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Affective Neuroscience and Theory of Mind: An Analysis on Neural Connections

Afektif Sinirbilim ve Zihin Kuramı: Nöral Bağlantılar Üzerine Bir Analiz

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ABSTRACT

Theory of mind is a neurobiological capability that is concerned with the social cognition of living organisms and studied widely in cognitive neuroscience. Affective neuroscience is a comprehensive neuroscientific theory that examines the affective systems of living things from a neurobiological perspective. Affective neuroscience posits that there are 7 different affective systems in the mammalian brain and these systems are activated by subcortical structures. The aim of this article is to try to explain the theory of mind ability described in cognitive neuroscience with affective neuroscience's affective systems and to propose a region for the neuroanatomical structure of the SELF system that encompasses the theory of mind ability. The paper connects the 3 positive affective systems of affective neuroscience, namely SEEKING, PLAY and CARE, through the relationship between theory of mind and empathy. The main conclusion of the study is that theory of mind, which has deep neural connections within the neocortical structures, may be based on subcortical structures. This connection was established through neural circuits extending from the ventral tegmental area to the medial prefrontal cortex for the SEEKING system. However for the PLAY and CARE systems, this connection was established through the anterior medial cingulate cortex and anterior insula for affective empathy; and through the dorsomedial prefrontal cortex, temporopatietal junction and superior temporal sulcus for cognitive empathy. We also argue that the theory of mind and SELF pathway may be encompassed in the pathways of the SEEKING, PLAY and CARE system, starting from the VTA and extending to mesolimbic and mesocortical regions.
Keywords: Cancer, radiotherapy, music therapy, anxiety, fatigue, pain

ÖZ

Zihin kuramı bilişsel nörobilimde tanımlanan ve canlıların sosyal bilişlerini kapsayan genel bir nörobiyolojik yetenektir. Afektif sinirbilim ise canlıların duygulanım sistemlerini nörobiyolojik perspektiften inceleyen kapsamlı bir nörobilim teorisidir. Afektif sinirbilime göre memeli beyninde 7 farklı duygulanım sistemi vardır ve söz konusu sistemler subkortikal yapılar tarafından aktive olur. Bu makalenin amacı bilişsel nörobilimde tanımlanan zihin kuramı yeteneğini afektif sinirbilimin duygulanım sistemleri ile açıklamaya çalışmak ve KENDİLİK sisteminin nöroanatomik yapısı için zihin kuramı yeteneğini kapsayan bir bölge önermektir. Afektif sinirbilimin tanımladığı 3 pozitif duygulanım sistemi olan ARAYIŞ, OYUN ve BAKIM sistemlerini zihin kuramının empati ile olan ilişkisi neticesinde birbirine bağlayabileceğimizi savunuyoruz. Neokorteks yapılarıyla derin nöral bağlantıları olan zihin kuramı işlevi subkortikal yapılardan temel alıyor olabilir. Bu bağlantının ARAYIŞ sistemi için ventral tegmental alandan medial prefrontal kortekse uzanan nöral devrelerle, OYUN ve BAKIM sistemleri için afektif empati açısından anterior medial singulat korteks ve anterior insula; bilişsel empati açısından dorsomedial prefrontal korteks, temporopatietal bileşke ve superior temporal sulkus üzerinden kurulabileceği önerilmektedir. Ayrıca, zihin teorisi ve KENDİLİK yolağının, VTA'dan başlayıp mezolimbik ve mezokortikal bölgeye uzanan ARAYIŞ, OYUN ve BAKIM sistemi yolaklarına dahil edilebileceği görüşündeyiz.
Anahtar sözcükler: Afektif sinirbilim, zihin kuramı, duygulanım, empati, kendilik

Introduction

The hard problem of consciousness, which connects neuroscience to philosophy and is one of the most controversial topics in the literature, investigates how and why the human species has the ability to experience a subjective phenomenon (Chalmers 1995). Panksepp (2017) emphasizes that we need to examine what self is and how it is related to emotions in order to explain conscious minds from a neurobiological perspective. A conscious mind is a mind that contains a "self" (Damasio 2020). Therefore, we need to look for a neurobiological substrate for the concept of the self in to solve the problem of consciousness, then we can define “the subject of phenomenal experiences". However, the theories about consciosness use philosophical concepts for the investigation of mind. Nevertheless, conducting research is also important, as the basic theories in neuroscience

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(e.g. behavioral, cognitive or affective neuroscience theories) seem to be irreconcilable as they approach the brain with different methodologies (Panksepp 2003a). When it comes to the anatomical structure and the functions of the brain, it is important to take a holistic view and to follow a methodology that allows us to consider conflicting theories together (Panksepp et al. 2016), so that we can gain important clues to problems we have yet to solve, such as consciousness and the self. Watt (2007) also puts the concepts together such as empathy and emotions from the perspective of both cognitive and affective neuroscience, and mentions that there is a lack of literature on how subcortical regions of the brain are related to the theory of mind. This gap, which is also pointed out by Singer (2006), overcomes the problem by elucidating the relationship between ToM ability with more primitive mechanisms in the brain.

Theory of mind (ToM) is a social skill associated with social behavior. The environment of the organism is of great importance for this ability because through ToM we can understand how the intentions of organisms differ from our own minds. ToM is a neurobiological ability that helps the organism to orient to organisms other than itself cognitively and to place them on a meaningful level (Frith and Frith 2003, Brüne and Brüne-Cohrs 2006). ToM is associated with neocortex regions (especially frontal regions) and is one of the higher cortical functions in humans, and in the majority of neuroimaging studies. ToM has been associated with the activation of frontal regions (Vogeley et al. 2001, Gallagher and Frith 2003, Singer 2006). Affective neuroscience (AN) is a general neuroscience theory that argues that the subcortical structures of the brain give rise to emotional experiences in the evolutionary process and the affective systems resulting from subcortical activation functionally determine the neocortex in the developmental process (Panksepp 2017, Panksepp and Biven 2021). AN provides a broad theoretical background to cover the ToM. AN combines subcortical and neocortical structures into 7 basic affective systems (SEEKING, PLAY, CARE, LUST, ANGER, FEAR and PANIC) and the SELF system, which is thought to be the basis of the phenomenal experiences of living beings (affective systems are capitalized in the affective neuroscience literature to distinguish between the emotions we use in everyday language and the affective systems in our brains, and in this article, we capitalize affective systems to be faithful to the literature). Affective systems as defined in AN require the brain to work holistically, including the neocortex. According to AN theory, affective systems are analyzed under two headings: Positive affects (SEEKING, PLAY, LUST and CARE) and negative affects (ANGER, FEAR and PANIC). The field of AN extends to almost all of the physiological functioning of the brain, the dynamics of mental functions, and more abstract states such as consciousness (Panksepp 2017, Panksepp and Biven 2021).

There are no studies on the neural connections of AN and ToM in the current literature, so we hope that this article will contribute to the literature. This article aims to reconcile the theory of AN with the ability of ToM with a neuroanatomical perspective, which plays an essential role in cognitive neuroscience; and to propose a neuroanatomical regional explanation for the SELF system based on the relationship between ToM and subcortical structures. Therefore, the study draws attention to the similarities of the neural connections between the affective systems in AN and the ToM. The study will first introduce the theory of AN and basic affective systems, then the neuroanatomical structure of the ToM ability, and in the discussion section, the neural connections between AN and ToM will be discussed, and defined neuroanatomical regions will be proposed for the mechanism of the SELF system.

Fundamental Theses of Affective Neuroscience

AN is a theory that examines the neurobiology of affect and has an important place in disciplines such as ethology, neurology, psychiatry, psychology and neuropsychoanalysis. The main claim of AN is that affective systems should have the capacity for subjective feeling states that reveal affective value in addition to basic psychological criteria (Panksepp 2017). A controversial principle of AN is that affective processes, including subjective experienced feelings play a key role in the causal chain of events. It has a central role in the execution of the actions of both humans and animals. Subjectively experienced feelings ultimately emerge from the interaction of various emotion systems that are the basic infrastructure of the self (Panksepp 2017). According to Panksepp and Biven (2021), the neocortex works as a kind of “tabula rasa”; subcortical structures are shaped through experiences and affect the neocortex, and through epigenetic changes caused by environmental factors. Then neocortex matures with a modular organization that appears to be “programmed” (Davis and Montag 2019, Panksepp and Biven 2021). Neural circuits in the neocortex are critical to the performance of our higher cortical functions: thinking, decision-making, speech, comprehension, etc. According to AN theory, the neocortex operates our cognitive functions and has some functional regions directly related to subcortical structures in emotion processing (Damasio et al. 2000, Panksepp and Biven 2021). AN attempts to provide an integrated interpretation of the behaviors of living beings based on their affective systems. The research is conducted in the different mammalian brains.

When negative affective systems associated with stress and aggression are activated, brain regions such as the amygdala and hypothalamus take an active role and a "fight-flight" response is often shown (Sapolsky 2004). However, activated negative affective systems by stress inhibits frontal lobe activity (Panksepp 1990, Arnsten et al. 2015). Moreover, frontal lobe damage or dysfunction of these regions is associated with aggression (Brower and Price 2001). Likewise, when positive affective systems, which play a role in the animal's survival and are associated with the approach response, are activated, frontal lobe activity increases (Burgdorf and Panksepp 2006). In this way, the brain has the necessary cognitive resources to fulfill its needs and SEEKING system arises. It is important to note that the SEEKING system has a significant direct or indirect relationship with all other systems. The SEEKING system is shown as the oldest evolutionary affective system in AN because it has a vital role in survival (Panksepp and Biven 2021).

The fundamental theses of AN theory can be listed as follows:

a. Mammals are conscious beings, and their survival capacity strengthens thanks to their affective systems; all mammals have evolved to feel emotions (Panksepp 2017, Davis and Montag 2019).

b. Experiencing affects does not require learning behavior, affective systems play an active role for organisms to learn environmental experiences and function as a reward-punishment system (Panksepp 2017, Davis and Montag 2019, see also Fuchshuber et al. 2022).

c. Neocortex activity is not required to experience affects. Affects are products of subcortical activation, and the function of the neocortex is emotion regulation or emotion inhibition. Therefore, cortical damage in the mammalian brain does not impact affective systems but can impact functions such as emotion regulation. On the other hand, damage to deep subcortical structures can negatively impact the entire emotional and cognitive performance of the animal (DeMolina and Hunsperger 1962). For these reasons, it can be inferred that the mammalian brain is based on an evolutionary hierarchy (Panksepp 2017, Davis and Montag 2019).

d. Neocortex structures are blank slates at the time of the birth of a living being and this blank slate is filled by interacting with subcortical structures during development. Therefore, living beings gain their experiences through subcortical structures, and the task of the neocortex is to provide cognitive and emotional control based on these experiences. In short, there is a bottom-up unilateral determinism between corticals 2023). Solms 2023).

e. Affective systems provide the psychobiological basis of personality. Therefore, knowing how the affective systems operates the organisms means that we can analyze their personality structures. Extremes or abnormalities in these systems lead to psychiatric disorders, and for AN theory, psychiatric disorders have a subcortical basis, just like personality (Özkarar-Gradwohl et al. 2014, Panksepp 2017, Davis and Montag 2019, Panksepp and Biven 2021).

f. Negative affective systems cause inhibition in neocortex activity, whereas positive affective systems cause excitation in neocortex activity (Damasio et al. 2000, Burgdorf and Panksepp 2006, Panksepp 2011a, Panksepp and Biven 2021).

This section will introduce the 7 basic affective systems and the SELF system.

SEEKING System

The SEEKING system is one of the oldest and fundamental affective systems based on the subcortical structures of the mammalian brain (Panksepp and Biven 2021). It constitutes the affective substructure that enables animals to care for their offspring, build social communities, and search for sexual partners and hunts. In humans, the ability to think strategically is a functional factor in the SEEKING system. In this respect, AN theory claims that higher cortical functions in humans are significantly linked to SEEKING (Panksepp and Biven 2021). The functions of the SEEKING system are listed in six items: 1- Providing general behavioral activation. 2- Creating a state of willingness to manage the stimulus. 3- Ensuring the continuity of behavior. 4- Providing/managing exchanges between behavioral teams. 5- Realizing simple approach behavior. 6- Modulating/creating reward anticipation error (Panksepp and Biven 2021). Motivational signals that impact the functioning of the neocortex come from subcortical structures, and one of the most critical subcortical structures related to this is the SEEKING system (Panksepp and Biven 2021).

The SEEKING system is anatomically originated from the lateral hypothalamus and, connects the limbic system with many brainstem regions, and extends to the neocortex through connections with the medial frontal cortex.

Through pathways extending from the prefrontal cortex, hippocampus and basolateral amygdala to the nucleus accumbens, the SEEKING system processes the data coming into the brain (Wright and Panksepp 2012). Furthermore, AN theory has linked the SEEKING system to the medial prefrontal cortex via three bundles originating from the ventral tegmentum, from the lateral hypothalamus to the nucleus accumbens, and from the medial prefrontal cortex to mesolimbic and mesocortical dopaminergic pathways. In this respect, the nucleus accumbens is considered as a critical region for the SEEKING system (Panksepp 2017, Panksepp and Biven 2021). Since activation in the nucleus accumbens is associated with motivational and affective functions, it has been suggested that it is a central component of the limbic-motor system, and studies revealed that dopaminergic neurons increases the activity in the limbic-motor system (Blackburn et al. 1992). Another study shown that the dopaminergic throught the nucleus accumbens allows living beings to direct their attentional resources to new situations and extract "meaning" from them. It helps them to establish dynamic relational connections between the events experienced and the values attributed to these events (Ikemoto and Panksepp 1999).

Dopamine is one of the prominent neurotransmitter in SEEKİNG system. It involves reward and learning mechanisms in the brain (Wright and Panksepp 2012). In addition, the SEEKING system is also linked to norepinephrine and serotonin pathways, especially acetylcholine, GABA and glutamate (Panksepp 2017, Montag and Davis 2018). NMDA receptors, a glutamate receptor, have been found to have a role in positive emotional learning in the medial prefrontal cortex (mPFC) and show similarities with mechanisms governing synaptic plasticity in the hippocampus (Burgdorf et al. 2011). In particular, neural integration of glutamate and dopamine signals in the nucleus accumbens is a critical element for the control of cellular plasticity underlying reward-based learning behavior (Hernandez et al. 2005). Furthermore, the dopamine systems of the ventral tegmental area and ventral striatum are essential for reward and arousal, to which we should add that the SEEKING system stimulates the anticipation of reward rather than the reward itself (Ikemoto 2010, Coenen and Schlaepfer 2012, Panksepp 2017). The neurotransmitter systems mentioned in these studies work as part of the SEEKING system. Orexin, a neuropeptide that stimulates affective systems such as FEAR by creating homeostatic imbalances, is also among the stimuli of the SEEKING system (Panksepp and Biven 2021). On the other hand, GABA has been shown to have an inhibitory effect on the reward-seeking system, so GABA can be considered to have an inhibitory function for the SEEKING system (Ikemoto 2010). Just like in other affective systems, the role of opioids is also essential in the SEEKING system; low doses of opioids release near the dopaminergic region can increase the activity of the SEEKING system, which is thought to be due to the inhibition of nearby GABA neurons by opioids (Ikemoto 2010, Panksepp and Biven 2021).

ANGER System

ANGER system is an affective system that can be easily aroused when physical activity is limited by an external factor, homeostatic imbalances caused by hunger or sensory displeasure on the body's surface. ANGER system can also be aroused when the activity of SEEKING system is inhibited (e.g. if a promised reward is suddenly withdrawn). ANGER system is system found in all mammalian brains, this is a higly effective mechanism for all the species (Panksepp and Biven 2021). In addition, Panksepp (2017) claims that classical conditioning of ANGER can develop quickly and states that conditioned rage responses can occur when certain neutral stimuli are paired with unconditioned stimuli related to rage. One of the best ways to achieve this is to stimulate specific brain regions related to ANGER.

Because it is possible to find some similarities between ANGER and SEEKING systems (e.g. aggression during hunting behavior or "calm biting"), two affective systems can be used instead wrongly. SEEKING system is a basic affective system that is tightly connected to the other affective systems, so when ANGER system is activated, and one of the organisms is going to attack the other, SEEKING system will necessarily be activated due to the orienting need of the aggression. The hunting rush seen in living things is controlled by SEEKING system rather than the ANGER system. The counterpart of this situation in humans can be exemplified by their effort to win an argument (Panksepp and Biven 2021).

The ANGER system starts from the medial amygdala and extends to medial hypothalamus and periaqueductal gray matter (PAG) via stria terminalis. ANGER system proceeds hierarchically, according to which subcortical structures are more important than neocortex in ANGER affect (Blair 2011, Panksepp and Biven 2021). The PAG is the critical structure here. The effect of PAG-induced ANGER can continue to be aroused even if the activation of higher brain regions (amygdala and hypothalamus) is inhibited (DeMolina and Hunsperger 1962). According to hierarchical structure of the system, the most critical importance lies first in the PAG, then in the hypothalamus and finally in amygdala. For example, ventromedial hypothalamic lesions intensely stimulate ANGER, although the exact cause is unknown. Animals being exposed to these lesions become untouchable

without protective clothing (Panksepp and Biven 2021). In brain imaging studies on the affect of ANGER, activations in parietal regions with inhibition in left frontal cortex were observed when people felt angry (Kimbrell et al. 1999). In other studies, activations were observed in anterior and posterior cingulate cortex, amygdala and orbitofrontal cortex. They are thought to be related to ANGER and it is plausible that the activation in orbitofrontal cortex occurs to inhibit ANGER (Blair et al. 1999, Berlin et al. 2004).

Chemicals that stimulate ANGER include testosterone, substance P, norepinephrine, glutamate, acetylcholine and nitric oxide combinations. Along with norepinephrine blockers, serotonin, GABA (since it is the main inhibitor), oxytocin, and endogenous opioids are chemicals that can inhibit the ANGER affect (Panksepp and Biven 2021).

FEAR System

Like other affective systems, FEAR system is evolutionarily innate in living beings and adapted to our social practices through learning mechanisms (Panksepp and Biven 2021). The FEAR system runs from PAG to amygdala and then back down again. Stimulation of these pathways can trigger chronic anxiety. Frontal lobe and amygdala can be stimulated even when fear stimuli are distant. This leads to the so-called "fight or flight" response. When parts of the PAG related to FEAR are directly stimulated, animals experience feelings of terror (Adamec 2001). Similarly, electrical stimulation of the amygdala elicits such behaviors similar to natural or conditioned fear states (Ressler 2010). Moreover, amygdala may exhibit plasticity that mediates both the acquisition and elimination of conditioned fear (Davis 1992). The anatomy of FEAR system depicts a bidirectional network extending from the central nuclei of the amygdala to the ventral-anterior and medial hypothalamus, enveloping the third ventricle and extending to specific dorsally located regions of mesencephalic PAG. Feeling of fear causes activation in deep subcortical affective systems and is shared by all mammalian brains, regardless of their level of cognitive ability (Panksepp 2017, Panksepp and Biven 2021). Just like ANGER system, FEAR system is known to evolve hierarchically, so the amygdala is not absolutely necessary for the feeling of fear to occur, but PAG and hypothalamus are absolutely critical (Panksepp and Biven 2021). In a human study, fear sensations were generated with stimulation of lateral and medial midbrain structures (Nashold et al. 1969).

Benzodiazepines are frequently encountered as drugs that can inhibit the FEAR system. Although the serotonin molecule is also known to inhibit the FEAR system, it is thought that antidepressants generally exhibit inhibition in all affective systems. In this case, serotonin is generally an inhibitory factor for FEAR system, not specifically (Panksepp and Biven 2021). It can also be accepted that GABA inhibits FEAR system since it is the main inhibitory molecule (Panksepp et al. 2011). The neurotransmitters mainly investigated regarding the FEAR system can be listed as follows: glutamate, oxytocin, alphaMSH (alpha melanocyte stimulating hormone), corticotropin and cholecystokinin (Montag and Davis 2018).

LUST System

The LUST system is divided into two distinct anatomical systems for biological sex function. In male brains, medial anterior hypothalamus plays a critical role for the rate of effectiveness of LUST. From an evolutionary perspective, interstitial part of anterior hypothalamus is an important anatomical area. However, the chemicals associated with sexual behavior are also important. In infants, testosterone is secreted just before and after birth. In females, ovarian estrogen matures and progesterone steroid production initiates puberty. In males, sexual arousal occurs when the testes produce abundant testosterone. Chemicals associated with female and male sexual behavior are linked to many subcortical brain regions, especially hypothalamus's anterior hyptothalamus. Sexual arousal in females, unlike in males, originates in ventromedial part of the hypothalamus. Male's sexual drive is linked to anterior hypothalamus's preoptic area (POA) (Panksepp & Biven 2021). The neuroanatomical correlates of sexual behavior are associated with neural connections including hypothalamus and PAG (Calabro et al. 2019). Moreover, a study with cats showed that PAG is particularly decisive in performing mating behavior (Holstege and Huynh 2011). This aligns with the neuroanatomical perspective of Panksepp and Biven (2021). In a review study about sexual function of brain, it has been suggested that neuroanatomical structures are related to sexuality and these have co-evolved with mesocortical pathways in evolutionary terms (Damasio and Carvalho 2013, Berridge and Kringelbach 2015). This may indicate that SEEKING system may contain LUST system, as it does the other affective systems. The behavior of seeking all pleasurable states, including dopamine-provided sexuality in affective euphoric movements, is linked to SEEKING system (Panksepp and Biven 2021). For example, Fuchshuber and his colleges (2022), developed a psychometric measurement tool of LUST system, and argued that the interconnection between SEEKING and LUST systems

is important for the learning process and that "desire" comes out with SEEKING system and the "liking" action in LUST system is involved to provide learning behavior. Since LUST system is a positive affect, it is not expected to inhibit neocortex activation, whereas a study on the sexual behavior of cats showed that left temporal lobe and ventral prefrontal cortex were strongly deactivated during sexual stimulation (Holstege and Huynh 2011). This contradicts the ideas proposed by Panksepp (Burgdorf and Panksepp 2006, Panksepp 2010, Panksepp 2011a) regarding the relationship of positive affective systems with the neocortex.

CARE System

The CARE system refers to some behavioral patterns of organisms such as feeding, nurturing, caring, and showing interest (Panksepp and Biven 2021). The release of oxytocin, a peptide hormone, is associated with maternal, sexual and social attachment behaviors (Kendrick 2000). These oxytocin-mediated behaviors in CARE system play an important role in positive social interactions (Uvnas-Moberg 1998). The CARE system is assumed to be evolutionarily intertwined with the LUST system (Panksepp 2010). Although the CARE system is conceptually an affective system that is not associated with sexuality, it is known that neurochemicals involved in sexual behavior (e.g. oxytocin) also play critical roles in CARE system (Panksepp et al. 1997, Kendrick 2000, Panksepp 2009, Feldman et al. 2010).

Oxytocin levels, which regulate social relationships in mammals are much higher in females than in males (Marazziti et al. 2019). The hormone estrogen accompanies oxytocin production throughout cells in anterior hypothalamus, including paraventricular nucleus (PVN) and dorsal preoptic area (dPOA) (Burbach et al. 2006). Lesions in PVN significantly inhibit maternal behavior in first-time mother rats (Insel and Harbaugh 1989). Rats that have never been mothers exhibit maternal behaviors when they are in the same cage with their mothers, and these behaviors are associated with increased activity in oxytocin neurons in PVN regions of non-maternal rats (Carcea et al. 2021). A lesion in the dPOA completely abolishes maternal behavior (Numan and Callahan 1980, Numan and Insel 2003). Estrogen and progesterone levels govern oxytocin receptors at several oxytocin-releasing sites, including the nucleus bed of stria terminalis (BNST) and ventromedial hypothalamus (Gimpl and Fahrenholz 2001, Acevedo-Rodriguez et al. 2015). Activation is BNST region is effective in regulating the pain of separation. Mothers experience restlessness when their babies are lost through activation of BNST (Panksepp and Biven 2021). At the same time, oxytocin injection produces a physiologically antistress effect, which is permanent despite the administration of oxytocin antagonists because it impacts opioid system (Uvnas-Moberg 1998).

A branch of the CARE system runs from ventral tegmentum to hypothalamus, incorporating SEEKING system (Panksepp 2017, Panksepp and Biven 2021). This part of CARE system may stimulate some behaviors that can be attributed to SEEKING system. In this respect, goal-directed behavior in maternal motivation to attend to infant's needs may result from coordinated work of SEEKING and CARE systems. Such maternal behaviors were observed when oxytocin was injected into VTA (Panksepp and Biven 2021). Likewise, a maternal behavior such as breastfeeding provides an increase in oxytocin equivalent to oxytocin injection in many subcortical regions, especially in VTA (Febo et al. 2005).

PANIC System

The arousal of the PANIC system makes us feel abandoned and sad, but once sadness subsides and we enter a safe space, we feel peace and security thanks to endogenous opioids and oxytocin systems of CARE system. Constant arousal in PANIC system is one of the factors that can cause chronic mood pathologies, and if young children grow up with inadequate attention (abandonment, neglect, abuse), then the resources of SEEKING system can be depleted, and mood disorders can occur (Panksepp & Biven, 2021). The feeling of sadness is prominent for PANIC system. It was shown in a study that activations were observed in the anterior cingulate cortex, dorsomedial thalamus, periaqueductal gray matter and some primitive cerebellum regions during feeling of sadness (Damasio et al. 2000).

In animals, PAG, dorsomedial thalamus, ventral septal region, and stria terminalis nucleus were related to sadness (Panksepp et al. 1988). It is thought that the PANIC system evolved from primitive pain mechanisms in brain stem. The inhibition by opioids of both physical pain and behaviors, such as "separation call" that occurs when animals experience abandonment, may provide evidence for this. Separation pain does not originate from cortical-cognitive mechanisms but from deep affective medial brain regions such as the PAG. Like the PANIC response, FEAR and ANGER responses are produced in dorsal PAG, which controls the affective aspect of physical pain. According to affective neuroscience, the affective sensation seen in the PANIC system has evolutionary is related to the old affective messages of physical pain (Panksepp and Biven 2021).

It can be said that PANIC responses also occur during irregular homeostatic imbalance; homeostasis is provided by the activity of SEEKING syste. In this respect, PANIC and SEEKING can be considered as two opposite systems (Coenen et al. 2011). The effect of amygdala in PANIC was shown in a study. Accordingly, there was activation in amygdala (negative) in the state of sadness and that this activation was modulated by dorsolateral prefrontal cortex and rostral anterior cortex (Freed et al. 2009). Another study found deactivation of μ-opioid neurotransmission in rostral anterior cingulate cortex, ventral pallidum, amygdala and inferior temporal cortex in sustained sadness (Zubieta et al. 2003).

Lastly, three different neuropeptides are known to inhibit PANIC responses. The first one is endogenous opioids, which can cause addictive behavior. The other two are oxytocin and prolactin, which are also related to CARE system. When the amount of neuropeptides decreases in brain, the organism may have a PANIC response. When the amount increases, social bonding may occur, in a positive way and the release or supplementation of opioids increases, symptoms such as depression and sadness may disappear (Panksepp et al. 1980, Panksepp 2017, Panksepp and Biven 2021). According to another study, three neurotransmitter systems that can explain PANIC responses were identified as follows: endogenous opioids, oxytocin and dopamine. Dopamine release may occur during sadness in response to cues reminiscent of the object of sadness (Freed and Mann 2007).

PLAY System

PLAY system, a positive behavior in the mammalian brain, is inherited (Burgdorf et al. 2007, Panksepp and Biven 2021). The PLAY system enables the creature to prepare for social life, develop hunting and searching impulses, and acquire social skills such as aggression, flirting, sexuality, competition, parenting, and coping with unexpected dangers (Spinka et al. 2001, Panksepp and Biven 2021). Social play is considered as a distinct and unique behavior (Vanderschuren et al. 1997). Although the studies related to neuroanatomy of PLAY system are still new, it is known that this system originates from subcortical structures and does not even require cortex (Pellis et al. 1992). Neonatal rodents that have had their cortex removed have been found to participate in play to fight as juveniles (Pellis et al. 1992, Panksepp et al. 1994). The sensory components of touch that lead to PLAY behaviors do not first send signals to neocortex but to posterior dorsomedial thalamic nuclei (Siviy and Panksepp 1987a). Some lesions in thalamus, which processes tactile information, have been shown to inhibit PLAY behavior (Siviy and Panksepp 1985, Siviy and Panksepp 1987b). Lesions in ventromedial hypothalamus (VMH) also impair PLAY behavior because they make animals pathologically aggressive (Lammers et al. 1988, Kruk 1991). Amygdala has also a important role in PLAY behavior; monkeys and cats with temporal lobectomy, including amygdala, have been found to exhibit hypersexual behavior and are not interested in PLAY behavior (Klüver and Bucy 1939 cited in Panksepp and Biven 2021). In addition, dorsomedial diencephalon, parafascicular region and PAG are also brain structures associated with PLAY system (Siviy and Panksepp 1985, Siviy and Panksepp 1987b, Montag and Davis 2018). However, the cortex is not completely dysfunctional in PLAY system. For example, it was shown in a rodent study that mPFC lesions indirectly impaired general social behavior, self-care and social play by affecting response selection and attention processes (Schneider and Koch 2005), and this is known to lead to the same results in humans (Anderson et al. 1999, Hall and Solowij 1998, Eslinger et al. 2004). Since the neuroanatomical findings of PLAY system are mostly based on studies on laboratory animals, we cannot directly say that these regions are related to PLAY system in humans. However, studies with Affective Neuroscience Personality Scale (ANPS) (Davis and Panksepp 2011, Montag and Panksepp 2017) and studies on attention deficit hyperactivity disorder (Panksepp et al. 2003, Panksepp 2007) draw attention to the fact that PLAY system are similar in humans and animals.

It is known that there is opioid release during PLAY behavior, especially in the preoptic area (an area also critical for the LUST and CARE systems), suggesting that opioid release (especially morphine, Vanderschuren et al. 1995) and PLAY system (and hence social behavior) work together (Panksepp and Bishop 1981). Along with opioids, neurochemicals such as glutamate, acetylcholine and endocannabinoids may also be related to PLAY system (Vanderschuren et al. 1997, Montag and Davis 2018).

SELF System

SELF system is a dynamic structure in brain. It is driven by primary process mechanisms and is originated in subcortical structures. The same subcortical circuits basically produce harmonious emotional movements and primary feelings. The term “core SELF” is used as a qualitative concept to explain subcortical processes that ensure the organism’s adaptation (Panksepp and Biven 2021). Human beings have become aware of their experiences throughout the brain’s evolutionary process. According to affective neuroscience, this awareness or “consciousness” requires a “core” system of “SELF” because as the organism gains awareness of its phenomenal

experiences, it becomes a subject of this awareness. The subject's most basic core state can be called "core SELF".. It was suggested in a study focusing on SELF and the evolution of consciousness from the perspective of affective neuroscience that SELF system could be neuroanatomically represented by hypothalamus, thalamic reticular nucleus, superior colliculus, optic tectum and PAG structures located in subcortical regions (Fabbro et al. 2015). Some studies linking to SELF and self-referential processing with cortical midline structures (medial orbital prefrontal cortex, ventromedial prefrontal cortex, supragenual anterior cingulate cortex, dorsomedial prefrontal cortex, medial parietal cortex, posterior cingulate cortex, pregenual anterior cingulate cortex and retrosplenial cortex) and subcortical structures have tie neural connections with each other, it has been concluded that cortical midline structures may provide a neuroanatomical basis of SELF system (Panksepp 2003b, Northoff et al. 2006, Northoff and Panksepp 2008, Panksepp and Northoff 2009).

Affective neuroscience hypothesizes that there are two types of phenomenal consciousness; first the ability to experience diversified positive and negative affects, and second, ability to percieve the outer world in experiential ways. These compose the basis of cognitive awareness. The first type of phenomenal consciousness (the ability to experience positive and negative affects) must have evolved with the evolutionary analysis of brain. Accordingly, it was noted that the first structure related to this ability correspond to primitive regions of the brain, namely medial and caudal parts. The most critical of these regions is PAG, which also plays an active role in many other affective systems. Homeostatic systems are concentrated in the midline structures of hypothalamus in the evoluiton. This may be one of the reasons why affective systems that try to respond to need systems (such as SEEKING, FEAR, ANGER) interact with hypothalamus. Moreover, these affective systems are directly linked to SELF system, and experience of SELF is neurodynamically involved in the activation of these affective systems. For example, the scent of predators activates FEAR system in animals, where core SELF experiences feelings of fear and dread (Panksepp 2017, Panksepp and Biven 2021).

Due to the difficulty of studying SELF system anatomically, subcortical structures of the system have not been fully characterized. Nevertheless, in comparison with other affective systems of affective neuroscience, some criteria have been proposed for the candidate regions for the anatomy of the SELF system: 1) the structures in the system should be located in primitive regions of the brain that formed during the evolutionary process, 2) they should be located in many parts of the neuro-axis and be multimodal, 3) the system should have a stable structure and its homeostatic deviations should be detectable, 4) the primary process should be excitable in certain situations in affective states, i.e. it should contain connections with the rest of brain (Panksepp and Biven 2021). The subcortical brain structures may meet these criterias as follows: (i) The deep nuclei in pons, the parabrachial area and dorsal motor nucleus of vagus. (ii) PAG and surrounding midbrain regions. (iii) Superior and inferior colliculus, especially their deep motor components. (iv) Ventral tegmental area (VTA). (v) Hypothalamus. (vi) A series of basal ganglia nuclei, especially amygdala and nucleus accumbens (Panksepp and Biven 2021). Among these circuits, the deep motor layers of the superior colliculi, VTA and hypothalamic circuits connected to them, and PAG nucleus are critical regions for SELF-consciousness because consciousness is not damaged in the absence of other regions (Panksepp 2017, Panksepp and Biven 2021).

Theory of Mind

Theory of mind (ToM), in its most general sense, refers to the capacity to perceive and think about what is happening around us. As one of the fundamental steps in human evolution and an essential element for social cognition, ToM is linked to the activity of certain neural pathways. Therefore, it is closely related to the concept of "social brain" (Brothers 1990). Historically, the emergence of the ToM dates back to a paper published by Premack and Woodruff (1978), primatologists who studied primate behavior. According to them, since a creature with some kind of inferential system cannot directly observe phenomenal states in other creatures, and since its inferential system is more capable of drawing possible conclusions and predictions from the behavior of other creatures, there is a "theory" of other minds, and our capacity to propose this theory is called as theory of mind (Premack and Woodruff 1978). When Premack and Woodruff (1978) examined the problem-solving styles of the chimpanzees they studied, they discovered that chimpanzees arrived at solutions based on the mental states of their trainers (i.e., the trainers' intended behaviors or information). Abilities such as empathy, reasoning capacity, blundering, belief, the capacity to lie, and the capacity to make guesses about what others are thinking require ToM mechanism. In this regard, for example, it was noted in a study that this ability is not operated properly in individuals with autism spectrum (Baron-Cohen et al. 1985). According to Keysers (2019), an individual with autism may lack the ability to think about what others might be thinking, even though he or she/ they may have sufficient logical reasoning skills to pursue a PhD in theoretical physics. A disruption in the neurobiological activities at the root of ToM will also affect our social behavior (Brüne and Brüne-Chors 2006).

Theory of mind is explained with developmental neurobiology. Accordingly, Neural plasticity and mirror neurons are generated during developmental stages (Sinigaglia and Rizzolatti 2019, Constandi 2019). It is generally accepted that by the age of 5 years, ToM is almost complete in children (Langley et al. 2022). According to Baron-Cohen's (1995 cited in Langley et al. 2022) developmental model, 6-month-old human infants can distinguish between the movements of animate and inanimate objects, around the age of 1 year, self-perception gradually begins to develop, and joint attention develops, and 14-18-month-old infants begin to recognize the causal relationship between desires, intentions and emotions and goals. The studies noted that genes and environment (epigenetic mechanisms) are also important in ToM. It has been shown that the genetic factor increases as the age ratio decreases, especially with language use, rapid development of ToM functioning is observed (Hughes and Cutting 1999). A study on twins showed that the genetic infrastructure was more important than environmental factors in TOM mechanisms (Roland et al. 2006). It was found in another twin study that ToM function was almost equally related to genes and environment (Isaksson et al. 2021). These findings are open to interpretation in opposition to the "tabula rasa" approach of AN theory.

The range of pathological conditions in which theory of mind is impaired is quite wide. It is possible to observe inhibition of ToM function in neurodevelopmental, psychological and neurobiological disorders. Although autism (Baron-Cohen et al. 1985) and schizophrenia (Değirmencioğlu et al. 2018, Braak et al. 2022) are frequently cited as examples in this regard, it is also observed that ToM function is impaired in conditions such as lesion studies, cases of early abuse, language impairment, deafness, attention deficit and hyperactivity disorder, dementia and Parkinson's disease (Westby 2014). ToM disorders are associated with social dysfunction in neuropsychiatric samples (Braak et al. 2022). In particular, research on brain damage provides us with a rich body of knowledge in terms of understanding both the neurobiology and psychopathology of ToM ability (Winner et al. 1998, Frith and Frith 2003).

Neuroanatomy of Theory of Mind

Functional magnetic resonance imaging (fMRI) is used chiefly in studies on the localization of ToM. The areas consistently associated with ToM are medial prefrontal cortex (mPFC), superior temporal sulcus (STS) and temporo-parietal junction (Fletcher et al. 1995, Vogeley et al. 2001, Kana et al. 2014, Jiang et al. 2017, Mukerji et al. 2019, Ogawa and Kameda 2019). In a review study (Siegal and Varley 2002) it was noted that some subcortical structures such as the amygdala showed activation during tasks requiring ToM included. In addition, frontal cortical regions and right temporal-parietal cortex are also important. For example, an fMRI study found that dorsolateral prefrontal cortex (DLPFC), temporo-parietal junction (TPJ), posterior STS and mPFC regions were activated in high eye contact compared to mouth fixation during verbal communication, and there was an increase in activation in the related regions as well (Jiang et al. 2017). In another fMRI study, mPFC was found to be associated with ToM (Gallagher et al. 2000). In addition to mPFC, orbitofrontal cortex (OFC) is also associated with ToM (Siegal and Varley 2002). In a study conducted with patients with bilateral damage to the OFC and unilateral damage to left DLPFC, patients with bilateral damage to OFC were successful in simple tests of ToM, but failed in tests requiring fine social reasoning skills such as faux pas. On the other hand, patients with unilateral damage to left DLPFC did not show a specific lack of ToM abilities but only had difficulty in tests requiring the use of working memory (Stone et al. 1998). This study suggests that OFC is associated with complex levels of ToM ability.

A study using positron emission tomography (PET) found that posterior cingulate, STS, mPFC and bilateral temporal poles were associated with ToM (Fletcher et al. 1995). Another study examining brain activation of watching and imitating emotional facial expressions found that passively watching emotional faces caused activation in right ventral premotor area while imitating emotional faces caused bilateral activation (Leslie et al. 2004). These studies showed that ToM is spread throughout the cortex, but certain regions are more active. It is known that frontal cortex is of great importance in ToM tests that require fine judgment, such as irony. In a related study, irony comprehension ability was tested in patients with prefrontal and posterior damage, and it was found that patients with prefrontal damage performed poorly. Especially in patients with right ventromedial PFC damage, irony skill performances were worse (Shamay-Tsoory et al. 2005). This study showed that prefrontal lobe plays a vital role in the complex levels of ToM. It is possible to examine ToM in studies conducted with both healthy children and children diagnosed with autism spectrum disorder (ASD). In an fMRI study conducted with children without ASD, more activation was found in bilateral TPJ, precuneus, and right STS during false belief when the false belief (ToM) condition was compared with a control condition containing non-mental false content (Mukerji et al. 2019). In a study conducted with children diagnosed with ASD, children who failed the tests showed less activation in the TPJ, right inferior frontal gyrus and left premotor cortex (Kana et

al. 2014). These regions were also activated in healthy adults in skills requiring ToM. For example, right TPJ plays a critical role in games against real people, whereas left TPJ plays an essential role in games against computers that require second-order inferences (Ogawa and Kameda 2019). As a result, trying to understand others' emotions activates some areas in temporal and mPFC (Corradi-Dell'Acqua et al. 2014).

In summary, MPFC, STS and TPJ are highly correlated with ToM. In the light of the conducted studies, it can be inferred that the regions associated with ToM are located in the temporal, parietal and frontal lobes and that ToM is also associated with some limbic-paralimbic structures (amygdala, mPFC, OFC, anterior cingulate cortex) (Şahin et al. 2019). While making sense of others' thoughts and orientations is defined by cognitive ToM ability, making sense of others' feelings and emotions is characterised by affective ToM ability (Shamay-Tsoory et al. 2009). Experimental studies on affective ToM show that affective ToM tasks are anatomically separated from cognitive ToM tasks by the ventromedial PFC (Shamay-Tsoory et al. 2005, 2006). The amygdala does not play a critical role in cognitive ToM tasks but is decisive in affective ToM tasks (Mier et al. 2010). Völlm et al. (2006) also observed activation of the parasingulate cortex, anterior cingulate cortex, posterior cingulate cortex and amygdala in affective ToM tasks. The overlapping regions in cognitive and affective ToM tasks focus more on the mPFC, TPJ, posterior STS and precuneus (Poletti et al. 2012, Schlaffke et al. 2015). On the other hand, according to another study, while cognitive ToM tasks require precuneus, cuneus and temporal lobe regions, affective ToM tasks require small structures of the posterior cingulate cortex and basal ganglia along with the structures of the prefrontal cortex (Schlaffke et al. 2015).

Possible Neural Connections between Theory of Mind and Affective Systems and their Relation to the SELF System

One of the aims of this article is to focus on possible neural connections between AN theory and ToM. First of all, we will look at the relationship between the ToM ability and the basic arguments of AN theory. The main arguments of AN theory were presented in the last part of section 2. According to arguments (a) presented here, it was argued that affective systems have contributed to evolutionary adaptation and that the ToM ability evolved as an adaptive ability for complex social interaction in primates (Gerrans 2002, Brüne and Brüne-Cohrs 2006, Chung 2021). These (b) are related to learning behavior and AN mechanisms, according to which the affective systems play an active role in enabling organisms to learn environmental experiences, and ToM also contributes to learning process (e.g., learning by imitation) (Gopnik and Meltzoff 1993). Thus suggesting that the affective systems and the ToM may work together in the learning process. According to argument (c), experiencing affect does not require the neocortex, so at first glance, it may seem that affect does not require the ToM. Still, studies on affective ToM suggest that ToM activity helps people experience emotions (Mier et al. 2010, Lane et al. 2015, Schlaffke et al. 2015). It is known that subcortical structures also play an active role in affective ToM tasks (Siegal and Varley 2002, Völlm et al. 2006, Mier et al. 2010). This does not make the argument false (c), because the fact that ToM is linked to the experience of affect does not exclude the necessity of affective systems. Another approach (d) argues that neocortex appears as a blank slate in the early developmental stages of living beings and is "filled in" through its interaction with subcortical structures. Therefore, most cortical regions associated with ToM may also develop by interacting with subcortical structures in the developmental processes. It means that AN systems may determine ToM. According to studies focusing on the development of ToM ability, ToM develops in children between 3-5 years of age (Perner and Lang 1999, Wellman et al. 2001, Langley et al. 2022). If we accept this approach (d) as true, we can also suggest that affective ToM ability, which is more related to subcortical structures, develops earlier than cognitive ToM ability (Montague and Walker-Andrews 2001, Saxe et al. 2004, Mier et al. 2010). Argument five (e) establishes a relationship between affective systems and personality. There is a lack of scientific literature on how ToM ability impacts personality, but there have been some statistical studies on ToM and personality disorders (e.g. Murphy 2006). Argument six brings that (f), neocortex activation is inhibited during negative affect and stimulated during positive affect. This suggests that neocortical structures associated with ToM should be inhibited during activation of intense negative affect and stimulated during positive affect. Thus, there may be a positive correlation between ToM activation and the activation of the positive affect systems of SEEKING, PLAY, CARE and LUST. Likewise, we can suggest a negative correlation between ToM activation and the activation of the negative affect systems ANGER, PANIC and FEAR. Based on this argument (f), we suggest that since the neuroanatomical structures of ToM are primarily located in cortical regions, possible neural connections between the ToM and AN could be established through positive affect systems.

The neurotransmitter networks of the SEEKING system is operated through dopaminergic pathways to cortical systems. The basis of the system is medial prefrontal cortex (mPFC), which is thought to be fundamental for both affective and cognitive ToM (Poletti et al. 2012, Schlaffke et al. 2015). A study conducted with rats found

that mPFC activation increased when a foreign rat was in the environment but not when it was with an inanimate object or in an empty environment (Lee et al. 2016). Accordingly, mPFC activation may occur as a response to the presence of foreign organisms in the environment. Overlapping regions in cognitive and affective ToM tasks focus more on mPFC and TPJ areas (Schlaffke et al. 2015). It can be suggested that the primary motivation for the activation of mPFC in creatures with ToM is the functioning of SEEKING system. The animal behaviorally scans the environment to animate and inanimate objects, and if there is a living object in the environment, mPFC is activated as predicted by SEEKING system. Thinking about the psychological state of a living being, whether human or dog, has been associated with increased activation in mPFC region compared to thinking about its body parts (Mitchell et al. 2005). Given that mPFC is activated when thinking about others (Amodio and Frith 2006), this may provide some clues about the concepts of self and otherness. For example, in individuals with autism, the ToM may not exhibit much activation due to the overlap of the self-focused perspective with the other-focused perspective (Isoda 2021). First of all, we know that mPFC is functionally related to social behavior (Wagner et al. 2012, Denny et al. 2012), so it is conceivable that SEEKING system, which is related to our social behaviors, is also associated with mPFC, just as the ToM, which is a social function, is associated with mPFC. A link between the two does not explain all our social relationships. Still, it can give us a neurobiological perspective on powerful concepts of our sociality, such as self and otherness. For example, from an evolutionary perspective, Fritz Heider argued that humans need to predict and understand the behavior of others (cited in Wagner et al. 2012). Predicting and understanding the behavior of others is achieved through ToM. From an evolutionary perspective, this need may be related to the primary process of brain events described by Panksepp (2017, Panksepp and Biven 2021).

The PLAY system prepares the animal for its social environment and is important for behaviors such as hunting, aggression, sexuality, competition, parenting, and coping with danger (Spinka et al. 2001, Panksepp 2017, Panksepp and Biven 2021). In fact, these behaviors are supported by PLAY system thanks to SEEKING system, e.g., searching for new hunts, seeking partners to reproduce, competing to become dominant in the social environment, etc. The same is true for the CARE system. Behaviors such as feeding, nurturing, caring, giving care are explained by the activation of CARE system. These activations are thought to have a close connection with social interaction in living things (Uvnas-Moberg 1998, Panksepp and Biven 2021). According to studies on ASD, problems with social bonding in individuals with autism were related to the deactivation of PLAY and CARE systems (Aitken 2008, Carré et al. 2015). It was found in a study conducted with children with autism that TPJ, right inferior frontal gyrus and left premotor cortex exhibited deactivation (Kana et al. 2014). In particular, the anterior cingulate cortex (Montag and Davis 2018), which is the neocortical region of PLAY and CARE systems, is also essential for affective ToM ability (Abu-Akel and ShamayTsoory 2011). Accordingly, the possible neural connection of the PLAY and CARE systems with ToM may be associated with the anterior cingulate cortex.

Possible neural connections between the PLAY and CARE systems and the ToM may also be established through the ability to empathize. Empathy refers to the ability to share the feelings of others (Singer and Tusche 2014). Empathy, by definition, arises from observing or imagining another person's emotional state, which requires especially affective ToM. Since social behaviors are at the forefront of CARE system, it is possible to discuss the importance of empathy. The relationship between empathy and CARE system can also be established through oxytocin (Stevens and Taber 2021). Panksepp (2011b) stated that primitive forms of empathy might be seen in the interest and sensitivity of mothers towards crying babies. This ability to empathize in the mammalian brain may have evolved through the struggle to survive in a social environment. The ToM, which is linked to empathy, must therefore also be linked to affective systems such as PLAY and CARE. These neural connections can be established through anterior medial cingulate cortex and anterior insula for affective empathy and through dorsomedial PFC, temporoparietal junction and STS for cognitive empathy (Stevens and Taber 2021). These neuroanatomical structures are known to be directly related to ToM. On the other hand, PLAY and CARE systems are linked to some neuroanatomical structures such as the ventral tegmental area, medial prefrontal cortex and anterior cingulate cortex (Watt 2007, Panksepp and Panksepp 2013).

Another aim of this study is to propose the neuroanatomical regions for SELF system based on the relationship between the ToM and subcortical structures. A meta-analysis focusing on self-referential processing (SRP) and the SELF system emphasizes the importance of cortical midline structures (Northoff et al. 2006). Northoff and Panksepp (2008) argued that self-referential processing works through subcortical-cortical midline structures in all mammalian brains. Subcortical midline structures include medial orbital prefrontal cortex, ventromedial prefrontal cortex, supragenual anterior cingulate cortex, dorsomedial prefrontal cortex, medial parietal cortex, posterior cingulate cortex, pregenual anterior cingulate cortex and retrosplenial cortex (Northoff et al. 2006). It is known that the ability of the ToM involves ventromedial prefrontal cortex, anterior cingulate cortex, dorsomedial prefrontal cortex and medial prefrontal cortex (Frith and Frith 2003, Saxe et al. 2004, Northoff et

al. 2006). According to Northoff et al. (2006), self-referential processing lies at the basis of the self, and self-referential processing generally enables organism to distinguish self-related stimuli from non-self-related stimuli. Accordingly, it can be argued that the ToM ability should be activated for self-referential processing, and therefore, ToM ability is the basis of SELF system. Fabbro et al. (2015) argue that it is not only language that makes people unique but also the ability to use ToM and capacity to travel through time mentally. The Tom ability is critical for the acquisition of social skills in humans, and since the human species is a social creature, there is an evolutionary need for the development of the ToM ability (Brüne and Brüne-Cohrs 2006). Subcortical midline structures serve as a buffer zone for the self models proposed so far in neuroscience (Northoff et al. 2006). It should be noted that not only cortical structures but also subcortical structures are significant in the mechanisms of self and consciousness (Panksepp 2017, Solms 2023). For this, Northoff and Panksepp (2008) propose three strong lines of evidence: (i) stimulation of the neocortex does not produce strong affect compared to stimulation of subcortical structures, except for the orbitofrontal cortex and medial frontal cortex, (ii) damage to subcortical structures that converge in the medial and intralaminar nuclei of thalamus, the mesolimbic dopaminergic channles and PAG significantly impairs consciousness and organismal competence, and finally (iii) consciousness is preserved in children born with neodecortication damage in infancy.

Taken together, this evidence suggests that consciousness is a high-level emotional-cognitive mechanism that evolved from the subcortical structures of mammalian brain. The core SELF mechanism required for conscious experience may also follow neural pathways starting from subcortical structures and extending to neocortex structures. Considering that human beings are social organisms, it can be argued that the ability of ToM lies at the basis of self-referential processing behavior. And since the ability of ToM has a connection with subcortical structures and develops by interacting with these structures, it can be suggested that neural connections between ToM and affective systems are necessary for the formation of the SELF system in humans. Therefore, we propose that the ToM ability that helps humans to interact socially also helps the formation of the SELF system, for which subcortical-cortical ToM pathways must be activated in humans. We argue that the ToM-SELF pathway may be implicated in pathways of the SEEKING, PLAY and CARE system that extend from VTA to mesolimbic and mesocortical regions. The reasons for this suggestion are that the cortical-subcortical structures responsible for the ability to ToM are involved in the SEEKING, PLAY and CARE pathways (especially anterior cingulate cortex, mPFC and amygdala, see Abu-Akel and Shamay-Tsoory 2011, Montag and Davis 2018, Panksepp 2017), the fact that SEEKING system is one of the oldest and fundamental affective systems based on subcortical structures and interacts with every affective system (see Panksepp and Biven 2021), and that PLAY and CARE systems are particularly associated with social cognition and empathy, and thus with ToM ability (see Abu-Akel and Shamay-Tsoory 2011, Montag and Davis 2018).

Since the findings of AN theory are mainly based on animal experiments (Cromwell and Panksepp 2011), it is challenging to investigate possible neural connections between the ToM and AN systems, which are mostly studied in human samples. One of the most critical limitations of this article is the lack of research findings from which we can generalize possible neuroanatomical connections, so we can only talk about possible neural connections. Future studies focusing on the statistical relationships between personality scales of AN theory and ToM scales in human samples may provide new findings on how AN theory can explain ToM ability. In addition, controlled laboratory experiments can be conducted in relation to our proposal regarding SELF system and ToM ability.

Conclusion

This article aims to examine the possible neural connections between AN and ToM and to propose a neuroanatomical region for the SELF system, including the possible ToM ability. According to the 6 main theses derived from the AN literature, the ToM ability may be linked to subcortical structures in the brain. This article argues that these connections may be established through positive affect systems according to thesis (f). Since the SELF system does not yet have a specific neuroanatomical region, this article argues that mesolimbic-mesocortical structures originating from the VTA and associated with positive affective systems are necessary for the development of the SELF system. It will be necessary to experimentally test the hypotheses established in this article in future studies to understand better the SELF system and the neural connections between ToM and AN.

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