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The role of hedonics in the Human Affectome

Susanne Becker[a,*,1], **Anne-Kathrin Bräscher**[b,1], **Scott Bannister**[c], **Moustafa Bensafi**[d], **Destany Calma-Birling**[e], **Raymond C.K. Chan**[f], **Tuomas Eerola**[c], **Dan-Mikael Ellingsen**[g,2], **Camille Ferdenzi**[d], **Jamie L. Hanson**[h], **Mateus Joffily**[i], **Navdeep K. Lidhar**[j], **Leroy J. Lowe**[k], **Loren J. Martin**[j], **Erica D. Musser**[l], **Michael Noll-Hussong**[m], **Thomas M. Olino**[n], **Rosario Pintos Lobo**[l], **Yi Wang**[f]

[a]Department of Cognitive and Clinical Neuroscience, Central Institute of Mental Health, Medical Faculty Mannheim, Heidelberg University, J5, 68159 Mannheim, Germany

[b]Department of Clinical Psychology, Psychotherapy and Experimental Psychopathology, University of Mainz, Wallstr. 3, 55122 Mainz, Germany

[c]Durham University, Palace Green, DH1 RL3, Durham, UK

[d]Research Center in Neurosciences of Lyon, CNRS UMR5292, INSERM U1028, Claude Bernard University Lyon 1, Lyon, Centre Hospitalier Le Vinatier, 95 bd Pinel, 69675 Bron Cedex, France

[e]Department of Psychology, University of Wisconsin-Oshkosh, 800 Algoma, Blvd., Clow F011, Oshkosh, WI 54901, USA

[f]Neuropsychology and Applied Cognitive Neuroscience Laboratory, CAS Key Laboratory of Mental Health, Institute of Psychology, Chinese Academy of Sciences, Beijing 100101, China

[g]Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Harvard Medical School, CNY149-2301, 13th St, Charlestown, MA 02129, USA

[h]University of Pittsburgh, Department of Psychology, 3939 O'Hara Street, Rm. 715, Pittsburgh, PA 15206, USA

[i]Groupe d'Analyse et de Théorie Economique (GATE), 93 Chemin des Mouilles, 69130, Écully, France

[j]Department of Psychology, University of Toronto Mississauga, Mississauga, ON L5L 1C6, Canada

[k]Neuroqualia (NGO), 36 Arthur Street, Truro, NS, B2N 1X5, Canada

[*]Corresponding author. Susanne.Becker@zi-mannheim.de (S. Becker).

[1]These authors contributed equally to this project and should be considered co-first authors; the remaining authors contributed equally and are listed in alphabetical order.

[2]Present address: Department of Psychology, University of Oslo, Forskningsveien 3A, 0317 Oslo, Norway.

Declarations of interest

None.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.neubiorev.2019.05.003.

[l]Department of Psychology, Center for Childen and Families, Florida International University, 11200 SW 8th St., Miami, FL 33199, USA

[m]Clinic for Psychiatry and Psychotherapy, Division of Psychosomatic Medicine and Psychotherapy, Saarland University Medical Centre, Kirrberger Strasse 100, D-66421 Homburg, Germany

[n]Temple University, Department of Psychology, 1701N. 13th St, Philadelphia, PA 19010, USA

Abstract

Experiencing pleasure and displeasure is a fundamental part of life. Hedonics guide behavior, affect decision-making, induce learning, and much more. As the positive and negative valence of feelings, hedonics are core processes that accompany emotion, motivation, and bodily states. Here, the affective neuroscience of pleasure and displeasure that has largely focused on the investigation of reward and pain processing, is reviewed. We describe the neurobiological systems of hedonics and factors that modulate hedonic experiences (e.g., cognition, learning, sensory input). Further, we review maladaptive and adaptive pleasure and displeasure functions in mental disorders and well-being, as well as the experience of aesthetics. As a centerpiece of the *Human Affectome Project*, language used to express pleasure and displeasure was also analyzed, and showed that most of these analyzed words overlap with expressions of emotions, actions, and bodily states. Our review shows that hedonics are typically investigated as processes that accompany other functions, but the mechanisms of hedonics (as core processes) have not been fully elucidated.

Keywords

Pleasure; Displeasure; Reward; Pain; Valence; Nucleus accumbens; Ventromedial prefrontal cortex; Orbitofrontal cortex

1. Introduction

Hedonics are experiences of pleasure and displeasure. Thus, hedonics are core processes and central components of emotional responses. For example, the emotion ‘fear’ consists of a continuum of automatically activated defense behaviors (Kozlowska et al., 2015) that can co-occur with ‘feelings of fear’, that are typically negative in valence (LeDoux and Pine, 2016). In general, the experience of emotions tends to be more complex than other feelings characterized by non-valenced mental experiences that accompany body states (based on the definition of feelings in Damasio and Carvalho, 2013; Berridge and Kringelbach, 2013; Fontaine et al., 2007). Feelings encompass a wide range of mental experiences, including, but not limited to, signifying physiological need (e.g., hunger), tissue injury (e.g., acute pain), optimal function (e.g., well-being), the dynamics of social interactions, and more (e.g., gratitude; Damasio and Carvalho, 2013). Hedonics are specific fundamental elements of the experience of feelings, contributing the core positive and negative valence to these phenomena. Specifically, pleasure as the positive valence of feelings involves feelings of enjoyment, happiness, and satisfaction. Pleasure is induced by events or stimuli that are perceived by an organism as beneficial and can be caused by the receipt of a desired stimulus or by the omission or withdrawal of an aversive stimulus or event (Cabanac, 2002).

In contrast, displeasure is a state of dissatisfaction, disgrace, or disfavor. It is induced by events or stimuli that are perceived by an organism as negatively valenced and can be caused by the reception of a punishment or by the omission or withdrawal of a reward (Cabanac, 2002).

We review findings from affective neuroscience on the core hedonic processes of feelings, as part of the *Human Affectome Project* (coordinated by the non-profit organization *Neuroqualia*). In addition to reviewing the current state of the art scientific literature, we also explore the English language words that are used in daily life to convey feelings. The project seeks to develop a comprehensive, integrated model of affect that can serve as a common focal point for affective neuroscience in the future. To that end, the current manuscript focuses specifically on the neuroscience of hedonics and the language used to express feelings relating to pleasure and displeasure. The review consists of three main parts. First, we broadly review the current scientific literature on pleasure and displeasure systems. This includes how pleasure and displeasure are mutually inhibited and promoted, as well as how they are modulated. Furthermore, we discuss impairments in hedonics in mental disorders, as well as optimal hedonic functioning in well-being, and the experience of aesthetics. Due to the vast amount of available literature in many of the fields investigated within this review, we selected representative key literature without claiming to be complete and refer the reader to reviews where appropriate. In the second part of the document, we review hedonics as they are represented in every-day language and consider how language might inform the way we approach hedonics-related neuroscience research. Lastly, we aim to identify the relationships that exist between hedonics and the other areas of affective neuroscience, particularly those reviewed within this special issue (i.e., actions, anger, attention, fear, happiness, motivation, physiological/bodily states, planning, sadness, the self, and social processing). The objective of this review is to give a broad overview of recent developments in hedonics within the field of affective neuroscience from basic research to applied areas of study, including clinical research.

2. Topic area review

2.1. Pleasure and displeasure as core hedonic processes

Positive and negative hedonic feelings are powerful motivators of behavior and likely evolved to facilitate decisions regarding which behaviors to pursue and which to avoid. For example, sensations from external stimuli with their accompanying pleasant and unpleasant qualities are integrated with an organism's learning history and current state. This allows an organism to quickly extract meaning and the significance of those sensations (Barrett and Bar, 2009; Miskovic and Anderson, 2018; Schacht and Vrticka, 2018). Further, hedonic experiences are modulated by homeostatic states and corresponding desires of an organism (Cabanac, 1971) that optimize their behavioral significance. Thus, hedonic valence is a property of a complex process of the individual and their perception.

Through the work of Osgood and Suci (1955), pleasure (or hedonic valence) emerged as the main factor of affect. However, after this initial formulation, controversies have ensued regarding whether hedonic valence should be described by a single bipolar dimension (Bradley and Lang, 1994; Russell, 1980) or two independent dimensions (Cacioppo and

Berntson, 1994; Watson and Tellegen, 1985). In addition, another ongoing and long-standing discussion in the field of hedonics relates to the hierarchical structure of affect, proposing either a dimensional model (Larsen and Diener, 1985; Tellegen et al., 1999) or models describing discrete emotion states (Barrett, 1998; Fredrickson, 2001; Izard, 1992; Zinbarg et al., 2016). Dimensional models argue for quantitative differences in orthogonal qualities (e.g., valence, arousal), while discrete models identify several qualitatively different states with different elicitors and functions (Fredrickson, 1998).

In addition to these ongoing conceptual discussions, hedonics are difficult to assess at a core phenomenological level. Hedonics are usually assessed through three distinctive output systems: subjective experience (e.g., self-reports), overt behavior (e.g., facial expressions, approach/avoidance, reaction time), and physiological responses (e.g., electrophysiology, brain imaging; Bradley and Lang, 1994; Gross and Barrett, 2011). Using behavior to identify the core processes of hedonics is complicated because such behavior typically reflects multiple aspects such as motivation and learned responses in addition to hedonics, and organisms are adaptive systems with highly flexible behavior (Simon, 1990; Smaldino and Schank, 2012). Further, although self-reports (in human research) allow introspective insights, they are easily confounded by various cognitive and social factors such as social desirability, response biases, memory effects, desires, and motivations, raising issues with the validity of self-reports. These facts may in part explain why it remains largely unknown how the brain creates affect (Lindquist et al., 2012). However, the development of mechanistic and/or computational models of affective responses has been suggested as a promising approach to overcome those limitations (Scherer, 2009; Smaldino and Schank, 2012; see Section 4.3).

In sum, research on core hedonic processes has shed light on the complex bio-psycho-social processes of an individual. However, controversies remain regarding multiple issues, including the dimensionality of hedonic valence and the structure of affect. The ultimate goal of affective neuroscience is to describe the neural mechanisms of emotion and accompanying aspects such as motivation, planning, feelings, etc. (Panksepp, 1992). Thus, more research is needed, particularly with methodologies that overcome past limitations, to solve these discussions.

2.2. Neurobiological systems of hedonics

As stated above, affective neuroscience focuses on the neurobiological underpinning of emotions and related phenomena. Accordingly, the following sub-sections of the review summarize the works on the neurobiological systems of hedonics. Since pleasure and displeasure have been typically investigated in separation, we review, first, the animal and human literature on pleasure and, second, on displeasure. However, pleasure and displeasure naturally do not occur in separation, rather they are closely linked. Thus, this section continues with a discussion on mutual inhibition and promotion of pleasure and displeasure.

2.2.1. Pleasure and reward—from animal to human models—Pleasure involves feelings of enjoyment, happiness, and satisfaction. However, the assessment of hedonic responses independent of motivational drives is challenging, as outline above. For this

reason, animal and human work on the neurobiology of pleasure has focused largely on the processing of rewards, encompassing both hedonic and motivational components.

2.2.1.1. Animal work.: Early investigations of the functional neuroanatomy of pleasure and reward in mammals stemmed from the seminal work by Olds and Milner (Olds and Milner, 1954). A series of pioneering experiments showed that rodents tend to increase instrumental lever-pressing to deliver brief, direct intracranial electrical stimulation of septal nuclei. Interestingly, rodents and other non-human animals would maintain this type of self-stimulation for hours, working until reaching complete physical exhaustion (Olds, 1958). This work led to the popular description of the neurotransmitter dopamine as the 'happy hormone'.

However, subsequent electrophysiological and voltammetric assessments as well as microdialysis clearly show that dopamine does not drive the hedonic experience of reward (liking), but rather the motivation to obtain such reward (wanting), that is the instrumental behavior of reward-driven actions (Berridge and Kringelbach, 2015; Wise, 1978). Strong causal evidence for this idea has emerged from rodent studies, including pharmacologically blocking of dopamine receptors or using genetic knockdown mutations in rodents. When dopamine is depleted or dopamine neurons destroyed, reward-related instrumental behavior significantly decreases with animals becoming oblivious to previously rewarding stimuli (Baik, 2013; Schultz, 1998). In contrast, hyperdopaminergic mice with dopamine transporter knockdown mutations exhibit largely enhanced acquisition and greater incentive performance for rewards (Pecina et al., 2003). These studies show that phasic release of dopamine specifically acts as a signal of incentive salience, which underlies reinforcement learning (Salamone and Correa, 2012; Schultz, 2013). Such dopaminergic functions have been related to the mesocorticolimbic circuitry: Microinjections to pharmacologically stimulate dopaminergic neurons in specific sub-regions of the nucleus accumbens (NA) selectively enhance wanting with no effects on liking. However, microinjections to stimulate opioidergic neurons increase the hedonic impact of sucrose reward and wanting responses, likely caused by opioid-induced dopamine release (Johnson and North, 1992). Importantly, different populations of neurons in the ventral pallidum (as part of the mesocorticolimbic circuitry) track specifically the pharmacologically induced enhancements of hedonic and motivational signals (Smith et al., 2011).

The double dissociation of the neural systems underlying wanting and liking has been confirmed many times (Laurent et al., 2012), leading to the concept that positive hedonic responses (liking) are specifically mediated in the brain by endogenous opioids in 'hedonic hot-spots' (Pecina et al., 2006). The existence of such hedonic hot-spots has been confirmed in the NA, ventral pallidum, and parabrachial nucleus of the pons (Berridge and Kringelbach, 2015). In addition, some evidence suggests further hot-spots in the insula and orbitofrontal cortex (OFC; Castro and Berridge, 2017).

Hedonic hot-spots in the brain might be important not only to generate the feeling of pleasure, but also to maintain a certain level of pleasure. In line with this assumption, damage to hedonic hot-spots in the ventral pallidum can transform pleasure into displeasure, illustrating that there is no clear-cut border between neurobiological mechanisms of pleasure

and displeasure but rather many intersections. For example sweet sucrose taste, normally inducing strong liking responses, elicits negative and disgust reactions in rats after the damage of a hedonic hot-spot in the ventral pallidum (Ho and Berridge, 2014). In addition to hot-spots that might be essential in maintaining a certain pleasure level, 'cold-spots' have been found in the NA, ventral pallidum, OFC, and insula. In such cold-spots, opioidergic stimulation suppresses liking responses, which in hot-spots causes a stark increase in liking responses (Castro and Berridge, 2014, 2017). A balanced interplay between cold- and hot-spots within the same brain regions such as the NA, ventral pallidum, OFC, and insula may allow for a sophisticated control of positive and negative hedonic responses (see 'affective keyboard' in Section 2.2.3). In line with such an assumed sophisticated control, it has to be noted that hedonic hot- and cold-spots are not to be hardwired in the brain. Depending, for example, on external factors creating stressful or pleasant, relaxed environments, the coding of valence can change in such hot-spots from positive to negative and vice versa (Berridge, 2019). Such phenomena have been observed in the NA (Richard and Berridge, 2011) and amygdala (Flandreau et al., 2012; Warlow et al., 2017), likely contributing to a fine-tuned control of hedonic responses dependent on environmental factors.

2.2.1.2. Human work.: Confirming results from animal research, a brain network termed the 'reward circuit' has been described in human research, which includes the cortico-ventral basal ganglia system, including the ventral striatum (VS) and midbrain (i.e., the ventral tegmental area; Gottfried, 2011; Richards et al., 2013). Within the reward circuit, reward-linked information is processed across a circuit that involves glutamatergic projections from the OFC and anterior cingulate cortex (ACC), as well as dopaminergic projections from the midbrain into the VS (Richards et al., 2013).

However, as previously described, reward cannot be equated with pleasure, given that reward processing comprises wanting and liking (Berridge et al., 2009; Reynolds and Berridge, 2008). Further, reward processing is modulated by subjective value and utility, which is formed by individual needs, desires, homeostatic states, and situational influences (Rangel et al., 2008). As such, pleasure as a core process is most closely related to 'liking' expressed during reward consumption. During such reward consumption, human neuroimaging studies have consistently noted a central role of the VS (including the NA) corresponding to results from animal research. The VS is consistently activated during the anticipation and consumption of reward (Liu et al., 2011). Interestingly, the VS is also activated during the imagery of pleasant experiences, including drug use in substance abusers, pleasant sexual encounters, and athletic success (Costa et al., 2010). Despite a vast literature emphasizing that the VS is implicated in the processing of hedonic aspects of reward in humans, this brain area has not been well parcellated into functional sub-regions (primarily because of limited resolution in human neuroimaging). Nevertheless, using an anatomical definition of the core and shell of the NA, one study successfully described differential encoding of the valence of reward and pain in separable structural and functional brain networks with sources in the core and shell of the NA (Baliki et al., 2013). This finding again high-lights the overlaps of pleasure and displeasure systems, rendering the separated investigation of pleasure and displeasure functions somewhat artificial.

In addition to the VS, the OFC has received much attention in human research on reward and hedonic experiences (Berridge and Kringelbach, 2015). Much of the current knowledge on the functions of the OFC in hedonic experiences is based on human neuroimaging, because the translation from animal work has proven to be challenging because of differences in the prefrontal cortex (PFC; Wallis, 2011). The OFC has been described in numerous human functional magnetic resonance imaging (fMRI) studies to represent the subjective value of rewarding stimuli (Grabenhorst and Rolls, 2011). More specifically, the OFC has been described as the first stage of cortical processing, in which the value and pleasure of reward are explicitly represented. With its many reciprocal anatomical connections to other brain regions important in reward processing, the OFC is in an optimal position to distribute information on subjective value and pleasure in order to optimize different behavioral strategies. For example, the OFC is well connected to the ACC, insular cortex, somatosensory areas, amygdala, and striatum (Carmichael and Price, 1995; Cavada et al., 2000; Mufson and Mesulam, 1982).

Besides the VS and the OFC, multiple other brain regions are involved in reward processing, including the caudate, putamen, thalamus, amygdala, anterior insula, ACC, posterior cingulate cortex, inferior parietal lobule, and sub-regions of the PFC other than the OFC (Liu et al., 2011). Reward involves processing of complex stimuli that involve many more components beyond wanting and liking, such as attention, arousal, evaluation, memory, learning, decision-making, etc.

In addition to higher-level cortical representations, pleasure also appears to be coded at very low levels of peripheral sensory processing. As an illustration, hedonic representations of smells are already present in peripheral sensory cells. There are differences in electrical activity of the human olfactory epithelium in response to pleasant vs. unpleasant odors (Lapid et al., 2011). Further, responses to the hedonic valence of odors involve differential activation of the autonomic nervous system (e.g., fluctuations in heart rate and skin conductance; Joussain et al., 2017). Together with the above-described results on central processing of pleasure, these findings highlight that extensive neurobiological systems are implicated in the processing of positive hedonic feelings including peripheral and autonomic components. In line with findings from the animal work, it can be assumed that environmental factors such as perceived stress affect these neurobiological systems leading to plastic changes (Juarez and Han, 2016; Li, 2013) and thus a sophisticated control of hedonic feelings adapted to situational factors.

2.2.2. Displeasure and pain—from animal models to human models—In contrast to pleasure, displeasure is a state of dissatisfaction, disgrace, or disfavor. However, while pleasure and positive valence of hedonics came into the focus of affective neuroscience in recent years, there is little work on the core processes of displeasure (Lindquist et al., 2012). Nevertheless, vast research on pain in animals and humans allows an approximation of core processes of displeasure. In addition, in humans, the role of the OFC in processing displeasure related to punishment and dyspnea (i.e., breathlessness), as an experience that is described as inducing strong displeasure, has been investigated.

2.2.2.1. Animal work.: Rodents naturally like consuming sweet tastes, burying objects, exploring enriched environments, interacting with companions, and exercising (Balcombe, 2006; Meijer and Robbers, 2014; Zukerman et al., 2009). When rodents stop engaging in these activities, we assume that they no longer find them pleasurable, satisfying, or enjoyable (Rygula et al., 2005). As such, in rodents, 'displeasure' is often characterized by measuring aversion or avoidance behavior that can be caused by a range of stimuli, including gastrointestinal distress (Best et al., 1973), chronic social stress (Lagace et al., 2010), fear (Krypotos et al., 2015), or pain (Pratt et al., 2013). Pain disrupts all of the aforementioned behaviors, and by proxy well-being, in lab animals (Burkholder et al., 2012). Therefore, pain is an especially well fitted stimulus to investigate processes related to displeasure, particularly because animal research relies largely on observable behavior.

In rodents, the 'unpleasantness' of pain and its affective component is usually characterized as an avoidance of the pain stimulus, while pain behaviors such as licking, jumping, and hypersensitivity are assumed to represent sensory-discriminative components of the processing of nociceptive input. Often, the conditioned place avoidance test, which measures the percentage of time spent avoiding an aversive context, is used to distinguish the affective component of pain from its sensory or reflexive aspects (Urien et al., 2017). Using conditioned place avoidance, multiple brain regions have been shown to play crucial roles in encoding the affective components of pain, including: the PFC, ACC, and prelimbic subdivisions (Jiang et al., 2014; Johansen et al., 2001), as well as the central and basolateral nuclei of the amygdala (BLA; Han et al., 2015; Neugebauer, 2015; Tanimoto et al., 2003), as discussed in the following section.

The medial PFC (mPFC) has a critical role in the modulation of aversive states and decision-making. In the context of pain avoidance, the prelimbic subdivision of the mPFC but not the infralimbic subdivision is necessary for acquiring and expressing the learned pain avoidance response (Jiang et al., 2014). In chronic pain, the mPFC has been shown to be responsible for the negative affect (both anxiety and depression phenotypes) developed as a result of chronic pain. Specifically, increased anxiety has been associated with sciatic nerve injury in rodents (Sang et al., 2018). Moreover, upregulation of mGluR5, a G-protein-coupled receptor, in the mPFC amplifies both pain and depressive behaviors in rats experiencing chronic neuropathic pain (Chung et al., 2017). Together, these studies suggest that the mPFC plays an important role in the affective responses towards pain and the affective responses as a result of chronic pain.

Relatd to pain avoidance, the ACC has been highlighted as well as critical for avoiding pain stimuli, in that ablation of ACC neurons disrupts the ability of rodents to avoid contexts, in which pain was experienced (Gao et al., 2004; Qu et al., 2011). Moreover, single-neuron recordings in the ACC reveal that specific populations of ACC neurons shift their firing rate from a pain-specific signal to encoding the anticipation of pain during conditioning of place avoidance (Urien et al., 2018). In contrast to acute pain, chronic pain states in animals have been shown to differentially impact upon sensory and affective abilities. For instance, chronic peripheral inflammation in rodents has been shown to alter acute pain representation in ACC neurons, resulting in increased aversion to noxious stimuli (Zhang et al., 2017), possibly increasing the feeling of displeasure.

In addition to the PFC and ACC, subcortical structures have been shown to be important in animal pain models. For example, the amygdala has been shown to encode sensory specific associations between environmental cues and painful stimuli in animal models. Several studies using conditioned place avoidance have shown that the amygdala (BLA and central nucleus of the amygdala, CeA) is necessary for the acquisition of an avoidance response to pain, but not the experience of pain itself (Ansah et al., 2010; Han et al., 2015). Further evidence suggests that kappa opioid receptor (KOR) signaling in the CeA specifically promotes the aversiveness of chronic neuropathic pain. Accordingly, blocking KOR in the CeA in rodents experiencing chronic pain reducing the aversiveness of the pain state (Navratilova et al., 2018).

In addition to inducing a state of aversion, pain appears to disrupt reward functions, possibly contributing to anhedonia in chronic pain and describing how long-term states of displeasure interact with functions of pleasure. A study by Taylor et al. (2015) revealed that persistent pain activates microglia in the ventral tegmental area in rodents, which disrupts the reward circuitry by increasing neuronal excitability resulting in impaired reward behavior. Furthermore, chronic pain changes galanin signaling, a neuropeptide known for its role in feeding in the NA, resulting in reduced motivation for food reward in two separate models of chronic pain in mice (Schwartz et al., 2014).

Altogether, these studies indicate a multifaceted neural network of displeasure and pain whereby the aversive nature of pain is encoded by regions, such as the ACC, prelimbic subdivisions, mesolimbic circuitry, and the amygdala. Further, chronic pain as a chronic stressor induced many changes in the underlying neurobiology, impressively illustrating how pain can induced neural plasticity, leading to an increase in negative affect. However, a fundamental difficulty that exists for neuroscientists in understanding displeasure is that there is no well-defined pain-specific neural circuit analogous to the discrete brain regions that encode pleasure (see Section 2.2.1.1).

2.2.2.2. Human work.: Many of the fine-grained results from animal research on displeasure and particularly pain cannot be directly replicated in humans. Despite a great advancement in technologies in recent years, broadly available methods used in human research, such as functional or structural MRI, still have a coarse spatial and/or temporal resolution.

Nevertheless, in line with animal work, a distributed pain processing brain network, in which affective and sensory components of pain processing can be dissociated, has been described in human research related to acute pain. In general, this network comprises the thalamus, ACC, insula, primary (SI) and secondary somatosensory cortices (SII), and PFC (Schweinhardt and Bushnell, 2010). More specifically, the so-called lateral and medial pain system have been identified, with the lateral system representing sensory-discriminative aspects of pain with SI and SII as the main structures implicated, and the medial system representing emotional-motivational aspects of pain with the main structures implicated being the ACC and the insula (Treede et al., 1999). Interestingly, in the context of negative hedonics and displeasure, it has been shown that perceived pain unpleasantness can be up-regulated, for example by hypnosis, independent of perceived intensity and vice versa with

corresponding increases in the medial or lateral pain brain system (Hofbauer et al., 2001; Rainville et al., 1997).

Similarly, sensory and affective components of pain are differently affected by different forms of cognitive-emotional pain modulation, which describes the top-down modulation of perceived pain by cognitive or emotional processes such as expectations, attention/distraction, and positive/negative affect (independent of the perceived pain; Bushnell et al., 2013, for review). While attention to pain and distraction from pain predominately affects perceived pain intensity, positive and negative affect induced, for example, by odors or music, predominately affects perceived pain unpleasantness, with positive affect leading to less perceived unpleasantness and negative affect to increased unpleasantness and thus displeasure (Loggia et al., 2008; Roy et al., 2008; Villemure and Bushnell, 2009; Villemure et al., 2003). These findings suggest predominant and direct interactions within the affective system and thus pleasure and displeasure, independent of the modalities of the inducing stimuli.

In line with such interactions and with the animal literature reviewed above (see Section 2.2.2.1), it has been proposed that chronic pain is accompanied by a shift in hedonic processing, leading to (1) impaired processing of rewarding stimuli resulting in diminished positive affect within the NA, and (2) an increase of a negative stress-related state resulting in enhanced negative affect (Combined Reward deficiency and Anti-Reward Model, CReAM; Borsook et al., 2016). Related to the latter, the habenula has been suggested as a hub in this increase of a negative stress-related state (Borsook et al., 2016), although evidence on such a central role of the habenula remains scarce. Such a shift may partially explain manifestations of anhedonia and impaired motivation, particularly when related to obtaining reward, that have been described in chronic pain (Marbach et al., 1983). These processes also may result in high comorbidity between chronic pain and affective disturbances such as depression (Rayner et al., 2016), which is characterized by impaired positive affect (see Section 2.4.1).

Corresponding to the described negative hedonic shift in chronic pain, a shift from nociceptive to emotional-motivational has been described (Hashmi et al., 2013), illustrating that the processing of pain and displeasure is not hard-wired in the brain but can shift depending on nociceptive input. Specifically, altered functional connectivity between medial PFC (incorporating parts of the OFC) and the VS (including the NA) has been shown to be predictive of the transition from sub-acute to chronic pain (Baliki et al., 2012), highlighting an interesting overlap with brain regions being involved in the processing of pleasure and reward.

Another intense sensation, beside pain, that allows the investigation of displeasure as a core process is dyspnea. Dyspnea or shortness of breath is an experience described as extremely unpleasant, sometimes even associated with feelings of impeding death (Banzett et al., 2008), inducing a strong feeling of displeasure. Different sensory qualities of dyspnea include air hunger (i.e., the urge to breathe), sense of excessive work of breathing (i.e., increased impedance of inspiration), and the feeling chest tightness, which is associated with bronchoconstriction (Lansing et al., 2009). Similarly to pain perception, sensory and

affective dimensions of dyspnea have been described (Lansing et al., 2009), which can be distinguished during experimentally induced hypercapnia (Wan et al., 2009). When breathing through an inspiratory resistive load, distraction led to a decrease in perceived unpleasantness compared to attention to the breathing load while perceived intensity was in both conditions comparable (von Leupoldt et al., 2007). The available literature suggests an overlap with brain structures implicated in pain processing (von Leupoldt et al., 2009). Early studies show an activation of the insular cortex by air hunger (Banzett et al., 2000) and during loaded breathing (Peiffer et al., 2001) along with activation of limbic structures including the ACC and amygdala (Evans et al., 2002; Liotti et al., 2001). More recent studies separate the affective from the sensory dimension and conclude that unpleasantness but not intensity related to dyspnea is processed in the anterior insula and amygdala (Stoeckel et al., 2018; von Leupoldt et al., 2008). This overlap with brain processing of acute painful stimuli is suggestive of a brain network of the processing of displeasure, independent of inducing stimuli and modalities. However, as mentioned above in the context of animal work on displeasure (see Section 2.2.2.1), it appears that there is no well-defined neural circuit, processing displeasure similar to the well-known discrete reward circuit (see Section 2.2.1.1).

Nevertheless, human research has emphasized the role of the lateral OFC in displeasure (Dunckley et al., 2005; O'Doherty et al., 2001; Seymour et al., 2007; Small et al., 2001). Activation in the lateral OFC has been related to the evaluation of punishing stimuli representing aversive value (Kringelbach and Rolls, 2004; O'Doherty et al., 2001). However, most studies on the role of the OFC have only investigated hedonics indirectly by examining processes such as aversive conditioning, reversal learning, or decision-making. Based on such studies, a consistent observation is that representations of aversive stimuli in the lateral OFC can result in a change of ongoing behavior (O'Doherty et al., 2001; Rolls et al., 2003). These study results have suggested that the lateral OFC codes signals to initiate escape behavior rather than displeasure being a core process (Berridge and Kringelbach, 2013).

In sum, a circuit comprising a set of distinct brain regions specifically processing displeasure has not been described yet. Overlaps in the neural correlates of affective dimensions of pain and dyspnea hint at such a possible discrete circuit, but more research is needed to specify such a circuit. Further, results on chronic pain suggest that such a circuit can be subject to change depending on input, resulting in increased negative hedonic responses. Similarly, the potential role of the lateral OFC as one distinct brain region involved in processing displeasure and/or related escape behavior has to be elucidated.

2.2.3. Mutual inhibition and promotion of pleasure and displeasure—As discussed above in several instances, the investigation of pleasure and displeasure in separation, with existing research often focusing on reward or pain, appears unnatural. Rather, many interactions between positive and negative hedonics are observable, corresponding to a traditional perspective from psychological research that there exists a hedonic continuum, ranging from pleasure on one end to displeasure (often described in terms of pain) on the other (Cabanac, 1979). This is an intuitive concept and is applicable in several instances. For example, it has been shown that experiencing pleasure induced by images or music, or obtaining a reward inhibits experienced pain (Becker et al., 2013;

Kenntner-Mabiala and Pauli, 2005; Roy et al., 2008). In clinical contexts, the experience of chronic pain suppresses positive feelings and pleasure (Marbach et al., 1983). The mutual inhibition of pleasure and displeasure in terms of pain may be mediated by endogenous opioids (Fields, 2007; Leknes and Tracey, 2008). Further, the NA and ventral pallidum have been described to contain both hedonic hot-spots and cold-spots (see Section 2.2.1.1). Moreover, an arrangement of an 'affective keyboard', describing graded affective responses related to neighboring anatomical representations, has been suggested specifically in the NA medial shell (Richard and Berridge, 2011). Moving from anterior to posterior locations in the NA medial shell results in a gradient of responses from appetitive through mixed to fearful. Those findings suggest a brain mechanism that may serve to control the balance between positive and negative affect, possibly particularly important if stimuli inducing pleasure and displeasure are present simultaneously. Importantly, the affective keyboard can be modulated by environmental factors. Exposure to stressful environments (i.e., bright lights and loud music) causes NA caudal fear-generating zones to expand rostrally in rats. Conversely, a preferred home environment (i.e., familiar, dark and quiet) caused NA appetitive-generative zones to expand caudally while shrinking the fear-generating zones (Reynolds and Berridge, 2008). Similarly, the roles of local D1 and D2 dopaminergic receptors in the NA shell switch roles depending on a positive or negative environmental context (Richard and Berridge, 2011). These findings highlight that the processing of positive and negative affect is not hardwired in the brain and that hedonic hot-spots underlie neural plasticity.

Similar to the concept of the affective keyboard, some brain regions are involved in the modulation of hedonic value in humans. For instance, mid-anterior and mid-lateral regions of the OFC and the medial edge have been shown to represent changes in perceived pleasure when the perceived pleasantness of food changes dependent on different states of satiation (Small et al., 2001). The medial OFC has further been shown to mediate perceived reductions in perceived pain due to a simultaneously obtained reward and thus the intersection of an un- pleasant and a pleasant experience (Becker et al., 2017b).

The assumed continuum and one-dimensional space between pleasure and displeasure is subject to modulatory influences as suggested by numerous examples in recent research (Ellingsen et al., 2015). Such modulatory influences are sensory, homeostatic, cognitive, and social-cultural factors that result in complex interactions of pleasure and displeasure. An example of such complexities is that of mutual promotion, in which pleasure may promote pain experiences and vice-versa, or pleasure and pain that are experienced concurrently. A deep massage or eating hot chili peppers serve as examples of such mixed affective experiences. Similarly, pain is not always perceived as negative. An intriguing example of this is experiencing moderate levels of pain as pleasurable, if this experience represents the avoidance of even stronger pain (Leknes et al., 2013). This 'hedonic flip' was found to be correlated with increased activation in the VS (including the NA), ventromedial (vm) PFC, and periaqueductal grey (PAG). Further, if told that the pain had beneficial effects, people could tolerate ischemic pain longer (Benedetti et al., 2013), with this effect being linked to the co-activation of opioid and cannabinoid neurochemical systems. Further, experiencing strong pain induced by a cold-stressor test increased the pleasure from eating chocolate (Bastian et al., 2014a). Possibly, enhanced pleasure following pain is caused by the release

of endogenous opioids, which both pain and reward can elicit (Smith and Berridge, 2007), leading to a positive shift in hedonic experiences (Leknes and Tracey, 2008). In addition, heightening of sensory processing and attention may cause pleasure following pain. Given the adaptive association between pain and action readiness, modulated by physiological arousal and awareness, it is suggested that during the brief period following the offset of pain, heightened arousal levels are maintained, possibly resulting in a higher level of attention to sensory inputs that are hedonically positive (Bastian et al., 2014b).

From the available literature, it cannot be concluded when mutual inhibition or promotion occurs. It may be that both effects can be present simultaneously, highlighting the complex nature of the interaction of pleasure and displeasure. Whether a study reports mutual inhibition or promotion could be explained in many instances by methodological aspects. For example, studies testing the pain-inhibiting effects of a pleasurable event such as viewing a pleasant picture or obtaining a reward (see above; Becker et al., 2013; Kenntner-Mabiala and Pauli, 2005; Roy et al., 2008) specifically tested the pain-inhibitory effects without assessing possible mutual promotion. Nevertheless, it is likely that in such situations participants perceived pleasure and displeasure simultaneously as well and possibly the pain enhanced the pleasure induced by the stimuli.

Focusing on co-occurring pain and reward, the Motivation Decision Model of Pain describes neurobiological mechanisms of mutual inhibition and promotion of pleasure and displeasure and when these effects are expected (Fields, 2006, 2007). According to the model, anything that is evaluated as more important than pain in a specific situation should have antinociceptive effects, leading to a simultaneous enhanced perception of reward and pleasure. In contrast, if the pain is viewed as more important, pronociceptive effects should occur, diminishing simultaneously the perception of the reward/pleasure. Supporting the model, mice trained to expect chocolate when standing on a hot plate that was turned off remained (and endured pain) for about twice as long when the hot plate was turned on compared to a control group, trained to expect regular food, before escaping (Dum and Herz, 1984). Similarly, if human volunteers had the choice between accepting a monetary reward that was coupled to a painful electrocutaneous stimulation or rejecting the reward at the benefit of avoiding the pain, pain was inhibited when participants accepted both reward and pain, suggesting anti-nociceptive effects, and facilitated when rejecting both, suggesting pro-nociceptive effects (Becker et al., 2017a). Mutual inhibitory and promotional effects are presumed in the model to be exerted via engagement or inhibition of descending opioidergic pathways, respectively (Fields, 2006, 2007).

In sum, positive and negative hedonic feelings affect each other, which is reflected in the underlying mechanisms. For example, some brain regions have been demonstrated to be specifically involved in the processing of such mutual influence. Further, a fine-grained modulation of the balance between positive and negative affect appears to be fostered by arrangements such as the affective keyboard, which itself is subject to neural plasticity dependent on environmental factors. Similarly, whether mutual inhibition or promotion occurs, depends on several internal and external factors of an organism and the surrounding situation.

2.3. Modulation of hedonic feelings

Positive and negative hedonic feelings are powerful motivators, facilitating decisions related to goal-directed behavior. However, in order to be useful, pleasure and displeasure need to be malleable to information about external context and internal state, needs, and motivations of the individual, since the utility of given actions and sensations depend on these factors. Such malleability mirrors (to some extent) the mutual inhibition and promotion of pleasure and displeasure, of which the direction and degree depend on internal and external factors, as discussed above (see Section 2.2.3). Hedonic value can be modulated by various factors such as behavioral and cognitive regulatory mechanisms, memory and learning, development and sensitivity windows, and biological factors, including sex differences, and external influences, which will all be considered in greater detail in the following sections.

2.3.1. Behavioral and cognitive regulation of hedonics—A powerful modulator of positive and negative hedonic feelings is expectation. The strong effect of expectations on pleasure and displeasure is impressively illustrated by placebo or nocebo effects, in which clinical outcomes, physical performance, or other feelings, are improved or deteriorated due to positive or negative expectations toward a treatment (Benedetti et al., 2007; Carlino et al., 2014; Finniss et al., 2010; Geuter et al., 2017). Placebo and nocebo effects have been investigated in positive affect (Ellingsen et al., 2013; McCabe et al., 2008; Plassmann et al., 2008) and extensively studied in pain (e.g., Amanzio and Benedetti, 1999; Atlas et al., 2012; Eippert et al., 2009; Jensen et al., 2015; Wager et al., 2004; reviewing the vast amount of literature on placebo and nocebo effects in pain is beyond the scope of this review and can be found elsewhere: Damien et al., 2018; Vase et al., 2016). Focusing on hedonics, placebo effects in pain are particularly interesting phenomena as they describe a transition of hedonic feelings from a negative affective state and displeasure (induced by pain) to a positive affective state and pleasure (induced by pain relief). Functional neuroimaging studies have investigated how expectations modulate brain activation to produce pain relief or pain increases related to placebo and nocebo effects (Wager and Atlas, 2015), showing that activation in regions such as PFC, OFC, rostral ACC, and PAG is increased in response to placebo treatment, while activation in somatosensory processing regions was reduced (Amanzio et al., 2013; Atlas and Wager, 2014). A similar modulatory circuit including rostral ACC and PAG seems to regulate nocebo hyperalgesia (Tinnermann et al., 2017), leading to increased activation in brain regions commonly associated with the processing of pain (Bingel et al., 2011; Geuter and Buchel, 2013; Kong et al., 2008; Schmid et al., 2015). Interestingly, studies investigating expectation-induced enhancement of perceived pleasantness have similarly found increases in this circuitry including the vmPFC, OFC, amygdala, and VS (Ellingsen et al., 2013; Plassmann et al., 2008), consistent with the view that there may be some common mechanisms involved in shifts of hedonic value – whether positive or negative.

In the context of pain research, it has also been shown that also several cognitive-emotional factors (other than expectation) can modulate the perception of pain and thus displeasure (Bushnell et al., 2013) including, perceived control of the painful event and cognitive reappraisal. Salomons and colleagues (Salomons et al., 2015) showed, for example, that acute pain that was perceived by participants to be controllable was associated with

decreased perceived pain accompanied by decreased activation in the amygdala and increased activation in the VS (including the NA). Other results highlight a possibly mediating role of the dorsolateral PFC in the effects of perceived control on acute pain (Bräscher et al., 2016; Wiech et al., 2006). Similarly, cognitive reappraisal of acute pain, leading to increased or decreased pain perception has been demonstrated to be mediated via the functional connectivity between the VS (including the NA) and vmPFC (overlapping with the OFC; Woo et al., 2015), again highlighting the role of brain regions central in pleasure and reward processing in the modulation of displeasure.

One strategy of modulating hedonic feelings, partially overlapping with cognitive reappraisal discussed before, is emotion regulation, by which pleasure and displeasure can be modulated with respect to duration, intensity, latency, onset/offset, and valence (Gross, 1998, 2014). According to the Process Model of Emotion Regulation, one of the most widely cited models in this context, emotion regulation can occur via behavioral strategies such as situation selection (i.e., choosing which context to put oneself into in order to experience or avoid a particular emotion) and situation modification (i.e., changing the context in a way that modifies one's emotions e.g., listening to music; Gross, 1998, 2014) and via cognitive strategies, such as attentional deployment (i.e., directing one's attention within a given context to modify one's emotions) and cognitive change (i.e., changing how one appraises a context to modify one's emotions; Gross, 1998, 2014). In addition, the model describes that emotion regulation can occur via response modulation (i.e., directly modifying the existing behavioral, experiential, or physiological correlates of one's emotions), involving behavioral and/or cognitive processes (Gross, 1998, 2014). Emotion regulation can serve to upregulate (i.e., to enhance) or downregulate (i.e., to dampen) components of an emotional response. Several brain regions that have been related before to the processing of pleasure and displeasure are implicated in emotion regulation such as the PFC, ACC, anterior insula, and VS, regardless of which strategy of emotion regulation is utilized (e.g., Diekhof et al., 2011; Frank et al., 2014; Kohn et al., 2014; Morawetz et al., 2017). Interestingly, emotion regulation can be employed consciously and is indeed part of cognitive behavioral therapy in affective disorders, which are characterized by impaired hedonic feeling as discussed in Section 2.4.

2.3.2. Learning and memory—Early writings by Darwin describe the striking link between stimuli and the affective states they elicit that can either be inherited or be associated by habit – in other words, through learning and memory (Anderson and Adolphs, 2014). Learning involves the acquisition of knowledge or skills through study, experience, or being taught, while memory comprises storing and remembering information.

Evidence suggests that learning plays a major role in the development and modulation of likes and dislikes, i.e., the experience of pleasure or displeasure in response to stimuli (Rozin and Millman, 1987; Wardle and Cooke, 2008), although in some cases preference is genetically programmed (e.g., preference for sweet taste; Steiner et al., 2001). Conditioned taste aversion is a prominent example, in which gastrointestinal malaise, especially nausea and vomiting, lead through classical conditioning to decreased hedonic value of the ingested taste in animals (Itoga et al., 2016; Roitman et al., 2010) and humans (Klosterhalfen et al., 2000). A real life equivalent to conditioned taste aversion is food poisoning, illustrating stark

changes in hedonic experience in one trial learning situations. Evidence shows that after inducing conditioned taste aversion in rats, the pattern of neural activation changes in NA (Roitman et al., 2010) and ventral pallidum (Itoga et al., 2016), suggesting that the NA-ventral pallidum circuit encodes innate preference as well as learned hedonic value (Itoga et al., 2016).

Evaluative conditioning as another type of learning can also modulate hedonic feelings, whereby a change in hedonic valence of a stimulus is induced by coupling this stimulus with another valenced stimulus that elicits an affective response. Evaluative conditioning has been investigated within and across different modalities, e.g. using odorant, visual, gustatory, auditory, and haptic stimuli (Fu et al., 2018; Heycke et al., 2017; van den Bosch et al., 2015). For instance, presenting photos of happy babies together with fragrances increased the pleasantness of those fragrances and increased activation in the OFC and VS (including the NA) compared to a coupling of the fragrances with affectively neutral pictures (Hummel et al., 2017). Further, observing the behavior of others can induce changes in hedonic value via observational learning. For instance, watching a model showing a facial disgust expression after consumption of a colored drink decreases the liking of the same colored drink in the observer (Baeyens et al., 2001).

In addition to associative learning, hedonic value can also be modulated by non-associative learning, for instance by the phenomenon called ‘mere exposure’. The mere exposure effect describes the phenomenon that (repeated) exposure to a neutral stimulus increases the liking of this stimulus (Zajonc, 1968). Irrespective of number of exposures, increased liking has been shown to be associated with increased activation in the anterior insula and the striatum (Green et al., 2012).

Not only different forms of associative and non-associative learning modulate hedonic feeling, but also how information on hedonic feelings is stored and remembered. The effect of memory on hedonic feelings can be seen in primacy and recency effects, whereby recency effects appear to have a stronger influence (Murdock Jr, 1962). Memory of the enjoyment at the end of an pleasant experience rather than the memory of the enjoyment at its beginning determines how people desire to repeat that experience, as shown in gustatory contexts (Garbinsky et al., 2014). It has been shown that memory for end moments, when people are most satiated, interferes with memory for initial moments. Consequently, end moments are more influential than initial moments when people decide how long to wait until consuming a food again (Garbinsky et al., 2014). This is related to the peak-end rule (Kahneman, 2000), which states that the retrospective evaluation of affective episodes does not depend on the feelings over the full duration of the episode, but on the average of the most intense feeling during the episode and the feeling at the end of the episode. An intriguing implication of this rule related to displeasure is that extending the duration of a painful episode while reducing the pain at its end should result in less remembered unpleasantness of the episode compared to when it would have terminated earlier. This has been confirmed in studies that recorded the pain reported by patients undergoing colonoscopy (Redelmeier et al., 2003) and students undergoing hand immersion in cold water (Kahneman et al., 1993).

2.3.3. Development and sensitive windows in the acquisition of hedonic responses—Learning and memory are processes that are based on prior experiences and thus an individual learning history. However, sensory hedonics (i.e., pleasurable or displeasurable responses to sensory stimuli) are characterized by predisposed (unconditional, universal, stereotyped) in addition to learned responses. Examples of the former are the positive response to sweet taste and the negative response to bitter taste, which are present at birth and have an adaptive function of approach and avoidance of edible and poisonous substances (Steiner et al., 2001). Some of these predisposed responses seem to be limited to sensitive windows during development. For example, the rabbit mammary pheromone attracts pups only during the very first days of life (Schaal et al., 2003). Similarly, in the visual domain, young primates display a preference for faces over non-face objects, independent of any experiences with faces (Sugita, 2008).

Such predispositions are added by very early, in utero learning experiences reminding of the phenomenon of mere exposure described in the section before (see Section 2.3.2). For instance, a fetus perceives in utero odors from the mother's diet and experiences the mother's voice and spoken language, resulting in preferences for these odors, their mother's voice and language, which is observable after birth (e.g., DeCasper and Fifer, 1980; Mennella et al., 2001; Moon et al., 1993). Sensitive windows occur also later in life. For example, exposure to particular odors during infancy and childhood lead to more positive hedonic responses in adulthood than if these odors were encountered less often or later in life (Haller et al., 1999; Poncelet et al., 2010). Despite these insights into the relevance of sensitive windows, it remains elusive whether deficiency of sensory stimulation during such sensitive periods interferes with later behaviors and experience of hedonics.

2.3.4. Biological and external modulators of sensory hedonics—In addition to behavioral, cognitive, and developmental factors, biological characteristics of the sensory system can affect hedonic feelings directly, modulating sensory hedonics. For example, hedonics in response to external stimuli are modulated by various internal and external factors such as biological (e.g., expression of sensory receptors), physiological (e.g., hormones, age), and psychophysical fac- tors (e.g., stimulus concentration/intensity, exposure), among others. This is particularly observable in the domain of olfaction: Due to direct projections from the olfactory bulb to the amygdala and hippocampus, olfaction has been considered a basic form of affective processing. Some olfactory hedonic responses are comparably stable across individuals (e.g., smells signaling a threat, such as spoiled food), but in general individuals differ in their responses to most chemical compounds from the environment. This variability is expressed at the level of olfactory receptors. Odor perception results from the activation of a combination of receptors, each receptor being the expression product of one of 400 olfactory genes. For example, individuals carrying one of two different alleles of the receptor for the body odor androstenone show contrasting hedonic responses (Keller et al., 2007). However, characteristics of odorant molecules, sensory exposure, hormonal status, and age are also strong modulators of hedonic responses to smells. For example, increasing intensity of odorants can lead to a decrease as well as an increase in pleasantness depending on the specific odorant (Cain and Johnson, 1978; Ferdenzi et al., 2014; Moskowitz et al., 1976). With respect to hormonal status, women

perceive the smell of androstenone as less unpleasant during their ovulatory phase than during other phases of the menstrual cycle (Hummel et al., 1991). Further, Joussain and colleagues (Joussain et al., 2013) showed that with age the hedonic valence of unpleasant odors remains unchanged, while pleasantness of positive odors decreases. Interestingly, geography and culture affect sensory hedonics as well, apart from different genetic backgrounds: Individuals are exposed and familiarized from birth to adulthood to very different olfactory environments, foods, and practices that shape hedonic experiences (Poncelet et al., 2010), likely directly at the level of the sensory system.

2.3.5. Sex differences—One biological factor that emerges as relevant in various contexts is sex differences – not only on the context of sensory hedonics, but also in pain processing and in general emotion processing.

With respect to sensory hedonics, one sex-related factor that causes variation is the hormonal status of women. Hummel et al. (1991) showed that women evaluate the smell of androstenone as less un-pleasant during their ovulatory phase compared to other phases. Further, pregnant women perceive some odors as more unpleasant than non-pregnant women (Kolble et al., 2001). Considering learning (including non-associative learning) and memory as discussed above (see Section 2.3.2), sex differences have been described with repeated exposure to odors. Liking ratings decrease significantly with respect to repeated exposures in men but not in women (Triscoli et al., 2014). Further, women have been shown to code odorants more often auto-biographically than men (Zucco et al., 2012). Interestingly, sex differences have been shown to moderate sensory hedonics related to the perception of odors in schizophrenia as a mental illness accompanied by impaired hedonics: Men suffering from schizophrenia rate pleasant odors as less pleasant than women suffering from schizophrenia (Moberg et al., 2003; for details see Section 2.4.1).

Beside olfaction and directly related to sensation, sex differences have been well described in pain research. Women are more sensitive to pain compared to men across pain modalities and are overrepresented as patients with chronic pain (Bartley and Fillingim, 2013; Berkley, 1997; Mogil, 2018). This may be underpinned by differences in expressions of NMDA-receptors (Dong et al., 2007), opioidergic processing (Chakrabarti et al., 2010; Liu and Gintzler, 2000; Loyd et al., 2008), sex chromosomes (Gioiosa et al., 2008), and psychosocial and cultural factors (Mattos Feijo et al., 2018; Sanford et al., 2002). However, higher pain sensitivity does not necessarily equate stronger un-pleasantness. When focusing specifically on pain unpleasantness, no differences in perceived unpleasantness between women and men were found, albeit neural correlates differed between sexes (Girard-Tremblay et al., 2014).

More general, sex differences have been intensely study in emotion processing. Early studies described that women show higher emotion expression compared to men, but men and women do not differ in the experience of emotion (Dimberg and Lundquist, 1990; Kring and Gordon, 1998). This finding has been replicated several times (e.g., Kret and De Gelder, 2012; Polackova Solcova and Lacev, 2017), although other studies also report some differences in the experience of emotion between women and men (e.g., Deng et al., 2016; Fernandez et al., 2012). In addition, differences in the neural correlates of emotions have been described, with women showing distinct activation in the amygdala, hippocampus, and

regions of the dorsal midbrain compared to men. Men show distinct activation in the mPFC, ACC, frontal pole, and mediodorsal nucleus of the thalamus compared to women, as recently shown in a large meta-analysis (Filkowski et al., 2017). However, these studies did not focus specifically on hedonic feelings and their neural correlates. In addition, although many studies found higher positive and negative valence ratings in women compared to men, this difference might be caused by a higher expressiveness in women compared to men, as described above.

2.4. Applied hedonics

Hedonics have not only been investigated in the context of basic research questions such as delineating underlying neurobiological systems and factors that modulate the experience of hedonic feelings, but also in applied contexts describing both maladaptive and adaptive functioning. As the fundamental elements of the experience of feelings and as powerful positive and negative motivators of behavior, maladaptive and adaptive functioning of hedonics can starkly influence well-being and daily life functioning. Malfunctions of hedonic processes have been described in several mental disorders resulting, for example, in anhedonia and impaired motivation. Thereby, malfunctions of hedonics can lead, in severe cases, to a complete loss of motivational drive and thus an inability to manage daily functioning. In contrast, adaptive functioning in terms of successful, well-functioning hedonics foster long-term well-being and flourishing, leading to good mastering of various daily and life obstacles and satisfaction. In this context, one aspect, namely the experience of aesthetics, begins to receive more and more attention, as a factor that affects humans in many daily situations by modulating hedonic states. For example, aesthetics as a modulator of well-being and inducing positive hedonic feelings has been discussed in the context of interior design and architecture in private and public places, surrounding the whole industry of wellness and spa-treatments, and as sources of recreation (Smith et al., 2012).

In the following, such maladaptive and adaptive functioning of hedonics will be discussed exemplary, focusing on a few notable examples of mental disorders associated with aberrant hedonic processing and well-being and flourishing as well as the experience of aesthetics as examples for adaptive hedonics.

2.4.1. Mental disorders—Mental disorder are commonly accompanied by impaired processing of pleasurable experiences and heightened processing of displeasurable experiences and thus malfunctioning of hedonics. As a prototypic example of such malfunctioning, major depression will be described in the following, added by a description of aberrant hedonics in schizophrenia and attention-deficit/hyperactivity disorder (ADHD) as less well-known examples. In addition, malfunctioning of hedonics has been considered as a possible mechanism across different mental disorder diagnoses, opening novel avenues to mechanism-based therapeutic approach, as detailed below.

2.4.1.1. Major depression.: Major depression is characterized by low mood for at least two weeks and across most situations. One of the primary symptoms of major depression is loss of interest and pleasure (American Psychiatric Association, 2013), which is referred to as anhedonia (Meehl, 1975). Individuals with depression often demonstrate significantly

lower levels of self-reported extraversion, which includes facets of reward seeking and well-being (Kotov et al., 2010) and behavioral activation system functioning (Pinto-Meza et al., 2006; Wilson et al., 2014). Correspondingly, individuals with major depression demonstrate diminished responsiveness during the anticipation and receipt of reward (Liu et al., 2014). Corresponding to these behavioral observations, several research groups have found decreased activation in the VS (including the NA) related to reward processing in patients with major depression compared to healthy controls (Zhang et al., 2013).

Independent of hedonics, women suffer roughly about twice as often as men do from major depression (Buckner et al., 2008; Salk et al., 2017). Interestingly, women with a current or lifetime diagnosis of major depression report more anhedonia as one core symptom compared to men (Thompson and Bland, 2018). A similar pattern has been found in the general population in the seasonality of depressive symptoms, with longer days correlating with reduced anhedonia in women but not in men (Lyall et al., 2018). Sex differences have also been described at the level of the brain, for instance, with depressed women showing altered prefrontal-limbic circuits while depressed men show altered prefrontal-striatal circuits (Kong et al., 2013), although it remains open how this relates to altered hedonics, since only few studies are available in this context (Bangasser and Valentino, 2014).

2.4.1.2. Attention-deficit/hyperactivity disorder.: ADHD has often been conceptualized as disorder of executive function, but recent work has established the need to integrate emotional and reward functioning into this conceptualization (Graziano and Garcia, 2016; Shaw et al., 2014). In general, ADHD is characterized by problems in paying attention, excessive activity, and difficulties in controlling behavior. However, several models of ADHD, including the Multiple Pathway Model (Nigg et al., 2004), suggest that ADHD is associated with disruptions in positive/approach emotions (preferring small immediate to larger delayed rewards) and emotion regulation as a modulator of hedonic feelings as discussed above (see Section 2.3.1). Several brain regions and networks have been proposed to underlie altered emotion and reward processing observed in ADHD (Rubia, 2018), including reduced activation in vmPFC, OFC, and VS (including the NA). Specifically, in the context of reward anticipation, individuals with ADHD tend to respond with reduced VS activation (Plichta and Scheres, 2014), while reward delivery has been associated with increased activation in the ventral and dorsal striatum (Furukawa et al., 2014). With respect to positive emotion, patients with ADHD have been shown to display greater activation in the dorsolateral PFC, left temporal and occipital cortex, vmPFC/subgenual ACC, striatum, and temporal parietal regions, as well as enhanced connectivity between amygdala, striatal, and occipital regions, during a positive emotion distraction task (Hwang et al., 2015; Passarotti et al., 2010; Posner et al., 2011; Rubia, 2018). Thus, ADHD appears to be associated with elevated hedonic responding at reward attainment, but reduced responding to reward anticipation.

The vast majority of studies examining hedonic responses and reward processes in individuals with ADHD have utilized exclusively male samples (Plichta and Scheres, 2014), although there are marked sex differences in the prevalence of ADHD with males outnumbering females at approximately 3 to 1 (Crowley et al., 2013). A recent study reported disruptions in fronto-subcortical functional connectivity specifically among girls

with ADHD in the context of a delay discounting task (Rosch et al., 2018), indicating individual preferences of smaller immediate rewards over larger, delayed rewards. However, delay discounting incorporates predominately motivational and cognitive aspects, because of which conclusions on hedonics as a core process are hard to derive. Other studies on hedonic and reward processes among individuals with ADHD have found no sex differences (Meinzer et al., 2012; Sternat and Katzman, 2016, for review).

2.4.1.3. Schizophrenia.: Anhedonia is one of several negative symptoms typically present in schizophrenia, which is also characterized by abnormal behavior and a decreased ability to understand reality. Symptoms frequently include false beliefs, confused thinking, and hallucinations. Nevertheless, an emotional paradox has been proposed in schizophrenia, describing a discrepancy between deficits in self-reported pleasurable experiences, but unaltered stimuli-induced experience of pleasure when assessed in the laboratory compared to healthy controls (Gard et al., 2007; Horan et al., 2006). This discrepancy can be resolved by taking into account wanting and liking or anticipatory and consummatory pleasure in this context (Kring and Barch, 2014). Findings from self-report measures (e.g., the Temporal Experience Pleasure Scale) suggest deficits in anticipatory pleasure in patients with schizophrenia, but not in consummatory pleasure (Gard et al., 2006; Li et al., 2015; Mote et al., 2014). Laboratory-based assessments that focus on consummatory pleasure reveal comparable hedonic ratings of positive stimuli in patients with schizophrenia and healthy controls as demonstrated in a meta-analysis (Cohen and Minor, 2010). Specifically distinguishing anticipatory and consummatory pleasure, the differential responding of deficits in anticipatory pleasure but not in consummatory pleasure was confirmed by using the Anticipatory and Consummatory Pleasure task in patients with schizophrenia (Gold et al., 2013; Lui et al., 2016; Moran and Kring, 2018). On a neurobiological level, hypoactivation of the VS has been found in patients with schizophrenia during reward processing using fMRI compared to healthy controls (Arrondo et al., 2015; Li et al., 2018).

Similar to the observations in depression and ADHD, sex difference related to positive and negative hedonic feelings have been described in schizophrenia. In general, men have a higher incidence of schizophrenia than women (1.4:1) and women show a later onset with more affective symptoms (Abel et al., 2010; Li et al., 2016). Specifically, using a network analysis approach, blunted affect was highlighted as a central symptom in women being closely interconnected to the presence of other negative symptoms such as alogia (i.e., inability to speak), and asociality (i.e., lack of motivation to engage in social interaction; Strauss et al., 2019). Despite this blunted affect, women with schizophrenia show increased pleasantness or unpleasantness in response to hedonically positive or negative pictures compared to men with schizophrenia (Heerey and Gold, 2007). Similarly, results on sensory hedonics related to smells in schizophrenic patients showed disrupted pleasantness ratings of the odorant molecule of amyle acetate (smelling like banana) in men but not in women, which could not be explained by an impairment of odor detection (Moberg et al., 2003). This result was confirmed by further studies, with men suffering from schizophrenia rating pleasant odors as more unpleasant than healthy men and no such difference in women (Walsh-Messinger et al., 2018; but see Kamath et al., 2013). Correspondingly, an impaired trait hedonic capacity assessed using self-reports has been described in male but not female

patients with schizophrenia (Yan et al., 2012). Further, negative picture viewing has been shown to evoke significantly greater activation in the thalamus, cerebellum, temporal, occipital and posterior cingulate cortex in men suffering from schizophrenia, while women suffering from schizophrenia exhibited greater activation in the left middle frontal gyrus (Mendrek et al., 2007).

2.4.1.4. Mechanism-based diagnostic groups.: The occurrence of impaired hedonics in several mental disorders led to the hypothesis of a common underlying disease mechanism. Supporting this hypothesis, cross-diagnostic comparisons on effort-cost decision-making in depression and psychosis show that both diagnostic groups are less willing to expend effort to obtain rewards compared to healthy controls. However, despite this phenomenological similarity, different mechanisms appear responsible: reduced reward responsivity in depression and deficits of cognitive control in psychosis (Anticevic et al., 2015; Culbreth et al., 2018). Nevertheless, because several mental disorders show altered hedonic responses such a cross-diagnostic approach promises important insights, likely revealing mechanisms that can be utilized in therapeutic approaches. This is in line with the National Institute of Mental Health Research Domain Criteria project (Insel, 2014), which aims for a new description of mental illnesses, based on dimensions of observable behavior and neurobiological measures with the goal is to understand the mechanisms of mental health and disease in terms of varying degrees of function and dysfunctions.

2.4.2. Hedonics and well-being—Given that numerous mental disorders can be characterized by malfunctioning hedonics, it is not surprising that adaptive hedonics have been associated with well-being. Contemporary discussions on well-being consider a distinction between hedonics and eudaimonia. In contrast to hedonics, which are typically short-term, immediate reactions, eudaimonia focuses on long-term and future goals such as life satisfaction, engagement in meaningful activity, flourishing, and long-term well-being (Peterson et al., 2005; Ryan and Deci, 2001). Importantly, eudaimonia is accompanied by positive affect and positive hedonic feelings.

From a neurobiological perspective, a small, but growing body of research has begun to connect eudaimonia and its related components, to variations in neural circuitry. From a structural perspective, eudaimonic well-being has been found to correlate with increased grey matter in the right insular cortex (Lewis et al., 2014). Specifically, Kong and colleagues (Kong et al., 2015) found a positive correlation between life satisfaction and grey matter volume in the right parahippocampal gyrus. Supporting these findings, causal evidence from a study of twins suggested that lower subjective well-being was associated with lower hippocampal volume (Ent et al., 2017). Further, two recent fMRI studies suggest relations between eudaimonia and the corticostriatal reward circuitry, bridging results on the neurobiology of eudaimonia to the neurobiological of hedonics. Heller and colleagues (Heller et al., 2013) showed that individuals with sustained activation in the dorsolateral PFC and striatum in response to positive visual stimuli reported greater well-being. Complementing these findings, Telzer and co-workers (Telzer et al., 2014) demonstrated in a longitudinal study that adolescents who showed higher VS activation during prosocial/ eudaimonic decisions had declines in depressive symptoms over the time course of one year.

2.4.3. Neuroaesthetics—As more research groups have investigated hedonics and well-being, there has also been an increase in investigations centered on the related construct of aesthetics and specifically neuroaesthetics as another example of adaptive hedonics. Neuroaesthetics investigate the biological processes underlying aesthetic experiences. Theoretical models of aesthetic engagement encapsulate perceptual, affective, and contextual components of the experience (Pelowski et al., 2017). Neurobiologically, these are parts of an aesthetic triad, understanding aesthetic experience as recruiting sensory-motor, emotion-valuation, and meaning-knowledge circuits in the brain (Chatterjee and Vartanian, 2014) and are predominantly relevant to hedonics is the emotion-valuation system. While it is under debate whether aesthetic emotions are distinct from adaptive emotions (fear, disgust, etc.), aesthetic liking and pleasure experiences appear to recruit similar brain circuits underlying reward processing and motivated behavior. Meta-analyses of neuroimaging studies on positive aesthetic appraisal show consistent activation of the OFC and the VS (Kühn and Gallinat, 2012). Peak moments of pleasure with music show significant activation of the VS (including the NA; Salimpoor et al., 2011). Furthermore, recent studies using transcranial magnetic stimulation exciting the left dorsolateral PFC increased liking of music (Mas-Herrero et al., 2017) and visual art (Cattaneo et al., 2014). Neuroaesthetics are particularly relevant for understanding hedonics when considering the phenomenon of finding pleasure in sadness or tragedy in art. However, the field is still young and further research is needed addressing, for example, the role of higher meaning and knowledge in aesthetic pleasure, and their accompanying neural correlates.

3. Linguistics

As the comprehensive review above illustrates, hedonic feelings impact a wide-array of behavior and functional domains. However, the approaches used in affective neuroscience do not always align with everyday life experience and behavior (e.g., the dissociation of wanting and liking is typically not readily comprehensible and traceable for a layperson). This misalignment should not be ignored, because affective neuroscience focuses on the investigation of neurobiological mechanisms of emotions highly relevant in daily life. With such a misalignment present, it is conceivable that science neglects aspects important in natural settings. In this context, an interesting observation is that many aspects and constructs related to hedonic feelings can be found in the spoken language (see below), but there seems to be variability in how hedonic feelings are talked about. Since language is a powerful representation of consciously and unconsciously ongoing processes in the human mind, the analysis of language might offer novel insights in areas and interconnections of hedonics with other processes such as motivation, planning, bodily processes, and the self, possibly neglected so far in research. To fill in this important gap, we conducted a review of the (English) language that people use to express feelings that relate to pleasure and displeasure, aiming at fostering new views and discussions on the neuroscience of hedonics.

3.1. Definition of feeling words

The centerpiece of this approach, reviewing the literature to identify possibly neglected areas of research, was a well-defined comprehensive definition of feelings. As mentioned in the introduction (Section 1), feelings are an important component of the emotional response, but

they are not emotions per se (LeDoux, 2015). Further, feelings are not limited to co-occur with specific emotions. Rather, they can signify physiological need (e.g., hunger), tissue injury (e.g., pain), optimal function (e.g., well-being), the dynamics of social interactions (e.g., gratitude; Damasio and Carvalho, 2013). Interestingly, this clear delineation between feelings and emotions, which is important in the context of research, is not represented in every-day language. Here, the expression of feelings, in particular the hedonic aspects of pleasure and displeasure, are commonly intermixed with expressions of emotions, bodily states, actions, etc.

Further, feelings are not consistently defined and our definitions for these terms evolve over time (Tissari, 2016) contributing to the observed divergence between common language and scientific definitions. Moreover, while some feelings may be universally experienced across cultures (e.g., hunger, pain, cold, fatigue, etc.), other feelings are understood to be culturally constructed (e.g., gratitude, Boiger and Mesquita, 2012; optimism, Joshi and Carter, 2013). Based on these considerations and in the attempt to create a linguistic inventory of articulated language, the *Human Affectome Project* first defined feelings in a manner that would allow understanding the full range of terms to be considered with the awareness that variations in terminology are going to exist in day-to-day usage, between languages, and across cultures as follows:

> *A "feeling" is a fundamental construct in the behavioral and neurobiological sciences encompassing a wide range of mental processes and individual experiences, many of which relate to homeostatic aspects of survival and life regulation* (Buck, 1985; Damasio and Carvalho, 2013; LeDoux, 2012; Panksepp, 2010; Strigo and Craig, 2016). *A broad definition for feeling is a perception/appraisal or mental representation that emerges from physiological/bodily states* (Damasio and Carvalho, 2013; LeDoux, 2012; Nummenmaa et al., 2014), *processes inside (e.g., psychological processes) and outside the central nervous system, and/or environmental circumstances. However, the full range of feelings is diverse as they can emerge from emotions* (Buck, 1985; Damasio and Carvalho, 2013; Panksepp, 2010), *levels of arousal, actions* (Bernroider and Panksepp, 2011; Gardiner, 2015), *hedonics (pleasure and pain)* (Buck, 1985; Damasio and Carvalho, 2013; LeDoux, 2012; Panksepp, 2010), *drives* (Alcaro and Panksepp, 2011; Kozlowska et al., 2015), *and cognitions (including perceptions/appraisals of self* (Ellemers, 2012; Frewen et al., 2013; Northoff et al., 2009), *motives* (Higgins and Pittman, 2008), *social interactions* (Damasio and Carvalho, 2013; Gilam and Hendler, 2016; LeDoux, 2012; Panksepp, 2010), *and both reflective* (Holland and Kensinger, 2010) *and anticipatory perspectives* (Buck, 1985; Miloyan and Suddendorf, 2015)). *The duration of feelings can vary considerably. They are often represented in language* (Kircanski et al., 2012) *(although they can sometimes be difficult to recognize and verbalize) and some feelings can* be influenced/shaped by culture (Immordino-Yang et al., 2014). *Feelings that are adaptive in nature* (Izard, 2007; Strigo and Craig, 2016) *serve as a response to help an individual interpret, detect changes in, and make sense of their circumstances at any given point in time. This includes homeostatic feelings that influence other physiological/body states, other mental states, emotions, motives, actions, and behaviors in support of*

adaptation and well-being (Damasio and Carvalho, 2013; Strigo and Craig, 2016). *However, some feelings can be maladaptive in nature and may actually compete and/or interfere with goal-directed behavior*.

A "feeling" is not a synonym for the term "emotion". There is standing debate between researchers who posit that discrete emotion categories correspond to distinct brain regions (Izard, 2010) *and those who argue that discrete emotion categories are constructed of generalized brain networks that are not specific to those categories* (Lindquist et al., 2012). *However, both groups acknowledge that in many instances, feelings are a discernable component/constituent of an emotional response (which tends to more complex).*

Based on this definition of feelings, a formal linguistic analysis was done resulting in nine broad categories of feelings: Physiological or Bodily states, Attraction and Repulsion, Attention, Social, Actions and Prospects, Hedonics, Anger, General Wellbeing, and Other (Siddharthan et al., 2018). Specifically, the hedonics category was described as *"Feelings that relate to pleasurable and painful sensations and states of mind, where pleasurable includes milder feelings related to comfort and pleasure (e.g. comfortable, soothed, etc.) and painful likewise includes feelings related to discomfort and suffering (e.g. suffering, uncomfortable, etc.) in addition to pain"*. It has to be noted that used terms such as 'painful' or 'pain' were based on a linguistic approach, not necessarily reflecting neuroscientific approaches, in which pain is separated into physical pain and emotional/psychological pain (Papini et al., 2015). The hedonics category did not include feelings of Anger, Fear, Attraction, and Repulsion or General Wellbeing (e.g., happiness or sadness).

3.2. Analysis of feeling words related to hedonics

Of the feeling words identified in the review of the (English) language (Siddharthan et al., 2018), 101 feeling words were assigned to the hedonics category based on the linguistic analysis and reviewed by subjective description (cf. Supplementary Table 1).

3.2.1. Hedonic continuum—Almost two thirds of the words were found to be related to pleasure (64%) and roughly one-third (34%) was related to displeasure. On one hand, this distribution mirrors a bias in the research literature with more research in different fields on positive hedonics and a major focus on pain in the context of displeasure with only few other research fields investigating negative hedonics. On the other hand, this distribution fits well with the finding that in humans, positive feelings predominate over negative ones, which has been confirmed across cultures (Diener and Diener, 1996). The reviewed feeling words involve different degrees of hedonic intensity and can be organized on a continuum, ranging from positive to negative valence, with extreme pleasure (e.g., euphoria) on one end, to pleasure (e.g., delight), comfort (e.g., languor), and relief (e.g., relief). The term 'bittersweet' can be located in the middle between positive and negative valence. The continuum proceeds in the negative range with discomfort (e.g., uncomfortable), to displeasure (e.g., hurt), to extreme displeasure (e.g., tormented), which represents the other end. Few words (7%), refer to a change in valence from negative to positive or less negative (e.g., alleviate) or a mixture between positive and negative valence (e.g., bittersweet). The affective keyboard that has been described in the NA and suggested to control hedonic

balance, particularly when pleasant and unpleasant stimuli are present simultaneously (see Section 2.2.3; Richard and Berridge, 2011), may be viewed as a neural correlate of such words that concurrently relate to positive and negative valence.

3.2.2. Overlap with topics other than hedonics—As mentioned above, although words in the hedonic category needed to be related to pleasure and displeasure by definition, they were not necessarily restricted to the pure sensation of such pleasure and displeasure. Subcategorizing the words, they can be differentiated into those that constitute such general descriptors for hedonic valence (e.g., pleasant) and others that are more specific and relate to other topics such as bodily states, attention, social, actions, anticipation, fear, sadness, happiness, and the self (cf. Fig. 1 and Supplementary Table 1).

However, no apparent connections to the categories of anger and motivation emerged with the words in the hedonics category. As discussed in Section 2, hedonic value is closely connected to motivation (see also Fig. 1). Organisms are motivated to repeat behavior that has been associated with pleasant feelings (approach behavior) and stop behavior that has been associated with displeasurable feelings (avoidance, escape behavior). This pattern of approach and avoidance/escape behavior can be linked to the concept of comfort zones (Panksepp, 2010). According to the free energy principle (Friston, 2005), any agent acting in an uncertain world needs to maximize its chances of visiting or staying at comfort zones (desired states). In the long-run, organisms must trade-off between consuming immediate rewards (exploitation) and acquiring new information (exploration) to avoid surprising (dangerous) encounters in the future. Pleasure and displeasure emerge from the movement toward and away from the comfort zones, respectively, and thus motivate behavior.

Anger appears to be an exception in this concept of comfort zones and motivated behavior. While pleasant feelings typically lead to approach behavior and negative feelings to avoidance/escape behavior, anger is somewhat counterintuitively associated with approach behavior although it represents a negative feeling (Carver and Harmon-Jones, 2009; Fig. 1). Neural correlates support this view by showing anger-induced brain activation mostly in the left hemisphere, which has been associated with approach-oriented motivational tendencies (Carver and Harmon-Jones, 2009). This is consistent with recent evidence that shows that motivational direction (approach vs. withdrawal) and affective valence (positive vs. negative) are not always aligned (Harmon-Jones, 2018). Interestingly, descriptions of anger are missing in the word list of the hedonic category, possibly reflecting this exceptional position of anger compared to the other categories of feelings.

The analysis of the feeling words related to hedonics identified fun (e.g., merry; Fig. 1) as an additional subcategory, which has not been addressed separately within the *Human Affectome Project*. Possibly, this category represents a linguistic equivalent to the proposed primary-process (basic) emotional system PLAY (Panksepp, 2010). The PLAY system characterizes intense social joy due to social engagement (e.g., festive). Activation of the PLAY system by rough-and-tumble play or tickling of rats is typically accompanied by specific ultrasonic vocalizations (chirping sounds) and might resemble laughter in humans, e.g., due to humorous cartoons or jokes (Panksepp, 2007). Intriguingly, laughter in humans and chirping sounds in rats have been described to activate the mesolimbic circuit, brain

regions that have been associated with other pleasurable feelings, as well (Panksepp, 2007). However, PLAY and the category of ‘fun’ are not broadly represented in the field of affective neuroscience, possibly highlighting a neglected area in research, which nevertheless make up a large part in human feelings of pleasure.

Notably, the words in the hedonic category frequently refer to bodily states. In the pleasurable range, a comparatively large subsample of words refers to love and sexuality (e.g., sensual); this observation has an equivalent in the neuroscientific literature because in many human studies sexually appealing images are used as a reward and in animal studies engagement in sexual behavior. With respect to negative valence, mostly pain states are addressed (e.g., lash) and this is, as well, reflected in neuroscientific research, as discussed above (see Section 2.2.2).

However, pain-related terms are also used to describe so-called states of emotional or psychological pain, induced for example by social rejection. In most of these cases, the same word has at least two meanings, one referring to actual bodily pain (e.g., sting: cause a stinging pain; “The needle pricked his skin”) and another one referring to emotional or psychological pain (e.g., sting: cause an emotional pain, as if by stinging; “His remark stung her”). In contrast, research clearly differentiates between pain related to nociception and (potential) tissue damage and displeasing feelings induced by social rejection, exclusion, and loss as a result of an intense discussion on overlaps and their functional meaning in the neural correlates of both phenomena. For example, neuroscientific research has started to explore neural correlates of states of emotional and psychological pain and found that during emotional/psychological pain compared to physical pain states, fine-grained differences in patterns of brain activation emerge, despite parallels in activated brain regions (Krishnan et al., 2016; Woo et al., 2014). However, with respect to language, it is obvious that context can bend linguistic applications, such that a single defined term can have different meanings for people based on their experiences or the situation that they are in.

Although vast overlaps in the explored feeling words and the neuroscientific literature were found, it stands out that terms describing feelings specifically elicited by tastes and smells are missing in the word list. In contrast, affective neuroscience related to hedonics has tastes and smells clearly in focus, particularly due to direct brain pathways promoting strong feelings and emotional responses to tastes and smells important for survival. Food stimuli are frequently used as rewards in human and animal experimental research to induce pleasurable states. Terms related to food emerge in the word list of the category on physiological/bodily states, but here, they only convey states of hunger and satiation without an obvious reference to hedonics (cf. Review on Physiological states; Pace-Schott et al., 2019, this issue). Correspondingly, evidence shows that olfactory and gustatory stimuli are typically not associated with modality-specific affective terms: Rather, they elicit - in many cultures - a wide variety of unspecific feelings (Ferdenzi et al., 2013) including some that refer to pleasurable and displeasurable affect (e.g., disgusted, repelled, pleasantly surprised, delighted).

4. Cross-topic relationships of hedonics

As touched already in the review section (see Section 2) and then linguistics section (see Section 3), there seems to be a natural overlap of hedonics as the core process of feelings, with emotions such as fear, anger, happiness, and sadness, as well as motivation, attention, and planning, i.e., the topics discussed in this special issue. Much work in the field of affective neuroscience has been dedicated to emotions, motivation, attention, and planning. In contrast, how the brain creates the core processes of pleasure and displeasure has not received as much attention (Lindquist et al., 2012). As noted previously (see Section 2), most of the work on hedonics has been done in relation to the processing of reward and pain, thus being almost inseparably linked to motivation. In these studies, affective and motivational aspects of reward and pain are not necessarily separated; reward and pain are sometimes even equated – falsely – with positive and negative affect, ignoring motivational aspects. A similar interconnection of hedonics with other processes was revealed in the analysis of the language represented in the hedonics category (see Section 3): While some of the words in the hedonics word list clearly relate to the pure sensation of pleasure and displeasure, the majority of words showed overlaps with other processes and topics of this special issue, such as fear, sadness, happiness, physiological/bodily states, etc., although the word lists were created with the prerequisite that a word will appear only on one list.

Commonly the assessment of hedonics is confounded by other related constructs, such as motivation, emotion, or attention, possibly contributing to the fact that research on pure hedonic aspects of feelings is limited. Often motivational aspects can be registered by external observers through behavior and are therefore easy to assess, while affective responses are in most instances not directly observable and thus have to be inferred indirectly. Even in human research, where subjects can be asked to evaluate pleasure and displeasure, on verbal and numerical rating scales, such assessments are often confounded, for example, by social desirability, cognitive biases, and demand characteristics. In addition, evaluation of hedonic aspects independent of, for example, the motivation to achieve or avoid something is very challenging.

In addition to assessments that might be confounded by other components of feelings, another reason for a focus of research on processes other than hedonics might be that pleasure and displeasure are not directly related to needs in terms of homeostasis. Healthy organisms strive to achieve states that maintain homeostasis and pleasure and displeasure are important indicators of homeostatic needs (e.g., the feeling of hunger is typically uncomfortable or aversive) and their satisfaction (e.g., eating, particularly of high-caloric food, feels pleasurable in hungry state). Possibly, without hedonic feelings, a driving factor important for well-being and even survival would be missing, leading to impaired motivational drive to satisfy various needs. Such effects can be observed, for example, in depression, in which anhedonia is one of the core symptoms and which is accompanied by impaired motivational drive, leading in severe cases to a strong neglect of homeostatic needs (Belujon and Grace, 2017; Husain and Roiser, 2018), as noted earlier in the context of malfunctioning of hedonics in mental disorders (see Section 2.4.1).

4.1. Relationship of hedonics with physiological/bodily states

One intersection of hedonics with other research topics discussed in this special issue can be found with physiological/bodily states. In this context, the ‘somatic marker hypothesis’ has gained significant recognition and acceptance in the field of affective neuroscience (Damasio and Carvalho, 2013; Damasio, 1996). This hypothesis proposes that feelings are represented bodily as ‘somatic markers’ and that these bodily representations guide behavior, in particular decision-making. Based on lesion studies, among other evidence, the OFC (and vmPFC) has been proposed to play an essential role in coding, processing, and utilization of somatic markers in decision-making, with lesions leading to impaired planning and organization of beneficial behavior represented, for example, in starkly increased risky and irrational behavior (Bechara, 2004; Pujara et al., 2015). Importantly, the hypothesis assumes a ‘body loop’, i.e., that physiological changes in the body can trigger emotions by inducing feelings with positive or negative valence. Similarly, a clear delineation between hedonics and bodily states appears lacking in situations, in which hedonics are directly induced by sensory stimuli such as in physical pain and olfaction. Here, a physiological process is needed as the basis for the induction of positive and negative affect.

4.2. Relationship of hedonics with emotions

In addition to the intersection with physiological/bodily states, hedonics seem inseparably interconnected with emotions such as fear, anger, sadness, and happiness. For example, hedonic well-being, as one component of subjective well-being, has been defined as consisting of the balance between feelings of happiness, anger, sadness, etc. (Steptoe et al., 2015). However, this intuitively compelling assumption is not necessarily represented in research. In research on fear conditioning, for example, affect and hedonics were even explicitly avoided as poorly defined concepts (LeDoux, 2000). In many instances of this research and other research on emotion, affective stimuli are used to induce emotions such as fear, anger, sadness, and happiness, but primary outcomes focus, for example, on physiological responses or emotion regulation. The latter concept of emotion regulation proves to be a particularly important topic in this context. In the context of such research on anger, an interesting intersection with hedonics is observable, namely the research on revenge. Revenge is associated with positive hedonic feelings and shows overlap, for example, in neural correlates with pleasure and reward processing (Chester, 2017). A similar paradox, i.e., the induction of pleasure by processes related to negative affect, received attention in the context of research on sadness: Listening to sad music can induce pleasure (Eerola et al., 2018). Interestingly, such ambivalent states where hedonics and the underlying emotion seem to contradict are represented in our everyday language, as discussed above (see Section 3.2.2).

Apart from this line of research, sadness and happiness are essential constructs in the concept of hedonic well-being (Steptoe et al., 2015), delineating a strong intersection with research on hedonics. In particular in the context of research on happiness, this intersection becomes obvious with pleasure being defined as a central component of happiness and a translation that has been made of results from hedonic responses to reward, to the investigation of happiness (Berridge and Kringelbach, 2011; Kringelbach and Berridge, 2009).

4.3. Relationship of hedonics with motivation, attention, planning, action, and social interaction

The strong intersection of research on hedonics and motivation has been outlined above (see Section 2). Despite these strong interconnections, research has aimed at doubly dissociating hedonics and motivation, highlighting dissociable underlying mechanisms. Nevertheless, hedonic feelings act as strong motivators driving behavior and decision-making. Moreover, hedonic feelings and motivation can enhance or diminish each other and are subject to other modulating factors as discussed above (see Section 2.3). Accordingly, hedonic feelings can be modulated by homeostatic states and corresponding desires of an organism (Cabanac, 1971), with this modulation resulting in a change of motivational drive. For instance, sugar consumption is known to be modulated by hunger (Berridge, 1991), and saline ingestion by sodium depletion (Berridge et al., 1984).

Illustrating the close relationship of affective valence, motivation, and learning (Rolls, 2000), hedonic experiences can serve, for example, as cues in Pavlovian learning, resulting in stimulus-stimulus associations that allow predictions in future situations. Further, (perceptual) control theory (Toates, 1986) suggests that affective valence is related to (prediction) error signals in the brain as important modulators of learning and approach/avoidance motivation. For instance, affective valence has been described as the rate of discrepancy reduction over time (Carver and Scheier, 1990; Chang et al., 2010; Hsee and Abelson, 1991), reward prediction error (Keramati and Gutkin, 2011; Rutledge et al., 2014), and the rate of change of prediction error over time (Joffily and Coricelli, 2013). Importantly, this brings hedonics to the realm of computational models of perception, learning, attention, and action in neurosciences and, more specifically, the predictive coding theory (Clark, 2013).

Despite this close relationship to motivation and learning, hedonics seem to play only a minor role in the research on attention, planning, and action. Yet hedonics clearly influence planning (to achieve pleasure and avoid displeasure) and actions can induce pleasure and displeasure, so greater focus on these relationships is needed. In contrast, hedonics are frequently included as considerations in research on social emotions. For example, social interactions are often a source of positive or negative affect, guiding such interactions and strongly affecting social behavior (Fehr and Camerer, 2007). Group behavior, cohesiveness, and group dynamics are also regulated by social hedonic feelings (Goldenberg et al., 2016).

4.4. Relationship of hedonics with the self

Another area of research represented in this special issue is the self, with feelings related to self-appraisal with respect to many different categories (e.g., size, weight, intelligence, fitness, self-esteem, identity, belonging, etc.). At a first glance, intersections with research on hedonics seem lacking. However, a few interesting intersections can be found. For example, research has pointed out that hedonic pleasure increases when related to conscious self-regulation in terms of self-licensing compared to impulsive hedonic consumption (de Witt Huberts et al., 2014). Similarly, self-regulation with respect to weight can be related to pleasure: Hedonic perception of food decreased in people after obesity surgery the more they perceived that they themselves invested in the procedure (Alfonsson et al., 2017;

Husted and Ogden, 2014). Further, self-interest can result in hedonic feelings, but only if such self-interest is externally imposed (Berman and Small, 2012).

5. Conclusions

Pleasure and displeasure are fundamental elements of life that affect behavior, cognitions, perception, and social interaction. Despite the apparent omnipresence of hedonics in daily life, hedonics have not been the main focus for the field of affective neuroscience. Truly subjective in their nature, assessment and quantification of hedonics require introspection and/or are confounded by closely coupled aspects such as motivation. Correspondingly, insights on the neurobiological basis of pleasure and displeasure predominantly come from research on reward and pain, which mainly elicit approach and avoidance behaviors (as manifestations of motivation). While animal research allows sophisticated methodological procedures creating the possibility of dissociating motivational and hedonic responses, this is not possible in human research. However, human research can make use of our access to introspection and verbal reports.

In addition to the description of psychobiological mechanisms of pleasure and displeasure, affective neuroscience has described mutual inhibition and promotion of positive and negative affect. This finding appears particularly interesting because it is relevant in clinical contexts: Several disorders seem to be characterized by increased negative affect with reduced positive affect at the same time, possibly leading to a self-sustaining negative feedback loop (e.g., such as described in chronic pain and depression). Besides alterations of hedonics by clinical states, the experience of pleasure and displeasure can be modulated by various factors either without awareness of a person or with awareness and possibly self-control. For example, early processing in perception, exposure in early childhood, learning, cognition, and memory can modulate pleasure and displeasure as well as active emotion regulation strategies. Such interactions and modulation highlight the complex nature of hedonics with a large inter- and intra-individual variation.

Although hedonics have been carefully considered in focused research on this topic, in some related fields such as psychology and in research on well-being, rich and rigorous work on the neurobiological mechanisms of hedonics as core processes is still lacking. For example, precise roles of genetics, culture, learning, and habit in explaining such variation remains largely unknown. Further, because research on pleasure and displeasure has focused on investigations of the processing of reward and physical pain, differences in brain representations of hedonic valence might have been underestimated. It is conceivable that a brain hub or circuit exists that processes hedonics independent of specific modalities and across positive and negative valence.

The idea of such a hedonic hub or circuit that strongly intersects with other brain regions would fit the observation that hedonics play a central role in many aspects of feelings such as actions, attention, motivation, physiological/bodily states, planning, the self, and social, and emotions such as anger, fear, happiness, sadness, as reviewed and discussed in the *Human Affectome Project*. Interestingly, such extensive intersections have also been found in the linguistic approach when analyzing the word list in the hedonics category. With the

only exceptions of ‘anger’ and ‘motivation’, all other above-mentioned aspects of feelings and emotions were represented in the word list of the hedonics category, in line with the conclusion that the neuroscientific investigation of hedonics as a core process is challenging, because hedonics seem almost inseparably linked to other processes.

In sum, hedonics as the core process of positive and negative affect need further investigation to better understand the different mechanisms and layers of hedonic experiences. Deeper knowledge of pure hedonic mechanisms might fertilize affective neuroscience as it might lead to a clearer separation of processes, resulting in precise models and new hypotheses on the role of hedonics. In clinical contexts when negative and positive affect are altered this knowledge could be used to establish novel mechanism-based treatments independent of specific diagnoses. By making progress on both basic and applied questions related to hedonics, we hope this review, as well as other publications from the *Human Affectome Project*, can advance progress in affective neuroscience and related disciplines.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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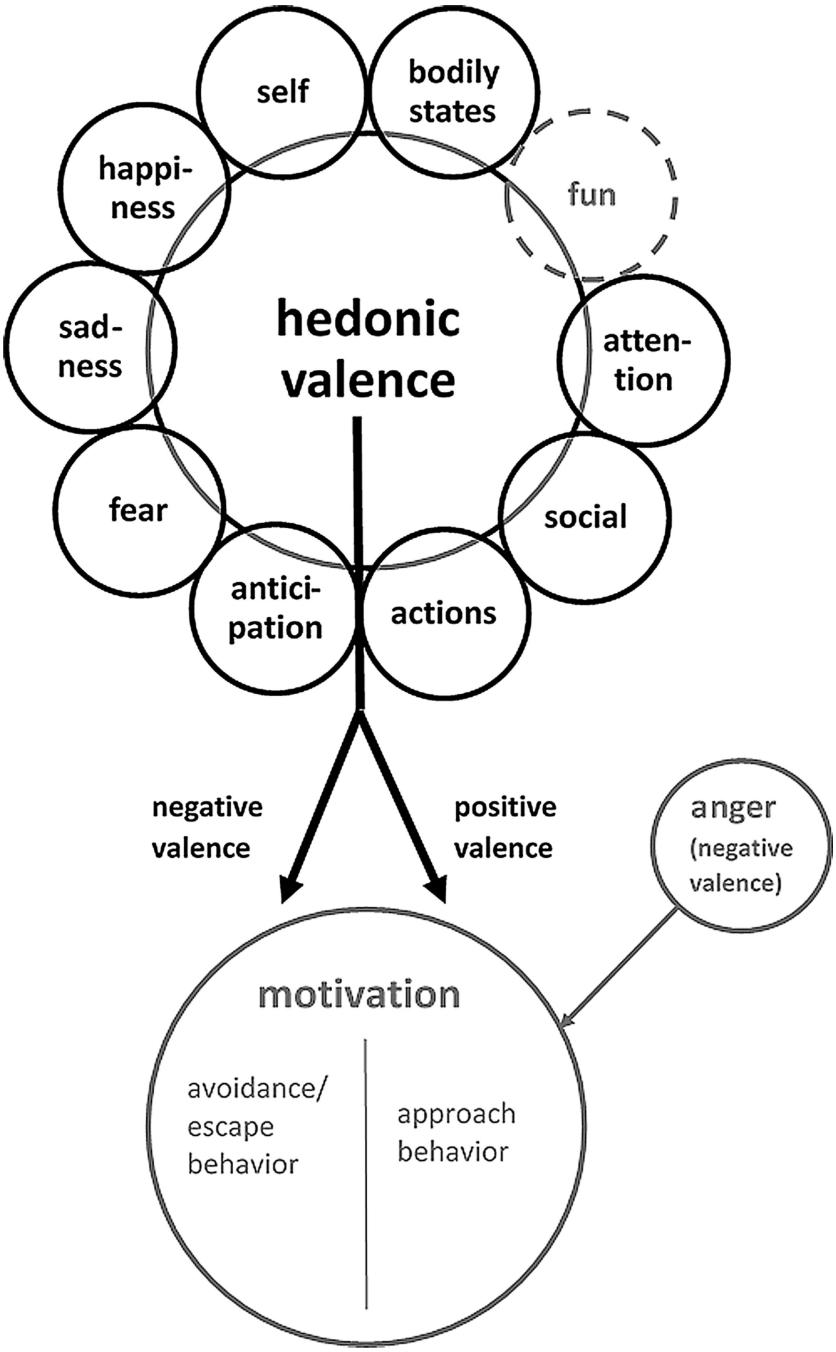

Fig. 1.

Organizational structure of the hedonics-related feeling words. The illustration shows that hedonic value is an integral part of most of the categories of feelings that have been investigated in the *Human Affectome Project*. Categories that were missing from or were additionally found in the analysis of the hedonic terms are displayed in grey. For example, fun has been identified as a potential additional category. Further, hedonic value and motivation (which did not emerge in the word list) seem to be closely connected, in the sense that, based on, for example, needs, preferences, and desires, positive hedonic value can

induce approach and negative hedonic value can induce avoidance/escape behavior thus motivating an organism. However, anger, which did not emerge in the hedonics-related word list, holds an exceptional position, as it refers to a negative affective state leading to approach behavior (cf. Section 3).