of *Medicina nei Secoli* is dedicated to *Memory in contemporary biomedicine: cross-disciplinary scenarios*. It hosts seven expert contributions to the field covering different areas of medical inquiry (i.e., immunology, neuroscience, gerontology) and humanistic-social perspectives (history, epistemology, ethics, and law).

**Keywords:** Memory - Cognition - Dementias - MMTs - Lie detection

### Introduction

The current issue of *Medicina nei Secoli* is dedicated to *Memory in contemporary biomedicine: cross-disciplinary scenarios*. As guest co-editors with different backgrounds in the medical humanities, we conceived of this issue as a continuation of an earlier issue, entitled

*Memory in antiquity\**. Like its predecessor, this issue is extensive and incredibly rich. It hosts seven expert contributions to the field covering different areas of medical inquiry (i.e., immunology, neuroscience, gerontology) and humanistic-social perspectives (history, epistemology, ethics, and law). As has been previously shown, the field of memory is interdisciplinary, inevitably overlapping with other fields and connecting a wide range of topics. As we will see in the present contributions, some ancient conceptualizations of memory still resist contemporary theories. We thus believed that, after a journal issue reflecting on ancient views of memory, another issue dedicated to contemporary research was due—the historical gap between the two notwithstanding. In any case, we do not preclude the possibility of another issue in the near future covering the historical or conceptual gaps.

Historically, memory has been a concern for many thinkers, including poets, novelists, painters, musicians, historians, philosophers, psychologists, natural scientists, and physicians. Although it is true that these thinkers developed relevant taxonomies of this phenomenon at the behavioral level and that some of these taxonomies are still in place today (long-term vs. short-term or working memory, declarative vs. procedural, episodic vs. semantic, etc.), only in the last century has our scientific understanding of the underlying brain mechanisms of memory progressed remarkably<sup>1</sup>. Famous lesion cases of amnesiac patients since the mid-twentieth century have opened the door to theoretical refinements in the neuroscience of memory. William Scoville's patient H.M. had his hippocampus resected bilaterally in an attempt to cure his severe epilepsy in the late 1950s<sup>2</sup>, and K.C., Endel Tulving's patient, had the hippocampus area in both lobes damaged in an accident in 1981<sup>3</sup>. While the two patients' lesions may appear similar at first sight, they provoked different kinds of amnesia. H.M. conserved short-term memory but showed anterograde amnesia—he could not remember events that occurred after his surgery—and only partial retrograde amnesia—he was incapable of remembering some events from several years before the surgery. K.C. showed a complete loss of episodic (anterograde and retrograde) memory but retained his semantic memory: he could report such details as his date of birth, the color of his car, and the names of the schools he attended. Both H.M. and K.C. retained their procedural memory; they could remember or acquire skills.

Building on earlier research on the mammalian hippocampus, Eric Kandel's work on invertebrates, such as the sea snail (*Aplysia*), was a breakthrough<sup>4</sup>. This research took 15 years beginning in the 1960s, involved different actors, and led to the discovery of the long-term potentiation (LTP) mechanism for implicit (procedural) memory, which was perceived as only quantitatively different from the explicit (declarative) memory we see in conscious beings. These and later advances undermined the standard view of consciousness's centrality for memory and significantly affected our philosophical and anthropological views of memory in recent decades.

Memory is the faculty that encodes, stores, and retrieves information when needed. Traditionally, we have derived a folk concept of memory intuitively from how con-

scious beings like us—endowed with minds/brains—memorize and recollect data, events, skills, and habits as well as emotions. However, conceiving of memory as merely cognitive or centered on cognition is misleading—unless we adopt the strategy of some biologists and enlarge the sense of cognition (generically information-processing) such that it applies to *aneural* organisms (e.g., microbes)<sup>5</sup>, classes of molecules (e.g., immunoglobulins), or even cell-intrinsic mechanisms (genes).

Some authors wonder if attributing memory to aneural entities is little more than a metaphorical strategy. They claim we can intentionalize processes occurring at minuscule levels of description in order to better understand and explain them while still claiming that memory is and has to be intended as a neural-based function. There are ongoing discussions over whether some given forms of memory – associative memory, for instance – may pertain only to higher species equipped with brains. For some scholars, including Kandel, cell-intrinsic mechanisms, such as genetic and epigenetic mechanisms, serve as function enablers but do not provide proper memory storage<sup>6</sup>. According to this view, storage memory can hardly be attributed to entities that lack synapses.

Alternatively, other scholars go further in interrogating whether speaking about genetic, immunological, or microbial memory has a phylogenetic meaning that sheds light on what memory really is, how it evolved in lower lifeforms and human beings, and whether observed differences between primitive and higher lifeforms are simply a matter of complexity. Memory is a broad concept; it may have different-level processors and realizers in both the biological domain (e.g., genes, molecules, cells, and multicellular networks) and the digital-electronic domain (e.g., IT and AI systems), and it, therefore, does not require any consciousness or intentionality.

Uncontestably, contemporary cross-disciplinary research has shown that memory is not just a functional or physiological process, but a structural or anatomical one as well. Functional changes are mirrored in observable physical modifications, and these modifications are governed in nature—and sometimes emulated in machines—by adaptive processes of natural selection. Crucially, memory is closely connected to learning, memory being the record of a learning process. Moreover, both learning and a biological brain's consolidation of memories are processes mediated by emotions or, better yet, processes that depend on emotional valance (positive vs. negative) and arousal intensity<sup>7</sup>. Emotional valance/intensity may determine good or bad outcomes (e.g., enhanced memory performance or traumatic onset disorders). Notoriously, performance in different types of memory tests varies individually and over the course of an individual's life. There is an extensive literature on how memory can be modified, enhanced, altered, compromised, or entirely suppressed. More recently, memory modification techniques (MMTs)<sup>8</sup> based on acquired knowledge have gone beyond mere psychological manipulation and now include a wide array of biotechnological tools (e.g., nanotechnological, optogenetic, pharmaceutical, brain stimulation, and surgical devices), which may be applied for clinical or non-clinical purposes. Memory-modifying poten-

tials include memory erasure, memory blunting, implantation of false memories, and switching the affective valence of a memory record. Such tools may heighten public expectations and excitement but also raise ethical concerns<sup>9</sup>. Nonetheless, MMTs' potentials for treating post-traumatic stress disorders is huge.

Finally, yet importantly, recent research has shown—counterintuitively—that conscious memory is fragile and deceptive. These drawbacks contrast with the tacit assumption of past psychological research that memory functions optimally, and thus veridically, in healthy subjects. In the past, an inability to recall something that had been presented was considered a sign of memory failure. We now recognize that conscious memory is fragmentary and reconstructive and thus a fallible and unreliable process. This reality complicates the investigation of the phenomenon of memory and has relevant epistemological implications for many other domains. Today, a lively philosophical debate exists between those who argue remembering should be intended as a form of (or even the same mental state as) imagining and those on the other side who list criteria for distinguishing between the two capacities<sup>10</sup>. Moreover, since memory continuity forms the base of various philosophical constructs we use to characterize the self (e.g., personal identity, self-knowledge, authenticity, conscious narrativity, etc.), these concepts have now assumed ambiguous and inconsistent facades. We should refrain from taking ideological positions on the cultural role of memory, and we must note that the celebrative narrative of (conscious) memory has sometimes also been used in controversial ways to orient prejudicial social and cultural practices. For example, collective or social identity, cohesion, and history have been used to justify nationalism, separatism, and racism. Additionally, in domains like medical care, recognizing the weakness of conscious memory suggests that relying solely on anamnesis—a patient's recollection of their medical history—is an unreliable and insufficient strategy for clinical diagnosis, especially when compared to direct examination and diagnostic tests. This conclusion is particularly relevant in psychiatry, where diagnosis still relies primarily on descriptive tools and the adoption of objective diagnostic measures for mental disorders is progressing far too slowly. These are only some examples of the notable implications recent findings on memory have for our daily lives. Researchers are now developing new measurements that can objectively detect whether someone is remembering or lying and may be used to determine or contest the truthfulness of a reported story. These tools are incredibly promising. The ethical implications of this research for such fields as forensics are enormous given that inaccuracies in a witness's or suspect's statements could undermine the fair resolution of legal disputes and result in rights abuses<sup>11</sup>.

The authors in this issue brilliantly address some of the issues in the biomedicine of memory sketched above while engaging with the humanities in a multi-faceted way. Javier Gómez-Lavin and Justin Humphreys argue that contemporary neuroscience's concept of working memory implicitly carries within it misleading conceptualizations

derived from Aristotle's notion of φαντασία (*phantasia*). After offering a detailed comparison of the two notions and highlighting some of their faults, they raise two objections that may affect contemporary research. First, we too easily conflate working memory with higher cognition (i.e., *cognition suffusion objection*). Second, we questionably tend to transfer the identifying criteria of peripheral faculties to some central faculty like working memory (i.e., *bottom-up mereological objection*). Gómez-Lavin and Humphreys, thus, pave the way for a post-Aristotelian faculty psychology.

Gilberto Corbellini engages with the complex conceptual history of immunological memory. Only traces of this idea can be found among the ancients; immunological memory did not become a concrete idea until the birth of bacteriology and immunology at the end of the nineteenth century and has been subject to experimental investigation only since the 1930s. Examining twentieth-century discoveries in the field, Corbellini highlights that some of them, like that of a class of receptors able to recognize the specific molecular structures on the surface of pathogens, favored the notion that immunological memory is not simply metaphorical and unspecific but may constitute a proper form of memory. Interestingly, immunological theories, like that of clonal selection, inspired Gerald Edelman's theory of neurobiological memory as a re-categorization within his influential approach called "Neural Darwinism".

Matteo Borri discusses memory loss as a symptom of Alzheimer's disease by showing, through historical analysis, that the relationship between this symptom and Alois Alzheimer's diagnosis was not as historically straightforward as is now assumed by popular belief. The story of the Alzheimer's patient Mrs. Auguste D. shows that Alzheimer was captivated first by symptoms and later by histopathological signs detected through the autopsy of Auguste D.'s brain. However, these manifestations were seen as indicators of aphasia rather than memory impairment. Borri claims that it was an intervention by Emil Kraepelin, who named the new category after Alzheimer and included it in his nosography, that shifted attention toward thought disorders in dementias—an idea surrounding a condition Kraepelin himself introduced, *dementia praecox*. The synthesis of memory decay and dementias was finally established, Borri explains, by the DSMs.

Giuseppe Sartori and Giulia Melis address the issue of memory malingering in court from a neuroscientific perspective. They review recent definitions and diagnoses, as well as the technological frontiers forensic scientists are currently exploring in order to be able to assess the truthfulness of a defendant's or witness's claims, detect intentionality in lying, and determine any possible association between intentional lying and psychopathology. Sartori and Melis discuss overt techniques, where the subject is aware of being observed, and the limitations of older devices of psychophysiological, behavioral, and cognitive lie detection, which they contrast with the benefits of more recent techniques (i.e., autobiographical version of the Implicit Association Test developed by their team and the Timed Antagonistic Response Alethiometer). They also

present a covert detection technique and the use of artificial intelligence to detect lies and explain the specifics of a clinical interpretation of malingering.

The last two contributions address the ethical debates surrounding MMTs. Alexander Erler addresses the critique that these procedures, especially those for memory erasure that is employed on both traumatic and non-traumatic memories, alter one's memory through direct brain interventions and may undermine a person's "truthful living." Erler supports two responses: the skeptical view that autobiographic memories are largely inaccurate and the view that truthfulness can be plausibly outweighed by other values, even in non-therapeutic use. However, even if the author identifies circumstances under which the second response to the truthfulness objection may not apply, the conclusion on the viability of applying these techniques is cautiously optimistic. While they are specifically focused on memory erasure in a therapeutic domain (i.e., treating post-traumatic stress disorders), Elena Nicolaou, Giulio Mecacci propose an original solution to the same issue Erler tackles. They consider individual and collective objections to this intervention, according to which MMTs might undermine an individual's authenticity or societal tools such as witness testimony or historical memory. To support individuals' memory modification decisions, Nicolaou and Mecacci appeal to patient autonomy, expressed through the informed consent process, and defend a combination of two fundamental rights—mental health and cognitive liberty—while conceding to some constraints (i.e., identity preservation and proportionality of the treatment).

These latest considerations bring us back to the significance of the "art of forgetting," to borrow a phrase from Aleksandr Luria's classic psychopathological work<sup>12</sup>. What if we could remember every single detail of our lives, or, in Luria's own words, "What changes occur in a person's inner world, in his relationships with others, in his very life style when one element of his psychic makeup, his memory, develops to such an uncommon degree that it begins to alter every other aspect of his activity?"<sup>13</sup> The historical case of Solomon Shereshevsky, the powerful mnemonist described by Luria since the 1920s, is illustrative. Shereshevsky possessed an exceptional capacity for episodic memory; he apparently could not forget. He could remember numbers, words, details of events, and even a list of 100 names given to him by Luria 17 years before. Luria diagnosed Shereshevsky with synesthesia, a condition that activates multiple senses simultaneously. However, Shereshevsky was prosopagnosic, meaning he could not remember people's faces. He had poor fluid thinking, no creativity, limited thought flexibility, and trouble socializing. Hypermnnesia may come, it seems, with non-negligible side effects. Memory's double-edged nature may contextualize the entire issue of memory capacity and the importance of investigating it, given its phylogenetic roots, in light of its evolutionary fitness-relevant purpose.



## Bibliography and notes

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