Psychopharmacology (1992) 107:160–174

Psychopharmacology

Complex motor and sensorimotor functions of striatal and accumbens dopamine: involvement in instrumental behavior processes

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Received May 9, 1991 / Final version September 6, 1991

Abstract. The suggestions that dopamine (DA) systems are involved in "motor control" and "reward" represent the classic working hypotheses on the behavioral functions of these systems. The research generated by these hypotheses has yielded results that are far more complicated than the simplest form of either hypothesis would indicate. Pharmacological or lesion-induced interference with DA function does not suppress all aspects of movement control, nor all aspects of reward, nor all aspects of motivation. The deficits produced by interference with DA systems are selective and dissociative in nature, affecting some aspects of motor or motivational function, but leaving others basically intact. In some sense the hypotheses that DA is involved in "motor" or "reward" or "motivational" processes are partly correct, but the processes to which these terms refer are too broad to offer an accurate and detailed description of the behavioral functions of brain DA. A review of the literature on the behavioral pharmacology of DA suggests that the behaviors most easily disrupted by DA antagonists are highly activated and complex learned instrumental responses that are elicited or supported by mild conditioned stimuli, and maintained for considerable periods of time. It is proposed that DA in accumbens and striatum modulates the ability of neocortical and limbic areas involved in sensory, associative, and affective processes to influence complex aspects of motor function, and also modulates the execution of complex motor acts organized by the neocortex. Thus, interference with DA systems produces a "subcortical apraxia", which dissociates complex stimulus processes from complex motor processes, but leaves aspects of those processes intact.

Key words: Dopamine – Motor control – Motivation – Sensorimotor function

The purpose of this paper is to offer a theoretical discussion of the behavioral functions of mesolimbic and nigrostriatal dopamine (DA) systems. However, there are some general conceptual problems that one must consider in order to elucidate the behavioral functions of any brain system. One such problem is the limitations imposed by the bewildering array of concepts and terms that are used. Language generated from psychology or physiology often was developed in one particular scientific or historical context, and may have limited applicability outside of that original context. Physiologists or pharmacologists with a genuine interest in behavior may be daunted by the subtleties and complexities of psychological terms. Some psychological concepts developed purely from behavioral work may not be useful in describing the functions of a particular brain system, or the effect of a particular drug. Yet it also is true that behavioral analysis and theory is necessary for organizing our understanding of brain function. Scientific understanding of the behavioral functions of brain DA systems probably has been limited by just such conceptual difficulties (see Neill 1982). Considerable discussion over the last several years has focussed on the question of whether DA antagonists suppress instrumental behavior because of effects on "reward", "motivation", or "motor" processes. One implication of this issue is that these constructs are independent and exclusive categories, and that this independence applies to physiological as well as behavioral analysis. However, it has been argued that motivation and motor control are constructs that overlap considerably, and share common brain mechanisms (Broekkamp 1975; Mogenson et al. 1980; Salamone 1986, 1987, 1988, 1991). In addition, there are problems with the use of terms like reward, motivation, or motor control, because these terms refer to very complex phenomena, which involve the combined operation of several different functions.

The key to understanding the behavioral functions of brain DA systems may lie in our ability to identify and define the relevant behavioral functions in a more precise manner, with reference to what we know from physiological or pharmacological experiments. In turn, this revised understanding of behavioral processes may lead us to

re-define theoretical aspects of how the brain controls behavior. In order to move toward this goal, the present paper will offer a discussion of the role of striatal and accumbens DA in the behavioral processes involved in instrumental conditioning.

Hypothesized motor and reward functions of brain DA systems

The behavioral functions of brain DA systems have been the subject of considerable research, and several hypotheses have been offered to organize our understanding of this work. The present paper is not intended to provide a detailed description of these hypotheses, because they have been the subject of several other reviews. Nevertheless, it is important to outline some of the more influential hypotheses.

Several lines of evidence suggest that DA in striatum and nucleus accumbens is involved in motor functions. Depletion of striatal DA leads to severe motor problems, which often are so debilitating that organisms are akinetic, aphagic, adipsic, and relatively unresponsive to some stimuli (Ungerstedt 1971; Marshall et al. 1976; Stricker and Zigmond 1976). Nucleus accumbens DA depletion does not produce debilitating motor effects, nevertheless, DA depletion in accumbens can suppress spontaneous and amphetamine-induced locomotion (Kelly et al. 1975; Koob et al. 1978). Parkinson's disease has been linked conclusively to a depletion in striatal DA (Hornykiewicz 1972), and can be accompanied by a depletion of DA in limbic areas. Administration of DA antagonists generally suppresses various motor activities. It has been suggested that interference with DA function impairs motor functions such as the initiation or maintenance of movement, or the execution of complex motor acts (Rolls et al. 1974; Fibiger et al. 1976; Ahlenius 1979). Relatively high doses of neuroleptics decrease locomotion and produce a state of cataleptic immobility (Janssen et al. 1965). Moderate doses of neuroleptics suppressed feeding and drinking (Janssen et al. 1965; Rowland and Engle 1977), and aversive and appetitive instrumental behavior (Posluns 1962; Neimegeers and Schelekens 1965; Rolls et al. 1974; Fibiger et al. 1976; Monti and Hance 1976; Wise 1982; see review by Salamone 1987).

The major alternative to the "motor hypothesis" of neuroleptic action is the "anhedonia hypothesis". According to this view, DA is important for the neural systems that mediate the rewarding impact of reinforcers such as food, water, drugs of abuse, and electrical brain stimulation (Wise et al. 1978a, b; Bozarth and Wise 1981a, b, 1986; Wise 1982, 1985). Early evidence in favor of this view came from studies showing that DA antagonists cause operant responding to decline over time in a way that is similar to extinction on some schedules of reinforcement (Wise et al. 1978a; b). This proposed deficit in reward processes has been described as being distinct from the motor effects of DA antagonists (Wise 1982, 1985). Rats pressing a lever to obtain food, or rats injected with the widely abused drug cocaine, both showed increases in extracellular DA in nucleus accumbens (Hernandez and Hoebel 1988). A variety of drugs of abuse have been shown to increase extracellular DA in nucleus accumbens (Di Chiara and Imperato 1986; Imperato and Di Chiara 1986; Hernandez and Hoebel 1988; Chen et al. 1990), and rats will self-administer amphetamine if it is injected directly into nucleus accumbens (Hoebel et al. 1983). Nucleus accumbens has received particular attention in research on the involvement of DA in reward processes, probably because this structure has important limbic inputs, and the limbic system is traditionally linked with emotion and motivation.

The anhedonia hypothesis has undergone considerable revision since it was first proposed. Initially, the hypothesized effects of DA antagonists on primary reinforcers were emphasized (Wise et al. 1978a, b). The implication of the use of the term "anhedonia" is that DA antagonists were thought to reduce the subjective pleasure produced by primary reinforcers, and that this effect was responsible for a neuroleptic-induced decline in operant resonding. According to Wise et al. (1978a, p 263) "neuroleptics appear to take the pleasure out of normally rewarding brain stimulation, take the euphoria out of normally rewarding amphetamine, and take the 'goodness' out of normally rewarding food". Subsequently, Gray and Wise (1980) suggested that DA antagonists interfere with "incentive-motivation" processes. By using the term incentive-motivation, Wise was employing concepts developed by Bindra (1974, 1978) that were designed as alternatives to the traditional response-reinforcement view of operant conditioning. Several researchers have used the concepts of incentive, or incentive-motivation, to explain some of the behavioral effects of DA antagonists (see discussion below). More recently, Wise (1988) has emphasized other ways in which interference with DA systems affects reward processes. According the the theory of Glickman and Schiff (1967), reinforcing events are those that facilitate activity in neural systems mediating species-specific consummatory acts. Wise (1988; Wise and Bozarth 1987) has suggested that DA antagonists may interfere with this type of reinforcement mechanism; he has observed that many drugs of abuse act by increasing DA activity and has suggested that the psychomotor activation thus produced is related to their reinforcing properties. Even some "sedative" drugs of abuse, such as ethanol, have behavioral stimulant properties at low doses (Sanders 1976; Sanders et al. 1978; Imperato and Di Chiara 1986).

Problems with the classic hypotheses of DA function

The suggestions that DA systems are involved in "motor control" and "reward" represent the classic working hypotheses in this area. In fact, there are several other hypotheses that will be considered below. Nevertheless, it is along the lines of these two seemingly incompatible views that much of the research on the behavioral functions of DA systems has been conducted. The research generated by the hypotheses that DA is involved in motor or reward processes has demonstrated that the situa-

tion is far more complicated than the simplest form of either hypothesis would indicate. Pharmacological or lesion-induced interference with DA function does not suppress all aspects of movement control, nor all aspects of reward, nor all aspects of motivation. In order to understand this research, it is important to emphasize functions that are preserved after interference with DA systems, as well as those that are impaired.

DA depletion or administration of DA antagonists does not produce a true paralysis. Interference with DA systems can suppress movement under some conditions, but the organism still retains considerable residual motor capacity, which can be demonstrated under different stimulus conditions. Environmental stimulation was able to reverse the decline in locomotor activity observed in haloperidol-treated rats (Lynch and Carey 1987). Parkinsonian patients who are akinetic or bradykinetic can show movement in response to intense stimuli (Schwab and Zieper 1965). Rats made akinetic with DA depleting brain lesions are capable of being activated by cold baths, tail pinch or forced swimming (Antleman et al. 1976; Marshall et al. 1976; Keefe et al. 1989). These data indicate that the response-suppressing effects of DA antagonists or DA depletion, even in extreme cases, can be overridden by changing the sensory input. The preservation of residual response capacity is even more evident in studies of instrumental behavior that involve moderate interference with DA systems. Doses of neuroleptics that impair active avoidance responses leave escape responses basically intact (Posluns 1962), despite the fact that the motor acts involved in these responses are similar. Neuroleptic-treated animals that have "extinguished" responding in operant tasks will show increased responding if they are exposed to a stimulus paired with reinforcement (Franklin and McKoy 1978; see review by Wise 1982). These results argue against the notion that DA systems directly mediate the execution of motor acts that are necessary for the performance of instrumental behavior, and make it difficult to explain all the effects of DA antagonists in terms of a direct interference with motor output.

A thorough examination of the literature reveals that there also is considerable evidence against the hypothesis that interference with DA systems blocks the "hedonic impact" of rewarding stimuli (see reviews by Salamone 1987, 1991). After the initial findings suggesting that DA antagonists produce effects that resemble extinction, numerous reports indicate that neuroleptic drugs and extinction do not produce equivalent effects (Phillips and Fibiger 1979; Mason et al. 1980; Tombaugh et al. 1980; Faustman and Fowler 1981, 1982; Evenden and Robbins 1983a; Asin and Fibiger 1984; Gramling et al. 1984; Ettenberg and Carlisle 1985; Salamone 1986, 1988; Spivak and Amit 1986; Willner et al. 1988). It has been suggested that the effects of interference with DA systems may resemble the effects of pre-feeding (Willner et al. 1988). However, the effects of DA depletion and haloperidol were shown not to resemble the effects of pre-feeding on a food consumption task (Salamone et al. 1990b) or an instrumental food-choice procedure (Salamone et al. 1991). Appetitive taste reactivity to sweet solutions in rats was preserved after extensive depletion of forebrain DA (Berridge et al. 1989). Kirkpatrick and Fowler (1989) used a force-proportional reinforcement paradigm to study the hypothesized effects of pimozide on reinforcement processes in rats, and observed that pimozide did not disrupt the emission of higher forces for sweeter sucrose solutions. Using an operant psychophysical procedure, Martin-Iverson et al. (1987) observed that haloperidol did not lower the perceived quantitity of food in a way that was consistent with a decrease in perceived reward value.

Several important aspects of appetitive motivation are left intact after DA antagonism or DA depletion. Discrimination performance is relatively spared after systemic neuroleptic administration (Beninger 1982; Tombaugh et al. 1983; Bowers et al. 1985). Low doses of DA antagonists that markedly suppressed the instrumental behavior of lever pressing for food or water did not suppress consumption of freely available food or water (Rolls et al. 1974; Fibiger et al. 1976; Ljungberg 1988, 1989, 1990). Gramling and Fowler (1985) reported that a conditioned instrumental licking response was more easily disrupted by neuroleptic drugs than was consummatory licking. In behavioral paradigms that offered separate indices of response rate or speed and response choice, DA antagonists impaired response rate or speed at doses that did not impair response choice (Evenden and Robbins 1983a; Tombaugh et al. 1983; Bowers et al. 1985). Doses of DA antagonists that impair lever pressing for brain stimulation have much less effect if nosepoking is the instrumental response (Ettenberg et al. 1981; Mekarski 1989). Salamone (1986, 1988) demonstrated that haloperidol disrupted food-induced locomotor activity but did not disrupt the instrumental response of simply being in proximity to the food dish. Thus, interference with DA systems does not produce a global disruption or all aspects of appetitively motivated behavior, nor a global interference with the effects of rewarding stimuli.

As described above, the reward process that is said to be interfered with in the anhedonia hypothesis has been described in several ways since it was first formulated. In some ways, this reflects the ambiguous understanding of the reinforcement process, which is due to the formidable scientific difficulty of identifying the characteristics of stimuli that can make them reinforcers. The intuitively attractive hypothesis that stimuli are reinforcing because they are hedonic does not command general assent. Although it should be obvious that such a proposition would be rejected by radical Skinnerians, a hedonic view of reinforcement also was rejected by learning theorists such as Hilgard and Marquis (1940) and by Meehl (1950). Non-hedonic descriptions of the effects of reinforcers have been offered, including drive reduction, activation of consummatory responses, drive induction, changes in sensation, or behavior-releasing effects. It has been suggested that reinforcing activities are those that are relatively highly preferred (Premack 1959) or deprived (Timberlake and Allison 1974).

The term "incentive" also has been defined in several ways by various theorists. According to Spence (1956)

incentive was used to describe the energizing effects of conditions such as amount of reward. Logan (1960, p 3) stated that incentive referred to the "expectation of reward". According to Logan and Wagner (1965, p 26) incentive learning refers to "a learning process that depends directly upon special incremental and decremental effects on performance that are produced by reward and punishment respectively". Cofer and Appley (1964) related incentive both to anticipation of reinforcement and invigoration of behavior. More recently, the term incentive has continued to be used to describe several different characteristics of the behavioral effects of stimuli. Stimuli act as incentives in that they are goals or hedonic stimuli towards which behavior is directed (Bindra 1974, 1978). Through associative processes, conditioned incentive stimuli can lead to expectation or anticipation of reinforcement (Bolles 1972; Bindra 1974, 1978). In addition, incentive stimuli act to activate or invigorate behavior (Cofer and Appley 1964; Bindra 1972; Cofer 1972; Killeen 1981).

Whether one considers "reward", "incentive-motivation" or "consummatory acts" as the basis for the behavioral phenomenon of reinforcement, there is not substantial evidence that impairment of DA systems produces a general or fundamental interference with all aspects of these processes. At moderate levels of interference with DA systems, there are too many effects of reinforcing stimuli that are left intact. As described above, at low doses of DA antagonists that impair instrumental lever pressing on most schedules for a variety of reinforcers, animals can engage in consummatory behavior, show taste preferences for and behavioral reactivity to sweet stimuli, lever press on a DRL schedule, show preserved response choice and discrimination, and show simple approach responses as the instrumental behavior. Most rats with forebrain DA depletions spend more time feeding than control rats (Salamone et al. 1990b). These features of behavior are not some epiphenomena, or some peripheral idiosyncracies of a particular operant task. Rather, approach, consummatory behavior and time allocation are *fundamental* to the process of appetitive motivation and reinforcement, as emphasized by Baum (1969), Bindra (1978), Glickman and Schiff (1967), Schneirla (1959) and Thorndike (1911).

Dopaminergic involvement in aversively motivated behavior

The ability of DA antagonists to interfere with instrumental responses is not unique to positively reinforced behavior. Numerous studies have demonstrated that DA antagonists interfere with active avoidance responses, whether the particular response is running in alleyways (Posluns 1962; Janssen et al. 1965; Beninger et al. 1980b) or pressing a lever to avoid shock (Niemegeers et al. 1969). Niemegeers et al. (1970) demonstrated that the DA antagonists haloperidol and chlorpromazine reversed the response-enhancing effects of amphetamine on a Sidman avoidance task. DA systems become activated during stressful or aversive stimulation. Very large increases in DA release or metabolism occur in the frontal cortex of rats exposed to footshock (Thierry et al. 1976; Fada et al. 1978; Abercrombie et al. 1989a; b). Increases in DA release and metabolism in nucleus accumbens resulting from shock stress also have been reported (Fada et al. 1978; D'Angio et al. 1987; Abercrombie et al. 1989a, b). The 30–60% increases in DA release or metabolism in nucleus accumbens that occur after shock are considerably smaller than the large (>100–200%) increases observed in frontal cortex. However, the magnitude of the changes in nucleus accumbens DA activity resulting from aversive stimulation are comparable to those produced in this same structure by naturally-occurring rewards (Hernandez and Hoebel 1988).

In general, there is a striking similarity between the characteristics of dopaminergic involvement in appetive and aversive motivation. Instrumental responses of both types are impaired by DA antagonists. The decline in responding over time that is shown when neuroleptics impair appetitive responses also is shown when DA antagonists impair avoidance responding (Sanger 1986). In both cases, the direct response to the motivational stimulus is less easily disrupted than the instrumental response that is related to that stimulus. For example, feeding is less easily disrupted by neuroleptics than lever pressing for food (Rolls et al. 1974; Fibiger et al. 1976), and escape is less easily impaired by neuroleptics than avoidance (Posluns 1962). As with appetitive stimuli, doses of neuroleptics that impair instrumental response rate or latency in avoidance tasks have little effect on discrimination (Ahlenius 1979; Corradini et al. 1984). Periodic presentation of shock (Abercrombie et al. 1989a) or food (McCullough et al. 1990) both increase accumbens DA release. Although it is true that DA antagonists have been shown to block the place preference produced by some drugs of abuse (Spyraki et al. 1983; Spyraki and Fibiger 1988), it has also been demonstrated that haloperidol blocked the place aversion produced by the anxiogenic compound FG 7142 (Di Scala and Sandner 1989). Thus, there is considerable evidence that DA systems are involved in responding to aversive as well as appetitive stimuli, and may be involved in processes that are common to both aspects of motivation.

Additional hypotheses of DA function

The deficits produced by interference with DA systems are selective and dissociative in nature, affecting some aspects of motor or motivational function, but leaving others basically intact. In some sense the simple statements that DA is involved in "motor" or "reward" or "motivational" processes are partly correct, and partly incorrect. Clearly, the processes to which these terms refer are too broad to offer an accurate and detailed description of the behavioral functions of brain DA. Therefore, it is important to consider hypotheses of DA function that are more specific than the global hypotheses described above.

Some investigators have characterized the behavioral functions of striatal DA as being sensorimotor, rather

than purely motor in nature (e.g. Ungerstedt and Ljungberg 1974; Lidsky et al. 1975). Teuber and Proctor (1964) described some of the deficits associated with basal ganglia dysfunction in humans as being neither sensory or motor, but rather reflecting sensory-motor interaction. Considerable evidence indicates that depletion of striatal DA, particularly in the lateral striatum, reduces responsivity to stimuli (Marshall et al. 1976; Dunnett and Iversen 1982; White 1986; Fairley and Marshall 1987). It has been hypothesized that neuroleptic drugs reduce the "efficacy" of stimuli (Dews and Morse 1961; Clody and Carlton 1980).

Marsden (1982) hypothesized that the basal ganglia are involved in "the automatic execution of learned motor plans" (p 514). In supporting this hypothesis, Marsden (1982) relied heavily on studies indicating that Parkinsonian patients have little difficulty in selecting correct motor responses (Angel et al. 1970), or executing slow or simple movements, but had great difficulty in executing sequential motor acts or performing two simultaneous voluntary motor acts (Schwab et al. 1954). Fowler and his colleagues have conducted several studies of learned limb and paw movements in rats, in which the instrumental response involves depression of a lever or small disk attached to a force transducer. Haloperidol was shown to increase response duration by slowing paw withdrawal (Fowler et al. 1986b). Fowler et al. (1986a) observed that DA antagonism has greater effects on the temporal characteristics of response output, as opposed the ability to exert high levels of force.

As has been noted by several authors (Wise 1982; Salamone 1986; Sanger 1986; Ettenberg 1989; Liao and Fowler 1990) a general feature of the effect of neuroleptic drugs is that they cause progressive impairments in responding. Rats treated with DA antagonists show difficulty maintaining movement induced by aversive stimulation (Anisman et al. 1979). Gaddy and Neill (1977) noted that DA depletion had greater effects on sustained behaviors than on behaviors that are emitted briefly. Salamone (1987) suggested that the duration of periods of movement was an important parameter that was sensitive to disruption by interference with DA systems. DA antagonism reduced the duration of bursts of feeding (Salamone 1988; Salamone et al. 1990c). Also, considerable evidence indicates that DA systems are involved in features of the temporal organization, sequencing or patterning of movement (Lyon and Robbins 1975; Koob et al. 1978; Cools 1980; Robbins and Everitt 1982; Evenden and Robbins 1983b; Kelley and Stinus 1985; Salamone 1988).

Mogenson et al. (1980) proposed that the nucleus accumbens represents a functional interface between the limbic system and the motor system, thereby providing a link between motivational and motor processes. Since it was originally offered, this view has gained considerable support from anatomical, physiological and behavioral studies. The nucleus accumbens receives inputs from hippocampus and amygdala (Kelley and Domesick 1982; Kelley et al. 1982; Yim and Mogenson 1982). Activation of ventral tegmental DA neurons decreases the exitatory effects of hippocampal stimulation on some accumbens neurons (Yang and Mogenson 1984). The nucleus accumbens, via actions on the ventral pallidum, can exert influence upon the pedunculopontine nucleus, which is involved in the control of locomotion (Swanson et al. 1984; Garcia-Rill 1986; Yang and Mogenson 1987).

Beninger (1983) hypothesized that DA is involved in the process of reward-related or incentive learning. According to this view, DA neurons are involved in modulating the response-eliciting properties of neutral stimuli, and the maintenance of the response-eliciting properties of previously conditioned stimuli. Concepts and terminology related to incentive processes also have been employed by Blackburn, Phillips and their colleagues (e.g. Blackburn et al. 1987, 1989) as a part of their emphasis on the importance of mesolimbic DA for preparatory behaviors. Using a conditioned feeding paradigm, pimozide and metoclopramide were shown to affect the latency and frequency of entry into the feeding niche at doses that did not alter food consumption (Blackburn et al. 1987, 1989b). Blackburn et al. (1989a) observed that DA metabolism in nucleus accumbens increased during exposure to a stimulus associated with food, but was not during food consumption.

The notion that mesolimbic DA is important for secondary reinforcement and for mediating some of the behavioral effects of "conditioned incentives" has also received considerable support (Taylor and Robbins 1984, 1986; Cador et al. 1989; Everitt 1990; Everitt et al. 1989). Systemic administration of pimozide disrupted the establishment of conditioned reinforcement (Beninger and Phillips 1980). Systemic or intra-accumbens injections of amphetamine increased the effects of secondary reinforcement (Robbins 1978; Taylor and Robbins 1984). Nucleus accumbens DA depletion reduced the effects of amphetamine on responding to secondary reinforcement (Taylor and Robbins 1986). In addition, the effects of amphetamine on responding to secondary reinforcement reflect interactions between amygdala and nucleus accumbens (Cador et al. 1989; Everitt et al. 1989).

Salamone (1988) suggested that low doses of DA antagonists impair activational aspects of motivation (response rate, vigor, or persistence), but have less effect upon relatively simple goal-directed features of behavior. This view is supported by studies, reviewed above, indicating that moderate-to-low doses of DA antagonists have minimal effect upon measures of response choice, discrimination, or food and water consumption. Depletion of accumbens DA reduced various activities induced by scheduled food presentation (Robbins and Koob 1980; Mittleman et al. 1990). Low doses of haloperidol suppressed schedule-induced motor activity, but not simple approach responses for food (Salamone 1986, 1988). Schedule-induced activity is accompanied by increases in DA release and metabolism in accumbens and striatum (Church et al. 1987; Salamone et al. 1989; McCullough et al. 1990).

It is useful to discuss the relations between the various hypotheses that have been offered. Some of the hypotheses described above (e.g. Marsden 1982; Fowler et al.

1986a, b) suggest that DA systems are involved in subtle features of motor control. Because there are several different aspects of motor control, there is little precision and no uniformity in the use of the term "motor deficit". It is a mistake to assume that an impairment of motor function implies paralysis, or a complete loss of motor capacity, because the exact nature of a motor deficit depends upon where in the nervous system the dysfunction is, and which functions are performed by the impaired structure. Flaccid paralysis, spastic paralysis, apraxia and difficulty with organizing and planning movement all represent impairments in aspects of motor function that are quite different from each other. In addition, it should also be recognized that there is considerable overlap between motivational and motor processes (Duffy 1963; Cofer and Appley 1964; Cofer 1972; Stricker and Zigmond 1976, 1984; Salamone 1986, 1987, 1988; Salamone et al. 1989). Broekkamp et al. (1977) stated that it was arbitrary to draw an absolute dichotomy between brain mechanisms involved in motor control and motivation.

Many of the hypothesized functions of DA systems are compatible with each other. For example, it is possible to integrate the hypotheses offered by Blackburn et al. (1987) and Salamone (1988) by considering that both instrumental and consummatory responses have activational and directional characteristics. The hypothesis that DA is involved in preparatory behavior (Blackburn et al. 1987) is related to the hypothesis that DA is involved in conditioned reinforcement (Taylor and Robbins 1984, 1986; Cador et al. 1989; Everitt et al. 1989), because many preparatory behaviors are supported by conditioned stimuli. Possibly, DA is more involved in mediating the activational effects of conditioned, as opposed to unconditioned, stimuli. One can integrate several of the hypotheses described above by stating that the behaviors most easily disrupted by DA antagonists are highly activated and complex learned instrumental responses that are elicited or supported by mild conditioned stimuli, and maintained for considerable periods of time. In contrast, the behaviors that are most resistant to disruption by DA antagonists are relatively simple and often unlearned responses to intense unconditioned stimuli. This summary statement is in general agreement with much of the work described above, and would suggest that the behavioral functions of brain DA are multifaceted. This may seem unparsimonious to some readers, but to others it may merely reflect the intricacies of the research findings themselves.

Behavioral model of instrumental processes

It is difficult to describe the behavioral functions of brain DA without reference to a particular set of behavioral terms and concepts. This section will describe a model of instrumental behavior that is consistent with much of the research on the role of DA systems in motivation. Motivation has been defined in several different ways, but for the present discussion it is defined as the processes that enable the organism to regulate the availability, probability, or proximity of stimuli (Salamone 1991). Defined in this way, motivation is not described in terms of hypothetical states, drives, desires or euphoria, nor is it used as an explanation of behavior. Rather, motivation is meant to describe the set of sensory, motor and other processes that characterize the interaction of the organism with its environment. It should be obvious that this is a very broad definition, which includes most behaviors demonstrated by whole organisms. It is because of this breadth, and the numerous processes involved in motivation, that one cannot simply state that a drug impairs motivation. Rather, it is more useful to identify the specific aspects of motivation that are influenced by a particular condition.

The definition of motivation given above did not offer a hedonic view, in which organisms are thought to seek stimuli because they are "pleasurable". The precise relation between emotion and motivation remains uncertain. Emotional effects of a stimulus can be the result of complex cognitive and physiological interactions (Schachter and Singer 1962; Schachter 1964). Cabanac (1971) suggested that "pleasure" may be a signal of the usefulness of a stimulus. Emotion, like motivation, is a difficult term to define, and I will define emotions as "the internal stimuli that occur in organisms in motivationally-relevant situations". Thus, emotions can be considered as an aspect of the sensory processes involved in motivation, involving sensation of visceral reactions, metabolic factors, facial expressions, inputs from various exteroceptive processes, and also cognitive processes.

The behavior of organisms regulates the environment such that stimuli are increased or decreased in probability, and through approach, escape or avoidance behaviors stimuli are either brought more proximal or placed further away. These properties of behavior may be so fundamental, and so essential to life processes, that there is not one single factor that determines the valence of motivational stimuli, and no simple or universal answer to the question of why some stimuli are motivationally relevant. Even the obvious motivational stimulus that is common to all organisms, food, is not regulated in a simple manner. Several stimuli are involved in food motivation, including blood glucose and other metabolic factors, taste, and gastric distention. Usually, food, water and sex are considered to be the naturally occurring motivational stimuli, yet several experiments indicate that behavior can be directed towards other types of sensory stimuli as well (Montgomery 1954; Berlyne 1967). Thus, appetitive motivation involves the tendency to approach or to increase the probability of occurrence of certain stimuli, and there appear to be many factors that cause organisms direct their behavior towards these stimuli.

Typically, the behaviors required for regulating stimuli involve chains of responses. The terminal end of the sequence involves some direct interaction with the motivational stimulus, including direct sensory experience, some consummatory response, or both. However, unless the motivational stimulus is freely and immediately available, there are responses that must occur in order for the terminal sensations or consummatory responses to oc-

cur. These responses are called instrumental behaviors, because the behavior of the organism is instrumental in obtaining access to a particular stimulus. Thus, if an organism is directed towards a stimulus, the organism will engage in sequences of responses that initially involve instrumental behavior, but which eventually lead to a direct interaction with that stimulus.

There is an important relation between directional aspects of motivation and the process of instrumental reinforcement. Thorndike (1911), in describing the law of effect, defined a "satisfier" as a stimulus that "the animal does nothing to avoid, often doing such things as to attain and preserve it". Premack (1959) noted that reinforcing activities are those that occur with a relatively high probability. Glickman and Schiff (1967) described positive reinforcers as stimuli that induce species-specific approach responses. According to Bindra (1978) positive reinforcers reliably produce approach reactions. However, organisms are not merely directed towards stimuli in a diffuse manner. In many cases, organisms can learn to emit very specific responses that lead to particular outcomes. Organisms can acquire novel combinations of responses and specific motor skills through instrumental learning, which may depend upon response-reinforcement associations (Mackintosh 1974, 1978; Colwill and Rescorla 1986; Stokes and Balsam 1991). Traditionally, the definition of reinforcement is restricted to the effect of the stimulus on the instrumental responses of the organism; thus, a positive reinforcer is said to increase response probability. However, if there is a contingent relation between the response and the reinforcer, then it must also be true that the organism is increasing the probability of reinforcement by engaging in the instrumental response. Consistent with this notion, a motivational corollary of the empirical law of effect is that a reinforcer is a stimulus that is increased in probability by the organism. Therefore, instrumental behavior is characterized by an organism-environment system in which the organism is regulating its environment, and responses of the organism are in turn modified by their environmental consequences.

Instrumental behavior often is initiated when the goal stimulus is not immediately present nor easily available. Conditioned stimuli are necessary for instigating and supporting many complex instrumental behaviors, and for providing information about access to motivational stimuli, and the response-reinforcement relation (Rescorla 1990). Also, energy barriers separate organisms from stimuli towards which they are directed, just as energy barriers prevent some chemical reactions from occurring spontaneously. Thus, instrumental behavior can involve considerable amounts of work. Rats will forage over wide areas of space, or vigorously press levers, to increase the availability of food. Scheduled food presentation or stimuli associated with food can induce a very high level of various motor activities (Campbell and Sheffield 1953; Staddon and Simmelhag 1971; Killeen 1975; Salamone 1988). The vigor and persistence of instrumental behavior, including those behaviors instigated by conditioned stimuli, can enable organisms to overcome the obstacles separating them from significant stimuli.

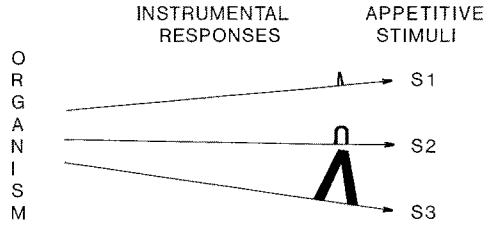

Fig. 1. A model depicting the interaction of an organism with three different appetitive stimuli. Different instrumental responses with distinct energetic and temporal requirements are necessary to obtain access to each stimulus. The particular instrumental response selected will be influenced by the value of each rewarding stimulus and the requirements of each of the different responses

The process of behavioral regulation typically involves several different stimuli and instrumental responses over time. Foraging animals can have several food sources, and in a complex environment food is only one of several stimuli that are available. In addition, different instrumental responses vary in terms of their difficulty, the general energetic requirements, and the time they take to execute (Fig. 1). According to optimal foraging theory, the profitability of a food source, in terms of the ratio of food gained to the expenditure of energy necessary to obtain it, is an important determinant of foraging patterns (Krebs 1978). Researchers using operant procedures or "economic" models of behavior also have emphasized how responding is affected by the balance between reinforcement value and response factors such as response costs, constraints, or temporal characteristics of responding (Herrnstein 1974; McDowell and Kessel 1979; Staddon 1979; Kaufman 1980; Rachlin 1981; Hursh et al. 1988; Timberlake et al. 1988). The allocation of responses with relation to various stimuli represents the highest level of motivational control.

At this point, it should be evident that the effects of motivationally relevant stimuli are multifarious. Motivational stimuli are regulated by the instrumental behavior of the organism; they are stimuli towards which behavior can be directed, and they can facilitate the acquisition of novel motor acts. Learned instrumental behavior can involve an elaborate associative structure linking conditioned stimuli, instrumental responses, and reinforcers (Rescorla 1990). The activating properties of motivational stimuli can feed back to the organism to support the maintainence of further responses. Motivational stimuli can produce internal effects that we label as emotions, which may be part of the stimulus processing involved in motivation, and may serve as internal discriminative stimuli that control instrumental behavior. Psychologists employ terms such as "incentive" and "reinforcement" to summarize these effects, but the fact that we can invent a term to describe a process does not make that process a simple phenomenon, or an elemental substrate for drug action.

Involvement of striatal and accumbens DA in motivational processes

The behavior of organisms is characterized by sensory-motor interactions at various levels of function. Reflexes represent the lowest level of sensory-motor integration. Classical conditioning involves another, more complex type of sensory-motor process. Motivational processes involve a variety of sensory-motor interactions. Some consummatory responses involve simple, often stereotyped patterns of motor activity. In many cases it has been determined that features of these responses are organized at spinal and brainstem levels. For example, decerebrate rats can consume food if it is placed in their mouth (Flynn and Grill 1983). Aspects of the motor pattern for locomotion are organized in the brainstem (Garcia-Rill 1986).

In its most complex sense, motivation involves the control of stimuli by the use of a variety of intrumental responses, ranging from simple locomotion to intricate manipulation of objects with the digits, forepaws or mouth. Organisms are capable of allocating these responses in relation to a vast array of stimuli. Many of the processes involved in motivation, such as coordination of learned motor acts in a temporal sequence, motor planning, execution of variable motor acts that achieve certain functional outcomes, conditioning, evaluation of density or rate of various reinforcers, or decision-making processes based on cost/benefit analyses, probably depend heavily on functions involving the neocortex, limbic system and basal ganglia. In order to generate adaptive behavior, these forebrain structures must influence the activity of brain areas directly involved in the execution of motor acts. It is proposed that DA in accumbens and striatum modulates the processes that enable neocortical and limbic areas to influence various aspects of motor function (Fig. 2).

The striatum and nucleus accumbens receive major inputs from the neocortex, cingulate cortex, hippocampus and amygdala. One major output of the striatum is directed at brainstem nuclei that have been implicated in aspects of motor control including oral behavior, rotation, locomotion, and control of trunk musculature (Redgrave et al. 1980; Taha et al. 1982; Vaccarino et al. 1985a, b; Garcia-Rill 1986). A second major output is directed at the frontal lobes. An important feature of the anatomy of the frontal cortex and basal ganglia is a series of parallel, segregated circuits that form partially closed "loops" linking specific frontal cortical areas with specific striatal subregions via connections in the globus pallidus and thalamus (Alexander et al. 1986). The functions of the frontal lobes are quite complex, and can include involvement in cognitive, affective and motor control processes. Although the specific details of frontal lobe organization depend upon the species, and the precise functions of each area remain to be determined, there is considerable evidence that the motor control functions of the frontal lobe are organized in a hierarchical fashion (see Kolb and Whishaw 1990). The frontal lobes of rats, non-human primates and humans are involved in processes ranging from control of fine distal and limb musculature, to planning of movements, to the temporal organization of movements.

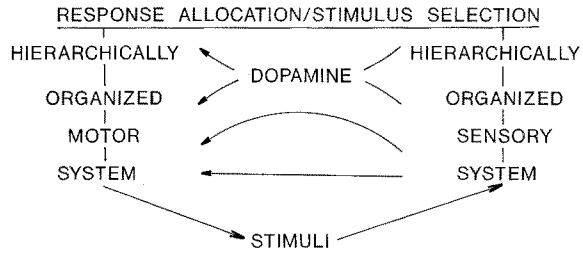

Fig. 2. Motor and sensory systems are organized in a hierarchical manner, with interactions at various levels. At the highest level is the ability to allocate responses with relation to the value of various stimuli. DA in accumbens and striatum is seen as modulating the ability of some high level sensory processes to influence aspects of motor control

There is considerable evidence that DA modulates the activity of neurons in accumbens and striatum, and it has been suggested that DA could serve a "gating" function, in which the ability of afferent neurons to influence output is partially regulated by DA. DA in accumbens and striatum inhibited the excitatory effects of cortical or limbic inputs on intrinsic neurons (Hirata et al. 1984; Vives and Mogenson 1986; Mogenson et al. 1988). Amphetamine modified the effects of sensory stimulation on striatal cells (Abercrombie and Jacobs 1985), and DA was shown to modulate the effects of glutamate and GABA on striatal cells (Chiodo and Berger (1986)). Rolls et al. (1984) observed that the inhibitory effects of DA on striatal movement related neurons could act to enhance the signal to noise ratio of these neurons, or set the threshold for their activation. The suggestion that DA modulates synaptic processes in accumbens and striatum is important in view of the fact that these structures are viewed as regulators of motor function. According to Neafsy et al. (1978) the basal ganglia do not directly cause movements to occur, but instead are involved in facilitating or enabling movements and regulating their organization. Salamone (1987) and Carli et al. (1989) suggested that striatal and accumbens DA does not participate directly in the selection of particular responses, but rather exerts a modulatory influence over features of response output.

DA in striatum and accumbens is seen as modulating the ability of some sensory, associative, and affective processes to influence complex aspects of motor function (Fig. 3). Thus, interference with DA systems produces a "subcortical apraxia", which dissociates complex stimulus processes from complex motor processes, but leaves aspects of sensory and motor processes essentially intact. Highly coordinated motor acts that have a high degree of temporal organization, and that are related to cortical mechanisms, are impaired by interference with DA systems (Marsden 1982; Evenden and Robbins 1984; Sabol et al. 1985; Whishaw et al. 1986; Salamone et al. 1990b). Temporal organization and planning are particularly disrupted in Parkinsonian patients (Ogden et al. 1990). Striatal and accumbens DA are seen as having little direct involvement in detection of sensory stimuli (Carli

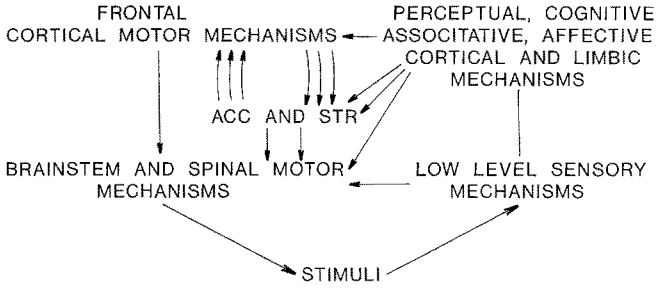

Fig. 3. Schematic representation of the behavioral functions of DA in accumbens *(ACC)* and striatum *(STR)*. It is suggested that DA in nucleus accumbens and striatum modulates the ability of cortical and limbic processes to instigate complex instrumental behavior. The connections shown are highly oversimplified, and are not meant to imply that accumbens and striatum perform the same functions (see text)

et al. 1985, 1989) and affect. DA is not seen as necessary for most aspects of stimulus-stimulus associative processes (Beninger et al. 1980a, b; Beninger 1983; Weiner et al. 1987; Weiner 1990). The residual motor capacity present after severe DA dysfunction occurs because striatal DA synapses are several steps removed from the motor neurons themselves, and because more powerful sensory stimulation can activate movement through processes that do not require DA. Thus, interference with accumbens or striatal DA is less likely to impair relatively simple responses to intense unconditioned stimuli (e.g. escape responses, forced swimming). An organism with a moderate impairment of DA function still is directed towards stimuli such as food provided that the intrumental and consummatory responses are relatively simple, and direct food-related stimuli are present (e.g. sight or smell of food).

Interference with DA has a pronounced effect on the ability of conditioned stimuli to elicit instrumental behavior. The effects of DA antagonists on place preference for food (Spyraki et al. 1982), avoidance (Posluns 1962), secondary reinforcement (Beninger and Phillips 1980) and response-reinstating effects of food during extinction (Horvitz and Ettenberg 1989) may all reflect a decrease in responsiveness to conditioned stimuli, or a deficit in the establishment of response-eliciting properties of conditioned stimuli. The hypothesized involvement of DA in learning about incentive stimuli (Beninger 1983, 1991) and in some aspects of memory for response-reinforcement relations (Packard and White 1991) may reflect dopaminergic involvement in sensory-motor integration or response-stimulus associations. It is not necessary to consider that these effects stem from a global interference with primary reinforcement or hedonia, but rather they can be considered as deficits in complex sensory-motor function.

Although it is useful to consider the overall behavioral functions of striatal and accumbens DA, it is necessary to emphasize that each particular DA terminal region is involved in distinct functions that reflect the different inputs and outputs of each region (Divac 1972; Simon and Le Moal 1988). However, it does not seem quite accurate to state merely that DA in striatum has a "motor" function, whereas accumbens DA is related to "limbic" or "motivational" types of functions. Neostriatum also receives limbic inputs (Kelley et al. 1982; Grabiel 1990), and the outputs of nucleus accumbens as well as striatum lead to motor areas of the brain. In addition, it may be inaccurate to assume that limbic inputs to accumbens and striatum are necessarily involved in "emotion", because limbic areas also are involved in memory/cognition. It may not be useful to make a simple dichotomy between the behavioral functions of accumbens versus striatum, because each of these areas may be composed of several functionally distinct subregions. Further research will be necessary to identify more precisely the behavioral functions of DA in each of the various subregions of nucleus accumbens and striatum. The lateral striatum of rodents and the putamen of primates may function in close association with motor cortex to control manipulation of objects and highly coordinated use of the forelimbs. The ventrolateral striatum of the rat is particularly involved in forelimb and oral motor control (Evenden and Robbins 1984; Sabol et al. 1985; Whishaw et al. 1986; Jicha and Salamone 1991; Kelley et al. 1988; Pisa 1988a, b; Salamone et al. 1990a, b). In rats, extensive depletion of DA in nucleus accumbens decreases spontaneous locomotion (Koob et al. 1978), whereas depletions in ventrolateral striatum do not (Jicha and Salamone, 1991). DA in nucleus accumbens is involved in responding for secondary reinforcement (Taylor and Robbins 1986), and complex aspects of movement involving planning and organization may be more related to caudate or nucleus accumbens DA. Possibly, different subregions of nucleus accumbens and striatum are organized in a hierarchical fashion that mimics the organization of the motor system in general and the frontal lobe in particular. The functions performed by each subregion could be dependent upon the types of stimulus inputs (e.g. conditioned versus unconditioned, distal versus proximal stimuli) and the features of motor control (e.g. large versus small behavioral units, locomotion versus manuipulation) being regulated.

Behavior is regulated with relation to a variety of available reinforcers, and each of these stimuli can only be obtained by overcoming the obstacles associated with the particular stimulus. It has been suggested that DA, particularly in nucleus accumbens, is involved in the process through which organisms forage or exert effort in gaining access to significant stimuli (Rosenblatt et al. 1979; Neill and Justice 1981; Sinnamon 1982; Kelley and Stinus 1985; Salamone 1987, 1988, 1991). Recently, rats were observed in a choice procedure in which the subjects could press a lever to obtain a more-preferred food, or approach and consume a less-preferred food that was freely available (Salamone et al. 1991). Normally, rats in this procedure press the lever to obtain the preferred food, and eat little of the less preferred food. However, intra-accumbens haloperidol or depletion of accumbens DA shifted the behavior of these rats, such that lever pressing was decreased but consumption of the less-preferred food increased. These results suggest that DA activity sets constraints upon the particular instrumental response that is selected in a given situation. The DA-depleted rat that was not pressing the lever was still

directed towards food acquisition and consumption, thus the rat reorganized its behavior and selected a new "path" to obtain food.

Conclusions

Rather than assuming that there is an absolute dichotomy between motivational and motor function, it is suggested that the brain mechanisms for these processes overlap, and that brain DA is important for modulating functions that are common to motivation and motor control. DA is involved in aspects of sensory-motor function, in the broadest sense of these terms. Thus, depending upon the particular terminal region, DA could act to facilitate the ability of cutaneous stimuli to elicit discrete body movements, or to enhance reactivity to rewarding stimuli. In a sense, the involvement of DA in facilitating the ability of conditioned stimuli to promote instrumental responding, or in acting to modulate a limbic-motor interface, represent special cases of this sensory-motor function.

It can be argued that some of the functions of DA represent more than just the stimulation of movement per se, but also represent the facilitation of particular interactions with the environment. Many of the behaviors that can be enhanced by stimulant drugs, such as lever pressing, nose poking, and gnawing are not simply muscle acts; these are activities that are dependent upon the presence of features of the environment. Stimulant stereotypies can be influenced by a variety of environmental conditions (Lyon and Randrup 1972; Ellinwood and Kilbey 1975; Kelley et al. 1986). Also, the relation between DA release and motor activity is diffuse. The activity of most substantia nigra or ventral tegmental DA cells is not associated with particular movements, but these cells have been shown to become generally active during periods of motor activity (Steinfels et al. 1983; Nishino et al. 1987). According to Buchwald et al. (1975) the basal ganglia act to affect the bias of neurons in other parts of the motor system, so that these neurons become more responsive to other inputs. These observations suggest that DA release in some regions may not simply instigate muscle acts themselves, but rather it may establish a state in which certain stimuli will be more able to elicit movement.

The complex nature of motivation and the variety of factors that can influence instrumental behavior has important implications for the role of DA in reward processes. The threshold for brain stimulation reward has been suggested as an index of the reward value of a stimulus that is independent of motor function (Edmonds and Gallistel 1974; Wise 1982). Thus, if a DA antagonist raises the stimulation threshold it is interpreted as a selective effect on "reward" processes. However, it has been shown that stimulation threshold is not a pure measure of reward, and can be increased by motor factors such as task difficulty (Frank and Williams 1985; Fouriezos et al. 1990). Another paradigm that has been used to assess the behavioral effects of DA antagonists is response-reinforcement matching, in which the relation between responding and reinforcement density on VI schedules is described by a rectangular hyperbola (Herrnstein 1974; Heyman and Monaghan 1987). Low doses of neuroleptics have been shown to change the response-reinforcement relation (Heyman 1983; Heyman et al. 1986; but see Morley et al. 1984) by causing an increase in the parameter that represents density of reinforcement necessary to maintain a half-maximal response rate (RL50, see Fig. 4). Although this parameter has been used as an index of the rewarding impact of the stimulus, it may not be a pure index of reward, and may instead reflect several factors. An analogy can be drawn to the ED50, a parameter in pharmacology that is very widely used. Although the ED50 is an index of potency, this parameter is determined by many factors such as affinity, drug penetration, and duration of action. Similarly, the behavioral parameters derived from curve-fitting analyses of VI responding probably do not reflect one single factor such as the hedonic value of the stimulus. The self-stimulation threshold or the RL50 may simply be indices of relative behavioral reactivity to reinforcing stimuli under specific conditions. As such, the effects of DA antagonists on these measures can be interpreted as a particular manifestation of the sensory-motor functions of DA systems (Salamone 1991).

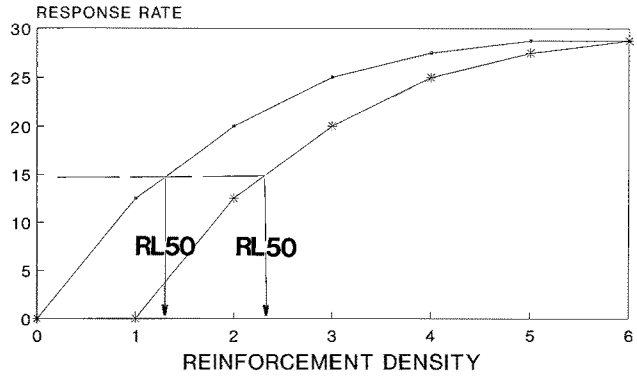

Fig. 4. Hypothetical data from a response-reinforcement matching experiment. Rats are exposed to VI schedules with different reinforcement densities, and response rate is related to reinforcement density. The RL_{50} is the reinforcement level that generates a response rate that is 50% of the maximum rate. Administration of DA antagonists has been shown to increase the RL_{50}. This effect could represent a decreased behavioral reactivity to a reinforcing stimulus, and thus may be a manifestation of the sensory-motor functions of DA. The ability of the neuroleptic-treated animal to obtain normal maximum response rates at higher densities of reinforcement reflects the reversibility of the behavioral effects of DA antagonists with increasing sensory input. (– □ –) Control; (– * –) DA antagonist

Manipulation of DA systems could have powerful indirect effects on affective processes. Reduced functional activity in accumbens and striatal DA would leave the organism less able to avoid aversive stimuli and less able to obtain positive stimuli, which would generate a less positive affective state (Willner 1985; Salamone 1991). In addition, enhanced DA transmission, as produced by activating stimuli or low doses of stimulant drugs, would render the organism more able to avoid aversive stimuli and more able to obtain positive stimuli, which would

generate a more positive affective state. It is possible that one of the functions of emotions is to act as internal stimuli that control and elicit instrumental behavior, much as external discriminative stimuli and drugs can. Thus, interference with DA systems may lessen the probability that internal stimuli related to emotions will instigate adaptive instrumental behaviors.

References

Abercrombie EA, Jacobs BL (1985) Dopaminergic modulation of sensory responses of striatal neurons : single unit studies. Brain Res 358:27–33

Abercrombie EA, Keefe KA, DiFrischia DA, Zigmond MJ (1989a) Differential effect of stress on in vivo dopamine release in striatum, nucleus accumbens and medial frontal cortex. J Neurochem 52:1655–1658

Abercrombie EA, Keefe KA, Zigmond MJ (1989b) Evidence that nerve terminal density is an important contributor to apparent differences in the activation of central dopamine systems. Behav Pharmacol 1 [suppl 1]:26

Ahlenius S (1979) An analysis of behavioral effects produced by drug-induced changes in dopaminergic neurotransmission in the brain. Scand J Psychol 20:59–64

Alexander GE, DeLong MR, Strick PL (1986) Parallel organizations of functionally segregated circuits linking basal ganglia and cortex. Annu Rev Neurosci 9:357–381

Anisman H, Zacharko R (1982) Stimulus change influences escape performance: Deficits induced by uncontrollable stress and by haloperidol. Pharmacol Biochem Behav 17:263–269

Anisman H, Remington G, Sklar LS (1979) Effect of inescapable shock on subsequent escape performance: catecholaminergic and cholinergic mediation of response initiation and maintenance. Psychopharmacology 61:107–124

Angel RW, Alston W, Higgins JR (1970) Control of movement in Parkinson's disease. Brain 93:1–14

Antleman SM, Rowland RE, Fisher AE (1976) Stress related recovery from lateral hypothalamic aphagia. Brain Res 102:346–350

Asin KE, Fibiger HC (1984) Force requirements in lever-pressing and responding after haloperidol. Pharmacol Biochem Behav 20:323–326

Baum WM, Rachlin HC (1969) Choice as time allocation. J Exp Anal Behav 12:861–874

Beninger RJ (1982) A comparison of the effects of pimozide and nonreinforcement on discriminated operant responding in rats. Pharmacol Biochem Behav 16:667–669

Beninger RJ (1983) The role of dopamine activity in locomotor activity and learning. Brain Res Rev 6:173–196

Beninger RJ (1991) Receptor subtype-specific dopamine agonists and antagonists and conditioned behavior. In: Willner P, Scheel-Kruger J (eds) The mesolimbic dopamine sytem: from motivation to action. Cambridge University Press, Cambridge, England, pp 273–300

Beninger RJ, Phillips AG (1980) The effect of pimozide on the establishment of conditioned reinforcement. Psychopharmacology 68:147–153

Beninger RJ, Maclennan AJ, Pinel JPJ (1980a) The use of conditioned defensive burying to test the effects of pimozide on associative learning. Pharmacol Biochem Behav 12:445–448

Beninger BJ, Mason ST, Phillips AG, Fibiger HC (1980b) Use of conditioned suppression to evaluate the nature of neuroleptic-induced avoidance deficits. J Pharmacol Exp Ther 213:623–627

Berlyne DE (1967) Arousal and reinforcement. In: Levine D (ed) Nebraska Symposium on Motivation. University of Nebraska Press, Lincoln, Nebraska, pp 1–110

Berridge KC, Venier IL, Robinson TE (1989) Taste reactivity analysis of 6-hydroxydopamine-induced aphagia: implications for arousal and anhedonia hypotheses of dopamine function. Behav Neurosci 103:36–45

Bindra D (1972) Neuropsychological interpretation of the effects of drive and incentive-motivation on general and instrumental behavior. Psychol Rev 75:1–22

Bindra D (1974) A motivational view of learning, performance and behavior modification. Psychol Rev 81:199–213

Bindra D (1978) How adaptive behavior is produced: A perceptual-motivational alternative to response-reinforcement. Behav Brain Sci 1:41–91

Blackburn JR, Phillips AG, Jakubovic A, Fibiger HC (1986) Increased dopamine metabolism in nucleus accumbens and striatum following consumption of a nutritive meal but not a palatable non-nutritive sacharin solution. Pharmacol Biochem Behav 25:1095–1100

Blackburn JR, Phillips AG, Fibiger HC (1987) Dopamine and preparatory behavior: I. Effects of pimozide. Behav Neurosci 101:352–360

Blackburn JR, Phillips AG, Jakubovic A, Fibiger HC (1989a) Dopamine and preparatory behavior: II. A neurochemical analysis. Behav Neurosci 103:15–23

Blackburn JR, Phillips AG, Jakubovic A, Fibiger HC (1989b) Dopamine and preparatory behavior. III: A neurochemical analysis. Behav Neurosci 103:15–23

Bolles RC (1972) Reinforcement, expectancy and learning. Psychol Rev 79:349–409

Bowers W, Hamilton M, Zacharcho RM, Anisman H (1985) Differential effects of pimozide on response-rate and choice accuracy in a self-stimulation paradigm in mice. Pharmacol Biochem Behav 22:521–526

Bozarth MA, Wise RA (1981a) Involvement of the ventral tegmental dopamine system in opioid and psychomotor stimulant reinforcement. Life Sci 28:551–555

Bozarth MA, Wise RA (1981b) Heroin reward is dependent on a dopaminergic substrate. Life Sci 29:1881–1886

Bozarth MA, Wise RA (1986) Involvement of the ventral tegmental dopamine system in opioid and psychomotor stimulant reinforcement. NIDA Res Monogr Ser 67:190–196

Broekkamp CL, van Dongen PA, van Rossum (1977) Neostriatal involvement in reinforcement and motivation. In: Cools AR, Lohman AM, van den Berken JH (eds) Psychobiology of the striatum. Elsevier Holland, Amsterdam

Brozoski TJ, Brown RM, Rosvold HE, Goldman PS (1979) Cognitive deficit caused by regional depletion of dopamine in prefrontal cortex of rhesus monkey. Science 205:929–932

Buchwald NA, Hull CD, Levine MS, Villablanca J (1975) The basal ganglia and the regulation of response and cognitive sets. In: Brazier MA (ed) Growth and development of the brain. Raven Press, New York, pp 171–189

Cabanac M (1971) Physiological role of pleasure. Science 173:1103–1107

Cador M, Robbins TW, Everitt BJ (1989) Involvement of the amygdala in stimulus-reward associations: interactions with the ventral striatum. Neuroscience 30:77–86

Campbell BA, Sheffield FD (1953) Relation of random activity to food deprivation. J Comp Physiol Psychol 46:320–322

Carli M, Evenden JL, Robbins TW (1985) Depletion of unilateral striatal dopamine impairs initiation of contralateral actions but not sensory attention. Nature 313:279–282

Carli M, Jones GH, Robbins TW (1989) Effects of unilateral dorsal and ventral striatal dopamine depletion on visual neglect in the rat: A neural and behavioral analysis. Neuroscience 29:309–327

Chen J, Paredes W, Li J, Smith D, Lowison J, Gardner EL (1990) tetrahydrocannabinol produces naloxone-blockable enhancement of presynaptic basal dopamine efflux in nucleus accumbens of conscious, freely-moving rats as measured by intracerebral microdialysis. Psychopharmacology 102:156–162

Chiodo LA, Berger TW (1986) Interactions between dopamine and amino acid-induced excitations and inhibition in the striatum. Brain Res 375:198–203

Church WH, Justice JB, Neill DB (1987) Detecting behaviorally relevant changes in extracellular dopamine with microdialysis. Brain Res 412:397–399
Clody DE, Carlton PL (1980) Stimulus efficacy, chlorpromazine, and schizophrenia. Psychopharmacology 69:127–131
Cofer CN (1972) Motivation and emotion. Scott, Foresman, Glenview, IL
Cofer CN, Appley MH (1964) Motivation: theory and research. Wiley, New York
Colwill RM, Rescorla RA (1986) Associative structures in instrumental learning. In: Bower GH (ed) The psychology of learning and motivation. Academic Press, New York, pp 55–104
Cools AR (1980) Role of neostriatal dopaminergic activity in sequencing and selecting behavioural strategies: facilitation of processes involved in selecting the best strategy in a stressful situation. Behav Brain Res 1:361–378
Corradini A, Tombaugh T, Anisman H (1984) Effects of pimozide on escape and discrimination performance in a water-escape task. Behav Neurosci 98:96–106
D'Angio MD, Serrano A, Rivy JP, Scatton B (1987) Tail-pinch stress increases extracellular DOPAC levels (as measured by in vivo voltammetry) in rat nucleus accumbens but not frontal cortex: antagonism by diazepam and zolpidem. Brain Res 409:169–174
Di Chiara G, Imperato A (1986) Preferential stimulation of dopamine release in the nucleus accumbens by opiates, alcohol and barbiturates: studies with transcerebral dialysis in freely moving rats. Ann NY Acad Sci 473:367–381
Di Scala G, Sander G (1989) Conditioned place aversion produced by FG 7142 is attenuated by haloperidol. Psychoparmacology 99:176–180
Divac I (1972) Neostriatum and functions of prefrontal cortex. Acta Neurobiol Exp 32:461–477
Duffy E (1963) Activation and behavior. Wiley, New York
Dunnett SB, Iversen SD (1982) Sensorimotor impairments following localized kainic acid and 6-hydroxydopamine lesions of the neostriatum. Brain Res 248:121–127
Edmonds PE, Gallistel CR (1974) Parametric analysis of brain stimulation reward in the rat: effect of performance variables on the reward summation function. J Comp Physiol Psychol 87:876–883
Ellinwood EH, Kilbey MM (1975) Amphetamine stereotypy— influence of environmental factors and prepotent behavior patterns on its topography. Biol Psychiatry 10:3–16
Ettenberg A (1989) Dopamine, neuroleptics and reinforced behavior. Neurosci Biobehav Rev 13:105–111
Ettenberg A, Koob GF, Bloom F (1981) Response artifact in the measurement of neuroleptic-induced anhedonia. Science 209:357–359
Ettenberg A, Carlisle HJ (1985) Neuroleptic-induced deficits in operant responding for temperature reinforcement. Pharmacol Biochem Behav 22:761–767
Evenden JL, Robbins TW (1983a) Dissociable effects of *d*-amphetamine, chlordiazepoxide and alpha-flupenthixol on choice and rate measures of reinforcement in the rat. Psychopharmacology 79:180–186
Evenden JL, Robbins TW (1983b) Increased response switching, perseveration and perseverative switching following *d*-amphetamine in the rat. Psychopharmacology 80:67–73
Evenden JL, Robbins TW (1984) Effects of unilateral 6-hydroxydopamine lesions of the caudate-putamen on skilled forepaw use in the rat. Behav Brain Res 14:61–68
Everitt BJ (1990) Sexual motivation: a neural and behavioral analysis of the mechanisms underlying appetitive and copulatory responses of male rats. Neurosci Biobehav Rev 14:217–232
Everitt BJ, Cador M, Robbins TW (1989) Interactions between the amygdala and ventral striatum in stimulus-reward associations: studies using a second-order schedule of sexual reinforcement. Neuroscience 30:63–75
Fada F, Argiolas A, Melis MR, Tissari AH, Onali PC, Gessa GL (1978) Stress-induced increase in 3,4-dihydroxyphenylacetic acid (DOPAC) levels in the cerebral cortex and in nucleus accumbens: reversal by diazepam. Life Sci 23:2219–2224
Fairley PC, Marshall JF (1987) Dopamine in the lateral caudate-putamen of the rat is essential for somatosensory orientation. Behav Neurosci 100:652–663
Faustman WO, Fowler SC (1981) Use of operant response duration to distinguish effects of haloperidol form non-reward. Pharmacol Biochem Behav 15:327–329
Faustman WO, Fowler SC (1982) An examination of methodological refinements, clozapine and fluphenazine in the anhedonia paradigm. Pharmacol Biochem Behav 17:987–993
Fibiger HC, Carter DA, Phillips AG (1976) Decreased intracranial self-stimulation after neuroleptics or 6-hydroxydopamine: evidence for mediation by motor deficits rather than by reduced reward. Psychopharmacology 47:21–27
Flynn FW, Grill HJ (1983) Insulin elicits injestion in decerebrate rats. Science 221:188–190
Fouriezos G, Bielajew C, Pagotto W (1990) Task difficulty increases threshold of rewarding brain stimulation. Behav Brain Res 37:1–7
Fowler SC (1990) Neuroleptics produce within-session decrements: facts and theories. Drug Dev Res
Fowler SC, Gramling SE, Liao RM (1986a) Effects of primozide on emitted force, duration and rate of operant response maintained at low and high levels of required force. Pharmacol Biochem Behav 25:615–622
Fowler SC, LaCerra MM, Ettenberg A (1986b) Effects of haloperidol on the biophysical characteristics of operant responding: implications for motor and reinforcement processes. Pharmacol Biochem Behav 25:791–796
Frank R, Williams H (1985) Both response effort and current intensity affect self-stimulation train duration thresholds. Pharmacol Biochem Behav 22:527–530
Franklin KBT, McCoy SH (1979) Pimozide-induced extinction in rats: stimulus control of responding rules out motor deficit. Pharmacol Biochem Behav 11:71–75
Gaddy JR, Neill DB (1977) Differential behavioral changes following intrastiatal applications of 6-hydroxydopamine. Brain Res 119:439–446
Garcia-Rill E (1986) The basal ganglia and the locomotor regions. Brain Res Rev 11:47–63
Glickman SE, Schiff BB (1967) A biological theory of reinforcement. Psychol Rev 74:81–109
Grabiel AM (1990) Neurotransmitters and neuromodulators in the basal ganglia. TINS 13:244–254
Gramling SE, Fowler SC (1985) Effects of neuroleptics on rate and duration of operant versus reflexive licking in rats. Pharmacol Biochem Behav 22:541–545
Gramling SE, Fowler SC, Collins KR (1984) Some effects of pimozide on nondeprived rats licking sucrose solutions in an anhedonia paradigm. Pharmacol Biochem Behav 21:617–624
Gray T, Wise RA (1980) Effects of pimozide on lever-pressing behavior maintained on an intermittent reinforcement schedule. Pharmacol Biochem Behav 12:931–935
Hernandez L, Hoebel BG (1988) Food reward and cocaine increase extracellular dopamine in the nucleus accumbens as measured by microdialysis. Life Sci 42:1705–1712
Herrnstein RJ (1974) Formal properties of the matching law. J Exp Anal Behav 21:159–164
Heyman GM (1983) A parametric evaluation of hedonic and motoric effects of drugs: pimozide and amphetamine. J Exp Anal Behav 40:113–122
Heyman GM, Monaghan MM (1987) Effects of changes in response requirement and deprivation on the parameters of the matching law equation: new data and review. J Exp Psychol [Anim Behav] 13:384–394
Heyman GM, Kinzie DL, Seiden LS (1986) Chlorpromazine and pimozide alter reinforcement efficacy and motor performance. Psychopharmacology 88:346–353
Hilgard ER, Marquis DG (1940) Conditioning and learning. Appleton Century, New York

Hirata K, Yim CY, Mogenson GJ (1984) Excitatory input from sensory motor cortex to neostriatum and its modification by conditioning stimulation of the substantia nigra. Brain Res 321:1–8

Hoebel BG, Monaco AP, Hernandez L, Aulisi EF, Stanley BG, Leonard L (1983) Self-injection of amphetamine directly into the brain. Psychopharmacology 81:158–163

Hornykiewicz O (1972) Dopamine and its physiological significance in brain function. In: Browne GH (ed) The structure and function of nervous tissue. Academic Press, New York

Horvitz JC, Ettenberg A (1989) Haloperidol blocks the response-reinstating effects of food reward: a methodology for separating neuroleptic effects on reinforcement and motor processes. Pharmacol Biochem Behav 31:861–865

Hursh SR, Raslear TG, Shurtleff D, Bauman R, Simmons L (1988) A cost-benefit analysis of demand for food. J Exp Anal Behav 50:419–440

Imperato A, Di Chiara G (1986) Preferential stimulation of dopamine release in the nucleus accumbens of freely moving rats by ethanol. J Psychol Exp Ther 239:219–228

Janssen PA, Niemegeers CJF, Schellekens KHL (1965) Is it possible to predict the clinical effects of neuroleptic drugs (major tranquilizers) from animal data? Arzneimittelforschung 15:104–117

Jicha GA, Salamone JD (1991) Vacuous jaw movements and feeding deficits in rats with ventrolateral striatal dopamine depletion: Possible relation to Parkinsonian symptoms. J Neurosci 11:3822–3829

Kaufman LW (1980) Foraging costs and meal patterns in ferrets. Physiol Behav 25:139–141

Keefe KA, Salamone JD, Zigmond MJ, Stricker EM (1989) Paradoxical kinesia in Parkinsonism is not caused by dopamine release: studies in an animal model. Arch Neurol 46:1070–1075

Keehn JD, Riusech R (1977) Schedule-induced water and saccharin polydipsia under haloperidol. Bull Psychonom Soc 9:413–415

Kelley AE, Domesick VB (1982) The distribution of the projection from the hippocampal formation to the nucleus accumbens of the rat: an anterograde- and retrograde-horseradish peroxidase study. Neuroscience 7:2321–2335

Kelley AE, Stinus L (1985) Disappearance of hoarding behavior after 6-hydroxydopamine lesions of the mesolimbic dopamine neurons and its reinstatement with L-dopa. Behav Neurosci 99:531–543

Kelley AE, Domesick VB, Nauta WJH (1982) The amygdalostriatal projection in the rat- an anatomical study by anterograde and retrograde tracing methods. Neuroscience 7:615–630

Kelley AE, Winnock M, Stinus L (1986) Amphetamine, apomorphine and investigatory behavior in the rat: Analysis of the structure and pattern of responses. Psychopharmacology 88:66–74

Kelley AE, Lang CG, Gauthier AM (1988) Induction of oral stereotypy following amphetamine microinjection into a discrete subregion of the striatum. Psychopharmacology 95:556–559

Kelly PH, Seviour PW, Iversen SD (1975) Amphetamine and apomorphine responses in the rat following 6-OHDA lesions of the nucleus accumbens septi and corpus striatum. Brain Res 94:507–522

Killeen P (1975) On the temporal control of behavior. Psychol Rev 82:89–115

Killeen P (1981) Incentive theory. In: Bernstein D (ed) Response structure and organization. University of Nebraska Press, Lincoln, Nebraska

Kirkpatrick MA, Fowler SC (1989) Force-proportional reinforcement: Pimozide does not reduce rats' emmission of higher forces for sweeter rewards. Pharmacol Biochem Behav 32:499–504

Kolb B, Whishaw IQ (1990) Fundamentals of human neuropsychology. W.H. Freeman, New York

Koob GF, Riley SJ, Smith SC, Robbins TW (1978) Effects of 6-hydroxydopamine lesions of the nucleus accumbens septi and olfactory tubercle on feeding, locomotor activity, and amphetamine anorexia in the rat. J Comp Physiol Psychol 92:917–927

Krebs JR (1978) Optimal foraging: Decision rules for predators. In: Krebs JR, Davies WB (eds) Behavioral ecology. Sinauer Sunderland, MA, pp 23–63

Liao RM, Fowler SC (1990) Haloperidol produces within-session increments in operant response duration in rats. Pharmacol Biochem Behav 36:199–201

Lidsky TI, Buchwald NA, Manetto C, Schneider JS (1985) A consideration of sensory factors involved in the motor functions of the basal ganglia. Brain Res Rev 9:133–146

Ljungberg T (1987) Blockade by neuroleptics of water intake and operant responding in the rat: anhedonia, motor deficit or both? Pharmacol Biochem Behav 27:341–350

Ljungberg T (1988) Scopolamine reverses haloperidol-attenuated lever pressing for water but not haloperidol-attenuated water intake in the rat. Pharmacol Biochem Behav 29:205–208

Ljungberg T (1989) Effects of the dopamine D–1 antagonist SCH 23390 on water intake, water-rewarded operant responding and apomorphine induced decrease of water in rats. Pharmacol Biochem Behav 33:709–712

Ljungberg T (1990) Differential attenuation of water intake and water-rewarded operant responding by repeated administration of haloperidol and SCH 23390 in the rat. Pharmacol Biochem Behav 35:111–115

Logan FA (1960) Incentive: How the conditions of reinforcement affect the performance of rats. Yale University Press, New Haven

Logan FA, Wagner AR (1965) Reward and punishment. Allyn and Bacon, Boston

Lyon M, Randrup A (1972) Dose-response effect of amphetamine upon avoidance behavior in rats seen as a function of increasing stereotypy. Psychopharmacology 23:334

Lyon M, Robbins TW (1975) The action of central nervous system stimulant drugs. Curr Dev Psychopharmacol 2:79–163

Lynch MR, Carey RJ (1987) Environmental stimulation promotes recovery from haloperidol-induced extinction of open field behavior in rats. Psychopharmacology 92:206–209

Mackintosch NJ (1974) The psychology of animal learning. Academic Press, London

Mackintosh NJ (1978) Limits on reinterpreting instrumental conditioning in terms of classical conditioning. Behav Brain Sci 1:67

Marsden CD (1982) The mysterious motor function of the basal ganglia: the Robert Wartenberg lecture. Neurology 32:514–539

Marshall JF, Levitan D, Stricker EM (1976) Activation-induced restoration of sensorimotor functions in rats with dopamine-depleting brain lesions. J Comp Physiol Psychol 90:536–546

Martin-Iverson MT, Wilke D, Fibiger HC (1987) Effect of haloperidol and *d*-amphetamine on perceived quantitiy of food and tones. Psychopharmacology 93:374–381

Mason ST, Beninger RJ, Fibiger HC, Phillips AG (1980) Pimozide-induced suppression of responding: evidence against a block of food reward. Pharmacol Biochem Behav 12:917–923

McCullough LD, Singer D, Salamone JD (1990) Periodic food presentation increases extracellular dopamine and metabolites in nucleus accumbens dialysis perfusates. Soc Neurosci Abstr 16:438

McDowell JJ, Kessell R (1979) A multivariate rate equation for variable-interval performance. J Exp Anal Behav 31:267–283

Meehl PE (1950) On the circularity of the law of effect. Psychol Bull 47:52–75

Mekarski JE (1989) Main effects of current and pimozide on prepared and learned self-stimulation behaviors are on performance not reward. Pharmacol Biochem Behav 31:845–853

Mittleman G, Whishaw IQ, Jones GH, Koch M, Robbins TW (1990) Cortical, hippocampal, and striatal mediation of schedule-induced behaviors. Behav Neurosci 104:399–409

Mogenson G, Jones D, Yim CY (1980) From motivation to action: functional interface between the limbic system and the motor system. Prog Neurobiol 14:69–97

Mogenson GJ, Yang CR, Yim CY (1988) Influence of dopamine limbic inputs to the nucleus accumbens. Ann NY Acad Sci 537:86–100

Montgomery KC (1954) The role of the exploratory drive in learning. J Comp Physiol Psychol 44:582–589

Morley MJ, Bradshaw CM, Szabadi E (1984) The effect of pimozide on variable-interval performance: a test of the 'anhedonia' hypothesis of the mode of neuroleptic action. Psychopharmacology 84:531–536

Neafsy EJ, Hull CD, Buchwald NA (1978) Preparation for movement in the cat. II. Unit activity in the basal ganglia and thalamus. Electroencephalogr Clin Neurophysiol 44:714–723

Neill DB (1982) Problems of concept and vocabulary in the anhedonia hypothesis. Behav Brain Sci 5:70

Neill DB, Justice JB (1981) An hypothesis for a behavioral function of dopaminergic transmission in nucleus accumbens. In: Chronister RB, Defrance JF (eds) The neurobiology of the nucleus accumbens. Huer Institute, Brunswick

Niemegeers CJE, Verbruggen FJ, Janssen PAJ (1969) The influence of various neuroleptic drugs on shock avoidance responding in rats. Psychopharmacology 16:161–174

Niemegeers CJE, Verbruggen FJ, Janssen PAJ (1970) The influence of various neuroleptic drugs on shock avoidance responding in rats. Psychopharmacology 17:151–159

Nishino H, Ono T, Muramoto K, Fukuda M, Sasaki K (1987) Neuronal activity in the ventral tegmental area (VTA) during motivated bar press feeding in the monkey. Brain Res 413:302–313

Ogden JA, Growden JH, Corkin S (1990) Deficits of visuospatial tests involving forward planning in high-functioning Parkinsonian. Neuropsychiat Neuropsychol Behav Neurol 3:125–139

Packard MG, White NM (1991) Dissociation of hippocampus and caudate nucleus memory systems by posttraining intracerebral injection of dopamine agonists. Behav Neurosci 105:295–306

Phillips AG, Fibiger HC (1979) Decreased resistance to extinction after haloperidol: Implications for the role of dopamine in reinforcement. Pharmacol Biochem Behav 10:751–761

Pisa M (1988a) Motor somatotopy in the striatum of rat: manipulation, biting and gait. Behav Brain Res 27:21–35

Pisa M (1988b) Motor functions of the striatum in the rat: critical role of the lateral region in tongue and forelimb reaching. Neuroscience 24:453–463

Posluns D (1962) An analysis of chlorpromazine-induced suppression of the avoidance response. Psychopharmacology 3:361–373

Premack D (1959) Toward empirical behavior laws. I: Positive reinforcement. Psychol Rev 66:219–233

Rachlin H (1981) Absolute and relative consumption space. In: Bernstein D (ed) Response structure and organization. University of Nebraska Press, Lincoln

Redgrave P, Dean P, Donohue TP, Pope SP (1980) Superior colliculus lesions selectively attenuate apomorphine-induced oral stereotypy: a possible role for the nigrotectal pathway. Brain Res 196:541–546

Rescorla RA (1990) The role of information about the response-outcome relation in instrumental learning. J Exp Psychol [Anim Behav] 16:262–270

Robbins TW (1975) The potentiation of conditioned reinforcement by psychomotor stimulant drugs: a test of Hill's hypothesis. Psychopharmacology 45:103–114

Robbins TW (1978) The acquisition of responding with conditioned reinforcement: Effects of pipradrol, methylphenidate, *d*-amphetamine and nomifensine. Psychopharmacology 58:79–87

Robbins TW, Everitt BJ (1982) Functional studies of central catecholamines. Int Rev Neurobiol 23:303–364

Robbins TW, Koob GF (1980) Selective disruption of displacement behaviour by lesions of the mesolimbic dopamine system. Nature 285:409–412

Rolls ET, Rolls BJ, Kelly PH, Shaw SG, Wood RJ, Dale R (1974) The relative attenuation of self-stimulation, eating and drinking produced by dopamine-receptor blockade. Psychopharmacology 38:219–230

Rolls ET, Thorpe SJ, Boytim M, Szabo I, Perret DI (1984) Responses of striatal neurons in the behaving monkey. 3. Effects of iontophoretically applied dopamine on normal responsiveness. Neuroscience 12:1201–1212

Rosenblatt WH, Hutchins K, Sinnamon HM (1979) Pimozide's effects on ICSS depend upon the interaction of reward and effort. Soc Neurosci Abstr 5:350

Rowland N, Engle DJ (1977) Feeding and drinking interaction after acute butyrophenone administration. Pharmacol Biochem Behav 7:295–301

Sabol KE, Neill DB, Wages SA, Church WH, Justice JB (1985) Dopamine depletion in a striatal subregion disrupts performance of a skilled motor task in the rat. Brain Res 335:33–43

Sahakian BJ, Sarna GS, Kantameneni BD, Jackson A, Hutson PH, Curzon G (1985) Association between learning and cortical catecholamines in non-drug-treated rats. Psychopharmacology 86:339–343

Salamone JD (1986) Different effects of haloperidol and extinction on instrumental behaviors. Psychopharmacology 88:18–23

Salamone JD (1987) The actions of neuroleptic drugs on appetitive instrumental behaviors. In: Iversen LL, Iversen SD, Snyder SH (eds) Handbook of psychopharmacology. Plenum Press, New York pp 575–608

Salamone JD (1988) Dopaminergic involvement in activational aspects of motivation: effects of haloperidol on schedule-induced activity, feeding and foraging in rats. Psychobiology 16:196–206

Salamone JD (1991) Behavioral pharmacology of dopamine systems: a new synthesis. In: Willner P, Scheel-Kruger J (eds) The mesolimbic dopamine system: from motivation to action. Cambridge University Press, Cambridge, England, pp 599–613

Salamone JD, Keller RW, Zigmond MJ, Stricker EM (1989) Behavioral activation in rats increases striatal dopamine metabolism measured by dialysis perfusion. Brain Res 487:215–224

Salamone JD, Johnson CJ, McCullough LD, Steinpreis RE (1990a) Lateral striatal cholinergic mechanisms involved in oral motor activities in the rat. Psychopharmacology 102:529–534

Salamone JD, Zigmond MJ, Stricker EM (1990b) Characterization of the impaired feeding behavior in rats given haloperidol or dopamine-depleting brain lesions. Neuroscience 39:17–24

Salamone JD, Steinpreis RE, McCullough LD, Smith P, Grebel D, Mahan K (1991) Haloperidol and nucleus accumbens dopamine depletion suppress lever pressing for food but increase free food consumption in a novel food-choice procedure. Psychopharmacology 104:515–521

Sanders B (1976) Sensitivity to low doses of ethanol and pentobarbital in mice selected for sensitivity to hypnotic doses of ethanol. J Comp Physiol Psychol 90:394–398

Sanders B, Sharpless SK, Collins AC, McClearn GE, Flanagan C (1978) Activating and anesthetic properties of general depressants. Psychopharmacology 56:185–189

Sanger DJ (1986) Response decrement patterns after neuroleptic and non-neuroleptic drugs. Psychopharmacology 89:98–104

Scatton B, D'Angio M, Driscoll P, Serrano A (1988) An in vivo voltammetric study of the response of mesocortical and mesoaccumbens dopaminergic neurons to environmental stimuli in strains of rats with differeing levels of emotionality. Ann NY Acad Sci 537:124–137

Schacter S (1964) The interaction of cognitive and physiological determinants of emotional state. In: Berkowitz L (ed) Advances in experimental social psychology. Academic Press, New York, pp 49–80

Schacter S, Singer JE (1962) Cognitive, social and physiological determinants of the emotional state. Psychol Rev 69:379–399

Schneirla TC (1959) An evolutionary and developmental theory of biphasic processes underlying approach and withdrawal. In: Jones MR (ed) Nebraska Symposium on Motivation. University of Nebraska Press, Lincoln, pp 1–42

Schwab RS, Zieper I (1965) Effects of mood, motivation, stress and alertness on the performance in Parkinson's disease. Psychiat Neurol 150:345–357
Schwab RS, Chaftez ME, Walker S (1954) Control of two simultaneous motor acts in normals and parkinsonism. Arch Neurol 72:591–598
Simon H, Le Moal M (1988) Mesencephalic dopaminergic neurons: role in the general economy of the brain. Ann NY Acad Sci 537:235–253
Simon H, Scatton B, Le Moal M (1980) Dopaminergic A10 neurons are involved in cognitive function. Nature 286:150–151
Sinnamon HM (1982) The reward-effort model: an economic framework for examining the mechanism of neuroleptic action. Behav Brain Sci 5:73–75
Spence KW (1956) Behavior theory and conditioning. Yale University Press, New Haven
Spivak KJ, Amit Z (1986) Effects of pimozide on appetitive behavior and locomotor activity: dissimilarity of effects when compared to extinction. Physiol Behav 36:457–463
Spyraki C, Fibiger HC (1988) A role for the mesolimbic dopamine system in the reinforcing properties of diazepam. Psychopharmacology 94:133–137
Spryaki C, Fibiger HC, Phillips AG (1982) Attenuation by haloperidol of place preference conditioning using food reinforcement. Psychopharmacology 77:379–382
Spryaki C, Fibiger HC, Phillips AG (1983) Attenuation of heroin reward in rats by disruption of mesocorticolimbic dopamine system. Psychopharmacology 79:278–283
Staddon JE (1979) Operant behavior as adaptation to constraint. J Exp Psychol Gen 108:48–67
Staddon JE, Simmelhag VL (1971) The superstition experiment: a re-examination of its implications for the principles of adaptive behavior. Psycho Rev 78:3–43
Steinfels GF, Heym J, Strecker RE, Jacobs BL (1983) Behavioral correlates of dopaminergic unit activity in freely moving cats. Brain Res 258:217–228
Stokes PD, Balsam PD (1991) Effects of reinforcing preselected approximations on the topography of the rat's bar press. J Exp Anal Behav 55:213–231
Stricker EM, Zigmond MJ (1976) Recovery of function after damage to central catecholamine-containing neurons: a neurochemical model for the lateral hypothalamic syndrome. In: Sprague JM (ed) Progress in psychobiology and physiological psychology. Academic Press, New York, pp 121–173
Stricker EM, Zigmond MJ (1984) Brain catecholamines and the central control of food intake. Int J Obesity 8 [suppl 1]:39–50
Swanson LW, Mogenson GJ, Gerfen CR, Robinson P (1984) Evidence for a projection from the lateral preoptic area and substantia innominata to the "mesencephalic locomotor region". Brain Res 295:161–178
Taha EB, Dean P, Redgrave P (1982) Oral behavior induced by intranigral muscimol is unaffected by haloperidol but abolished by large lesions of superior colliculus. Psychopharmacology 77:272–278
Taylor JR, Robbins TW (1984) Enhanced behavioral control by conditioned reinforcers following microinjections of D-amphetamine into the nucleus accumbens. Psychopharmacology 84:405–412
Taylor JR, Robbins TW (1986) 6-Hydroxydopamine lesions of the nucleus accumbens but not the caudate nucleus attenuate responding with reward-related stimului produced by intra-accumbens D-amphetamine. Psychopharmacology 90:390–397
Teuber H-L, Proctor F (1964) Some effects of basal ganglia lesions in subhuman primates and man. Neuropsychology 2:85–93
Thierry AM, Tassin JP, Blanc G, Glowinski J (1976) Selective activation of mesocortical dopaminergic system by stress. Nature 263:242–244
Thorndike EL (1911) Animal intelligence. MacMillan, New York
Timberlake W, Allison J (1974) Response deprivation: an empirical approach to instrumental performance. Psychol Rev 81:146–164
Tombaugh TN, Anisman H, Tombaugh J (1980) Extinction and dopamine receptor blockade after intermittent reinforcement training: failure to observe functional equivalence. Psychopharmacology 70:19–28
Tombaugh TN, Szostak C, Mills P (1983) Failure of pimozide to disrupt acquisition of light-dark and spatial discrimination problems. Psychopharmacology 79:161–168
Ungerstedt U (1971) Aphagia and adipsia after 6-hydroxydopamine induced degeneration of the nigro-striatal dopamine system. Acta Physiol Scand 82 [suppl 367]:95–122
Ungerstedt U, Ljungberg T (1974) Central dopamine neurons and sensory processing. J Psychiatr Res 55:149–150
Vaccarino FJ, Franklin KBJ, Prupas D (1985a) Opposite locomotor asymmetries elicited from the medial and lateral substantia nigra: Role of superior colliculus. Physiol Behav 35: 741–747
Vaccarino FJ, Franklin KBJ, Prupas D (1985b) The role of the midbrain reticular formation in the expression of two opposing nigral denervation syndromes. Physiol Behav 35:749–752
Vives F, Mogenson GJ (1986) Electrophysiological study of the effects of D1 and D2 dopamine antagonists on the interaction of converging inputs from the sensory motor cortex and substantia nigra neurons in the rat. Neuroscience 17:349–359
Weiner I (1990) Neural substrates of latent inhibition: the switching model. Psychol Bull 108:442–461
Weiner I, Feldon J, Katz Y (1987) Facilitation of the expression but not the acquisition of latent inhibition by haloperidol in rats. Pharmacol Biochem Behav 26:241–246
Whishaw IQ, O'Connor WT, Dunnet SB (1986) The contributions of motor cortex, nigrostriatal dopamine and caudate-putamen to skilled forelimb use in the rat. Brain 109:805–843
White NM (1986) Control of sensorimotor functions by dopaminergic nigrostriatal neurons: influence on eating and drinking. Neurosci Biobehav Rev 10:15–36
White NM (1988) Effect of nigrostriatal dopamine depletion on the post-training, memory-improving action of amphetamine. Life Sci 43:7–12
Willner P (1985) Depression: a psychobiological synthesis. Wiley, New York
Willner P, Chawala K, Sampson D, Sophokleus S, Muscat R (1988) Tests