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Clinical Affective Neuroscience

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Affective neuroscience is a promising young field in neuroscience for understanding the basis of many types of psychopathology. It describes the scientific investigation of the neural basis of affect, emotion, and feelings. These phenomena arise from mental processes that are not always directly observable, which complicates discovering their neural basis. Still, as it has done for other inferred processes, such as memory and language, neuroscience should transform our emotion-based patient formulations and lead to novel, targeted therapeutics for emotional issues. In this Translations, we aim to provide a brief introduction to affective neuroscience for clinicians, beginning with defining key terms and then reviewing clinical applications.

First, it is noteworthy that common clinical terms have different meanings in affective neuroscience. In the influential *Affective Neuroscience*, Panksepp defined affect as a primitive mental process based in subcortical structures, found across species that places an organism in a particular behavioral state.¹ Of course, affects have evolved for a purpose, and the affective systems proposed by Panksepp (Table 1) are hallmark examples. A general neuroscientific definition of emotion is a conscious experience that has at least two components – stimulus and response. An emotion incorporates the cognitive interpretation or experience of the stimulus, overt behavioral response, physiologic response, and feeling, which may be considered the subjective synthesis of internal sensations. Emotions are also typically considered to have a valence component, the degree to which they are experienced as pleasurable (positive valence) or aversive (negative valence). Emotions are relatively brief in their duration as opposed to other internal states, though their associated physiologic arousal may last for hours.

Basic emotion is a term for a core, discrete emotional experience that is shared among all people.² However, exactly which basic emotions exist and how universal they may be continues to be debated. When considering the literature on emotions, it is important not to confuse basic emotions with affective systems. Affects are basic, evolutionarily conserved processes which may not be consciously experienced. Emotions are conscious experiences which may involve multiple affective systems, physiological arousal, and cognitive processes.

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Clinical Applications of Affective Neuroscience

Motivation

Some major, contemporary theories of emotion consider brain-based motivational processes to be a core organizing dimension. One influential example of how a motivational system has been formulated in affective neuroscience is the “seeking system” in Table 1.

Motivational processes are normal and always active in the brain, underlying behavior intended to approach or avoid. They are supported by the mesolimbic dopamine systems. These systems are defined by dopaminergic projections from the ventral tegmental area to the nucleus accumbens and areas of the neocortex, notably the ventral and medial prefrontal cortex.

Motivation-related dysfunction has influenced psychiatric practice, appearing in early formulations of psychiatric illness, e.g. Freud’s pleasure principle. It is implicated in several psychiatric conditions as a core affective component. Perhaps most familiar to clinicians is its central role in substance use disorders. For interested readers, the National Neuroscience Curriculum Initiative (NNCI; www.nncionline.org) has produced a web-based module “Addiction” describing the motivational circuitry in substance use disorders.³ The module is intended to aid clinicians in understanding and communicating the neural pathophysiology of substance use disorders and provides an accessible overview of the motivational system.

Motivation system disturbances have been established in obsessive compulsive, eating, disruptive behavioral, psychotic, and mood disorders. An affective neuroscience approach may refine prognosis and treatment for such disorders. Consider the example of eating disorders, a fitting one, since food is a fundamental stimulus for motivation. When something important such as food is detected, an individual may have an approach response with a corresponding dopamine change in the mesolimbic system. The association between dopamine change and approach response is so reliable that there are well-established mathematical models that predict it. Recent work applied such models to understanding the motivation system dysfunction in anorexia, finding the response is dysfunctional. Rather than having a simple lack of dopamine response to food, the motivational system demonstrates extreme fluctuations. The discovery of these fluctuations, even after recovery, may help explain the relapsing course and suggest novel treatments. For example, an intriguing new hypothesis suggests that dopamine partial agonists may treat core symptoms of anorexia nervosa by attenuating these fluctuations, effectively stabilizing the motivational neural circuit.⁴

Fear and Anxiety

Neural systems underlying threat detection, response, and experience are critical for understanding anxiety disorders as well as other threat related disorders such as disruptive behavioral and posttraumatic stress disorders. A few definitions are helpful prior to describing how affective neuroscience has improved our understanding of these conditions. A threat is anything that has the potential to harm. Fear is typically defined as a type of response to a stimulus that is threatening or associated with threat. Anxiety is a more generalized state in response to an ambiguous threat.

Early models of fear proposed that it originated in an “innate fear circuit” with the amygdala playing a central role as a sort of threat detector. While the amygdala is critical, contemporary theories in affective neuroscience extend this understanding to broader neural systems. LeDoux and Pine recently described a two-system model that disentangles the behavioral and physiologic response to threat from the subjective experience of fear.⁵ The threat response system processes information through the amygdala to the nucleus accumbens that controls defensive actions such as freezing, escape, and defensive aggression. The second system in this model describes the experience of fear, relying on neurocircuitry that engages conscious awareness, specifically the frontoparietal network. This account describes the generation of a conscious experience of fear as separable from more basic, defensive, physiologic reactions.

Neuroscience has informed the distinction between fear and anxiety. Recent, influential work by Davis and others has discovered unique associations between aspects of fear and anxiety and specific areas of the amygdala or its extensions, particularly the bed nucleus of the stria terminalis (BNST).^{6,7} The discovery of these more anxiety-related areas has led to promising developments in the study of anxiety disorders in children. For example, changes in the BNST are clearly seen in children with anxiety-related temperaments who develop anxiety disorders.⁸

An increasing understanding of how fear, threat, and anxiety circuitry adapt will clearly impact on learning-based treatments. For example, the neural basis of reducing threat response through extinction has inspired modifications to exposure therapy. When providing exposures of a threat stimulus, neuroscience suggests a therapist might focus on maximizing the discrepancy between the expectation of harm and the experience of safety.⁹

Resources are available that translate affective neuroscience in more depth. An accessible overview of basic concepts in affective neuroscience is the “Emotion” chapter of Gazzaniga, Ivry and Mangun’s *Cognitive Neuroscience: The Biology of the Mind*.¹⁰ For those wishing to take a deeper dive in the fundamentals of affective neuroscience, Roll’s *Emotion and Decision-Making Explained*¹¹ introduces theoretical issues and investigational techniques. Gross’s *Handbook of Emotion Regulation*,¹² deals with control processes of emotional and affective systems. These works remain grounded in neuroscience and all discuss some translations to clinical work where possible. Concise, clinical translations that are less technical or cover specific types of mental illness are emerging. Some NNCI topics and reviews in psychiatry journals increasingly touch on affective neuroscience. The National Institute of Mental Health updates a set of translations in its Research Domain Criteria matrix. There are some authoritative translational books such as *Anxious: Using the Brain to Understand and Treat Fear and Anxiety* by LeDoux.¹³

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Table 1:Affective Systems as Described by Panksepp¹⁴

AFFECTIVE SYSTEM	KEY BRAIN REGIONS	ASSOCIATED EMOTIONAL PHENOMENON
Lust	Cortico-medial amygdala, BNST, preoptic hypothalamus, VMH, PAG	Erotic feelings, jealousy
Care	Preoptic area, anterior cingulate, VTA, PAG, BNST	Love, attraction
Panic	Anterior cingulate, BNST, dorsomedial thalamus, PAG	Separation distress, guilt, embarrassment
Play	Dorso-medial diencephalon, parafascicular area, PAG	Joy, playfulness
Fear	Central and lateral amygdala to medial hypothalamus and dorsal PAG	Anxiety, worry
Rage	Medial amygdala to BNST, perifornical hypothalamus to PAG	Anger, irritability
Seeking	Nucleus accumbens, VTA, mesolimbic and mesocortical outputs, lateral hypothalamus, PAG	Interest, frustration, craving

BNST = bed nucleus of stria terminalis, VMH = ventromedial hypothalamus, PAG = periaqueductal gray, VTA = ventral tegmental nucleus