Neuropharmacology 76 (2014) 342–350

Contents lists available at SciVerse ScienceDirect

Neuropharmacology

journal homepage: www.elsevier.com/locate/neuropharm

Invited review

Interoception and drug addiction

Martin P. Paulus [a,b,*], Jennifer L. Stewart [a]

[a] Department of Psychiatry, University of California San Diego, La Jolla, CA, USA
[b] Psychiatry Service, VA San Diego Healthcare System, La Jolla, CA, USA

ARTICLE INFO

Article history:
Received 12 February 2013
Received in revised form
2 July 2013
Accepted 3 July 2013

Keywords:
Interoception
Insula
Embodiment
Relapse
Cue reactivity

ABSTRACT

The role of interoception and its neural basis with relevance to drug addiction is reviewed. Interoception consists of the receiving, processing, and integrating body-relevant signals with external stimuli to affect ongoing motivated behavior. The insular cortex is the central nervous system hub to process and integrate these signals. Interoception is an important component of several addiction relevant constructs including arousal, attention, stress, reward, and conditioning. Imaging studies with drug-addicted individuals show that the insular cortex is hypo-active during cognitive control processes but hyper-active during cue reactivity and drug-specific, reward-related processes. It is proposed that interoception contributes to drug addiction by incorporating an "embodied" experience of drug uses together with the individual's predicted versus actual internal state to modulate approach or avoidance behavior, i.e. whether to take or not to take drugs. This opens the possibility of two types of interventions. First, one may be able to modulate the embodied experience by enhancing insula reactivity where necessary, e.g. when engaging in drug seeking behavior, or attenuating insula when exposed to drug-relevant cues. Second, one may be able to reduce the urge to act by increasing the frontal control network, i.e. inhibiting the urge to use by employing cognitive training.

This article is part of a Special Issue entitled 'NIDA 40th Anniversary Issue'.

1. Interoception, homeostasis, and drug-taking behavior

Interoception (Craig, 2002, 2009), i.e. receiving, processing, and integrating body-relevant signals with external stimuli to affect ongoing motivated behavior, is an important process that contributes to the degree to which individuals approach or avoid drugs of abuse. Interoception can be viewed as a state of the individual, i.e. the way a person "feels" at a particular point in time (Craig, 2010), or it can be viewed as sensing body-related information in terms of awareness (Pollatos et al., 2005), sensitivity (Holzl et al., 1996), or accuracy of the sensing process (Vaitl, 1996). Interoception is thought to serve a homeostatic function (Craig, 2003) such that an individual's approach or avoidance behavior toward stimuli and resources in the outside world is aimed at maintaining an equilibrium. For example, a person will approach a heat source in a cold environment but avoid it when the ambient temperature is high. Interoception provides an anatomical framework for identifying pathways that are focused on the modulating the internal state of the individual. This framework comprises peripheral receptors (Vaitl, 1996), c-fiber afferents, spino-thalamic projections, specific thalamic nuclei, posterior and anterior insula as the limbic sensory cortex and the anterior cingulate as the limbic motor cortex (for reviews see Augustine, 1996; Craig, 2007). Whether viewed as an integral individual state of "feeling" or as specific sensing of body-related afferents, interoception has profound effects on other brain processes such as cognitive control, emotion, decision-making, reward, stress, and conditioning.

Since the central component of interoception is the body-relevant feeling state, one way to conceptualize the contribution of interoception to these processes is to consider the notion of embodiment (Niedenthal, 2007) of an experience. The basic notion of embodiment theories is that higher-level cognitive and affective processing is grounded in the organism's sensory and motor experiences (Winkielman et al., 2009). For example, the individual's original neural state when information was initially acquired is reinstantiated when a stimulus, an option in a decision-making context, or the reception of a reward is processed. As a consequence, the experience of an emotional state, e.g. anger, is intrinsically linked with the internal body state, e.g. muscle tension. Since the insula cortex is critically important in processing physiological states of an individual, one may view this brain area as an important neural basis for the embodiment of approach or avoidance behaviors.

* Corresponding author. Laboratory of Biological Dynamics and Theoretical Medicine, Department of Psychiatry, University of California San Diego, 8939 Villa La Jolla Drive, Suite 200, La Jolla, CA 92037-0985, USA. Tel.: +1 858 534 9442.
E-mail address: mpaulus@ucsd.edu (M.P. Paulus).

0028-3908/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.neuropharm.2013.07.002

The homeostatic aspect of interoceptive processing is often overlooked but quite important for approach and avoidance behavior. Specifically, the degree to which a stimulus is approached or avoided is a function of the degree to which the reception of this stimulus brings this individual closer to a homeostatic state. For example, a hungry person will seek out and consume available food but a satiated person may engage in much less food-seeking and consumption behavior. The relationship between a stimulus and the associated degree of approach or avoidance as a function of the internal state of the individual was described as by Cabanac as alliesthesia (Cabanac, 1971). The internal state can enhance approach or avoidance behavior, which has been called positive alliesthesia, or attenuate such motivated action, which refers to negative alliesthesia. There is some evidence that deprivation states such as hunger and thirst enhance the responsivity of neural systems to internal stimuli (Tataranni et al., 1999). In other words, a hungry individual may experience visceral afferents more intensely than a satiated person (Piech et al., 2010). Internal state dependent changes in approach or avoidance behavior can transcend the specific reward stimulus, e.g. food restriction also confers positive alliesthesia to alcohol preference (Soderpalm and Hansen, 1999). The relationship between deprivation state and intensity of interoceptive processing has important consequences for drug abuse research. For example, the degree to which cognitive control systems influence ongoing behaviors could be a function of the deprivation state and the associated intensity of interoceptive afferents. Specifically, optimal control could be an inverted U-shape function of the interoceptive state. As a result, low levels of “embodied” experience may not engage the cognitive control system to adjust ongoing behavior. In comparison, a highly “embodied” experience may “overwhelm” the cognitive control system by providing a highly emotionalized experience.

One way to conceptualize drug-taking behavior is to pose that individuals take substances to feel better or to avoid feeling worse. The positive and negative reinforcing aspects of drugs of abuse have given rise to a tremendous insight into the behavioral processes (Koob and Le Moal, 1997; Robinson and Berridge, 2003), neural systems (Everitt and Robbins, 2005; London et al., 2000), and molecular mechanisms (Kalivas and Volkow, 2005; Nestler and Aghajanian, 1997) of drug addiction. More recently, there has been an increased realization that body-relevant information and its associated neural circuits may also play an important role in drug addiction (Naqvi and Bechara, 2010; Naqvi et al., 2007). However, the framework for this approach is much less developed and needs further empirical validation. In particular, the relationship between previously examined constructs important for drug addiction and interoception needs a more detailed evaluation. Thus, in this review we delineate the relationship between interoception and other important behavioral processes with high relevance for drug addiction. Evidence for insula dysfunction is summarized for four substance use populations: nicotine, marijuana, amphetamine, and cocaine dependent individuals. Lastly, we integrate the findings to suggest three important topics of future research that will help to determine the role of interoceptive processing in drug addiction.

2. A brief introduction to the insular cortex: the interoceptive hub

The insular cortex (Augustine, 1985) is a complex brain structure that can be most easily viewed as organized macroscopically along an anterior–posterior (Craig, 2002) and superior–inferior axis (Kurth et al., 2010). This macroscopic organization is partially consistent with the microscopic structure of the insula, which shows granular, dysgranular, and agranular columnar organization from posterior to anterior insula (Chikama et al., 1997; Shipp, 2005). A recent meta-analysis shows that the anterior–posterior subdivision is delineated more clearly on the right side. The anterior cluster is predominately activated by effortful cognitive processing, whereas the posterior is mostly activated by interoception, perception and emotion (Cauda et al., 2012). Moreover, the anterior insula, potentially together with the anterior cingulate cortex, appears to pivotally influence the dynamics between large-scale brain networks subserving both default-mode and executive control network information processing (Sutherland et al., 2012). One has to be careful to engage in extensive inverse inference statements, i.e. the degree to which one ascribes activation in a particular context in a brain structure to a process that involves this brain structure in another context. However, the paucity of studies examining the neural basis of direct interoceptive assessments in individuals with drug addictions compels one to carefully consider the insula involvement in various studies as contributing to the embodied experience.

3. The interface between interoception and basic behavioral processes

3.1. Arousal

Arousal, conceptualized as the degree to which an individual reacts physiologically and psychologically to stimuli, involves the activation of the reticular activating system in the brain stem (Moruzzi and Magoun, 1949) as well as the autonomic, endocrine, and limbic systems (Quinkert et al., 2011). Individual differences in levels of arousal have long been thought to contribute to susceptibility to using drugs (Zuckerman, 1974). Specifically, it has been hypothesized that subjects use drugs to adjust to an optimal level of arousal. As pointed out above, visceral afferents are mapped hierarchically in the brain and influence efferent signals. The neural circuits involved in processing these afferents overlap substantially (de Morree et al., 2013) with those involved in arousal-related processing (Critchley, 2009). Thus, interoceptive processing involves components of arousal and this conceptual relationship is supported empirically by a number of different studies. For example, anterior insula showed sustained activity during extended emotional contexts that tracked positively with levels of arousal (Somerville et al., 2012). Monitoring skin conductance as a measure of arousal, the degree of anterior insula activity was correlated with the interaction between accuracy and sensitivity to biofeedback (Critchley et al., 2002). Furthermore, modulation of interoceptive afferents such as rectal distention, which leads to substantial increase in plasma adrenaline and sympathetic arousal as characterized by increased heart rate as well as low versus high frequency heart rate variability, shows among other areas significant insula activation that correlates with indices of sympathetic arousal (Suzuki et al., 2009). Thus, interoceptive processing, indexed by the sensitivity and accuracy of sensing visceral afferents, may be both affected by and – in turn – affect general levels of arousal. However, it is unclear whether “embodiment” of arousal implies that insula-integrated afferents, which modulate levels of arousal, are necessary or sufficient to change arousal levels, i.e. whether the insula simply acts as a “driver” for different arousal states. Alternatively, one may consider that drug-induced changes act via this route to bring an individual to an optimal level of arousal, i.e. afford the individual access to a particular embodied state to select an optimal response. These are important questions for future research.

3.2. Attention

Attention can be conceptualized as the degree to which cognitive resources are allocated to favor processing specific stimuli of the external and internal environment as opposed to others.