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CLINICAL NEUROSCIENCE OF ADDICTION: NEUROBIOLOGICAL DISRUPTIONS AND TRANSLATIONAL MODELS OF SOCIAL DYSFUNCTION

NEUROCIENCIA CLÍNICA DE LA ADICCIÓN: DISRUPCIONES NEUROBIOLÓGICAS Y MODELOS TRASLACIONALES DE DISFUNCIÓN SOCIAL

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Clinical Neuroscience of Addiction: Neurobiological Disruptions and Translational Models of Social Dysfunction

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ABSTRACT

Background: A comprehensive understanding of the neurobiological substrates that modulate social behavior is essential for identifying etiologies and proposing effective approaches to social dysfunction and addiction. Rather than relying on speculative or metaphysical premises, this framework is based on measurable neurological alterations resulting from chronic environmental stress and early relational deficits. These conditions may lead to maladaptive engrammatic patterns and dysregulated neurocircuitry, with direct implications for the emergence of compulsive behaviors. **Aims:** This study aims to propose a conceptual refinement in the field of clinical neuroscience, with emphasis on the integration of addiction medicine within a neuroevolutionary and precision-based model. **Methods:** The methodological approach combines descriptive observational analysis with a neuroethological perspective, incorporating data from peer-reviewed literature in behavioral neuroscience and neuroimaging studies (fMRI), focused on the identification of patterns consistent with dysregulation in dopaminergic and prefrontal-limbic pathways. **Conclusion:** Based on consistent neuroscientific parameters, we delineate a structured framework to interpret addiction-related phenomena, introducing a neurobiologically grounded model that contributes to clinical and theoretical advancement in the understanding of addictive behaviors.

Keywords: addiction, neurocircuitry, social behavior, dopaminergic pathways, neuroevolutionary model

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Neurociencia Clínica de la Adicción: Disrupciones Neurobiológicas y Modelos Traslacionales de Disfunción Social

RESUMEN

Antecedentes: Una comprensión integral de los sustratos neurobiológicos que modulan el comportamiento social es esencial para identificar las etiologías y proponer enfoques efectivos frente a la disfunción social y la adicción. En lugar de basarse en premisas especulativas o metafísicas, este marco se fundamenta en alteraciones neurológicas medibles, producto del estrés ambiental crónico y de déficits relacionales tempranos. Estas condiciones pueden conducir a patrones engramáticos desadaptativos y a una neurocircuitería disfuncional, con implicaciones directas en la aparición de conductas compulsivas. Objetivos: Este estudio busca proponer un refinamiento conceptual en el campo de la neurociencia clínica, con énfasis en la integración de la medicina de la adicción dentro de un modelo neuroevolutivo y basado en la precisión. Métodos: El enfoque metodológico combina un análisis observacional descriptivo con una perspectiva neuroetológica, incorporando datos de literatura científica revisada por pares en neurociencia del comportamiento y estudios de neuroimagen (fMRI), centrados en la identificación de patrones consistentes con la desregulación de las vías dopaminérgicas y prefronto-límbicas.Conclusión: Basándonos en parámetros neurocientíficos consistentes, delineamos un marco estructurado para interpretar fenómenos relacionados con la adicción, introduciendo un modelo con base neurobiológica que contribuye al avance clínico y teórico en la comprensión de las conductas adictivas.

Palabras clave: adicción, neurocircuitería, comportamiento social, vías dopaminérgicas, modelo neuroevolutivo

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INTRODUCTION

According to the American Society of Addiction Medicine (ASAM), addiction is defined as "a chronic, treatable medical disease that involves complex interactions among brain circuits, genetics, environment, and an individual's life experiences. People with substance use addiction engage in compulsive behaviors and often continue despite harmful consequences"[1]. This classification aligns with the neurobiological frameworks that currently inform evidence-based approaches to addiction treatment.

Recent neurobiological advances, supported by molecular tracing techniques such as Arc-driven mGRASP, in conjunction with behavioral neuroscience and functional neuroimaging methods, have contributed to a broader understanding of synaptic connectivity and memory-related processes in addiction. These findings allow for the refinement of clinical constructs in addiction medicine, with a focus on measurable maladaptive neural configurations rather than speculative multidimensional models[2].

Empirical data continue to demonstrate that exposure to early life stressors and emotionally adverse conditions increases the risk for multiple psychopathologies, including substance use disorders (SUDs). Computational models of memory engrams reveal that overlapping neural circuits may sustain pathological associations in response to such experiences. These patterns can persist into adulthood and influence the development of comorbid conditions such as post-traumatic stress disorder and affective dysregulation[3].

In the context of clinical research and decision-making, the investigation of addiction-related phenomena requires precision in interpretation and methodological restraint. The presence of interpretative errors due to attentional network dysfunctions has been documented in studies examining the relationship between structural damage and functional outcomes, suggesting the need for a cautious and evidence-based analysis of neurocognitive data[4].

The accurate identification of etiologies and therapeutic targets for social behavior dysfunctions depends on the recognition of specific neurological correlates. These include dysfunctional network patterns and altered connectivity signatures that typically emerge under sustained environmental stress or lack of affective stimulation. These neurological anomalies have been observed in clinical presentations

involving visual-spatial processing impairments and attention deficits, reinforcing the argument that social deficits in addiction may be rooted in identifiable cerebral alterations[5].

Clinical neuroscience provides a valid pathway for integrating these observations into a structured model of precision medicine. Evidence from white matter disconnection studies supports the premise that disruptions in connectivity, rather than isolated gray matter lesions, play a central role in syndromes affecting awareness and executive function. This conceptual shift informs the understanding of addiction not as a singular behavioral manifestation but as a complex, network-level dysfunction[6].

Primary Neuro Determinism

The interaction between familial psychosocial dynamics and genetic-epigenetic influences contributes to the development of identifiable personality traits rooted in specific neurobiological dysfunctions. This configuration, involving eight commonly observed clinical neurodysfunctions (CNDs), appears to precede socioeconomic and educational variables in its impact on the early formation of emotional and behavioral regulation patterns[6].

These dysfunctions, when acting in interpersonal contexts, particularly within early relational environments, may give rise to maladaptive behavioral responses characterized as neurodysfunctional interpersonal relationships (RINs). The observed microstructural personality elements are primarily oriented toward affective survival in both internal and social domains, particularly under emotionally inconsistent conditions[7].

Such dysfunctional interpersonal patterns within family systems have been associated with increased resistance to treatment and a higher risk of relapse in individuals with substance use disorders and other behavioral addictions. These phenomena are understood to arise from neurobiological triggers, involuntary emotional unavailability, and impairments in volitional control and agency across members of the relational group (8).

Within this framework, it becomes necessary to consider clinical approaches that target family-level dynamics. Specifically, strategies incorporating the understanding of Family Coping processes and Family Schema configurations—both of which are grounded in neurobiological and psychological structures—may enhance intervention outcomes by addressing the emotional survival systems that sustain maladaptive cycles (8).

The set of ONCs (Observed Neuroclinical Conditions) refers to a cluster of behavioral tendencies formed through early affective interaction. These configurations are partially dependent on neurobiological substrates and are linked to a spectrum of psychological phenomena, including internalizing and externalizing temperaments, personality traits, affective dysregulation, and mechanisms of stress response (9).

According to current literature, the ONCs involve the following clinical and neurobiological features (10):

1. Neurological Deficit of Family Synchrony (DNSF),
2. Maladaptive amygdalar-limbic modulation related to family schemas,
3. Hormonal and immune-inflammatory dysregulation,
4. Dysfunctions in neuropsychodynamic feedback and mirror systems within family interactions,
5. Dysregulation of the dopaminergic reward system and dopamine homeostasis,
6. Neural network impairments involving emotional engrams and deficits in both primary and higher-order cognitive processing (associated with the conceptual framework of Neuroschematic Survival Syndrome),
7. Secondary simultanagnosia and executive cognitive limitations (1),
8. Dissociative neuroadaptive disorders of consciousness.

Specific manifestations within this framework include:

- Secondary Simultanagnosia: a visual-perceptual limitation preventing the simultaneous recognition of multiple elements within the visual field (1);
- Secondary Alexithymia: reduced access to internal affective states, impairing emotional self-awareness;
- Secondary Anosognosia: inability to accurately infer or recognize others' affective states;
- Anosodiaphoria: attenuated concern or awareness regarding one's health status, often accompanied by affective indifference.

These dysfunctions, collectively representing a survival-based emotional personality architecture, reflect a form of maladaptive habituation embedded in disrupted neurocognitive circuits. The resulting

engrammatic structures function as stable, but dysfunctional, neural patterns—also referred to as emotional engrams, neural signatures, or maladaptive cognitive schemas (11).

Neurobiopsychosocial Conditioning

Biopsychosocial conditioning within family environments involves the simultaneous activation of multiple cognitive-affective schemas over extended periods. These schemas are frequently reactivated by specific environmental or interpersonal cues originating within the family context (12). This process is associated with adaptive mechanisms for coping with chronic stressors, often involving abrupt amygdala hyperactivation. This hyperactivation leads to a restricted attentional field and decreased affective modulation, which in turn may contribute—implicitly and without deliberate intention—to patterns of emotional neglect (12).

Vygotsky's theoretical model distinguishes between elementary and higher psychological functions, offering a developmental framework for understanding cognitive complexity (13). Higher psychological functions encompass operations such as voluntary attention, intentional memorization, conceptual abstraction, symbolic thought, reasoning, imagination, goal-directed behavior, and language-mediated cognition. These functions are considered “higher” because they emerge through cultural mediation and are not reducible to reflexive or instinctual responses, which are more characteristic of elementary biological mechanisms shared with non-human species (13,14).

When biopsychosocial conditioning becomes neurofunctionally dysregulated, it reflects impairments in neurocognitive systems responsible for attentional anchoring, intersubjective perception, and emotional-cognitive integration. This includes deficits in neural connectivity associated with value-directed attentional capture (VDAC), reduced attention during interpersonal exchanges across verbal, nonverbal, and symbolic domains, and disruptions in the recognition of agency and intentionality (14–16).

Further dysfunctions encompass disturbances in motivation processes regulated by valence attribution, involuntary emotional responses such as alexithymia, deficits in visuospatial awareness like simultanagnosia, and limitations in recognizing internal or external states consistent with anosognosia. Memory systems—both episodic and schematic—are also implicated, contributing to the consolidation of maladaptive emotional engrams within these disrupted circuits (17–20).

These conditions are often subtle and difficult to detect in standard clinical assessments. However, their impact is significant, manifesting as micro-level distortions in awareness (micro-dissociations), cognitive-affective biases, and decision-making errors anchored in survival-oriented emotional frameworks. These processes undermine neurosemantic integration and contribute to persistent patterns of social dysfunction (21).

Engrams

An engram refers to a persistent and detectable physical or molecular alteration within a neural network, resulting from activity-dependent processes in specific neuronal populations. These changes occur in response to episodic stimuli and can be reactivated by partial or complete re-exposure to the original conditions, thereby enabling memory retrieval (22). Experimental evidence shows that repeated exposure to the same contextual stimulus leads to consistent activation of the same cell ensembles, commonly tracked through the expression of immediate early genes (IEGs) such as c-Fos, Arc, and the activity-regulated cytoskeleton-associated protein (22).

In the hippocampus, engram cells have been identified as forming synaptic connections with other neurons participating in the encoding of the same memory episode (22). These engram networks operate as coordinated assemblies of memory-encoding cells, and their reactivation is both necessary and sufficient for the conscious retrieval of stored experiences (22–27).

Furthermore, experimental models have demonstrated that artificial activation of engram circuits can produce memory distortions, including the generalization of fear to unrelated contexts or the induction of context-specific memories never actually experienced (22–27). Evidence from optogenetic studies, such as those conducted by Kitamura et al., indicates that engrams form simultaneously in the hippocampus and the medial prefrontal cortex (mPFC) during the initial phase of memory encoding, although mPFC engram cells remain inactive during recent memory retrieval and are classified as “silent engrams” (22–27).

The relatively low degree of overlap between neuronal populations activated during memory acquisition and later recall—typically between 10 and 40 percent—suggests a dynamic restructuring of engrams throughout the memory consolidation process. This reorganization reflects the capacity of neural

networks to adapt their composition to optimize selectivity and behavioral relevance of stored information (22–27).

Competition among neurons within a brain region for inclusion in an engram is modulated by neuronal excitability. Cells with higher excitability levels have an increased probability of being recruited into the memory trace, influencing the spatial and functional configuration of the engram ensemble (28–30). Structural plasticity in engram cells includes increased synaptic strength and dendritic spine density, along with preferential downstream connectivity to other engram-encoded neurons, even during resting or offline states (28–30).

Advances in molecular neuroscience have enabled selective manipulation of these cell populations using promoter-specific gene expression strategies, allowing for precise targeting of engram-related processes at the cellular and circuit levels. These methodologies incorporate constitutively active proteins or activity-inducible genetic markers to isolate and characterize engram cell subtypes (28–30).

Conceptual Memory

The encoding and retrieval of memory are mediated by specific subpopulations of neurons, referred to as cellular engrams. In the human brain, memory formation frequently involves the association of semantically or perceptually related concepts, a process supported by distributed yet selective neural assemblies (31–33).

According to the Hebbian learning principle, synaptic connections between neurons exhibiting temporally correlated activity are progressively strengthened, whereas those between neurons with weakly correlated activity tend to undergo synaptic depression or elimination. This process enhances the probability that the neural activation pattern present during encoding will be reactivated during subsequent retrieval, establishing a synaptic engram as a memory substrate within coactive neuronal ensembles (31–33).

In the human medial temporal lobe (MTL), individual neurons referred to as “concept cells” exhibit invariant responses to representations of specific persons, places, or abstract elements. These neurons selectively increase their firing rates upon exposure to stimuli associated with a particular conceptual domain (34–37). The activity of a concept cell reflects the encoding of a discrete representational unit, suggesting that each concept is represented by a distinct and distributed subset of neurons. When a

stimulus is presented, the coactivation of γN neurons defines the engram of a single concept, while the overlap between two unrelated concepts is estimated as $\gamma^2 N$, where N denotes the total number of neurons in the relevant cortical region (34–37).

Experimental data confirm that individual neurons can become responsive to newly learned associations, particularly when two concepts are presented in paired configurations. In such cases, the proportion of shared neurons increases from less than one percent for unrelated concepts to approximately four to five percent for concept pairs that have undergone associative learning, supporting the hypothesis that neuron sharing facilitates cognitive integration and memory binding (38–39).

Theoretical models such as those proposed by Romani and Tsodyks demonstrate that memory engrams maintain structural independence from network size constraints. Nonetheless, they allow for statistically significant overlap between certain engram pairs, enabling sequential activation under conditions of oscillatory or periodic background input. This mechanism may underlie the neurobiological basis for concept sequencing and inferential reasoning (40–43).

Persistent structural connectivity has also been observed in animal models. Long-term potentiation of Arc-expressing neurons between hippocampal subfields such as dCA3 and CA1 has been demonstrated following continuous learning, confirming the stability and traceability of functional engrams in vivo. These findings contribute to the clinical characterization and potential targeting of memory circuits (40–43).

Neurodysfunctional Family Interpersonal Relationships

The quality of early family interactions plays a central role in child development, attachment formation, and mental health outcomes. Several studies have established the correlation between caregiver responsiveness and neuropsychological maturation in the child (45–47). Exposure to childhood adversity, including chronic stress and parental depression, has been shown to affect the dynamics of the mother-father-child triad, disrupting interactional quality and emotional attunement within the family system (45–47).

Triadic synchrony—defined as temporally coordinated behaviors involving physical proximity, affectionate contact, and mutual gaze between both parents and their infant—has been associated with

parental oxytocin levels. These synchronous interactions contribute to the formation of secure relational patterns during early development (45–47).

Oxytocin has emerged as a key modulator of social behavior, implicated in mechanisms underlying trust, empathy, affiliation, and the regulation of interpersonal interactions, particularly in parent–child bonding. Behavioral studies suggest that parental sensitivity correlates positively with endogenous oxytocin production, reinforcing its role in shaping attachment-specific behaviors (48,49).

Evidence also supports the intergenerational transmission of stress-related vulnerabilities. Parents with histories of adverse childhood experiences (ACEs) often display increased levels of depressive symptoms, which in turn compromise their responsiveness to their children. This reduced sensitivity affects both dyadic and triadic interactions within the family, contributing to less effective emotional regulation and behavioral involvement in children (48,49).

Maternal and paternal sensitivity appear to be mutually reinforcing. Higher sensitivity in parent–child dyads is associated with more adaptive triadic coordination, enhancing the child's capacity for emotional regulation and relational engagement. Conversely, reduced synchrony correlates with the emergence of internalizing symptoms in children, particularly in contexts where parental mental health is compromised (48,49).

Notably, improvement in children's psychological outcomes has been observed when maternal depressive symptoms are alleviated. However, this effect is not uniform across cases. In families where mothers report histories of early trauma—such as emotional abuse, sexual abuse, or physical neglect—traditional interventions may have limited efficacy. In these contexts, maladaptive parenting strategies, including lower acceptance and increased psychological control, tend to persist independently of perinatal factors (48,49).

These findings underscore the necessity of early, targeted interventions that address both the psychological health of the parent and the relational mechanisms that mediate parent–child interaction. Enhancing positive parenting behaviors through structured, neurobehavioral frameworks may contribute to improved developmental trajectories in at-risk offspring (48,49).

Intrusive Neurodysfunctional Interpersonal Relationships

The concept of alienation encompasses multiple dimensions in interpersonal dynamics and is frequently observed in family systems. Functionally, it is characterized by bidirectional influence. One individual may encroach upon the rights or autonomy of another through overt or covert behaviors, often driven by affective control mechanisms, behavioral regulation, volitional imposition, and financial self-interest. These behavioral patterns, commonly associated with parental affective neglect and authoritarianism, manifest within a relational context where the alienator exhibits dominance and the alienated assumes a submissive role (50).

Such intrusive interactions are often subtle and normalized within dysfunctional environments. They are maintained by maladaptive conditioning mechanisms that serve momentary relief functions, frequently co-occurring with other interpersonal strategies that obscure their pathological nature (50). These behaviors typically originate during early developmental stages and reflect alterations in familial role expectations. These may involve role inversion, hyper-authoritarianism, or deficits in caregiving due to emotional absence or neglect (51–52).

Violations of relational boundaries and personal autonomy are consistent with maladaptive expressions of selfishness. These are hypothesized to emerge from involuntary neuroadaptive patterns linked to neurodevelopmental emotional dysfunctions (NDE) or ONCs. In this context, the punitive or aversive nature of the behavior is tied to a diminished perception of relational responsibility (51–52).

Individuals exhibiting these traits may present selective deficits in affective processing, despite retaining functional cognitive capacity in survival-oriented domains. This dissociation is reflected in reduced flexibility of thought, impaired conceptual reasoning, and compromised social-affective functioning. Symptomatically, such profiles may resemble traits observed in pervasive developmental conditions, including restricted empathy, underdeveloped communication, diminished resilience, and a narrow range of social interests (51–52).

Neurobiological evidence suggests that affiliative bonds—mediated by systems such as oxytocin—can rapidly shift from attraction to aversion. Feldman and colleagues have demonstrated that the same neural substrates implicated in attachment and empathy also contribute to antagonistic emotional responses.

These systems, initially structured within the maternal-infant bond, are later adapted for broader social functioning and group cohesion among mammals (51–52).

The concept of the affiliative brain, as defined in these studies, has been associated with vulnerabilities to specific psychopathologies, including dissocial personality disorder, borderline personality disorder, and subtypes with sociopathic or psychopathic features (53–54). Trajectories leading to antisocial behavior include disorganized attachment, early life maltreatment, parental rejection, negative attribution of others' mental states (low mentalization), verbal deficits, impulsivity, and increased peer affiliation with antisocial individuals (53–54).

A key factor in the emergence of these dysfunctions is the absence of sensitive parental responsiveness, also known as mentalism. This refers to the caregiver's inability to detect and appropriately respond to the child's affective and developmental cues. Intrusive parenting behaviors, which involve disregarding the child's autonomy and imposing adult-centric priorities, reflect a disruption in the neural substrates responsible for family synchrony (53–54).

Intrusive parental conduct is characterized by a pattern of adult-centered interactions, in which parents assert control over tasks that the child is developmentally capable of handling independently. This behavior suppresses autonomy, disregards the child's emotional feedback, and often reflects an immaturity in caregiving capacity (55). Consequences of such patterns include restricted emotional exploration, inhibition of independent coping skills, and heightened physiological arousal in the child. These responses interfere with emotional regulation, particularly the ability to manage fear and perceptions of safety (55).

As a result, parental intrusiveness is considered a significant risk factor for altered neurodevelopment in socioemotional domains. It may result in persistent neurobiological alterations and sequelae that compromise healthy psychological maturation (56).

Secondary Neuro Determinism

Secondary Neuro Determinism (SND) refers to unconscious and involuntary stress-response mechanisms primarily oriented toward emotional survival, often manifesting as adaptive strategies within physical, economic, or relational contexts. These responses are frequently observed in both

family systems and occupational environments, where behavioral patterns emerge as coping mechanisms under chronic stress exposure (57).

In this state of neuroactivation, individuals often remain unaware of the presence of secondary emotional gains, particularly those mediated by dysfunctional relational dynamics within neurodysfunctional interpersonal relationships (RINs). Behaviors such as compulsive routines or dopaminergic reinforcement cycles may arise as attempts to manage psychosocial stress. However, these behaviors also paradoxically induce instability and reinforce maladaptive affect regulation strategies (57).

Both primary and secondary survival-based neurodeterminisms may operate concurrently, giving rise to observable behavioral deviations such as exaggerated self-importance or maladaptive conduct in professional contexts (58).

Coping and Addiction

Behaviors initiated as stress-coping strategies may, under certain conditions, evolve into habitual patterns. When these behaviors serve dual functions—both alleviating aversive emotional states and activating reward circuitry—the risk of transition into addiction increases, particularly in the presence of genetic predispositions or highly pleasurable reinforcement cycles (59).

Addiction is clinically characterized by a neuropsychological dependency on the coping behavior, evidenced by the inability to cease the behavior despite genuine attempts and preserved motivation to change (59). Across different forms of addiction, individuals commonly experience deficits in judgment, reduced predictive awareness, and impaired self-referential processing (59).

Functional neuroimaging studies have shown evidence of abrupt, automatic activations within the amygdala, which operate as neurobiological triggers for mesolimbic reward pathways. These findings support the hypothesis that maladaptive coping behaviors are reinforced through dysregulated connectivity between affective and dopaminergic systems (59). Despite this evidence, no comprehensive synthesis of mediating or moderating factors has been established to inform structured prevention or treatment programs for substance use disorders (SUDs) (59).

Most existing studies focus on isolated moderators or mediators within individual levels of the socioecological framework, which limits the understanding of multifactorial contributors to behavioral pathology. A broader, integrative model could guide more conscious and effective clinical interventions

(59). Furthermore, variations in exposure, individual response patterns, and access to services significantly influence clinical outcomes and should be included in evaluative frameworks (59).

Although some meta-analyses have attempted to address contextual factors in relational environments, results have not demonstrated sufficient robustness. This suggests the need for evaluators to adopt a critical and motivated stance, regardless of clinical specialization, to facilitate meaningful behavioral change (60).

In several cases, behaviors such as problem gambling may not conform strictly to addiction models but instead reflect maladaptive coping strategies developed to manage unmet emotional needs. Dysregulated coping and internet addiction are not mutually exclusive; rather, dysfunctional coping can act as a predictor of addictive behaviors. This positions certain maladaptive behaviors as forms of psychological self-medication (60).

The dopaminergic midbrain, particularly the substantia nigra and ventral tegmental area (SN/VTA), plays a central role in processing reward stimuli (60). This region is also sensitive to novelty, indicating shared mechanisms between novelty detection and reward processing. The hippocampus, which is implicated in encoding novel experiences, exhibits anticipatory responses distinct from those of the SN/VTA when processing expected versus unexpected novelty (61).

Memory recall is significantly enhanced for anticipated novel stimuli when compared to those that are unexpected, suggesting differential encoding and consolidation pathways (62). These differences are reflected in functional connectivity profiles of SN/VTA regions during reward prediction tasks (63). Specifically, stimuli predictive of reward that are novel enhance the functional connectivity between medial SN/VTA and mesolimbic targets, including the nucleus accumbens, hippocampus, and primary visual cortex (64).

This connectivity likely enables the integration of novelty and reward signals, contributing to the modulation of memory processes associated with emotionally salient or motivationally relevant events. The medial SN/VTA may act either as a convergence point for novelty-reward interactions or as a modulatory hub for memory encoding related to reward-predictive novelty (65).

METHODS

The methodological design adopted in this study was descriptive and observational, with field-based ethnographic components. This was integrated with an extensive literature review focused on behavioral neurobiology in both human and animal models. The selected studies were primarily based on analyses using functional magnetic resonance imaging (fMRI) and were retrieved from indexed databases such as PubMed and Web of Science. Article inclusion followed a contextual analysis protocol to ensure relevance and alignment with the neurobiological framework under investigation.

DISCUSSION

The application of a pragmatic research paradigm reflects a methodological alignment with the need to address complex, real-world phenomena through empirical inquiry. This approach prioritizes functional solutions to social and clinical problems, emphasizing translational potential. In the context of addiction medicine, the integration of experiential data with structured observational protocols aligns with pragmatic epistemology, which posits that meaning is derived from lived experience and is essential for constructing applicable knowledge.

This study presents a comprehensive model within the domain of precision medicine that offers a structured, evidence-informed framework for clinical decision-making in addiction. The methodology enabled the identification of functional patterns and clinical categories relevant to complex, uncontrolled behavioral disorders.

Mixed methods research continues to be adopted in healthcare sciences, where pragmatism serves not only as a philosophical foundation but also as a practical strategy for integrating patient-oriented perspectives and empirical rigor. The synergy between methodological pluralism and stakeholder engagement enhances both the depth and applicability of health-related research outcomes (66–67).

CONCLUSION

Based on descriptive observational field research, a novel conceptual and clinical model was identified. This model contributes to the understanding of addiction as a multifactorial condition and opens new investigative pathways by offering a resolution-oriented framework for intervention.

Declaration of Conflicts of Interest

The authors declare no conflicts of interest relevant to the content or execution of this study.

BIBLIOGRAPHIC REFERENCES

1. Kampman K, Jarvis M. American Society of Addiction Medicine (ASAM) National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use. J Addict Med. 2015 Sep-Oct;9(5):358-67. doi: 10.1097/ADM.0000000000000166. PMID: 26406300; PMCID: PMC4605275.
2. Murthy BKB, Somatakis S, Ulivi AF, Klimmt H, Castello-Waldow TP, Haynes N, Huettl RE, Chen A, Attardo A. Arc-driven mGRASP highlights CA1 to CA3 synaptic engrams. Front Behav Neurosci. 2023 Jan 30;16:1072571. doi: 10.3389/fnbeh.2022.1072571. PMID: 36793796; PMCID: PMC9924068.
3. Gastaldi C, Schwalger T, De Falco E, Quiroga RQ, Gerstner W. When shared concept cells support associations: Theory of overlapping memory engrams. PLoS Comput Biol. 2021 Dec 30;17(12):e1009691. doi: 10.1371/journal.pcbi.1009691. PMID: 34968383; PMCID: PMC8754331.
4. Ptak R, Schnider A. The attention network of the human brain: relating structural damage associated with spatial neglect to functional imaging correlates of spatial attention. Neuropsychologia. 2011 Sep;49(11):3063-70. doi: 10.1016/j.neuropsychologia.2011.07.008. Epub 2011 Jul 19. PMID: 21787795.
5. Cui Y, Liu Y, Yang C, Cui C, Jing D, Zhang X, Chen Y, Li B, Liang Z, Chen K, Zhang Z, Wu L. Brain structural and functional anomalies associated with simultanagnosia in patients with posterior cortical atrophy. Brain Imaging Behav. 2022 Jun;16(3):1148-1162. doi: 10.1007/s11682-021-00568-8. Epub 2021 Nov 17. PMID: 34787788; PMCID: PMC9107404.
6. Doricchi F, Thiebaut de Schotten M, Tomaiuolo F, Bartolomeo P. White matter (dis)connections and gray matter (dys)functions in visual neglect: gaining insights into the brain networks of spatial awareness. Cortex. 2008 Sep;44(8):983-95. doi: 10.1016/j.cortex.2008.03.006. Epub 2008 May 23. PMID: 18603235.
7. Price CJ, Weng HY. Facilitating Adaptive Emotion Processing and Somatic Reappraisal *via* Sustained Mindful Interoceptive Attention. Front Psychol. 2021 Sep 8;12:578827. doi: 10.3389/fpsyg.2021.578827. PMID: 34566738; PMCID: PMC8457046.

8. Price CJ, Thompson EA, Crowell S, Pike K. Longitudinal effects of interoceptive awareness training through mindful awareness in body-oriented therapy (MABT) as an adjunct to women's substance use disorder treatment: A randomized controlled trial. Drug Alcohol Depend. 2019 May 1;198:140-149. doi: 10.1016/j.drugalcdep.2019.02.012. Epub 2019 Mar 23. PMID: 30928884; PMCID: PMC6467707.

9. Umarova RM, Saur D, Kaller CP, Vry MS, Glauche V, Mader I, Hennig J, Weiller C. Acute visual neglect and extinction: distinct functional state of the visuospatial attention system. Brain. 2011 Nov;134(Pt 11):3310-25. doi: 10.1093/brain/awr220. Epub 2011 Sep 23. PMID: 21948940.

10. Chechlacz M, Rotshtein P, Hansen PC, Riddoch JM, Deb S, Humphreys GW. The neural underpinings of simultanagnosia: disconnecting the visuospatial attention network. J Cogn Neurosci. 2012 Mar;24(3):718-35. doi: 10.1162/jocn_a_00159. Epub 2011 Nov 8. PMID: 22066584.

11. May AC, Davis C, Kirlic N, Stewart JL. Mindfulness-Based Interventions for the Treatment of Aberrant Interoceptive Processing in Substance Use Disorders. Brain Sci. 2022 Feb 17;12(2):279. doi: 10.3390/brainsci12020279. PMID: 35204042; PMCID: PMC8870441.

12. Price CJ, Hooven C. Interoceptive Awareness Skills for Emotion Regulation: Theory and Approach of Mindful Awareness in Body-Oriented Therapy (MABT). Front Psychol. 2018 May 28;9:798. doi: 10.3389/fpsyg.2018.00798. PMID: 29892247; PMCID: PMC5985305.

13. Duquette P, Ainley V. Working With the Predictable Life of Patients: The Importance of "Mentalizing Interoception" to Meaningful Change in Psychotherapy. Front Psychol. 2019 Sep 26;10:2173. doi: 10.3389/fpsyg.2019.02173. PMID: 31607993; PMCID: PMC6774393.

14. Dębska A, Wójcik M, Chyl K, Dzięgiel-Fivet G, Jednoróg K. Beyond the Visual Word Form Area - a cognitive characterization of the left ventral occipitotemporal cortex. Front Hum Neurosci. 2023 Jul 28;17:1199366. doi: 10.3389/fnhum.2023.1199366. PMID: 37576470; PMCID: PMC10416454.

15. Darby, RR, Edersheim, J., & Price, BH (2016). O que pacientes com demência frontotemporal de variante comportamental podem nos ensinar sobre responsabilidade moral. *AJOB Neuroscience* , *7* (4), 193-201.

16. Skipper JI. Uma voz sem boca não mais: A neurobiologia da linguagem e da consciência. NeurosciBiobehav Rev. 2022 Sep;140:104772. doi: 10.1016/j.neubiorev.2022.104772. Epub 2022 Jul 11. PMID: 35835286.

17. Herman AM. Interoception Within the Context of Impulsivity and Addiction. Curr Addict Rep. 2023;10(2):97-106. doi: 10.1007/s40429-023-00482-7. Epub 2023 Apr 29. PMID: 37266189; PMCID: PMC10148627.

18. Karim AKMR, Proulx MJ, de Sousa AA, Likova LT. Do we enjoy what we sense and perceive? A dissociation between aesthetic appreciation and basic perception of environmental objects or events. Cogn Affect Behav Neurosci. 2022 Oct;22(5):904-951. doi: 10.3758/s13415-022-01004-0. Epub 2022 May 19. PMID: 35589909; PMCID: PMC10159614.

19. Akyüz N, Marien H, Stok FM, Driessen JMA, de Wit J, Aarts H. Obedience induces agentic shifts by increasing the perceived time between own action and results. Sci Rep. 2024 Jul 22;14(1):16769. doi: 10.1038/s41598-024-66499-8. PMID: 39039144; PMCID: PMC11263708.

20. Rho HJ, Kim JH, Lee SH. Function of Selective Neuromodulatory Projections in the Mammalian Cerebral Cortex: Comparison Between Cholinergic and Noradrenergic Systems. Front Neural Circuits. 2018 Jun 22;12:47. doi: 10.3389/fncir.2018.00047. PMID: 29988373; PMCID: PMC6023998.

21. Schmahmann JD, Smith EE, Eichler FS, Filley CM. Cerebral white matter: neuroanatomy, clinical neurology, and neurobehavioral correlates. Ann N Y Acad Sci. 2008 Oct;1142:266-309. doi: 10.1196/annals.1444.017. PMID: 18990132; PMCID: PMC3753195.

22. Septien S, Rubin MA. Transtornos da Consciência: Questões Éticas de Diagnóstico, Tratamento e Prognóstico. SeminNeurol. 2018 Out;38(5):548-554. doi: 10.1055/s-0038-1667384. Epub 2018 15 de outubro. PMID: 30321893.

23. Graham M, Doherty CP, Naci L. Usando a Neuroimagem para Detectar Consciência Encoberta e Determinar o Prognóstico de Pacientes em Coma: Informando os Tomadores de Decisão Substitutos sobre os Resultados Individuais dos Pacientes. SeminNeurol. 2018 Out;38(5):555-560. doi: 10.1055/s-0038-1667385. Epub 2018 15 de outubro. PMID: 30321894.

24. Padmala S, Sambuco N, Pessoa L. Interactions between reward motivation and emotional processing. Prog Brain Res. 2019;247:1-21. doi: 10.1016/bs.pbr.2019.03.023. Epub 2019 Apr 17. PMID: 31196430.

25. Graham M, Wallace E, Doherty C, McCann A, Naci L. Da Consciência ao Prognóstico: Implicações Éticas de Descobrir Consciência Oculta em Pacientes Comportamentalmente Não Respondentes. Ética em Saúde Camb Q. 2019 Oct;28(4):616-631. doi: 10.1017/S0963180119000550. PMID: 31526429.

26. Di Perri C, Bahri MA, Amico E, Thibaut A, Heine L, Antonopoulos G, Charland-Verville V, Wannez S, Gomez F, Hustinx R, Tshibanda L, Demertzi A, Soddu A, Laureys S. Correlativos neurais de consciência em pacientes que emergiram de um estado minimamente consciente: um estudo de imagem multimodal transversal. Lancet Neurol. 2016 Jul;15(8):830-842. doi: 10.1016/S1474-4422(16)00111-3. Epub 2016 27 de abril. PMID: 27131917.

27. Calabrò RS, Bramanti P, Naro A. Rumo a novos métodos de diagnóstico em distúrbios de consciência. Lancet Neurol. 2016 Out;15(11):1114-5. doi: 10.1016/S1474-4422(16)30202-2. PMID: 27647635.

28. McFadyen J, Mattingley JB, Garrido MI. An afferent white matter pathway from the pulvinar to the amygdala facilitates fear recognition. Elife. 2019 Jan 16;8:e40766. doi: 10.7554/eLife.40766. PMID: 30648533; PMCID: PMC6335057.

29. Throuvala MA, Pontes HM, Tsaousis I, Griffiths MD, Rennoldson M, Kuss DJ. Exploring the Dimensions of Smartphone Distraction: Development, Validation, Measurement Invariance, and Latent Mean Differences of the Smartphone Distraction Scale (SDS). Front Psychiatry. 2021 Mar 8;12:642634. doi: 10.3389/fpsyt.2021.642634. PMID: 33762981; PMCID: PMC7982468.

30. Anderson ED, Barbey AK. Investigating cognitive neuroscience theories of human intelligence: A connectome-based predictive modeling approach. Hum Brain Mapp. 2023 Mar;44(4):1647-1665. doi: 10.1002/hbm.26164. Epub 2022 Dec 20. PMID: 36537816; PMCID: PMC9921238.

31. Di Perri C, Thibaut A, Heine L, Annen J, Laureys S. Rumo a novos métodos de diagnóstico em transtornos de consciência - Resposta dos autores. Lancet Neurol. 2016 Oct;15(11):1115-6. doi: 10.1016/S1474-4422(16)30205-8. PMID: 27647636.

32. Jox RJ, Bernat JL, Laureys S, Racine E. Distúrbios da consciência: estamos prontos para uma mudança de paradigma? - resposta dos autores. Lancet Neurol. 2013 Fev;12(2):132. doi: 10.1016/S1474-4422(12)70286-7. Epub 2012 21 de dezembro. PMID: 23260191.

33. Septien S, Rubin MA. Transtornos da Consciência: Questões Éticas de Diagnóstico, Tratamento e Prognóstico. SeminNeurol. 2018 Out;38(5):548-554. doi: 10.1055/s-0038-1667384. Epub 2018 15 de outubro. PMID: 30321893.

34. Shu J, Qiang Q, Yan Y, Wen Y, Ren Y, Wei W, Zhang L. Distinct Patterns of Brain Atrophy associated with Mild Behavioral Impairment in Cognitively Normal Elderly Adults. Int J Med Sci. 2021 Jun 11;18(13):2950-2956. doi: 10.7150/ijms.60810. PMID: 34220322; PMCID: PMC8241773.

35. Byram AC, Lee G, Owen AM, Ribary U, Stoessl AJ, Townson A, Illes J. Considerações Éticas e Clínicas na Interseção de Neuroimagem Funcional e Transtornos da Consciência. Ética em Saúde Camb Q. 2016 Oct;25(4):613-22. doi: 10.1017/S0963180116000347. PMID: 27634713.

36. Farisco M, Laureys S, Evers K. Externalização da consciência. Possibilidades científicas e implicações clínicas. Curr Top BehavNeurosci. 2015;19:205-22. doi: 10.1007/7854_2014_338. PMID: 25146416.

37. Dollberg DG, Hanetz-Gamliel K, Levy S. COVID-19, problemas de comportamento infantil e ansiedade e mentalização da mãe: um modelo de moderação mediada. CurrPsychol. 2021 Nov9:1-12. doi: 10.1007/s12144-021476-y. Epub antes da impressão. PMID: 34776719; PMCID: PMC8577641.

38. Dollberg DG, Hanetz-Gamliel K. Ligações de Mediação-Moderação Entre ECAs das Mães, Sintomas de Psicopatologia de Mães e Crianças e Mentalização Materna Durante a COVID-19.

Psiquiatria Frontal. 2022 Mar 17;13:837423. doi: 10.3389/fpsyt.2022.837423. PMID: 35370808; PMCID: PMC8968198.

39. Behrendt HF, Scharke W, Herpertz-Dahlmann B, Konrad K, Firk C. Como mãe, como criança? Determinantes maternos do desenvolvimento socioemocional precoce das crianças. Saúde Infantil J. 2019 Mar;40(2):234-247. doi: 10.1002/imhj.21765. Epub 2019 7 de fevereiro. PMID: 30731022.

40. Brazeau N, Reisz S, Jacobvitz D, George C. ENTENDENDO A CONEXÃO ENTRE O TRAUMA DO APEGO E A AUTOEFICÁCIA MATERNA EM MÃES DEPRIMIDAS. Saúde Infantil J. 2018 Jan;39(1):30-43. doi: 10.1002/imhj.21692. Epub 2017 27 de dezembro. PMID: 29281747; PMCID: PMC5814850.

41. Park M, Brain U, Grunau RE, Diamond A, Oberlander TF. As trajetórias da depressão materna desde a gravidez até 3 anos após o parto estão associadas ao comportamento das crianças e às funções executivas aos 3 e 6 anos. Arch

42. WomensMent Health. 2018 Jun;21(3):353-363. doi: 10.1007/s00737-017-0803-0. Epub 2018 16 de janeiro. PMID: 29340801.

43. Vaever MS, Pedersen IE, Smith-Nielsen J, Tharner A. A depressão pós-parto materna é um fator de risco para a variabilidade emocional infantil aos 4 meses. Saúde Infantil J. 2020 Jul;41(4):477-494. doi: 10.1002/imhj.21846. Epub 2020 14 de fevereiro PMID: 32057136.

44. Kingston D, Kehler H, Austin MP, Mughal MK, Wajid A, Vermeyden L, Benzies K, Brown S, Stuart S, Giallo R. Trajetórias de sintomas depressivos maternos durante a gravidez e os primeiros 12 meses pós-parto e comportamento de externalização e internalização infantil aos três anos. PLoS Um. 2018 Abr 13;13(4):e0195365. doi: 10.1371/journal.pone.0195365. PMID: 29652937; PMCID: PMC5898728.

45. Aoyagi SS, Tsuchiya KJ. A depressão pós-parto materna afeta os resultados de desenvolvimento das crianças? J ObstetGynaecol Res. 2019 Sep;45(9):1809-1820. doi: 10.1111/jog.14064. Epub 2019 18 de julho. PMID: 31321836.

46. Whittle S, Simmons JG, Hendriksma S, Vijayakumar N, Byrne ML, Dennison M, Allen NB. Maus-tratos na infância, psicopatologia e o desenvolvimento de sub-regiões hipocampais

durante a adolescência. Comportamento Cerebral. 2016 Nov 30;7(2):e00607. doi: 10.1002/brb3.607. PMID: 28239518; PMCID: PMC5318361.

47. Donges US, Suslow T. Alexitimia e processamento automático de estímulos emocionais: uma revisão sistemática. RevNeurosci. 2017 1 de abril;28(3):247-264. doi: 10.1515/revneuro-2016-0049. PMID: 28099136.

48. Mair RG, Miller RL, Wormwood BA, Francoeur MJ, Onos KD, Gibson BM. The neurobiology of thalamic amnesia: Contributions of medial thalamus and prefrontal cortex to delayed conditional discrimination. Neurosci Biobehav Rev. 2015 Jul;54:161-74. doi: 10.1016/j.neubiorev.2015.01.011. Epub 2015 Jan 20. PMID: 2561618

49. Phillips JM, Kambi NA, Redinbaugh MJ, Mohanta S, Saalmann YB. Disentangling the influences of multiple thalamic nuclei on prefrontal cortex and cognitive control. Neurosci Biobehav Rev. 2021 Sep;128:487-510. doi: 10.1016/j.neubiorev.2021.06.042. Epub 2021 Jun 30. PMID: 34216654; PMCID: PMC8393355..

50. Saalmann YB. Intralaminar and medial thalamic influence on cortical synchrony, information transmission and cognition. Front Syst Neurosci. 2014 May 9;8:83. doi: 10.3389/fnsys.2014.00083. PMID: 24847225; PMCID: PMC4023070.

51. Varela C, Moreira JVS, Kocaoglu B, Dura-Bernal S, Ahmad S. A mechanism for deviance detection and contextual routing in the thalamus: a review and theoretical proposal. Front Neurosci. 2024 Feb 29;18:1359180. doi: 10.3389/fnins.2024.1359180. PMID: 38486972; PMCID: PMC10938916.

52. Hallett M, Aybek S, Dworetzky BA, McWhirter L, Staab JP, Stone J. Functional neurological disorder: new subtypes and shared mechanisms. Lancet Neurol. 2022 Jun;21(6):537-550. doi: 10.1016/S1474-4422(21)00422-1. Epub 2022 Apr 14. Erratum in: Lancet Neurol. 2022 Jun;21(6):e6. doi: 10.1016/S1474-4422(22)00179-X. PMID: 35430029; PMCID: PMC9107510.

53. Wang J, Deng Y, Booth JR. Automatic semantic influence on early visual word recognition in the ventral occipito-temporal cortex. Neuropsychologia. 2019 Oct;133:107188. doi: 10.1016/j.neuropsychologia.2019.107188. Epub 2019 Sep 6. PMID: 31499046.

54. Oegema R, Barakat TS, Wilke M, Stouffs K, Amrom D, Aronica E, Bahi-Buisson N, Conti V, Fry AE, Geis T, Andres DG, Parrini E, Pogledic I, Said E, Soler D, Valor LM, Zaki MS, Mirzaa G, Dobyns WB, Reiner O, Guerrini R, Pilz DT, Hehr U, Leventer RJ, Jansen AC, Mancini GMS, Di Donato N. International consensus recommendations on the diagnostic work-up for malformations of cortical development. Nat Rev Neurol. 2020 Nov;16(11):618-635. doi: 10.1038/s41582-020-0395-6. Epub 2020 Sep 7. PMID: 32895508; PMCID: PMC7790753.

55. Rogers JC, De Brito SA. Cortical and Subcortical Gray Matter Volume in Youths With Conduct Problems: A Meta-analysis. JAMA Psychiatry. 2016 Jan;73(1):64-72. doi: 10.1001/jamapsychiatry.2015.2423. PMID: 26650724.

56. Degré-Pelletier J, Danis É, Thérien VD, Bernhardt B, Barbeau EB, Soulières I. Differential neural correlates underlying visuospatial versus semantic reasoning in autistic children. Cereb Cortex. 2024 May 2;34(13):19-29. doi: 10.1093/cercor/bhae093. PMID: 38696600; PMCID: PMC11065103.

57. Webb CE, Turney IC, Dennis NA. What's the gist? The influence of schemas on the neural correlates underlying true and false memories. Neuropsychologia. 2016 Dec;93(Pt A):61-75. doi: 10.1016/j.neuropsychologia.2016.09.023. Epub 2016 Sep 30. PMID: 27697593; PMCID: PMC5354939

58. Dennis NA, Bowman CR, Vandekar SN. True and phantom recollection: an fMRI investigation of similar and distinct neural correlates and connectivity. Neuroimage. 2012 Feb 1;59(3):2982-93. doi: 10.1016/j.neuroimage.2011.09.079. Epub 2011 Oct 7. PMID: 22001165.

59. Carpenter CM, Webb CE, Overman AA, Dennis NA. Within-category similarity negatively affects associative memory performance in both younger and older adults. Memory. 2023 Jan;31(1):77-91. doi: 10.1080/09658211.2022.2123524. Epub 2022 Sep 21. PMID: 36131610; PMCID: PMC9991946.

60. Naspi L, Hoffman P, Devereux B, Morcom AM. Perceptual and Semantic Representations at Encoding Contribute to True and False Recognition of Objects. J Neurosci. 2021 Oct 6;41(40):8375-8389. doi: 10.1523/JNEUROSCI.0677-21.2021. Epub 2021 Aug 19. PMID: 34413205; PMCID: PMC8496201.

61. Chambon V, Sidarus N, Haggard P. From action intentions to action effects: how does the sense of agency come about? Front Hum Neurosci. 2014 May 15;8:320. doi: 10.3389/fnhum.2014.00320. PMID: 24860486; PMCID: PMC4030148.

62. Duquette P. More Than Words Can Say: A Multi-Disciplinary Consideration of the Psychotherapeutic Evaluation and Treatment of Alexithymia. Front Psychiatry. 2020 May 25;11:433. doi: 10.3389/fpsyt.2020.00433. PMID: 32523552; PMCID: PMC7261853.

63. Murty VP, Tompary A, Adcock RA, Davachi L. Selectivity in Postencoding Connectivity with High-Level Visual Cortex Is Associated with Reward-Motivated Memory. J Neurosci. 2017 Jan 18;37(3):537-545. doi: 10.1523/JNEUROSCI.4032-15.2016. PMID: 28100737; PMCID: PMC5242406.

64. Ezzyat Y, Inhoff MC, Davachi L. Differentiation of Human Medial Prefrontal Cortex Activity Underlies Long-Term Resistance to Forgetting in Memory. J Neurosci. 2018 Nov 28;38(48):10244-10254. doi: 10.1523/JNEUROSCI.2290-17.2018. Epub 2018 Jul 16. PMID: 30012697; PMCID: PMC6262147.

65. Ekeres MJ, Winocur G, Moscovitch M. The hippocampus and related neocortical structures in memory transformation. Neurosci Lett. 2018 Jul 27;680:39-53. doi: 10.1016/j.neulet.2018.05.006. Epub 2018 May 4. PMID: 29733974.

66. Duquette P. More Than Words Can Say: A Multi-Disciplinary Consideration of the Psychotherapeutic Evaluation and Treatment of Alexithymia. Front Psychiatry. 2020 May 25;11:433. doi: 10.3389/fpsyt.2020.00433. PMID: 32523552; PMCID: PMC7261853.

67. Tompary A, Davachi L. Consolidation Promotes the Emergence of Representational Overlap in the Hippocampus and Medial Prefrontal Cortex. Neuron. 2017 Sep 27;96(1):228-241.e5. doi: 10.1016/j.neuron.2017.09.005. Erratum in: Neuron. 2020 Jan 8;105(1):199-200. doi: 10.1016/j.neuron.2019.12.020. PMID: 28957671; PMCID: PMC5630271.

68. Dixsaut L, Gräff J. The Medial Prefrontal Cortex and Fear Memory: Dynamics, Connectivity, and Engrams. Int J Mol Sci. 2021 Nov 9;22(22):12113. doi: 10.3390/ijms222212113. PMID: 34830009; PMCID: PMC8619965.

69. Lyman GH, Kuderer NM. Perception, Cognition and Thought: Part III: Reasoning, Judgement and Decision-Making. Cancer Invest. 2023 Sep;41(8):699-703. doi: 10.1080/07357907.2023.2238944. Epub 2023 Jul 27. PMID: 37467515.