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Dose-dependent dissociable effects of haloperidol on locomotion, appetitive responses, and consummatory behavior in water-deprived rats

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ABSTRACT

We studied whether a cascade of different phases of ingestive behavior were governed by different doses of the dopamine D2 receptor system. A wide spectrum of doses (0, 0.025, 0.05, 0.1, 0.2, and 0.4 mg/kg) of a D2 receptor antagonist, haloperidol, were administered to 6 groups of water-deprived rats. 45 min following administration of the drug a 15 min water intake session was allowed to assess the effect on (a) locomotion, (b) appetitive response and (c) consummatory responses. The procedure was repeated for 5 days. Results: The doses of 0.025 to 0.1 mg/kg had no effects on any measured behavior compared with the control group. The 0.2 mg/kg dose induced catalepsy during sessions 3 and 5 and impaired consummatory (decreased lick numbers and intake volume) behaviors during sessions 1–5. The 0.4 mg/kg dose affected appetitive behavior (increased latency to contact the water tube) during session 2 and consummatory behavior during all five water sessions. The 0.2 mg/kg dose appeared to dissociate appetitive and consummatory behavior, and the 0.4 mg/kg dose locomotor activity and motivational behavior (including consummatory and appetitive responses). These results, that the three elements of ingestive behavior (locomotion, appetitive responses, and consummatory behavior) have different sensitivity to haloperidol, suggest that separable D2 mechanisms are involved in governing the ingestive behavior.

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1. Introduction

The dopamine D_2 receptor subtype is broadly distributed throughout the brain and is highly expressed in the neostriatum, olfactory bulb, substantia nigra, nucleus accumbens, and prefrontal and entorhinal cortices (Levey et al., 1993; Weiner et al., 1991). D_2 receptor systems in the brain may play a crucial role in a wide range of functions, including cognition (Nordstrom et al., 1993; Swerdlow et al., 1994; Von Huben et al., 2006), locomotor activity (Fowler and Liou, 1994; Fowler and Wang, 1998; Stuchlik et al., 2007), and reinforcement behaviors (Beninger et al., 1987; Di Chiara et al., 2004; Hoffman and Beninger, 1989; Nakajima, 1989; Smith et al., 1997; Wise, 2005; Wolterink et al., 1993).

According to White (1989), "reinforcement refers to the tendency of certain stimuli to strengthen learned stimulus-response tendencies" (p. 181). Thus, reinforcement connects certain environmental stimuli (e.g., light) with responses (e.g., running speed). Subsequently, the presence of this stimulus elicits approach or appetitive behavior (Salamone and Correa, 2002). Elimination of reinforcers would then attenuate this appetitive response (i.e., extinction). Craig (1917) stated that "when the appeted stimulus is at length received it releases a consummatory reaction, after which the appetitive behavior ceases and is succeeded by a state of relative rest, a state of satisfaction" (p. 685). Thus, a chain of behaviors (such as orienting and running) can serve as appetitive behavior that occurs prior to consummatory behavior (e.g., eating food). The appetitive behavior is removable from the consummatory behavior and may involve the reinforcing process (Berridge and Robinson, 1998; Wolgin et al., 1988). The appetitive response is induced by the reinforcement, but the consummatory behavior is not; however, whether the appetitive response and the consummatory behavior are both governed by D_2 receptor system remains to be further clarified.

The functions of brain D_2 receptors on locomotor activity, appetitive responses, and consummatory behavior are controversial (Fouriezos and Wise, 1976; Gallistel and Davis, 1983; Horvitz and Ettenberg, 1988; Wise, 1978). One viewpoint is that D_2 receptors mediate appetitive, conditioned behaviors and locomotor activity but not consummatory behavior. The D_2 receptor has been shown to regulate conditioned operant eating responses (Rolls et al., 1974) and operant drinking behavior (Ljungberg, 1990) but not the unconditioned consummatory acts of eating and drinking (Fibiger et al., 1976; Ljungberg, 1987). Moreover, studies using D_2 receptor knockout mice (Fowler et al., 2002) or antagonist treatment (Fowler, 1999) show

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that conditioned appetitive responses are blunted (Adams et al., 2001). Additionally, D_1 or D_2 antagonist injections into the nucleus accumbens (Salamone et al., 1991) or intraperitoneal injections of dopamine blockers (Cousins et al., 1994; Salamone et al., 1996) have been shown to impair lever pressing for food, but food intake remains intact. Lesions of dopamine neurons with neurotoxin 6-hydoxydopamine at the ventrolateral striatum elicits motor deficits without influencing food consumption. Furthermore, a neurotoxic lesion at the nucleus accumbens decreases instrumental lever pressing for food but does not affect consummatory responses (Cousins et al., 1993). Blockade of D_1 or D_2 receptors within the nucleus accumbens shell or core with specific doses of dopamine antagonists suppresses spontaneous locomotor activity without impairing food consumption (Baldo et al., 2002). However, few studies have shown that D_2 receptor antagonism attenuates the likelihood of behavioral responses (i.e., consummatory behavior) without affecting the latency to emit a learned response (i.e., appetitive responses; Horvitz and Eyny, 2000). D_2 receptors in the brainstem modulate the suppression of consummatory behavior, whereas D_2 receptors in the shell of the nucleus accumbens do not appear to mediate the appetitive intake response (Sederholm et al., 2002).

Finally, D_2 receptors have been demonstrated to control all functions related to locomotor activity, appetitive responses, and consummatory behavior. For example, Fowler and colleagues reported that low doses of haloperidol induce forelimb tremor (Fowler et al., 1990) and block tongue extension during licking behavior in rats (Fowler and Mortell, 1992). These authors also administered D_1 and D_2 antagonists to disrupt microcatalepsy and forelimb responses (Fowler and Liou, 1994) and injected various D_2 antagonists to elicit catalepsy (an active immobility phenomenon; Fowler and Liou, 1998) and parkinsonism-like symptoms (Fowler and Wang, 1998). Clifton (2000) demonstrated that 0.05–0.2 mg/kg haloperidol increases meal size but decreases the rate of feeding. These authors also related these findings to extrapyramidal side effects observed in humans taking neuroleptic drugs (Lee and Clifton, 2002) and suggested that D_2 receptor system mediates both appetitive and consummatory behavior. Whether the dopamine system controls appetitive, consummatory, and simple motor responses needs further clarification.

The present study used a wide spectrum of doses of the D_2 antagonist haloperidol to study whether the effects of haloperidol on reinforcement-seeking behaviors (including appetitive and consummatory responses) and locomotive activity could be dissociated.

2. Methods

2.1. Subjects

Sixty male Sprague–Dawley rats (weighing 200–260 g at the beginning of the experiment) were purchased from BioLASCO Taiwan Co., Ltd. Rats were housed at a constant temperature (20 ± 2 °C) with food available *ad libitum*. All subjects were group-housed, two per cage, in a colony room with a 12 h/12 h light/dark cycle (lights on 08:00–20:00). All experiments were carried out in compliance with the Animal Scientific Procedures Act of 1986 and received local ethics committee approval. All efforts were made to minimize animal suffering and to use a minimal number of animals.

2.2. Apparatus

Licking behavior during the test session was measured by a Lickometer, which consisted of a wire-mesh cage, a white panel, and a 25 ml burette with 0.1 ml graduations. The panel was mounted in front of the wire-mesh cage and connected to a burette. When the rat's tongue contacted the burette, the circuit was closed. A 0.01 mA current passed through the circuit without influencing the licking response. Simultaneously, the electrical signal was detected by a computer program (Pico Soft Technology Co. Ltd., Cambridgeshire, UK) to time each lick to the nearest 1 ms. Total intake for each session was deduced by measuring the final volume remaining in the burette. When the rat's tongue initially contacted the licking tube, the Lickometer recorded the time. Thus, three indices of licking behavior were analyzed: intake volume, the number of licks, and the latency to first lick the drinking tube.

2.3. Procedure

Rats were water-deprived for 23.5 h per day and given 30 min water access at about 16:00 throughout the experiment, with the exception of some specific water treatments. At the beginning of this experiment, all rats were adapted to a water-deprivation regimen in which they were given access to water for 15 min in the morning for each of 2 consecutive days. Animals were then tested for an additional 5 days as described below. Rats were randomly assigned to one of six groups ($n = 10$ per group) and given 0, 0.025, 0.05, 0.1, 0.2, or 0.4 mg/kg (i.p.) haloperidol (2% w/v) in tartaric acid solution (pH 3.5–4) 45 min prior to a 15 min water intake session over 5 consecutive days in the morning. All treatments were administered in a volume of 1 ml/kg. All chemical compounds were purchased from Sigma (St. Louis, MO).

2.4. Statistical analysis

Mean latency was calculated from the rat's first contact with the licking tube and was based on the methods of assessment proposed by Horvitz and Eyny (2000) to define the mean latency time as an appetitive response. The number of licks and intake volume during the 15 min sessions were considered consummatory behaviors (Ljungberg, 1987; Silvestre et al., 1996). Additionally, almost all of the rats in the 0.4 mg/kg group and some of the rats in the 0.2 mg/kg group exhibited immobility; therefore, these data served as cataleptic responses (Fowler and Liou, 1998).

Appetitive responses and the two consummatory behaviors were analyzed by a mixed 2 × 5 two-way repeated-measures analysis of variance (ANOVA), with dose and session as factors for each experimental group (0.025, 0.05, 0.1, 0.2, and 0.4 mg/kg haloperidol) compared with the 0 mg/kg dose. When appropriate, *post hoc* tests were conducted using Tukey's Honestly Significant Difference (HSD) test. A p value less than 0.05 was considered significant in all comparisons. The numbers of cataleptic rats and haloperidol doses were analyzed using Spearman correlation.

3. Results

Table 1 shows the effects of haloperidol on locomotor activity during five water access sessions. The doses of haloperidol were positively correlated with catalepsy ($r = 0.85$, $p < 0.05$). Catalepsy in the 0.2 and 0.4 mg/kg haloperidol groups was observed in 30% and

Table 1
Effects of haloperidol on locomotor activity over five water access sessions.

Haloperidol dose (mg/kg)	Catalepsy		Non-catalepsy	
	Number of rats	%	Number of rats	%
0	0	0	10	100
0.025	0	0	10	100
0.05	0	0	10	100
0.1	0	0	10	100
0.2	3	30	7	70
0.4	7	70	3	30

Spearman correlation = 0.85, $p < 0.05$*.
Note that catalepsy indicates active immobility during the water access sessions.

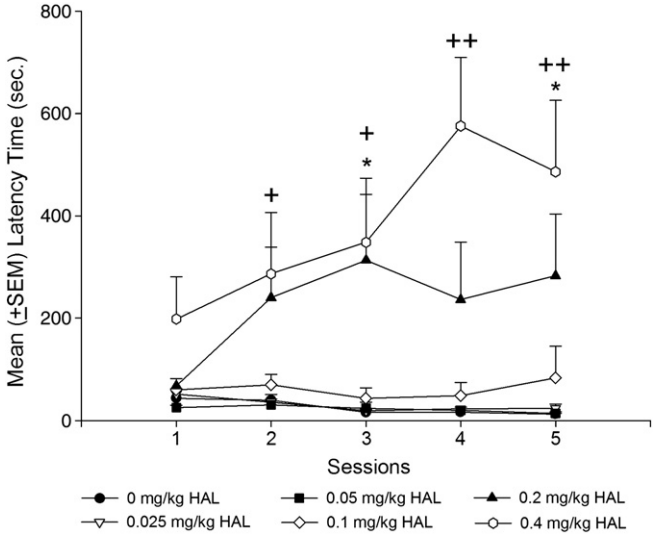

Fig. 1. Effects of various doses (0, 0.025, 0.05, 0.1, 0.2, and 0.4 mg/kg) of haloperidol on the mean latency to first contact the licking tube. Studies were conducted in water-deprived rats over five consecutive daily sessions. Data are expressed as the group mean latency (±SEM) ($n=10$ per group). $^{*}p<0.05$, significant difference between 0.2 mg/kg haloperidol and control (0 mg/kg haloperidol) groups. $^{+}p<0.05$, $^{++}p<0.01$, significant difference between 0.4 mg/kg haloperidol and control (0 mg/kg haloperidol) groups. HAL, haloperidol.

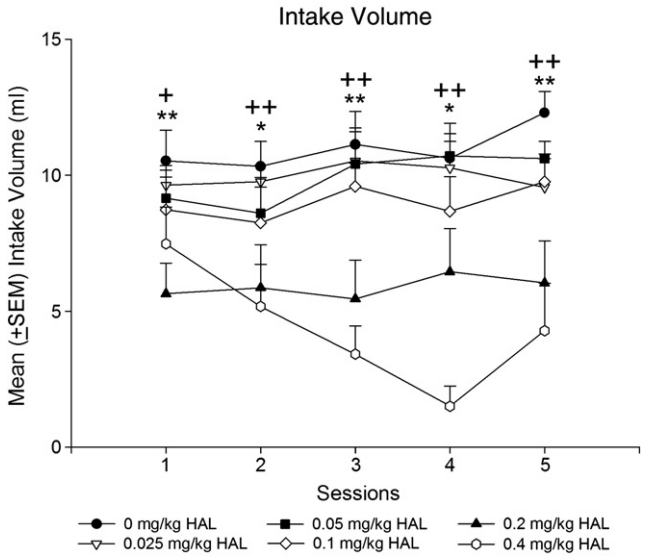

Fig. 2. Effect of various doses (0, 0.025, 0.05, 0.1, 0.2, and 0.4 mg/kg) of haloperidol on water intake (volume) in water-deprived rats over five consecutive daily 15 min sessions. Data are expressed as mean intake volume (±SEM) ($n=10$ per group). $^{*}p<0.05$, $^{**}p<0.01$, significant difference between 0.2 mg/kg haloperidol and control (0 mg/kg haloperidol) groups. $^{+}p<0.05$, $^{++}p<0.01$, significant difference between 0.4 mg/kg haloperidol and control (0 mg/kg haloperidol) groups. HAL, haloperidol.

70% of subjects, respectively. The 0–0.1 mg/kg haloperidol doses induced catalepsy in 0% of subjects, suggesting that the higher doses of haloperidol resulted in greater inhibition of locomotion (i.e., cataleptic effect). Thus, haloperidol doses need to be greater than 0.2 mg/kg to induce immobility (Table 1).

Appetitive responding was assessed by the latency to first contact to the licking tube (Fig. 1). A 2×5 ANOVA with repeated sessions was used to asses the effect of each dose of haloperidol compared with the 0 mg/kg dose. For 0.025 dose the main effect is not significant ($F_{1,18}=0.44$, $p>0.05$). The effect was not significant for 0.05 mg/kg ($F_{1,18}=0.12$, $p>0.05$), and 0.1 mg/kg ($F_{1,18}=1.76$, $p>0.05$). Significant effects were observed with 0.2 mg/kg ($F_{1,18}=6.51$, $p<0.05$) and 0.4 mg/kg ($F_{1,18}=24.35$, $p<0.01$). However, a significant main effect of session was observed in the 0.025 mg/kg and 0.05 mg/kg groups compared with the control group ($p<0.05$), but no main effect of session was found in the 0.1–0.4 mg/kg groups compared with the control group ($p>0.05$). No dose × session interaction was found for any dose compared with the control group ($p>0.05$). *Post hoc* analysis over the five sessions revealed that the significant dose effects were entirely attributable to the differences observed in the 0.2 and 0.4 mg/kg groups. Using Tukey's HSD test, the significant effect observed in controls and the 0.2 mg/kg group was found during sessions 3 and 5 ($p<0.05$). Moreover, significant effects of 0.4 mg/kg were found from session 2 to session 5. Thus, significant differences in latency were found between the 0.2 mg/kg and 0.4 mg/kg groups. The 0.4 mg/kg dose exerted the strongest effect on latency compared with the other haloperidol doses (Fig. 1).

Consummatory behavior was evaluated using the following behavioral indices: intake volume and the number of licks. Water intake and licking behavior in each group are summarized in Figs. 2 and 3, respectively. The average intake volume during the entire test session is shown in Fig. 2. A 2×5 repeated-measures ANOVA revealed a significant main effect of 0.2 mg/kg ($F_{1,18}=6.51$, $p<0.05$) and 0.4 mg/kg ($F_{1,18}=24.35$, $p<0.01$). However, no significant main effects of 0.025–0.1 mg/kg were observed ($p>0.05$). A significant main effect of session was found with doses of 0.025 mg/kg ($F_{4,72}=6.88$, $p<0.01$) and 0.05 mg/kg ($F_{4,72}=3.66$, $p<0.01$), but the other doses (0.05–0.4 mg/kg) did not have significant effects compared with the control group ($p>0.05$). Additionally, no significant dose × session interaction was observed with any of the doses ($p>0.05$). Tukey's HSD *post hoc* test indicated significant differences between the 0 mg/kg and 0.2 mg/kg groups during sessions 1–5 ($p<0.05$). *Post hoc* tests also indicated that the 0.4 mg/kg dose was significantly different from the 0 mg/kg dose over each of the five sessions ($p<0.05$). Therefore, the main effect of dose may have been attributable to significant differences between the control group and the 0.2 mg/kg and 0.4 mg/kg groups. The 0–0.1 mg/kg doses did not affect intake volume (Fig. 2).

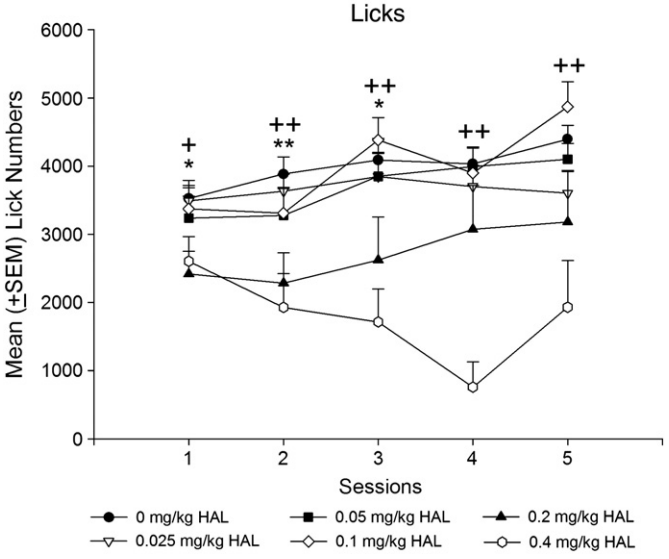

Fig. 3. Effect of various doses (0, 0.025, 0.05, 0.1, 0.2, and 0.4 mg/kg) of haloperidol on water intake (licking behavior) in water-deprived rats over five consecutive daily 15 min sessions. Data are expressed as group mean number of licks (±SEM) ($n=10$ per group). $^{*}p<0.05$, $^{**}p<0.01$, significant difference between 0.2 mg/kg haloperidol and control (0 mg/kg haloperidol) groups. $^{+}p<0.05$, $^{++}p<0.01$, significant difference between 0.4 mg/kg haloperidol and control (0 mg/kg haloperidol) groups. HAL, haloperidol.

Fig. 3 summarizes the mean number of licks during the 15 min test. A 2×5 repeated-measures ANOVA revealed a significant main effect of dose for 0.025 mg/kg ($F_{1,18}=1.50$, $p<0.05$), 0.05 mg/kg ($F_{1,18}=0.88$, $p<0.05$), 0.1 mg/kg ($F_{1,18}=0.00$, $p<0.05$), 0.2 mg/kg ($F_{1,18}=7.43$, $p<0.05$), and 0.4 mg/kg ($F_{1,18}=38.16$, $p<0.01$) compared with the control group. A significant main effect of session was observed only for 0.05 mg/kg ($F_{4,72}=5.62$, $p<0.01$) and 0.1 mg/kg ($F_{4,72}=7.04$, $p<0.01$). No significant effect of session was observed for 0.025, 0.2, and 0.4 mg/kg ($p>0.05$). No significant dose × session interaction was found for the 0.025–0.4 mg/kg doses compared with the control group ($p>0.05$). Furthermore, Tukey's HSD *post hoc* test indicated significant differences between the 0 mg/kg and 0.2 mg/kg groups during sessions 1–3 ($p<0.05$) and between the 0 mg/kg and 0.4 mg/kg groups during sessions 1–5 ($p<0.05$). Therefore, the main effect of dose may have been attributable to significant differences between the control group and the 0.2 mg/kg or 0.4 mg/kg groups. The 0–0.1 mg/kg doses did not affect the number of licks during the five 15 min sessions.

4. Discussion

The present results indicate that, depending on doses, haloperidol could dissociate locomotor responses from appetitive and consummatory behaviors. The 0.4 mg/kg dose impaired locomotion (i.e., catalepsy) during session 1. However, the cataleptic effect of 0.2 mg/kg haloperidol occurred after session 2 and not during session 1. Regarding the assessment of appetitive behavior, the 0.4 mg/kg dose significantly increased the latency to access water during session 2–5. The 0.2 mg/kg dose increased the latency for the appetitive response during sessions 3 and 5. Only the 0.2 mg/kg and 0.4 mg/kg doses significantly decreased the consummatory behavior (intake volume and the number of licks), over all five sessions. The doses ≤0.1 mg/kg appeared to have no effect on any behavior. Therefore, the 0.2 mg/kg dose of haloperidol during session 1 appeared to be critical for dissociating appetitive responses from consummatory responses. However, the 0.4 mg/kg dose dissociated locomotor activity from motivational behaviors (including appetitive and consummatory responses) during session 1. Additionally, a cumulative effect of the 0.2 mg/kg dose during session 2 dissociated locomotor activity and appetitive responding. Thus, the haloperidol doses greater than 0.2 mg/kg impaired consummatory drinking behavior as well as appetitive approach behavior and locomotion, but doses lower than 0.2 mg/kg had less of an effect on consummatory behavior. Locomotor activity and appetitive and consummatory responding were differentially sensitive to the haloperidol injection sessions. Locomotor activity and appetitive and consummatory behavior were blunted by 0.2 mg/kg haloperidol in the second, third, and first sessions, respectively (see Table 2 and Fig. 4). Therefore, dopamine regulation of both motor and motivational behaviors (i.e., including appetitive responding and consummatory behavior) cannot be explained by a simple yes or no of D_2 receptor mechanism. Rather, it is the matter of differential sensitivity to dopamine blocking.

4.1. Neural substrates and the dissociating motor from motivational functions

Previous studies have shown different neural pathways subserve motoric and motivational pathways (Melis and Argiolas, 1995): the nigrostriatal dopamine projections regulate motor behavior, and the mesolimbic dopaminergic projections mediate motivational circuits (Alcaro et al., 2007; Di Chiara et al., 2004; Smith, 1995; Stellar et al., 1983; Strange, 1993; Yoshida et al., 1992). A similar dissociation has been observed with the opioid system in which opiate-induced motivation is associated with anterior ventral tegmental area (VTA) glutamatergic activity, whereas the psychomotor effects of opiates are more associated with posterior VTA glutamatergic activity (Shabat-Simon et al., 2008; Zangen et al., 2002). Thus, within the dopaminergic and opioid systems, the motivational effects from motoric effects can be dissociated.

4.2. Dopamine system: appetitive and consummatory behaviors

In a recent review, Salamone et al. (2007) summarize some relevant dopamine data and propose a similar dissociation viewpoint in which "these manipulations appear to separate aspects of primary food motivation from features of instrumental responding for food" (p. 465). The responding of the primary food motivation is similar to our concept of a motivational stimulus-induced consummatory behavior. The instrumental responding is similar to the appetitive responses. Some crucial dopamine studies are suggested to distinguish between appetitive and consummatory behaviors (Salamone, 1988; Blackburn et al., 1989; Ikemoto and Panksepp, 1996; Salamone, 1991; Barbano and Cador, 2007; Burgdorf and Panksepp, 2006; Czachowski et al., 2002). For example, 0.2 and 0.4 mg/kg doses of D_2 antagonist haloperidol were shown to impair the activational aspects

Table 2
Effects of haloperidol on locomotor activity and appetitive and consummatory licking behavior.

Haloperidol dose (mg/kg)	Locomotion	Appetitive response	Consummatory behavior	
			Licks	Intake volume
0	–	–	–	–
0.025	–	–	–	–
0.05	–	–	–	–
0.1	–	–	–	–
0.2	+ (until session 2)	+ (sessions 3 and 5)	+ (sessions 1–3)	+ (sessions 1–5)
0.4	++ (until session 1)	++ (sessions 2–5)	++ (sessions 1–5)	++ (sessions 1–5)

$^{+}p<0.05$, $^{++}p<0.01$, significant effect compared with 0 mg/kg haloperidol group. –, nonsignificant effect.

HAL Doses (mg/kg)	Stimulus Properties	Relevant Behaviors	Functions	
0.2~	Hedonic	Consummatory responses	Liking	Motivation
0.2~0.4	Reinforcing (i.e. reinforcement)	Appetitive responses	Wanting	
0.4~		Locomotion	Motor activity	

Fig. 4. Schematic of the dissociation between locomotor activity and motivation with 0.4 mg/kg haloperidol. Administration of 0.2 mg/kg haloperidol further dissociated appetitive responding from consummatory responding.

(appetitive behavior) of food-motivated behavior without influencing directional behavior toward food consumption, but 0.1 mg/kg did not affect any feeding behaviors (consummatory behavior; Salamone, 1988). Dopamine blockers metoclopramide and thioridazine were used to test feeding behaviors; the result indicates that 2.5–7.5 mg/k doses of metoclopramide attenuate conditioned preparatory responses (appetitive behavior) for food but only high dose 7.5 mg/kg affects consummatory responses, whereas 10–30 mg/kg thioridazine doses do not influence any measure of feeding behavior (Blackburn et al., 1989). The data of dopamine antagonists cis-flupentixol (1, 5, 25 μg/0.5 μl /site) microinjection into the nucleus accumbens are shown to block anticipatory behaviors (appetitive responses), but consummatory responding for a sucrose solution intake remains intact (Ikemoto and Panksepp, 1996). The D_2 antagonist raclopride was injected prior to a sucrose sham feeding test; indicating that the lick rate and lick pattern of consummatory behavior under raclopride injection were similar to dilution of the sucrose concentrations from 10% to 5% (Schneider et al., 1990); suggesting that D_2 receptor inhibition blunted the hedonic processing of the orosensory sucrose stimulus but did not affect the motoric activity of ingestive behavior (Davis, 2004; Hsiao and Smith, 1995). Also, 5, 10, 15 mg/kg doses of D_2 antagonist remoxipride were shown to decrease ethanol-seeking behavior (appetitive responses) rather than ethanol intake (consummatory behavior; Czachowski et al., 2002). Therefore, some conditions of a dopamine dose range and antagonists restriction are seemingly to merely impact anticipatory/preparatory behavior without affecting the consummatory aspects of feeding behavior (Barbano and Cador, 2007).

Similar dose-related effects are observed in sexual and ethanol-seeking behaviors (Balthazart et al., 1997; Castagna et al., 1997): 0.05–0.2 mg/kg haloperidol, 0.1–1 mg/kg pimozide, and 0.1–0.5 mg/kg clozapine (all dopamine antagonists) block appetitive anticipatory behavior, but bilateral infusions of haloperidol into the nucleus accumbens reduced the appetitive behavior without the consummatory copulatory behavior (Pfaus and Phillips, 1991). Similarly, intra-nucleus accumbens or intraperitoneal injections of a D_2 antagonist raclopride (1, 3, and 10 μg/subject) attenuated appetitive ethanol-seeking behavior and consummatory intake behavior in rats (Czachowski et al., 2001), and this effect was more pronounced on appetitive ethanol-seeking behavior than on the consummatory behavior of ethanol intake (Samson and Chappell, 2004; Silvestre et al., 1996). However, there are conflicting data that do not support a role for dopamine in appetitive and consummatory behavior (Bednar et al., 1995; Bratcher et al., 2005; Volkow et al., 2002). For example, a D_1 receptor agonist SKF38393 (1, 10, and 20 mg/kg) and a D_2 receptor agonist quinpirole (0.25, 0.5, 1 mg/kg) were administrated to influence the lever pressing behavior for primary food reward; the results indicate that D_1 agonist SKF38393 but not D_2 quinpirole injections were prone to the dose-dependent response for food reinforcement. However, estimates of bias and estimates of goodness of fit did not significantly change at all doses of a D_1 agonist SKF38393 and a D_2 agonist quinpirole. Therefore, these authors suggest that D_1 receptor is probably involved in the inhibition of consummatory behavior rather than a D_2 receptor (Bratcher et al., 2005). In addiction, 1 mg/kg D_1 agonist SKF38393 and 0.1 mg/kg D_2 agonist LY-171555 have been demonstrated to blunt the intraoral infusion intake of sucrose solution reward (i.e. consummatory behavior), and reversed this inhibition effect, respectively, by a D_1 antagonist SCH39166 (0.1 mg/kg) and a D_2 antagonist raclopride (0.6 mg/kg); suggesting that D1 and D2 receptors may only control the consummatory ingestive behavior, but this paradigm cannot discriminate consummatory ingestive behavior from appetitive ingestive behavior (Bednar et al., 1995). By contrast, some studies reported that the dopamine system only mediates the reinforcing aspects of feeding behavior (Epstein and Leddy, 2006).

4.3. Wanting and liking v.s. appetitive and consummatory behaviors

Robinson and Berridge (1993) have performed a series of experiments to dissociate "wanting" and "liking" in motivation-induced appetitive and consummatory behavior (Robinson and Berridge, 1993). They suggested that the dopamine system controls the incentive salience of rewarding stimuli and modulate the motivational value in a manner separable from hedonia and reward learning. According to their hypothesis, the concept of "wanting" is a dopamine-related function elicited by the reinforcing property of the stimulus, and this reinforcing property reflects the incentive value (salience) of the positive motivational stimulus. We suggest that this reinforcing property elicits appetitive responses. Conversely, the definition of "liking" posited by Robinson and Berridge (1993) reflects the hedonic property of the positive motivational stimulus. Thus, we propose that this hedonic property causes the consummatory performance; thus the motivation can be divided into "wanting" and "liking" components. Notice, for example, that Fig. 4 in the present study depicts the relationships between the stimulus properties, relevant behaviors, and functions with various doses of haloperidol. After systematically ruling out other dopamine hypotheses, these authors suggest that the brain dopamine system plays a crucial role only for incentive salience processing (Berridge, 2007). That is, the dopamine neural substrates selectively control the "wanting" function (appetitive behavior) independent of the "liking" function (consummatory behavior). Meanwhile, the "liking" function has been shown to be sensitive to the benzodiazepine diazepam, which enhances the hedonic reaction pattern in rats subjected to a taste reactivity test paradigm (Berridge and Robinson, 1998). Additionally, this "liking" effect is also hypothesized to be influenced by the opioid system (Barbano and Cador, 2007; Wilson et al., 2006).

5. Conclusion

Important to consider is that the 0.2 mg/kg haloperidol dose blocked appetitive, consummatory, and locomotor responses in the present study. However, the 0.2 mg/kg dose was more potent and had a more pronounced effect on consummatory behavior compared with appetitive responses and locomotion. The 0.2 mg/kg dose had the weakest effects on locomotion compared with the other behavior. Therefore, the present results seem to support the incentive salience hypothesis proposed by Robinson and Berridge. That is, consummatory behavior (liking) and appetitive responses (wanting) could be dissociated by an appropriate dose of haloperidol (0.2 mg/kg). Moreover, the highest dose of haloperidol (0.4 mg/kg) dissociated locomotion (motor activity) and appetitive responses (motivation). These findings suggest that D_2 receptors may mediate all responses, including locomotor activity and appetitive and consummatory behavior, and underscore the importance of considering the dose of haloperidol used for studies investigating motor, appetitive, and consummatory behavior. However, some interesting issues emerge from this study. One issue is whether the 0.2 mg/kg haloperidol dose dissociating locomotor activity from motivational behaviors (appetitive and consummatory responses) could "map," respectively, on the mesolimbic or nigrostriatal dopamine pathways. Another issue is that the present data suggest that dopamine blockade impairs different motoric or motivational systems at various haloperidol doses. However, haloperidol presumably has the same neuropsychological effect at all doses, but the different behavioral measures are differentially sensitive to common impairment. The current data cannot clearly discern why the same neuropsychological effect of haloperidol can induce differentially sensitive behavioral effects. These effects may be partially attributable to the varying intensities of the effects of haloperidol, and therefore the qualitative changes in specific neural pathways. These two issues should be investigated in future studies.

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