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NEUROBIOLOGY OF THE CHILDHOOD ADVERSITY MODEL AND SUBCLINICAL EMOTIONAL PARENTAL NEGLECT

**NEUROBIOLOGÍA DEL MODELO DE ADVERSIDAD
INFANTIL Y NEGLIGENCIA PARENTAL EMOCIONAL
SUBCLÍNICA**

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Neurobiology of the childhood adversity model and subclinical emotional parental neglect

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ABSTRACT

Introdução: Research in neurogenetics and human neurobiology, through the use of functional neuroimaging with proton emission (fMRI), we describe in an objective and analytical way, a clinical set based on neurobiology and social neurosciences, which organizes a series of situations by the individuation of objectivity and subjectivity, such as the current Syndrome Z. The most predominant neurological mechanisms are biobehaviors, all dependent on the neurological component, and develop in response to the quality of affective attention of biological parents, and present a hierarchical nosology of cumulative causal factors that were delimited from descriptive clinical practice, like all most diseases in Medicine. **Métodos:** We present a clinical pre-diagnosis construct, based on neuropathophysiology, which was carried out in the practical field, and helps in the understanding and organized identification of a serious public health problem, and a hidden setback in family courts. It aims to contribute to the problem of NP, and its medical and specialized characterization, as well as its already known social and psychological consequences. **Resultados:** The quality of care is directly reflected in maladaptive neurological development, with deficits in emotional regulation, in intelligence and family and social skills, family synchrony and chronic states of cognition and behavior that distort the real values of mental health and the importance of interpersonal relationships (IR). **Discussão:** Several pieces of evidence have shown that complex PTSD or a history of childhood abuse (or both), and also in the presence of four or more situations of Adverse Emotions in Childhood (ACE), negatively impact parenting and multiple comorbidities, physical and mental, and social risk behaviors, in addition to generating "intergenerational cycles" of trauma. **Conclusão:** This study should be reflected upon by professionals in family law and Family Medicine, as there is no assessment and much less protective care interventions for child neurodevelopment, which is sensitive to ACEs, which determine or limit the social, mental and organic life of the child.

Keywords: z syndrome, metabolic syndrome, hypodopaminergic, addiction, dopamine

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Neurobiología del modelo de adversidad infantil y negligencia parental emocional subclínica

RESUMEN

Introducción: La investigación en neurogenética y neurobiología humana, a través del uso de neuroimagen funcional con emisión de protones (fMRI), nos permite describir de manera objetiva y analítica un conjunto clínico basado en la neurobiología y las neurociencias sociales, que organiza una serie de situaciones mediante la individuación de la objetividad y la subjetividad, como es el caso del actual Síndrome Z. Los mecanismos neurológicos más predominantes son los biocomportamientos, todos dependientes del componente neurológico, que se desarrollan en respuesta a la calidad de la atención afectiva de los padres biológicos, y que presentan una nosología jerárquica de factores causales acumulativos delimitados a partir de la práctica clínica descriptiva, como ocurre con la mayoría de las enfermedades en Medicina. **Métodos:** Se presenta un constructo de prediagnóstico clínico, basado en la neuropatofisiología, que fue elaborado en el campo práctico y que contribuye a la comprensión e identificación organizada de un grave problema de salud pública, además de ser un obstáculo oculto en los tribunales de familia. Este modelo busca aportar a la problemática del NP y a su caracterización médica y especializada, así como a sus ya conocidas consecuencias sociales y psicológicas. **Resultados:** La calidad del cuidado se refleja directamente en un desarrollo neurológico desadaptativo, con déficits en la regulación emocional, en la inteligencia y en las habilidades familiares y sociales, en la sincronía familiar y en estados crónicos de cognición y comportamiento que distorsionan los valores reales de la salud mental y la importancia de las relaciones interpersonales (RI). **Discusión:** Diversas evidencias han mostrado que el TEPT complejo o los antecedentes de abuso infantil (o ambos), así como la presencia de cuatro o más situaciones de Experiencias Adversas en la Infancia (ACE), impactan negativamente en la crianza y en múltiples comorbilidades físicas, mentales y conductas de riesgo social, además de generar “ciclos intergeneracionales” de trauma. **Conclusión:** Este estudio debe ser considerado por los profesionales del derecho de familia y de la Medicina Familiar, dado que actualmente no existen evaluaciones ni mucho menos intervenciones de cuidado protector para el neurodesarrollo infantil, el cual es sensible a las ACE y determina o limita la vida social, mental y orgánica del niño.

Palabras clave: síndrome Z, síndrome metabólico, hipodopaminérgico, adicción, dopamina

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INTRODUCTION

The care of children and adolescents is culturally and legally the responsibility of the parents who have custody and the coexistence of these children is the potentially most protective and appropriate space for their development. The community and the State carry out complementary protection, information, and collective policies, as established by Brazilian legislation, always aiming at well-being and thus ensuring the best possible state of health.¹ The expression “potentially more protective” reflects that although there is an expectation regarding the care offered within families, it is also known that this is not always an effective space of protection, and the family environment can also be hostile, with violations of children's rights that are often hidden and vices.¹ The violations are diverse and multiple: physical, psychological, sexual violence, abandonment, and neglect. Parental neglect (PN) is the most reported type of violence and the one that most motivates the removal of children and adolescents from their family context¹. According to the World Health Organization (WHO -2020), PN corresponds to the failure of parents or caregivers to ensure the child's development, whether in terms of health, education, shelter, nutrition and safe living conditions. Child abuse can also be defined as the failure to provide care when protective resources are available and which have repercussions on one or more areas of development.² According to the WHO, child abuse is defined as: "Child abuse or mistreatment includes all forms of physical and/or emotional mistreatment, sexual abuse, neglect or negligent treatment, or commercial exploitation, resulting in actual or potential harm to the health, survival, development or dignity of the child, in the context of a relationship of responsibility, trust or power."² In the scientific reality, particularly behavioral neurobiology studies, there is a voluminous and overwhelming amount of evidence on childhood adversity and presents an accumulation of clinical data on damage in various dimensions of children's mental health (MH), such as psychological, social, neurological, genetic, epigenetic, hormonal, inflammatory and psychiatric.²⁻⁷ However, there are no objective and precise studies, combined with the hidden flaw of methodological preference for research dependent on statistics. There are no initiatives and concern from responsible communities in organizing minimum care, even if reductionist, and the reality of the epidemic of family conflicts and Mental Disorders (MD) that are influenced by psychosocial factors, shows a progressive and subtle increase,



especialmente después de la epidemia de Covid-19.⁸⁻¹² Actualmente, en la red básica de salud en Brasil, no se presta atención a la salud mental, además de persistentes narrativas profesionales, que alimentan la cultura de subestimar la MD, a menudo justificada por falta de evidencia significativa, o creencia en problemas complejos que son difíciles de resolver, y por lo tanto hay una falta de atención a la salud mental, que es tan importante como la salud orgánica, pero con diferentes valores.⁸⁻¹² La falta de conocimiento técnico, en profundidad y especializado en el área de la salud familiar y del trabajador es evidencia de desinformación, desorganización y conocimiento científico obsoleto, que no es una prioridad en las políticas de salud pública, además de la falta profesional de motivación para conducir investigaciones y acciones, y los conflictos sociales están directamente relacionados con trastornos sociales como delitos familiares, violencia doméstica y alienación parental, que se reflejan en la salud de los trabajadores y el gasto público.¹³⁻¹⁷ Actualmente, la Medicina no aborda profesionalmente la MD familiar de manera técnica y comprensiva, y actualmente el Derecho Familiar está causando complicaciones en la salud de los niños, en varios casos de conflictos familiares que son neurodisfuncionales e incluso patológicos, debido a la falta de un enfoque médico, combinado con la falta de comprensión y sentido del problema real o base concreta, que solo el médico tiene la capacidad de identificar las enfermedades.¹³⁻¹⁷ El foco central es la salud y los derechos de los niños y las familias, que sufren de negligencia y imprudencia profesional por parte de los abogados, y negligencia e incompetencia por parte de los médicos, ya que no hay planes prácticos para el cuidado de la MD en la familia.¹³⁻¹⁷ Los comportamientos neurodisfuncionales o neuromaladaptativos presentan disfunciones emocionales y afectivas, que tienen predominio en sus mecanismos, junto con disfunciones hormonales y mecanismos epigenéticos de larga duración, ya que el niño presenta un desarrollo activo del neurodesarrollo hasta los ocho años, y las emociones adversas deben evitarse.¹⁸⁻²⁵ Sin embargo, con avances en los últimos años en la investigación sobre neurogenética y neurobiología humana, a través del uso de neuroimagen funcional con emisión de protones (fMRI), podemos describir objetivamente y analíticamente un conjunto clínico basado en neurobiología y neurociencias sociales, que organiza una serie de situaciones por la individuación de la objetividad y la subjetividad, como el actual Síndrome Z. Los mecanismos neurológicos más predominantes y aquellos con la mayor presentación clínica son los biocomportamientos, todos dependientes del componente neurológico, y se desarrollan en respuesta a la calidad de la atención afectiva de los padres biológicos, y presentan una nosología jerárquica



of cumulative causal factors that were delimited from descriptive clinical practice, like most diseases in Medicine.²⁶⁻³²

Neurodysfunctional Interpersonal Relationships in the Family Environment/Syndrome Z

According to *Leisman G et al*, children are suffering harm as a natural consequence of universal child development and therefore **NOT** a consequence of variations in child-rearing practices and financial status, but rather initially resulting from the processing of components of affective attention, with economic and educational factors being built *in a posteriori*, and consequently resulting in specifically predictable behavioral patterns.³³⁻⁴⁵ The activity of the human mind has been increasingly demonstrated to depend on the functioning of the neurobiological complex that consists of natural phenomena involving neuronal activities, hormones, action potentials, neurotransmitters, genetic products and others.³³⁻⁴⁵

Human consciousness presents objective (neurobiological) and subjective components in which each person has a unique narrative of how volition, habituation, performance capacity and the environment interact and influence over time, and thus provide experiences and learning.³³⁻⁴⁵ A better understanding of the presented network may help advance treatments for neuropsychiatric conditions related to aberrant predictive processing and promote cognitive improvement in healthy individuals.⁴⁷⁻⁵¹ The neurocognitive variable related to the development of executive attention is called effortful control, representing the ability of the infant or an adult to inhibit a dominant response to execute a subdominant response.⁴⁷⁻⁵¹ Being responsible for an action is to have the sense, notion and judgment, in the sense of feeling the effect of a means or stimulus (whether positive or negative) and the reactions of the causal chains that led to the existence of the conscious intention that determined the action, whether active or passive, as well as self-control.⁴⁷⁻⁵¹ Individual values are personal convictions with a sense of consideration and importance, which generate significant motivation to seek or do, and can be derived from culture, belief, beauty, ethics, morals and others .⁴⁷⁻⁵¹ Interests are related to the pleasure of doing something and are reflected in a preference for certain activities over others, and may or may not be congruent with values .⁴⁷⁻⁵¹ Volition Is the cognitive and behavioral process by which an individual decides to perform an action that he or she desires. It is defined as a psychological function of mental state, and a neurological function of deliberate effort .⁴⁷⁻⁵¹ A complex, continuous and standardized



volitional process that involves the causality of personal cognitive acts and states, values and interests, which can be neurodysfunctional and even pathological. ⁵²⁻⁵⁶ When determining a choice to do an activity, this state is called imminent volition, and when we execute it, this act is called immanent, executive or imperative volition. ⁵²⁻⁵⁶ When an immanent or determined choice controls or governs a series of voluntary acts, we classify it as a state of predominant volition, while subordinate volitions are those acts of will that put into practice the object desired by the predominant or governing volition. ⁵⁷⁻

⁶⁷ Volitional processes can be applied consciously and can be automated as habits over time, therefore it consists of a state and an act, such as a thought or a behavior. ⁵⁷⁻⁶⁷ Several neuroscientists and researchers of the psychic apparatus have highlighted the importance of the defense mechanisms of the human mind, but a comorbidity has emerged that is exclusive to these, which affects interpersonal relationships and has an elementary function, Emotional Survival. ⁶⁸⁻⁶⁹ The presence of family synchrony is fundamental and necessary for the adequate neurodevelopment of the entire emotional cascade of the newborn. ⁶⁸⁻⁶⁹ When affective attention is absent or deficient, a series of maladaptive mechanisms occur in the child's brain in response, which have the primary function of avoiding the initial discomfort of the absence of family synchrony, with amygdala behaviors, and a series of associated dysfunctions described below occur. ⁶⁸⁻⁶⁹

A set of **eight** Common Neurodysfunctions (ONDs) has been identified and described in clinical practice, which in a hierarchical construction, represent a initial microstructure of the personality, as it precedes and contributes to the onset of the development of some psychopathologies and some Personality Disorders (PD). ⁶⁸⁻⁶⁹ Thus, an ONCs microstructure is initially formed, is clearly delimited, with several neuromaladaptive pathophysiological mechanisms, and expresses neurocognitive and behavioral states with affective attention deficit, and simultaneously involuntary affective neglect that is hidden in several cases. The microstructure can evolve with internalizing or externalizing states and typical association with different types of stress. ⁶⁸⁻⁶⁹ Several empirical evidences have established that the long-term response profiles of the stress system are programmed to correspond to the quality of the social and physical environments experienced during the first sensitive windows of life. The following are the clinical and neurobiological elements of ONCs:



- (1) *Neurological Familial Synchrony Deficit (DNSF),*
- (2) *and limbic neuromaladjustment (Family Schemas)*
- (3) *Hormonal and immunoinflammatory dysfunctions,*
- (4) *Dysfunctions of family neuropsychodynamics and neuromirroring,*
- (5) *Neurodysfunction of the reward system and dopamine homeostasis,*
- (6) *Neurodysfunctions of neural networks with emotional Engrams, with deficits in primitive and higher mental functions (Neuroschematic Survival Syndrome)*
- (7) *Simultanagnosia ¹ and cognitive limitation,*
- (8) *Dissociative Disorders of Neuroadaptive Consciousness*

They are subtle and automatic states such as Alexithymia ² , Anosognosia ³ , Anosodiaphoria ⁴ , dissociation of Consciousness, deficit of cognitive intelligence due to secondary simultanagnosia, deviant behaviors, secondary to pathological activated neurobehaviors , such as family schemes, automatisms, fear and stress. They produce illusions of emotional survival.

1) Secondary Simultanagnosia: Inability to effectively identify more than four objects at the same time.

2) Secondary Alexithymia : Inability to effectively self-observe (self-identify) emotional and affective awareness at the same time.

3) Secondary Anosognosia: Inability to effectively identify another person's emotional and affective state.

4) Anosodiaphoria : Inability to identify one's own health condition, associated with denial of one's state.

The neural mechanisms underlying these difficulties are the same in individuals with dysfunctional parenting, and other traits of PD and family and occupational social RINs. In the current literature, there is a growing number of clinical methods of emotional measurement, which analyze using physiological markers, associated with other underlying markers that influence the pathophysiology of physical and mental clinical diseases, and in addition to social interfaces and disorders. ⁶⁸⁻⁶⁹ According to Miglin R et al., there is a growing number of transdiagnostic clinical approaches that evaluate behavioral functioning in real time, and thus it is possible to measure the emotional socialization of parents, together with children's emotionality, as well as the quality and

effectiveness of these interactions in everyday life.⁷⁰⁻⁷³ A history of childhood adversity should be considered in the differential diagnosis of developmental delay, dyslexia, dermatitis, asthma, recurrent infections, somatization, sleep disorders, but also for psychological and behavioral functioning similar to Autism Spectrum Disorders (ASD) and ADHD.⁷⁰⁻⁷³ With a prolonged ontogeny, relatively high levels of glucocorticoid receptors, and persistent postnatal neurogenesis, the hippocampus is particularly vulnerable to the effects of stress.⁷⁰⁻⁷³

Engrams

Neural representations of context, dependent on repeated activation of neural ensembles, remain stable over a period of time to facilitate recall and integration.⁷⁴⁻⁷⁷ An engram is a significant and lasting physical or chemical change in a neural network due to activity in a subset of neurons caused by episodic stimuli, which can be reactivated upon presentation of all or part of the original stimulus ensemble, leading to memory retrieval.⁷⁴⁻⁷⁷ Furthermore, engrams can be described as networks of individual engram cells that act together to store the components of memories, and reactivation of this network is necessary and sufficient for recall of that encoded memory.⁷⁴⁻⁷⁷ *An engram can be understood as the physical record of a representation, with the activated ensemble becoming reactivatable within a given stimulus ensemble (context), resulting in recall.*⁷⁴⁻⁷⁷ Engram activation may even be sufficient to induce a false memory in the form of generalization of a fear response in one context to a neutral context or even to construct a representation of a context that has never been physically experienced.⁷⁴⁻⁷⁷ *Kitamura et al.* found that engrams are actually formed simultaneously in the early stage of context memory acquisition in both the HPC and the medial prefrontal cortex (mPFC), where long-term memory is stored.⁷⁴⁻⁷⁷ The Standard Consolidation Model states that newly acquired episodic memories are initially stored only in the HPC and then transferred to the cortex as long-term memories, accompanied by the “deletion” of engrams from the HPC over time.⁷⁴⁻⁷⁷ The mPFC engram cells that were generated in the early stage are not reactivated during the recent memory retrieval state but exist as “silent engrams.”⁷⁴⁻⁷⁷ These silent engrams become functionally mature over time, concurrent with the transition of memory to the basolateral amygdala (BLA), which is required for fear memory, while HPC engram cells gradually become silent over time.⁷⁴⁻⁷⁷ *Matos et al.* demonstrated that the activity of a small subset of mPFC neurons is sufficient and necessary for the expression of remote memory,



and selective disruption of cAMP response element binding protein (CREB) function in mPFC engram cells after CFC impairs remote memory formation. Several studies have demonstrated that neurons activated by experience play a key role in memory. Learning-activated neurons are a cellular substrate for memory storage and retrieval and constitute engram cells.⁸⁰⁻⁸⁸ The relatively low overlap between sets of neurons activated during learning and recall (10–40%) shows how engrams change throughout memory consolidation, through the dynamism of neurons ‘leaving’ or ‘entering’ the engram.⁸⁰⁻⁸⁸ Knowledge of the temporal profile of engrams elucidates how their composition is related to mnemonic properties, such as memory selectivity, an essential characteristic for adaptive behavior. *Tomé DF et al.*, demonstrated through a spiking neuronal network model, that memory engrams are dynamic and that changes in their composition are mediated by inhibitory plasticity.⁸⁰⁻⁸⁸ Thus, they are fundamental for the emergence of memory selectivity, during recall and memory consolidation.⁸⁰⁻⁸⁸ Fear generalization is a maladaptive response to harmless stimuli or situations that is characteristic of post-traumatic stress disorder and other anxiety disorders.⁸⁰⁻⁸⁸ Competition between engram and non-engram cells in the dentate gyrus determines fear generalization. The overgeneralized fear response to innocuous cues may result from oversensitized memory retrieval resulting from dysfunctional activity in the hippocampus.⁸⁰⁻⁸⁸ Currently, research on engrams is growing. Eligible neurons within a given brain region have been shown to compete for allocation to an engram, and relative neuronal excitability determines the outcome of this competition, which determines how the engrams interact. Studies have shown long-lasting changes in engram cells such as increased synaptic strength and spine density in resting-state (offline) neurons, as well as preferential connectivity with other downstream engram cells.⁸⁹⁻⁹⁰ Therefore, both increased intrinsic excitability and synaptic plasticity act simultaneously in engram formation, in addition to participating in memory consolidation and retrieval processes.⁸⁹⁻⁹⁰ Technological advances have allowed targeting of individual cell subtypes through gene expression, which can include constitutively active proteins or more transient expression caused by neuronal activity.⁸⁹⁻⁹⁰ According to *Albarran et al.*, increasing the stability of neocortical dendritic spines improves learning, while decreasing the size of neocortical dendritic spines leads to impaired performance in a motor task.⁸⁹⁻⁹⁰ Recently, it has become possible to label synapses between neurons, thanks to *GFP Reconstitution Across Synaptic Partners* (GRASP), which was adapted for pre- and



postsynaptic engram neurons with a genetic method based on the *Immediate Early Gene* (IEG) *cFos* and allowed visualizing the engram at the synaptic level.⁸⁹⁻⁹⁰ However, the genetic system based on the *cFos IEG* provides only transient labeling and it is unclear whether other genetic schemes based on other IEGs would aid in the labeling of structural synaptic engrams.⁸⁹⁻⁹⁰ Murthy BKB *et al*., demonstrated through the use of the GRASP system in the dorsal hippocampus of mice, under the control of two different IEG promoters, commonly used to identify neuronal engrams: *cFos* and *Arc*, and demonstrated the possibility of identifying and labeling functional engrams for different periods.

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States chronic neuro determinists

Second *Vygotsky*, the human mind has two types of functions: elementary psychological and higher psychological. The human species is essentially social, as it is only through interpersonal interactions that the development of humanization occurs.⁹¹⁻⁹³ The microstructure of the ONCs emotional survival personality presents a series of dysfunctions of the higher and primitive psychic functions, which function as neural networks, which are true engrams of maladaptive emotional systems, which are synonymous with neuronal signatures or cognitive and behavioral schemes, and present dysfunction of neuronal hyperconnectivity.⁹¹⁻⁹³ Such cognitive states with associated dysfunctional alterations are subtle and subtle, and can generate micro-illusions, dissociation of consciousness, self-deceptions, choices, convenient values of emotional survival, which impair neurosignification⁹¹⁻⁹³. The set is composed of chronic neuroschematic activations, with variations of dysfunctions of general intelligence, executive function, processing speed, volition, emotional memory, reasoning, perceptive, verbal comprehension, interpersonal communication deficit, language dysfunction, fixation of survival values, family and occupational RINs.⁹¹⁻⁹³ In a second plane of cognitive dysfunctions, which are objective and involuntary in onset, permeate the sense of voluntarism in what is presented in our everyday consciousness, in which a group of neuro-schemas of memories, of psychosocial coping (*social coping*).⁹⁴⁻⁹⁵ The routine functioning of these underlying network systems and subnetworks, can present functional and neurofunctional networks working simultaneously, in which represents emotional Neurodeterminism.⁹⁴⁻⁹⁵



Neuro biopsychosocial conditioning

Biopsychosocial conditioning in the family environment, it represents the activity of several schemes simultaneously, for long periods, as they are activated by the family context, with environmental or family clues.⁹⁴⁻⁹⁵ They present function of coping with biopsychosocial stress, and begin with sudden onsets of amygdala hyperactivity, which produces a narrowing of consciousness, since the amygdala system is the main component of momentary Mastery and Control and its maintenance, as well as being responsible for sudden emotional defenses and excess reason that brings resistance and rigidity, making irrational interaction or behavior, which is illusory and based on belief, non-self-perceptible.⁹⁴⁻⁹⁵ The amygdala system expresses the clinical schemas in the family environment, habituated in a dysfunctional way in self-attention, presenting insufficiency of interoception (alexithymia), cognitive inflexibility of correlating several pieces of knowledge simultaneously (secondary simultanagnosia).⁹⁶⁻
⁹⁸ Presence of neuronal hyperconnectivity dysfunction in value -oriented attentional capture (VDAC), or fixation, associated with attention deficit in interpersonal and written communication.⁹⁶⁻⁹⁸ A large body of literature suggests that neural activity consists of predictions and prediction errors that are common throughout the brain, and thus the vast majority of fMRI experiments in affective neuroscience are designed to limit predictability, including clinical data from visual, auditory, somatosensory, and motivated behaviors.⁹⁶⁻⁹⁸ Predictions are important for emotional and material survival control function, but they can be derived from semantic cues (verbal instruction) or recently learned associations stored in memory (conditioning).⁹⁶⁻⁹⁸ The ascending connections of the Superior Colliculus are candidates for an *early plastic effect on higher, more “experience-dependent” circuits* of the social brain.
⁹⁶⁻⁹⁸ Evidence shows that the Superior Colliculus contains the largest amounts of GABA and the highest density of GABAergic synaptic terminals in the brain.⁹⁶⁻⁹⁸ They can refer to stimulus attributes (from low-level sensory features to object perception to complex social interactions), stimulus timing (even when “jittery”), expected motor responses (button presses, eye movements), expected somatosensory stimulation (sensation of pressing a button), predicted stimulus sampling given motor responses (eye movements, pupil dilation), and also visceral changes (changes in heart rate, respiration), and among others⁹⁶⁻⁹⁸ Given that the prestimulus period likely consists of different brain states at different times (rather than a stable baseline), this raises the question of whether the prestimulus brain state has



implications for the brain–behavior relationship.^{96–98} The brain is in constant motion, and when a stimulus disrupts its trajectory, the functional activity observed in response to the stimulus reflects a deviation from the trajectory.^{96–98} The predictions developed over the years vary among individuals as a function of their personal developmental history and are likely to be difficult to modify.^{96–98} Research in animals has shown that early sensory areas exhibit plasticity related to valence processing, which is considered a “core” affective feature of our emotional lives.^{96–98} Alternatively, a predictive processing account suggests that greater activity in these early areas may be driven by prediction error at relatively lower levels of the hierarchy.^{96–98} In typical picture-viewing task designs in affective neuroscience, low-level predictions might concern when and where to position the eyes, how much to dilate the pupils, and the expected changes in visual sensory information given these motor movements (“active inferences”), as generated from eye movements.^{99–101} To the extent that affect involves a multilevel cascade of predictions and prediction errors, it is quite possible that predictions are generated in sensory cortical areas other than those that receive direct input.^{99–101} An evocative image of a screaming child might drive predictions in the auditory cortex, and these predictions might play a constitutive role in affective experience.^{99–101} A psychological state might engage different brain regions at different times (degeneration) depending on how a stimulus disrupts (introduces prediction error into) ongoing brain activity.^{99–101} The complete set of predictions constitutes a person's internal model and may be idiosyncratic to a person's experience. Direct inference involves inferring the probability of activation in a brain region *given the previous brain state*, in addition to the psychological state induced by a stimulus.^{99–101} Chikazoe *et al.*, employed representational similarity analysis and identified brain regions that exhibit continuous activity and reflect a continuous dimension of subjective valence, spanning neurological states from negative to positive affect. While simple feature detection models show that there is a specific and reliable pattern of activation, and therefore underlies affective experience, located in limbic and paralimbic regions.^{99–101} Because predictions are not stationary and because prediction errors are naturally contingent on predictions, the neural activity underlying affective experience will depend on which aspects of an evocative stimulus are meaningful, and present ongoing predictions of threat or violation.^{99–101} Current models of predictive processing suggest that there may be many different brain states that give rise to feelings of (dis)pleasure or arousal. The idea that



the baseline state involved low levels of activity spread evenly across the brain gave way to the discovery that a certain set of “default mode” brain regions were actually more active during rest than during task engagement.^{99–101} Some of the key regions of the default mode network include portions of the anterior medial prefrontal cortex, ventrolateral prefrontal cortex (PFC), posterior cingulate complex, hippocampus, and other medial temporal lobe structures, and lateral temporal and parietal areas.^{99–101} This “default mode” is not an inert or “resting” baseline for psychological function. Although default mode areas often experience reduced overall activity during certain cognitive and attentional performance tasks, they do experience increased activity during social cognitive tasks.¹⁰² Thus, the brain does not return to a stable functional baseline, at least at the spatiotemporal resolution of fMRI data. When a higher-order common factor is used to model the correlations between response inhibition, working memory updating, and mental set shifting, this common factor predicts the inhibition factor almost perfectly. However, there is significant variation in the updating and shifting factors that are unrelated to the common factor. Resting-state and functional connectivity data suggest several distinct configurations (networks) of PFC and other brain regions, the lateral “fronto-parietal” (“central executive”) network (FPN), anchored in the dorsolateral (dl) and dorsomedial PFC and posterior parietal cortex; the “cingulo-opercular” network (CON), which overlaps with a “salience” network and includes the ACC, insula, and subcortical regions; the “ventral attention” network, which includes the inferior frontal gyrus, regions of the insula, and the temporoparietal junction; and the “dorsal attention” network, which includes the frontal field and intraparietal sulcus; and the “default mode network” (DMN) comprising medial PFC regions that interact with certain posterior cortical regions. The brain processes three sources of motivation: extrinsic rewards, moral values, and image concerns. According to decision neuroscience, when choosing whether to accept or reject an offer that weighs two types of attributes (moral values and money), the brain assigns a value to each option and compares them by calculating their difference. This scheme has been applied successively in the field of value-based decision-making in relation to various types of benefits (money) and costs (waiting for a long delay). A neurobehavioral and cognitive pattern that shares the same brain activation mechanisms characterizes the primary NDE with an emotional survival function and the secondary NDE with a financial/physical survival function. Although it may seem like a split-second phenomenon, deliberating about which



emotions we perceive unfolds in several stages of decision-making processing. General neurocognitive models of perception postulate that our brain first extracts sensory information about the world, then integrates this data into a percept, and finally interprets it. Furthermore, the left amygdala was responsive across all classes of decision-making paradigms, regardless of task demands. Bilateral brain processes for nonverbal decisions, left brain processes for verbal decisions. The mechanistic explanation of emotion perception consists of constructivist theories, which argue that the emotions of others can be accurately inferred from a combination of perception of motor expression, contextual processing, and conceptual knowledge about the relationships between emotions, desires, and beliefs. Perception of motor expressions can inform the process of emotion inference not because motor expressions reflect emotions per se (there is *no one-to-one mapping*), but because the observer has learned through experience to associate certain motor expressions with certain emotional experiences through a process of *bootstrapping*.

Perception

Our perception of free will is composed of a desire to act (volition) and a sense of responsibility for our actions (agency).⁸⁹⁻¹⁰⁹ Lesions that disrupt agency also occur in many different locations, but they fall within a separate network defined by connectivity with the precuneus.⁸⁹⁻¹⁰⁹ Together, these networks may underlie our perception of free will, with implications for neuropsychiatric diseases in which these processes are impaired.⁸⁹⁻¹⁰⁹ Recent research has therefore focused on understanding this perception by dividing it into two processes: the intention or motivation to act, termed volition, and the sense of responsibility for one's own action, termed agency.⁸⁹⁻¹⁰⁹ This view has received considerable empirical support from studies showing that spatial and temporal discrepancies between performing an action and seeing visual feedback of the action reduce the sense that the observed action is one's own.⁸⁹⁻¹⁰⁹ Thus, introducing a spatial transformation between an action and its visual consequences reduces participants' sense of agency in proportion to the induced mismatch.⁸⁹⁻¹⁰⁹ The so-called "intentional binding" effect provides another line of evidence for the role of temporal contiguity between action and outcome in the construction of agency. The intentional binding effect was first reported by *Haggard et al.* and refers to the subjective compression of the temporal interval between a voluntary action and its external sensory consequences.⁸⁹⁻¹⁰⁹ The intentional binding effect would constitute an implicit but

reliable measure of agency, since it only occurs when events in the external environment are accurately recognized as *consequences* of one's action.^{89–109} In comparative accounts, a positive sense of agency is the default operation when no mismatch occurs between anticipated and actual states. Thus, a reliable and explicit sense of agency can only be formed when reafferent signals (visual, motor, or proprioceptive) become available for matching with intentions.^{89–109} Thus, one cannot feel agency over any event until that event has been registered and processed in the brain. As a consequence, agency can only be attributed *retrospectively*, although it is informed by *on-line signals* about motor orientation and control. However, an alternative possibility is that the sense of agency is also generated *prospectively*, before the action itself and before the actual effect of the actions is known. The onset of a random-dot visual stimulus marks the beginning of the decision process. The useful information is encoded by a set of neurons in the visual cortex. The flow of information from the stimulus is processed by specific regions in the visual cortex, which provide a stream of evidence for downstream processes.^{89–109} The stream of momentary evidence comes from neurons in the visual cortex, concentrated in the middle temporal (MT) brain region. Other neurons, residing in the association cortex, represent the accumulation of this momentary evidence.^{89–109} A fundamental property of neurons in these areas—the vast majority of the cortical mantle in primates—is their ability to sustain firing for long periods in the absence of immediate sensory input or immediate motor effect. While MT neurons are spiking at a roughly constant rate, neurons in the LIP gradually increase or decrease their firing rate as more evidence accumulates for or against one of the choices.^{89–109} If the stimulus is turned off and a delay period occurs, MT neurons return to their baseline firing rates, but LIP neurons whose response fields contain the chosen target emit a sustained discharge that indicates the outcome of the decision. However, the firing pattern of neurons representing momentary evidence is entirely caused by input from other neurons, many of which are already in a *continuum* of activity and others are “dormant.” The prefrontal cortex plays an important role not only in determining which events to perceive but also which of the corresponding response dispositions to select and actualize in overt behavior.^{89–109} Thus, action selection is the result of competition between response tendencies in the context of prefrontal bias signals that represent goal drives and strivings.^{89–109} Action selection can be decoupled from drives and strivings as a result of a lowering of the threshold for action selection. The emotional inhibition task

engaged the OFC and amygdala, whereas a think-no-think task engaged the hippocampus, consistent with work by *Anderson*, who demonstrated that memory retrieval can be inhibited by a dlPFC- to-hippocampal pathway via relays in the mediotemporal lobe or retrosplenial cortex.⁸⁹⁻¹⁰⁹ The term categorical perception describes the subjective experience in which a perceived dimension jumps abruptly from one category to another at a certain point along a continuum, rather than changing gradually.⁸⁹⁻¹⁰⁹ Categorical and continuous perception often occur simultaneously when processing the emotions of others: the former allows for a gestalt perception of a single emotion, while the latter allows us to perceive subtle variations within an emotional construct.⁸⁹⁻¹⁰⁹ However, categorical perception seems to dominate the way we process and attribute emotions in others, and the reason for this may be to achieve cognitive efficiency by parsing information into meaningful but limited chunks of information. The influence of context and language also increases in the inference of emotional state, because the richer the emotional expression in situational information (a booming laugh), the less need there is to rely on context to infer the respective emotional state. To date, less attention has been paid to how higher cognitive functions (language processes, access to semantic knowledge) contribute to the formation of holistic perception and its interpretation in various contexts. Perception occurs when incoming sensory information is made available to higher-order brain regions and compared to a mental model. In the ventral stream, this mental model consists of semantic categorical representations, such as a prototype of a stimulus, or how a familiar face involuntarily stimulates. In the dorsal stream, the mental model consists of visuo- optic and audio-motor sequences potentially stored in our procedural memory, demonstrating how emotional expressions and emotional statements evolve over time. These models allow us to perceive and discriminate the actions of other individuals, including facial movements and speech. A later stage in the process of emotional perception concerns emotional categorization or verbal labeling. By converting the set of sensory information into a percept that can be communicated, an individual is able to relate to and describe the emotional state of another individual. In relation to this stage, a significant task-dependent role is assigned to the frontal cortex in matching incoming sensory information with a mental model. Although there are reviews and meta-analyses on the multiple roles of the inferior frontal cortex (IFC) in the perception of a large class of stimuli, there are no systematic reviews for the perception of emotional expressions, despite abundant empirical



data.^{103–105} Another frontal brain structure consistently recruited during perceptual decisions about emotions is the dorsomedial frontal cortex (dmFC).^{103–105} This structure is predominantly involved in social cognition, such as forming impressions about others and inferring beliefs, desires , and intentions. Emotional expressions conveyed by others are inherently social stimuli and are processed differently than other classes of stimuli, such as inanimate objects. The involvement of the dmFC in this specific decision-making process suggests that facial, bodily, and vocal emotional expressions are not only proxies for mental states, but also that observers spontaneously infer mental traits and states (beliefs, desire, intention) that are integrated into emotional appraisal.^{103–105} In addition to the frontal brain structures targeted by the ventral and dorsal processing streams, other brain structures that do not belong exclusive leither processing stream also contribute to perceptual decisions about emotions.^{103–105} One such structure is the amygdala, which works concurrently with sensory and higher-order cortices to tag incoming sensory information with contextual relevance and subsequently detect this relevance upon the next encounter with that stimulus.^{103–105} The fear conditioning procedure instills an initially neutral stimulus with the aim of eliciting biologically relevant responses and behaviors (freezing or fleeing) upon consistent association with an unconditioned aversive stimulus.^{89–109} Furthermore, the amygdala likely processes various emotional expressions, such as facial expressions and vocal prosody features, as relevant social cues. The amygdala may serve as one of the interfaces between sensory cortices and higher-order brain structures.^{89–109} The overwhelming evidence suggests that the right pSTS is involved in decoding and understanding meaningful social actions conveyed by gaze direction, body movement, and other types of meaningful goal-directed movement or implied by spoken words.

89–109

Neurodysfunctional Attention

Attention plays an essential role in motivating behavior and cognition, such as language and memory, and selectively enhances the processing of relevant sensory information. Attention is our ability to focus on relevant information rather than irrelevant information. Attention has qualities and intensities. When focusing on a task, attention can be distracted by new, unexpected, but task-irrelevant events. This is the case with distracting sounds, which impair performance in children, as they are part of the long-term development of attention control. The ability to focus attention and ignore novel sounds that are



irrelevant to the task develops considerably from age 4 to 6. Different sources of motivation contribute to the regulation of sensory processing in the cortex and perceptual behavior, such as goal-directed attention to cognitively demanding tasks, which is often driven by external incentives. Attention levels can also be heightened by an internal desire to complete a task without any apparent change in external incentives, but it does require cognitive effort. The ability to act on the basis of the current incentive value of the outcomes of the action is a defining characteristic of purposeful or goal-directed behavior, distinguishing goal-directed responses from stimulus-elicited habits that are unaffected by changes in outcome values. Some studies show that V4 neuronal activity in the visual cortex is increased as a result of increased cognitive effort in response to increased attentional task demands. *Poort et al.* demonstrated that distinct mechanisms of response suppression are carried out by inhibitory and excitatory neurons in the visual cortex, associated with top-down input models, and thus generate improved sensory processing due to learning and attention.^{.103-105} The social brain in a neuromaladaptive state promotes dysfunctional inattention, with the aim of avoiding threats of emotional distress and indirectly generates effects of neglect and low diligence processes.^{.103-105} The term “unity and diversity” (UD) is used by neuroscientists to describe the relationships between these diverse frontal lobe processes, responsible for an “irrational variety” in human reactions, even with restricted and non-progressive lesions of the prefrontal regions, characterized as “compulsivity” or “abnormally stimulus-linked behavior”. The common and basic element of UD is “neglect of goal or disregard for a known task requirement”.^{.103-105} The study of the PFC is a great ally in deducing the organization of the mediation of the variety of cognitive processes, such as the dominance of automatic or dominant responses, interference controls, task alternations and coordination, updating of working memory, monitoring and planning. Social cognition is the process that guides behaviors towards other individuals of the same species. Several brain structures play a key role in controlling social behaviors: the ventromedial prefrontal cortex, the amygdala, the right somatosensory cortex and the insula. What we pay attention to is influenced by the reward of learning. Humans automatically attend to stimuli previously associated with reward and to stimuli that have been experienced and conditioned during visual search, even when it is disadvantageous in current situations. Several studies have shown that associative reward learning alters the brain's processing mechanisms of visual stimuli, in the face of



learned reward cues that are difficult to ignore.^{.103-105} The neuroanatomical connectivity of the PFC associated with most cortical and subcortical regions mediates several neural networks, and thus generates cognitive states of control and attention in different functional domains (spatial, visual and verbal).^{.103-105} However, changes in mental state require several subprocesses, such as interference control, recovery and reconfiguration of task sets. Changes due to the influence of previously learned stimulus-reward associations, but which can currently be considered irrelevant, is a phenomenon called "value-driven attentional capture" (VDAC).^{.103-105} The VDAC are representations of stimulus associated with reward undergo plasticity in the sensory cortex, automatically capturing attention during the initial processing of any lived experience.^{.103-105} Behavior directed toward goals or associated outcomes presents motivational elements based on cognitive values, which influence decision making and aid in interpretation in order to distinguish motivational control from value-based processes.^{.103-105} Studies of selective attention typically consider the role of task goals, but attention can also be captured by stimuli previously associated with reward or emotional defense.^{.103-105} Many studies show that reward learning induces visual cortical plasticity, which modulates early visual processing to capture attention; learned value modulates spatial signals in visual cortical areas, an effect that correlates with VDAC.^{.103-105} Attentional capture by previously rewarded targets as the modulatory effect of reward on *priming*, as well as the decoupling of reward history and prior task relevance in value-driven attention. Studies using magnetic encephalography have investigated modulations by reward learning, and have shown that VDAC is supported by learned value signals that modulate spatial selection throughout the posterior visual and parietal cortex, which can still occur in the absence of changes in visual processing in the cortex.^{.103-105} This value modulation is influenced by the strength of the behavioral VDAC effect and persists in subsequent target processing. Recent studies have demonstrated that VDAC is based on Pavlovian conditioning, and behavioral evidence distinguishes VDAC from other established control mechanisms, suggesting a distinct underlying neurobiological process.^{.103-105} The VDAC persists perennially even without reinforcement, unlike other forms of learning, where removal of reinforcement typically leads to extinction.^{.103-105} Evidence suggests that the time course of resource and reward is flexible, with some constraint on learning the resource–reward association. When these value-cuing stimuli appeared as distractors in the test phase, they continuously shaped

attentional selection despite their task irrelevance. ¹⁰³⁻¹⁰⁵ Rule-guided allocation of attention to different stimulus dimensions produced discriminate patterns of activation in visual cortex, providing a signature of top-down bias in perception. Survival in a changing environment requires qualities that predict social reality. Our reasoning seeks patterns of information that provide predictions. The brain tries to make it easier for itself to predict the behavior of others without communication, since coordinated repetitive movements of closely related individuals are more predictable to the brain. Cognitive development and social cognition require individuals to connect with and coordinate with relatives (and/or peers) to capture patterns of information that provide predictions. The differentiation of “facial expressions” is a process of increased mental activity, which has considerable applications in the clinical setting of emotions, as attentional bias toward threat is implicated in the etiology and maintenance of anxiety disorders. ¹⁰³⁻¹⁰⁵ In The fMRI studies of adults exposed to familiar and unfamiliar videos, it was shown that neuroadaptations led to tighter connectivity between the ACC and the anterior insula, consolidating an interface combining information from exteroceptive and interoceptive sources to support attachment representations. Viewing one's own child versus a familiar child was associated with activation in the amygdala, insula, anterior paracingular cortex, and posterior superior temporal sulcus Viewing. The face of an unfamiliar child compared with that of an unfamiliar adult engages areas associated with attention as well as face perception. In response to pictures of children, parents also exhibit higher plasma oxytocin concentrations, as well as stronger activation in brain regions important for decoding facial emotions (caudal middle frontal gyrus), mentalizing (temporoparietal junction), and reward processing (medial orbitofrontal cortex). In summary, socioemotional studies show a mixed pattern of affected functions; fMRI and neural hodology studies have shown connectivity dysfunctions in the amygdala and parietal networks, aberrant frontoparietal and temporoposterior networks with relative preservation of the posterior part of the default mode network and the visual network. They also showed a significant disconnection in the frontal pathways. Several neuroscientists have shown that value signals automatically guide attention to new situations and associations, which may or may not be beneficial, depending on their congruence with current goals. Cognitive control allows stimulus-response processing to be aligned with internal goals and is therefore central to intelligent and purposeful behavior. Control depends on the active representation of task

information in the prefrontal cortex (PFC), which provides a source of contextual bias in perception, decision-making, and action. Studies that analyzed the strength of neuronal connectivity in the PFC have shown that the inferior frontal sulcus and intraparietal sulcus during context-dependent decision-making are functionally active at rest and during task performance. Attentional focusing ensures that emotionally salient features of complex events are preferentially retained in memory, which may be an evolutionary disadvantage. The superior colliculus (SC) dominates visual behavior during the first months of life, is active at birth for complex visual tasks, and has a significant influence on several hemispheric regions. The SC is the main brain center, with a subcortical structure, that permanently integrates visual and nonvisual, external and internal (bottom-up and top-down, respectively) information, and has the enigmatic ability to make nonconscious decisions about where to focus attention. It is also a sentinel that triggers the subcortical mechanisms that drive *social motivation* to follow faces from birth and automatically respond to emotional stimuli.⁹⁹⁻¹⁰² Through indirect connections, it also simultaneously activates several cortical structures necessary for the development of *social cognition* and the multiattentional task required for conscious social interaction in real-life scenarios. It also plays a crucial role in the integration of external and internal senses with emotional, autonomic, and endocrine functions, as well as in visual/motor transformation, target selection, and goal-directed motor responses.⁹⁹⁻¹⁰² Its multiple *direct connections* from the cortex are responsible for the shift from covert to overt attention and the interaction of medial and lateral cortical brain networks, which regulate and integrate endogenous attention with external attention, respectively.¹⁰³⁻¹⁰⁵ With the description of the “*Sprague effect*”, a *hemineglect syndrome* produced by a unilateral lesion of the SC, or the resolution of hemineglect in a patient with a frontal lesion, after inactivation of the contralateral SC, evidence was given to the significant influence of the SC on hemispheric functions. In blindsight, the primary visual cortex is compromised, but the SC and the magnocellular visual pathway are spared and the individual is able to react to stimuli.⁹⁹⁻¹⁰² This is evidence of the role of the SC in ongoing, multi-attentional, non-conscious emotional processing, including autonomic and motor reactions. Affective and motivational aspects of visual attention and saccadic control activate the “*Emotional System*” or “*Alarm System*” of the SC, and thus *simultaneously trigger attentional, autonomic, endocrine, and cognitive functions* via the dopaminergic *reward system*, the adrenergic *alert*



system, the cholinergic system, and the endocrine system .⁹⁹⁻¹⁰² Abstraction is a intellectual operation which consists of isolating, in a concept, an element to the exclusion of others, from which abstraction is then made. The notion of abstraction is important for understanding some philosophical controversies in relation to empiricism, universalism and evidence-based medicine. Abstraction is the cognitive operation through which something is chosen as an object of perception, attention, observation, consideration, research, study, judgment and others. It is isolated from other things with which it is in a greater relationship. Spatial cognition corresponds to the ability of an individual to perceive the spatial relationships between objects as well as to present themselves with the notions of depth, solidity and distance. The Heteromodal Association Area of the Posterior Parietal Cortex is important because it is associated with different syndromes that significantly involve deficits in spatial cognition.⁹⁹⁻¹⁰² The main sensory pathways (visual, tactile, proprioceptive, auditory and vestibular) that receive stimuli for the development of the spatial cognition process. A spatial fixation point is the site of conscious attention, where we usually focus attention; where we fixate, it is possible to allocate some attention away from the fixation point (covert attention).⁹⁹⁻¹⁰² This covert attention is known to shift or compress receptive visual fields toward the attended location, to improve visual acuity at the locus of attention, although covert attention also defines a center of reference that affects the visuomotor response.⁹⁹⁻¹⁰² This cognitive ability is closely correlated with spatial perception, which is formed by the end result of the organization and integration of diverse sensory stimuli, which aim to assist in the comprehension of consciousness in a general panorama of the relationships and forms of the external environment.¹⁰³⁻¹⁰⁵

Neuroesthetics

Perhaps it is more appropriate to say that beauty is in each sense of the perceiver. The experience of the world is primarily multisensory and integrated across different sensory modalities, so many of our decisions are based on aesthetics as perceived by multiple sensory modalities rather than a single sensory modality. Aesthetics can refer only to external, or material, design, as if a food looks good but does not taste good, most of us will not choose to eat that food, and we will not buy a scent just by seeing its color, but by smelling it as well. Thus, multisensory cues can, separately or in combination, influence our perceived attractiveness or aesthetics of an individual or object, and our attitudes and actions toward

that person or object. It is therefore important to deepen our understanding of how the human aesthetic process operates across sensory modalities and how this process is distinct from basic perceptual processing. Karim AKMR *et al.* , present a model based on hierarchical information processing styles, disentangling aesthetic processing from basic perceptual processing, and demonstrate how affective and cognitive influences interact to modulate aesthetic preferences under both top-down and bottom-up control. In support of this model, we present findings from cognitive neuroscience, neuroaesthetics, affective science, psychology, and the arts that highlight the crucial role that different cortical regions play in recognizing objects or stimuli and appreciating their beauty in visual and nonvisual modalities, and how their roles may be mediated by experience. *Basic perception* depends on the explicit properties of the stimulus and the perceptibility of the cognitive agent, while *aesthetic perception or appreciation* may or may not depend on the explicit properties of the stimulus, but from the individual characteristics of the observer's cognitive agent. Personal characteristics of the cognitive agent that may further shape aesthetic preference include culture, experience, interest , aesthetic mindset, emotional state, or motivation. These arise from the dynamic interaction between the cognitive agent and the object, rather than just explicit "objective" properties of the object or "subjective" characteristics of the cognitive agent. A projected image may not be appreciated by a particular religious community because people in that community believe that there is no place for images, and thus it goes against religious code, belief systems, and value, and so is perceived as unaesthetic and unbeautiful, suggesting that beauty depends on value and is in the eye of the beholder.⁹⁹⁻¹⁰² Thus, the perceived quality of an object reflects the observer's opinion or judgment about its quality (aesthetics) independent of its actual physical qualities, and thus an unfair opinion or judgment may arise. An aesthetic property is distinguished from a descriptive or basic physical property in that the perception of an aesthetic property involves cognitive evaluation, hedonic valuation, and often knowledge-dependent concepts, but the perception of a descriptive physical property does not.⁹⁹⁻¹⁰² A descriptive property, such as being rectangular or being red, can be attributed without any belief about its evaluation and hedonic status, whether positive, negative, or neutral, are natural attributes.⁹⁹⁻¹⁰² The perception of the descriptive property (being a circle, a triangle, or a square; lexical status of letter strings) can operate with or without consciousness, or attention, but the perception of the aesthetic property does not.⁹⁹⁻¹⁰² Thus, *basic*



perception is a non-evaluative form of cognitive process or a purely non-cognitive process that generally does not induce any emotional feelings, whereas *aesthetic perception or appreciation is not only a* definite cognitive evaluative process , but also induces emotional feelings). However, a complexity associated with *aesthetic perception* is the conflicting aesthetic emotions elicited by the composition of multifaceted stimuli. The coexistence of aesthetic and non-aesthetic properties in the same stimulus is likely to induce simultaneously positive and negative emotions in the cognitive agent. In such an *approach- avoidance* dilemma , aesthetic preference may be determined by the resulting impact of the two opposites on the elicitation of aesthetic emotions.

Automatisms and cognitive control Automatic information processing is not a unitary construct, but rather diagnosed considering the presence of different characteristics such as uncontrollable, efficient, unconscious, and sudden. The characteristics of automaticity are not intrinsic to the processes , but point to the conditions under which the neural processes operate or to the variables that influence their occurrence. Psychological processes should not be diagnosed as automatic or non-automatic in a categorical way, but rather as more or less automatic than other processes, depending on the number and extent of the characteristics. Distraction is a functional strategy of emotional regulation used to alleviate a state of discomfort or emotional distress. Within the perspective of the attention economy, distraction is increasingly associated with the use of digital technology, performance deficiencies , and interference with higher-order cognitive processes. Distraction can be conceptualized as the result of a reaction to exogenous (orientation system) or endogenous (alert system) signals, or as the result of a conflict between these two networks that are competing for attentional resources. Endogenous signals (alert system) are the bottom-up signals in the form of expectations, worries, and persistent thoughts that lead to distraction or daydreaming. The executive system is implicated when a conflict arises between exogenous and endogenous signals, leading to discontinuity of attention and, therefore, to poor deployment of attention, causing difficulties in inhibitory or executive control, which are dependent on dopaminergic neurons. Cognitive control (CC) is a term generally associated with the healthy functioning of the PFC and its related regions, such as the cingulate cortex, and is considered synonymous with the earlier notion of executive function (EF).⁸⁹⁻⁹⁵ It also involves a central process of behavioral regulation that optimizes its goal-directedness and counteracts automaticity.⁸⁹⁻⁹⁵ The CC



allows stimulus-response processing to be aligned with internal and external goals, which is essential for conscious (purposeful), intelligent, and rational action. ⁸⁹⁻⁹⁵ The role of the PFC in the CC consists essentially of contextually biasing attention (through instructions) to resolve conflicts and exert attentional control. ⁸⁹⁻⁹⁵ Several fMRI studies show that ACC activation was accompanied by activation of the dorsolateral (dl) PFC associated with top-down adjustments of response control, which can be termed a “multiple demand” (MD) system. ⁸⁹⁻⁹⁵ The cellular physiology of these regions is characterized by rapid firing of neurotransmitters such as dopamine, and they present neural plasticity properties that allow functions such as goal maintenance in working memory. ⁸⁹⁻⁹⁵ The three functional abilities of the CC are inhibition of a prepotent response (stopping an automatic response, sometimes to make an alternative response), updating working memory (continually replacing no longer relevant information in working memory with newly relevant information as it is detected in the environment), and switching mental sets (alternating between two alternative tasks). The CC operates in different internal and external states, such as stress, which alters the neurochemical environment, and the “inverted U-shaped” functioning of the PFC, which translates into job performance effectiveness and general intelligence. *Individual* differences in response inhibition tasks may be particularly related to this ability, because if a goal is inactive or ineffective, more automatic or prepotent responses will take over, leading to poor performance on these tasks. ⁹⁹⁻¹⁰² They characterized the unity of frontal lobe functions in terms of goal-related processes, specifically the ability to form and realize goals at multiple levels of abstraction. ⁸⁹⁻⁹⁵ Studies have shown that goal neglect was more closely related to general brain atrophy than to focal frontal lesions, and that these general goal-related processes are related to the MD network, a network of frontal and parietal regions that are commonly activated across tasks. ⁸⁹⁻⁹⁵ Several studies have demonstrated moderate to large correlations between measures of intelligence, particularly measures of fluid intelligence (such as reasoning), and measures related to the CC. ⁸⁹⁻⁹⁵ Hybrid organizational systems may incorporate features of MD in certain PFC regions, but also allow for specificity of neural connectivity to mediate specific aspects of response inhibition, updating, and cognitive flexibility. ⁸⁹⁻⁹⁵ In the case of *memory of work*, the lateral frontal cortex in primates, already implicated in the spatial delayed response task, was known to contain cells that exhibited activity in delay periods in response to stimuli in several sensory modalities. ⁸⁹⁻⁹⁵ Electrophysiological evidence,

as well as human functional imaging, suggests that the inferotemporal/perirhinal and anterior parietal cortex also exhibited maintenance operations, although the dlPFC appeared to have important roles in resisting interference (distraction) in working memory. Recent studies have shown the role of posture in alertness and found evidence for top-down executive control in the maintenance of alertness. Alerting has been linked to the norepinephrine system that modulates frontal and parietal structures. The executive network is involved in error detection, conflict resolution, and other aspects of performance, and involves the anterior cingulate and anterior insula (operculum).⁸⁹⁻⁹⁵ Many psychiatric and neurological disorders are associated with specific symptoms that may be at least in part a product of impaired CC, or with more general cognitive deficits that, when accompanied by emotional behaviors, may express prolonged neurocognitive states and moments of “moral dementia.” Many theories and debates about human intelligence have presented theories as single regions, or overlapping specific networks, but the discoveries of neural hodology and the reconnection of interhemispheric neurons may help to better understand. The emphasis on whole-brain multinet network connectivity, and the inclusion of dysfunctions of weak connections in some regions and strong connections in others, motivates the prediction that intelligence will depend on functional connections that are distributed globally throughout the connectome. Using resting-state fMRI data, we expand our understanding of the neurobiological substrates that give rise to intelligence and emphasize the importance of considering neural representations of lower activity in emotional and maladaptive neurosystems.

Alexithymia and Anosognosia

According to *Taylor et al.*, alexithymia is a personality trait essentially characterized by deficits in the ability to identify and describe emotions and reduced tendencies to engage in fantasies and reflect on emotional experiences.⁸⁹⁻⁹⁵ The term alexithymia, which literally means “lack of words for emotion”, is thus an identification of a neurological state based on clinical observations in many patients with psychosomatic illnesses, who have a restricted affective life and hardly benefit from psychodynamic therapy. Some authors define it as a personality trait characterized by difficulties in recognizing (identifying) and then accurately verbalizing one’s own emotions, using a cognitive style oriented towards external events, rather than intrapsychic experiences.⁸⁹⁻⁹⁵ Attention predominates in the awareness of external reality and thus presents difficulties in identifying feelings, deficits in automatic

facial expressions in neuroadaptation states. The neuropsychological state of alexithymia is associated with several psychiatric disorders, such as depression, anxiety, and eating disorders, and is therefore considered a general vulnerability factor for the development of mental disorders. Furthermore, it seems likely that alexithymic individuals receive negative feedback from the social environment about their deficits in perceiving, feeling, and communicating emotions and their superficial ways of thinking.⁸⁹⁻⁹⁵

Nemiah presented a deficit model in which a reduced capacity for fantasy formation and experience of feelings is proposed, and a deficient representation of feelings and a diminished affective response are assumed. Different neurobiological models have been proposed to explain the etiology of alexithymia. It has been suggested that inadequate neural connections between limbic and neocortical areas may be a contributing factor to the development of alexithymia. According to *Buchanan et al.*, since a right hemisphere advantage has been described in the perception of emotion, it has been hypothesized that alexithymia could reflect disturbances in the functioning of the right hemisphere. A popular etiological model of alexithymia represents the interhemispheric transfer deficit or functional commissurotomy model according to which emotional material is disconnected from the left hemisphere when verbally expressive situations occur. According to the hypoarousal model, alexithymic individuals are characterized by dampened sympathetic nervous system activation in response to affective stimuli. Individuals who spontaneously develop stronger physiological responses to emotional stimuli should become more quickly aware of them and also make them more accessible to conscious reflection. Alexithymic individuals show low reactivity to negative emotional stimuli, in which the brain regions responsible for evaluation, encoding and affective response, such as the occipitotemporal areas, amygdala and insula, work less, and are characterized simultaneously with anosognosia with the same deficits in perceiving others, by automatic activation again of the alexithymic circuits. The fMRI studies in alexithymic individuals have demonstrated poor states of feelings, few affective responses and deficits in emotional reactivity. Alexithymic individuals suffer in interpersonal relationships due to deficits in expressing themselves, feeling, perceiving, communicating, in front of "normal" people who also do not perceive, the real problem of alexithymics. Alexithymic individuals show low reactivity to negative emotional stimuli, in which the brain regions responsible for evaluation, encoding and affective response, such as the occipitotemporal areas, amygdala and insula, work less. fMRI



studies in alexithymics have demonstrated poor states of feelings, few affective responses and deficit of emotional reactivity. These are dysfunctions of neuronal connection, between limbic and neocortical areas. The reduced response of the fusiform gyrus to facial emotions with The poor physical perception in alexithymic individuals may affect the brain's visual processing, and thus impair the recognition of emotional facial expressions of others. This process is currently classified by modern neuroscience as anosognosia. fMRI studies in alexithymic patients and masked individuals have observed fewer harsh responses and have shown little amygdala activation to unidentifiable faces, with or without threat. Alexithymic features may be consequences of deficits in interhemispheric communication, low limbic-neocortical connectivity and/or right hemisphere dysfunction and excessive amygdala activity. It is conceivable that alexithymic features phenomenologically represent a kind of final common pathway to the automatic processing deficits in alexithymia. Several studies show that children who are maltreated show deficits in the recognition, expression and understanding of emotions. Higher levels of maltreatment in childhood or adolescence have been associated with higher levels of alexithymia. Researchers suggest its presence as a transdiagnostic mechanism. Other pathological situations of alexithymia are when patients present with schizophrenia, psychopathy, autism, acute neurointoxication of substances, neurodysfunctions and long-lasting epigenetics, such as relapse states, allostatic cycles, pathological demotivation. *Duan et al.*, showed negative associations between the subscale difficulties in identifying feelings and activity in response to masked facial surprise, in the fusiform, parahippocampal and superior temporal gyri. *Pollatos et al.*, presented results of difficulties in identifying and describing feelings, associated with smaller electrodermal responses to briefly presented negative images (but not to positive or neutral images). *Sonnby-Borgström* examined facial electromyographic (EMG) activity of the corrugator and zygomaticus muscles in response to masked (and unmasked) emotional facial expressions in patients with alexithymia, and found that individuals with severe alexithymia showed less corrugator muscle imitation in response to masked stimuli (and lower levels of automatic processing). Reduced activation in this network in response to emotional stimuli, as observed in alexithymia, may impede the effortless and unintentional computation of their affective value. Although most of the available evidence from neurobiological *priming studies* relates to visual emotional stimuli, there are also early indications that rapid and unintentional processing of

auditory emotional stimuli may be impaired in alexithymia. However, it should be noted that not all findings from neurobiological studies on automatic emotion processing and alexithymia suggest that alexithymia is related to brain hyporesponsiveness during emotion processing. In particular, the results of *Mériaux et al.* demonstrate that activation of the anterior cingulate cortex to task- irrelevant threatening faces is increased in alexithymia. *Van der Velde et al.* have argued that the increased response of the anterior cingulate gyrus to emotional stimuli in alexithymic individuals may reflect increased cognitive demands to attend to and understand the emotional value of stimuli. Alexithymic features may be consequences of deficits in interhemispheric communication, low limbic-neocortical connectivity, and/or right hemisphere dysfunction. Although emotions are generally elicited involuntarily and arise without conscious effort, it is surprising that little attention in the etiological considerations of alexithymia has been given to deficits in automatic emotion processing and their neurobiological underpinnings .

Memory

Over the past decade, advances in cognitive neuroscience have begun to unravel the biological mysteries surrounding the persistence of emotional experiences in humans, with implications for understanding memory disorders in affective disorders. According to *Josselyn SA et al.*, memory is the ability to use the past in the service of the present or future; it is central to our daily lives and defines who we are; without it, we are condemned to an eternal present. Episodic memories are encoded by neuronal ensembles activated by experience that remain necessary and sufficient for recall. Emotion has significant influences on learning and memory that involve several brain systems at different stages of information processing. They are influenced by arousal and valence of the amygdala, and its interactions with the frontal and temporal lobes. Currently, studies present accumulated data on the effects of emotion on memory systems, such as declarative memory (events, episodic, explicit) and non-declarative memory (implicit, fear conditioning). Recognition memory has two dissociable processes: familiarity discrimination and recollection. Familiarity discrimination for individual visual stimuli is performed in the perirhinal cortex of the temporal lobe. A systematic review has shown that the number of memories stored by a familiarity detection network depends on the rule of synaptic plasticity (storage depends on processes that produce synaptic weakening). Neural signals of visual familiarity were

observed as reductions in responses to repeated presentations of a stimulus, a phenomenon known as repetition suppression. Memory for a stimulus is degraded in two ways: plasticity events obscure existing memories, and plastic weights weaken over time. Memory-selective neurons prefer either novel or familiar stimuli, and scale response as a function of confidence. They signal subjective choices, independent of truth and values. Confidence-selective neurons signal confidence, independent of stimulus familiarity. Together, this functional separation reveals the action-independent encoding of familiarity based on declarative memory and confidence in individual choices. Currently, multisensory neuroscience research uses clinical stimuli to investigate the impact of their content on intermodal integration, and their functional variations are translated by the term "semantic". In several studies, most tasks that influence semantic factors were found without cortical networks that are more likely to mediate these effects. Cortical regions are particularly responsive to variations in content and states of semantic correspondences ("congruent") and incompatibilities ("incongruent"). Recent fMRI studies point to functional differentiation of temporal and frontal cortical regions, the former being more responsive to semantically congruent stimulation and the latter to semantically incongruent audiovisual stimulation. *Doehrmann and Naumer*, showed that in "normal" individuals with angry faces, they were associated with increased processing and effective connectivity of the inferior occipital regions, in relation to the ventrolateral prefrontal regions, and thus transmit disapproval with subsequent evocation of excessive fear responses and negative cognitions.

Emotional episodic memory

The memory-enhancing effects of emotional arousal involve interactions between subcortical and cortical structures and engagement of central and peripheral neurohormonal systems that are coordinated by the amygdala but limit the range of consciousness. Memory enhancement by arousal involves similar brain systems in positive and negative valences. However, the retention advantages of emotional valence in the absence of high arousal partially reflect semantic and strategic processes that are regulated in the frontal lobe and that benefit declarative memory without central amygdala involvement. The contributions of the amygdala, PFC, and MTL memory systems extend beyond the initial period of memory consolidation to initiate the retrieval of emotional memories, including especially those from the personal and intimate past. According to *Hamann*, autobiographical memory

research allows ethical evaluations of more intense and remote emotional episodes, as well as investigations of emotional influences on the phenomenology of memory but not on memory accuracy. The exact time course of consolidation is subject to considerable debate, and the stabilization of memory traces is a lengthy process that can last months to years. Emotional arousal has complementary and immediate effects during encoding that are time- invariant and are interpreted to reflect attentional influences on memory. Recent studies have demonstrated the retrieval of items from emotional contexts with activation of limbic structures (amygdala, insula, and cingulate) and several regions of the temporal and frontal neocortex. Studies of retrograde amnesia support. *Markowitsch* 's proposal that retrieval of remote personal memories involves interactions between the inferior PFC and its connections with the anteromedial temporal lobe that courses through the uncinate fasciculus. Furthermore, fMRI studies that analyzed autobiographical retrieval in healthy adults demonstrated activity in the frontotemporal regions, as well as in other regions, such as the medial PFC, retrosplenial cortex, and extrastriate cortex, which perform self-referential processing and visuospatial images. Emotional intensity affects the perceptual and phenomenological properties of autobiographical memories, such as the degree to which the memory is revived upon retrieval, the vividness of the memory, and the narrative details. Understanding how emotion transforms the remembrance experience that accompanies autobiographical memories can advance knowledge about the complex and subjective characteristics of emotional memory. Surface beliefs are illusory or self-deceiving , in relation to a deep or concrete belief.

Contextual memory

Contextual learning is a critical component of episodic memory and important for living in any environment. Although we may be focusing on a specific event or person at the moment, many other information streams occur simultaneously around the target to initiate the formation of contextual memory or “context.”. External components collected by sensory systems, such as visual, odor, sound, and touch information, contribute to the formation of spatial-contextual information. External information and internal states are used. Internal elements are collected through the emotional states, hormonal states, or stress experienced within the situation . The effects of internal states can predispose a circuit to be more or less responsive to a given cue.⁷⁷⁻⁹⁸ External components are the elements of the environment or an object. We can describe *context as the specifics of a place that are not the place itself* .



⁷⁷⁻⁹⁸ Thus, external elements are easier to manipulate and are often used as the primary means of modifying contexts.⁷⁷⁻⁹⁸ According to *Marks et al.*, context modulates decisions, recall processes, and plays an important role in the initial processing and reconstruction of episodic memories. It also aids in the agility of object representations, motivational determination, and evaluation of actions.⁷⁷⁻⁹⁸ There are several tasks in which place memory can be included as part of a context-dependent memory paradigm, such as contextual fear conditioning (CFC).⁷⁷⁻⁹⁸ The entorhinal cortex (EC), a major contributor to the functionality of the hippocampal circuit, plays a key role in contextual memory processes. Lesions in this region result in decreased contextual learning, but not in avoidance learning.⁷⁷⁻⁹⁸ Hippocampal injury disrupts the CFC in a time-sensitive manner, with recent memories being deleted by the lesion and long-term contextual memories being undamaged.⁷⁷⁻⁹⁸

Conceptual Memory

The storage and retrieval are mediated by subpopulations of neurons that are therefore considered cellular engrams. Human memory makes associations between different concepts.⁷⁷⁻⁹⁸ According to the Hebbian postulate, connections between neurons with correlated activity patterns are strengthened, while connections between neurons whose activity patterns are clearly correlated are depressed or even lost.⁷⁷⁻⁹⁸ This phenomenon increases the likelihood that neural activity patterns that occur during encoding will reoccur at later time points. Therefore, the subset of synapses between coactive neurons can also be considered a memory substrate, or a synaptic engram.⁷⁷⁻⁹⁸ The episode “with my friend in this place” gave rise to an association between two existing concepts: before the trip (the episodic event), you already knew your friend (first concept) and had seen the place (second concept), but only after the trip do you associate these two concepts. Concepts are encoded in the human middle temporal lobe (MTL) by neurons called “concept cells” that respond selectively and invariably to stimuli representing a specific person or place. Each concept is thought to be represented by a set of concept cells that increase their firing rates simultaneously upon presentation of an appropriate stimulus. With shared neurons, activation of a first assembly (place) can also activate a second assembly (person). First, for the brain to function properly as a memory network, it must remain possible to remember the two associated concepts separately (place without its friend) rather than automatically both together.⁷⁷⁻⁹⁸ However, if concepts share many neurons, it becomes likely that the two memory items can no longer

be distinguished but are merged into a single, larger concept encoded by a larger number of active neurons. Shared concept cells can be visualized as an overlap between two memory engrams. Associative memory in recurrent networks, such as area CA3 of the hippocampus, has been modeled with attractor neural networks where each memory item is encoded as a memory engram in a fixed random subset of neurons “pattern”, so that no pattern has an overlap above chance with another. Association chains can form the basis of a “stream of thought” where the direction of transitions from one concept to the next is based on learned associations⁷⁷⁻⁹⁸ According to *Romani-Tsodyks et al.* , memory engrams are independent of finite-size effects and stimulate neuron sharing in some engram pairs above chance, which allows sequential retrieval in the presence of periodic background input. ⁷⁷⁻⁹⁸ *Gastaldi C et al.* , showed that in large sparse coding-level networks, neurons shared by chance are not sufficient to reliably induce the retrieval of a chain of concepts, since overlaps greater than chance, represented by associations learned experientially, are required. ⁷⁷⁻⁹⁸ Instead of transitions triggered by oscillations, transitions can also be triggered by two adaptation mechanisms that act on different time scales without the need for periodic inhibition. Attractor networks with sparse patterns and random connectivity are suitable candidate models for biological memory, due to two features: memory retrieval after stimulation with a partial cue and sustained activity after a stimulus has been removed. ⁷⁷⁻⁹⁸

Objective

The objective of this article is to assist in the resolution with the use of medical evaluation based on neuroscience and neurobiology, which were organized from clinical practice faithful to reality, with the identification of a phenomenon harmful to collective integral health, observed with methodology and systematization of accumulated data from scientific publications from the Pubmed digital library, all selected with clinical abstraction and thus convenience, when identifying a clinical and pathophysiological causal link, which follows from a “continuum” of research after the initial description of Syndrome Z in 2022, Marília, interior of São Paulo, in a therapeutic community for drug addicts and from self-experienced experiences and empirical findings. In this work, we describe the cognitive and behavioral aspects that influence the quality of care and the effects on development in contexts of parental neglect, and in situations where there is unavailability of care resources.



METHOD

We present a clinical pre-diagnostic construct, based on neuro physiopathology, which was carried out in the practical field, and helps in the understanding and organized identification of a serious public health problem and a hidden setback in family courts. It aims to contribute to the problem of NP, and its medical and specialized characterization, as well as its already known social and psychological consequences. With concrete clinical updating and delimitation, with the organization of disorders with a clinical and physiopathological causal link, which present significant influence of genetic, epigenetic, neurodysfunctional, hormonal, inflammatory, immunological and metabolic orders.

RESULT

The quality of care is directly reflected in maladaptive neurological development, with deficits in emotional regulation, intelligence and family and social skills, family synchrony and chronic states of cognition and behavior that distort the real values of mental health and the importance of interpersonal relationships (IR), in addition to influencing various aspects of stress in children and adolescents, and have a significant and direct influence on MD such as depression and anxiety and psychosomatic and metabolic disorders. The studies reviewed, together with the description of neurodysfunctional behaviors that interfere with affective attention, as other types of attention and values predominate, which are distorted in many cases for predominantly neurological reasons. Currently, there is no attention to this problem, and here, like other studies on Syndrome Z, they provide resources with real chances of prevention and improvement in various treatments of MD and chronic organic diseases that have an important neuropsychological component.

DISCUSSION

Instead of applying psychological tests , we identify syndrome Z through clinical neuromarkers, neurodysfunctional behavioral and cognitive states, and amygdala automatisms, which are expressed by alexithymia and anosognosia, family schemas, chronic oscillatory hypodopaminergic state, which are neurodevelopmental responses in EAI environments and consequently NP in a subtle and hidden way. In addition to these momentary activation states, there is concomitant deficit of Mentalism or affective attention, which presents mechanisms dependent on neurobiology such as peripheral dopaminergic and

oxytocin neurons. And with the habit of not intervening in harmful behaviors, what is neuromaladaptive and even pathological becomes normal, and the normal and the merely adaptive are scarce and are not identified, with consonant concepts. The evidence shows that reality is not in the same direction as current legal laws, human rights, and objective medical ethics codes are moving in the opposite direction, even if the reference we should follow were civil laws, laws on children's rights, human rights, and codes of ethics. In Brazil, there is much research on the judicialization of Medicine, in which a major problem is medical error, which in many cases is due to professional negligence, or due to bodily injury or due to an ineffective doctor-patient relationship. Several pieces of evidence have shown that complex PTSD or a history of childhood abuse (or both), and even the presence of four or more situations of Adverse Childhood Experiences (ACE), have a negative impact on parenting and on multiple comorbidities, physical and mental, and social risk behaviors, in addition to generating "intergenerational cycles" of trauma.

CONCLUSION

This work described common and predominant states that occupy the space and time of emotional and affective attention, which is currently subtle and hidden from professionals and family members, elucidating a significant participation of neurobiological order, which always acts simultaneously with subjective or personal components, and experienced as experience, and begins to understand the danger of the rigidity of a pattern that is believed to be normal, where the normal does not present neuromaladaptation, but rather adaptation. This study should be reflected upon by professionals in family law and Family Medicine, as there is no assessment and much less protective care interventions for child neurodevelopment, which is sensitive to ACEs, which determine or limit the social, mental and organic life of the child.

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