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Mini-Review

The Impact of Stress in Decision Making in the Context of Uncertainty

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For a number of decades, different fields of knowledge, including psychology, economics, and neurosciences, have focused their research efforts on a better understanding of the decision-making process. Making decisions based on the probability of future events is routine in everyday life; it occurs whenever individuals select an option from several alternatives, each one associated with a specific value. Sometimes subjects decide knowing the precise outcomes of each option, but commonly they have to decide without knowing the consequences (because either ambiguity or risk is involved). Stress has a broad impact on animal behaviors, affects brain regions involved in decision-making processes, and, when maladaptive, is a trigger for neuropsychiatric disorders. This Mini-Review provides a comprehensive overview on how stress impacts decision-making processes, particularly under uncertain conditions. Understanding this can prove to be useful for intervention related to impairments to decision-making processes that present in several stress-triggered neuropsychiatric disorders.

Key words: stress; decision making; uncertainty

During the past decades, different fields of knowledge, including psychology, economics, and neurosciences, have focused on the decision-making process, highlighting its broad impact and huge complexity and contributing to the rise of a new area devoted to the study of brain computations implicated in valued decisions (Rangel et al., 2008). Making decisions based on the probability of future events is routine in everyday life; it occurs whenever individuals select an option from several alternatives, each one associated with a specific value. To manage limited resources, living organisms have to make critical decisions that have survival value, which means that being a good decider has selective and evolutionary impact (Kalenscher and van Wingerden, 2011). Conversely, impaired/poor decision making can have catastrophic consequences and constitutes an important feature of several neuropsychiatric disorders, such as schizophrenia, anxiety disorders, substance abuse disorders, obsessive compulsive disorder, and pathological gambling (for review see Ernst and Paulus, 2005).

Decisions are driven by values, subjective attributes tagged to the different options at the beginning of the decision-making process and representing the benefits/gains expected from each. This valuation process and the following decisions are modulated by several variables, including uncertainty, cost and effort, delay, and social modulators, the contribution of which will be briefly reviewed.

Sometimes individuals decide knowing the precise outcomes of each option, but more often they have to bet without an exact knowledge of the consequences (Hsu et al., 2005). "Uncertainty" refers to this lack of knowledge concerning the outcomes of a specific choice (Hsu et al., 2005). Uncertain events can be categorized by the confidence in the probability assignment to each outcome. "Ambiguity" refers to situations in which the outcomes cannot be fully specified and/or their probability is completely unknown, and "risk" refers to situations in which the distribution (or probability) of each possible outcome is (at least partially) known, with a continuum between both extremes. It is believed that the processing of ambiguity and risk is supported by distinct neural mechanisms involving different brain regions (activation within the lateral prefrontal cortex is related to ambiguity, whereas activation of the posterior parietal cortex is predicted by risk preference; Huettel et al., 2006). In contrast, whether value and uncertainty share common neuronal circuits/mechanisms is still an open question.

Uncertainty about an outcome is thought to modulate our choices according to a simple linear model in which its probability weighs the utility of the outcome (the expected-utility model, devised by Bernoulli in

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1738, "p × u"). An individual deviating from the predictions of the model would be risk prone if he or she overvalued p and risk-averse if he or she undervalued it. The expected utility models are useful as frameworks for understanding decision making under uncertainty but are subject to frequent violations across a wide range of common situations (Platt and Huettel, 2008). Uncertainty is the main contributor to these deviations, not only because the probability of outcomes in real life is commonly unknown but also because of limitations in the human capacity to estimate probabilities. These limitations are easily recognized in pathological gamblers and include overvaluation of winning outcomes and undervaluation of losing outcomes, overrepresentation of rare events, overgeneralization based on sparse data, and superstitious beliefs relating to game-controlling outcomes.

Making good decisions implies an estimate not only of the value and the likelihood of each reward but also of the costs and the efforts implied in obtaining it. This valuation integrates the hedonic properties of a stimulus ("liking"), characteristics that remain constant in addition to changes in motivation or devaluation procedures, and the disposition to overcome costs in order to obtain a goal ("wanting"; Kurniawan et al., 2011). Animals (including humans) experience effort as a burden and tend to avoid effortful actions when reward magnitude is kept constant (Kool et al., 2010). Furthermore, to reach a desired goal, animals are ready to expend efforts that encompass an accurate integration of costs and benefits of each action. Disorders of the dopamine system, such as schizophrenia or stimulant addiction, are associated with impairments in effort-based decision making. Whereas schizophrenic patients tend to avoid high-effort options (Fervaha et al., 2013), amphetamine users display enhanced willingness to exert effort, particularly when reward probability is lower (Wardle et al., 2011).

Another relevant factor for decisions that has been extensively studied in recent years is the delay in obtaining the outcome. Along with risk and effort, individuals usually include the time lag involved in obtaining the reward in the decision algorithm. Preference for small rewards delivered immediately over larger rewards delivered after a delay is commonly known as *delay discounting*. Higher rates of delay discounting result in a pattern of impulsive choice and are associated with attention deficit hyperactivity disorder (Barkley et al., 2001), addictive disorders (Kirby and Petry, 2004), and pathological gambling (Madden et al., 2009), disorders in which the ability to delay gratification is significantly impaired.

Decisions are commonly made in social contexts and are frequently subjected to judgment by others; the latter is, particularly in humans, an important modulator of decision-making behaviors. Social interactions may affect decisions in several aspects, including the social learning that has been shown to be crucial for adaptive decision making because it avoids the costs and the risks associated with individual learning (Laland, 2004), the inclusion of the potential benefits of cooperation and the putative costs of competition in the valuation of competing options (West et al., 2007), the tendency to adapt behaviors to match the rest of the group (conformity; Laland, 2004), and the exhibition of coordinated patterns of behaviors by social groups (such as traffic flow in human crowds; Helbing and Molnar, 1995). Some studies have explored neurobiological correlates of social modulation in decision making and contributed to identifying aberrant neural substrates underlying social abnormalities observed in psychiatric disorders, such as frequent withdraw from social interactions in depression and late phases of schizophrenia; incorrect interpretation of social interactions in antisocial personality disorder, borderline personality disorder, and autism; and persistent violation of social norms and elevated levels of aggressive behaviors in antisocial personality disorder (for review see Rilling et al., 2002; van den Bos et al., 2013). Here we review the impact of stress in decisions and its modulators, with a particular focus on the processing of risk and uncertainty.

STRESS

Stress is defined by the physiological response of the organism to any challenging or demanding stimulus (Selye, 1998). Independently of the nature of such stimuli, the stress response is characterized by a neuroendocrine response under control of the hypothalamus. Acutely, there is sympathetic nervous system activation and the consequent release of cathecolamines from the adrenal medulla. This fast-acting but short-lived response is accompanied by an activation of the hypothalamus–pituitary–adrenal (HPA) axis that results in the sequential release of corticotrophin-related factor by the hypothalamus, adrenocorticotropic hormone by the pituitary, and corticosteroids by the adrenal cortex (mainly cortisol in primates and humans and corticosterone in rodents; Sapolsky et al., 1986). The activation of the HPA axis with an increase in cortisol levels is the hallmark of the stress response, particularly in chronic conditions in which the fast catecholaminergic response has long waned. Although the consequences of sympathetic overactivation are observed mainly in the periphery, the glucocorticoids can easily enter the central nervous system and modulate its activity via both mineralocorticoid and glucocorticoid receptors, which are widely present in the brain. The stress response is considered adaptive, contributing to the restoration of homeostasis (de Kloet et al., 2008). However, when the exposure to a stressful stimulus is of sufficient intensity or prolonged in time, it can become deleterious and have a particular impact in the structure and function of the brain (for review see Sousa and Almeida, 2012).

Thus, when analyzing the impact of stress, it is of utmost importance to differentiate acute from chronic stress because these have very distinct and, sometimes, opposite consequences. For example, whereas acute stress (via corticosteroids) might promote memory consolidation, chronic stress impairs memory consolidation and retrieval (Roozendaal, 2002). Thus, in the remainder of this Mini-Review, the impact of chronic and acute stress exposures will be separately presented and discussed.

CHRONIC STRESS AND THE NEURONAL NETWORKS IMPLICATED IN DECISION MAKING

Decision-making processes are mediated by parallel circuits linking the cerebral cortex and the basal ganglia that encode three distinct (and, somehow, conflicting) valuating systems, goal-directed, habit-based, and pavlovian/conditioning systems. These circuits are key targets of chronic stress exposure, mainly but not exclusively through activation of glucocorticoid receptors (Sousa and Almeida, 2012).

The goal-directed system requires top-down processing of numerical and abstract concepts that encompass the consistency of choices and is modulated by variables related to cognition, attention, and expertise. The medial prefrontal cortex (mPFC), in particular the prelimbic region and the dorsomedial striatum (DMS; caudate in humans), is a key components of the corticostriatal circuit regulating goal-directed choice, called the *associative network* (Balleine and O'Doherty, 2010; Fig. 1). The DMS, in particular, is central in this circuit and is crucial for learning and expressing goal-directed behaviors (Yin et al., 2005); it receives inputs directly from association cortices and projects to areas known to participate in action control, such as the substantia nigra pars reticulata and the mediodorsal nucleus of the thalamus. In addition, the DMS is also involved in assigning value to outcomes (Balleine, 2005). In contrast to the DMS, the specific role of the mPFC is less well understood. Although it does not appear to be crucial to goal-directed action (Ostlund and Balleine, 2005), it is involved in updating the assignment of predicted values for each possible outcome (St. Onge and Floresco, 2009), a specific feature of goal-directed behavior. In this regard, the intense dopaminergic projection from the ventral tegmental area (VTA) to the prelimbic cortex is particularly noteworthy (Naneix et al., 2009), given that dopamine-producing cells have been shown to compute the difference between the expected and the actual value of an outcome, often called *reward prediction error* (Cohen et al., 2012). It is noteworthy that the anterior cingulate cortex, another mPFC region, has also been shown to encode the expected value of an outcome, factoring the real magnitude of the reward and its cost (including its risk, its delay, and the effort necessary to retrieve it; Knutson et al., 2005; Kable and Glimcher, 2007; Rushworth and Behrens, 2008); its activation increases as a function of cognitive control demanded by the task (Brown and Braver, 2005). Chronic stress response induces an overall atrophy and hypofunction of this network that correlates with a facilitated shift from goal-directed to habit-based decisions (Dias-Ferreira et al., 2009, for rodents; Soares et al., 2012, for humans). Indeed, chronic stress exposure is known to decrease the overall volume and the size of dendritic trees of neurons in the anterior cingulate cortex and in the prelimbic area of the PFC (Radley et al., 2005; Cerqueira et al., 2007b) and the DMS (Dias-Ferreira et al., 2009; Soares et al., 2012) and to disturb other key functions of these regions, including working memory (Mizoguchi et al., 2000; Cerqueira et al., 2007b) and reversal learning (Cerqueira et al., 2007a). Paradoxically, in rodents, chronic stress exposure has been shown to increase the power of the local field potentials in these regions, particularly at lower frequency bands (Oliveira et al., 2013), together with neuronal spiking frequency, whereas the firing bursts were generally decreased (Lee et al., 2011). Stress also impairs the dopaminergic inputs (mainly from the VTA) to the mPFC (Mizoguchi et al., 2000), which might interfere with the reward prediction error signaling mechanism discussed above. Additionally, other cortical and subcortical areas that play a role in goal-directed decision making, including the ventromedial prefrontal cortex (vmPFC; Cook and Wellman, 2004; Cerqueira et al., 2007a) and the medial orbitofrontal cortex (OFC; Dias-Ferreira et al., 2009), are similarly affected by chronic stress. These two, in particular, constitute the vmPFC that encodes the expected future reward attributable to a chosen action (Gläscher et al., 2009) and are associated with action–outcome but not stimulus–response decisions (Valentin et al., 2007). In contrast, the OFC has been shown to be critically involved in goal-directed behaviors by holding information on relationships between environmental patterns and somatic states induced by those patterns. Interacting reciprocally with the OFC, the basolateral amygdala (BLA) plays an important role in forming representations linking cues to outcome expectancies (Pickens et al., 2003) and promoting the assignment of incentive value to predicted outcome (Balleine and O'Doherty, 2010), a function that seems to be mediated by local opioid receptors (Wassum et al., 2009). The OFC seems to be essential to keep these representations updated and stored in memory (Pickens et al., 2003). Additionally, the BLA, by its known connections with the hypothalamus, seems to be responsible for processing affective and motivational properties of outcomes. The BLA influences the corticostriatal circuit through its direct projections to the prelimbic cortex, DMS, and mediodorsal thalamus and its indirect projections to the ventral striatum via the insular cortex. The stress-induced hypertrophy (Vyas et al., 2002; Pêgo et al., 2008) and increased activation of the BLA (Zhang and Rosenkranz, 2012) could result in increased modulation of the goal-directed circuit, although the specifics of such influence are still to be defined. Finally, the ventral striatum, specifically the core part of the nucleus accumbens, has also been shown to be crucial for instrumental performance, participating in translating motivation into actions (for review see Balleine and O'Doherty, 2010) and also being targeted by chronic stress (Bessa et al., 2013).

With intensive training and repetition, control of actions can be transferred to the habit-based system. Habitual actions involve an ordered, structured action sequence that can be quickly elicited by particular rewards (Graybiel, 2008) and can be neutral, desirable, or undesirable. The sensorimotor network, a circuit that includes

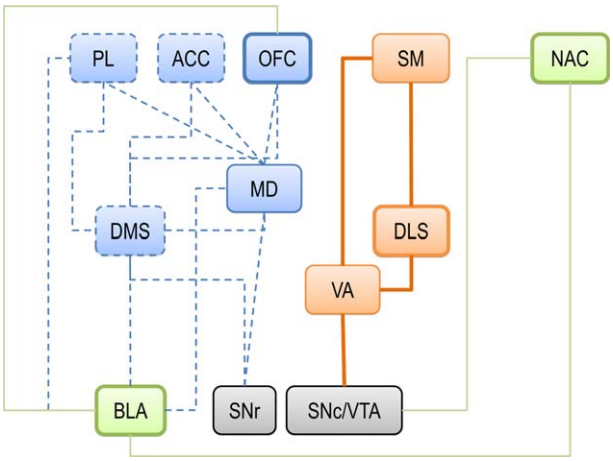

Fig. 1. Schematic representation of chronic stress effects on structures and circuits involved in instrumental and pavlovian conditioning. Chronic stress induces a shift from the associative network (blue), involved in goal-directed behaviors, through the sensorimotor network (orange) responsible for habit-based behaviors. Pavlovian conditioning (green) was also affected by stress. PL, prelimbic cortex; ACC, anterior cingulate cortex; OFC, orbitofrontal cortex; SM, sensorimotor cortex; NAC, nucleus accumbens; BLA, basolateral amygdala; DMS, dorsomedial striatum; DLS, dorsolateral striatum; MD, mediodorsal thalamus; VA, ventral anterior thalamus; SNr, substantia nigra pars reticulate; SNc, substantia nigra pars compacta; VTA, ventral tegmental area. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

the sensorimotor cortex and the dorsolateral striatum (DLS; putamen in humans) as key components, has been shown not only to be implicated in habit formation but also to be affected by stress in both rodents (Dias-Ferreira et al., 2009) and humans (Soares et al., 2012). Indeed, whereas the sensorimotor cortex seems to be resilient to the impact of chronic stress, the DLS and its neurons enlarged upon chronic stress exposure, which correlates with an increased propensity toward habitual behavior (Dias-Ferreira et al., 2009; Soares et al., 2012). This propensity might not depend only on such structural changes, given that after an instance of acute stress human subjects showed a similar potentiation of habitual behavior (Schwabe and Wolf, 2009). It is known that the habitual stimulus–response learning is modulated by dopaminergic projections from the substantia nigra and the VTA into the DLS, encoding the assignment of a specific value for each action and promoting the acquisition of a response to conditioning stimulus by striatal neurons (Aosaki et al., 1994).

With the pavlovian conditioning system, individuals learn to associate a particular cue/stimulus with a reward. This is an innate passive learning procedure, associated with a limited repertoire of actions that include automatic behaviors, such as preparing to eat when approaching a table with food or approaching the reward magazine when an outcome is delivered in a decision-making apparatus (Rangel et al., 2008). The neural basis of the pavlovian system includes responses to stimuli with specific spatial organization in the dorsal periaqueductal gray (Keay et al., 2001) and is encoded in a neural network involving the OFC, ventral striatum, and BLA (Gottfried et al., 2003; Ostlund and Balleine, 2007). As mentioned above, all these regions are impacted by chronic stress exposure, which might explain why chronic stress exposure was recently shown to affect pavlovian-to-instrumental transfer (Morgado et al., 2012b). The OFC stores information on the relationships between environmental cues and somatic states induced by them; thus, it is crucial not only to action–outcome learning but also to stimulus–response conditioning. It seems that lateral and central parts of the OFC, receiving inputs from sensory areas, are involved in pavlovian valuing, whereas medial parts participate in associative learning networks.

From thios it becomes clear that stress, in particular chronic stress, exposure has a major impact on the brain networks involved in decision making. However, similarly to other behaviors, this impact appears to be bidirectional, impairing the functioning of some areas and networks while promoting that of others. Globally, stress favors the sensorimotor network subserving habitual behaviors at the expense of the goal-associative network. To oversimplify, this fact results in more habit-based responses and a general impairment of actions based on goals. More importantly, however, is the impact of stress on the other areas that process the different parameters that modulate decisions, including risk and uncertainty, in which its actions are only starting to be elucidated.

STRESS AND RISKY DECISION MAKING

Exposure to chronic stress has been shown to disrupt several brain functions that are associated with significant impairments in memory (Sousa et al., 1998; Sousa and Almeida, 2012), working memory (Mizoguchi et al., 2000; Cerqueira et al., 2007b), behavioral flexibility (Cerqueira et al., 2007a), anxiety (Pêgo et al., 2006), mood (Bessa et al., 2009), habit formation (Dias-Ferreira et al., 2009), and pavlovian-to-instrumental transfer (Morgado et al., 2012b). Because these functions are crucial for decision making, several studies have been conducted to explore this impact. In a recent review, Starcke and Brand (2012) explored the impact of stress on decisions, specifically those taken by patients suffering from stress-related disorders or under the influence of acutely induced laboratory stress. Stress was found to affect decisions significantly; however, its effects and subsequent decision strategies vary according to type of decision task and type of stressor applied. Additionally, these (almost acute) laboratory situations do not mimic some features of chronic and/or natural stress that humans experience in daily life.

For a number of years, few studies have focused specifically on the impact of stress on risk-based decision making (Table I summarizes some articles on stress and decision making). In contrast to other types, risk-based decisions are not strictly divided into favorable and unfavorable options, allowing other types of calculations based on an individual's proneness to risk and not based merely

TABLE I. Selected Recent Studies on Stress and Decision Making

Original reference	Animal	Age	Task(s)	Reward (punishment)	Type of stressor	Duration of stress	Behavioral effect of stress
Starcke et al., 2008	Human	Adult	Game of Dice Task	Money	Speech anticipation	Acute (20 min)	More risky
Lighthall et al., 2009	Human	Adult	Balloon Analog Risk Task	Money	Cold pressure task	Acute (2 min)	Men: more risky; women: less risky
Dias Ferreira et al., 2009	Rat	Adult	Outcome devaluation and contingency degradation	Sucrose pellets and sucrose solution	Chronic unpredictable stress	Chronic (28 days)	Habit-based behavior
Porcelli and Delgado, 2009	Human	Adult	Financial Decision Making Task	Money	Cold pressure task	Acute (2 min)	Increased reflection effect
Putman et al., 2010	Human	Adult	Decision making task	Money	Cortisol	Acute	More risky
Morgado et al., 2012a	Rat	Adult	Pavlovian instrumental transfer	Sucrose pellets and sucrose solution	Chronic unpredictable stress	Chronic (28 days)	Pavlovian Instrumental Transfer impaired
Soares et al., 2012	Human	Adult	Outcome devaluation and contingency degradation	Food (hungry subjects)	Chronic psychosocial stress	Chronic (months)	Habit-based behavior
Porcelli et al., 2012	Human	Adult	Card guessing task	Money	Cold pressure task	Acute (2 min)	No effects reported
Shafiei et al., 2012	Rat	Adult	Effort discounting	Sucrose pellets	Restraint stress	Acute (20/60 min)	Decrease of high effort choices
Johnson et al., 2012	Human	Adolescent	Balloon Analog Risk Task + Tower of London + Cognitive Reflection Test	Money	Trier Social Stress Test (TSST)	Acute (18 min)	More risk taking
Galvan and McGlennen, 2012	Human	Adolescent	Risky decision making	Money	Daily stress	Acute	More risk choices under stress
Morgado et al., 2012b	Rat	Adult	Risk-based decision-making task	Sucrose pellets	Chronic unpredictable stress	Chronic (28 days)	Less risky
Koot et al., 2013	Rat	Adult	Rat gambling task	Sucrose pellets (quinine pellets)	Corticosterone injection	Acute (3 days)	More risky, less advantageous choices
Pabst et al., 2013a	Human	Adult	Game of Dice Task	Money	Trier Social Stress Test (TSST)	Acute (18 min)	Less risky (5 and 18 min); More risky (28 min after)
Reynolds et al., 2013	Human	Adolescent	Balloon Analog Risk Task	Money	Trier Social Stress Test (TSST)	Acute (18 min)	More risky
Kandasamy et al., 2014	Human	Adults	Lottery Choice Task	Money	Hydrocortisone administration	Chronic (8 days)	Less risky choices (gender differences)

on the ability to perform advantageous choices. Moreover, these reports display great disparity in duration of stress exposure, nature, and/or types of stressors and task design that greatly increases complexity when analyzing the results. The following analyzes the effects of acute and chronic stress on decision making.

Effects of Acute Stress

Acute stress leads to improved performance in decision tasks (Bourne and Yaroush, 2003) that can be correlated with enhanced learning from positive outcomes and decreased learning from negative outcomes (Petzold et al., 2010; Lighthall et al., 2012). However, such a positive effect is dependent on the complexity of the task, the intensity of the stressor, the level of the arousal, and the individual characteristics of the subjects, such as cognitive and technical skills (Bourne and Yaroush, 2003; Lupien et al., 2009).

When decisions have involved some degree of uncertainty, the reported effects of acute stress have been consistent, independent of the experimental paradigm. In general, stressed individuals tend to display increased levels of risk taking or increased rates of risky choices whether outcomes are advantageous (Lighthall et al., 2009) or disadvantageous (van den Bos et al., 2009). This effect was described by Johnson et al. (2012) and Galván and McGlennen (2012) in adolescents subjected to daily stress or to the Trier Social Stress Test, respectively, and also in experiments using the Iowa Gambling Task (Preston et al., 2007) and the Game of Dice Task (Starcke et al., 2008), paradigms in which participants have to choose between large-disadvantageous and small-advantageous options. In the same vein, acute stress has been shown to bias choices for risky options when decisions involve losses rather than gains (Porcelli and Delgado, 2009). These latter effects seem to be mediated by glucocorticoids because, as with stress, animals acutely injected with corticosterone displayed an increased rate of high-risk options in an equivalent rodent task, emphasizing the decreased sensitivity to losses induced by these hormones (Koot et al., 2013).

Despite this consistent pattern of increased risk preference induced by acute stress, effects were observed to be dependent on age, gender, and other individual characteristics. Acute stress was found to exacerbate risk seeking in men and risk aversion in women (Lighthall et al., 2009), a gender effect replicated by van den Bos et al. (2009), who found a stress-induced improvement on performance in females (by using a more conservative pattern of choice) and poorer decisions in males when performing the Iowa Gambling Task. In another human study, Porcelli and Delgado (2009) highlighted the critical relevance of individual characteristics in the evaluation of stress impact on decisions. By using a financial decision-making task, they found that acute stress exacerbates behavioral biases in decision making, showing that people who are generally risk averse tend to play more safely, whereas those who tend to be risk seekers make more risky choices.

Paradoxical effects of acute stress were reported from a study using the Game of Dice Task; risk taking was promoted when the task was performed 28 minutes after stress induction, and risk aversion was favored when the task was performed 5 or 18 minutes after stress (Pabst et al., 2013a). These stress-induced effects seem to be ameliorated if an executive task is performed simultaneously (Pabst et al., 2013b). Despite methodological limitations (small samples and absence of significant differences between stress and controls at two time points), these results illustrate the differential roles of catecholamines and cortisol as mediators of acute stress effects on risky decision making, a research line that has not been adequately addressed.

Humans are intrinsically averse to risk and, even more, to ambiguity. Even when risky options have a positive expected value, subjects preferred to play it more safely (Platt and Huettel, 2008). Therefore, even when decisions are preferably risky, risk taking is likely to be viewed as inappropriate. Several studies have been designed to understand the neurobiological mechanisms that contribute to the occurrence of such misprocessing of risk. For example, individuals with decision-making impairments that lead to increased risk taking displayed high insular activation compared with controls, which is consistent with increased insular activation seen when healthy individuals choose higher-risk outcomes (Paulus et al., 2003). This increased activation might contribute to the natural risk-averse pattern of choice by its putative role in representing somatic states related to potential negative consequences of risk and loss (Damasio, 1996; Paulus et al., 2003). Although data on the impact of chronic stress in insular structure and function are scarce, recent studies have shown that both patients with posttraumatic stress disorder and persons with increased cumulative life adversity display decreased insular volumes (Ansell et al., 2012; Herringa et al., 2012). Moreover, acute stress-induced changes in insular activation correlated with performance in a risky decision-making task (the Balloon Analog Risk Task, see below) and were gender specific, with males showing increased activation and higher reward collection, whereas females showed the opposite pattern (Lighthall et al., 2012). By using neuroimaging tools, a recent study examined the effects of different types of uncertainty on neural processes of decision making; compared with risk, ambiguous conditions produced higher activation of the OFC, amygdala, and dorsomedial prefrontal cortex, whereas the DMS (caudate nucleus) and precuneus cortex were more activated during risk (Hsu et al., 2005). Altogether, these findings provide useful insights on how brain functions are altered under acute stress and on the regions involved in risk-based decision making processes.

Effects of Chronic Stress

Few studies have addressed the impact of chronic and repetitive stress on risk-based decision-making processes. Honk et al. (2003) have established that individuals

with low baseline cortisol levels display higher rates of risk choices in the Iowa Gambling Task. They hypothesized that this disadvantageous behavior was related to insensitivity to losses and increased reward dependence among these individuals. In contrast, Kandasamy et al. (2014) described how administration of hydrocortisone (a corticosteroid) increased risk aversion in a lottery game, an effect whose magnitude is gender dependent. However, this contradiction between the two studies is only apparent. Whereas in the Honk et al. study choice patterns were related to basal cortisol levels, which are a constitutive characteristic of individuals, Kandasamy and colleagues evaluated the impact of cortisol elevation, replicating in a more natural way the impact of chronic stress. Preliminary data from our laboratory demonstrate that a risk-averse pattern of choice is induced by chronic stress in a rodent risk-based decision-making paradigm (Morgado et al., 2012a, 2014), in line with Kandasamy et al.'s observations.

These results might be related to a chronic-stress induced impairment of reward processing in the mPFC. Indeed, in a functional magnetic resonance imaging study, Tom et al. (2007) observed that gains and losses promote changes in similar regions, including the striatum, vmPFC, and anterior cingulate cortex, with putative gains enhancing activation and putative losses decreasing activation. However, decreased activity induced by losses in the striatum and the vmPFC was greater than increased activity induced by similar gains in other regions of interest. Additionally, the same study showed an interesting correlation between behavioral and loss aversion in several regions, such as the ventral striatum and the vmPFC. Because these regions are a key target of chronic stress, which hampers their structure and function (Soares et al., 2012), this suggests a direct link between stress exposure and changes in loss-aversion patterns. In this regard, acute stress was shown to induce reduction in reward-related PFC function (Ossewaarde et al., 2011), whereas a recent study correlated higher levels of perceived stress with blunted mPFC responses to gains and losses (Treadway et al., 2013).

These findings are in accordance with literature that identifies decision impairments in patients suffering from stress-related psychiatric disorders. In obsessive compulsive disorder, for instance, patients consistently displayed a risk-averse pattern of choices while showing significantly elevated levels of blood cortisol and self-reported stress (Morgado et al., 2013). Thus, it can be assumed that impairments observed in decision making could be provoked and/or exacerbated by chronic stress, which points to the reduction of stress and the development of more adaptive coping strategies as putative interventions to ameliorate behavioral alterations associated with that psychiatric condition.

CONCLUSIONS

Making decisions is one of the most complex cognitive processes, involving sequential steps that include analysis of internal and external states, valuation of different options available, and action selection. Because decisions are often made under stress, it becomes critical to know how stress impacts decision making in the context of uncertainty. Acute stress seems to enhance decision biases, mainly increasing risky choices in accordance with personal characteristics such as gender and individual proneness to risk. Less is known about the effects of chronic stress on decision-making processes that involve risk, a field that requires attention because it might open new perspectives of approach to different neuropsychiatric conditions in which these impairments are central.

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REFERENCES

Ansell EB, Rando K, Tuit K, Guarnaccia J, Sinha R. 2012. Cumulative adversity and smaller gray matter volume in medial prefrontal, anterior cingulate, and insula regions. Biol Psychiatry 72:57–64.

Aosaki T, Graybiel AM, Kimura M. 1994. Effect of the nigrostriatal dopamine system on acquired neural responses in the striatum of behaving monkeys. Science 265:412–415.

Balleine BW. 2005. Neural bases of food-seeking: affect, arousal, and reward in corticostriatolimbic circuits. Physiol Behav 86:717–730.

Balleine BW, O'Doherty JP. 2010. Human and rodent homologies in action control: corticostriatal determinants of goal-directed and habitual action. Neuropsychopharmacology 35:48–69.

Barkley RA, Edwards G, Laneri M, Fletcher K, Metevia L. 2001. Executive functioning, temporal discounting, and sense of time in adolescents with attention deficit hyperactivity disorder (ADHD) and oppositional defiant disorder (ODD). J Abnorm Child Psychol 29:541–556.

Bessa JM, Ferreira D, Melo I, Marques F, Cerqueira JJ, Palha Ja, Almeida OFX, Sousa N. 2009. The mood-improving actions of antidepressants do not depend on neurogenesis but are associated with neuronal remodeling. Mol Psychiatry 14:764–773, 739.

Bessa JM, Morais M, Marques F, Pinto L, Palha JA, Almeida OF, Sousa N. 2013. Stress-induced anhedonia is associated with hypertrophy of medium spiny neurons of the nucleus accumbens. Transl Psychiatry 3: e266.

Bourne LE, Yaroush RA. 2003. Stress and cognition: a cognitive psychological perspective. National Aeronautics and Space Administration Grant Number NAG2-1561: outline stress and cognition: a cognitive psychological perspective.

Brown JW, Braver TS. 2005. Learned predictions of error likelihood in the anterior cingulate cortex. Science 307:1118–1121.

Cerqueira JJ, Mailliet F, Almeida OF, Jay TM, Sousa N. 2007a. The prefrontal cortex as a key target of the maladaptive response to stress. J Neurosci 27:2781–2787.

Cerqueira JJ, Taipa R, Uylings HBM, Almeida OF, Sousa N. 2007b. Specific configuration of dendritic degeneration in pyramidal neurons of the medial prefrontal cortex induced by differing corticosteroid regimens. Cereb Cortex 17:1998–2006.

Cohen JY, Haesler S, Vong L, Lowell BB, Uchida N. 2012. Neuron-type-specific signals for reward and punishment in the ventral tegmental area. Nature 482:85–88.

Cook SC, Wellman CL. 2004. Chronic stress alters dendritic morphology in rat medial prefrontal cortex. J Neurobiol 60:236–248.

Damasio AR. 1996. The somatic marker hypothesis and the possible functions of the prefrontal cortex. Philos Trans R Soc Lond B Biol Sci 351:1413–1420.

de Kloet ER, Karst H, Joels M. 2008. Corticosteroid hormones in the central stress response: quick-and-slow. Front Neuroendocrinol 29:268–272.

Dias-Ferreira E, Sousa JC, Melo I, Morgado P, Mesquita AR, Cerqueira JJ, Costa RM, Sousa N. 2009. Chronic stress causes frontostriatal reorganization and affects decision-making. Science 325:621–625.

Ernst M, Paulus MP. 2005. Neurobiology of decision making: a selective review from a neurocognitive and clinical perspective. Biol Psychiatry 58:597–604.

Fervaha G, Foussias G, Agid O, Remington G. 2013. Neural substrates underlying effort computation in schizophrenia. Neurosci Biobehav Rev 37:2649–2665.

Galván A, McGlennen KM. 2012. Daily stress increases risky decision-making in adolescents: a preliminary study. Dev Psychobiol 54:433–440.

Gläscher J, Hampton AN, O'Doherty JP. 2009. Determining a role for ventromedial prefrontal cortex in encoding action-based value signals during reward-related decision making. Cereb Cortex 19:483–495.

Gottfried Ja, O'Doherty J, Dolan RJ. 2003. Encoding predictive reward value in human amygdala and orbitofrontal cortex. Science 301:1104–1107.

Graybiel AM. 2008. Habits, rituals, and the evaluative brain. Annu Rev Neurosci 31:359–387.

Helbing D, Molnar P. 1995. Social force model for pedestrian dynamics. Phys Rev E Stat Phys Plasmas Fluids Rel Interdiscip Topics 51:4282–4286.

Herringa R, Phillips M, Almeida J, Insana S, Germain A. 2012. Posttraumatic stress symptoms correlate with smaller subgenual cingulate, caudate, and insula volumes in unmedicated combat veterans. Psychiatry Res 203:139–145.

Honk JV, Schutter D, Hermans E, Putman P. 2003. Low cortisol levels and the balance between punishment sensitivity and reward dependency. Neuroreport 14:1993–1996.

Hsu M, Bhatt M, Adolphs R, Tranel D, Camerer CF. 2005. Neural systems responding to degrees of uncertainty in human decision-making. Science 310:1680–1683.

Huettel SA, Stowe CJ, Gordon EM, Warner BT, Platt ML. 2006. Neural signatures of economic preferences for risk and ambiguity. Neuron 49:765–775.

Johnson SB, Dariotis JK, Wang C. 2012. Adolescent risk taking under stressed and nonstressed conditions: conservative, calculating, and impulsive types. J Adolesc Health 51:S34–S40.

Kable JW, Glimcher PW. 2007. The neural correlates of subjective value during intertemporal choice. Nat Neurosci 10:1625–1633.

Kalenscher T, van Wingerden M. 2011. Why we should use animals to study economic decision making: a perspective. Front Neurosci 5:82.

Kandasamy N, Hardy B, Page L, Schaffner M, Graggaber J, Powlson AS, Fletcher PC, Gurnell M, Coates J. 2014. Cortisol shifts financial risk preferences. Proc Natl Acad Sci U S A 111:3608–3613.

Keay KA, Clement CI, Depaulis A, Bandler R. 2001. Different representations of inescapable noxious stimuli in the periaqueductal gray and upper cervical spinal cord of freely moving rats. Neurosci Lett 313:17–20.

Kirby KN, Petry NM. 2004. Heroin and cocaine abusers have higher discount rates for delayed rewards than alcoholics or nondrug-using controls. Addiction 99:461–471.

Knutson B, Taylor J, Kaufman M, Peterson R, Glover G. 2005. Distributed neural representation of expected value. J Neurosci 25:4806–4812.

Kool W, McGuire JT, Rosen ZB, Botvinick MM. 2010. Decision making and the avoidance of cognitive demand. J Exp Psychol Gen 139:665–682.

Koot S, Baars A, Hesseling P, van den Bos R, Joëls M. 2013. Time-dependent effects of corticosterone on reward-based decision-making in a rodent model of the Iowa Gambling Task. Neuropharmacology 70:306–315.

Kurniawan IT, Guitart-Masip M, Dolan RJ. 2011. Dopamine and effort-based decision making. Front Neurosci 5:81.

Laland KN. 2004. Social learning strategies. Learn Behav 32:4–14.

Lee YA, Poirier P, Otani S, Goto Y. 2011. Dorsal–ventral distinction of chronic stress-induced electrophysiological alterations in the rat medial prefrontal cortex. Neuroscience 183:108–120.

Lighthall NR, Mather M, Gorlick Ma. 2009. Acute stress increases sex differences in risk seeking in the balloon analogue risk task. PloS One 4:e6002.

Lighthall NR, Sakaki M, Vasunilashorn S, Nga L, Somayajula S, Chen EY, Samii N, Mather M. 2012. Gender differences in reward-related decision processing under stress. Soc Cogn Affect Neurosci 7:476–484.

Lupien SJ, McEwen BS, Gunnar MR, Heim C. 2009. Effects of stress throughout the lifespan on the brain, behaviour, and cognition. Nat Rev Neurosci 10:434–445.

Madden GJ, Petry NM, Johnson PS. 2009. Pathological gamblers discount probabilistic rewards less steeply than matched controls. Exp Clin Psychopharmacol 17:283–290.

Mizoguchi K, Yuzurihara M, Ishige A, Sasaki H, Chui DH, Tabira T. 2000. Chronic stress induces impairment of spatial working memory because of prefrontal dopaminergic dysfunction. J Neurosci 20:1568–1574.

Morgado P, Ribeiro B, Marques F, Sousa N, Cerqueira JJ. 2012a. Stress-induced risk aversion is reverted by a D2/D3 agonist. Program No. 282.04/SS10. 2012 Neuroscience Meeting Planner. New Orleans, LA: Society for Neuroscience.

Morgado P, Silva M, Sousa N, Cerqueira JJ. 2012b. Stress transiently affects pavlovian-to-instrumental transfer. Front Neurosci 6:93.

Morgado P, Freitas D, Bessa JM, Sousa N, Cerqueira JJ. 2013. Perceived stress in obsessive–compulsive disorder is related with obsessive but not compulsive symptoms. Front Psychiatry 4:1–6.

Morgado P, Marques F, Silva MB, Sousa N, Cerqueira JJ. 2014. A novel risk-based decision-making paradigm. Front Behav Neurosci 8:45

Naneix F, Marchand AR, Di Scala G, Pape J-R, Coutureau E. 2009. A role for medial prefrontal dopaminergic innervation in instrumental conditioning. J Neurosci 29:6599–6606.

Oliveira JF, Dias NS, Correia M, Gama-Pereira F, Sardinha VM, Lima A, Oliveira AF, Jacinto LR, Ferreira DS, Silva AM, Reis JS, Cerqueira JJ, Sousa N. 2013. Chronic stress disrupts neural coherence between corticolimbic structures. Front Neural Circuits 7:10.

Ossewaarde L, Qin S, Van Marle HJF, van Wingen Ga, Fernández G, Hermans EJ. 2011. Stress-induced reduction in reward-related prefrontal cortex function. Neuroimage 55:345–352.

Ostlund SB, Balleine BW. 2005. Lesions of medial prefrontal cortex disrupt the acquisition but not the expression of goal-directed learning. J Neurosci 25:7763–7770.

Ostlund SB, Balleine B. 2007. Orbitofrontal cortex mediates outcome encoding in Pavlovian but not instrumental conditioning. J Neurosci 27:4819–4825.

Pabst S, Brand M, Wolf OT. 2013a. Stress and decision making: a few minutes make all the difference. Behav Brain Res 250:39–45.

Pabst S, Brand M, Wolf OT. 2013b. Stress effects on framed decisions: there are differences for gains and losses. Front Behav Neurosci 7:142.

Paulus MP, Rogalsky C, Simmons A, Feinstein JS, Stein MB. 2003. Increased activation in the right insula during risk-taking decision making is related to harm avoidance and neuroticism. Neuroimage 19:1439–1448.

Pêgo JM, Morgado P, Cerqueira JJ, Almeida OF, Sousa N. 2006. Mismatch between anxiety status and morphometric parameters in the amygdala and bed nucleus of the stria terminalis. Behav Brain Res 173:320–325.

Pêgo JM, Morgado P, Pinto LG, Cerqueira JJ, Almeida OF, Sousa N. 2008. Dissociation of the morphological correlates of stress-induced anxiety and fear. Eur J Neurosci 27:1503–1516.

Petzold A, Plessow F, Goschke T, Kirschbaum C. 2010. Stress reduces use of negative feedback in a feedback-based learning task. Behav Neurosci 124:248–255.

Pickens CL, Saddoris MP, Setlow B, Gallagher M, Holland PC, Schoenbaum G. 2003. Different roles for orbitofrontal cortex and basolateral amygdala in a reinforcer devaluation task. J Neurosci 23:11078–11084.

Platt ML, Huettel Sa. 2008. Risky business: the neuroeconomics of decision making under uncertainty. Nat Neurosci 11:398–403.

Porcelli AJ, Delgado MR. 2009. Acute stress modulates risk taking in financial decision making. Psychol Sci 20:278–283.

Porcelli AJ, Lewis AH, Delgado MR. 2012. Acute stress influences neural circuits of reward processing. Frontiers in neuroscience 6:157.

Putman P, Antypa N, Crysovergi P, van der Does WaJ. 2010. Exogenous cortisol acutely influences motivated decision making in healthy young men. Psychopharmacology 208:257–263.

Preston SD, Buchanan TW, Stansfield RB, Bechara A. 2007. Effects of anticipatory stress on decision making in a gambling task. Behav Neurosci 121:257–263.

Radley JJ, Rocher AB, Janssen WG, Hof PR, McEwen BS, Morrison JH. 2005. Reversibility of apical dendritic retraction in the rat medial prefrontal cortex following repeated stress. Exp Neurol 196: 199–203.

Rangel A, Camerer C, Montague PR. 2008. A framework for studying the neurobiology of value-based decision making. Nat Rev Neurosci 9: 545–556.

Reynolds EK, Schreiber WM, Geisel K, MacPherson L, Ernst M, Lejuez CW. 2013. Influence of social stress on risk-taking behavior in adolescents. Journal of anxiety disorders 27:272–277.

Rilling J, Gutman D, Zeh T, Pagnoni G, Berns G, Kilts C. 2002. A neural basis for social cooperation. Neuron 35:395–405.

Roozendaal B. 2002. Stress and memory: opposing effects of glucocorticoids on memory consolidation and memory retrieval. Neurobiol Learn Mem 78:578–595.

Rushworth MF, Behrens TE. 2008. Choice, uncertainty, and value in prefrontal and cingulate cortex. Nat Neurosci 11:389–397.

Sapolsky RM, Krey LC, McEwen BS. 1986. The neuroendocrinology of stress and aging: the glucocorticoid cascade hypothesis. Endocr Rev 7: 284–301.

Schwabe L, Wolf OT. 2009. Stress prompts habit behavior in humans. J Neurosci 29:7191–7198.

Selye H. 1998. A syndrome produced by diverse nocuous agents. 1936. J Neuropsychiatry Clin Neurosci 10:230–231.

Shafiei N, Gray M, Viau V, Floresco SB. 2012. Acute Stress Induces Selective Alterations in Cost/Benefit Decision-Making. Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology 37:1–16.

Soares JM, Sampaio A, Ferreira LM, Santos NC, Marques F, Palha JA, Cerqueira JJ, Sousa N. 2012. Stress-induced changes in human decision-making are reversible. Transl Psychiatry 2:e131.

Sousa N, Almeida OF. 2012. Disconnection and reconnection: the morphological basis of (mal)adaptation to stress. Trends Neurosci:1–10.

Sousa N, Almeida OF, Holsboer F, Paula-Barbosa MM, Madeira MD. 1998. Maintenance of hippocampal cell numbers in young and aged rats submitted to chronic unpredictable stress. Comparison with the effects of corticosterone treatment. Stress 2:237–249.

St. Onge JR, Floresco SB. 2009. Dopaminergic modulation of risk-based decision making. Neuropsychopharmacology 34:681–697.

Starcke K, Brand M. 2012. Decision making under stress: a selective review. Neurosci Biobehav Rev 36:1228–1248.

Starcke K, Wolf OT, Markowitsch HJ, Brand M. 2008. Anticipatory stress influences decision making under explicit risk conditions. Behav Neurosci 122:1352–1360.

Tom SM, Fox CR, Trepel C, Poldrack RA. 2007. The neural basis of loss aversion in decision-making under risk. Science 315:515–518.

Treadway MT, Buckholtz JW, Zald DH. 2013. Perceived stress predicts altered reward and loss feedback processing in medial prefrontal cortex. Front Hum Neurosci 7:180.

Valentin VV, Dickinson A, O'Doherty JP. 2007. Determining the neural substrates of goal-directed learning in the human brain. J Neurosci 27: 4019–4026.

van den Bos R, Harteveld M, Stoop H. 2009. Stress and decision-making in humans: performance is related to cortisol reactivity, albeit differently in men and women. Psychoneuroendocrinology 34:1449–1458.

van den Bos R, Jolles JW, Homberg JR. 2013. Social modulation of decision-making: a cross-species review. Front Hum Neurosci 7:301.

Vyas A, Mitra R, Shankaranarayana Rao BS, Chattarji S. 2002. Chronic stress induces contrasting patterns of dendritic remodeling in hippocampal and amygdaloid neurons. J Neurosci 22:6810–6818.

Wardle MC, Treadway MT, Mayo LM, Zald DH, de Wit H. 2011. Amping up effort: effects of d-amphetamine on human effort-based decision-making. J Neurosci 31:16597–16602.

Wassum KM, Ostlund SB, Maidment NT, Balleine BW. 2009. Distinct opioid circuits determine the palatability and the desirability of rewarding events. Proc Natl Acad Sci U S A 106:12512–12517.

West SA, Griffin AS, Gardner A. 2007. Evolutionary explanations for cooperation. Curr Biol 17:R661–R672.

Yin HH, Ostlund SB, Knowlton BJ, Balleine BW. 2005. The role of the dorsomedial striatum in instrumental conditioning. Eur J Neurosci 22: 513–523.

Zhang W, Rosenkranz JA. 2012. Repeated restraint stress increases basolateral amygdala neuronal activity in an age-dependent manner. Neuroscience 226:459–474.