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DORSOMEDIAL STRIATUM LESIONS AFFECT ADJUSTMENT TO REWARD UNCERTAINTY, BUT NOT TO REWARD DEVALUATION OR OMISSION

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Abstract—The dorsomedial striatum (DMS) has been implicated in the acquisition of reward representations, a proposal leading to the hypothesis that it should play a role in situations involving reward loss. We report the results of an experiment in which the effects of DMS excitotoxic lesions were tested in consummatory successive negative contrast (reward devaluation), autoshaping training with partial vs. continuous reinforcement (reward uncertainty), and appetitive extinction (reward omission). Animals with DMS lesions exhibited reduced lever pressing responding, but enhanced goal entries, during partial reinforcement training in autoshaping. However, they showed normal negative contrast, acquisition under continuous reinforcement (CR), appetitive extinction, and response facilitation in early extinction trials. Open-field testing also indicated normal motor behavior. Thus, DMS lesions selectively affected the behavioral adjustment to a situation involving reward uncertainty, producing a behavioral reorganization according to which goal tracking (goal entries) became predominant at the expense of sign tracking (lever pressing). This pattern of results shows that the function of the DMS in situations involving reward loss is not general, but restricted to reward uncertainty. We suggest that a nonassociative, drive-related process induced by reward uncertainty requires normal output from DMS neurons.

Key words: reward devaluation, reward omission, reward uncertainty, successive negative contrast, partial reinforcement, extinction spike.

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Abbreviations: CR, continuous reinforcement; cSNC, consummatory successive negative contrast; DLS, dorsolateral striatum; DMS, dorsomedial striatum; ERK, extracellular signal-related kinase; PBS, phosphate buffered saline; pCREB, phosphorylated cyclic adenosine monophosphate response element-binding protein; PR, partial reinforcement; PRAE, partial reinforcement acquisition effect; PREE, partial reinforcement extinction effect.

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INTRODUCTION

There are theoretical and empirical reasons to think that the adjustment to situations involving reward devaluation (e.g., successive negative contrast), reward uncertainty (e.g., partial reinforcement), and reward omission (e.g., appetitive extinction) share a common set of mechanisms (Daly and Daly, 1982; Amsel, 1992; Flaherty, 1996; Gray and McNaughton, 2000; Papini, 2014; Papini et al., 2015; Anselme, 2015, 2016). Amsel's (1992) behavioral theory, for example, suggests that the devaluation or omission of an otherwise expected reward unconditionally induces an aversive emotional state (called primary frustration), which can then be associatively reactivated by the presentation of stimuli that were present at the time of the loss event (called secondary frustration). In the consummatory successive negative contrast (cSNC) situation, devaluation from a large to a small reward (e.g., 32% to 4% sucrose) is accompanied by the release of stress hormones (Mitchell and Flaherty, 1998; Pecoraro et al., 2009), influenced by anxiolytic (Flaherty et al., 1986; Kamenetzky et al., 2008; Ortega et al., 2014a) and opioid treatments (Pellegrini et al., 2005; Wood et al., 2005, 2008), followed by preference for substances with addictive potential (Manzo et al., 2015a,b), modulated by genetic influences (Torres and Sabariego, 2014), dependent on the integrity of brain structures involved in emotion (Ortega et al., 2011; Kawasaki et al., 2015), and affected by the post-training administration of memory enhancing drugs (Bentosela et al., 2006; Ruetti et al., 2009; Norris et al., 2011). Many of these features are also present in appetitive extinction and reward uncertainty situations based on instrumental training procedures (Feldon and Gray, 1981; Coe et al., 1983; Kawasaki and Iwasaki, 1997; Thomas and Papini, 2001; Rosas et al., 2007; Gómez et al., 2008, 2009; Shaw et al., 2009; Cuenya et al., 2012; Manzo et al., 2014, 2015a,b). Thus, reward loss (herein denoting reward devaluation, uncertainty, and omission) involves emotional activation and the development of aversive emotional memories (Papini and Dudley, 1997; Papini, 2003; Papini et al., 2015). However, these neurobehavioral factors are usually studied separately in various reward-loss situations.

The goal of the present experiment was to determine the role of the dorsomedial striatum (DMS) in reward

devaluation, uncertainty, and omission in the same animals (see Glossary for task descriptions). A similar design to that employed here was used before in two other studies. Ortega et al. (2013) trained animals with lesions of orbital or medial prefrontal cortex in a cSNC task followed by an autoshaping task involving either continuous or partial reinforcement (CR, PR). In that study, lesions of the orbital cortex attenuated cSNC and also eliminated the enhancement of autoshaped lever pressing responding during PR training, relative to CR training (the partial reinforcement acquisition effect, PRAE). Unlike in this case, lesions of the medial prefrontal cortex affected neither task. Similarly, Ortega et al. (2014b) reported that after six generations, animals selectively bred for fast recovery from a 32-to-4% sucrose downshift exhibited a reduced cSNC effect; however, no change was observed in a line of animals selected for slow recovery or in a randomly paired control line. Interestingly, fast recovery animals also displayed no evidence of the PRAE or of the PREE (i.e., partial reinforcement extinction effect, i.e., increased persistence of lever pressing during extinction after PR training; Boughner and Papini, 2006). None of these correlated effects were observed in either slow-recovery or randomly selected animals. In both cases the authors (Ortega et al., 2013; Ortega et al., 2014b) concluded that the attenuation of the cSNC and PRAE/PREE was consistent with a common neural mechanism activated by exposure to episodes involving reward loss, whether in terms of devaluation, omission, or uncertainty.

Here we sought to extend this approach to lesions of the DMS. The DMS was selected based on four sources of evidence. First, the DMS has been shown to be critical in reward devaluation situations. For example, DMS expression levels of phosphorylated cyclic adenosine monophosphate response element-binding protein (pCREB, a marker of synaptic plasticity) were higher after the first devaluation session than after the second devaluation in the cSNC situation (Glueck et al., 2015). Comparable results were obtained with the extracellular signal-related kinase (ERK, also a marker for cellular plasticity). Shiflett et al. (2010) reported that infusion of the ERK inhibitor U0126 into the posterior region of the DMS abolished the reduction in instrumental behavior induced by reward devaluation based on presession feeding. These data suggest a role of the DMS in situations involving reward devaluation.

Second, using instrumental training procedures and the presession feeding devaluation technique, Yin et al. (2005) reported that lesions of the posterior DMS after limited amounts of training abolished the reward-devaluation effect. Interestingly, similar lesions in the dorsolateral striatum (DLS) induced the reward-devaluation effect after extensive training, an effect absent in sham animals (Yin et al., 2004). These results provide support for the hypothesis that different sections of the dorsal striatum (DMS, DLS) are involved in the transition from the acquisition of instrumental actions to the performance of instrumental habits (Gasbarri et al., 2014; Hart et al., 2014).

Third, the DMS has been implicated in decision making, specifically involving choice behavior under risky/uncertain conditions in humans (e.g., Brevers et al., 2015), and choice after serial discrimination reversals in rats (Castañé et al., 2010). Paradoxically, DMS lesions did not impair extinction performance assessed after the last reversal, despite disrupting reversal performance as noted above (Castañé et al., 2010). Tasks such as serial discrimination reversals not only involve reward uncertainty, but they require a choice between competing alternatives and a degree of behavioral flexibility that may promote learning-set formation (Bushnell and Stanton, 1991; Ragozzino, 2007; Floresco et al., 2009).

Fourth, although the involvement of the DMS in reward-loss situations is largely unknown, its afferent-efferent connections (Voorn et al., 2004; Striedter, 2016) point to structures known to regulate actions triggered by worse-than-expected outcomes. Evidence from structures that send inputs to the DMS, whether directly or indirectly (mediated by ventral striatum and thalamus), include the prelimbic cortex, which expresses pCREB during cSNC (Glueck et al., 2015), the orbitofrontal cortex, whose lesion attenuates the cSNC effect (Ortega et al., 2013), the anterior cingulate cortex, whose lesion prolongs the cSNC effect (Ortega et al., 2011), the amygdala, whose reversible inactivation attenuates the cSNC effect (Kawasaki et al., 2015), and the nucleus accumbens, whose neurons show reduced dopamine release during reward devaluation and omission (Genn et al., 2004; Biesdorf et al., 2015). Outputs from the dorsal striatum also reach the lateral habenula, which inhibits dopaminergic neurons of the mesostriatal reward pathway (Christoph et al., 1986) and whose lesion retards extinction of lever pressing after sucrose reinforcement (Friedman et al., 2011). Altogether, these sources of evidence pointed to a key role of the DMS in situations involving reward loss such as those studied in the present experiment.

The approach implemented here was to compare the effects of DMS lesions in three tasks administered in succession: cSNC, PR vs. CR training, and appetitive extinction, the last two based on autoshaping training. The cSNC task evaluated the role of the DMS in reward devaluation in a consummatory response situation (i.e., licking for sucrose). We assessed reward uncertainty in terms of the PRAE (PR vs. CR during acquisition) and PREE (PR vs. CR in extinction) using the autoshaping situation. The transition from acquisition to extinction provided two sources of evidence on the role of the DMS on reward omission: the extinction spike and extinction rate. The extinction spike (or burst) refers to a tendency in the autoshaping preparation for lever pressing to increase early in extinction relative to the terminal acquisition level of responding (Thomas and Papini, 2001). The extinction spike has not been reported after PR training in acquisition. Appetitive extinction after CR training was used to evaluate the effects of DMS lesions on reward omission. Serial reversal learning and similar tasks including risky/uncertain reward conditions involve choice between alternatives as well as shifts in