Molecular imaging of the human emotion circuit

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Abstract

Emotions modulate behavioural priorities at the central and peripheral nervous system. Understanding emotions from the perspective of specific neurotransmitter systems is critical, because the central role of affect in multiple psychopathologies, and the role of specific neuroreceptor systems as corresponding drug targets. Here we provide an integrative overview of molecular imaging studies that have targeted the human emotion circuit at the level of specific neuroreceptors and transmitters. We focus specifically on opioid, dopamine and serotonin system given their key role in modulating motivation and emotions, and discuss how they contribute to both healthy and pathological emotions.
Introduction

Emotions prepare us for action. They coordinate systemic activation patterns at multiple physiological and behavioral scales to promote survival. Most modern emotion theories consider emotions as modulatory systems interacting with both lower-order systems such as those involved in homeostasis, as well as higher-order cognitive circuits supporting decision making. Categorical models of emotions propose that the evolution has carved out a set of basic emotions—usually including anger, fear, disgust, happiness, sadness, and surprise but possibly also others—that support specialized survival functions (Cordaro et al., 2018; Cowen & Keltner, 2017; Ekman, 1992; Nummenmaa & Saarimäki, 2017; Panksepp, 1982). These basic emotions are characterized by discrete neural and physiological substrates, distinctive subjective feelings (such as “I feel happy”), expressions, and discrete functional neural basis (Kreibig, 2010; Nummenmaa et al., 2014; Nummenmaa et al., 2018; Saarimäki et al., 2016; Tracy & Randles, 2011). Much of recent neuroimaging work has aimed at mapping the functional organization of the emotion circuits in the brain using functional magnetic resonance imaging (Nummenmaa & Saarimäki, 2017; Wager et al., 2015), and these studies have been successful in delineating the neurobiological architecture of emotions (Figure 1).

Meta-analyses of the BOLD-fMRI data have however yielded inconsistent support for the discrete neural basis of emotions. One proposed explanation for this is the low spatial resolution of BOLD-fMRI coupled with univariate analysis: if specific neural populations coding different emotions are intermixed within one voxel, their activation differences cannot be revealed by univariate techniques. In line with this view, multivariate pattern recognition studies have consistently provided support for discrete neural basis of different basic and complex emotions (Kragel et al., 2016; Kragel & Labar, 2015; Saarimäki et al., 2018; Saarimäki et al., 2016). Even though multivariate analysis techniques improve the discriminability and specificity of data patterns across different classes or conditions (Norman et al., 2006), they cannot resolve one of the main limitations of the BOLD-EPI data – that the signal is completely unspecific with respect to the underlying neurotransmitter circuits.

A single voxel in an EPI image may contain neurons operating with a multitude of different neurotransmitters, whose net activation is reflected in the BOLD signal. Understanding emotions from the perspective of specific neurotransmitter systems is however critical, because the central role of affect in multiple psychopathologies, and the role of specific neuroreceptor systems as drug targets. For example, the most commonly assumed working mechanism of antidepressants involve either increased neurotransmission by increasing synaptic neurotransmitter levels (such as norepinephrine or dopamine (DA)), or specific agonist effects of the targeted receptors. Thus, it is imperative to delineate not just the anatomical but also neuromolecular organization of the emotion circuits in the brain. Here we provide an overview on the molecular mechanisms of emotions, with specific focus on in vivo imaging of specific neurotransmitter and neuroreceptor studies in humans. We focus specifically on the opioidergic, dopaminergic and serotonergic mechanisms, as they can be readily studied in vivo in the human brain (Figure 2).

![Diagram of brain regions](image)
Figure 1. Statistical summary of brain regions involved in emotional processing based on NeuroSynth database (Yarkoni et al., 2011).

Studying human neuroreceptor systems in vivo
Most commonly used functional imaging (fMRI) and electromagnetic (MEG / EEG) techniques for recording brain activation do not yield information regarding the underlying mechanisms of neurotransmission. Because pharmacological microstimulation studies are not feasible in humans, main approaches for studying emotion-related neurotransmission involve different activation, blockade and depletion studies, as well as nuclear medicine imaging techniques for direct in vivo measurements.

Pharmacological activation and blockage studies
The classical behavioral pharmacological approach involves delivering specific receptor agonists or antagonists or other pharmacologically active agents into the circulation (or directly in the target tissue in the case of animal studies). In humans these studies are difficult to conduct, because oral or intravenous administration leads to systemic rather than regionally specific effects, and it is well established in animal studies that the effects of receptor agonists / antagonists can be regionally highly selective (Berridge & Kringelbach, 2015). One way for overcoming this limitation is to use pharmacological imaging approach, where functional imaging or electromagnetic recordings are performed during a pharmacological challenge versus placebo condition, which allows inferring the brain regions where drug action leads to neural responses. However, these regional responses may still be influenced by systems-level effects, and pinpointing the specific regions whose pharmacological manipulation leads to altered BOLD signal is difficult. Furthermore, these studies employ potent pharmacological agents (such as morphine or dexamphetamine) thus requiring strict clinical supervision. Finally, pharmacological manipulations may lead to physiological effects that may directly confound the BOLD signal, such as respiratory depression caused by opioid agonists (Pattinson, 2008), further complicating their interpretation.

Monoamine depletion studies
A complementary approach to pharmacological activation and blockage studies involves techniques that temporarily lower the functioning of monoamines (usually serotonin, dopamine, catecholamine), typically by restricting the intake of the precursor amino acids or blocking their synthesis. The three most widely used techniques involve acute tryptophan depletion (ADT) blocking the 5-HT serotonin transporter synthesis by dietary restriction of 5-HT precursor L-tryptophan. The effect is amplified by consumption of large quantity of other amino acids that will compete with tryptophan at the blood-brain barrier (Booij et al., 2003b). The phenylalanine/tyrosine depletion (APTD, in turn, targets the dopaminergic / catecholamic systems by restricting the dietary intake of its precursors phenylalanine and tyrosine. Such techniques result in specific short-term effects in distinct neurotransmitter systems rather than on general protein metabolism in the brain (Booij et al., 2003a), however the interpretation of these results is complicated due to the system-level effects on transmitter synthesis. Nevertheless, these techniques are valuable when investigating the involvement of monoamine system function in specific mood disorders.

Molecular imaging with positron emission tomography
Functional molecular imaging using positron emission tomography (PET) is the current gold standard for in vivo molecular imaging in humans. It is based on injecting radiolabeled, biologically active molecules to the circulation. The molecules will bind to the target sites, and the unstable isotopes will undergo positron emission decay. The radioisotope emits a positron (an antiparticle of an electron) which will travel in the tissue losing kinetic energy. After certain degree of deceleration the positron can interact with an electron, leading to annihilation event producing two gamma photons (rays) moving in opposite directions. The gamma rays are recorded by the detector units of the PET camera, and on the basis of
simultaneously detected gamma rays on the opposite sides of the detector ring, the location of the annihilation event can be computed. This subsequently allows reconstruction of the tracer uptake in the tissue. When combined with measurements of tracer input and output, these raw radioactivity counts can be transformed to biologically meaningful information such as binding of the radioligand.

This technique provides excellent biological resolution due to the possibility to develop highly selectively binding radioligands for different protein targets, and as it also allows spatial resolution of a few millimeters. Despite its high sensitivity for in vivo tracing of biomarkers, PET lacks capability for resolving the underlying tissue morphology thus this information needs to be acquired through separate MR or CT scan. Functional imaging of slow-acting neurotransmission is however possible (Backman et al., 2011; Zubieta et al., 2001), although the temporal resolution is in the of tens of minutes for most neurotransmission studies. Modern integrated PET-MRI -systems (Judenhofer et al., 2008) also allow simultaneous measurement of, for example, perfusion with both PET and arterial spin labelled MRI (Heijtel et al., 2014; Zhang et al., 2014), or perfusion with MRI and neuroreceptor occupancy (PET) significantly broadening the usability (Sander et al., in press). All in all, the PET technique is currently the most accurate and specific tool available for investigating neurotransmission in vivo in humans.

**Figure 2.** Distribution of type 2 dopamine receptors, µ-opioid receptors and 5-HT1A serotonin transporters measured using PET radioligands.

**Dopamine system**

Rewards exert a powerful influence on our behaviour. Both humans and animals are motivated for obtaining various types of rewards ranging from food and sex to social contact, and the pleasurable sensations upon reward consumption reinforce the motivation for repeated consumption of the rewards. Monoamine neurotransmitter dopamine and its receptors D1-D5 are classically known for their role in motor control as well as reward-motivated behaviour and pleasure. There are multiple dopaminergic pathways in the brain that consist of projection neuros synthesizing and releasing dopamine (Figure 3). The **mesolimbic** pathway projects from the ventral tegmental area (VTA) to the ventral striatum. This pathway is particularly involved in processing incentive salience, generating pleasure responses and reinforcement learning. The **mesocortical** pathway projecting from the VTA to the prefrontal cortex is, in turn, more involved in executive functions although it also contributes to reward processing. The **nigrostriatal** pathway connects substantia nigra to the striatum (putamen and caudate), and contributes critically to motion control. Finally, the **tuberoinfundibular pathway** connects the hypothalamus and the pituitary gland. Importantly, all the main functions of the dopamine system are also central to reward processing, and it comes as no surprise that dopamine system has been implicated as one of the primary molecular pathways for reward (Wise & Rompre, 1989).
PET studies using radioligand [11C]raclopride in humans have demonstrated central dopamine release during reward processing. Due to the poor temporal accuracy of PET, it is impossible to dissect the contribution of reward expectation and consumption phases to the dopamine release: It is simply practically difficult to design sufficiently long (~45 min) tasks where rewards would be only anticipated but not delivered. Henceforth, these types of studies mix both anticipation and consumption related effects. This type of studies have shown that feeding – one of the most salient biological rewards – triggers dopamine release in striatum. Because the magnitude of the dopamine release is associated with the subjective pleasantness evaluation of the meal, these data have been interpreted as evidence for hedonic (rather than homeostatic) responses to feeding (Small et al., 2003). This is further supported by another series of studies, which measured dopamine release during intravenous glucose / placebo delivery, thus precluding the subjective evaluation of the reward value of the glucose, yet systemically altering the blood glucose levels simulating postprandial state (Haltia et al., 2008; Haltia et al., 2007). These studies found no differences between the glucose and placebo conditions, suggesting that alterations in circulating glucose levels are not enough for central dopamine release. Instead, the hedonic responses driven by the orosensory and chemical taste pathways might be curial for the feeding-triggered dopamine response.

There is less evidence for dopaminergic processing of other primary reward signals, but some studies point that romantic (Takahashi et al., 2015) and maternal attachment-related rewards (Atzil et al., 2017) might be processed via the dopamine system in humans. However, these studies are difficult to interpret as the other (Atzil et al., 2017) reported dopamine activations in regions where [11C]raclopride has either low or no specific binding that would be sensitive to even D2/D3R antagonist challenge (Svensson et al., 2019), and the other was based in individual differences approach (Takahashi et al., 2015) and did not report main effects of dopamine release across the whole group of subjects. Also, in murine models dopamine typically decreases (rather than increases as suggested by human PET data) social contact seeking (Manduca et al., 2014), yet this might also be accounted by cross-species differences. Striatal dopaminergic reward signaling however extends beyond biologically significant rewards. For example, more “cognitive” rewards such as listening to favorite music (Salimpoor et al., 2011), gambling (Joutsa et al., 2012) and playing video games (Koepp et al., 1998) leads to striatal dopamine release. In all of these tasks the reward value is learned rather than intrinsic, suggesting that both intrinsic (“natural”) and acquired reward signals are processed in comparable fashion via dopaminergic signaling. This is most clearly highlighted by data that shows that simple cognitive tasks such as task switching may trigger striatal dopamine release as soon as they are coupled with rewards (Jonasson et al., 2014).

However, also negative emotions induce dopamine release. One study using [18F]fallypride revealed increased dopamine release in the amygdala and mediolateral frontal cortex during processing of negative
emotional words (Badgaiyan et al., 2009), a subsequent study using [11C]raclopride found similar effects in caudate and putamen (Badgaiyan, 2010). There are multiple possibilities for these, on surface level slightly contradictory DA activations during displeasure. It is however possible that they can reflect the preparatory avoidance behavior triggered by the aversive stimulus, reflected in motor preparation related dopamine release. This might be reflected in similar activation as the preparatory approach for rewards in. Finally, dopamine system also contributes to nociceptive processes, and pain induces consistent dopaminergic activation particularly in the striatum (Scott et al., 2006; Wood et al., 2007). Finally, type 2 dopamine receptors (D2R) have also been linked with executive control and working memory (Backman et al., 2011), thus it these effects might reflect prediction and planning of escape responses in the executive system. Recent PET-fMRI fusion work has also tried to dissect the specific role of dopamine in processing different aspects of emotions, specifically pleasure-displeasure (valence) and arousal axis. This approach is based on separate PET measurement of neuroreceptor distribution, which can then be used to predict emotion-dependent BOLD responses in subsequent fMRI experiment (Karjalainen et al., 2017). The logic of these experiments is to look whether interindividual variation in the regional BOLD responses would be dependent on corresponding variability on neurotransmitter availability, which would be indicative of DA involvement in the emotional processes targeted in the fMRI experiment. However, this work has failed to establish associations between DR availability and emotion-specific BOLD responses (Karjalainen et al., 2018) and instead suggests the key role of opioid system in modulating basic affective responses (see below).

Given the central role of dopamine in modulating motivation and reward, it is not surprising that dysregulated dopaminergic neurotransmission is the hallmark of numerous addictive disorders (Volkow et al., 2009). Human imaging studies have demonstrated that alcohol and drug dependence are associated with lowered D2R availability (Martinez et al., 2012; Volkow et al., 2001; Volkow et al., 1996). Additionally, drug-induced striatal dopamine responses are blunted in metamphetamine abusers (Volkow et al., 2014). With behavioural addictions and addiction-like behaviours the results are less clear. Animal studies on obesity suggest that striatal D2R would be downregulated in the obese state (Johnson & Kenny, 2010). Human studies have yielded mixed results with some finding lower (de Weijer et al., 2011; Volkow et al., 2008; Wang et al., 2001) and others unaltered (Haltia et al., 2008; Haltia et al., 2007; Steele et al., 2010) D2R availability in the striatum. Finally, pathological gambling is not associated with altered D2R availability (Joutsa et al., 2012). However, gambling-dependent dopamine signalling is amplified (rather than blunted as in amphetamine abusers upon drug administration (Volkow et al., 2014)) in pathological gamblers versus controls (Joutsa et al., 2012). In sum, it seems that substance abuse markedly downregulates the D2R system possibly via direct pharmacological effects, whereas behavioural addictions and addiction-like states are modulated by at least partially independent pathways.

Opioid system

Endogenous opioids are expressed widely throughout the human central nervous system and numerous high-density sites constitute of central nodes of the human emotion circuit. Among the three classes (μ, δ, and κ of opioid receptors), the μ receptors mediate the effects of endogenous β-endorphins, endomorphins, enkephalins, and various exogenous opioid agonists (Henriksen & Willoch, 2008). The predominant action of μ-opioids in the central nervous system is inhibitory, but they have also excitatory effects. The neurons synthesizing β-endorphin are found in the arcuate nucleus in hypothalamus and the nucleus tractus solitarius medulla, from where rich projections originate throughout the CNS. Dopamine is oftentimes considered as the primary neurotransmitter for reward processing (Wiseman & Rompre, 1989). Opioid and dopamine systems are however closely interlinked at cellular level (Tuominen et al., 2015), and opioids can produce reward independently of dopamine (Hnasko et al., 2005), likely via partially independent molecular pathways. Opiates are commonly used illicit drugs particularly in the US, where the lifetime prevalence of opioid use disorder exceeds 2% (Grant et al., 2016). Such high misuse potential is attributed to the strong ‘liking’ responses - the pleasurable subjective experiences produced by drug consumption (Comer et al., 2012). However, experiments with drug-naïve volunteers have not provided
consistent results on opioid agonist derived liking or pleasure. Some studies report increased pleasure upon μ receptor agonist delivery (Riley et al., 2010; Zacny & Gutierrez, 2003, 2009), whereas others have not corroborated these findings (Ipser et al., 2013; Lasagna et al., 1955; Tedeschi et al., 1984). These discrepancies likely pertain to differences in the route of administration, receptor affinity and genetically determined variation in receptor expression (Levran et al., 2012). Some recent experiments have found that opioid agonists shift the evaluation of external stimuli, making them seem more pleasant, without necessarily directly influencing tonic subjective emotional state per se (Heiskanen et al., in press). Thus, it is possible that opioid agonists influence primarily the evaluative processing of emotions, rather than modulating directly the acute subjective feeling. Consequently, opioids might alleviate stress and dysphoria by shifting the evaluation of the internal and external world towards more positive directions.

Figure 4. Organization of the human opioid system in the brain. Note that as the specific opioid neuron projections cannot be established, thus the figure characterizes the relative expression of different receptor subtypes in the some of the key nodes of the emotion circuit.

Molecular imaging however shows consistently that reward consumption triggers endogenous opioid release. Feeding leads to increased endogenous opioid release in the reward circuit and also elsewhere in the brain (Burghardt et al., 2015; Tuulari et al., 2017). This response is however observed for both palatable and non-palatable meals, and is actually stronger for faster-metabolizing, non-appetizing liquid meal than for palatable pizza. Thus, the response is likely a combination of low-level homeostatic pleasure of feeding after fasting (which is presumably more intense during fast-metabolized liquid meal), and possibly a partially independent effect of subjective hedonic responses. Corroborating evidence for the role of the opioid system processing primary rewards comes from studies showing that pleasurable social interaction (Hsu et al., 2013; Manninen et al., 2017) and strenuous physical exercise (Boecker et al., 2008; Saanijoki et al., 2017) induce central opioid release. As with dopamine, these effects extend beyond primary rewards, and for example positive mood induced by mental imagery (i.e. in the absence of external sensory stimulation) induces opioid release in the amygdala (Koepp et al., 2009). Fusion imaging with PET and fMRI suggests that the opioid system governs particularly the arousal dimension of emotions. The more opioid receptors an individual has in their limbic system, the weaker are their arousal-dependent BOLD responses in the brain’s emotion circuits (Karjalainen et al., 2018). Accordingly, opioid system might act as an buffer against socioemotional stressors, alleviating the negative feelings associated with one’s own or others’ misfortunes (Karjalainen et al., 2017).
Whereas the general role of dopamine system in drug addictions is fairly clear-cut, the story is more nuanced with the opioid system. Alcohol dependence is associated with elevated MOR levels in the striatum (Heinz et al., 2005; Weerts et al., 2011), whereas cocaine dependence results in similar effects in more widespread, particularly cortical and cingulate areas (Gorelick et al., 2005). However, chronic opiate abuse is associated MOR downregulations (Koch & Hollt, 2008; Whistler, 2012). Thus, the effects of drug abuse on MOR seem to be drug-specific. More consistent data come from studies on obesity, that have implicated downregulated µ receptor action as the pathophysiological mechanism (Burghardt et al., 2015; Karlsson et al., 2016; Karlsson et al., 2015; Tuominen et al., 2015). These effects seem also specific to obesity rather than a general feature of behavioural addictions, as µ receptor downregulation is not observed for example in pathological gambling (Majuri et al., 2016). Finally, despite the centrality of the opioid system in hedonia and affective functioning, there is no clear evidence of its involvement in the pathophysiology of mood disorders. PET imaging data are limited in scope, and the existing studies have yielded conflicting evidence on opioidergic alterations in major depression (Hsu et al., 2015; Kennedy et al., 2006).

Serotonergic system

Monoamine neurotransmitter serotonin and its receptors 5HT₁-5HT₇ are involved in regulation of sleep, appetite, mood and pleasure, but it is also involved in cognitive and physiological processes. In the central nervous system serotonin is produced in the Raphe nuclei in the brainstem, from where the serotonergic projections originate to striatum and to the neocortex (Figure 5). Brain’s serotonergic systems also play a critical role in avoidance behaviour and fear and anxiety. Activation of the serotonergic system is critical for avoidance behaviour in rodents (Deakin & Graeff, 1991), and genetic variations of serotonin transporter (SERT) expression influence fear circuit’s responsiveness to acute threat signals in humans (Hariri et al., 2002). Thus, major categories of anxiolytic drugs also inhibit SERT.

Figure 5. Main serotonin pathways in the brain.

Whereas dopamine and opioid systems are centrally involved in pathophysiology of addictive disorders, the SERT system is consistently implicated in mood regulation and consequently in pathogenesis of mood disorders (Mann, 1999). Although initial reports on 5-HTT in mood disorders were variable, meta-analyses suggest that serotonin transporter availability is consistently lowered in depression (Ichimiya et al., 2002) (but see (Andrews et al., 2015)) and altered serotonergic neurotransmission is considered also hallmark of depression (Drevets et al., 1999). Accordingly, most widely used and effective of antidepressants act by increasing extracellular serotonin levels. Importantly, individual differences in the expression of the serotonin transporter mediate the effects of stressful life events on the onset of depression (Risch et al., 2009). In similar fashion, serotonin transporter availability varies seasonally,
suggest that altered serotonergic function may also underlie pathophysiology of seasonal affective disorders (Praschak-Rieder et al., 2008).

Functional molecular imaging of the serotonergic system has been limited due to the lack of radioligands that would be sensitive to endogenous serotonin levels, essentially preventing activation studies with PET. However, fusion PET-fMRI imaging has elucidated the role of SERT in emotional processing.

A number of studies indicate that the serotonergic system regulates amygdala responsiveness to facial expressions of emotions (Fisher et al., 2009; Fisher et al., 2006; Rhodes et al., 2007; Selvaraj et al., 2015). For instance, PET-fMRI studies have found an inverse relationship between 5-HT1A receptor density in the dorsal raphe nucleus (DRN) or HT2A density in the prefrontal cortex and the magnitude of amygdala BOLD response to emotional faces (Fisher et al., 2009; Fisher et al., 2006; Fisher et al., 2011; Selvaraj et al., 2015). Some studies have also yielded conflicting results, with no association between 5-HT1A binding and emotional face processing (Kranz et al., 2018). For practical and economical reasons, these types of multimodal neuroimaging studies have limited statistical power (oftentimes ns < 30), which may yield inconsistent effects in correlational designs. However, pharmacological activation studies provide corroborating evidence for serotonergic modulation of amygdala responses to threat. Multiple studies have documented that serotonin reuptake inhibitors (SSRIs) modulate amygdala reactivity to emotional facial expressions (Anderson et al., 2007; Bigos et al., 2008; Harmer et al., 2006; Murphy et al., 2009). These effects are however not just face-specific, but extend to emotional processing in general, but also to emotions derived from natural speech. Serotonin receptor (and norepinephrine) antagonist mirtazapine attenuates responses to unpleasant events in sensorimotor areas and anterior while modulating responses to arousing events in cortical midline structures. These effects are paralleled with increased functional connectivity between cortical midline and limbic areas during pleasant events (Komulainen et al., 2017), suggesting large-scale modulation of affective processing by serotonergic drugs.

From clinical viewpoint, subjective emotional feelings are also an important facet of mood disorders. Particularly negative self-concept and increased self-focus play and important role in the pathophysiology of depression. Some studies suggest that serotonergic system can influence how subjects interpret and process self-relevant affective information. Mirtazapine attenuates self-referential emotional processing in healthy volunteers, as manifested in decreased cortical midline activation (Komulainen et al., 2016). This mechanism could underlie one serotonin-dependent antidepressant action, this is further evidenced in clinical trials, that show how short-term escitalopram treatment normalizes self-referential processing in patients with major depressive disorder (Komulainen et al., 2018). Thus, serotonergic modulation seems to occur at multiple levels of the human emotion circuit, ranging from sensory to evaluative, cognitive and self-referential processes, and the serotonergic action of antidepressants probably targets all these levels.

**Conclusions**

Recent advances in nuclear medicine imaging have helped to elucidate the role of opioid, dopamine, and serotonin systems in human emotions. There is clear evidence that dopamine and opioid systems modulate hedonic processes. However, both dopaminergic and opioiergic activation is observed during negative emotions too, suggesting that they may also support general-level motivational arousal-modulation components of emotions. At pathophysiological level, dopamine system is more clearly linked with substance abuse and addictive disorders, whereas opioidergic activations vary from substance to substance, with clear downregulation observed particularly in obesity. The serotonin system links more clearly to negative emotions including fear and sadness, yet outside pharmacological and clinical studies, majority of these data come from pharmacological fMRI studies and those correlating transporter availability with BOLD-fMRI responses.
There is no clear one-to-one mapping between specific emotions or emotional behaviours and specific neurotransmitters. Obviously numerous neurotransmitters have a wide variety of roles, and their specific actions are not limited to emotional behaviour. Human imaging studies are challenging to conduct, and are limited by the radioligand pharmacokinetics and affinity. For the major neurotransmitter systems implicated in emotion, reliable radioligands exist for imaging serotonin, dopamine, opioid and endocannabinoid receptors and transmitters. For opioid and dopamine systems, there exist also radioligands that are sensitive to endogenous transmitter levels, whereas this has yet to be achieved for serotonin and endocannabinoid systems. In sum, targeting neurotransmitter mechanisms of emotions using PET is a powerful tool for dissecting the molecular mechanisms of emotions, further potentiated by the next-generation PET-MRI devices allowing addressing the molecular specificity of the emotion-related BOLD activations.

References


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