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Review

Infantile Amnesia can be Operationalized as a Psychological Meta Norm in the Development of Memory

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Abstract

This paper offers a syncretic synthesis of the highlights of the scientific knowledge accumulated to date on the mechanisms of infantile amnesia (IA). IA can be conceptualized as a meta-norm of memory development. The review shows that the neurobiological and neuropsychological evidence for IA converges within a common metacognitive framework of inquiry. The involvement of consciousness in the conditioning of memory traces and the association between infantile knowledge and implicit memory allow IA to be analyzed as a phenomenon with complex, universal neuropsychic regulation of a higher order. This approach overcomes the paradox of understanding IA.

Keywords: infantile amnesia; inhibitory learning; memory trace conditioning; infantile knowledge

1. Introduction

The inability of adults to recover memories before age 3–4 is a phenomenon first described by Caroline Miles in 1895. Sigmund Freud later labeled this phenomenon "infantile amnesia" while studying the psychology of autobiographical memory. This phenomenon encompasses the veracity and vividness of childhood memories, the formation of memory traces, and the role of emotions and forgetting in traumatic experiences, extending to the loss of memories from later childhood. Freud interpreted infantile amnesia (IA) as a memory failure during the first few years of life, emphasizing the psychoemotional impact of early experiences throughout life [1]. IA is characterized by the inability to recall the early life memories, along with the challenge of retrieving these memories. People often depend on triggers such as photographs, stories, or narratives to recall anything. Two periods of IA are distinguished: the first, where there are little or no autobiographical memories from before the age of 3–4 years, and the second, where more organized autobiographical memories begin to emerge between the ages of 5 and 7 years [2]. The current understanding of IA is shaped by evidence from both neurobiological perspectives, encompassing neurogenesis, neurotransmission, and the ontogenesis of memory, and the phenomenon's less explored but intriguing neuropsychological perspective.

This review summarizes the evidence accumulated to date in explaining IA, examining this phenomenon from an incremental scientific perspective. Specifically, we integrate existing IA theories with principles concerning the organization of higher neural memory structures. First, we discuss the hippocampal neurogenesis hypothesis, which postulates that the immaturity of the brain and its continued development after birth contribute to IA. Another large set of studies examines the connection between gammaaminobutyric acid (GABA)-ergic neurotransmission in fear memory. Next, the theory of associative learning in the extinction of fear memories extends the conception of memory trace conditioning in the following principles: (1) According to classical conditioning, the timing of an unconditioned stimulus and an unconditioned response is a process of associative learning; (2) Within classical conditioning, stimulus elimination is a process of new associative learning; (3) Therefore, through altered learning and memory extinction, two different associations are maintained. Extinction of fear memory is a process of new associative learning. We use this idea as a bridge for presenting IA as a complex neurocognitive and psychological phenomenon. This approach implies a deep insight into both the neurophysiology modulation of various memory processes (e.g., short-term memory, long-term memory, Ribault's law, memory consolidation, decay of memory traces, reverberant circuits, and their trophic effect) and the neuropsychoanalytic phenomena of memory (e.g., infantile knowledge, conscious, unconscious).

Touching on the topic of the essence of infantile amnesia, we cannot help but discuss some memory processes that we find essential for the development of the phenomenon.

Of course, in recent years, the thesis that memory is a function of multiple systems that are structurally and functionally different but are in a dynamic relationship and work in an integrated manner has been increasingly advocated, and we are far from aiming to discuss all of them [3]. Forty years ago, Tulving equated autobiographical and episodic memory [4] but subsequently raised the question of whether this is really so or not every episodic memory is autobiographical—and in order to become such, it is necessary to be related to personal experience. Bauer, therefore, defines autobiographical memory as personal-episodic [5]. Autobiographical memory is believed to be key to the emergence of consciousness [2]. Episodic memory involves the conscious activation (excitation) of brainstem core structures of stored patterns of cortical connectivity (facilitated synaptic networks) representing previous perceptual events. The directories of such connections are encoded through the hippocampus, which is tightly connected to the limbic system. "Episodic memories are not simply stored, but rather lived." (p.66, [6]). Episodic memory is an act of consciousness, and self-generated states are intrinsically emotional. Humans retrieve events in an episodic form in order to remember what they felt like. Due to the fact that the hippocampus is immature during the first two years, the encoding of episodic, explicit memories is not possible at this time. It is more likely that memories encoded at this early age take the form of habits and beliefs or of procedural and semantic knowledge. In this way, infantile knowledge is stored as implicit knowledge of how the world works and as body memory. Episodic memory work in psychotherapy is an individual reconstruction drawn from sources other than episodic memory. Sources can also be constructs derived from later episodes and projected back onto the early years [6].

IA provides invaluable resources for insight during the psychotherapeutic process and overall management of a large scale of mental disorders. From this perspective, it is seen as a part of the evolution of normal early mental defense mechanisms. On the other hand, from a medical perspective, amnesia per se may be defined as a psychopathological phenomenon.

The aim of our study is to provide a narrative review of the available evidence to highlight an understanding of IA as a psychological meta-norm. A meta-norm is defined as a variation of mental health that exists beyond the individual level of explanation, thereby serving the process of mental development and adaptation. It does not always meet standard operational criteria and range for what is presumed "normal" across the lifespan. Conversely, the meta-norm is not stable and universal but depends on age, culture, and values-specific determinants. For instance, what is evaluated as normal in childhood (fantasies, fears) or in the discourse of IA is not observed primarily as an effect of traumatic processing of early experiences but seems to be a development phenomenon in a nonlinear, universal way. The 1930s cultural identity is regarded as abnormal at a later stage of development, in adulthood or in modern times. Cognitive and memory functions represent one significant asset for mental health and well-being. Amnesia, on the other hand, is interpreted as a psychopathological phenomenon [7]. This study will explore the common normal mechanisms of memory development and, therefore, revisit infantile amnesia as a stage in it. The inherent difficulty in defining IA as a memory deficit, along with the observations regarding the impact of early development on individual vulnerability to potential psychopathological disorders [8], highlight the complex and nonlinear dynamics of this phenomenon. IA is not observed primarily as an effect of the cognitive processing of early traumatic experiences but seems to be a phenomenon regulated by development and emotional learning [9] in a nonlinear, universal way.

2. Methods

The search strategy involved using the Google Scholar and PubMed databases. We considered only full-text articles and books without restricting the publication period while prioritizing the most recent publications. Key search terms included: "infantile amnesia", "infantile amnesia and neurogenesis", "infantile amnesia and memory", "infantile amnesia and memory trace", and "infantile amnesia and psychoanalysis". We encountered numerous empirical papers exploring the neurogenesis hypothesis in infantile amnesia. However, there is a notable shortage of publications in neuroscience and neuropsychology that attempt to conceptualize this phenomenon comprehensively.

3. Neurodevelopmental Perspective in the Explanation of Infantile Amnesia

One key approach to defining the meta-norm of IA is to investigate it from a neurodevelopmental perspective. From this viewpoint, we tend to forget early childhood memories because our brain is maturing. The main argument of neurobiological theories regarding the origin of IA revolves around the ongoing maturation and immaturity of the human brain after birth. According to these theories, the immature structures responsible for memory formation and storage, such as the cortex and the hippocampus, encounter challenges in processing early life experiences, thereby contributing to IA. Cortical maturity, including adult synaptic connectivity and myelination, continues to develop during puberty and beyond. The hippocampus, particularly the dentate gyrus (DG) region, shows prolonged postnatal development in many species, not just humans. Although the hippocampal formation is structurally identical to that of an adult as early as the end of the second trimester of pregnancy, new neurons are added to the dentate gyrus long after birth. The dynamics of the continuing development of the nervous system in children seem most strongly and paradoxically related to the adult's inability to recover memories from early childhood. The most

commonly interpreted reason for this is the replacement of synaptic connections in memory circuits in the hippocampus [10]. The neuroanatomical development of individual hippocampal subdivisions has also been suggested to relate to variations in memory [11]. A larger anterior dentate gyrus volume (CA2-4 subfields) correlates with lower memory accuracy in younger children, while in older children, a smaller volume correlates with more accurate memories [12]. Better episodic memory was observed with larger hippocampal head volume in 6-year-olds but not in 4-year-olds [13]. In fact, changes at the neuronal level should be analyzed as a priority in the course of children's neuropsychological and social development. The natural course of development suggests that the purpose of memory changes over time. While younger children and infants do not attach importance to the details of events, they extract more general information. For older children, details gain importance. Figuratively speaking, the biomechanics of memory, understood as a global neurocognitive function, is nonlinear.

Age-dependent (ontogenetic) changes in memory stability oppose the maturational process, not the maturational state, compromising the storage of memories from early childhood. In this sense, the continuing maturation of the brain likely interferes with the stabilization or consolidation of memory. An extremely valuable insight is the finding that the inability to form stable and persistent memories in early life coincides with a period of high neurogenesis. Conversely, the ability to form stable, persistent memories appears in later periods of development when the rate of neurogenesis decreases. The integration of new neurons has been proposed to degrade existing memories by increasing the excitability (and hence instability) of hippocampal memory networks or by replacing synaptic connections in existing hippocampal memory circuits [14–16]. Specifically, the integration of new neurons alters the network architecture of hippocampal neurons, with memory fidelity closely dependent on the precision of their spatiotemporal activation. At the same time, the formation of afferent and efferent synaptic connections is a competitive process where the synaptic connections of newborn neurons coexist with or replace the synaptic connections of established neurons [17,18]. Immature granule neurons exhibit higher excitability compared to mature granule neurons. The addition of new, excitable neurons to hippocampal circuits can lead to an increase in overall excitatory drive in the DG (via recurrent DG networks) and in downstream CA3 networks (via direct mossy fiber connections). Homeostatic mechanisms for regulating these neurons and circuits include a reduction in their overall excitability or synaptic scaling at the neuron level (e.g., loss/endocytosis of synaptic GluA2 receptors) [17,19], leading to silencing of synapses and compromising information storage [20].

Levels of hippocampal neurogenesis have been studied in rats and guinea pigs. At different ages, the two species were trained in an aversion-motivated place discrimination task. Memory retention was tested over a two-week period, revealing that younger rats exhibited forgetting within this timeframe, whereas older rats demonstrated stable retention. The experiment demonstrated differences in DG development between the two species. No age-dependent difference in memory persistence was observed in guinea pigs, which can walk and see at birth. The relative maturity of the DG and correspondingly low levels of neurogenesis allow the formation of stable memories in newborns. It is likely that the maturity of other brain structures also contributes to the stability of their memory [17]. In humans, hippocampal neurogenesis declines with age but persists into aging. Ongoing neurogenesis is thought to support cognitive function throughout life, and its decline is associated with impaired cognitive-emotional resilience [21–24].

IA is also studied as an effect of critical periods for learning and memory when the brain is particularly sensitive and responsive to experience. It is believed that the hippocampal memory system undergoes a critical period of development, which is an ontogenetic principle observed in the sensory systems of birds, animals, and humans. According to this intriguing recent hypothesis, the immature hippocampal system is highly sensitive to stimuli and experiences during a critical period in order to mature and achieve functional competence (the brain's ability to store expressible and accessible information in the long term). It is assumed that during the so-called critical windows of sensitivity, the hippocampal system stores information through immature but highly active mechanisms in a latent form because it is in the process of learning how to learn and remember. This view describes the ontogenesis of learning itself as a process unfolding in sequences of critical periods for learning and memory. Therefore, the maturation of hippocampal-dependent functions of increasing complexity (e.g., the ability to retrieve memory traces) implies the building of already established (in previous critical periods) gradients of functional competence. In turn, functional achievements from previous periods activate critical periods or a switch driven by experience rather than by default by development. It should be emphasized that the entire hippocampal-dependent memory system, including the functional connectivity between the hippocampus, cortical areas, and amygdala, matures during the infantile critical period in response to experience [25,26].

4. Neurobiological Mechanisms and Pathways Underlying IA: Selective Forgetting is Programmed as a Normal Process

The current scientific understanding of IA has been shaped by studies on retention, brain regions, and neurotransmitter systems crucial for learning and memory. These studies have primarily involved experiments conducted with altricial animal species. In humans, IA is emerging

as a phenomenon of increasing importance in the fields of psychology, psychotherapy, and neuroscience, particularly concerning its role in spontaneous forgetting beyond memory pathology.

The lingering questions primarily revolve around the mechanism of forgetting in IA: Does the memory trace disappear or decay? Is IA explained by a failure to restore or by a storage failure? Is it a result of accelerated forgetting or insufficient learning? Interviews with older adults examining the content and age of their earliest memories do not provide independent verification of content because childhood memories are susceptible to confabulation. Children learn to formulate their own autobiographical memories in the process of developing their language skills as they talk about past events with their caregivers. The emergence of a cognitive sense of self is critical as it relates to the organization of memories or a personal frame of reference [27].

IA cannot be explained by differences in the strength of initial learning and altered parameters of learning (e.g., increased stimulus intensity). When rats were retrained with prolonged shock duration in passive and active avoidance tasks, the long-term memory of young rats was effectively enhanced, but they continued to show accelerated forgetting and lower retention compared to adults [27–29]. A stimulus (e.g., a foot strike) that elicits sympathetic activation has been found to facilitate more effective recall than conditioning stimuli. The shock causes the release of noradrenaline in the amygdala, the amount of which varies according to the intensity of the shock and predicts the effectiveness of restraint [27,30–32]. Direct administration of adrenaline prior to the conditioning stimuli had the same effect on the reinstatement of learned fear as foot shock. Norepinephrine activity in the amygdala is involved in mediating the influence of emotional arousal on memory consolidation, thereby enabling the strong recall of emotionally significant events. The amygdala is critically important for the acquisition and expression of conditioned fear [27,33].

Accumulated evidence suggests that GABAergic neurotransmission plays a significant role in modulating the reactivation of a forgotten fear memory [27,34]. Post-training administration of GABA A receptor agonists has been found to impair memory retention for fear, while GABA A receptor antagonists facilitate it [34]. Dysfunction of the GABAergic system of the brain is one of the main mechanisms of depression and anxiety. The same has been found in animals. GABA receptors are involved in various aspects of fear memory—acquisition and consolidation, retention, reconsolidation, and extinction [35]. Relevant to the phenomenology of IA is the proposition that fear memory extinction results from new inhibitory learning, which prevents the expression of the initially acquired conditioned fear. Extinction is closely linked to the emotional domain of adaptive behavior [36]. We would like to emphasize the highlights of this theory without neglecting the unimaginable complexity of neural structures, networks, nodes, transmitter systems, and plasticity involved in memory processes. Impairment of fear memory extinction is a core cognitive symptom in post-traumatic stress disorder (PTSD), depression, and panic anxiety. Resistance to fear extinction has been observed in both humans and rodents during adolescence, a vulnerable period for the onset of depression and/or anxiety. Extinction is a form of emotional regulation employed in the treatment of disorders characterised by elevated levels of fear and/or anxiety. Essentially, all brain activity is under inhibitory GABAergic control [37,38]. The therapeutic effect of medications like benzodiazepines, used to treat generalized/panic anxiety, sleep disorders, and epilepsy, is supported by the active inhibition of GABA [39,40], as well as in neurodevelopmental disorders [41]. While benzodiazepines are commonly prescribed for anxiety and also play a beneficial role in reducing the reconsolidation of unwanted memories, there is no conclusive scientific evidence for their contribution to the treatment of fear memory extinction impairment. However, extinction represents new learning in the ongoing course of experience—the repeated and systematic repetition of a conditioned stimulus, unpaired with an unconditioned one (for example, punishment or pain), is in itself a process of forming a new association according to the schema: conditioned stimulus and absence of pain/punishment. According to the principles of classical conditioning, the elimination of a stimulus can be seen as a change in association. Fear memory learning and extinction refer to the maintenance of two different associations supporting the corresponding plasticity in the GABAergic system in circuits of the amygdala, prefrontal cortex, and hippocampus. GABAergic system functioning in the amygdala has been shown to decrease during the acquisition of a conditioned fear response [42], and GABA transmission increases during extinction [36,43,44]. It makes sense that similar studies of GABA transmission could be replicated in the context of memory extinction for traumatic and/or emotionally significant experiences when dealing with emotions other than fear.

In terms of the neural trace of a forgotten memory or memory engram, activation of the mitogen-activated protein kinase (MAPK) signaling pathway in the amygdala is thought to correspond to the physical memory trace. MAPK is known to be part of the intracellular signaling pathway involved in experience-dependent plasticity [27,45,46]. After immunohistochemistry of brain tissue, increased phosphorylated mitogen-activated protein kinase (pMAPK) was found in the amygdala of rats conditioned in fear of discrete white noise (CS, conditioned stimulus) and shock (US, unconditioned stimulus). This finding was absent in the tissue of the control groups of rats in the same experiment [47]. Initial fear learning activates complex intracellular signals involving glutamate release, activation of protein kinases (such as MAPK), and protein synthesis, and disruption of any part of their cascade impairs initial learning [48–50].

Molecular, genetic, and epigenetic mechanisms also contribute to the alteration of neural plasticity, interrelated with memory functions, such as the epigenetic immunomodulators brain-derived neurotrophic factor (BDNF), methyl-CpG-binding protein 2 (MECP2), DNA methyltransferases (DNMTs), and histone deacetylase (HDAC) inhibitors [51–53]. Recent studies suggest that specific patterns of connectivity of engram cells contribute differently to memory storage and retrieval. After contextual fear conditioning, mice were immediately injected with the protein synthesis inhibitor anisomycin (ANI) or saline (SAL) as a control to examine engram pathways in the hippocampal DG and related areas as entorhinal cortex (EC) and amygdala. Findings after artificial disruption of memory consolidation indicate altered pathways of memory engram reactivation. Comparing the artificial disruption of consolidation (retrograde amnesia induced by protein synthesis inhibitor) and the subsequent memory recall (light-induced activation of DG engram cells) shows altered pathways for reactivating memory engrams. Specifically, optogenetic activation of DG engram cells leads to memory retrieval by reactivating engrams in downstream regions (hippocampal subfield CA3 and basolateral amygdala in particular) that have also been affected by systemic ANI injection. Researchers assume that augmented synaptic strength is not crucial for stored memory, but a rapid increase in synaptic strength is likely to be more important during the encoding phase [54]. It is assumed that all forms of forgetting correspond to neuroplasticity associated with remodeling synaptic circuits or switching engram cells from an accessible to an inaccessible state, as these processes are sensitive to the mismatch between expectations and the environment [55]. The function and purpose of forgetting in humans are not yet fully understood [56].

The conditioning of memory traces is dependent on the hippocampus, with the following in mind—the hippocampus is preferentially needed to acquire a trace association when the stimuli are distant in time, but not when the relationship between them is already known. Changing the time intervals between the conditioned, unconditioned stimulus and trace conditioning (delay conditioning) in animal experiments shows that they are able to shift the conditioned response to accommodate a new temporal relationship (new time of onset of the unconditioned stimulus) [57,58]. Moreover, it is the prefrontal cortex, rather than the hippocampus, that is involved in the tracking response. The deep nuclei of the cerebellum are also involved in the establishment and maintenance of the conditioned response [59]. The hippocampus responds to stimuli of all kinds, not just those that suggest a trace [57,60–62].

Animals with severely reduced neurogenesis, achieved through the use of an anti-mitotic agent, exhibited impaired learning in a trace fear conditioning task [63]. However, they were still able to learn the task when utilizing the delay paradigm, demonstrating a shift in conditioned response. Thus, artificial reduction of neurogenesis corresponds to an altered learning trajectory. Reduced neurogenesis led to increased memory persistence (in infant mice) following contextually conditioned fear, while increased neurogenesis (via voluntary running in adult mice) was associated with increased forgetting [64]. In another experiment, animals treated with bromodeoxyuridine (BrdU) to mark cells in the S phase of mitosis were tested for differences (one week after marker application) in learning in delay conditioning and conditioning with explicit unpaired stimuli (the time between random and unpredictable stimuli). In animals that acquired memory traces, twice as many new neurons were counted. Experience shows that the type of training does not save neurons from death, but newly created hippocampal neurons are sensitive to the formation of memory traces. More difficult-to-learn tasks depend on the hippocampus. For example, learning with spatial cues is more challenging than learning with visual cues in a water maze. Learning the change in discrimination is also more difficult than the discrimination between two tones. Trace conditioning depends on the hippocampus, whereas delay conditioning does not [57]. A human study examined the role of consciousness in the conditioning of memory traces. Delay conditioning and eyeblink conditioning paradigms were tested by having participants simultaneously watch a silent film about which they were then debriefed. The acquisition of a conditioned response was found to be related to levels of awareness of the stimulus contingencies. The authors believe that people's expectations for tracking tasks determine the probability of a conditioned response. Specifically, high expectations increase the likelihood of a conditioned response. Age-dependent deficits were observed in trace discrimination but not in forgetting discrimination. These results suggest that the awareness or knowledge of contingent stimuli may account for the acquisition of a conditioned response in higher-order discrimination tasks [63,65].

Recent insights into the anatomy and neurobiology of memory trace and the involvement of consciousness postulate a higher-order organization of memory in the central nervous system (CNS), modulated by learning, social experience, and neuroplasticity. It is likely that multimodal methods that simultaneously assess a person's cognitive and affective functioning, as well as data from neuroimaging, microbiological, and genetic studies, would be more reliable in providing evidence for the complex organization of memory processes. This, in turn, could lead to a better understanding of IA. After all, IA is not manifested by memory deficits but by the difficult or impossible recovery of autobiographical memories from early childhood despite mature and preserved cognitive function. Whether it is objectified and what accounts for the selectivity of memory (forgetting) in the context of IA is primarily a problem of normal psychology.

5. Experimental Assessment of IA in Humans

A challenge in the study of IA is that experimental tasks require a non-verbal nature, both in human infants and in animal studies. The limited motor capabilities of children under 1 year and the duration of the studies further complicate the experimental process. The assessment of IA in humans was originally based on the evaluation of memory and learning, situated in three groups of methods—visual recognition memory (VRM) paradigms, operant conditioning paradigms, and deferred imitation paradigms. Imitation paradigms are based on the tendency of infants to repeat the actions of people in their environment. They will not be discussed in this article because we share the idea that the ability to imitate is particularly dependent on the child's age and the level of his social, cognitive, and motor development, which limits the application and full reliability of these paradigms and makes them too relative [66]. Additionally, research on deferred imitation in humans has primarily concentrated on the preverbal developmental stage, which limits the discussion to nonverbal declarative memory [67]. We will reflect on the neuropsychological mechanisms of memory throughout the lifespan in terms of IA.

Assessment of visual recognition memory involves measuring fixation times when viewing a novel and a familiar visual stimulus. A variation of the method is the so-called habituation task, in which a single stimulus is presented repeatedly until the infant's interest in it wanes. A new stimulus is then introduced, and the time to loss of interest is again measured. These two times are then compared [68,69]. Using operant conditioning methods, the learning ability of infants has been investigated. For example, in high-amplitude sucking tasks, infants receive a stimulus in the form of a sound [70], visual [71], or taste [72] signal when they reach a certain speed and interval between suckings. This method revealed a perceptible preference for the mother's voice [73] in 3-day-old infants who had a maximum of 12 hours of postnatal contact with their mothers. The infants had to suckle at a certain frequency to reproduce the mother's voice, adjusting the interval between individual suckles. Additionally, newborn human infants can recognize their mother's voice, having perceived it during their prenatal development [74]. Previous study has documented infants' preference for their mother's voice and recognition of language samples in children's stories heard during pregnancy [75]. Pregnant women were asked to read the same text to their unborn babies twice a day for six weeks before their due date. Three days after birth, the scientists gave the newborns the opportunity to change their sucking speed to reproduce the paragraph read to them by their mothers or another text. Regardless of who reads the passage—the mother or another woman—babies change their sucking speed just to hear the familiar text. Such dependency was not observed in control groups of babies who had not systematically heard read-aloud texts before birth [73]. Currently, the concept of prenatal learning and memory is well-defended in the literature [76,77].

Mobile conjugate reinforcement (MCR) experiments in infants involve motor production, similar to the deferred imitation concept [67]. In the classic demonstration of the experiment, a band is attached to a baby's leg and connected to a stand with a brightly colored cell phone. When the baby kicks, the cell phone moves, creating feedback labeled as conjugate reinforcement. The harder or faster the baby kicks, the more effective the audio and visual feedback. Each session begins with a no-reinforcement period where the band is not connected to the cell phone, and movements remain unrewarded. The experiment is repeated at fixed time intervals, comparing the kicking frequencies during the non-reinforcement stages [78]. For some babies, a periodic reminder is applied before the session. In the first minutes of conjugate reinforcement, infants' kicking rate tripled compared to control infants presented with identical but unconditioned visual, auditory, and kinesthetic stimulation (cord instead of cell phone) [78]. Earlier MCR experiments demonstrated topographic response differentiation and functional equivalence in young infants. More recently, with a more sophisticated biofeedback system, infants have been found to detect and reproduce specific hip and knee movements of varying duration and direction when mobile movements and sound are added. The continuous information flow generated by the mobile device (movements and sound) and the proprioception from the self-generated movement is simultaneously analyzed [79,80]. A study demonstrates that painful experiences in the infantile period can influence the infant's behavior during subsequent painful experiences. The research involved comparing the pain response to routine vaccination in two groups of male babies—those circumcised with and without local anesthesia. The study showed that boys circumcised without local anesthesia cried significantly more and experienced greater physical and emotional distress from the vaccination. It is unlikely that this experience will be retained in the autobiographical memory. However, it implicitly raises the question of the association between pain, trauma, and memory [81].

6. Discussion

This paper presents key neurobiological mechanisms in IA research, shifting the focus from conclusions mainly based on animal studies to a deeper understanding of human neuropsychological organization. What researchers call the IA paradox is related to the lack of memories from an early age, and it is different from memory loss or impaired memory. In practice, IA is a phenomenon observed in mentally healthy individuals and is not primarily determined by a traumatic experience. The most influential theories propose neurogenesis, learning, and neuroplasticity as crucial mechanisms in explaining IA. However, they have not been sufficiently investigated in humans, likely due to

ethical concerns. On the other hand, inductive and robust scientific approaches rely on shared neurobiological structures between humans and certain animal species. Assuming that research on the phenomenology of IA in humans is inherently vulnerable and that there are no medical considerations for such studies, we would like to revisit IA from the perspective of neuropsychoanalysis.

As ontological development progresses, mechanisms of inherited memory undergo modification and individualisation. At the operational level, learning and memory become intricately woven into the nervous system, forming a unified cognitive function of perception. Neuroscientific knowledge of the subprocesses integrated in memory function provides the most profound paradigm for understanding IA. The function of memory is not reduced to just encoding, retention, storage, and retrieval of information. Consolidation is an independent encoding process that persists in storage. Consolidation has been convincingly demonstrated in studies of memory decay following brain injury or disease. While some aspects of memory are vulnerable, others are indestructible. More recent memories, formed hours, days, weeks, or months before the injury, are more valuable to neurological pathology. In contrast, older, more distant memories are more persistent. We know this time gradient as Ribault's Law. Short-term memory (immediate, working) and long-term memory represent a more global mode of subprocessing. Short-term memory is engaged with immediately perceived information, what a person is currently experiencing and learning, but "long-term memory begins a few seconds ago" (p.55, [6]). The inability to retrieve a memory of an event from an hour ago or the previous day is already a problem of long-term memory. Short-term memory has two aspects: (1) active recall, in which a person consciously keeps something in his mind for some reason, and (2) passive, corresponding to perception (objective reality, stimulus) [6]. The content of consciousness is stored in the so-called buffer of consciousness, which has a limited capacity. The buffer is maintained through continuous rehearsal and can hold approximately seven units of information. The momentary effects of external perceptual stimuli in the basic core consciousness (existing only at the moment) are described by terms such as ultra-short-term or iconic memory. Humans cannot encode and store everything experienced. Much of the information is excluded from attention during perception. Consolidation continues the process of sifting (filtering) within memory storage systems. In this way, consolidation not only anchors but also releases memories that one does not want (or cannot) keep. Trace decay is marked as active forgetting, and suppression is marked as passive forgetting. Physiologically, short-term memory is maintained by reverberating circuits or groups of cells that work together in closed (self-activating) circuits. The firing pattern plays a role in information retention, serving as the neural correlate of retention. The principle of this connectivity is known as Hebb's law: cells that fire together are wired together. An established reverberating circuit is more likely to be reactivated. The wiring process transforms short-term memories into long-term memories in two dimensions. On the one hand, through purely physiological cellular changes—synapses connecting the cells in the circuit become more permeable, so the cell is more likely to fire in response to stimuli at the synapses that previously activated it. On the other hand, through a constant anatomical process, the continuous firing of cells at certain junctions activates genetic mechanisms in them, which in turn promotes the growth of additional synapses at the same junctions. Temporary reverberating circuits have been shown to have a permanent, trophic effect on the cells involved by producing increased nerve tissue density. The trophic effect lasts throughout life and is highly activity-dependent. Inactive synapses atrophy and die [6]. The formation of synapses, as well as the influence of various endogenous and exogenous events on their stability, predispose to neuropsychiatric disorders [82]. The requirements for synaptic plasticity change during ontogenetic development. Immediately after birth, the human brain develops neural networks for perception and programming innate behavior, with synaptic contact formation in the absence of sensory input. Processing new information, such as language, family, culture, etc. requires higher levels of synaptic plasticity in contrast to mature age stages [83]. The environment of birth and life activates part of synaptic connections. They are strengthened, and underused ones are deleted—a process called synaptic pruning. This pattern mechanistically suggests that neural connections activated in childhood may be discarded during later stages of development simply because they are not needed. It also suggests that people do not rely on the same circuits in adulthood, as their life circumstances can change unpredictably and radically. In this way, displaced childhood memories disappear. These arguments suggest that IA may be understood as a matter of memory decay [6]. Experiments prove that fragmented memories - isolated moments, presented most often in the form of a picture or emotion, appear about half a year earlier than those for remembered whole events. This leads to the question of whether the end of infantile amnesia should be considered as the emergence of the earliest fragmentary memory (at 3 and 1/3 years) or of the entire episodic memory (at 4 years of age) [84].

There are two arguments against the idea that IA is a matter of memory decay. Firstly, the distinction between conscious and unconscious mechanisms. Conscious and unconscious remembering are two qualitatively different processes. Activating a trace is not the equivalent of conscious remembering. Long-term memory can be activated and brought to awareness without accompanying experience; an example of this is reminiscence. The fact of being unaware of early childhood events does not mean that traces are not activated. Neural networks that survive pruning processes can serve as templates for the organization of

later memories, functioning as stem circuits. They would activate regularly, even without consciousness accessing the events that originally formed them. Implicit memory corresponds to the unconscious, and explicit memory corresponds to the conscious in the psychoanalytic paradigm. Secondly, the IA phenomenon disrupts Ribault's Law. According to psychoanalysts, childhood memories appear to be forgotten, but they are robust and inaccessible to consciousness due to repression. The inability of a person to recall something consciously does not mean that he does not implicitly know what happened. What a person remembers, consciously or not, primarily depends on the involvement of certain memory systems in the encoding and retrieval of the memory. Specifically, if the episodic memory system and early consolidation are involved in encoding the experience, one explicitly remembers it. If they are not engaged, the event will fade from consciousness, but its indirect effects on behavior and beliefs may persist, as observed in some forms of repression [6].

As is known, critical periods of development are associated to changes in neuroplasticity, during which the nervous system is particularly responsive to certain experiences. Sensitive periods are also observed in affective development. Affective neural circuits in humans, or affective plasticity, have been described that support affective learning [85]. Unlike motor and sensory systems, these circuits undergo functional and structural changes in young adulthood [86]. Variations in early life experiences may permanently alter the development and function of affective circuits [87]. It has been found that the process of fear learning maturation is nonlinear and influenced by experience-dependent plasticity, including age epochs and critical developmental periods. Both the prefrontal and subcortical circuits that regulate fear learning undergo changes from childhood to adulthood [86]. The last observations in neuroscience largely support our proposal for IA as an aspect of higher-order neurocognitive regulation.

The neurobiological evidence accumulated from the studies on the mechanisms of IA supports the involvement of functional and anatomical immaturity, along with the ongoing development of the nervous system, during the early years of life in both humans and animals [10–24]. The influence of critical (sensitive) periods of learning and development and age-dependent changes in memory [25,26], in the study of IA follows the causal logic of the classic scientific experiment, which is technically linear (chronology of experience and observation). The concepts of consciousness's role in conditioning memory traces and inhibitory learning, along with the extinction of fear memory, propose a new approach. This approach suggests the formation of a new association, a variety of reverse classical conditioning, where a conditioned stimulus is paired with the systematic absence of an unconditioned stimulus (such as the withdrawal of pain or punishment involved in the initial fear association) [36]. This proposed approach objectifies a possible research direction, favoring a natural experiment. In this perspective, we should consider the following: IA is not specific to humans; it is a universal phenomenon. IA implies emotional regulation of learning (conditioning and inhibitory learning). The mechanisms of IA are better delineated in the context of traumatic experiences (memory extinction and repression). However, they do not fully explain its nature, as it is universally observed in healthy and cognitively preserved adults. The joint interpretation of the neurobiological and neuropsychological dimensions of IA, based on the neuroscientific knowledge of the memory subprocesses (encoding, information retention, storage, retrieval, consolidation) and memory subsystems (short-term memory, long-term memory, implicit memory, explicit memory, episodic memory, etc.), as well as psychological and psychoanalytic constructs (perception, conscious, unconscious, behavior, habits, beliefs) [6], seems to overcome the paradox in understanding IA. Speculatively speaking, IA is not a form of amnesia, rather, it is an effect of higher-order memory function. Such an analysis requires us to recognize that IA is a matter of more complex universal neural encoding and regulation, allowing us to conceptualize IA as a meta norm in memory development.

7. Conclusions

Infantile amnesia is a complex psychodynamic phenomenon, which emerges from nonlinear and complex neurobiological processes. It is considered as a critical part in the development of both cognitive-affective mental systems and their biological underpinnings in terms of neural circuits. As a part of development and adaptation, infantile amnesia should be regarded as an adaptive mechanism in the maturation of mind-brain mechanisms in response to environmental interactions. From that point of view we define IA as developmental meta-norm rather than disturbance in the normal memory functions. That would be one possible future perspective of research, in particular with focus on experimental paradigms, investigating IA in adult humans.

Author Contributions

KS conceptualised and designed the manuscript. BS collected and sorted references. BS and KS wrote the manuscript. DS designed the manuscript, critically reviewed and supervised the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

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Conflict of Interest

The authors declare no conflict of interest. Drozdstoy Stoyanov is serving as one of the Guest editors of this journal. We declare that Drozdstoy Stoyanov had no involvement in the peer review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to Gernot Riedel.

References

[1] O'Donoghue, D. Amnesias of a Freudian Kind. American Imago 2021; 78: 55–77. https://dx.doi.org/10.1353/aim.2021.0001.

[2] Occhionero M, Tonetti L, Giovagnoli S, Natale V. The infantile amnesia phenomenon and the beginning of autobiographical memories. Applied Sciences. 2023; 13: 1158. https://doi.org/10.3390/app13021158.

[3] Fivush R. The development of autobiographical memory. Annual Review of Psychology. 2011; 62: 559–582. https://doi.org/10.1146/annurev.psych.121208.131702.

[4] Tulving E. Elements of episodic memory. 1983.

[5] Bauer PJ. A complementary processes account of the development of childhood amnesia and a personal past. Psychological Review. 2015; 122: 204–231. https://doi.org/10.1037/a0038939.

[6] Turnbull O, Solms M. Memory, amnesia and intuition: a neuropsychoanalytic perspective. In Viviane G (ed.) Emotional development in psychoanalysis, attachment theory and neuroscience (pp. 63–92). Routledge: London. 2004.

[7] Jaspers, K. General psychopathology (Vol. 2). JHU Press: London. 1997.

[8] Callaghan BL, Richardson R. Early experiences and the development of emotional learning systems in rats. Biology of Mood & Anxiety Disorders. 2013; 3: 8. https://doi.org/10.1186/2045-5380-3-8.

[9] Callaghan BL, Graham BM, Li S, Richardson R. From resilience to vulnerability: mechanistic insights into the effects of stress on transitions in critical period plasticity. Frontiers in Psychiatry. 2013; 4: 90. https://doi.org/10.3389/fpsyt.2013.00090.

[10] Josselyn SA, Frankland PW. Infantile amnesia: a neurogenic hypothesis. Learning & Memory. 2012; 19: 423–433. https://doi.org/10.1101/lm.021311.110.

[11] Riggins T, Canada KL, Botdorf M. Empirical Evidence Supporting Neural Contributions to Episodic Memory Development in Early Childhood: Implications for Childhood Amnesia. Child Development Perspectives. 2020; 14: 41–48. https://doi.org/10.1111/cdep.12353.

[12] Canada KL, Ngo CT, Newcombe NS, Geng F, Riggins T. It's All in the Details: Relations Between Young Children's Developing Pattern Separation Abilities and Hippocampal Subfield Volumes. Cerebral Cortex. 2019; 29: 3427–3433. https://doi.org/10.1093/cercor/bhy211.

[13] Riggins T, Blankenship SL, Mulligan E, Rice K, Redcay E. Developmental Differences in Relations Between Episodic Memory and Hippocampal Subregion Volume During Early Childhood. Child Development. 2015; 86: 1710–1718. https://doi.org/10.1111/cdev.12445.

[14] Josselyn SA, Frankland PW. Memory Allocation: Mechanisms and Function. Annual Review of Neuroscience. 2018; 41: 389–413. https://doi.org/10.1146/annurev-neuro-080317-061956.

[15] Campbell BA, Spear NE. Ontogeny of memory. Psychological Review. 1972; 79: 215–236. https://doi.org/10.1037/h0032690.

[16] Chambers RA, Potenza MN, Hoffman RE, Miranker W. Simulated apoptosis/neurogenesis regulates learning and memory capabilities of adaptive neural networks. Neuropsychopharmacology. 2004; 29: 747–758. https://doi.org/10.1038/sj.npp.1300358.

[17] Toni N, Teng EM, Bushong EA, Aimone JB, Zhao C, Consiglio A, *et al*. Synapse formation on neurons born in the adult hippocampus. Nature Neuroscience. 2007; 10: 727–734. https://doi.org/10.1038/nn1908.

[18] Kim WR, Christian K, Ming GL, Song H. Time-dependent involvement of adult-born dentate granule cells in behavior. Behavioural Brain Research. 2012; 227: 470–479. https://doi.org/10.1016/j.bbr.2011.07.012.

[19] Fröhlich F, Bazhenov M, Sejnowski TJ. Pathological effect of homeostatic synaptic scaling on network dynamics in diseases of the cortex. The Journal of Neuroscience. 2008; 28: 1709–1720. https://doi.org/10.1523/JNEUROSCI.4263-07.2008.

[20] Meltzer LA, Yabaluri R, Deisseroth K. A role for circuit homeostasis in adult neurogenesis. Trends in Neurosciences. 2005; 28: 653–660. https://doi.org/10.1016/j.tins.2005.09.007.

[21] Boldrini M, Fulmore CA, Tartt AN, Simeon LR, Pavlova I, Poposka V, *et al*. Human Hippocampal Neurogenesis Persists throughout Aging. Cell Stem Cell. 2018; 22: 589–599.e5. https://doi.org/10.1016/j.stem.2018.03.015.

[22] Wu A, Zhang J. Neuroinflammation, memory, and depression: new approaches to hippocampal neurogenesis. Journal of Neuroinflammation. 2023; 20: 283. https://doi.org/10.1186/s12974-023-02964-x.

[23] Grabrucker S, Marizzoni M, Silajdžić E, Lopizzo N, Mombelli E, Nicolas S, *et al*. Microbiota from Alzheimer's patients induce deficits in cognition and hippocampal neurogenesis. Brain. 2023; 146: 4916–4934. https://doi.org/10.1093/brain/awad303.

[24] Alonso M, Petit AC, Lledo PM. The impact of adult neurogenesis on affective functions: of mice and men. Molecular Psychiatry. 2024; 29: 2527–2542. https://doi.org/10.1038/s41380-024-02504-w.

[25] Alberini CM, Travaglia A. Infantile Amnesia: A Critical Period of Learning to Learn and Remember. The Journal of Neuroscience. 2017; 37: 5783–5795. https://doi.org/10.1523/JNEUROSCI.0324-17.2017.

[26] Travaglia A, Bisaz R, Sweet ES, Blitzer RD, Alberini CM. Infantile amnesia reflects a developmental critical period for hippocampal learning. Nature Neuroscience. 2016; 19: 1225–1233. https://doi.org/10.1038/nn.4348.

[27] Madsen HB, Kim JH. Ontogeny of memory: An update on 40 years of work on infantile amnesia. Behavioural Brain Research. 2016; 298: 4–14. https://doi.org/10.1016/j.bbr.2015.07.030.

[28] Feigley DA, Spear NE. Effect of age and punishment condition on long-term retention by the rat of active- and passive-avoidance learning. Journal of Comparative and Physiological Psychology. 1970; 73: 515–526. https://doi.org/10.1037/h0030234.

[29] Schulenburg CJ, Riccio DC, Stikes ER. Acquisition and retention of a passive-avoidance response as a function of age in rats. Journal of Comparative and Physiological Psychology. 1971; 74: 75–83. https://doi.org/10.1037/h0030350.

[30] Galvez R, Mesches MH, McGaugh JL. Norepinephrine release in the amygdala in response to footshock stimulation. Neurobiology of Learning and Memory. 1996; 66: 253–257. https:

//doi.org/10.1006/nlme.1996.0067.
[31] Quirarte GL, Galvez R, Roozendaal B, McGaugh JL. Norepinephrine release in the amygdala in response to footshock and opioid peptidergic drugs. Brain Research. 1998; 808: 134–140. https://doi.org/10.1016/s0006-8993(98)00795-1.
[32] McIntyre CK, Hatfield T, McGaugh JL. Amygdala norepinephrine levels after training predict inhibitory avoidance retention performance in rats. The European Journal of Neuroscience. 2002; 16: 1223–1226. https://doi.org/10.1046/j.1460-9568.2002.02188.x.
[33] Haroutunian V, Riccio DC. Effect of arousal conditions during reinstatement treatment upon learned fear in young rats. Developmental Psychobiology. 1977; 10: 25–32. https://doi.org/10.1002/dev.420100105.
[34] Kim JH, Richardson R. A developmental dissociation of context and GABA effects on extinguished fear in rats. Behavioral Neuroscience. 2007; 121: 131–139. https://doi.org/10.1037/0735-7044.121.1.131.
[35] Makkar SR, Zhang SQ, Cranney J. Behavioral and neural analysis of GABA in the acquisition, consolidation, reconsolidation, and extinction of fear memory. Neuropsychopharmacology. 2010; 35: 1625–1652. https://doi.org/10.1038/npp.2010.53.
[36] Dubrovina NI. GABA-Receptors in Modulation of Fear Memory Extinction. Zhurnal Vysshei Nervnoi Deiatelnosti Imeni i P Pavlova. 2016; 66: 131–147.
[37] Thomas GM, Huganir RL. MAPK cascade signalling and synaptic plasticity. Nature Reviews. Neuroscience. 2004; 5: 173–183. https://doi.org/10.1038/nrn1346.
[38] Hoerndli FJ, Brockie PJ, Wang R, Mellem JE, Kallarackal A, Doser RL, *et al*. MAPK signaling and a mobile scaffold complex regulate AMPA receptor transport to modulate synaptic strength. Cell Reports. 2022; 38: 110577. https://doi.org/10.1016/j.celrep.2022.110577.
[39] Treiman DM. GABAergic mechanisms in epilepsy. Epilepsia. 2001; 42: 8–12. https://doi.org/10.1046/j.1528-1157.2001.042suppl.3008.x.
[40] Pallanti S, Zohar J, Kasper S, Möller HJ, Hollander E. Revisiting benzodiazepines (GABA Enhancers): A transdiagnostic and precision medicine approach. Journal of Psychiatric Research. 2024; 170: 65–72. https://doi.org/10.1016/j.jpsychires.2023.11.042.
[41] Tang X, Jaenisch R, Sur M. The role of GABAergic signalling in neurodevelopmental disorders. Nature Reviews. Neuroscience. 2021; 22: 290–307. https://doi.org/10.1038/s41583-021-00443-x.
[42] El Matine R, Kreutzmann JC, Fendt M. Chronic unilateral inhibition of GABA synthesis in the amygdala increases specificity of conditioned fear in a discriminative fear conditioning paradigm in rats. Progress in Neuro-Psychopharmacology & Biological Psychiatry. 2023; 124: 110732. https://doi.org/10.1016/j.pnpbp.2023.110732.
[43] Omoumi S, Rashidy-Pour A, Seyedinia SA, Tarahomi P, Vafaei AA, Raise-Abdullahi P. Corticosterone injection into the infralimbic prefrontal cortex enhances fear memory extinction: Involvement of GABA receptors and the extracellular signal-regulated kinase. Physiology & Behavior. 2023; 265: 114156. https://doi.org/10.1016/j.physbeh.2023.114156.
[44] Liu Y, Ye S, Li XN, Li WG. Memory Trace for Fear Extinction: Fragile yet Reinforceable. Neuroscience Bulletin. 2024; 40: 777–794. https://doi.org/10.1007/s12264-023-01129-3.
[45] Schmidt-Wilcke T, Fuchs E, Funke K, Vlachos A, Müller-Dahlhaus F, Puts NAJ, *et al*. GABA-from Inhibition to Cognition: Emerging Concepts. The Neuroscientist. 2018; 24: 501–515. https://doi.org/10.1177/1073858417734530.
[46] Koh W, Kwak H, Cheong E, Lee CJ. GABA tone regulation and its cognitive functions in the brain. Nature Reviews. Neuroscience. 2023; 24: 523–539. https://doi.org/10.1038/s41583-023-00724-7.
[47] Kim JH, Li S, Hamlin AS, McNally GP, Richardson R. Phosphorylation of mitogen-activated protein kinase in the medial prefrontal cortex and the amygdala following memory retrieval or forgetting in developing rats. Neurobiology of Learning and Memory. 2012; 97: 59–68. https://doi.org/10.1016/j.nlm.2011.09.005.
[48] Kandel ER. The molecular biology of memory storage: a dialogue between genes and synapses. Science. 2001; 294: 1030–1038. https://doi.org/10.1126/science.1067020.
[49] Phasuk S, Pairojana T, Suresh P, Yang CH, Roytrakul S, Huang SP, *et al*. Enhanced contextual fear memory in peroxiredoxin 6 knockout mice is associated with hyperactivation of MAPK signaling pathway. Molecular Brain. 2021; 14: 42. https://doi.org/10.1186/s13041-021-00754-1.
[50] Moreno A. Molecular mechanisms of forgetting. The European Journal of Neuroscience. 2021; 54: 6912–6932. https://doi.org/10.1111/ejn.14839.
[51] Nayak M, Das D, Pradhan J, Ahmed RG, Laureano-Melo R, Dandapat J. Epigenetic signature in neural plasticity: the journey so far and journey ahead. Heliyon. 2022; 8: e12292. https://doi.org/10.1016/j.heliyon.2022.e12292.
[52] Creighton SD, Stefanelli G, Reda A, Zovkic IB. Epigenetic Mechanisms of Learning and Memory: Implications for Aging. International Journal of Molecular Sciences. 2020; 21: 6918. https://doi.org/10.3390/ijms21186918.
[53] Kupke J. DNA methylation and transcriptional control in memory formation, persistence and suppression [Doctoral dissertation]. Combined Faculty of Mathematics, Engineering and Natural Sciences of the Ruprecht Karls, University Heidelberg. 2023.
[54] Ryan TJ, Roy DS, Pignatelli M, Arons A, Tonegawa S. Memory. Engram cells retain memory under retrograde amnesia. Science. 2015; 348: 1007–1013. https://doi.org/10.1126/science.aaa5542.
[55] Ryan TJ, Frankland PW. Forgetting as a form of adaptive engram cell plasticity. Nature Reviews. Neuroscience. 2022; 23: 173–186. https://doi.org/10.1038/s41583-021-00548-3.
[56] Zaki Y, Cai DJ. Memory engram stability and flexibility. Neuropsychopharmacology. 2024; 50: 285–293. https://doi.org/10.1038/s41386-024-01979-z.
[57] Shors TJ. Memory traces of trace memories: neurogenesis, synaptogenesis and awareness. Trends in Neurosciences. 2004; 27: 250–256. https://doi.org/10.1016/j.tins.2004.03.007.
[58] Beylin AV, Gandhi CC, Wood GE, Talk AC, Matzel LD, Shors TJ. The role of the hippocampus in trace conditioning: temporal discontinuity or task difficulty? Neurobiology of Learning and Memory. 2001; 76: 447–461. https://doi.org/10.1006/nlme.2001.4039.
[59] Takehara-Nishiuchi K. Prefrontal-hippocampal interaction during the encoding of new memories. Brain and Neuroscience Advances. 2020; 4: 2398212820925580. https://doi.org/10.1177/2398212820925580.
[60] Shors TJ, Miesegaes G, Beylin A, Zhao M, Rydel T, Gould E. Neurogenesis in the adult is involved in the formation of trace memories. Nature. 2001; 410: 372–376. https://doi.org/10.1038/35066584.
[61] Duff MC, Covington NV, Hilverman C, Cohen NJ. Semantic Memory and the Hippocampus: Revisiting, Reaffirming, and Extending the Reach of Their Critical Relationship. Frontiers in Human Neuroscience. 2020; 13: 471. https://doi.org/10.3389/fnhum.2019.00471.
[62] Opalka AN, Wang DV. Hippocampal efferents to retrosplenial cortex and lateral septum are required for memory acquisition. Learning & Memory. 2020; 27: 310–318. https://doi.org/10.

1101/lm.051797.120.
[63] Gould E, Beylin A, Tanapat P, Reeves A, Shors TJ. Learning enhances adult neurogenesis in the hippocampal formation. Nature Neuroscience. 1999; 2: 260–265. https://doi.org/10.1038/6365.
[64] Akers KG, Martinez-Canabal A, Restivo L, Yiu AP, De Cristofaro A, Hsiang HLL, *et al*. Hippocampal neurogenesis regulates forgetting during adulthood and infancy. Science. 2014; 344: 598–602. https://doi.org/10.1126/science.1248903.
[65] Knuttinen MG, Power JM, Preston AR, Disterhoft JF. Awareness in classical differential eyeblink conditioning in young and aging humans. Behavioral Neuroscience. 2001; 115: 747–757. https://doi.org/10.1037//0735-7044.115.4.747.
[66] Jones SS. The development of imitation in infancy. Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences. 2009; 364: 2325–2335. https://doi.org/10.1098/rstb.2009.0045.
[67] Meltzoff AN. What infant memory tells us about infantile amnesia: long-term recall and deferred imitation. Journal of Experimental Child Psychology. 1995; 59: 497–515. https://doi.org/10.1006/jecp.1995.1023.
[68] Scarf D, Gross J, Colombo M, Hayne H. To have and to hold: episodic memory in 3- and 4-year-old children. Developmental Psychobiology. 2013; 55: 125–132. https://doi.org/10.1002/dev.21004.
[69] Morgan K, Hayne H. Age-related changes in visual recognition memory during infancy and early childhood. Developmental Psychobiology. 2011; 53: 157–165. https://doi.org/10.1002/dev.20503.
[70] Eimas PD, Siqueland ER, Jusczyk P, Vigorito J. Speech perception in infants. Science. 1971; 171: 303–306. https://doi.org/10.1126/science.171.3968.303.
[71] Siqueland ER, DeLucia CA. Visual reinforcement of nonnutritive sucking in human infants. Science. 1969; 165: 1144–1146. https://doi.org/10.1126/science.165.3898.1144.
[72] Sameroff AJ. An apparatus for recording sucking and controlling feeding in the first days of life. Psychonomic Science. 1965; 2: 355–356.
[73] DeCasper AJ, Fifer WP. Of human bonding: newborns prefer their mothers' voices. Science. 1980; 208: 1174–1176. https://doi.org/10.1126/science.7375928.
[74] DeCasper AJ, Spence MJ. Prenatal maternal speech influences newborns' perception of speech sounds. Infant Behavior and Development. 1986; 9: 133–150.
[75] Moon C. Prenatal Experience with the Maternal Voice. In Filippa, M., Kuhn, P., Westrup, B. (eds.) Early Vocal Contact and Preterm Infant Brain Development (pp. 27–45). Springer: Cham. 2017. https://doi.org/10.1007/978-3-319-65077-7_2.
[76] Kumar N, Kamath S, Kumar G, Vaishali K, Sinha MK, Amin R, *et al*. Prenatal Learning and Memory: Review on the Impact of Exposure. Current Pediatric Reviews. 2023; 19: 108–120. https://doi.org/10.2174/1573396318666220601160537.
[77] Krueger C, Garvan C. Emergence and retention of learning in early fetal development. Infant Behavior & Development. 2014; 37: 162–173. https://doi.org/10.1016/j.infbeh.2013.12.007.
[78] Kelso JAS, Fuchs A. The coordination dynamics of mobile conjugate reinforcement. Biological Cybernetics. 2016; 110: 41–53. https://doi.org/10.1007/s00422-015-0676-0.
[79] Angulo-Kinzler RM. Exploration and selection of intralimb coordination patterns in 3-month-old infants. Journal of Motor Behavior. 2001; 33: 363–376. https://doi.org/10.1080/00222890109601920.
[80] Angulo-Kinzler RM, Ulrich B, Thelen E. Three-month-old infants can select specific leg motor solutions. Motor Control. 2002; 6: 52–68. https://doi.org/10.1123/mcj.6.1.52.
[81] Taddio A, Katz J, Ilersich AL, Koren G. Effect of neonatal circumcision on pain response during subsequent routine vaccination. Lancet. 1997; 349: 599–603. https://doi.org/10.1016/S0140-6736(96)10316-0.
[82] Rakic P, Bourgeois JP, Goldman-Rakic PS. Synaptic development of the cerebral cortex: implications for learning, memory, and mental illness. Progress in Brain Research. 1994; 102: 227–243. https://doi.org/10.1016/S0079-6123(08)60543-9.
[83] Lohmann C, Kessels HW. The developmental stages of synaptic plasticity. The Journal of Physiology. 2014; 592: 13–31. https://doi.org/10.1113/jphysiol.2012.235119.
[84] Bruce D, Wilcox-O'Hearn LA, Robinson JA, Phillips-Grant K, Francis L, Smith MC. Fragment memories mark the end of childhood amnesia. Memory & Cognition. 2005; 33: 567–576. https://doi.org/10.3758/bf03195324.
[85] Hartley CA, Lee FS. Sensitive periods in affective development: nonlinear maturation of fear learning. Neuropsychopharmacology. 2015; 40: 50–60. https://doi.org/10.1038/npp.2014.179.
[86] Raznahan A, Shaw PW, Lerch JP, Clasen LS, Greenstein D, Berman R, *et al*. Longitudinal four-dimensional mapping of subcortical anatomy in human development. Proceedings of the National Academy of Sciences of the United States of America. 2014; 111: 1592–1597. https://doi.org/10.1073/pnas.1316911111.
[87] Lupien SJ, McEwen BS, Gunnar MR, Heim C. Effects of stress throughout the lifespan on the brain, behaviour and cognition. Nature Reviews. Neuroscience. 2009; 10: 434–445. https://doi.org/10.1038/nrn2639.