Review

New Insights on Neural Basis of Choice

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Abstract

Identifying the neural mechanisms underlying decision-making is a fundamental issue in neuroeconomics, a branch in neuroscience that is still in its infancy. Although choosing among different types of goods and products might be very challenging, our brains are able to compute our choice with a fascinating velocity. A large number of experiments have investigated the neural correlates of choice and identified a number of core structures that are consistently involved in decision-making. These structures include the prefrontal cortex (orbitofrontal cortex, ventromedial and dorsolateral prefrontal cortex), striatum, amygdala, insular cortex and cingulate cortex. However, it is still unclear how those brain regions interact with each other to collectively process choice. In this review, I have searched through the current literature with a focus on the neural basis of choice and described the choice process by dissecting it into three main parts: Valuation, Choice, and Social decision-making. Based on the literature, I found significant evidence to assign brain regions to each part of the decision-making process. As such, the OFC/vmPFC and the striatum/midbrain seem to play a critical role in the valuation of goods, while the amygdala, insula and the anterior cingulate cortex are mainly associated with encoding of costs of choice (action, price, risk, ambiguity etc.) and initiation of emotional response associated with the choice. In addition, the AIC and the ACC are shown to be involved in many aspects of social decision-making, which are in this review limited to empathy and Theory of Mind.

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Introduction

Making decisions is something which humans, but also animals, do more often than one might think. Although making choices sounds like a straight-forward process, the opposite seems to be true. Decision making is a complex neural process involving many aspects such as action and perception, valuation and learning, which implies a heavy interaction and cooperation among different brain areas (Rangel & Hare, 2010). Understanding the mechanism of valuation and decision-making is of high interest to psychologists and neuroscientists, but quite reasonably, economists and marketers are also being aware of the importance of this topic of research. Not surprising, since understanding how humans value goods and how they make choices would improve the effectiveness of marketing strategies. Especially unraveling those factors that might interfere with valuation of goods, and consequently affecting the ultimate choice, is of high importance. Of course, there may be internal or bodily (homeostatic) factors that might influence valuation of goods, such as affective state, emotional (e.g., anger) and motivational (e.g., hunger) state and illness, but external factors such as risk, costs and ambiguity might influence valuation as well. In addition, the effects of social contexts on valuation are also interesting, as it is obvious that people behave differently with changing social contexts. Given these considerations, the emerging interdisciplinary field of research that focuses on the neural mechanism of choice, also called neuro-economics, has generated considerable recent research interest.

In this review, we attempted to conduct a search of the currently available literature on the neural basis of valuation and choice. For this purpose, we have made us of a significant amount of recent data and evidence originating from numerous experiments that have been established already, providing an updated picture of our current knowledge about the neural framework of choice. Hence, this review is composed of three main chapters, addressing the topics of valuation, choice and social decision-making. First, in "Chapter 1", we start with elaboration on the valuation systems in the brain, and provide a brief description of each associated brain regions. Second, in "Chapter 2" we shortly describe different decision-making systems in the brain, discuss about costs that might negatively affect valuation of goods, and attempt to clarify how choice might finally be established after integrating costs with (subjective) value. Third, we review recent results on social decision-making, and outline the most relevant neural processes in detail.

1. Valuation

As we have stated above, decision-making is a complex neural process that involves multiple component processes (Rangel and Hare, 2010). Especially, choosing between two or more different types of reward initiates heavy interactions among broad range of brain regions, which starts with a *valuation* process that will guide us to our final decision. Valuation is a critical component of decision-making that enables us to attach values to each reward option, using their (multi)sensory properties, but also using information about the internal and motivational state of the body and evolutionary desires (e.g. sex, high caloric food) (Grabenhorst & Rolls, 2011). For example, fatty foods are preferred by the brain, because of their high energy content that can provide an important survival advantage in resource scare environments. In the review of (Grabenhorst & Rolls, 2011), the authors describe the process of valuation, value-based decision-making and action selection by breaking them into three 'Tiers' or stages. During Tier 1, reward identity and sensory properties of rewards are computed by sensory cortices independently of subjective valuation of those rewards. Subsequently, sensory cortices send the sensory information primarily to a subregion of the frontal cortex, called orbitofrontal cortex (OFC), where valuation of the reward is processed (Tier 2).

As studies show, neural activity in the OFC correlates with subjective value (Rolls & Grabenhorst, 2008). After identity of reward is determined, OFC will compute if the object or reward is desirable or not at that very moment, e.g. a tasty food would be desirable, but would be less if consumed to satiety. This system actually protects us from consuming only one kind of food, and instead helps us to consume a variety of foods, in order to have a balanced intake of energy, minerals, vitamins etc. Besides valuation, the OFC also compares two or more different kinds of rewards (consumable or non-consumable) at neural level by encoding both absolute value and relative value of a reward. (FitzGerald, Seymour, & Dolan, 2009; Keiflin, Reese, Woods, & Janak, 2013). One could think about a situation in which a thirsty person is provided with either water only, or in combination with a (chilled) refreshing drink. Although absolute value of water in the first situation would be high, its relative value would be somewhat lower in the second situation. Finally, during Tier 3, information about (subjective) value is send to subsequent brain regions in the valuation and decision-making relay and further processed to establish a final decision and to initiate decision-based motor action.

Interestingly, there is some confusion about the distinction between the OFC and the very closely located ventromedial prefrontal cortex. In their book, Zald DH & Rauch SL state that these two regions are often used interchangeably in the literature which causes this confusion. However, they provide the following description:

"The OFC is the entire cortex occupying the ventral surface of the frontal lobe, dorsal to the orbital plate of the frontal bone. We have used the term VMPFC to designate a region that encompasses medial portions of the OFC along with ventral portions of the medial prefrontal cortex."

In addition, in a short online article, several pioneers in the field of neuroeconomics were asked why OFC and vmPFC are so often used interchangeably, and among them, Dino Levy gave the following answer:

"Because, as you mentioned some people will call an area OFC and others vmPFC. Moreover, to make things even more complicated, there is also differences between the lateral and the medial OFC. The origin of the problem is that the anatomy is very different in these areas but many papers tend to ignore these differences. Furthermore, fMRI is not good enough to actually differentiate between all these small subregions. Some scholars will address vmPFC and OFC as different. But be careful. It may be that they talk about humans or monkeys. There is no direct homology between these areas across species. Note, that rats don't even have an actual vmPFC or OFC, but only what is termed cingulate cortex."

In short, sensory information of reward objects are firstly processed by sensory cortices in order to identify the object. After identification, OFC then calculates subjective value for the reward, and in case of comparison between two or more options, it rescales its absolute value to a relative value. In the first section of this review, we will mainly focus on valuation (Tier 2) and decision-making (Tier 3), and to lesser extend perception and action (Tier 1 & partly Tier 3).

1.1 | The prefrontal cortex

Consisting of about 100 billion (or maybe more) neurons in humans, and highly efficient neural networks, the brain is capable to execute vast number of complex behavior. Those neurons are all grouped into distinct anatomical regions, based on their correlation with each set of behavior and perhaps the most complex region among all, responsible for many higher-order behaviors such as planning, cognitive control and thought, is the prefrontal cortex (PFC). The PFC is located in the forebrain and comprises a large part of the whole brain. It is heavily interconnected with almost all brain regions (Ongür & Price, 2000). Especially, the basal ganglia, subcortical areas, hypothalamus, hippocampus, motorcortex and cortical sensory areas are intimately interconnected with the PFC. However, the PFC can be divided in different sub-regions, which are specialized in coordinating of some part of all the inputs and outputs from and to other parts of the brain. For example, the dorsolateral PFC (dlPFC) has dense afferent projections originating from the visual, auditory and somatosensory cortices and efferent (indirect) projections towards brain regions involved in motor functions. Additionally, the dlPFC is interconnected with the cingulate, primary motor cortex, the cerebellum and the superior colliculus. On the other hand, the ventromedial PFC (vmPFC) and the orbitoPFC (OFC), are more closely related with subcortical structures (i.e. (hypo)thalamus, hippocampus, basal ganglia) and limbic structures (i.e. ventral tegmental area (VTA) and amygdala), and thereby receiving information like (long-term) memory, emotional and motivational state. These regions, in turn, use this information to conduct a proper response via loop-back system or inter-PFC

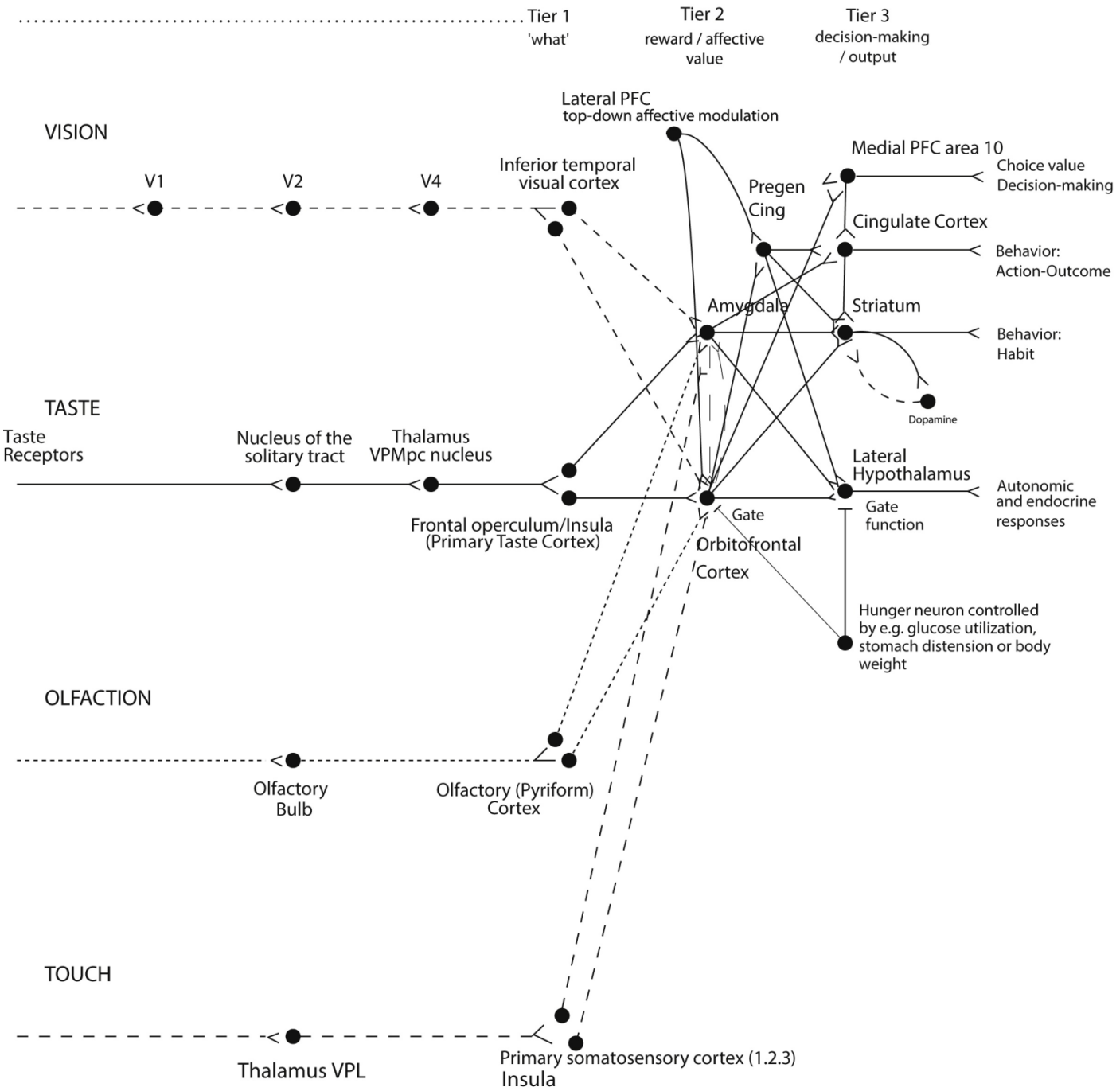

Figure 1 | A schematic overview of the neural system underlying decision-making (Adopted from Rolls & Grabenhorst, 2008)

connections. Thus, the PFC is the point at which all internal and external signals join, processed and further directed to their proper destinations.
It is known that the OFC itself, as a critical valuation region within the PFC, receives many afferent projections from very different brain regions, especially sensory cortices like the visual cortex (Thorpe, Rolls, & Maddison, 1983), olfactory cortex (Rolls & Baylis, 1994), (primary) somatosensory cortex (Rolls, Critchley, Browning, Hernadi, & Lenard, 1999; Rolls, Verhagen, & Kadohisa, 2003), (primary) taste cortex (Baylis, Rolls, & Baylis, 1995; Rolls, Yaxley, & Sienkiewicz, 1990), auditory cortex (Romanski & Goldman-Rakic, 2002); but also from dorsolateral PFC (DLPFC), subcortical areas like the midbrain and the basal ganglia (particularly from the ventral striatum); parietal cortex, insula and the amygdala (Ongur & Price, 2000; Price, 2007). Similarly, there are efferent projections originating from the OFC to very broad range of brain regions including the amygdala (Barbas, 2007), ventral tegmental area, ventral striatum (Ferry, Ongur, An, & Price, 2000), the vmPFC, the cingular cortex (Carmichael & Price, 1996), hypothalamus (Burton, Rolls, & Mora, 1976), but also indirect connections to motor cortex and hippocampus, to exercise motor control and to influence memory processing (Ongur & Price, 2000; Rolls & Xiang, 2005). While the motivational aspect of a certain reward is encoded by the midbrain dopamine system, the emotional aspect is especially encoded by the amygdala (Fiorillo, 2013; Dolan, 2007). It is then thought that the vmPFC/OFC use these many different inputs to encode the subjective value of different reward types (Miller & Cohen, 2001). Notably, it has been suggested that the OFC and the vmPFC have distinct anatomical localizations (Price & Drevets, 2010). Specifically, as partially described above, while OFC receives signals from sensory cortices and limbic areas in major, the vmPFC especially receives (and sends) projections from (to) the hypothalamus and brain stem, and based on these findings, it has been suggested that OFC is involved in gathering all sensory and motivational inputs to generate a value signal, and that the vmPFC is largely involved in autonomic functions and visceromotor responses (Price, 1999). Studies show that regions such as amygdala, the insula and the parietal cortex also correlates to some extend with reward magnitude, although the insula, and especially the anterior part of it, correlates in a negative way. Finally, by interacting with the parietal cortex the final decision will be made and the necessary motor-action will be initiated via the motor cortex.

1.2 | OFC and valuation

Studies have shown that, in order for the brain to compare between two or more reward types, values should be encoded to a single neural currency, which is referred as a *neural common currency* (Montague & Berns, 2002; Levy & Glimcher, 2012). To further describe this issue, we will introduce an example of a situation in which we have to choose between equal amount of apples and strawberries at a green market. The brain will immediately start with valuing the two options. Which one of them will have the highest value, the juicy apple or the sweet strawberry?

In the past decade, numerous experiments have reported that the orbitofrontal cortex (OFC) plays a critical role in the valuation process (Bartra et al., 2013). Evidence for a neural common currency comes from a fMRI study which shows that equal behavioral value equates to equal BOLD signals in the OFC (and vmPFC), or in other words, the neural activity in the OFC correlates with the subjective value for an option (Levy & Glimcher, 2012; Louie & Glimcher, 2012). Other fMRI studies in combination with (monetary) choice-tasks revealed that increased activity in the OFC (and vmPFC) precedes, but also remains after, the final decision-making, and that this activity correlates significantly with the reward magnitude, subjective-value and expected reward-value.[..]. However, some researchers suggest that different kind of rewards are transformed to a common scale, thereby retaining the identity of the reward; rather than transformation to a common currency, in which the identity of the object is lost. We will discuss this later in this section (Rolls & Grabenhorst, 2008; Grabenhorst & Rolls, 2011).

In order for vmPFC/OFC to attach a value for a reward (in the example case provided earlier it is the apple or the strawberry) it needs some information about its sensory, emotional and motivational properties. This information could either be retrieved from real-time perceptions signaling the vmPFC/OFC about the sensory properties of the reward (as described above) or from the memory system, stored in from a previous experience. (Padoa-Schioppa, 2009) has shown that OFC neurons encode subjective value in a so-called abstract manner, which basically holds that value is encoded independent of sensorimotor contingencies. Moreover, earlier studies have shown that the OFC, and to some extend cortical regions involved in processing of sensory stimuli, responds to a variety of sensory stimuli and encodes the pleasantness of stimuli (Montague et al., 2004; Pessoa & Engelmann, 2010) . Some olfactory stimuli or odor, although without any association with other taste or visual stimuli, elicit an increased activation in the OFC, and this activation correlates with subjective rating of pleasantness of the specific odor. (Critchley & Rolls, 1996). The same is true for taste stimuli, which may act as primary reinforcer, in that it can increase neural activity in the OFC, but this activation gradually decreases when feeding to satiety, providing evidence that OFC encodes subjective value of the stimuli (Rolls, Critchley, Wakeman, & Mason, 1996). Further, using the visual system, OFC is then capable to form an association between sight and other sensory stimuli like taste and odor, and subsequently contributes to memory formation of novel objects (Petrides, 2007). A study of Fery & Petrides (2002) showed that a subregion of the OFC (area 11 and 25) was activated during a task in which subjects were instructed to memorize novel objects that were shown to them, and no significant increase in firing of other brain regions was observed during this task.

Since there are many different types of rewards, a possible question that might arise is whether the OFC is capable to encode the subjective value for all types of rewards, i.e. primary rewards (such as food or warm touch) and secondary rewards (monetary gain, non-consumable goods). First of all, there are numerous studies that show that variety of neurons in the OFC encodes subjective value for almost all kind stimuli or reward, and no evidence has been found yet for a brain region that correlates specifically with subjective valuation of one type of reward. (Chib, Rangel, Shimojo, & O'Doherty, 2009). For example, OFC encodes value for taste stimuli (flavor) (Padoa-Schioppa & Assad, 2006), but also olfactory (Grabenhorst, Rolls, Margot, da Silva, & Velazco, 2007), somato-sensory (thermal) (Grabenhorst, D'Souza, Parris, Rolls, & Passingham, 2010), and visual stimuli (J. O'Doherty et al., 2003). Thus, OFC encodes value for consumable rewards, as well as for inconsumable rewards like an attractive face, a warm touch or monetary gains (Knutson, Rick, Wimmer, Prelec, & Loewenstein, 2007), though a recent meta-analysis showed that anterior part of the OFC seem to encode value for monetary (secondary) rewards while the posterior part of the OFC encodes subjective value for food rewards and erotic stimuli (Sescousse, Caldu, Segura, & Dreher, 2013). In addition, several lesion studies, both in rodents and monkeys, have further proven that OFC is critical in valuation of reward, in that OFC lesion abolishes satiety-induced devaluation of a preferred reward (Kazama & Bachevalier, 2009; Machado & Bachevalier, 2007a; Machado & Bachevalier, 2007b; Pickens et al., 2003). To be precise, rodents and monkeys were offered free-access to their preferred food (proven to be the preferred food

BOX 1 | Basal ganglia controls goal-based saccades

The basal ganglia is, as described earlier, involved in goal-based execution of motor control. In the review of (Hikosaka et al., 2006), they described one such goal-based motor control mechanism in which basal-ganglia is involved, namely goal-based saccades. As shown by anatomical studies, the caudate nucleus of the basal ganglia receives heavy input from the cerebral cortex, and sends projections to different regions, including the substantia nigra pars reticulate (SNr). The SNr, in turn, has projections to the superior colliculus (SC), a brain region involved in controlling eye movements, or saccades. Projections between the caudate and SNr, and between SNr and SC, are mainly inhibitory. Thus, activation of neurons in the caudate leads to inhibition of neurons in the SNr, disinhibiting neurons in the SC. It is then thought that the caudate controls saccades by orienting the eyes on the spatial localization of an expected reward. In a study in which monkeys are trained to associate a visual target, which appears on the left or on the right side of a screen, with either big or small reward. They found that when subjects expect a big reward, for example, on the right side, caudate neurons contralateral to target position (left) are activated. Subsequently, this leads to disinhibition of (left) SC projection SNr neurons, thereby creating a pre-target bias of a saccade towards the right side (reward position).These SC neurons now have increased excitability, and will quickly start firing upon receiving excitatory signals from the cerebral cortex, informing that visual target indeed appeared at the right side. Note that this bias is purely a result of expectation, since no visual target cue is presented yet. When the visual target cue appears on the right side, as expected, especially left cortical areas are activated, which in turn activates the SC via direct excitatory projections. Because, in response to reward position expectation, those neurons have already increased excitability due to activation of (left) caudate neurons, latency of saccade execution will be significantly low. By contrast, if visual target appears on the left (associated with small reward), right cortical areas activate SC neurons. Notably, these neurons were kept inhibited by SNr projections, which were not inhibited by activation of (right) caudate neurons, and consequently latency of saccade execution is increased.

These findings clearly show that caudate neurons, as a part of the basal ganglia, respond to reward expectation, which in turn influences motor control. In addition, it is also shown that caudate neurons, and other sub regions within the basal ganglia associated with motor control, are modulated by midbrain dopamine neurons (SN,

option from earlier test sessions) prior to a test session, allowing them to feed to satiety. Subsequently, when the same subjects were then offered with both the same preferred (but fed-to-satiety) food and a less-preferred food, they were choosing the less-preferred food. Thus, the more-preferred food is now devaluated to a level beneath the value of the less-preferred food. Remarkably, this devaluation is diminished after OFC lesion, and as a result, subjects consistently choose for the more-preferred food despite pre-feeding.

Emerging evidence show that different sub-regions of the OFC are involved in different aspects of valuation and decision-making. As described above, the first stage of decision-making is valuation of each option under consideration. However, valuation in itself consists of multiple dimensions, in that different population of neurons in the OFC encodes distinct aspects of valuation. In the study of (Padoa-Schioppa & Assad, 2006), they identified three different populations of neurons within the OFC, based on their correlation with different stages of valuation. First, they found a population of neuron that correlated with the subjective value of each option available, and they labeled them as "offer value" neurons. Second, they found another population of neurons that correlated with the subjective value of the chosen option, regardless of their identity, encoding the net value of the chosen option represented in a common neural currency, and they labeled those neurons as "chosen value" neurons. Finally, they found a third population of neurons, labeled as "taste" neurons, responding in a binary fashion to the offered juices, regardless of their quantity. Interestingly, in another study performed by (Hare, O'Doherty, Camerer, Schultz, & Rangel, 2008), they show that "goal value", which is similar to "offer value", is encoded primarily in the medial OFC (but also mPFC and amygdala); and that "decision value, which is similar to "chosen value", is encoded primarily in the central OFC. Interestingly, in their study they describe an additional element of valuation, called "prediction error", observed in the ventral striatum, that encodes for the difference between predicted value and the outcome value However, this activity is shown to occur in the final stages of decision-making and it is considered as an important feature of learning (will be further described below). The latter is a remarkable finding; since it has long been thought that striatum together with OFC/vmPFC encodes subjective value, but now seems to have a dissociable role in valuation process. From this study, we again observe that the OFC is important in collecting and preparing essential information to be used as input for decision-making, by computing both the subjective values of independent reward options, as well as the net value of each option, in which the gains and costs are taken into account. The subsequent fundamental issue is to understand how other (limbic) brain areas interact with the OFC and contribute to value encoding.

1.3 | Valuation in basal ganglia

The basal ganglia is a large brain structure comprising many sub regions such as the striatum (including the nucleus accumbens, caudate nucleus, and putamen globus pallidus) and substantia nigra. In general, basal ganglia sub regions are known for their roles in reward expectation, evaluation of reward outcome, and reward-based action selection. Since the basal ganglia receives heavy dopaminergic input, and sends heavy projections to motor areas, it is an ideal location for reward encoding and controlling (anticipatory) locomotion activity. Movement-related deficiencies that are seen in Parkinson patients, is a result of degeneration of dopaminergic neurons within the substantia nigra, causing loss of dopaminergic innervations into the (dorsal striatum). Interestingly, there are two main hypotheses that rises from numerous experiments focusing on the function of the basal ganglia in valuation and decision-making, namely the basal ganglia is either primarily involved in action selection or evaluating action outcome. The intriguing question now is whether the basal ganglia is indeed able to encode both processes? In their well-designed experiment, (Kim, Sul, Huh, Lee, & Jung, 2009)) show that the basal ganglia is primarily involved in evaluating action outcome rather than action selection. They only found neural activity in the basal ganglia that is related to action value, but not action selection per se. They propose that the basal ganglia prepares the necessary information to guide action selection, but the actual action selection would take place somewhere else in the

brain. They argue that these findings are consistent with previous findings (Lau & Glimcher, 2008; Samejima, Ueda, Doya, & Kimura, 2005). In contrast, they show that the basal ganglia, is involved in evaluating of action selection, by updating action outcome and to use this information in the future. Additionally, based on their finding that value signals in the basal ganglia are not static in each trial, they suggest that value and choice signals, encoded elsewhere (vmPFC/OFC) are send to the basal ganglia to evaluate action outcome, and if necessary update with new information. They also found some *reward prediction error* signals in the striatal region of the basal ganglia, which is a critical element in evaluation of reward outcome, and thus further confirming the above statement.

The functions of the striatum can be roughly divided over its two main sub regions, the ventral and dorsal striatum. The ventral striatum encompasses the nucleus accumbens and olfactory tubercle, while the dorsal striatum encompasses the caudate/putamen and globus pallidus. Many studies are performed to address a specific role either ventral or dorsal striatum. The ventral striatum is commonly associated with functions such as reward-encoding, reward prediction error, controlling anticipatory/motivational behaviour, and transforming motivation into action (Hare et al., 2008; J. P. O'Doherty, 2004). Contrary to ventral striatum, activity in dorsal striatum is mainly correlated with reward or chosen value, though the dorsal striatum is also shown to control movement and action selection (Daw & Doya, 2006; Hikosaka, Nakamura, & Nakahara, 2006; Schultz, 2006). Correlation studies in the dorsal striatum provided evidence for this statement, and showed that the activity in the caudate and the putamen significantly correlates with subjective action value of options, in a similar fashion as OFC encodes for goods based subjective values (Lau & Glimcher, 2008; Samejima et al., 2005). In these studies, monkeys were trained to associate a specific action (e.g. left or right lever press) with a certain reward (e.g. small or large reward), and caudate/putamen neurons responded linearly with reward magnitude or probability associated with corresponding action. The striatum receives extensive glutamergic inputs from the whole cortex and thalamic regions (Tepper, Abercrombie, & Bolam, 2007). To consider the neuronal population within the striatum, it is heavily populated (approx. 90%) by inhibitory (GABAergic) neurons called Medium Spiny Neurons (MSN's). Activation of MSN's is known to cause local inhibition, and they may be activated either by glutamergic inputs from the cortex or by afferent dopaminergic projection from the midbrain structures. In principle, those MSN's can be subdivided into at least two distinct populations based on the presence of different dopamine binding receptors, called either striatopallidal MSN's (projecting primarily to the globus pallidus and expressing high levels of D2 receptors) or striatonigral (projecting primarily to the substantia nigra *pars reticulata* and expressing high levels of D1 receptors) (Gerfen et al., 1990). Dopamine receptors which will be described in more detail below. Early neuroanatomical studies have shown that dopaminergic inputs to the ventral striatum origins from the ventral tegmental area, while dopaminergic input to the dorsal striatum originates from the substantia nigra *pars compacta* (Beckstead, Domesick, & Nauta, 1979; Swanson, 1982). Both structures contain large proportions of dopaminergic neurons, i.e. ~90% for the SNc and 60% for the VTA (Swanson, 1982). Thus, these findings have suggested that striatal neurons are under modulatory control of dopaminergic neurons, and due to the fact that they receive both glutamergic as well as dopaminergic inputs (which are thought to be the critical basis for plasticity and thus learning in the striatum), there is a general agreement that striatum is closely involved in learning en reward expectation. However, it is still a debate whether the striatum is also involved in encoding of reward values, since Hare et al. (2008) showed that striatum is preferentially involved in encoding the reward prediction error rather than encoding subjective value of different options. Due to the fact that the OFC is closely linked with the striatum, it might be true that the actual valuation of novel rewards is first encoded in the OFC, but this information is then provided to the striatum, possibly in parallel with other inputs from other regions linking these information with reward identity and predictive cues, to initiate motivational response. Subsequent confrontation with the same reward might then lead to early anticipatory response in the striatum and the midbrain. Any deviation from the prediction (in size, taste, calorie, etc.) would in turn lead to an update of the existing data, by means of prediction error signals. Finally, one should note that there are also other brain regions with strong interactions with the striatum and OFC/vmPFC, like the amygdala and cingulate cortex to mention a few, which seems to have overlapping functions.

1.4 | Learning and positive reinforcement

As described in past sections, valuation and especially decision making involves learning from past experiences. The mesolimbic dopamine network, which includes brain regions such as the midbrain (VTA, Substantia nigra pars compacta (SNc)) and ventral striatum, encodes the rewarding properties of motivational experiences, both positive as well as negative. We described in the previous section that dopaminergic projections from the midbrain modulates striatal neurons. This modulation occurs due to distinct modes of firing of dopaminergic neurons. To make this clear, dopaminergic neurons fire *tonically* during resting state (i.e. in the absence of specific stimuli), which basically holds that they have low activity, and thus generating low level of dopamine release at projection sites (Goto & Grace, 2005; Schultz, 2007). However, when experiencing (or expecting) something positive, e.g. receiving an unexpected salient reward, these neurons can significantly increase their firing frequencies with bursts of action potentials, also called *phasic* mode of firing, generating high level of dopamine release at projection sites (Ljungberg, Apicella, & Schultz, 1992; Schultz, Apicella, & Ljungberg, 1993). We already mentioned that dopamine has a modulatory function, and depending on which dopamine-binding receptors are present on post-synaptic neurons, it could either cause excitation or inhibition in the post-synaptic neuron. In order to have a better insight in actions of VTA dopamine neurons, one should know what receptors are present at target sites of those neurons and in what density. Dopamine receptors can be categorized into two groups, i.e. D1-like receptors (referred as D1 receptor hereafter), including D1 and D3 receptors; and D2-like receptors (referred as D2 receptor hereafter), including D2, D4 and D5 receptors. D2 receptors have higher affinity to dopamine compared to D1 receptors, and activation of these receptors leads to a neuronal inhibition. D1 receptors, in contrast, have rather excitatory effects within a neuron. As a consequence, during tonic firing dopamine neurons (in which low levels of dopamine is released by pre-synaptic neurons to the synaptic cleft, creating a situation in which the proportion of dopamine molecules at synaptic cleft is relatively low compared to the amount of D2 receptors) dopamine will preferentially bind to (post-synaptic) D2 receptors, but not (or less) to D1 receptors, and will have an inhibitory action on post-synaptic neurons. Conversely, during phasic firing of neurons (in which high levels of dopamine is released to the synaptic cleft, and thus D2 receptors are fully occupied by the abundance of dopamine molecules) dopamine is provided with the opportunity to bind D1 receptors, resulting in excitatory signals within post-synaptic neurons. To simplify, dopamine is able to modulate striatal MSN's, by firing in distinct modes, and thereby activating either D2 receptor expressing striatopallidal MSN's (suppressing locomotion) or activating D1 receptor expressing striatonigral MSN's (facilitating locomotion). In addition, activation of D2 and D1 receptors in combination with glutamine release at post-synaptic sites also contributes to either

long-term potentiation (LTP) or long-term depression (LTD), which are found to be critical elements of learning (Surmeier, Plotkin, & Shen, 2009).

The sensational properties of a reward or other stimuli that might cue a certain reward will cause midbrain dopamine neurons to start firing phasically at the next encounter with these reward predicting stimuli. This will help animals to form associations between the stimuli and the reward, and as a result, animals will anticipate more quickly in response to sensory perception of these reward predicting stimuli. The same is true for unpleasant experiences, although in that case animals show avoiding behavior rather than anticipatory behavior when perceiving the negative stimuli. This phenomenon is called positive reinforcement (Schultz, Dayan, & Montague, 1997; Tobler, Fiorillo, & Schultz, 2005). It is an essential mechanism for the animal's survival in the nature. Moreover, as stimuli repeatedly precede the reward, midbrain dopamine neurons will cease firing at the moment of receiving reward, and instead, the firing will slowly shift towards the moment of perceiving the reward predicting stimulus. In other words, the preceding stimulus includes some information about the value of the reward that is expected. To make it clear, a novel rewarding food or sensation causes increased activation of dopaminergic neurons in the midbrain only after receiving the reward, but this activation slightly shifts towards the predicting cue, and diminishes at time point of receiving the reward itself. Thus, immediately after receiving a novel reward, a valuation process starts and the reward will be labeled with a subjective value. It is thought that this value encoding originates from the OFC (Rolls, 2005), and it might be plausible that the OFC in turn sends the information about subjective value to midbrain dopaminergic neurons which respond to it with increased firing and causes the animal to exert motivational behavior. Simultaneously, information about reward identity and reward value, including any possible cues that might predict the reward, might then be stored in the memory. Finally, when the animal has properly associated the cue with the reward, information about the reward could be retrieved from the memory including the reward value, and will cause the animal to start anticipating for the reward. However, when the expected reward is omitted, VTA dopamine neurons shortly stop firing at time-point at which normally the reward was expected and this is called the *reward prediction error*. This is also true when the magnitude of the reward is different in size than expected, though in this case the activity of these neurons increase if reward magnitude is larger or smaller than expected, respectively. Basically, this signal encodes for the variation between the subjective predicted value and the subjective outcome value, including difference in magnitude and temporal allocation of the reward, and any difference will lead to an update of the information about the stimulus that is already been stored in the memory. In this context, receiving a reward which was not predicted, might also be assigned as deviation from the expectation and will therefore cause a positive prediction error, as it is 'more' than expected. Reward prediction encoding is, as stated above, also assigned to striatal neurons by Hare et al. (2008), and since the (ventral) striatum is strongly interconnected with the VTA, reward prediction error signals in the striatum are likely to be rooted in the VTA dopaminergic neurons. Thus, from these findings we might assume that the striatum, together with midbrain dopamine neurons, correlates with expected reward magnitude and evaluates reward outcome, and any difference between the expected reward magnitude and reward received will lead to a reward prediction error (though real negative reward prediction errors are not been observed in the VTA or striatum, but seems to be encoded somewhere else in the brain). The OFC/vmPFC, on the other hand, encodes the real-time subjective value of rewards only at perception. For this reason, it is plausible that striatum is continuously updated with new information each time a reward is perceived that is (in part) provided by the OFC/vmPFC.

To allow striatal and VTA neurons to respond on novelty, incoming stimuli should be compared with existent data stored in the memory. Increasing number of publications show the existence of a hippocampal-VTA loop, as a role for novelty encoding (Lisman & Grace, 2005). Legault and Wise (2001) showed that an output region of the hippocampus, the subiculum, sends excitatory glutamergic projections to the VTA, which in turn cause a dopamine release in the nucleus accumbens (ventral striatum). This dopamine release in the accumbens is totally abolished when glutamate receptors in the VTA is blocked by TTX injection, which strongly suggests that VTA is involved in this loop. The hippocampus also sends glutamergic projections to the PFC, which in turn has glutamergic projections to the VTA. Though, the PFC is not an essential part of the hippocampal-VTA loop, since blocking glutamergic receptors with TTX in the PFC does not affect hippocampus-dependent VTA dopamine activation.

To concise, VTA neurons, and especially dopaminergic ones, have heavy interactions with many different brain regions, including the OFC for value encoding, the (ventral) striatum for locomotion and anticipatory behavior, the hippocampus for memory processing, sensory cortices for sensory inputs and many more. However, due to the small size of the VTA and other midbrain structures, and due to heavy physiological artifacts within these regions, limited amount of fMRI studies are conducted that focus on the role of the midbrain in valuation and decision-making

1.5 | Amygdala encodes emotional value

Another brain area that seems to be critical in valuation is the amygdala, a heterogeneous region commonly associated with emotional processes. Its close interaction with both OFC/vmPFC and the striatum, but also emerging findings from correlation studies already suggests that is likely to be involved in valuation and decision-making, or even action-selection. However, the exact function of the amygdala in valuation of reward is still a topic of debate. Amygdala activity is shown to be strongly correlated with emotional processes such as fear-conditioning (i.e. predicting aversive events), observing emotional facial expressions or erotic stimuli. Apart from encoding incoming emotional stimuli, amygdala is able to initiate emotional response via its innervations to the hypothalamus, resulting in physiological changes (increased hart beat, skin conductance, and startle response). Basically, amygdala represents emotional value to be used as input for encoding of (reward) of values, but is also capable to transform this information into an (emotional) output. Lesion studies of amygdala in animals show significant impairments in sensitivity to rewarding and emotional stimuli, and exerting emotional/motivational response to these stimuli (Corbit & Balleine, 2005; Holland & Gallagher, 2003). Noticeably, the amygdala is not a single nucleus, but rather consists of multiple nuclei, and subregions that are most relevant to our topic of review are the basolateral amygdala (BLA) and the centromedial amygdala (CeA). The BLA has heavy afferent inputs from sensory cortices and the thalamus, while the CeA has extensive efferent projections to the striatum (especially to dorsal striatum), to the brainstem (controlling autonomic responses), and to somato- and visceromotor controlling areas. Besides, these two regions are also connected to each other via direct projections. It is demonstrated that the BLA is responsible for representing and evaluating emotional value of incoming stimuli, and the CeA is responsible for executing emotional response to these incoming emotional stimuli. Although the amygdala has been repeatedly shown to be involved in (e)valuation and decision-making (Murray, 2007; Paton, Belova, Morrison, & Salzman, 2006; Pickens et al., 2003), it is still not clear how the amygdala contributes to these

processes. Remarkably, a quite recent single neuron recording experiment conducted by (Grabenhorst, Hernadi, & Schultz, 2012) demonstrated that amygdala neurons predicted economic choice, independently of action-selection, although this might be related to so called emotion-based learning (EBL). EBL is thought to be the underlying mechanism of decision-making that is based upon emotional experiences with previous choices, which is likely to occur unconsciously. Brain regions, such as amygdala and vmPFC that guide EBL are shown to predict outcome of complex decisions by means of emotional response to available choices (Damasio, 1996). Moreover, in a special designed gambling task, well-known as the Iowa Gambling Task (IGT), in which both healthy subjects as well as subjects with vmPFC lesion are allowed to choose cards from four different decks of cards. Each card that is chosen from one of the four decks will reward or punish the subject with different monetary gains or losses. Although decks A and B contain cards with higher monetary amounts compared to decks C and D, they do contain cards with higher monetary penalties as well. Obviously, this is information is not shared with the subjects, forcing them to learn to develop the best strategy to end with as much as possible monetary sum (selecting more cards from decks C and D will eventually lead to a higher yield). Subjects are allowed to pick up new cards from the decks until they have reached 100 cards. Researcher have found that subjects start to realize that decks A and B are more riskier than decks C and D after approximately 50 cards (assessed by asking subjects whether they understand the game or not with 10-card intervals). Remarkably, although subjects indicate conscientiously that they think that A and B is more riskier after 50 cards, they show a non-conscientious emotional response to risky decks already after 10 cards as they move with their hands above those cards, which is measured by increased skin conductance. Importantly, no such pre-conscientious emotional response was observed in patients with vmPFC lesion (Bechara, Damasio, Tranel, & Damasio, 1997), indicating that the vmPFC is critical for EBL. Subsequent studies have shown that besides vmPFC, the amygdala and the insula are equally important in encoding of such decision-making (Bechara, Damasio, Damasio, & Lee, 1999; Bechara, Damasio, & Damasio, 2003) . Finally, recent developments increasingly points to a cooperative role for OFC and amygdala in value encoding. All in all, it seems that the amygdala, known for encoding emotion and related behaviors, plays an important role in valuation and decision-making, even more than it was previously thought, though additional studies are necessary for better understanding.

1.6 | The Insular and the Cingulate Cortex

The insular cortex is located within the Sylvian fissure, containing agranular and granular neuronal population with a gradual transition between the AI to posterior insula (PI), respectively (RW.ERROR - Unable to find reference:170; Gallay, Gallay, Jeanmonod, Rouiller, & Morel, 2012). The insula is primarily associated with sensational, emotional, affective, and cognitive processes, although there is a clear separation between the roles of the two sub regions. We largely mentioned the role of AI in many neural processes related to topic of this review. This is hardly surprising, since the functional connectivity of the AI with other regions allows such operations to be executed. The AI is tightly connected with prefrontal regions encompassing the OFC and DLPFC, regions close the temporal lobe, such as the amygdala, parahippocampus, cingulate cortex, and subcortical regions including the basal ganglia, brain stem and thalamus (Augustine, 1996; Fudge, Breitbart, Danish, & Pannoni, 2005; Mesulam & Mufson, 1982b; Mufson & Mesulam, 1982). Recent developments in functional connectivity of the insula indicate that PI mainly receives signals informing the AI about the physiological state of the body, and that the AI, in turn, translates these signals to emotion and conscious affective sensation (Craig, 2009).

Besides having some large overlapping role with the AI in affect, emotion and cognition, the cingulate cortex plays an important role in other distinct processes such as action-selection. It has been suggested that cingulate cortex and the insula are the limbic sensory and motor cortices, that cooperate to execute emotional aspects of feeling and motivation, respectively (Craig, 2009). The cingulate cortex, lying over the corpus callosum, encompasses four sub regions, called the ACC, MCC, posterior cingulate cortex, and retrosplenial cortex (Vogt, Vogt, Farber, & Bush, 2005). When considering empathy, strikingly the dorsal part of the ACC (dACC) and the anterior part of the MCC (aMCC) are those sub-regions that show up consistently, especially through their dense connectivity with other regions like the insula (Mesulam & Mufson, 1982a; Mufson & Mesulam, 1982), amygdala (Morecraft et al., 2007), ventral striatum (Kunishio & Haber, 1994), and PAG (Hardy & Leichnetz, 1981). Communication with the frontal cortices is established via the rostral part of the ACC, which has connections with the OFC (Pandya, Van Hoesen, & Mesulam, 1981). Nonetheless, the dACC and aMCC are also heavily involved in the pain circuitry (Dum, Levinthal, & Strick, 2009). Finally, the AI and the ACC are populated by a distinct class of neurons called spindle or Von Economo neurons, and it has been suggested that the characteristics of these neurons allow efficient communication between these regions. Such a property is crucial for fluent processing of affective states, emotion, and motivation in rapidly changing contexts.

To summarize the first section, it becomes increasingly evident that the OFC/vmPFC is the central spot in the brain for the computation of the subjective value, which is referred as the first stage of the choice process. In order to compute a subjective value, however, the OFC/vmPFC relies on three main types of value related inputs. The first type of inputs originates from the (somato)sensory areas, informing the OFC/vmPFC about the sensory properties of an option (i.e. visual, taste, smell etc.). The second type of input, provided by the striatum/midbrain, contains information about the motivational state of the body, while the third type of input, provided by the amygdala, contains information of subject's emotional state. Thus, it seems that the striatum and the amygdala compute the motivational and emotional value of an option, respectively, and transfer these information to the OFC/vmPFC, at which they are further integrated with (somato)sensory inputs to form a final subjective value. Importantly, one should note that the OFC does not simply respond to the (sensory) intensity of an option, but encodes its pleasantness at that very moment of decision-making. Moreover, the OFC/vmPFC is able to compute the subjective value both in an absolute manner, as well as in a relative manner, or also called a *neural common currency.* The latter is thought to be an important precursor for choice selection, since it allows comparison of multiple options. However, the exact mechanism underlying these valuation systems remain to be elucidated.

2. Choice

Thus far, we described how our brain is able to attach value to goods or rewards. Let us consider our example from the previous chapter: we were in a situation in which we had to choose between a strawberry and an apple at a green market. Having described the process of valuation, we now have labeled each option with a certain value. If we are in a thirsty condition, the juicy apple might have a lead to a higher subjective value. In contrast, if we desire something sweet, the strawberry might then be the option that scored the highest subjective value. However, we still did not make

any choice between them, and the subsequent question is whether we will choose for the strawberry or the apple. We already described that the OFC is able to encode the absolute value for both options under consideration, and even, the relative value. In addition, it is evident that expectancies about options is important for decision-making, because in most cases we do not have the opportunity to 'taste' the options before we choose, and therefore we have to imagine 'tasting' or expect the options. We have described that the hippocampus, together with the striatum and midbrain, but also OFC itself, are brain regions that represent expectations. Next, we will describe how value containing information and representations of expectations are further transformed and shaped into a choice.

2.1 | No single decision-making

Although we did not explicitly mentioned it in previous chapters, one should note that there are different types of decision-making systems, and each are thought to involve distinct, yet overlapping neural circuits (Padoa-Schioppa, 2011). There are three main type of decision-making or action-selection mechanisms that are mentioned by (van der Meer, Kurth-Nelson, & Redish, 2012): a *Pavlovian* action-selection mechanism, a *habit* action-selection mechanism, and a *deliberative* action selection mechanism. The Pavlovian system involves learning a stimulus-action association for motivationally significant outcomes, but the number of actions that are initiated in response to stimuli is rather limited (for example salivation, freezing, and approaching). This system includes the periaqueductal gray (PAG), VTA, amygdala, ventral striatum and OFC (McDannald et al. 2011). The habitual mechanism, in contrast, might involve more complex set of behaviors. In general, habits are established after extensive and time consuming training, but once learned, they can be initiated very rapidly, though they are quite fixed and highly insensitive to changes in context (e.g. failing to press slowly on the brake pedal with your left foot if you are used to drive cars with manual gears, because the left foot is then 'trained' to press heavily on the (clutch) pedal. Brain regions that are correlated with this system are (SNc), dorsolateral striatum, ventral striatum, and motor cortex (Cicek and Kalaska, 2010; Yin and Knowlton, 2004). Deliberative action-selection is the most complex one among the three systems, since it involves predicting and evaluating outcomes by integrating both information about our internal state and external signals, and selecting actions with the highest value determined by calculating gains and losses associated with each action. The deliberative system is also highly flexible, allowing us the make decisions in dynamic environments. Finally, deliberative decision-making system are thought to involve the hippocampus, the prefrontal cortex (OFC, vmPFC, dlPFC) ventral striatum, VTA and dorsomedial striatum (Johnson and Redish, 2007; Schacter and Addis, 2011; van der Meer and Redish, 2009; Yin and Knowlton, 2004). Extensive amount of studies are conducted to elucidate the underlying mechanism in these systems, though there is still a large gap in our knowledge concerning how these circuits establish decision and to what extent different decision-making circuits overlap each other.

2.2 | Costs in decision-making

Decision-making might not only depend on (positive) subjective value, but also with negative values, which are costs associated with a given option, that should also be integrated in the decision-making process. To sum the different types of (external) costs that can be associated to a choice, as decribed by Padoa-Schoppa (2011), there is cost of action, cost of delay, risk, ambiguity and of course monetary costs which is exclusive to humans, though we will describe the latter separately in chapter 3, which is about pain of paying . As different types of decision-making involves different circuits in the brain, different types of cost also seems to involve different neural circuits.

2.2.1 Cost of action

First, the cost of action is the effort of obtaining a reward, occurring very frequently in the nature, but also in our daily lives. We can think of a lion deciding whether or not to hunt a pray he has spotted. Although consuming this meal might be highly attractive, the lion should first consider the fact that he has to spend some energy in advance to chase the pray. The lion should now weigh the reward against the cost. If the pray he has spotted is a large deer, the value of the reward would probably exceed the cost of action, and thus resulting in a positive net value. By contrast, if the pray is just a little rabbit, its value would probably not exceed the cost of action, resulting in a negative net value. In case of a rabbit, the lion would probably decide to ignore it and seek for a bigger meal. A mechanism should therefore be available that encodes the net subjective value of each option by subtracting potential cost of action from the subjective value encoded by the OFC. Anterior cingular cortex (ACC), striatal regions and the midbrain seem to encode the net value of option, which is basically the value associated with an action or choice after substracting its cost, in contrast to the OFC, which is commonly associated with good-based valuation (Rudebeck et al., 2008). In addition, the ACC, and especially the dorsal part (ACCd), is shown to encode the net value. Neurons in monkey ACCd correlated with the amount of action that was required to obtain a reward, as there were neurons that increased with increasing reward expectation, and decreased with increased effort to obtain reward (Croxson, Walton, O'Reilly, Behrens, & Rushworth, 2009). Interestingly, in another study, there are actually two dissociable population of neurons found that either correlated with net value, i.e. increased firing in response to increased reward expectation; or reversely correlated with net value, i.e. increased firing with increased effort associated with reward (RW.ERROR - Unable to find reference:120).

2.2.2 Cost of delay

Second type of cost is delay. Postponing a purchase of a car to save for a better one is a simple example of a situation with a cost of delay. In this example, decision is made now, but the reward will take place later in the distant future. This process typically involves some imagination of future situations in which the reward with the delay is utilized. If the person thinks that the future reward is indeed more attractive than the current reward, he or she might then decide to accept the delay. Vice versa, if the value of the future reward does not exceed the value of the currently available option, then that person will go for the immediate reward. Generally, animals and humans prefer immediate rewards over delayed rewards, even if the immediate reward is smaller than the delayed reward. The future reward will be chosen only if its value is still larger than the smaller reward after discounting the cost of delay. As it is with other processes, it is still largely unclear how the brain computes this cost of delay. One might already suggest that delay as a cost is somewhat different than action cost, and consequently distinct circuits might therefore be responsible for representing these different types of costs. Indeed, although we described above that ACCd is largely responsible for encoding action-cost, this is not the case for encoding the cost of delay. Experiments have shown that the OFC, but also the ventral striatum, VTA, subregion of the hippocampus and posterior cingulate cortex as well, is able to encode cost of delay, as their activity correlated with the amount of delay associated with a reward and reward magnitude (Kable & Glimcher, 2007; Roesch, Calu, & Schoenbaum, 2007), and lesions in these regions resulted in increased impulsivity in rats, which confirms that these regions plays a role in decision-making between delayed rewards (Cardinal, Pennicott, Sugathapala, Robbins, & Everitt, 2001; Cardinal, 2006; Ghods-Sharifi, St Onge, & Floresco, 2009). Moreover, in a study in which subjects were asked to choose between immediate and delayed monetary rewards,

activity in the above mentioned brain structures, or limbic regions as they classified them, is shown to be greater for immediate rewards and gradually decreases with increasing delays (McClure et al 2004). These regions therefore seem to be responsible for anticipatory behavior (or Pavlovian decision-making) in response to immediate rewards. Interestingly, in patient subjects who are less sensitive to delay, and therefore applying less discount on delayed choices, the difference in activity in the ventral striatum and VMPFC between immediate and delayed reward is smaller compared to more impulsive subjects who apply larger discounting for delayed rewards (Ballard and Knutson, 2009; Kable and Glimcher, 2007; Peters and Buchel, 2009). These individual differences in discounting seem to depend on the magnitude of temporal perception (Kim and Zauberman, 2009; Kim and Zauberman, 2013). In contrast, another class of brain structures including especially the lateral prefrontal cortex, are shown to have a greater activity when subjects choose delayed rewards, and gradually increase with increasing delay. This suggests that lateral part of the prefrontal cortex, comprising subregions such as dorsolateral prefrontal cortex (dlPFC) and ventrolateral prefrontal cortex (vlPFC), play a role in future planning and decision-making. Indeed, lPFC seems to oppose with VMPFC and ventral striatum when choosing between immediate and delayed rewards, and that lPFC is involved in higher cognitive processes that might influence decision-making. Remarkably, there are currently contradicting theories and findings regarding the role of VMPFC and ventral striatum in encoding temporal discounting. Despite the fact that some hypotheses predict that suppressing activity in these two regions would cause subjects to exhibit more patient behavior, a recent study conducted by (Cooper, Kable, Kim, & Zauberman, 2013) have challenged these proposals, as they showed that patient subjects have different pattern of activity in these regions instead of reduced activity. They observed that subjects that apply less discounting for delayed rewards even show increased activity in the regions VMPFC and ventral striatum in response to delays with larger distance in the future. The intriguing question now is how delay is encoded by these regions. It has been thought that it starts with DA neurons in the midbrain that respond to unexpected immediate rewards, and thereby encoding the reward prediction error. Cues that predict immediate reward elicited higher activity in the VTA, compared to cues that predict delayed reward, but notably, as the delay increases the predictability of reward decreases, which in turn increases the probability that the reward is obtained unexpectedly, eliciting again an increased activation in VTA DA neurons. These signals are then further transferred to the OFC, which then encodes the discounted value of a reward, apart from cost of action and even independently of reward magnitude (Roesch, Taylor, & Schoenbaum, 2006; Schoenbaum & Roesch, 2005). In addition, it is shown that there are dissociable neuronal populations within the OFC that respond with increased activity to either immediate rewards or delayed rewards (Roesch et al., 2006).

To clarify the above section, it is evident that OFC/vmPFC and ventral striatum are strongly correlated with delay, as these regions are increasingly activated by immediate rewards and gradually decrease their firing with increasing delay. However, delays introduced in many studies are rather short-term delays, and as we mentioned above, OFC/vmPFC and ventral striatum increase their activity again to delays with longer temporal distances. Thus, their activities show a parabolic-like pattern. On the other hand, the dlPFC is opposing vmPFC by increasing its activity in response to longer delays.

DlPFC has repeatedly been shown to play a critical role in self-control, in that it encodes rather long-term consequences of choices. Given that dlPFC has strong connectivity with vmPFC, it is likely that dlPFC exert influence on the neural activity in the vmPFC. An interesting study that supports this hypothesis comes from (Hare, Camerer, & Rangel, 2009). In their study, they investigated both successful as well as unsuccessful dieters, in which the first group considers both health and taste attributes when provided with tasty but unhealthy food, while the latter group only considered taste. Although they have found similar value encoding activity in the vmPFC between the groups during time of choice, they have observed interesting differences in the left dlPFC. In successful dieters, left dlPFC show increased connectivity with the vmPFC, while this connectivity has not been observed in unsuccessful dieters. Strikingly, reducing activity in the left, but not right, dlPFC using TMS stimulation resulted in subjects choosing preferentially for immediate rewards and was less likely to wait for rewards (Figner et al., 2010). In their most recent study, (Hare, Hakimi, & Rangel, 2014)) further confirmed that dlPFC is able to modulate activity in the vmPFC (probably including the OFC) in situations in which monetary reward outcome is delayed, through the existing interconnectivity between these regions. Here, I would like to cite a clarifying statement originating from their paper:

"Choice seems to be driven by the stimulus value signals encoded in a vmPFC-based valuation system, but the activation of dlPFC is critical for deployment of self-control, because it appears to promote increased weighting of foresighted stimulus attributes in the vmPFC value signals as evidenced by increased effective connectivity to vmPFC during larger delayed rewards".

2.2.3 Risk and Ambiguity

Another factor that influences decision-making process is undoubtedly the amount of risk. Our brains are, interestingly enough, able to mathematically compute risk in an uncertain world. Increasing amount of studies contributed to a better understanding of the neural process underlying this feature. Humans, but definitely also animals, continuously cope with at least some degree of risk, that is, the chance an action will not lead to desired outcome (something positive), and instead the opposite comes true (commonly experienced as something negative). In animals, we could use the same example used in the previous chapter to make this clear. A hungry predator that encounters a pray would consider the risk prior to attacking it, i.e. it is not fully certain whether the predator is able to successfully hunt it's pray. The valuable energy that is invested, by means of physical effort, to obtain more energy in return might be totally lost in case of a failure, further endangering its own survival. Therefore organisms tend to minimize risk, in order to maximize their outcomes. Humans, on the other hand, are also confronted with risky situations, in which the basic principle is largely similar. There are of course many examples in which we make choices involving risk, such as investment in shares or saving money for pension. Obviously, most of the studies that focus on the neural mechanism of risk involve gambling tasks, although one should be aware that gambling as we know from casino games also heavily involves some amusement and fun. Consequently, while gambling tasks are suitable to explore the neural correlates of risk, they may lead to engagement of reward related brain regions as well. Nevertheless, several brain regions are identified that show correlations with risk and risk prediction. One such region is the anterior insular cortex (AIC). Neural activity in the AIC is shown to increase when subjects make risky choices, and this activity decreases as choices became surer (Paulus, Rogalsky, Simmons, Feinstein, & Stein, 2003). In addition, AIC activity correlated well with risk prediction. In a gambling task in which subjects are asked to pick up two cards from a deck with randomly ordered numbers between 1 and 10. Subjects were able to either win or lose $1 by respectively predicting correctly or incorrectly if the second card was going to be a higher or lower number than the first card. A delay of approximately 6 seconds was introduced between seeing the first card and picking the second card to measure neural activity in

response to risk prediction. They show that reward prediction would linearly increase with increasing chance of winning the reward, as can be predicted by observing the number on the first card. In contrast, risk prediction showed a reversed-U pattern, that is, the risk is at maximum when the number on the first card is 5, while it is at minimum (zero) when the first number is either 1 or 10. Same pattern has been observed in neural activity of the AIC during the delay period. More convincing finding is that inactivation of the AIC decrease risk taking in subjects while inactivation of OFC increase risk taking (Ishii, Ohara, Tobler, Tsutsui, & Iijima, 2012). Furthermore, there are some additional regions that are close associated with the insular cortex in risk encoding, which are together seem to form a network of emotion encoding. These regions include the ACC, inferior frontal gyrus (IFG) and the amygdala. A study of (Christopoulos, Tobler, Bossaerts, Dolan, & Schultz, 2009) revealed that ACC encodes risk in a purely objective manner, while IFG more related with encoding aversive response to risk. To elaborate, they showed that activity in the ACC increased in response to increasing risk, and this was not influenced by risk aversion as ACC activity did not vary among subjects. The IFG, on the other hand, is proven to be insensitive to objective risk evaluation, and instead correlates with subjective attitude towards risk. Increased activation of IFG is observed for safer choices, suggesting that risk averse people have stronger activations of IFG. In their study, they have also focused on the role of ventral striatum, and they showed that in line with other literature increasing activation of the ventral striatum increased with increasing (expected) value or magnitude of choice. While increased activation in the ACC and ventral striatum frequently precede a risky choice, in the IFG it precedes a safe(r) choice.

The role of amygdala in risk, however, is not clear yet. It is suggested that amygdala more involved in ambiguity, or also called estimation uncertainty, rather than encoding risk itself, since no correlation has been observed during task in which outcome probabilities were known. Activity in amygdala increased solely when outcome probabilities were unknown (Hsu, Bhatt, Adolphs, Tranel, & Camerer, 2005). Notably, in its review, (Bossaerts, 2010) defines risk as what remains after learning is finished, which cannot be avoided or reduced; while estimation uncertainty, or ambiguity, can be reduced over time by learning. Finally, although most of the studies with a focus on the role of insula in risk indicate an objective way of encoding, it could not be excluded that the insular cortex attaches some subjective value to risk signals, as it is known for encoding of several emotional processes. Further work is necessary to have a better understanding.

2.2.4 Pain of Paying

In the above sub-sections, we described different neural mechanisms underlying different types of 'costs' that contribute to devaluation of choices, and these are in main lines commons in all mammals. Though, there is one type of cost remaining, we did not described yet, a cost that is exclusively assigned to humans, and the one in which economists are mostly interested in; the monetary cost.

Money, defined as "*current medium of exchange in the form of coins and banknotes (Oxford dictionaries),* differs from primary rewards, such as food or sex, in that its value should be learned over time, and it is therefore called a secondary reward. For example, as a result of evolutionary process, newborns are able to value primary rewards, whereas they are senseless to secondary rewards like money. In other words, money becomes rewarding only when its value is learned, and once learned, spending or giving-away might be an unpleasant experience. Indeed, spending money is another type of cost when making economic choices. Practically in all our purchasing's we give away some amount of money to obtain a desired item or service in return, but how do we decide if the price is acceptable or not? The point at which humans decide to buy varies significantly among each other. While some people are eager with spending, other people may be less reluctant to spend money. Consequently, the former group may accept higher prices for same items in comparison with the latter group. In this review, we are especially interested in the neural correlates of purchasing decisions. A side from 'buy or not buy' situations, we particularly aim to understand how we make choices in situations in which we make choices between two or more goods with different prices. To elaborate on our aforementioned case of choosing between a strawberry and an apple, even though we have already assigned a subjective value to both, it is still necessary to integrate costs associated to each. In our case example, however, only cost of price is concerned, but not any other costs we described above. We might prefer strawberries over apples, but after considering the prices our final decision might shift towards the oranges. Basically, the subjective value of the item we are willing to buy should outweigh its cost, the cost of price in this case, in order to choose it. But how does our brain computes this cost of price, and integrates it to the decision-making process? Brain regions that are preferentially activated upon monetary gains (like almost all kind of rewards) are the ventral striatum (NAcc), the medial PFC and the (posterior) cingulate cortex. Activity in these regions increases with increasing monetary gain, but decreases with increasing loss (Riba, Kramer, Heldmann, Richter, & Munte, 2008). Since OFC is one of the major output regions of the ventral striatum, activity in this area is strongly decreased in response to reduced activity in the ventral striatum upon monetary loss. When we consider the role of OFC in valuation, we might suggest that this decrease in activity observed in the OFC is a result of integrating cost of money in the valuation process. Reduced activity in the ventral striatum in response to monetary loss might be one explanation for devaluation in the process. Since OFC, as well as the ventral striatum, receives many inputs, another explanation for devaluation could be the fact that there are other brain regions that correlates with monetary losses, and consequently send inhibitory signals towards the OFC or the ventral striatum. One such candidate is the amygdala, which seem to process monetary losses. But given the fact that amygdala is responsible for emotion, as we have described earlier, it is more plausible that amygdala, in this context, represents emotional response to monetary loss rather than computing monetary loss. A more plausible candidate might be the insular cortex, a region closely related to the amygdala, and having a similar negatively correlated neural response to monetary gains. In addition, insula is repeatedly shown to respond with increased activation during anticipation of physical pain (i.e. electric shock) or losses (Chua, Krams, Toni, Passingham, & Dolan, 1999; Paulus & Stein, 2006), during risky decisions (Paulus et al., 2003) and to visually aversive stimuli. Collectively, insula activation is thought to be responsible for aversive behavioral responses. Exemplifying studies of Knutson and colleagues shed light on the role of insula in encoding cost of price. Namely, they have shown that activation in the insula is also increased when human subjects were confronted with a price after viewing attractive products, and strikingly, this activation correlated with rate of expensiveness. Because of the fact that purchasing activates a region commonly related to aversiveness and pain, this phenomenon is referred as *pain of paying,* despite that additional studies are required to confirm whether this signal genuinely represents pain (Knutson et al., 2007; Knutson & Bossaerts, 2007; Knutson & Greer, 2008). Interestingly, it seems that activation in the insula even predicts rejection of those desired products when the associated price is experienced as too expensive, while activation in the ventral striatum predicts purchasing of desired products. Hence, there are two critical brain regions, the ventral striatum versus the insula, that have opposing responses to monetary gains and losses. Subsequent fundamental issue is to investigate how a winner is selected between these regions to

either accept or reject the purchase, since they are counteracting each other. It is important to note, however, that for better understanding of neural mechanism underlying such processes, we should analyze the functional connectivity among different brain regions, since it is hardly possible that one process is restricted to one region. It is therefore likely that activity in one region should have similar pattern of activity elsewhere in the brain.

Here we have listed some important negative attributes that can be integrated into the choice process. Although we attempted to describe different neural mechanism underlying encoding costs separately, in reality this seems unlikely. Different brain regions might have overlapping functions in distinct processes. For example, we have seen that ventral striatum is associated with very different processes, although it is mainly known for its role reward processing and initiating proper behavioral response. Furthermore, we have described that future planning and delay encoding is encoded by dlPFC, that risk prediction and related behaviors are encoded by the insular, ACC, IFG and the amygdala, and finally that cost of action is mainly encoded by the ACC. These negative attributes, together with positive attributes should converge at some point, and this point is thought to be the OFC/vmPFC. As we have already mentioned it in the first part of this review, these regions are then able to encode the subjective value for each choice, and to allow comparison, transform these values into a common currency.

2.3 | Transforming value into choice

Importantly, we have already mentioned three different kind of decision-making processes described in the literature: i) Pavlovian system, in which association between stimuli and outcome is learned, with an anticipation or withdrawal response. ii) Habitual system, in which a stimulus automatically elicits a certain action response, and is therefore less flexible and less sensitive to changes. iii) goal-based system, in which the association between response and outcome is learned. The latter is the most flexible one in that it can rapidly adjust to changing choice contingencies. All of these systems requires decision-making, but is not clear whether the underlying mechanism is the same for all, or are there different circuits for each system that might partially overlap each other. For the purpose of this review, the habitual and Pavlovian decision-making will not be described extensively; instead, the focus will be on the deliberative decision-making.

The key question now is how the brain is able to select the option with highest value (a comparator), a system that is likely to show choice predicting signals (probably with categorical response to inputs from OFC/vmPFC), and is able to initiate the proper motor action response. Indeed, there are brain regions identified that show such choice predicting signals, and activity within these regions closely precede motor response. Dorsomedial PFC (DMPFC) and intraparietal sulcus (IPS) seem to fulfill the comparator role, i.e. receive value information from OFC/vmPFC, compare and select the one with the highest net value, and transform choice into motor response (Hare, Schultz, Camerer, O'Doherty, & Rangel, 2011). Specifically, the DMPFC found to be more heavily involved in action-based decision-making, while the IPS is more involved in perceptual decision-making. The assumption that DMPFC might fulfill the comparator role for action-based decision-making is further strengthened by the fact that i) this region has strong connections with both value encoding areas like OFC and vmPFC, as well as motor areas (Beckmann, Johansen-Berg, & Rushworth, 2009); and ii) different decision variables are found in this region.

Moreover, the ACC has also been repeatedly reported to play a role in the selection of choice, as lesion in the ACC impaired establishment of choice based on action outcome. In addition, other studies revealed binary signals in the ACC representing chosen/not-chosen not action. It is suggested that action is selected through inhibition of the opposite action. Considering our previously mentioned findings that ACC correlated with the difference in (action) value signals between two options, a comparator role for ACC is reasonable, though many researchers state that a strong interaction between the mPFC and the ACC is the neural basis of choice selection.

3. Social Decision-making

In the previous chapters we attempted to describe the underlying neural mechanism of choice, but rather on individual base. In the following sections we will touch upon another dimension of decision-making, namely social decision-making. Social decision-making is a broad area of research with a focus on the effects of social interaction on decision-making behavior. It comprises many different social aspects, but owing to limitations in time and space, only two subjects will be considered. Empathy and Theory of Mind (or perspective-taking) will be treated in the next section, and to my knowledge, these are one the most important elements of social decision-making.

3.1 | Empathy

An additional interesting and highly debated feature of humans, non-human primates and some other animals that enables feeling or even imitating the emotions of others, and influences human or animal behavior accordingly is undoubtedly *empathy*. Indeed, it has been shown that same neural (emotional) responses are observed in an observer who engages empathy (Preston & de Waal, 2002). On top of that, observing someone suffering from pain, besides 'feeling' the pain, might trigger a help response in the observer (Hein, Silani, Preuschoff, Batson, & Singer, 2010). Preston & de Waal (2002) even suggest that all processes related to empathy are based mainly upon a perception action mechanism. Moreover, there are different forms of empathy, such as emotional and cognitive empathy. The latter is also called 'theory of mind' which we will discuss in the next section. It is thought that separate neural mechanisms underlie these different forms of empathy. Accordingly, lack of empathy (in general) was considered as the causal for autism spectrum disorder (ASD), but emerging studies now show that only cognitive empathy seems to be impaired in ASD patients, while emotional empathy is still intact (Rogers, Dziobek, Hassenstab, Wolf, & Convit, 2007; Shamay-Tsoory, Aharon-Peretz, & Perry, 2009). Furthermore, there are many states that might involve empathy, but obviously pain has the strongest impact. Consequently, studies focusing on empathy mainly use pain (mainly by painful, yet harmless electrical shocks) to investigate the neural mechanism of empathy, especially because of the fact that the pain network is well described. Brain regions that come up from those pain studies are the primary and the secondary somatosensory cortices, some regions in the frontal cortex, the brainstem, thalamic regions, the ACC, mid cingulate cortex (MCC), and at last the anterior insula (AI). Those regions show increased activity in response to pain, although not restricted to, and they can be classified either as objective encoders of brain, i.e. correlating with intensity of pain; or as subjective encoders, i.e. correlating with subjective rating of pain intensity (Duerden & Albanese, 2013). While ACC/MCC and AI belong to the latter, the rest mainly belong to the former (Kong et al., 2008). A remarkable experiment conducted by Singer and colleagues provided new insights in the neural basis of empathy. Using fMRI, female subjects underwent two scanning sessions. In the first session, they were scanned while they received painful electrical shock via an electrode attached to her hand. In the second session, their male partners joined the session by sitting next to the MRI scanner with electrode attached to their hands, and using mirrors they were visible to female subjects in the scanner. This time, female subjects did not receive

any electrical shock, but instead saw their partners receiving it. Hence, neural activity of female subjects were scanned both while they received the shock themselves, as well as while they saw their partners receiving the shocks. Importantly, in both conditions, neural activation has been observed in similar brain regions, which are the ACC, AI, the brainstem and the cerebellum (Singer et al., 2004). Subsequent studies confirmed this finding, as they showed that facial observation of pain activated the same pain network (Lamm, Batson, & Decety, 2007). A quite recent comprehensive meta-analysis conducted by Lamm and colleagues strongly proved that the AI and ACC/MCC have a critical role in empathy for pain, since these regions are consistently showed correlation with empathizing in variety of studies (Lamm et al., 2007). Furthermore, AI and ACC/MCC are not restricted to empathizing to pain, as they play critical role in empathizing with other states such as, disgust (Jabbi, Bastiaansen, & Keysers, 2008), anxiety (Prehn-Kristensen et al., 2009), taste (Jabbi, Swart, & Keysers, 2007)and even social exclusion (Masten, Morelli, & Eisenberger, 2011). Considering previous sections, these same regions are highly involved in the valuation and decision-making circuit. Logically, these findings strongly suggest that these brain regions exercise influence on decision-making process. In addition, the AI and ACC/MCC initiate behavioral or emotional responses depending on their distinct connections with other brain regions, such as the motor cortex or thalamic/brainstem regions.

3.2 | Theory of Mind

Consider, after a 'long journey' of perception, valuation, comparing, and action-selection in front of the fruit-and-vegetables stand at the green-market, you finally decided to buy some strawberries instead of the apples, despite the fact that strawberries were more expensive. You are now in a position to start a conversation with the grocer to confirm your purchase. However, you are not willing to pay the full price for the strawberries, and consequently you kindly ask for some discount, and start bargaining with grocer about the price. The outcome of this haggling will depend on your own haggling skills, but also definitely depend on the response of the grocer. The grocer may try to convince you that those strawberries are high quality, and therefore worth the price. Subsequently, you might be convinced or you might be simply not, but what makes us sensitive to such interactions?

The above text is a simple example of perspective-taking or also known as *Theory of Mind* (ToM). Although commonly associated with empathy, ToM can be considered as distinct neural process, involving different neural circuits. While empathy involves sharing emotions of others, ToM is thought to be a more cognitive process of acknowledging the thoughts, intentions, feelings, and taking the perspective of others. Obviously, ToM is an essential mechanism for development of social communication. Basically, empathy and ToM are complementary processes which are crucial for successful socializing. A person with a well-developed ToM, but a less developed empathy, might therefore be able to place itself in the situation of another person, even knowing how the other would think or feel. However, due to a lack of empathy, that person would probably not be able to experience any emotional and motivational feelings in response to perspective-taking that might influence their choices or behaviors. Such cases are commonly observed in criminals and patients with antisocial disorder. Conversely, missing ToM might impair perspective-taking, and consequently disturb communication and social interaction with others, as observed in patients with autism spectrum disorder (OSD) and schizophrenia. A large literature has already been established on ToM, and its neural correlates. An important hallmark of ToM is undoubtedly the attribution of false beliefs, allowing one to predict other's behavior. The cognitive capacity for ToM is commonly tested using a false-belief test. During this test the subject is confronted with an event in which the location of an object changed while the protagonist is absent. The subject is then asked where the protagonist will start looking for the object. Subjects with a strong ToM mainly indicate correctly that the protagonist will look at the original location of the object, since the protagonist is unaware of the change (false belief). By contrast, patients with OSD mainly answer by indicating that the protagonist will start looking from the new location, since they are unable to take perspective of the protagonist and therefore cannot predict the behavior of the protagonist.

Discussion

In the present review, I have attempted to provide a detailed description of the decision-making process, focused mainly on the core systems such as valuation, choice-selection and social influences to choice, by analyzing a large set of (recent) literature that are published on PubMed using keywords such as "valuation", (social) "decision-making", and "choice".

The highly complex nature of the (human) brain, with its strongly interconnected neuronal network challenges neuroscientists to map the neural process of choice. Until the finding of functional Magnetic Resonance Imaging (fMRI) technique in the 90's, it was hardly possible to see what was going on in our brain, and to functionally observe the dynamics of neural processes globally, and in real-time fashion. Consequently, fMRI has been extensively used by neuroscientist and psychologists to investigate the underlying neural mechanism, mainly by means of neural activity, of almost all kind of animal and human behavior. Hence, the provided literature in this review contains data mainly originating from fMRI experiments conducted with both human as well as animal subjects. However, in order to map the neural process of a certain behavior, it is critical that such fMRI experiments are carefully and properly designed. Furthermore, it is important to note that fMRI signals are based on BOLD-signals, which basically reflects neural activity indirectly, and with some degree of temporal delay (15-20 sec.). These facts should therefore be taken into account when considering results of such experiments. Another downside of the fMRI method is the lack of spatial resolution. Although there is a positive trend regarding the imaging resolution of MRI scanners, it is still not possible to scan the brain at neuronal level; rather, activity is scanned from specific brain regions, which may contain different genetically defined populations of neurons. Thus, while it is a useful technique to attribute brain regions to different sets of behaviors, it lacks the property to distinguish neuronal populations. A combination of fMRI with techniques such as optogenetics, which, although invasive (and therefore only applicable on animal subjects at the moment), have high spatial and temporal resolution, and allow inhibition or activation of specific type of neurons in real-time. Identifying and measuring distinct populations of neurons is especially of importance for dissecting many different processes and behaviors that are currently assigned to a single brain area.

Despite its above-mentioned limitations, fMRI experiments have provided powerful insights about neural correlates of choice, and led to identification of brain regions that play a crucial role in decision-making. Researchers share a common ground regarding the role of the OFC and the striatum as the most critical brain regions for valuation and processing of choice. Based on the literature, these regions have indeed shown to be the primary stations for determining the subjective value of options, and consequently have strong influence on the establishment of final choice. The broad range of inputs from different brain regions, including the sensory areas, provides the OFC with the necessary elements to encode a real-time subjective value for choice, as activity in the OFC has repeatedly shown to correlate with

(behaviorally) measured subjective value. Another finding, which is even more interesting, is that OFC seems to be able to transform these values into a so-called neural common currency, enabling comparison between multiple options. It is, however, unclear how these value signals in the OFC are established, and how this information is used for choice selection. Although a strong correlation has repeatedly shown, the exact role of the striatum in the valuation process is still poorly defined. A generally accepted role of the striatum is anticipation to rewards and initiating a motivational response, as activation in the striatum is commonly observed to rewarding options, with increasing activation to increasing magnitude of rewards. As we have seen from the literature, the striatum is involved in many stages of decision-making. During the valuation stage, it seems that the striatum mainly act as an input source for the OFC/vmPFC, transferring information about the motivational state of the body and the rewarding properties of options. During the final stage of decision-making, however, the striatum is likely to act as one of the several output stations of the OFC/vmPFC, and may initiate an anticipatory movement towards the chosen option. The same principle seems to hold true for the amygdala, though in this case emotion related aspects of choice are transferred between the amygdala and the OFC/vmPFC. To elaborate, while the amygdala seems to encode and transfer emotional value of choice to the OFC/vmPFC during the valuation stage, it is able to trigger emotional responses, such as increased heartbeat and transpiring, after a choice has been selected. In combination with other (sensory) inputs from other brain regions, signaling information like bodily state, hunger and sensory properties of options, the striatum and the amygdala thus contributes significantly for the encoding of option value within the OFC/vmPFC.

In summary, there are many regions that respond to value in some fashion, and some of these regions (e.g. OFC and the striatum) even respond simultaneously to different types of rewards which raises the question whether there is a single or multiple valuation systems present in the brain. Especially, a very recent review paper of Stott & Redish discuss this issue in detail (Stott & Redish, 2015). In their paper they provide some data from Strait et al., which show that reward expectation coding and value-related signals occur earlier in the VS, compared to the OFC (Stott & Redish, 2014; Strait et al., 2015). Although these are highly interesting findings that makes us aware for the fact that there may be multiple valuation systems instead of a single system, and remarkably show that value signals occur earlier in the VS, there are some point worth to note.
First of all, as we have mentioned in the beginning of this paper, there is still some confusion about the anatomical localization and the role between the OFC and vmPFC. While talking about OFC in the papers mentioned above, it could be well that they are talking about the vmPFC or another subregion in the PFC.
Second, are the value signals that are found in the VS and OFC reward or experiment specific or can we assume that this is the case in general. It might be the case that neurons in the VS responds faster to choice in order to initiate immediate anticipatory behavior towards highly motivational rewards, while OFC/vmPFC takes into account many other factors by receiving inputs from many other brain regions, and therefore responds somewhat later.

As new techniques evolve, new possibilities in elucidating the brain functioning do arise. Neuroimaging techniques such as fMRI, EEG and TMS, together with correlation studies already contributed to a large literature about functional neuroanatomy, which in turn allowed us to identify brain regions that play role in processing of choice. Undoubtedly, new techniques that allow observation of functional connectivity among different brain regions or clusters of neurons will provide us new insights about how they interact with each other. Eventually, mapping the functional connectivity of the brain will significantly improve our understanding about the human decision-making.

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