THE EFFECTS OF REWARD UNPREDICTABILITY ON PIGEONS' FORAGING DECISIONS AND DOPAMINE'S ROLE ON PIGEONS' CHOICE

by

Neslihan Edeş

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APPROVED BY:

Assoc. Prof. Dr. Ibrahim Raşit Bilgin . . . .
Thesis/Dissertation Advisor

Dr. Patrick Anselme (Germany) . . . . . .
Thesis/Dissertation Co-Advisor

Prof. Dr. Andrzej Furman . . . . . .

Assoc. Prof. Dr. Uğur Aksu . . . . . .

Assist. Prof. Dr. Berat Haznedaroğlu . . . . . .

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ABSTRACT

THE EFFECTS OF REWARD UNPREDICTABILITY ON PIGEONS' FORAGING DECISIONS AND DOPAMINE'S ROLE ON PIGEONS' CHOICE

In nature, animals face various anthropogenic and abiotic conditions, which can affect food distribution and availability. Animals have to make right foraging decision to survive under these variable conditions. Mammals' foraging decisions under uncertainty and the neurobiology behind this mechanism have been discussed in the literature. Even though there is a vast literature on mammals, more information is needed to determine whether birds use the same mechanisms. Experiment 1 and 2 tested the drug free preference of pigeons for a constant over a variable delay option. Then their preference was examined under the systemic administration of a dopamine agonist, apomorphine (Apo). Our results suggest that preference for a variable over a constant delay was insensitive to dopaminergic activity in birds in contrast with mammals. Also, sensitization to Apo was long-lasting and partly independently of Pavlovian conditioning. In Experiment 3, Apo-sensitized and saline pigeons' drug free preference was examined for a 50% probability option over a 5-s delay option, then again, their preference was observed under the systemic administration of Apo or saline. The Apo-sensitized and saline pigeons showed indifference between two options that shows Apo-sensitization has no effect on the development of a preference for variable-delay and probabilistic schedules of reinforcement.

ÖZET

ÖNGÖRÜLEMEZ ÖDÜLÜN GÜVERCİNLERİN YEM BULMA DAVRANIŞLARI ÜZERİNDEKİ ETKİSİ VE DOPAMİNİN GÜVERCİNLERİN SEÇİMİNDEKİ ROLÜ

Doğada hayvanlar besin dağılımını ve bulunurluğunu etkileyen antropojenik ve abiyotik şartlar ile yüzleşmektedirler. Hayvanların bu koşullar altında hayatta kalmak için doğru yem bulma stratejisini seçmeleri gerekir. Memelilerin belirsiz koşullar esnasında yem bulma stratejileri ve bu mekanizmanın ardındaki nörobiyoloji literatürde kapsamlı olarak tartışılmıştır. Memeliler hakkında geniş ölçüde literatür olmasına rağmen, kuşların da yem bulma aşamasında karar vermelerinde aynı mekanizmayı kullanıp kullanmadığını belirlemek için daha fazla bilgi gerekmektedir. Deney 1 ve 2'de, ilk olarak güvercinlerin herhangi bir enjeksiyon almadan sabit ve değişken opsiyonlar arasındaki seçimi test edildi. Sonrasında seçimleri sistemik olarak enjekte edilen dopamin agonisti apomorfin (Apo) ardından test edildi. Deney sonuçlarımız kuşlarda değişken ve sabit opsiyonlar arasındaki seçimin dopamin aktivesinden bağımsız olduğunu göstermiştir. Ayrıca Apo sensitizasyonu kalıcıdır ve Pavlov'un klasik koşullanmasından bağımsız olarak gerçekleşmektedir. Deney 3'de Apo duyarlılığı oluşan güvercinlerin ve kontrol saline güvercinlerinin beş saniye rötar ve %50 olasılık opsiyonları arasındaki seçimleri enjeksiyonsuz olarak test edildi ve tekrardan güvercinlerin opsiyonlar arasındaki seçimleri Apo ya da saline enjeksiyonlarının ardından tekrardan test edildi. Fakat Apo ve saline güvercinleri beş saniye rötar ve %50 olasılık opsiyonları arasında değişkenlik göstermedi bu da Apo sensitizasyonunun rötar ve olasılık opsiyonlarını içeren deney düzeneğinde bir seçim oluşturmada etkisiz olduğunu gösterdi.

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LIST OF SYMBOLS/ABBREVIATIONS

Apo	Apomorphine
APO	Apormorphine Pigeons
CS	Conditioned Stimulus
DD	Dopamine Deficient
FD	Fixed Delay
FR	Fixed-Ratio Schedule
ITI	Inter-Trial Interval
NAc	Nucleus Accumbens
PD	Parkinson’s Disease
PFC	Prefrontal Cortex
SAL	Saline Pigeons
VD	Variable Delay
VR	Variable-Ratio Schedule
VTA	Ventral Tegmental Area
UCS	Unconditioned Stimulus

1. INTRODUCTION

Humans have had a long history of modifying prehistoric environments. They have changed landscapes through deforestation and erosion (McGlone, 1983; Van Andel et al., 1990). In addition, competitive species and new predators have been introduced to the environment. The results of people's interactions with their environment range from relatively beneficial to the extreme of landscape degradation and extinction (Nagaoka, 2002). Besides anthropogenic effects; in nature, animals often face abiotic effects such as seasonal change, and variable temperatures. All these factors play crucial roles in food distribution and food availability. Therefore, animals have to make the right foraging decisions to cope with stochastic environments.

Especially for the small-sized animals, the right foraging decisions create the difference between life and death. For instance, rufous hummingbirds (*Selaphorus rufus*) migrate from Mexico to their breeding grounds 1400 m up in the Canadian Rocky Mountains. The migration of these birds that weigh 3-5 g ends in May, when the birds have to face freezing nighttime temperatures and heavy snowfall. From dawn until dusk, they have to forage approximately every 10-15 min, to satisfy their energetic needs. They drop their metabolic activity and go into torpor during the night until the morning when they are able to feed. A bird prevented from foraging because of snowfall or making poor foraging decisions might be unable to maintain its body temperature during the cold nights, and hence would not survive until the next morning (Bateson, 2002).

Nature provides different sizes of food. While large food items may contain more energy than smaller ones, they may be harder to find and sparsely distributed. Therefore, foraging decisions consist of trade-offs between a food item's energy content, the energetic cost of obtaining that food item, and the delay before it can be obtained. According to the optimal foraging theory, natural selection favors the animals whose foraging behavior is energetically efficient (Caraco,1980). In other words, the theory predicts that organisms should maximize the mean rate of food intake during the food search.

The work of Caraco (1980), which explained a model of foraging in a stochastic environment, and the work of Real (1981) that especially focused on fitness and uncertainty, were among the first studies that incorporated risk-sensitivity to foraging theory. In the presence of the alternative foodsources, many foraging animals are sensitive to variability in reward availability. Environmental stochasticity, which is typically referred to as 'risk', provides variable foraging options to animals.

Both psychologists and behavioral ecologists try to understand the effects of risk on the foraging decisions that are made by animals. Experimentally, risk can be produced by varying the amount of food, the time delay before the delivery of food, or the number of responses required to obtain food (Kacelnik and Bateson, 1996). Kacelnik and Bateson (1996) also listed different studies for the effect of the variable dimension (amount or delay) on the risk-sensitive preferences of different taxonomic groups (insects, fish, birds, and mammals). Among the studies that focused on responses to variability in amount of risk with no manipulation of energy budgets, most reported risk- aversion, a few showed risk proneness and some results were close to indifference between risk aversion and proneness. In these studies, the risk-averse animals were generally on positive energy budgets and the risk-prone animals were on negative energy budgets. But this rule (referred to as the energy budget rule) is not well confirmed (Kacelnik and Bateson, 1997). For example, responses to the effects of variability in delay with no manipulation of energy budgets show that animals are mostly risk-prone. Also, variable-ratio (VR) schedules are often preferred to fixed-ratio (FR) schedules, even when reward rate is lower.

2. THEORETICAL BACKGROUND

2.1. Risk Sensitive Foraging

2.1.1. Stochastic environments

For individuals, environment is a complex of many unstable abiotic and biotic factors, such as temperature, sunlight, nutrient availability, predators, and conspecifics. It is a critical challenge for animals to deal with all these factors. These unstable abiotic and biotic factors are responsible for environmental stochasticity, which may result in unpredictable local changes. For instance, while the yearly temperatures may only fluctuate on the order of 2 °C in caves, extreme seasonal flooding may be responsible for the variations in food availability from non-cave sources (Poulson, 1964). Thus insect populations living outside of caves are influenced by seasonal flooding, and they represent a major food sources for bats, which live in caves. In consequence, not only bats but also some other cave animals that get their food from nematodes in bat feces or fungus on the guano, face variations in food availability. Unpredictable environments also provide different foraging options, and animals, which require food to survive and reproduce, are sometimes unable to predict the future state of their environment.

2.1.2. Definition of risk

Food sources may vary in quality and are distributed in space and time, therefore foragers experience a number of decisions while searching for food. In the foraging literature, the study of risk concerns how foragers choose between probability distributions to optimize patch choice, and subsequently increase their chances of survival. While risk is referred to as ‘variance’ in the foraging literature, this term is also used in connection with danger of predation that has been implicated as a major selective force in the evolution of several morphological and behavioral characteristics of animals (Kacelnik and Bateson 1996, Lima and Dill 1990).

In real life, an action or event whose consequences cannot be fully predicted is a potential source of risk. Researchers use microeconomic models to explain how animals and humans make decisions under risky conditions. Whereas they maximize their gains and minimize losses during good decisions, bad decisions have the reverse effect. Knight (1921) conventionally distinguished decisions under risk and under uncertainty, and this convention has influenced the use of these terms in current

microeconomic models. While a measurable probability of future events is referred as risk, uncertainty (referred to as ambiguity) denotes an unknown probability of possible outcomes. Kaufman (2012) described risk as 'known unknowns'. In a Russian roulette game with a six-chamber revolver, if the player knows how many bullets the revolver includes, the decision to pull the trigger is stated as risk. With X bullets, where the probability of dying is X/6, the probability of staying alive is (6-X)/6. If the player doesn't know the number of bullets in the revolver (zero to six bullets can be in the revolver), then the decision is said to be made under uncertainty. In uncertainty cases, it is not possible to predict the future reliably, based on the past events. In the experiments that are conducted with animals and humans, the 'unpredictability=risk' principle is traditionally used to guide the study of their risk-taking behavior. Individuals are trained to freely choose between two options. In the constant option, an animal can learn exactly how much food it will obtain, how much time will be needed to take the food, or how many times it will have to respond to gain the reward. In the variable option, the animal can face variance in delay, in the amount or in the number of responses to get the food. Individuals are said to take risk when they choose the option associated with variability instead of choosing the more reliable constant option. Bateson and Kacelnik (1997) stated that distinguishing the effects of risk and uncertainty is impossible, because they cannot be tested separately. Anselme (2015) has extended this presupposition, suggesting that in the absence of the unpredictability there is no risk, but unpredictability alone does not cause the occurrence of risk. In the risk-taking experimental methods, individuals have no resources of their own to potentially lose. When an individual's own resources are limited or jeopardised, then reward variability can be associated with risk. However, all experimental manipulations maintain animals' energy budget constant over the training sessions, hence their own resources are not at stake. If an individual could not obtain enough food because of choosing the bad key, extra food will be provided in its own cage to maintain its constant weight. In experiments, loss is only represented as an absence of optimal/desired gain, therefore they investigate the effects of uncertainty rather than the effects of true risk. Despite the differences that distinguish the use of the word "risk" in natural and experimental conditions, we will refer to risk as a synonym of variance, parallel to the existing literature.

2.1.3. Risk-sensitive foraging theory

In nature, foragers encounter variable feeding options, and their daily energy intake can exhibit changes. For example, Guillemette et al. (1993) showed that when feeding on small mussels, the total daily intake of a wintering eider (*Somateria mollissima*) could vary between about 800 and 1,800 kJ (with a coefficient of variation around 12%). Eiders experience even more variance when feeding on large crabs (coefficient of variation around 23%). Even if food is abundant in the environment, and

the animals do not face life-or-death foraging decisions, they must have adequate energy for life-sustaining objectives such as mating, reproducing, and raising offspring. Therefore, animals should be sensitive to these variances in order to acquire adequate energy for these objectives. Animals tend to be risk-sensitive; when an animal is allowed to choose between two foraging conditions that differ in their risk levels, it may show a preference for risky option even if this might mean choosing the option that offers a somewhat lower average rate of gain (Kacelnik and Bateson, 1996). There are some natural and artificial factors in unpredictable environments that can push animals to adopt this type of strategy.

2.1.3.1. Energy budget rule. Caraco (1980) proposed energy budget rule and formulated the risk-sensitive foraging theory in this rule's context. It has been influential not only in behavioral ecology (Kacelnik and Mouden, 2013) but also in other fields such as psychology, economics, and anthropology (Kalenscher and van Wingerden, 2011; McDermott et al., 2008; Mishra, 2014; Winterhalder et al., 1999). The energy budget rule states that an animal under a positive energy budget should be risk-averse, and prefer alternatives that offer constant amount of food as this preference can reduce the chances of an energetic shortfall that could cause starvation (Caraco, 1980; Stephens & Krebs, 1986). Likewise, an animal under a negative energy budget should be risk-prone, and prefer the variable alternatives for the possibility of receiving a large amount of food to meet its energy requirements. A sigmoidal relationship between an animal's energy state and fitness briefly clarifies the energy budget rule (Caraco, 1980; Real and Caraco, 1986): an animal under a negative energy budget may tend to be risk-prone because the average fitness for a variable energy state exceeds that for a constant energy state. On the flip side, an animal under a positive energy budget loses more than it gains by a variable energy state, which may lead to risk-averse choices (Figure 2.1).

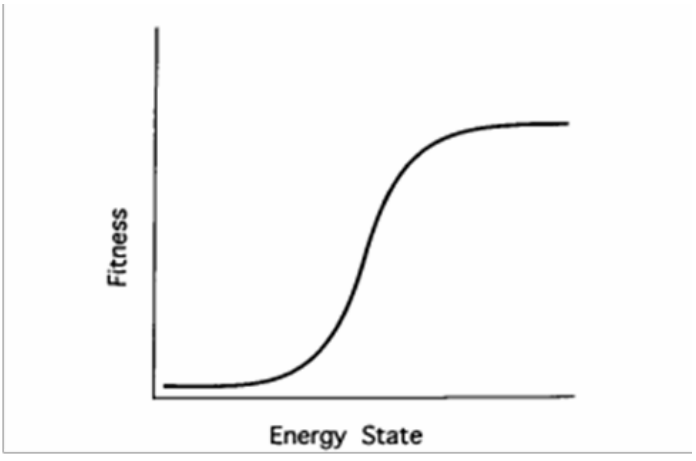


Figure 2.1. A sigmoidal relationship between energy state and fitness. An animal with negative energy state (concave-up region) may be risk-prone, an animal with a positive energy state (concave-down region) may be risk-averse (Smallwood, 1996).

Caraco et al. (1990) tested yellow-eyed juncos (*Junco phaeonotus*) under both negative and positive energy budgets. Negative and positive energy budgets were maintained at 1 °C, at 19 °C respectively. When expected energy budgets were negative, significant preference for high reward variance was observed. During the positive energy budget, low variance was preferred generally. Also in response to a temperature change, there was a shift between risk-prone and risk-averse behavior. According to the energy budget rule, when the expected rate of energy falls below the required level, low variance can contribute to starvation and high variance can provide better chances for survival. In contrast, when an animal is on a positive energy budget, low variance can ensure survival and high variance can increase the probability of starvation (Caraco 1981, 1982).

Despite its initial successes, the energy budget rule has been challenged. Kacelnik and Bateson (1996) and Kacelnik and Mouden (2013) reviewed published empirical studies that manipulated the energy budget rule, and stated that there is a lack of robust support for the energy budget rule. They classified all papers that supported the rule since 1980, or not (Figure 2.2), and showed that empirical support for the energy budget rule has declined with time. Despite its logical implications, when risk-sensitivity theory is formulated in terms of the budget rule, it fails to predict behavior. One of the major failures in a lot of experiments of budget rule is an insufficient understanding of the actual energetic status of the animals, and how it relates to fitness and the utility function (Mayack and Naug, 2011). The experiments yielding negative results against the budget rule involve larger species than those yielding positive results (Kacelnik and Bateson,1996). The application of the energy budget rule to large species is perhaps not suitable, because short-term energy requirement does not impact their survival, as opposed to the situation in the small animal groups (Caraco et al., 1990).

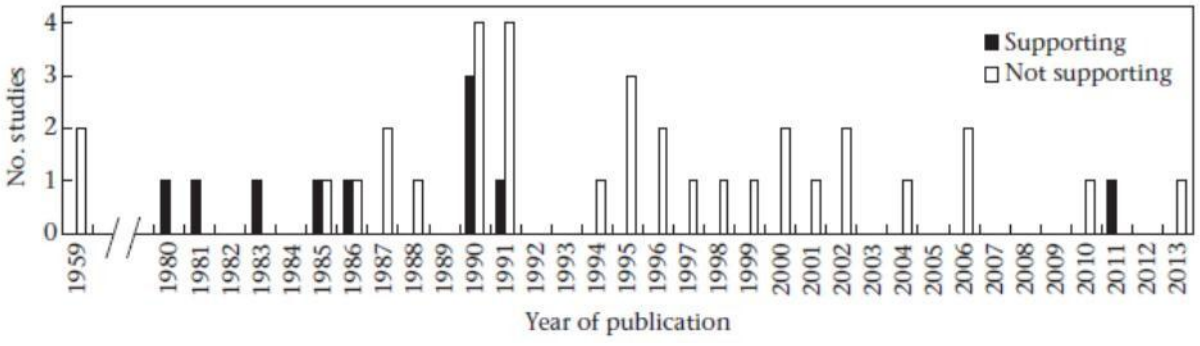


Figure 2.2. Studies that has supported or not supported energy budget rule since 1980 (Kacelnik and Mouden, 2013).

2.1.3.2. Natural and artificial effects on foraging. Animals search, detect, capture and consume many preys in order to survive and reproduce. Especially for the small-sized animals, the right foraging

decisions highlight the struggle for life and death as mentioned previously. Hurly and Oseen (1999) tested the risk-sensitive foraging preferences of rufous hummingbirds with three types of artificial flowers. All types of flowers provided the same mean volume of sucrose (30 μL), but they differed in terms of reward variability: constant, low variance and high variance. In trinary comparisons, birds preferred low variance reward over the constant reward, and the constant reward over the high variance reward. However, when the subjects were tested under binary conditions, they selected the constant reward over the low and high variance. This reversal emphasized the effects of the local context on foraging decisions.

Like birds, well-directed foraging decisions are crucial for mammals that have to maintain a high and constant body temperature during their daily activities. The common shrew, *Sorex areneus*, has an extremely high mass-specific metabolic rate, and due to its small body size, its body surface area is very large relative to body volume. A high surface/volume ratio results in rapid energy loss due to elevated thermic exchange with the external environment. This means that shrews are unable to sleep longer than a few hours at a time; a few hours without feeding can lead to death. During foraging, they have to take into account the energy gain associated with the consumption of prey, but also the costs associated with searching and handling. When they encounter a single prey or prey's nest, they have to estimate the pay-off and make the right decision to survive. Whereas handling a single prey and searching for a new one takes some time, nests are dispersed in the environment, and finding nests also requires a stroke of luck (Saarikko, 1989).

In addition to these natural effects, an animal must cope with the results of destructive human actions on their environment. Humans have altered their surroundings through deforestation and erosion (McGlone, 1983; Van Andel et al., 1990). Also invasive species, which have high biological flexibility, and can alter food web dynamics in an ecosystem through destruction or replacement of native food sources, have been introduced by humans. These nonnative species alter animals' survivorship and reproductive success. While vulnerable animals are faced with extinction, others can habituate to the presence of detrimental human activities and modify their behavior. For instance, due to a human-caused "biodiversity crisis", almost 2000 bird species have gone extinct in the tropical Pacific (Steadman, 1995). In contrast, Peck et al. (2014), tested the behavioral responses of native garden birds to the presence of a rose-ringed parakeet (*Psittacula krameri*), which is listed as one of the top 100 most invasive alien species in Europe (Vilà et al. 2009), versus the presence of a similar sized and also dominant native bird species, the great spotted woodpecker (*Dendrocopos major*). Under the influence of parakeet, reduced feeding rates and increased vigilance was observed among native birds, when compared to the control treatments.

2.1.3.3. How risk is generated in the lab conditions. Kacelnik and Bateson (1996) listed studies on different taxonomic groups (insects, fish, birds, and mammals) to show that animals are sensitive to variance; depending on testing conditions, animals may tend to prefer, avoid, or show indifference to risky food sources relative to alternative non-risky food sources. Several methods exist to test risk-sensitivity in animals.

In ratio schedule experiments, a constant option always provides reward following a fixed number (ratio) of responses, and a variable option provides reward following a variable number (ratio) of responses. During the training sessions, the animal learns that the constant option is more reliable than the variable option, for which the number of responses to obtain reward is unknown in advance. For instance, in one study, pigeons were given choices between a fixed-ratio (FR) schedule of food delivery that required 15, 30, or 60 responses and bivalued variable-ratio schedules of one and 120 with an arithmetic mean of 60.5 (Ahearn et al. 1992). The bivalued schedule was preferred by the pigeons. There was a shift of preference for a bivalued schedule of 15 and 105, most notably in the FR-15 condition.

Another method focuses on responses to variability in amount of reward. In amount schedules, animals have to choose between a constant option that provides small certain reward (e.g. three items) and a variable option (e.g. one or five items). Real (1981) discovered the influence of variability in nectar reward per flower on the foraging behavior of individual bumblebees (*Bombus sandersoni* FkIn.) and paper wasps (*Vespula vulgaris* L.) with combined amounts and probabilistic schedules. In a first experimental set, blue and yellow flowers, that offered equal volumes of nectar reward, were prepared for the bumblebees. Individual foraging bees showed increased preference for the yellow flowers. However, when the blue flowers were kept constant in terms of nectar volume (2 μL in each) and the yellow flowers offered a variable nectar volume (6 μL with a 33% probability and nothing in the remaining flowers), the individual foraging bees preferred the blue flowers, even though the expected gain from the two floral types was equal. In order to control that bees were avoiding uncertainty rather than the empty flowers, a new experiment was conducted. In this case, the constant floral type contained 2 μL of nectar in every flower, while the variable type contained 5 μL with a 33% probability. Individual foraging bees again preferred the constant type (Figure 2.3). Wasps behaved in a similar way; when one floral type was variable and the other was constant, wasps preferred the constant type (Real, 1981).

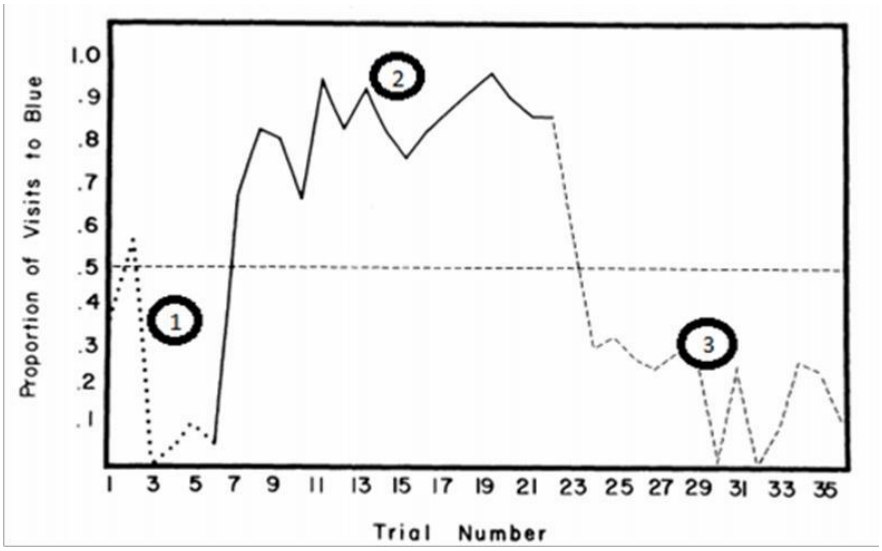


Figure 2.3. The influence of variability in nectar reward per flower on the foraging behavior of individual bumblebees (*Bombus sandersoni* FkIn.). Individual foraging bumblebees' visits to blue flowers. 1- Yellow and blue flowers were of equal quality. 2- Blue flowers were constant and yellow flowers were variable. 3- Yellow flowers were constant and blue flowers were variable. Constant flowers contained 2 μL nectar each; variable flowers contained 6 μL with a 33% probability or nothing (Real, 1981).

In other types of experimental setups, the risk was generated by variability in delay. Bateson and Kacelnik (1997) examined starlings' (*Sturnus vulgaris*) preferences for predictable and unpredictable delays in obtaining food. The 12 wild-caught European starlings (six males and six females) were divided into two groups, categorized as the 'risk-free' and the 'risky'. In each group, the birds had to choose between a 'variable option' and a 'fixed option'. As illustrated in Figure 2.4, for both options a single trial had six delayed reinforcements. In the fixed option the six delays of reinforcement were identical (τ). In the variable option each of the six delays of reinforcement was either 3 seconds (short) or 18 seconds (long). The risk-free group's first variable option was always short and the sequence was predictable (3, 18, 3, 18, 3, 18 seconds). The risky group's first variable option was also short; however, the rest of the sequence was unpredictable. Within a session, there were two types of trials, 'forced trials' and 'choice trials'. In the forced trials, the birds were exposed to only one option (fixed or variable) in order to experience them separately. In the choice trials, the risk-free and risky options were presented simultaneously, and the birds had to show their preference in every trial.

Depending on their preference for the constant or the variable option, animals are referred to as risk-averse or risk-prone, respectively. Whether animals are risk-averse or risk-prone not only depends on the type of variance, but also on the energetic status of the forager. The results showed that on negative energy budget, both of the groups above were significantly risk-prone. A comparison

between the risky group and the risk-free group indicated that the former was more risk-prone than the latter. Also switching the birds from negative to positive energy budget did not have any significant effects on preference. According to the risk-sensitive foraging theory, preference for one or the other option should be observed only in the risky treatment, where the variability also involved unpredictability. Since both risky and risk-free groups of starlings were significantly risk-prone on negative and positive energy budgets, the outcomes of this experiment did not support the earlier prediction strongly that claims the energetic status of the forager is mainly effective on animals' tendency for being risk averse or risk prone.

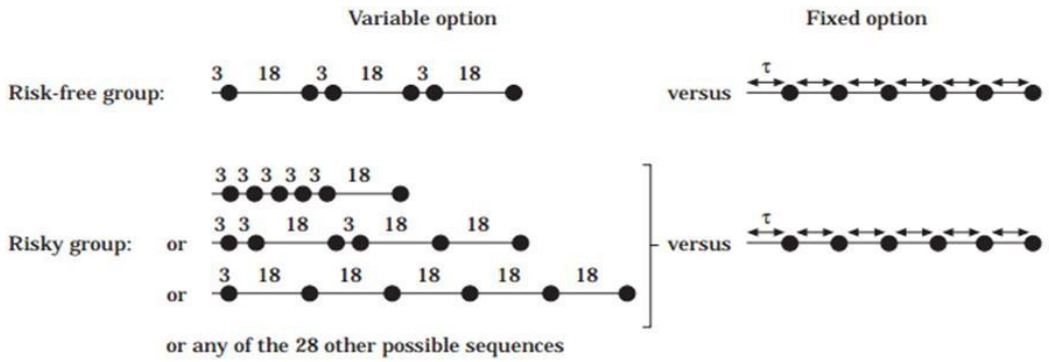


Figure 2.4. Starlings' (*Sturnus vulgaris*) preferences for predictable and unpredictable delays to obtaining food. In the variable option of the risk-free group, the sequence was predictable (3, 18, 3, 18, 3, 18). There were 31 possible sequences for the risky group's variable option. For both groups, the delay was adjusted in the fixed option (Bateson and Kacelnik, 1997).

2.2. Dopamine's Role on Pigeons' Foraging Decisions

Rewards and conditioned stimuli (any signal that predicts reward delivery-CS) are crucial components of life; they motivate animals and humans to eat, drink and mate (Schultz,2015). According to behavioral scientists, a reward is an event that increases the rate and probability of approach behavior (White et al., 2007). Besides this simple explanation, reward is a complex process containing several psychological components: 'liking', 'wanting', and associative learning. 'Liking' is the hedonic impact of a reward, that is, the pleasure/displeasure felt during its consumption. Associative learning is the change in associative strength between a reward and its predictive CS over repetitions. The third component of reward, 'wanting' or incentive salience, promotes the approach toward and the physical contact with the rewards (Berridge et al., 2009). In this thesis, I am only interested in the process of incentive salience. The aim of this chapter is to describe incentive salience and incentive sensitization theories, therefore 'wanting' component of reward will be discussed with more details.

2.2.1. Incentive salience theory

The central premise of incentive salience theory is that rather than altering 'liking' or learning, dopamine mediates the 'wanting' component of reward; dopamine is pivotal in causing motivational attraction for rewards (Robinson and Berridge, 1993). Incentive salience is mediated by mesocorticolimbic brain systems (Robinson and Berridge, 1993; Berridge, 2007). When something rewarding occurs, such as the smell of a delicious food and the anticipation of winning a lottery game, the brain responds by increasing the release of dopamine. The mesolimbic dopamine pathway is known to play a major role in the reward system. It connects the ventral tegmental area (VTA), one of the principal dopamine-producing area in the brain, with nucleus accumbens (NAc). Following the (unexpected) delivery of rewards like food, water, and sex, dopamine neurons in VTA get activated. These dopamine neurons project to the NAc via the mesolimbic dopamine pathway, and their activation increases the dopamine levels in NAc, where dopamine receptors D1 and D2 are abundant. The other reward-related pathway is the mesocortical dopaminergic pathway, which also originates in VTA but travels to prefrontal cortex (PFC), and is known to be important for a wide range of functions, such as motivation, emotion, and executive functions (Figure 2.5).

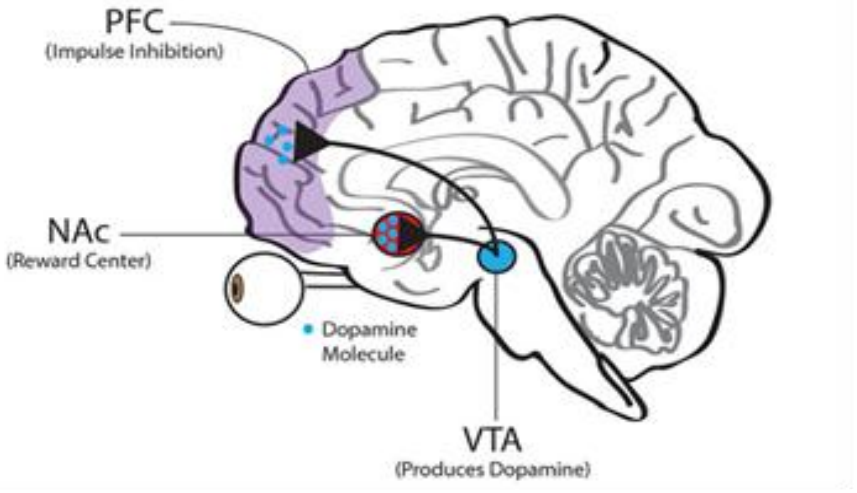


Figure 2.5. Rewards activate dopamine neurons in VTA, and increase dopamine levels in NAc (mesolimbic dopamine pathway). When a reward occurs, PFC also receives dopamine from VTA (mesocortical dopamine pathway).

To illustrate the role of dopamine on reward components, many experiments have been conducted with different animals. For example, Berridge and Robinson (1998) tested rats to observe the effect of dopamine on the liking component of reward. Experimental rats received a dopamine-selective neurotoxin (6-hydroxydopamine) to cause extensive dopamine depletion in the neostriatum

and NAc, while control rats were injected with the vehicle (saline) solution only. A sucrose solution was used to elicit the hedonic appetitive reactions in both groups. The sucrose-elicited hedonic responses (such as tongue protrusions, lateral tongue protrusions, and paw licks) did not differ between the two groups. These data suggested that extensive dopamine depletion in the neostriatum and NAc did not change rats' 'liking' responses to sweet stimuli. Also, dopamine deficient (DD) mice have been used to examine the connection of reward learning and dopamine. DD mice lack the tyrosine hydroxylase enzyme and cannot synthesize dopamine in their brain (Berridge, 2007). Cannon and Palmiter (2003) showed 'reward learning without dopamine' in DD mice. Although the DD mice had no dopamine in their brain, they could still learn the preference for a spout that delivered sucrose solution over a spout that delivered water. Their learned spout preference was comparatively equal to that of the control mice, which showed that dopamine was not sufficient for 'learning' by itself.

Besides these experiments, dopamine antagonists, whose action is to pharmacologically block access to dopamine receptors, have been used to show the role of dopamine in obtaining rewards. For instance, Ikemoto and Panksepp (1996) monitored appetitive behaviors of rats which had received microinjections of the dopamine D1/D2 receptor antagonist cis-flupentixol into the NAc, and they showed the requirement of dopamine to approach rewards. Rats' approach speed to the reward and anticipatory shuttle box activity were severely reduced under cis-flupenthixol. Cousins et al. (1996) also trained rats on a T-maze task under 6-hydroxydopamine which is used to selectively destroy dopaminergic neurons in the brain. In the first test condition, one arm of the maze that was obstructed by a barrier provided a high reinforcement density (4 x 45 mg pellets), whereas the other arm contained a low reinforcement density (2 x 45 mg pellets) without any barriers. In the other test condition, a separate group of rats was trained in the same T-maze in which there were four food pellets in the arm that was obstructed by a barrier, yet there were no food pellets in the unobstructed arm. After training, these two groups of rats were injected with 6-hydroxydopamine or ascorbate vehicle into the NAc. The results indicated that compared to the control group, dopamine-depleted rats decreased the number of selection of the obstructed arm with the high reinforcement density when the unobstructed arm contained two food pellets. When the unobstructed arm provided no food pellets and the only way to gain the food was to climb the barrier, dopamine-depleted rats showed significantly higher barrier crossing than the dopamine-depleted rats that were tested with food in the unobstructed arm.

In laboratory studies, the cues paired with reward gain incentive salience; they act as motivational 'magnets' that pull the animals to approach the reward. In some cases, attribution of incentive salience to reward predicting cues may make the cues 'wanted' as much as the reward itself

(Robinson et. al,2013). Moreover, the cues may become more irresistibly attractive, the animals may even try to eat or drink levers that predict food or water, rather than to be away from the real reward and lose it. For instance, some cocaine addicts can be found checking the floor for a white speck that is more likely to be a pebble rather than crack cocaine. They may even try to smoke this noncocaine pebble (Berridge, 2007)). Likewise, a pigeon may try to eat-peck or drink-peck a CS that is just an illuminated plastic key and previously associated with unconditioned stimulus (UCS) like grain or water (Figure 2.6) (Jenkins and Moore,1973).

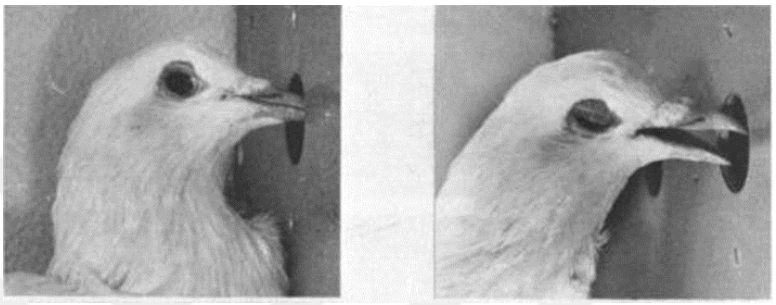


Figure 2.6. Pigeon's responses to CSs. The photograph on the left shows the response to the cue that was paired with water; the photograph on the right shows the response to the cue that was paired with food (Jenkins and Moore,1973).

2.2.2. Incentive sensitization theory

Most people have used a potentially addictive drug at least once in their lifetime (if we count nicotine, alcohol and caffeine, in addition to illegal drugs). While the vast majority of individuals does not face problems, for relatively few people the casual use of these drugs leads to compulsive patterns of abuse with detrimental outcomes (Thomsen et al., 2014). Incentive sensitization theory suggests a promising description of how drug-induced alteration in psychological functioning can cause a transition to addiction, which implies a pathological and compulsive pattern of drug-seeking and drug-taking behaviors (Hasin et al. 2006), as well as accounts of relapse.

Incentive sensitization theory was put forward by Robinson and Berridge (1993), which states that prolonged exposure to a drug of abuse (such as cocaine and amphetamine) causes a gradual sensitization (hypersensitivity) of dopamine neural systems that normally attributes incentive salience to reward cues, such as food. Neural sensitization is responsible for the abnormally strong appetency for such drugs and may cause addiction. Sensitized neural systems also react powerfully to drug-relates cues, which predict that drug is to be delivered soon: a drug acts as an UCS, and its repeated administration in association with CS makes these stimuli attractive as well (Braga et al., 2009). Drug

CS gets to be desired (Robinson and Berridge, 1993), preferred (Moeller and Dougherty, 2002), capture attention (Franken, 2003; Field and Cox, 2008; Lubman et al., 2000), and cause a variety of physiological and psychological responses (Childress et al., 1993; Childress et al., 1999; Volkow et al., 2003). Robinson and Berridge (1993) suggested that even though each of the reward components ('liking', 'wanting' and 'learning') plays a role in the development of drug use, the 'wanting' component alone makes drug addiction compulsive and resistant to recovery. Even though 'wanting' and 'liking' of the drug are strongly connected in the initial use of drug use, just 'wanting' becomes sensitized and addiction occurs (Figure 2.7). Drug detoxification may remove the withdrawal symptoms like dysphoria, anxiety, and irritability. However, even a significant period of drug abstinence in addicts does not suppress neural sensitization, whose effects are assumed to be quasi-permanent. When the mesolimbic system has been sensitized to the incentive motivational value of drug-associated cues, some proportion of individuals re-exposed to those cues (objects, location, friends, etc.) can relapse even after a long period of recovery.

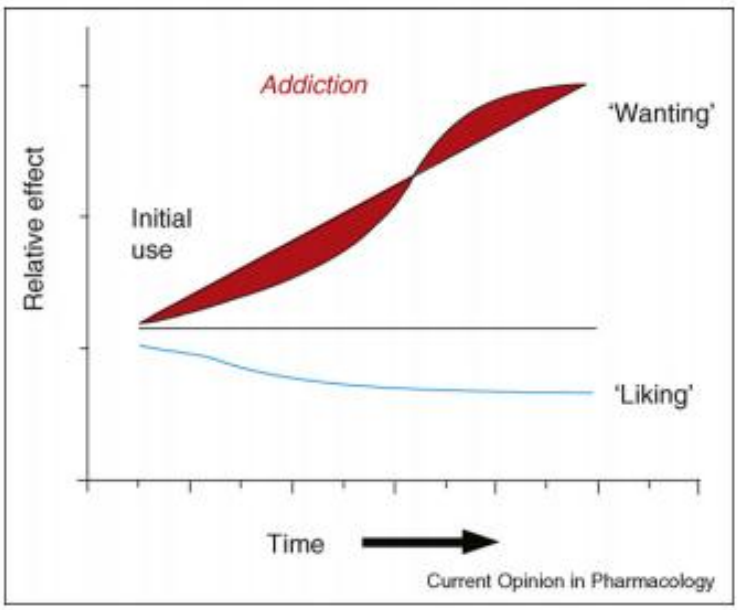


Figure 2.7. Incentive-sensitization model of addiction. 'Wanting' to take drugs may increase over time independently of 'liking' - the pleasure from using drugs. Sensitization does not increase 'liking' reactions. Humans who are becoming drug tolerant report that the dose of drug no longer gives as much pleasure as it did initially, although drug 'wanting' may increase over time (Berridge et al., 2009).

Sensitization is a complex process that is affected by the dose, the timing, and the time interval between the drug administrations, the environment in which drug is taken, and the predispositions of the consumer (genes, sex, hormonal status, etc.) (Robinson et al., 2013). Sensitization becomes

stronger with intermittent injections at high dosages. To illustrate the dose-effect relationship, Ferraio et al. (2005) allowed rats extended (six hours/session) or limited access (one hour/session) to self-administrated cocaine in an experimental chamber that had one active nose-poke port (resulting in the delivery of cocaine) and one inactive nose-poke port (no consequences). One month after the last exposure to cocaine, they were tested for sensitization with a challenging dose of cocaine. Rats, which had been allowed an extended cocaine access showed greater drug-seeking behavior, and made more responses to the active nose-poke port in the experimental chamber that was correlated with cocaine before. Also, their head movements were more intense than those of the rats which were exposed to more limited levels of cocaine, suggesting that they were sensitized to the psychomotor activating effects of cocaine. Crombag et al. (2001) examined the importance of environmental context on the development of sensitization. Rats were divided into three groups; the first group was housed in the test cages where they were injected and tested, a second group was not habituated to the test cages (they were transported each day from their home cage in the animal colony room to the test cages, and they immediately received the injections), and the last group was housed in the main animal colony, similar to the second group, and they were transported daily to the test cages and were injected after one or six to eight hours of habituation. Injections were made intravenously, and for all groups the test cages were identical. When amphetamine was injected immediately after placement into the behavioral test environment, they observed rotational behavior on the first test day, and robust sensitization developed with repeated daily injections. When the same treatment was applied to the first group, there was a small acute response and sensitization did not occur. The enhanced acute response seen in the behavioral test environment was significantly decreased after one hour of habituation to the test environment, and completely disappeared after six to eight hours of habituation.

2.2.3. Dopamine and reward uncertainty

Birds and mammals tend to prefer the uncertain option, whether in autoshaping or during free-choice. In a typical autoshaping experiment with rats, a metal lever emerges from a wall for several seconds as a CS to foresee an immediately subsequent presentation of a rewarding UCS such as palatable food (Robinson et al., 2014). No action is needed to gain the food, but rats are mostly active: sign-trackers approach and interact with the CS (vigorously sniffing, nibbling, biting, grabbing, pressing lever), goal-trackers approach and interact with the food dish (sniffing and nibbling the location where the sucrose reward will appear). There are also some other individuals showing comparable amounts of attention to both CS and UCS. By traditional views, CS-USC association may enhance the attractiveness of CS. However, in some cases, lower predictability might result in greater motivation. For instance, Anselme et al. (2013) demonstrated that reward unpredictability has an

incentive value. This study showed that an uncertain CS (50% trials were rewarded) that predicts an uncertain magnitude of UCS (reward was either one, two or three sucrose pellets on a random basis) could attract more approaches and nibbles than a CS that predicted reward delivery (one sucrose pellet) with 100% certainty. Cocker et al. (2012) also investigated rats' risk-taking behavior in a free-choice task. On every trial, rats selected between a safe lever delivering a known number of sugar pellets (range 1–3), versus an uncertain lever providing 50% chance of twice as much as the safe lever or receiving nothing. Overall rats showed risk-seeking behavior by choosing the uncertain lever on more than 60% of the trials. Bateson and Kacelnik (1997) manipulated reward distribution and showed starlings' tendency to a variable-delay option as opponent to a fixed-delay option is higher when variance is unpredictable than when variance is predictable. Johnson et al. (2011) examined rat's choices to earn food reinforcement by completing VR or FR response cases under other dopamine D2/D3 receptor agonist, pramipexole. While VR mimics a gambling-like preference, FR represents predictable rewards. There was a measurable increase in gambling-like behavior when pramipexole was administered acutely, it magnified preference for a VR over a FR in rats. This suggests that pramipexole promotes a preference for reward unpredictability over reward maximization.

While unpredictable rewards have an excitatory effect on behavior, and can cause an increase in the CS-directed motivation, the reasons underlying this mechanism must be investigated. In this respect, pharmacobehavioral researches mainly focus on mesolimbic dopamine, which is the chief neuromediator of incentive motivation. Zald et al. (2004) examined what happens in the human brain during unpredictable reward situations, such as gambling. They used positron emission topography scanner to observe brain activity. Different unpredictable and predictable scenarios were used. In the unpredictable scenario, the participations selected one of four cards and knew a monetary reward of $1 but they were not sure when it would occur. In the predictable scenario, the participants knew in every fourth card they selected, they would be rewarded by $1. In control condition, the same task was applied without rewards. Compared to the control condition, the predictable scenario caused only modest increases in dopamine transmission and no decreases. In contrast, unpredictable scenario generated significant increases in dopamine transmission in the left medial caudate nucleus, while simultaneously producing significant decreases in neighboring regions. This data showed the specific influence of unpredictability on dopamine transmission.

Dopamine's role in coding reward uncertainty has been supported by many behavioral studies, with mammals and birds responding more strongly to conditioned cues that predict uncertain rewards (Collins et al., 1983; Anselme et al., 2013). For instance, Tremblay et al. (2017) examined the effects

of a dopamine $D_{2/3}$ receptor agonist (ropinirole) on rats. After receiving saline or ropinirole injections, the subjects had to choose between a safe lever that delivered a guaranteed amount of sugar reward or an uncertain lever that delivered either double the safe reward or nothing with a 50% probability. Ropinirole application increased the selection of the uncertain option in two thirds of the rats, compared to the baseline values (Figure 2.8).

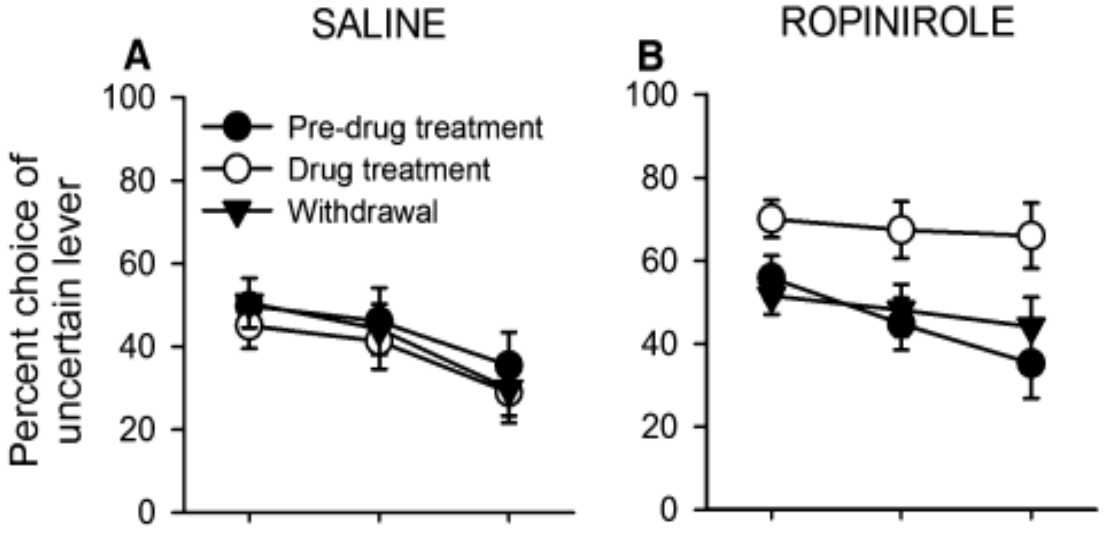


Figure 2.8. Percent choice of the uncertain lever for all rats in the saline (A) and in the ropinirole-treated (B) animals. Compared with baseline selection, ropinirole injected rats increased their choice on the uncertain option (Tremblay et al., 2017).

Besides these animal studies, the mesolimbic dopamine's role in gambling-like choice was also investigated in humans. Compared with healthy controls, pathological gamblers exhibited higher dopamine levels during a gambling episode (Linnet et al., 2011; Joutsa et al., 2012). In line with the animal data, the unpredictability of reward delivery in humans is also more effective in releasing dopamine than the reward per se. This suggests that the inability to foresee reward occurrence is strongly responsible for the motivation behind gambling behavior. Despite the fact that players attempt to maximize their gains, unpredictability holds their interest, because full predictability is dull (Anselme and Robinson, 2016). According to the traditional view, the primary motivation of gamblers is money, but Linnet et al. (2010) showed that pathological gamblers losing money had significantly higher dopamine release than pathological gamblers winning money. There was no dopamine release difference between pathological gamblers and healthy controllers who gained money. Other studies conducted with both monkeys and healthy human participants have shown that reward uncertainty rather than reward per se, increases dopamine (Fiorillo et al., 2003; de Lafuente and Romo, 2011; Preuschoff et al., 2006).

Pathological gambling is also a rare potential complication related to the treatment of Parkinson's disease (PD). Likewise, other impulsive control disorders like compulsive shopping and hypersexuality associated with dopaminergic therapy are common in PD, and occur in 13,6% of patients (Weintraub et al., 2010). PD is primarily treated with drugs that improve or restore the brain dopaminergic neurotransmission (Dodd, et al., 2005). Dodd et al. (2005) investigated 11 PD patients who suffered from pathological gambling and from other impulsive control disorders. Eighty-two percent of the patients were cured with pramipexole, though increasing dopamine levels in brain. Riba et al. (2008) reported that healthy humans placed larger bets following unexpected wins when given acute pramipexole (0.5 mg).

2.2.3.1. Apomorphine as a Dopamine Agonist. Apomorphine (Apo) is one of the first dopaminergic drug shown to improve impulsive disorders (Subramony, 2006). Apo is a dopamine agonist because its molecules add their effects to those of dopamine in the brain, and this drug has a pharmacological action on any type of dopamine receptor (D1-like and D2-like). It has been used in many experiments involving animals. For instance, Voikar et al. (1999) examined Apo-induced behavioral sensitization in male Wistar rats. The acute administration of Apo (0.5 mg/kg) did not alter the locomotor activity of rats, and only stereotyped behaviors such as gnawing, licking and sniffing were observed. After repeated injections of Apo (0.5 mg/kg twice a day for 14 consecutive days), a significant increase in locomotor activity was detected (Figure 2.9). Locomotor activity was measured in the open-field test on the 1st, 7th and 14th day of injections, through the counts of line crossing that is described as the frequency with which the rodent crossed a grid line with all four paws. One third of the rats did not react with increased locomotor activity even after two weeks of Apo injections (weak responders), whereas another one third increased locomotion after a few injections (strong responders). The last third group's responses were between the weak and strong responders (intermediate responders). In another study, Bloise et. al. (2007) showed that one or two days of Apo administration (0.5 and 2.0 mg/kg) caused behavioral locomotor sensitization on rats. This result suggests that sensitization processes can occur with a single drug exposure and increase with exposure to a higher drug dosage. The sensitization effect was context-specific; the same Apo treatment given outside of the test environment did not produce sensitization. The sensitization effect was observed with respect to locomotor behavior; other behavioral measures like sniffing and rearing did not provide indication of sensitization. To investigate the differential dose-effect relation, two treatments with 2.0 mg/kg and 0.5 mg/kg Apo were applied. While two treatments of 2.0 mg/kg Apo increased locomotor sensitization, compared with a single treatment of 2.0 mg/kg, two treatments with 0.5 mg/kg did not increase the sensitization effect more than the single 0.5 mg/kg treatment.

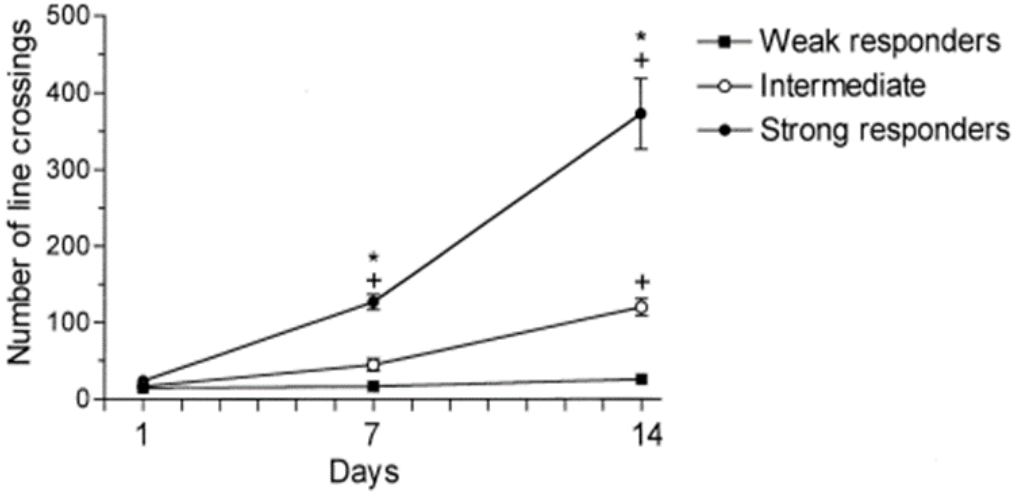


Figure 2.9. Apo-induced sensitization in Wistar rats. Rats were injected with Apo (0.5 mg/kg s.c. twice a day) for two weeks. On the 1st, 7th and 14th day on injection, locomotor activity was measured in the open-field test (Voikar et al., 1999).

In birds, the intramuscular injection of 1 mg/kg Apo induces a protracted bout of pecking involving several thousands of pecks within 30 min and lasting for more than one hour (Brunelli et al. 1975). In contrast, a control injection of saline caused a maximum of around a dozen of pecks during the same period of time. Acerbo and Delius (2004) also investigated Apo infusion effect in pigeons. Under anesthesia, pigeons were implanted (into the caudal striatum) with osmotic pumps. Half of the pumps were filled with an Apo solution (0.5 mg/kg/day), and the other half were filled with a saline solution. During the infusion, pigeons were kept in white-walled, green-dotted experimental cages. When the infusion had ended, pigeons were placed into their home cages and no injections were given for two days. Next, for six consecutive days, all the pigeons were injected daily with 0.5 mg/kg Apo and placed into the experimental cages for 20 min. On day 1, the Apo-preinfused pigeons pecked significantly more than the control saline preinfused pigeons (698 ± 157 against 205 ± 150 pecks/20 min). On the other hand, the near-asymptote level reached by the Apo preinfused group was lower than the saline preinfused group (day 6: 1986 ± 187 against 2950 ± 237 pecks/20 min, $p < 0.01$), which can be explained as a tolerance effect. Thus, with intermittent Apo administration, infusion may induce the development of Apo tolerance rather than sensitization. Godoy et al. (2000) pointed out to a similar result when pigeons were presensitized with 0.2 mg/kg Apo, and switched to a daily treatment dose of 0.5 mg/kg Apo. They observed higher pecking rates on day 1, compared to the other treatment days. Pharmacobehavioral studies have shown that the activation of both D_1-type and D_2-type receptors are involved in the pecking stereotypy elicited by

Apo in birds (Zarrindast et al.,1992). Acerbo et al. (2005) showed that compared to pigeons injected with saline, pigeons injected repeatedly with Apo have a higher density of dopamine D_1 receptors and a lower density of the dopamine D_2 receptors in the basal telencephalon. Studies on mammals also showed similar results. Mattingly et al. (1994) used selective D_1 (SCH 23390) or D_2 (sulpiride) antagonists on rats to determine if either could block the behavioral sensitization to Apo. Rats were injected with one of the antagonists, followed by an Apo injection. The results indicated that Apo caused a greater increase in locomotor activity, and that this Apo-induced increase in activity was completely blocked by both antagonists. While both antagonists blocked Apo-induced activity, only SCH-23390 prevented the behavioral sensitization to Apo. Rats pretreated with SCH-23390 and Apo did not show sensitization when subsequently tested with a challenging dose of Apo alone.

After repeated treatments with dopamine agonists or dopamine agonist-like drugs (such as Apo, amphetamine, bromocriptine, cocaine, and quinpirole), behavioral sensitization is either not observed or is significantly reduced, if the treatments are given in the animal's home cage rather than the test environment (Post et al., 1981; Mattingly and Gotsick, 1989). Battisti et al. (1999) designed a study to determine whether sensitization of the stereotyped behavioral effects caused by a single dose of Apo is dependent on environmental context in mice. While mice were pretreated with 40 mg/kg Apo and later tested in the same environment exhibited sensitization to Apo, mice which were placed in a distinct environment after 40 mg/kg Apo injection did not induce sensitization to Apo. Keller et. al. (2002) suggested that, like with rodents, increasing response to the drug in pigeons is partly dependent on the environmental context in which Apo takes effect. After Apo injections, before being returned to their home cages, pigeons were placed in an experimental cage for different durations (5 to 60 min-overall drug effect lasted for about one h). Subsequent tests in the experimental cage and home cage showed that after training with a 20 and 60 min of post-exposures, the pigeons pecked almost three times more in the experimental cage than in the standard cage (Figure 2.10). As another part of the study, groups of pigeons were placed either into the same experimental cage or into different experimental cages after Apo injections. Compared to the 'different-cage' group, the 'same-cage' group showed significantly stronger sensitization.

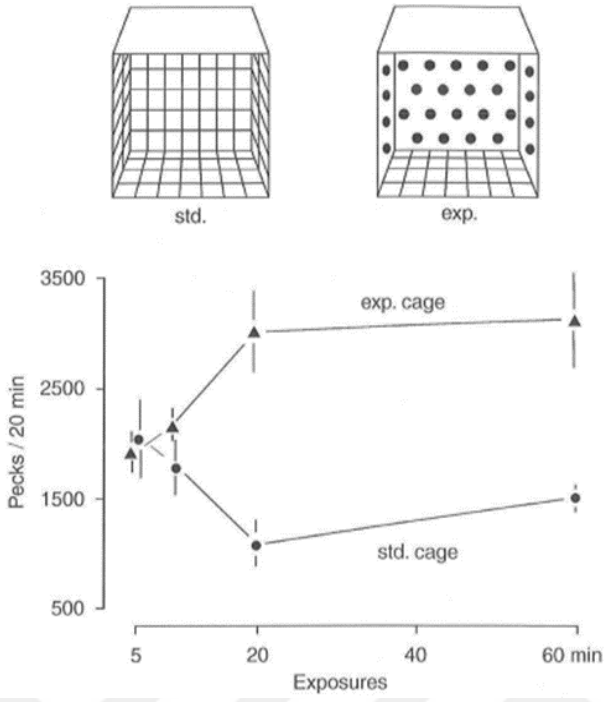


Figure 2.10. Pigeons' mean pecking scores during the test sessions in the experimental and standard home cages as a function of the exposure durations under the influence of Apo in the experimental cage during the training (Keller et al., 2002).

2.3. The Aim of the Study

Decision making under uncertainty has been extensively discussed in the literature. However, the exact role of uncertainty in controlling preference is not well understood. Also, the neurobiology of decision making under uncertainty has not been investigated in birds. Birds and mammals have diverged around 310 million years ago (Nei and Glazko, 2001), and there is evidence that important brain structures, such as the mammalian PFC and the avian nidopallium caudolaterale, evolved separately while being functionally equivalent (Güntürkün, 2012). Dopaminergic innervations in the nidopallium caudolaterale are similar to those observed in the PFC, so it is likely that dopamine exhibits comparable functions in these two brain structures. Nevertheless, more information is needed to determine whether birds use the same mechanisms as mammals making decisions.

The present study is the first to examine preference for variability under the systemic administration of a dopamine agonist, in birds. As previously stated, Apo has been used in pigeons and the exact dose-effect relations for pigeons is known. In this thesis, this dopamine agonist (Apo) is applied to add to the knowledge about decision processes in birds. More information about decision

making under uncertainty in birds will allow us to know whether its neurobehavioral relation can be generalized among higher vertebrates, including humans.

3. MATERIALS AND METHODS

This study comprised three experiments that aimed to understand the effects of Apo in decision making processes in pigeons. In Experiment 1, the pigeons were tested with a variable-delay (1-7 s) and a constant delay (4 s) in a free-choice task. Next, their preference was controlled under the systemic administration of Apo. In Experiment 2, different delay times were used for the variable delay option (2-12 s) and the constant delay remained same (4 s). Differently from Experiment 1, Apo sensitization phase was applied in a context that differed from that in which the pigeons were tested with variable and constant options. Next, the pigeons were subjected to an incubation phase without any treatment for 10 days. After incubation, to control their preference, the pigeons were retested again in a free-choice task. In Experiment 3, in addition to nine naïve saline pigeons, Apo-sensitized pigeons from Experiment 2 were reused. Differently from the previous two experiments, in this experiment the pigeons had to choose between a 50% probability of food delivery and a fixed 5-s delay in a free-choice task. Again, their preference was examined under the systemic administration of Apo.

3.1. Experiment 1

In this experiment, pigeons were given access to a fixed-delay option and a variable-delay option. The aim of this experiment was to determine whether Apo sensitization would induce a preference for a variable delay over a fixed delay.

3.1.1. Animals and housing conditions

The subjects were 9 adult homing pigeons (*Columba livia*- irrespective of gender) obtained from local breeders, which were previously used in unrelated experiments. All the pigeons were housed in individual wire-mesh cages with a 12 h dark-light cycle (lights on at 8 a.m.) (Figure 3.1). Pigeons were food-deprived and maintained at 80-85% of their free-feeding body weight while water was accessible ad libitum. All procedures (subjects' health and care, training period, etc.) were approved by a national ethics committee of the State of North Rhine-Westphalia, Germany.



Figure 3.1. Individual wire-mesh cages

3.1.2. Apparatus and stimuli

In all experiments for this thesis, pigeons were tested in a custom-designed training (or Skinner) box (35 cm height, 35 cm length and 40 cm width), illuminated by a house light. The training box was equipped with a feeder that was moved up or down to make food accessible or inaccessible to pigeons. It was located on the front panel of the Skinner box, equidistant from two transparent plastic keys (4 cm x 4 cm), on which the pigeons could peck. The pecking keys could be illuminated and displayed a specific pattern by means of an LCD flat screen behind the front panel (Figure 3.2).

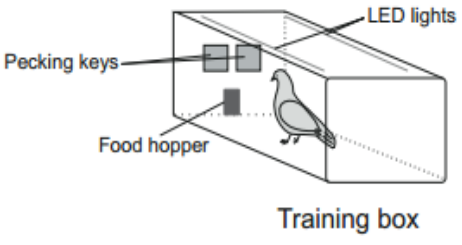


Figure 3.2. Schematic drawing of the Skinner box, which was equipped with a feeder and two pecking keys (Stacho et al. 2016).

In the forced-choice and free-choice tasks, one conditioned stimuli (CS) was hollow yellow star with a blue background and the other CS was hollow pentagon with a blue background (Figure 3.3). To eliminate the color preference effect during the tasks, the same color and contrast with background was used for both CSs. At the beginning of a CS presentation, a tone (1000 Hz) was presented in order to attract the pigeon's attention towards the CS. The Skinner boxes were sound insulated to avoid potential distractors that could disturb the pigeons while performing a task. There was a camera on the back wall, which allowed us to observe pigeons' behavior during the experiment. The programs for the experimental sessions were controlled by the MATLAB-Biopsy Toolbox (Rose et al. 2008).

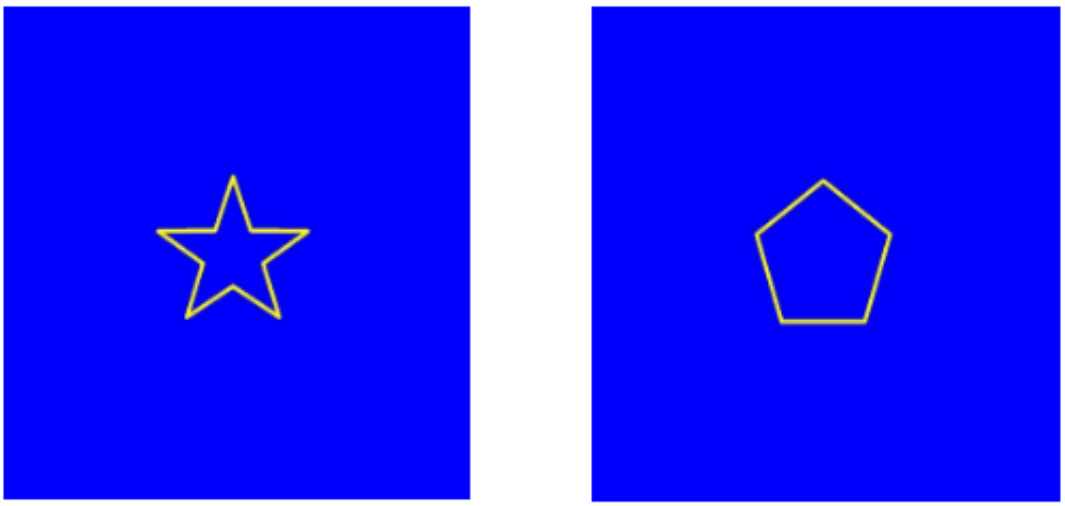


Figure 3.3. Experiment 1's stimuli.

3.1.3. Drug

For sensitization and the challenging dose, Apo hydrochloride that was obtained from BioMol (Hamburg-Germany), used. It was diluted in a saline solution to 0.5 mg/ml and 0.05mg/ml, respectively, and injected with a volume of 1 ml/kg into the pectoral muscle (half of the volume on each side). As a control condition, an equal amount of saline was injected before each session.

3.1.4. Procedure

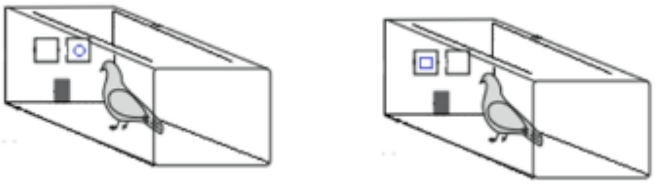
As the pigeons had previously been used in another experiment, they had already learned to peck at CSs. Therefore, they did not have to receive any Pavlovian autoshaping training. They received one daily session of forced-choice trials for 14 consecutive days. Specifically, they were trained for five days with a CS associated with a variable delay of 1 or 7 seconds, five days with another CS associated with a fixed delay of 4 seconds, and then four more days with a daily alternation of each

CS. Each session contained 40 trials, and the inter-trial interval (ITI) was 45 s. The sessions started with an ITI. After initial ITI termination, a CS was presented for 10 seconds, and then turned off. To be rewarded, the pigeons had to peck on the illuminated key at least one time. After termination of the CS presentation, pigeons were exposed to a delay (variable or fixed, depending on the CS) before food became available for 3 s. After forced-choice training, the pigeons were tested for 10 days in a free-choice procedure (four days with 30 sessions, six days with 40 sessions). The same CSs mentioned above were used here, among which the pigeons had to choose, with one presented on each key simultaneously.

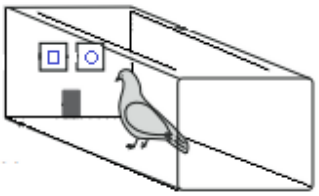
Upon the assumption that Apo can alter the preference for variable and fixed delays, as other dopamine agonists can, it was important to make both options equally attractive to pigeons. The delay values for which the pigeons showed no preference for either option (indifference point) was established for each individual. Depending on each pigeon's initial preference, the variable delay was gradually altered (increased or decreased) in order to make them equivalent to the fixed delay in terms of response rates.

Once the indifference point was reached for each pigeon, they were tested in the free-choice task under saline. To obtain a baseline, the next four consecutive days, Apo (0.5 mg/kg) was injected for sensitization. The pigeons were tested with the free-choice task only on the first and the last days of injections, they remained in their home cage on the other two days. Immediately after, the pigeons were subjected to 10 days of drug incubation. The pigeons stayed in their home cage without any injection and training during this period. After incubation, the pigeons were tested in the free-choice task with a saline and then with an Apo challenging dose (0.05 mg/kg) (Figure 3.4.).

A



B



C

Drug injection phase
1 day saline + free-choice task
4 days Apo (0.5 mg/kg) - 1st and 4th day free-choice task
10 days incubation-no treatment
1 day saline + free-choice task
1 day challenging dose (0.05 mg/kg) + free-choice task

Figure 3.4. Summary of Experiment 1. **(**A) *Forced-choice trials:* Pigeons were trained for five days with one CS associated with the variable delay (1-7 s) and five days with the other CS associated with the fixed delay (4 s), and then four more days with an alternation of each CS. (B) *free-choice trials:* Pigeons were tested with the free-choice task for five days (same variable and fixed delays). Then several days were necessary to reach the indifference point for each pigeon. (C) *Drug injection phase:* The first day, saline was administered for control purposes and the pigeons were tested in the free-choice task. For four consecutive days, they were injected intramuscularly with Apo and tested on 1st and 4th day with free-choice task. They were then subjected to 10 days of drug incubation without any treatment. After incubation, they were retested under the saline and challenging dose (0.05 mg/kg) within the free-choice task.

3.1.5. Statistical analyses

We used ANOVAs with repeated measures to compare the pigeons' responses during the different training phases. Standard error was used to calculate the p values.

3.2. Experiment 2

In Experiment 2, we decreased the attractiveness of the variable delay by increasing the delay times to make the pigeons prefer the fixed delay. This allowed us to test whether repeated Apo injections could change their preference and increase the attractiveness of the variable delay.

3.2.1. Animals and housing conditions

In Experiment 2, irrespective of their gender we used nine experimentally 9 naive homing pigeons. Apart from the fact that 8 of these pigeons were housed in an aviary cage (Figure 3.5) and one of them in an individual cage, their housing conditions were the same as in Experiment 1. These nine pigeons were also used as their own controls.



Figure 3.5. Aviary cage, in which eight individuals could be housed at the same time.

3.2.2. Apparatus and stimuli

The CS used in autoshaping was a white dot (8 mm in diameter) placed in the middle of a black background. For the forced and free-choice trials, the CSs were the same as used in Experiment 1. Delius et al. (2015) stated that, after repeated intramuscular Apo injections, pigeons showed excessive pecking responses within 20 min. We created an environment capable of recording pecks. To do that, we used cardboard boxes with carbon papers and normal papers fixed on the walls – referred to as "carbon boxes" thereafter. On each wall of these boxes, we fixed an A4-format white paper that contained small dark-gray dots. Behind these dark-grayed dotted papers, there were carbon papers and A4-format white papers. While pigeons were incited to peck on these dark-grayed dotted papers, carbon paper caused marks that were observed on the A4-format white paper (Figure 3.6).

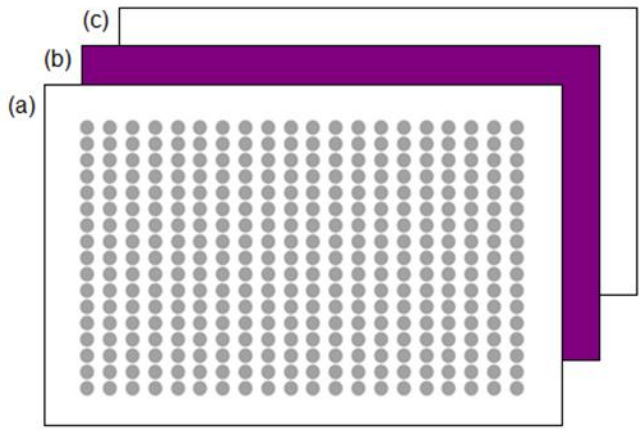


Figure 3.6. Carbon boxes' design. Pigeons' pecking responses after an Apo or a saline injection were recorded with this design. Pigeons pecked on the dark-gray dotted paper (a), and because of the carbon paper placed behind it (b), the carbon-marked pecks appeared on the white paper (c). (Anselme et al., 2018).

3.2.3. Procedure

Pigeons received one daily session of Pavlovian autoshaping (40 trials with a variable (30-90 s) ITI) in order to learn to peck when a CS was presented on the response keys. On each trial, the same CS was presented on the right or left key randomly for 10 s, and food was accessible for 3 seconds regardless of whether the pigeons pecked the CS or not. The autoshaping procedure was administered for eight days until each CS received a mean of three-four pecks per session. After autoshaping, pigeons were trained with forced-choice trials. As distinct from Experiment 1, the CSs had different delay values; one CS was associated with a variable delay of 2 or 12 s, and the other CS was associated with a fixed delay of 4 s. During the forced-choice trials, pigeons had to peck at least one time to the

illuminated key for food delivery. They were trained for five days with one CS, for five days with the other CS, and then for four more days with a daily alternation of each CS. During the next four consecutive days, pigeons were tested in the free-choice procedure, where they had to choose between the two CSs. The next day, they were tested again in the free-choice procedure under saline as a control condition. Prior to the phase of repeated Apo injections, pigeons were placed in the carbon boxes without injection for 30 min to habituate them to this new, narrow environment. On the second day, they were injected with saline and placed in the carbon boxes for the same duration. This time, their pecks were recorded by means of the carbon paper. For the next eight consecutive days, the pigeons were injected with Apo (0.75 mg/kg) and placed in the carbon boxes for 30 min to test the effects of neural sensitization immediately. Their pecks were also recorded by means of the carbon paper. Before the incubation phase, they were tested in the free-choice task without injection for three days. Then, they were subjected to an incubation period of 10 days. During incubation, pigeons remained in their home cage. Finally, they received a challenging dose (0.05 mg/kg) and were retested in the free-choice task for three more days (Figure 3.7).

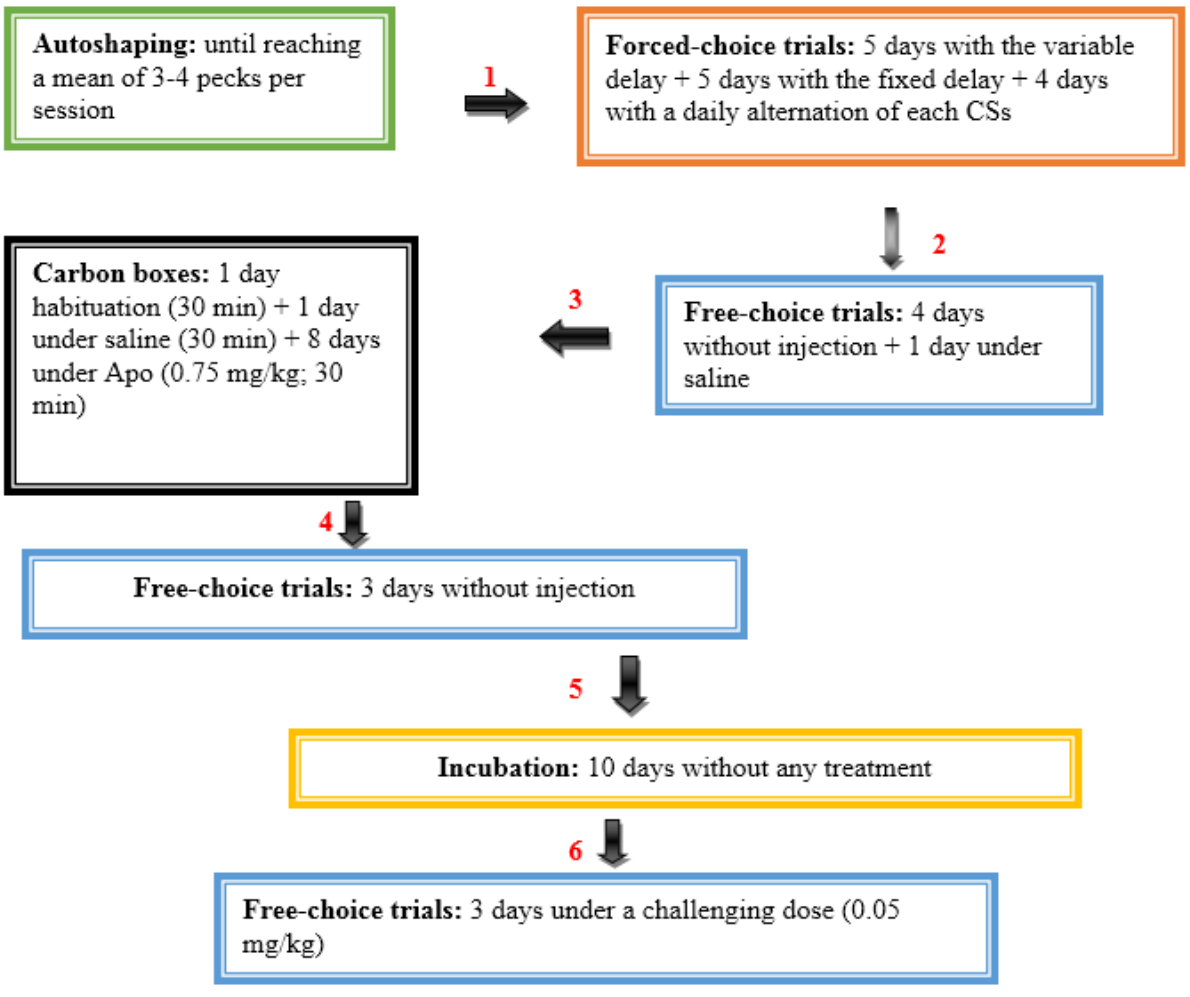


Figure 3.7. Summary of Experiment 2.

3.2.4. Statistical analyses

Pecking responses in this experiment were analyzed by means of repeated measures ANOVAs. Standard error was used to calculate all the p values. Data collected from the carbon boxes were analyzed with the Image Processing Toolbox of MATLAB in order to create digital images of the white paper containing the carbon-marked pecks. A custom-made MATLAB code was used to count the number of carbon-marked pecks. Before counting the pecks from the digitalized images, a Wiener filter was applied to remove some artifacts caused by pigeons' body movement in the carbon boxes. This filter helped minimize the overall mean square error. Upon the assumption that peck-induced spots had a higher density than artifact-induced spots, the images were converted to binary images by means of a suitable threshold. After thresholding, spots that had a high probability of being caused by pigeons' pecks were automatically counted.

3.3. Experiment 3

In the previous experiments, we expected that repeated Apo administration would increase preference for the variable delay over the fixed delay. In the first experiment, pigeons tended to prefer the variable delay before Apo injection, and we failed to reach the indifference point to observe the preference reverse. In the second experiment, they pecked the fixed delay slightly more than the variable delay, therefore the absence of that indifference point between the fixed and variable delays may be responsible for the lack of variable delay preference under Apo.

In Experiment 3, we aimed to obtain relative indifference between two options before Apo injections, and we designed a new task. In this new task, the pigeons had to choose between a probability of food delivery and a fixed delay for the same food. The removal of the drug from the body might have been the reason for the absence effect after sensitization in the previous experiments, therefore we did not use an incubation phase in this experiment. We trained the pigeons in the free-choice task two hours after the pigeons received their Apo injection.

3.3.1. Animals

In Experiment 3, we tested two groups of pigeons. In one group, the nine pigeons previously sensitized to Apo (in Experiment 2) were reused. The other group consisted of 10 naive pigeons, housed in aviary cages (irrespective of gender).

3.3.2. Apparatus and stimuli

To change the learning context with respect to the pre-sensitized pigeons, the CSs were changed in Experiment 3. One CS was a full blue triangle with a white background, and the other CS was a full blue square with a white background (Figure 3.8). Here, the task did not consist of choosing between two delays. One CS was associated with a 50% probability of food after 1 s delay and the other CS was associated with a 100% probability of food after a fixed 5-s delay. When available, food was delivered for 3 s.

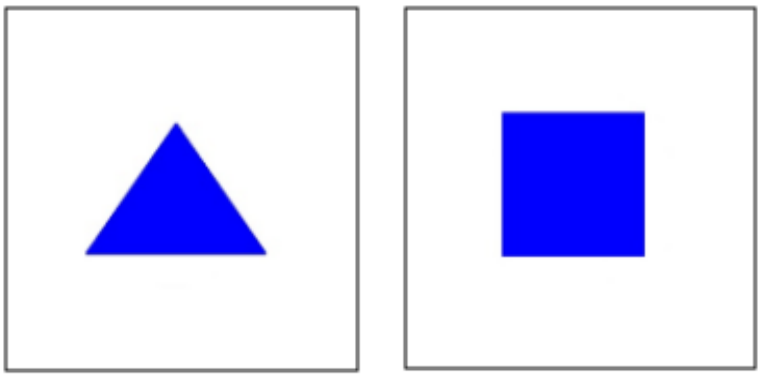


Figure 3.8. CSs used in Experiment 3. While one CS was associated with a 50% probability of food after a 1-s delay, the other CS was associated with a 100% probability of food after a 5-s delay (counterbalanced across pigeons).

3.3.3. Procedure

As forced-choice trials were systematically rewarded whether the pigeons pecked or not, the pigeons did not receive Pavlovian autoshaping. During the forced-choice trials (40 trials per session and 45-s ITI), both groups (Apormorphine-APO and saline-SAL), were trained with the 50% probability or with the 5-s delay separately. The pigeons from the SAL group had not been tested previously, therefore, the training period was longer for this group. After forced-choice training, both groups received five free-choice sessions of 40 trials (ITI:45 s). Like in the previous two experiments, the pigeons had to select one pecking key to be rewarded. The other key was then turned off. After training, for three consecutive days, depending on their group, the pigeons were injected intramuscularly with Apo (0.75 mg/kg) or saline, immediately placed in the carbon boxes for 30 min, and their pecks were recorded by means of the carbon paper. Then they were returned to their home cages for 90 min. After two hours following their injection, the pigeons were tested again in the free-choice task.

3.3.4. Statistical analyses

We used mixed ANOVAs with repeated measures for group comparisons. Standard error was used to calculate the p values.

4. RESULTS and DISCUSSION

4.1. Experiment 1

As reported in Figure 4.1, during the forced-choice task pigeons were trained with each CS for seven days. Pigeons were pecking both conditioned stimuli (CSs), and there were no significant differences in the number of pecks between the two conditions for any training days ($F(1,22) \leq 1.167$, $p \geq 0.292$).

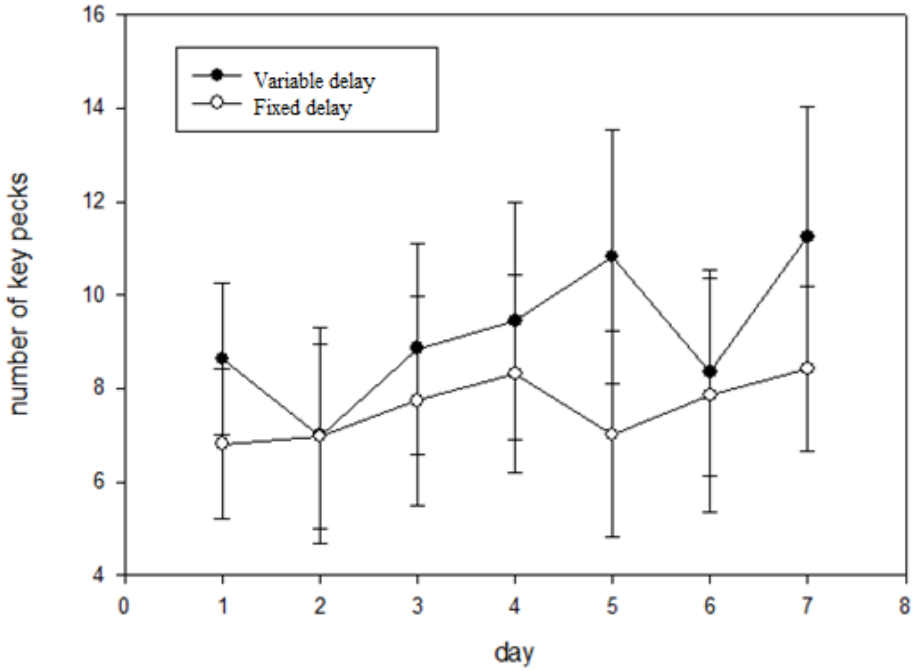


Figure 4.1. Pigeons' responses during the forced-choice training.

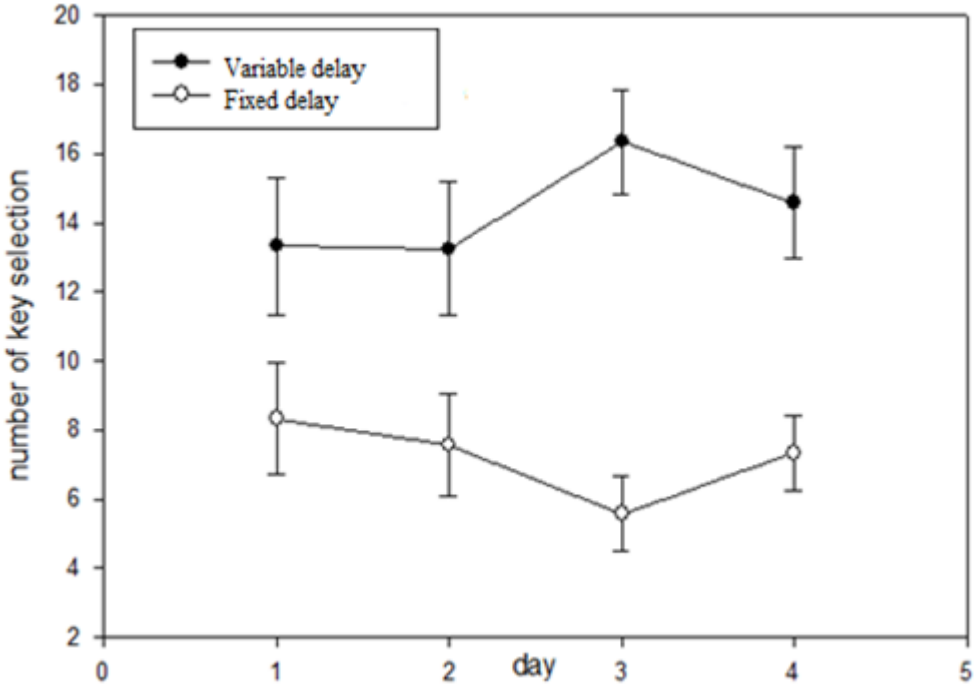


Figure 4.2. Pigeons' responses during four days of free-choice trials (30 sessions).

After forced-choice training, pigeons were immediately tested for four days within the free-choice task which contained 30 sessions (Figure 4.2), and six more days in the free-choice task that consisted of 40 sessions (Figure 4.3). During the first two days, effect of the day was not significant; the number of key selection for both variable delay (VD) and fixed delay (FD) remained similar (for VD: $F(3,33) = 1.278$, $p = 0.298$; for FD: $F(3,33) = 1.307$, $p = 0.288$), but the difference was significant during the last two days (Day 3: $F(1,11) = 18.417$, $p = 0.001$; Day 4: $F(1,11) = 7.724$, $p = 0.018$).

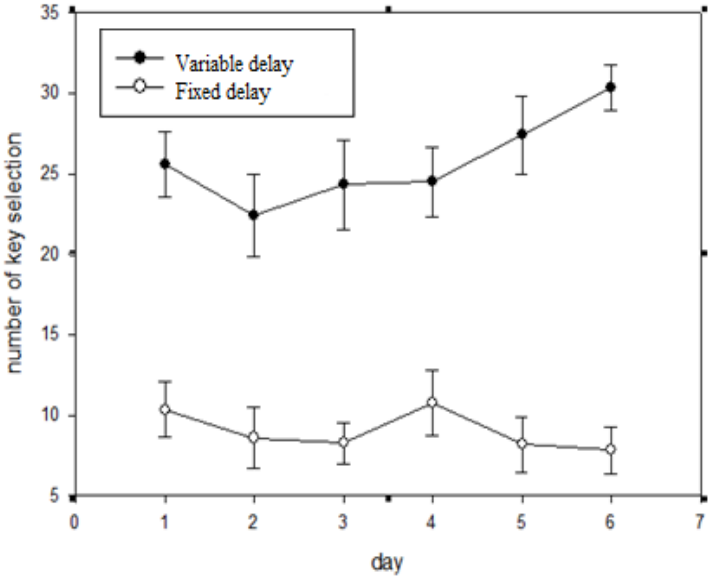


Figure 4.3. Pigeons' responses during the six days of free-choice trials (40 sessions).

Like in the four days free-choice task, the number of key selection for each key remained similar during the six days of free-choice task that consisted of 40 sessions (for VD: $F(5,55) = 2.045$, $p = 0.087$; for FD: $F(5,55) = 0.950$, $p = 0.457$). Pigeons strongly chose to peck the variable-delay key rather than the fixed-delay key on all days (Figure 4.3). During the first and the last days of training, the difference was significant (Day 1: $F(1,11) = 27.209$, $p<0.01$; Day 6: $F(1,11) = 63.461$, $p<0.01$).

In this experiment, the variance was low and the pigeons were risk prone like rufous hummingbirds (Hurly and Oseen, 1999). The arithmetic mean for the VD (1 or 7 s delay) was 4 s, and equivalent to the FD (4 s). In this case, they preferred VD which offered food sooner. For deprived animals like our pigeons, the attractiveness of the fixed option, which offered delayed reward, was lower (Cardinal, 2006; Estle et al., 2006). Paradoxically, offering a quicker delivery of food, made VD key more certain than the FD key and this can be explained by its subjective value. The subjective value associated with immediate rewards is higher than that associated with delayed rewards (Cardinal, 2006), therefore pigeons tended to prefer the variable option.

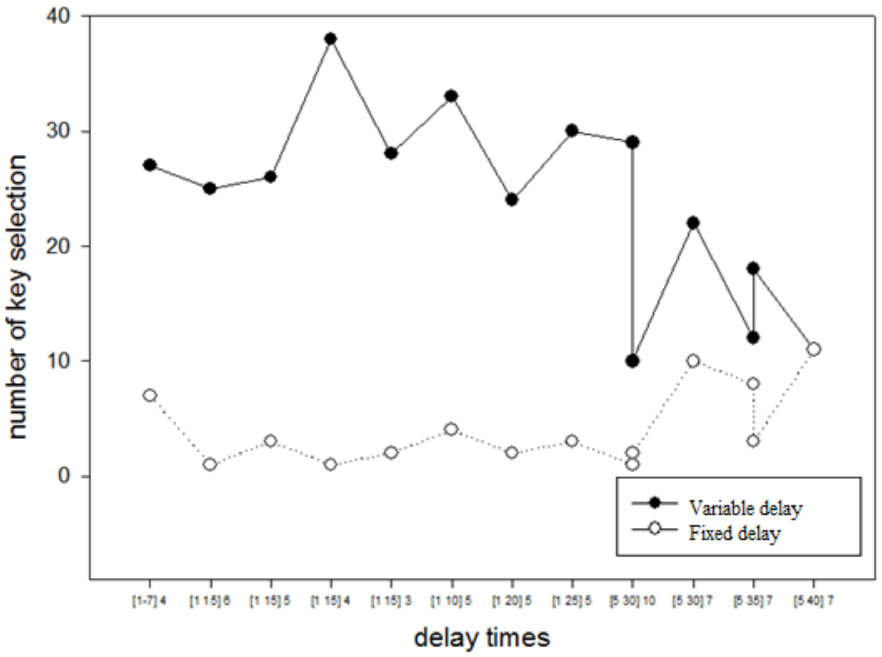


Figure 4.4. Indifference point for pigeon 656. It was trained with different variable and fixed delay times for several days. The number of key selections was equal when the VD was 5-40 seconds and FD was 7 second.

To observe the Apo effects on pecking choice, we used adjusting delay procedure (Mazur, 1987), where the delay time was changed from day to day. Before the injections, pigeons were trained with different delay times depending on their initial preference to reach the indifference point for each pigeon. VD was gradually altered to become equivalent to the FD in terms of response rate. A

hyperbolic discounting function suggests that as the delay to a reward increased, its present subjective value decreases inversely (Mazur, 1987). Therefore, pigeons were expected not to be prone to the VD key after increasing its delay times. Despite the fact that pigeons were trained with different delay times for several days, indifference point was observed just in one pigeon (Figure 4.4). In the literature, for both humans and nonhuman animals indifference points were reached (Rachlin et al., 1991; Evenden and Ryan, 1996). In our experiment, before the indifference points, pigeons were trained with identical delay times during the forced-choice and free-choice tasks for a long period (14 days with forced-choice task + 10 days with the free-choice task). After all these training days, they may have ignored to associate new delay values with CSs, and persist on their initial preference.

Before receiving apomorphine (Apo), the pigeons were given one session under saline (1 SAL inj) (Figure 4.5). Compared to the last day of the free-choice task, pecking at the VD key decreased significantly ($F(1,11) = 22.397$, $p = 0{,}000$), while pecking at the FD did not change ($F(1,11) = 3.462$, $p = 0.090$).

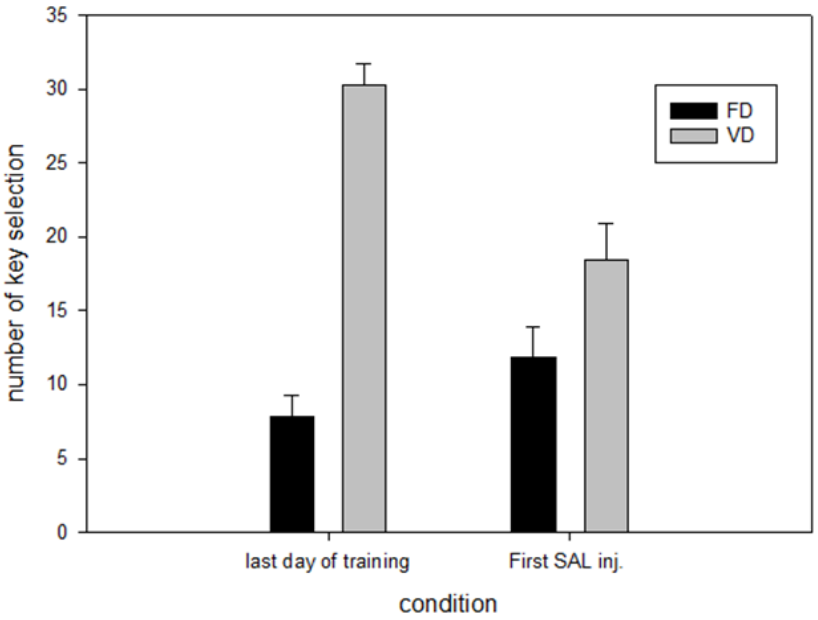


Figure 4.5. Pecking comparison between the last day of training and the first saline injection.

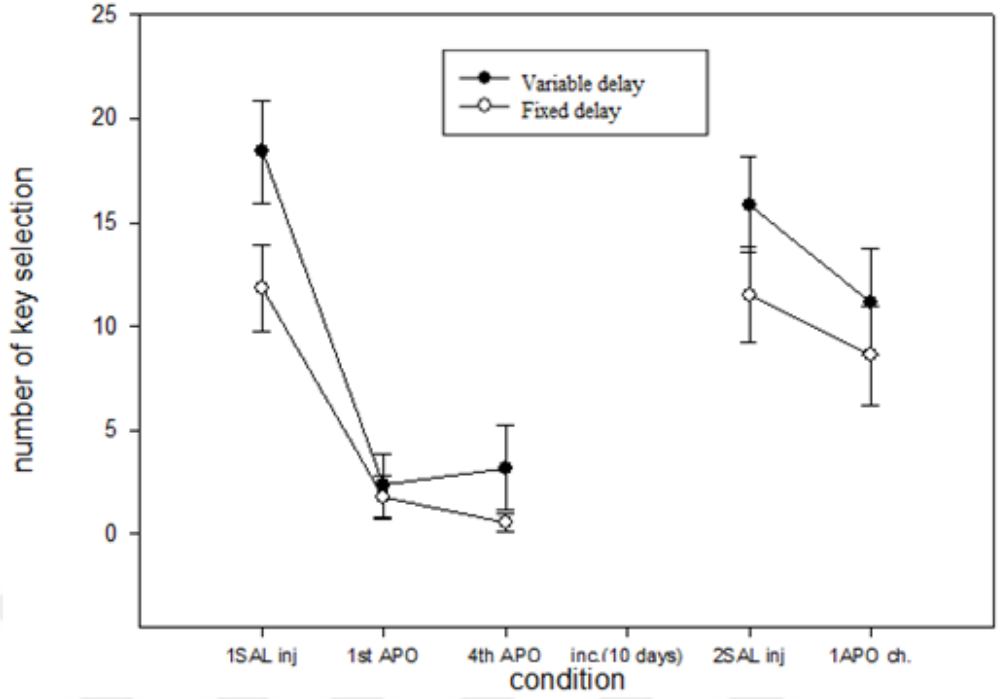


Figure 4.6. Apomorphine sensitization process

The day after the saline injection, sensitization to apomorphine started and continued for four consecutive days (Figure 4.6). On the first (1st Apo) and fourth (4th Apo) day of the injections, the pigeons were tested in the free-choice task, where it was observed that they almost completely stopped pecking any keys. Then the pigeons subjected to 10 days of incubation during which they remained in their home cage without any treatment. After incubation, testing pigeons with an Apo challenging dose (1APO ch., 0.05 mg/kg) did not show significant effects relative to the saline injection (2 SAL inj.) irrespective of the key (VD: $F(1,11) = 2.138$, $p = 0.171$; FD: $F(1,11) = 1.374$, $p = 0.266$).

Dopamine agonists' effect on preference for a variable (over a fixed option) has been studied in different animal groups previously (Dodd et al., 2005; Johnson et al., 2011; Voon et al., 2011 Tremblay et al., 2017). Also in many studies, Apo-induced pecking was recorded in pigeons (Wynne and Delius 1995; Acerbo and Delius 2004; Delius et al. 2014). These studies have examined how Apo affects pecking behavior in an experimental design where no food rewards or food related CSs were presented. In contrast, we tested pigeons under Apo in tasks involving food rewards and food related CSs. While they were pecking skinner box's walls randomly, no pecking was recorded on the keys. Ljungberg and Ungerstedt (1977) also observed some behavioral anomalies like increased locomotion, sniffing, repetitive head and limb movement elicited by apomorphine injection on rats. Our pigeons' behavior may have been caused by the same acute effect of Apo. In our free-choice task under the Apo challenging dose, pigeons' selection of number of keys did not change for either the variable or fixed delay options after an incubation period. Hence, contrary to other studies that were

conducted with dopamine agonists, our experiment failed to report evidence for the effect of Apo on preference for a variable option over a fixed option. This may have been due to a number of factors. On explanation is that Apo may have no influence on decision making during the free-choice tasks, a hypothesis which can be explained by considering Day et al. (2010) who showed that rats' dopamine release in the NAc is higher in a 0-s delay condition than in a 5-s delay condition during forced-choice training. However, dopamine signals during the free-choice task were identical for both options, therefore their choice was not correlated with dopamine release. It is also possible that environmental context was responsible for the absence of sensitization. Crombag et al. (2001) showed that rats that were habituated to a test environment before the injection did not show sensitization. In our experiment, the same experimental boxes were used for forced-choice, and free-choice training before the Apo injections, therefore, pigeons were familiar with their test environment. Bloise et. al. (2007) indicated that one or two-day of Apo administration caused behavioral locomotor sensitization in rats, and single drug exposure could trigger sensitization. On the contrary, Delius et al. (2015) suggested that drug dose administered and the repetition of drug injection could modulate the effectiveness of Apo. Hence, it is possible that four consecutive days of Apo injection (0.5 mg/kg) was not sufficient to obtain sensitization in our experiment.

4.2. Experiment 2

In Experiment 2, autoshaping sessions were used for naïve pigeons that were not used in an experimental task before. As reported in Figure 4.7, pigeons learned to peck in response to the presentation of a CS during the autoshaping (day 1: 6.897 ± 3.109; last day: 16.958± 1.125). On Day 4, significant differences appeared ($F(1,5) = 26.355$, $p= 0.004$).

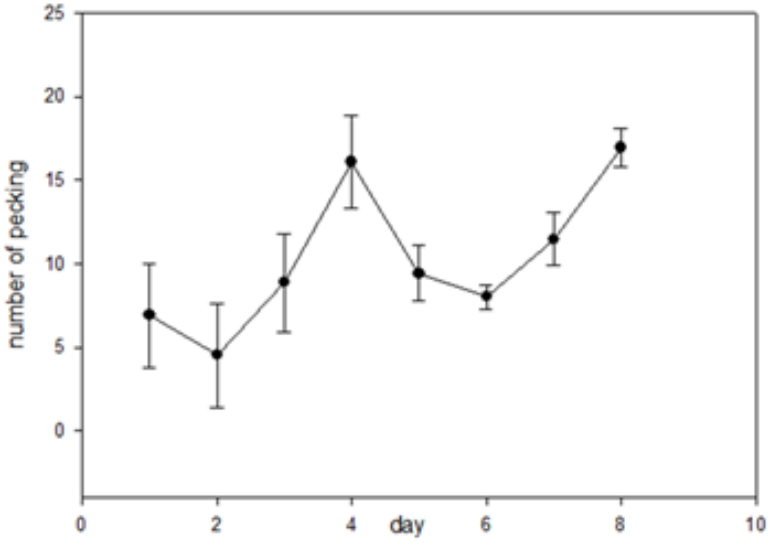


Figure 4.7. Number of pecking during the autoshaping.

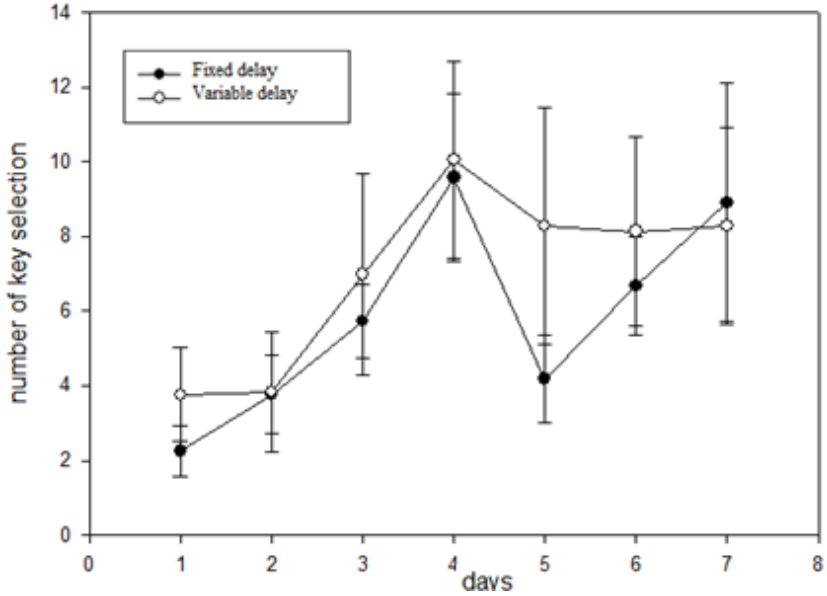


Figure 4.8. Pigeons' responses during the forced-choice trials.

After autoshaping, the pigeons were trained with the forced-choice trials for seven days (Figure 4.8). Pigeons were pecking both CSs and there was no significant difference in the number of pecks between two conditions ($F(1,5) = 0.130$, $p = 0,734$). A significant effect of day was obtained $F(1,5) = 10.357$, $p = 0.023$. But this effect was only visible for the VD between Day 1 and Day 4 ($F(1,5) = 7.188$, $p = 0.044$) and between Day 1 and Day 8 ($F(1,5) = 7.303$, $p = 0.043$).

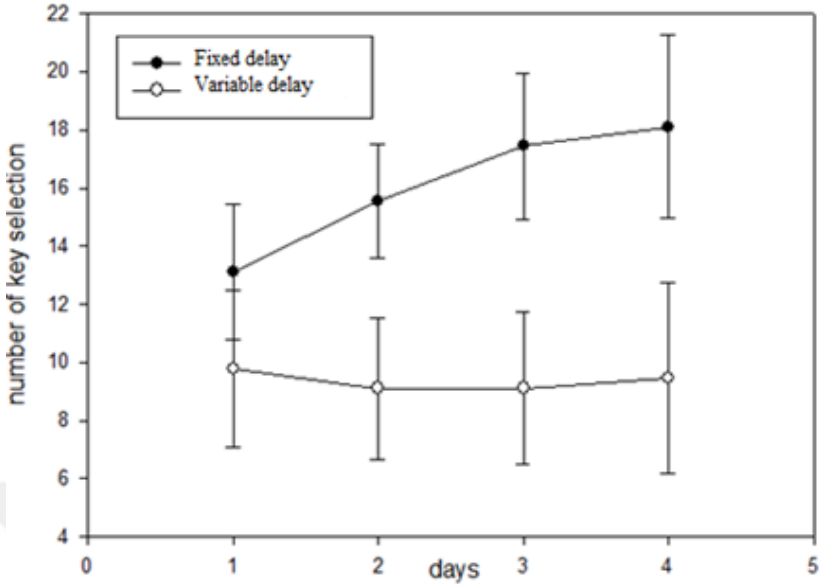


Figure 4.9. Pigeons' responses during four days of free-choice trials.

As reported in Figure 4.9, the pigeons were tested in the free-choice directly after forced-choice training. From Day 1 to Day 4, the number of FD key selection was slightly increased compared to that of VD key selection (FD; $F(1,8) = 2.980$ $p = 0.122$, VD; $F(1,8) = 0.074$ $p = 0.792$). There was no effect of day on the number of key selections (for FD; $F(3,24) = 2.207$ $p = 0{,}113$, for VD; $F(3,24) = 0.131$ $p = 0.940$). The difference between FD and VD key selection was only slightly increased from Day 1 ($F(1,8) = 0.591$ $p = 0.464$) to Day 4 ($F(1,8) = 1.843$ $p = 0.212$). As also seen in Figure 4.9, pigeons tended to prefer the fixed delay over the variable delay. This allowed us to evaluate whether Apo could increase the attractiveness of the VD over FD. The average value for the VD was 7 s and higher than the FD (4 s) in this experiment, therefore pigeons were inclined to prefer constancy (4 s) to variability (2 or 12 s). This result confirms that pigeons are delay-averse and this tendency can be explained by temporal discounting. Hwang et al. (2009) mentioned that compared to delayed rewards of similar magnitudes, humans and animals are more likely to go into action for immediate rewards because the subjective utility of the expected reward decreases with its delay. Cardinal (2006) and Estle et al. (2006) also illustrated the attractiveness of sooner rewards.

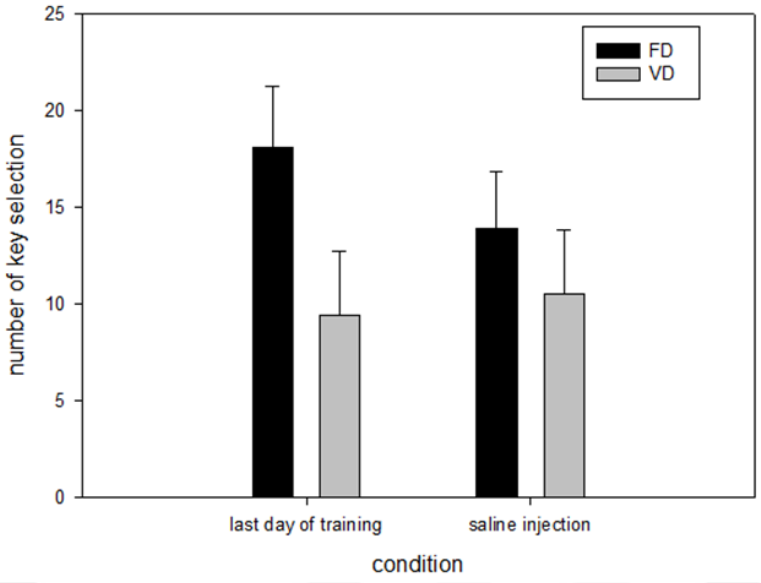


Figure 4.10. Pecking comparison between the last day of the free-choice training and saline control day.

Before receiving Apo, the pigeons were retested under saline. As illustrated in Figure 4.10, there were no significant differences between the last day of free-choice test and saline control day for both keys (for VD; $F(1,8) = 0.406$ $p = 0.542$, for FD; $F(1,8) = 2.590$ $p = 0.146$).

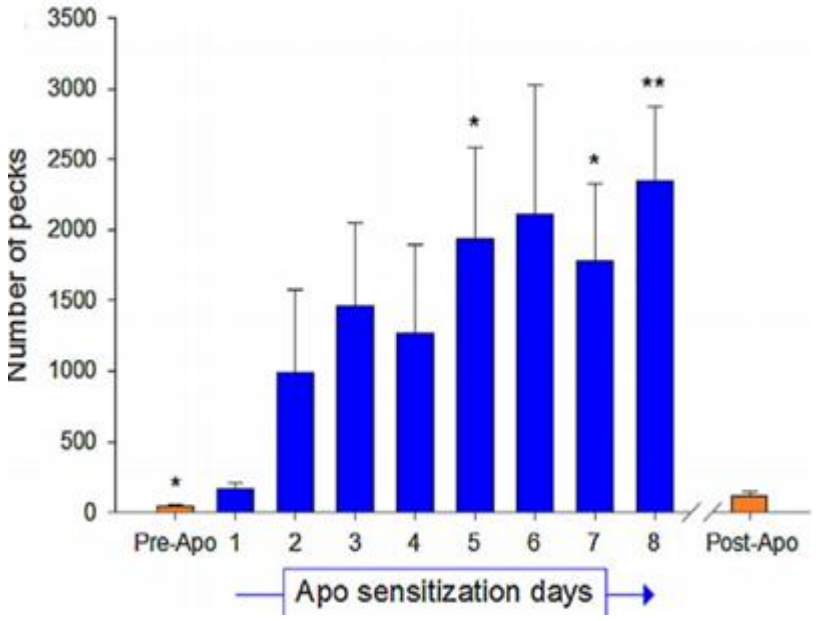


Figure 4.11. Pigeons' pecking responses under first control saline (pre Apo), eight days of repeated Apo injections, and last control saline (post Apo).

Figure 4.11 shows the pigeons' pecking responses under one day of saline injection (pre Apo), eight days of Apo injections in the carbon boxes, and one more day of saline injection after sensitization (post Apo). As reported in multiple studies (Acerbo et al. 2002, 2003; Acerbo and Delius 2004; Delius et al. 2014), our experiment showed the sensitized effect of Apo on pecking responses over the days of training in the carbon boxes; repeated Apo injection over the eight injections days in the carbon boxes induced a sensitization of pecking responses ($F(7,56) = 2.609$, $p = 0.021$). Pigeons were pecking on the carbon boxes' walls which can be considered as strange for domestic pigeons, as they are predominantly ground feeders. Pinkston and Lamb (2012) concluded that Apo-induced pecking is not related to forage pecking. This different pecking pattern may be an aggressive pecking that was also observed in domestic fowl chicks after Apo-treatment (Osuide and Adejoh, 1973). The number of pecks was increased significantly on the first day of Apo injection (Apo 1) compared to the control saline injection (pre Apo) ($F(1,6) = 7.922$ $p = 0.030$). Pigeons' pecking responses showed high incidence of variability over the eight injection days, and only the last days (5, 7, and 8) showed a significant alteration in the number of pecks in comparison with the first Apo injection day (Day 5: $F(1,8) = 7.889$, $p = 0.023$; Day 7: $F(1,8) = 9.528$, $p = 0.015$; Day 8: $F(1,8) = 17.526$, $p = 0.003$). On the saline injection day that occurred almost 30 days after the last Apo injection (post Apo), a strong decrease was observed on pigeons pecking responses in comparison with the last day of apomorphine injection ($F(1,6) = 18.225$, $p = 0.005$). The 30 days of intermission may have resulted in the pigeons forgetting the cue-drug association. Acerbo et al. (2005) showed that repeated Apo applications alters dopamine receptor densities, and Keller et al. (2002) stated that these alterations are long-lasting processes and have been assumed to be conditioned. Also, Wynne and Delius (1995) claimed that Apo-sensitized responding is conditioned. They trained the same pigeons under Apo in one context and under saline in another context on alternate days. Then these pigeons were injected with saline in both contexts on alternate days. They observed that the pigeons pecked significantly more in the context that associated with Apo. However, if sensitized pecking is a conditioned process, because of the absence of the Apo induced response, a decrease in pecking would have occurred under saline injection in the context that associated with Apo. The acute effect of Apo caused around 250 pecks on the first day of their training, and on the last day of the training the pigeons pecked about 380 times. The conditioning effect of the Apo should be equal to $380 – 250 = 130$ pecks. However, their pecks under saline in the Apo associated context was again around 380. Their data show sensitization is a context-specific process. In our experiment, the acute effect of the Apo caused 168 pecks on average. On the last day of the sensitization, they pecked about 2350 times. The expected conditioned pecking rate was 2350-168=2182. On post-Apo day, pigeons pecked around 113 times on average under saline. This result shows that the long-lasting effects of Apo sensitization on pecking responses are independent of conditioning.

Figure 4.12 depicts the density of pecks during the eight days of Apo sensitization. This figure indicates that, compared to the Apo injection days, pre-Apo and post-Apo days generated very low numbers of pecks.

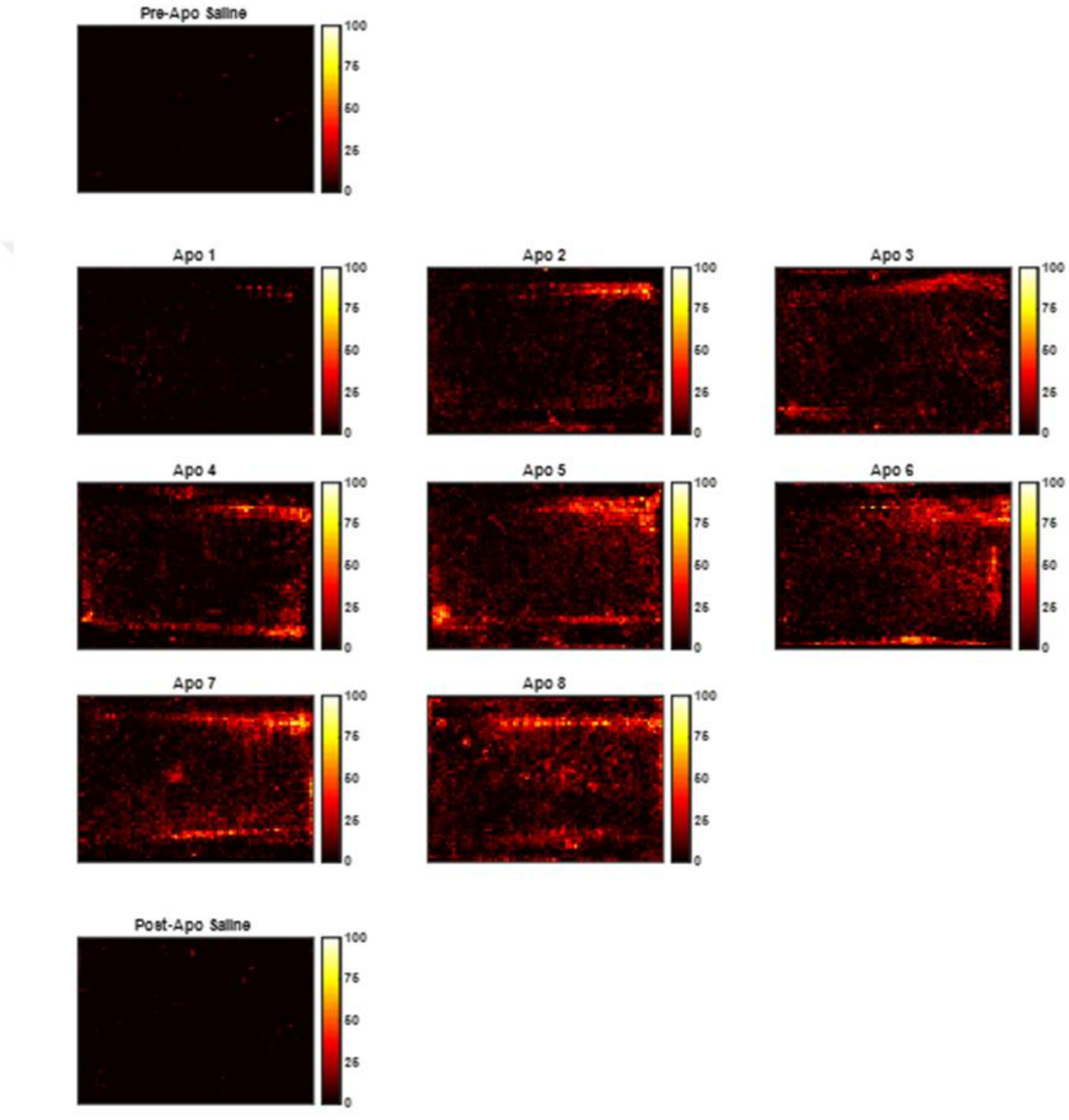


Figure 4.12. Density of pecks for the saline control days (pre-Apo saline and post-Apo saline) and for the eight days of sensitization to Apo.

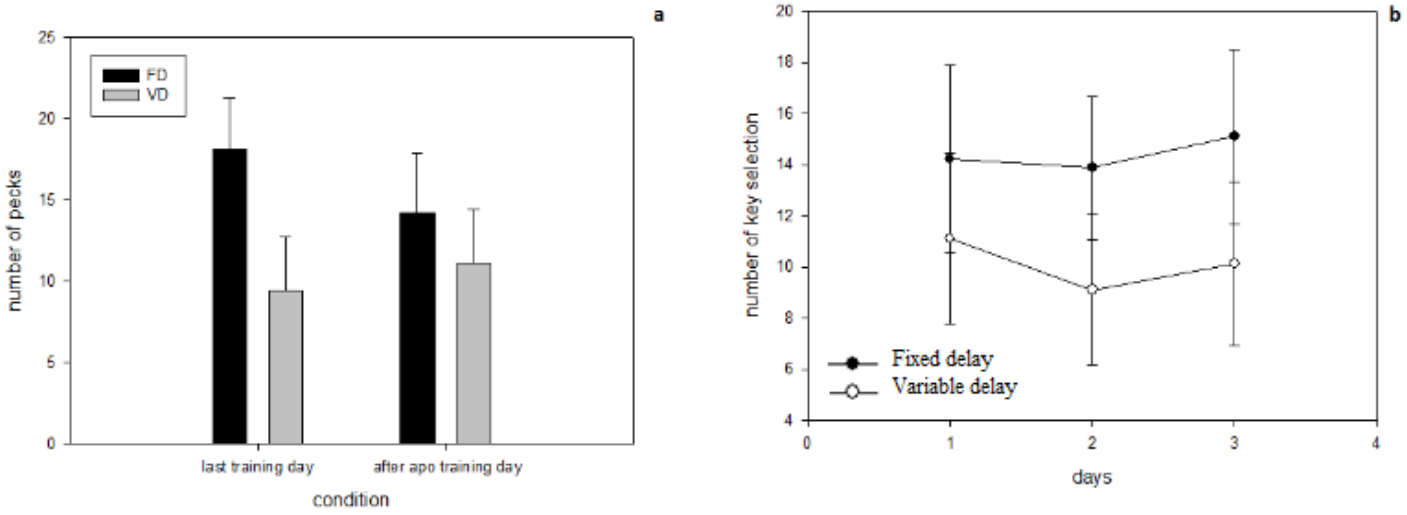


Figure 4.13. (a) Pigeons' pecking responses on the last day of training before Apo injections and first day of training after Apo sensitization. (b) Pigeons' responses during three days of training after Apo sensitization.

Following this treatment, the pigeons were retested in the free-choice task for three days without injection. There were no significant differences between the last training day and the first sensitized day for any key option (FD: $F(1,8) = 2{,}383$ $p = 0.161$; VD: $F(1,8) = 0.645$ $p = 0.445$) (Figure 4.13a). During the next three days of training, no differences were observed (FD: $F(2,16) = 0.444$ $p = 0.650$; VD: $F(2,16) = 2.634$ $p = 0.102$) (Figure 4.13b).

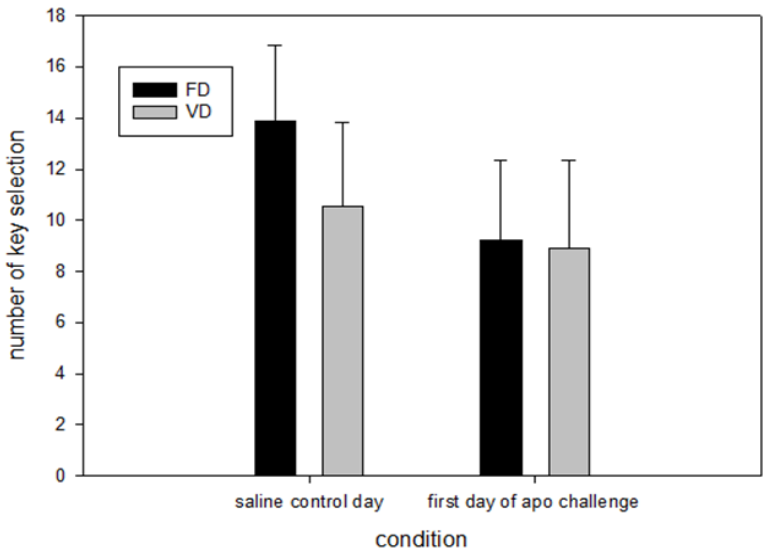


Figure 4.14. Pecking comparison between saline control day and the first Apo challenge.

Next, the pigeons were subjected to a 10 days incubation phase without any treatment. After this period, pigeons were tested with an Apo challenge (0.05 mg/kg) in the Skinner boxes for three days. Compared to the saline control injection before Apo sensitization, no significant effect was observed for any key on the first day of Apo challenge injection (Figure 4.14) (FD: $F(1,8) = 3.770$, $p = 0.088$; VD: $F(1,8) = 0.272$, $p = 0.616$). In an identical manner to Experiment 1, our free-choice task under Apo challenging dose, the pigeons' selection of number of keys did not change for either the variable or the fixed delay options, after an incubation period. This again suggests that Apo is not effective in controlling decision-making during the free-choice task.

As reported in Figure 4.15, no significant differences were observed over the three training days, for any keys (FD: $F(2,16) = 2.119$, $p = 0.153$; VD: $F(2,16) = 0.879$, $p = 0.434$).

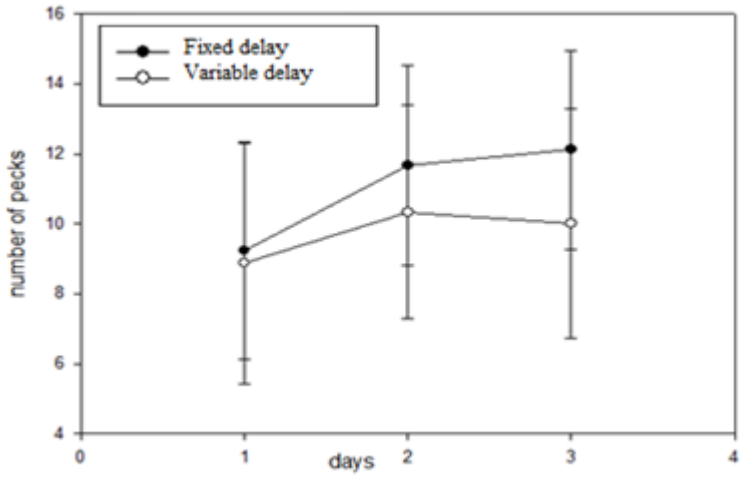


Figure 4.15. Pigeons' responses during the three days of training after ten days of incubation.

4.3. Experiment 3

In this experiment, we reused the pigeons that were sensitized to Apo in Experiment 2 in order to test whether neural sensitization could affect conditioned responding in a new task. Figure 4.16 shows the APO and SAL pigeons' pecks on the relevant (illuminated) key during the forced-choice trials. As reported in the figure, APO pigeons pecked the relevant key more than the SAL pigeons; there was an effect of day ($F(2,72) = 5.541$, $p = 0.005$), group ($F(1,36) = 17.652$, $p<0.01$) and group x day interaction ($F(2,72)=3.378$, $p=0.041$). These results may be demonstrating that apomorphine sensitization develops conditioned responding, as APO pigeons' pecks were focused. During the first and the last days of training, the group differences were significant with respect to the 5-s delay (first day: $F(1,34) = 4.790$, $p = 0.035$; last day: $F(1,34) = 9.678$, $p = 0.004$). The group differences were

significant for training days in the 50% probability condition (first day F(1,34) = 8.598, p = 0.006; middle of training: F(1,34) = 10.542, p = 0.003; last day: F(1,34) = 8.780, p = 0.005).

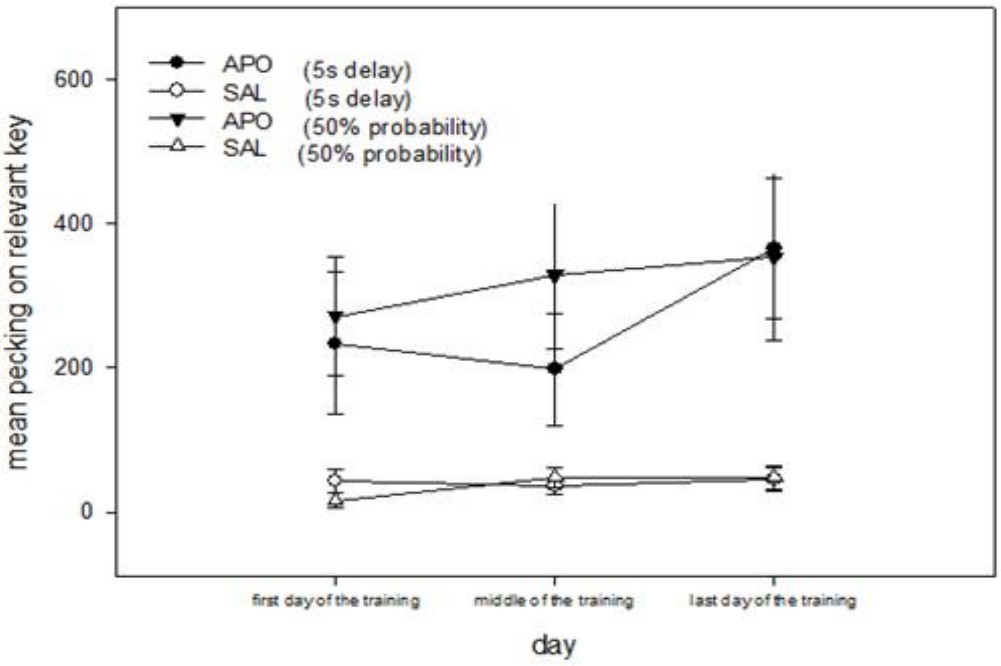


Figure 4.16. Pigeons' pecking responses on the relevant (illuminated key) during the forced-choice training.

We also recorded pigeons' pecking on the irrelevant (unilluminated) key (Figure 4.17). The pigeons in both groups pecked the irrelevant key, and a group difference was observed (F(1,36) =7.870, p = 0.008). There were no significant differences in day (F(2,72) = 0.950, p = 0.391) and group x day interaction (F(2,72) = 2.016, p = 0.140).

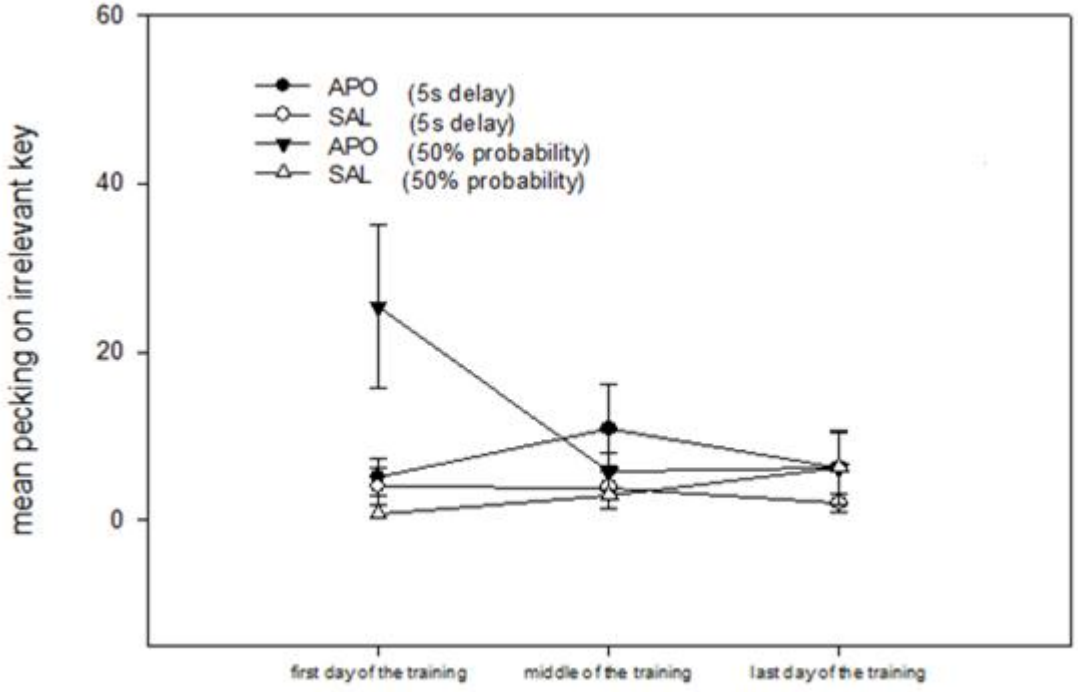


Figure 4.17. Pigeons' pecking on irrelevant key during the forced-choice task.

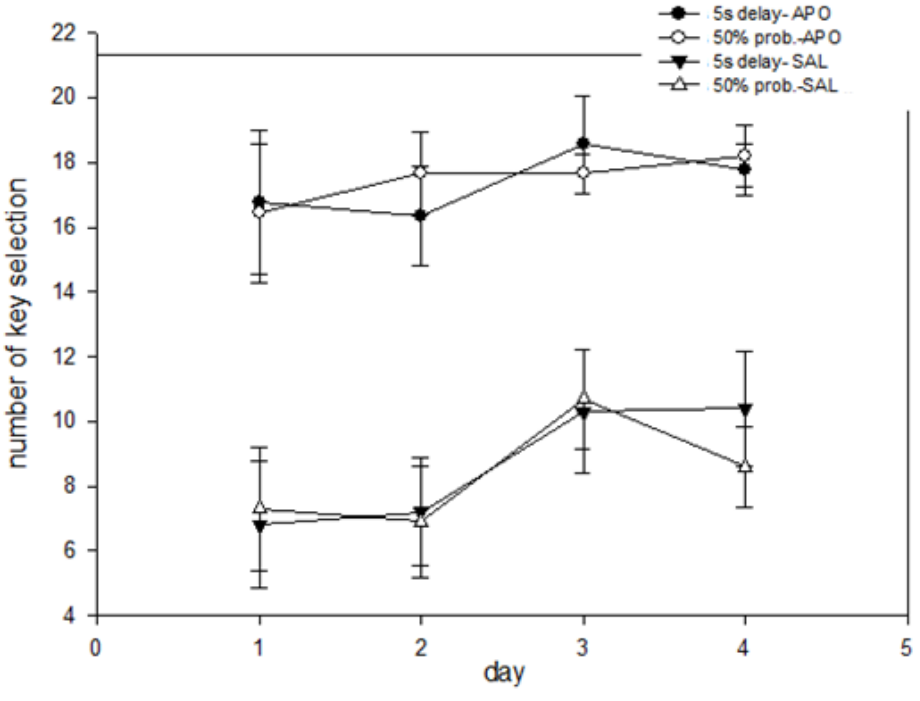


Figure 4.18. APO and SAL pigeons' pecking responses during the free-choice task.

After forced-choice training, the pigeons were tested in a free-choice task which had a 5-s delay and 50% probability options presented simultaneously (Figure 4.18). There was a significant effect of day ($F(3,102) = 5.854$, $p < 0.01$) and group ($F(3,34) = 14.063$, $p < 0.01$). It is appeared that the

number of pecks of APO pigeons on each key was higher than that of the SAL pigeons (APO 5-s delay versus SAL 5-s delay: $F(1,34) = 20.054$, $p < 0.01$; APO 50% probability versus SAL 50% probability: $F(1,34) = 22.132$, $p < 0.01$). While APO pigeons' number of pecks remained similar over training ($F(1,34) = 1.557$, $p = 0.221$), SAL pigeons' number of pecks increased ($F(1,34) = 6.040$, $p = 0.019$). The reason behind this different pattern may be that APO pigeons were trained previously (in Experiment 2), therefore they were already familiar with the experimental setup. Reaching an indifference point was easy because the two options were altered to become equivalent for each group. Both APO and SAL pigeons selected the 5-s delay and the 50% probability options in a similar fashion.

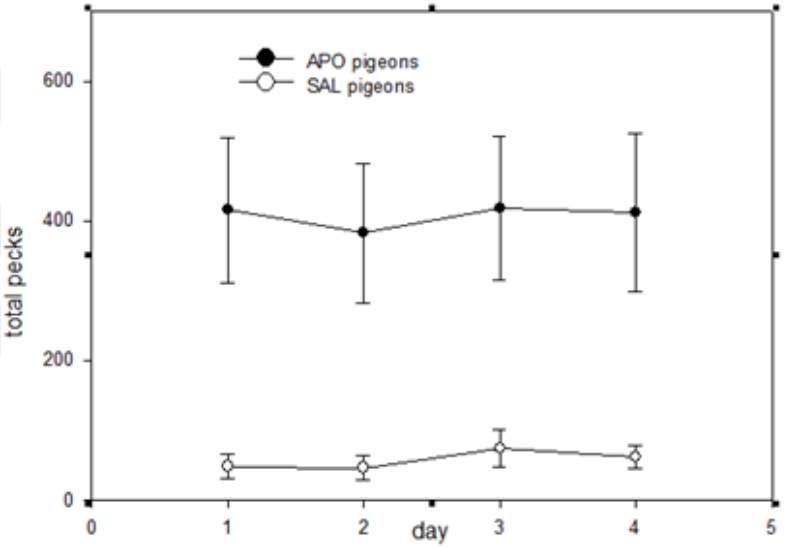


Figure 4.19. APO and SAL pigeons' total pecking during the free-choice task.

As reported in Figure 4.19, with respect to pigeons' total pecks, there was a significant effect of group ($F(1,17) = 12.340$, $p = 0.003$), but no effect of day ($F(4,68) = 1.150$, $p = 0.340$) and no day x group interaction ($F(4,68) = 0.211$, $p = 0.931$). APO group's total pecking was significantly higher than that for the SAL group (Day 1: $F(1,17) = 13.495$, $p = 0.002$; Day 4: $F(1,17) = 10.858$, $p = 0.004$).

After four days of free-choice training, both APO and SAL pigeons were retested under saline for one more day. Compared to the last day of training, pigeons' key selection remained similar in both groups (Figure 4.20).

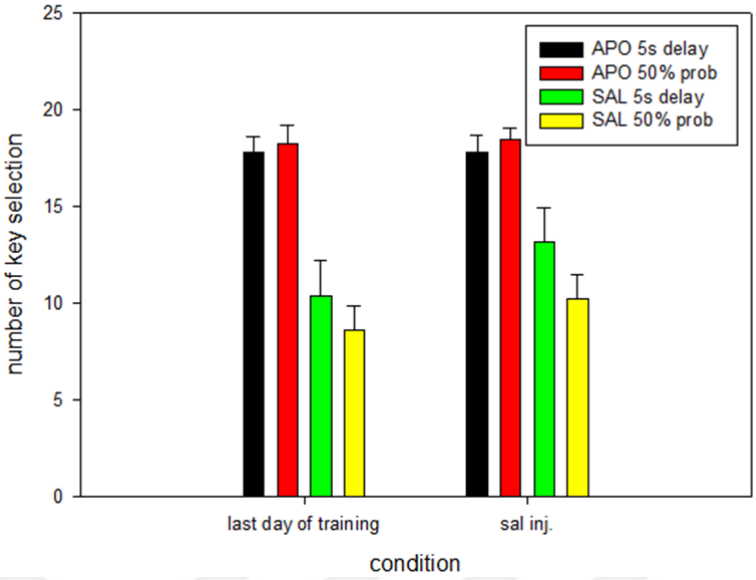


Figure 4.20. Pecking comparison between the last day of training and the saline injection for both APO and SAL groups.

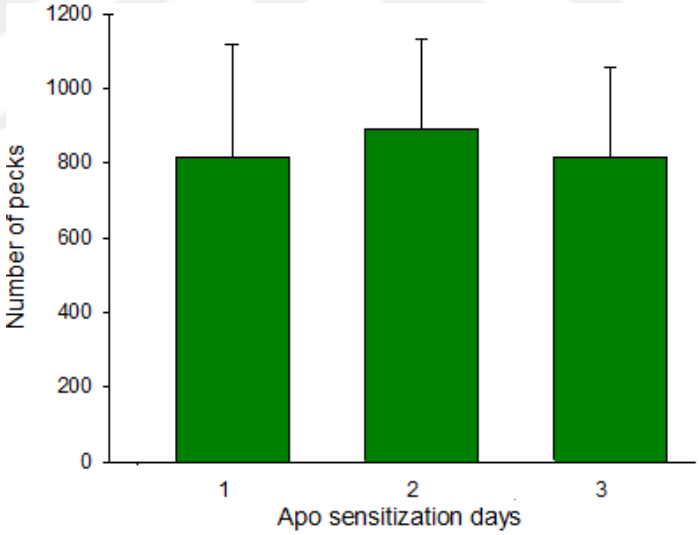


Figure 4.21. The response rates of the presensitized pigeons were elevated (relative to the Apo-1 day in Figure 4.11), as early as the first day of injection.

Immediately after the saline injection, for three consecutive days, the SAL pigeons received a saline injection and the APO pigeons received Apo injection two hours before the free-choice test, and were placed in the carbon boxes for 30 min and their pecks were recorded via the carbon papers (Figure 4.21). When reexposed to the carbon boxes under Apo, the presensitized pigeons pecking response rates on Day 1 was fivefold more than the performance they showed on the first day of Apo injection in Experiment 2, the difference between these two days was not significant ($F(1,8) = 3.931$,

p = 0.083), and saline pigeons gave no pecks at all. This indicates that Apo-induced neuroadaptations were present in the pigeons' brains throughout Experiments 2 and 3.

Two hours after the injections, pigeons were tested in the free-choice task (Figure 4.22). APO pigeons' responses fluctuated over training; on the first and the second day they selected 5-s delay key more than 50% probability key, and the last day probability key was preferred to the delay key (Day 1: $F(1,33) = 3.353$, $p = 0.076$; Day 2: $F(1,33) = 0.453$; $p = 0.506$, Day 3: $F(1,33) = 1.120$, $p = 0.298$). SAL pigeons' responses remained similar throughout the training (Day 1: $F(1,33) = 0.456$, $p = 0.504$; Day 2: $F(1,33) = 0.670$, $p = 0.419$; Day 3: $F(1,33) = 0.017$, $p = 0.896$).

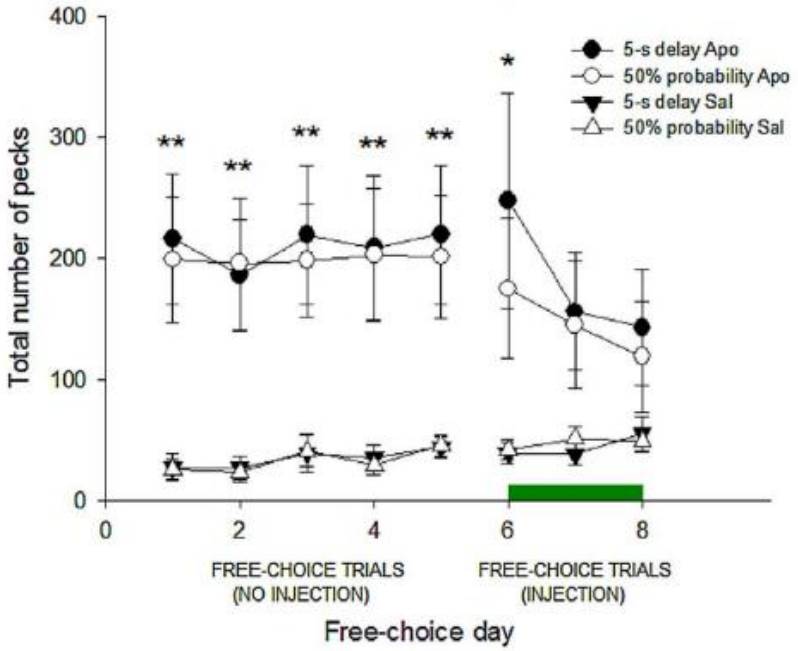


Figure 4.22. APO and SAL pigeons' pecking responses during free-choice training after Apo and saline injections

There were no significant effects of group ($F(3,33) = 2.7111$, $p = 0.061$), day ($F(2,60) = 0.750$, $p = 0.476$), and group x day interaction ($F(6,66) = 2.046$, $p = 0.071$). In both groups, the pigeons selected the 50% probability and the 5-s delay similarly (APO: $F(1,33) = 0.263$, $p = 0.611$; SAL: $F(1,33) = 0.378$, $p = 0.543$). Therefore, we could not find any evidence that Apo can affect the preference for reward uncertainty. This can be explained by dopamine receptors potentially not being active in the choice between delay and probability in pigeons (Day et al., 2010). To confirm this hypothesis, new experiments should be designed with other dopamine agonists like pramipexole, rotigotine or ropinirole.

5. CONCLUSIONS

In this study, we examined the drug free preference of pigeons for a constant delay over a variable delay, and a 50% probability option over a 5-s delay option. Next their preference was examined under the systemic administration of a dopamine agonist, Apo.

Conclusions of this study are given below:

1. The strong sensitizing effect of Apo on pecking responses in the carbon boxes verified that pigeons were sensitive to the drug, as reported in other studies that were conducted with rodents and pigeons.

2. A high pecking rate under the Apo injections showed that Apo-sensitized pecking is more about motivation rather that consumption of the food. This has been also shown by Pinkston and Lamb (2012); Apo-induced pecking is unrelated to the opportunity to get the food reward.

3. Our experiments showed that the long-lasting sensitization to Apo can occur independently of a conditioning process. This result conflicts with earlier findings that claim sensitized response to a drug is conditioned, therefore it is elicited by the environmental cues that surrounded the animal when it was exposed to the drug previously (Acerbo et al., 2003; Wynne and Delius, 1995). However, the design of these earlier studies were not adequate to fully support conditioning interpretation. Their data only demonstrated that sensitization is a context-specific process.

4. Contrary to other studies in the literature, our experiment failed to report evidence for the prediction that Apo pre-treatment would generate a preference for a variable option, over a constant option. Although Apo sensitization decreased the number of pecks in the constant option, it did not induce a preference for the variable delay. This may suggest that preference for variable delay over a constant delay is insensitive to dopaminergic activity in a bird brain. More detailed investigation with different dopamine agonists like pramipexole, rotigotine or ropinirole is needed to provide a satisfactory explanation for these observations.

6. REFERENCES

Acerbo, M. J., Delius, J. D., 2004. Behavioral Sensitization to Apomorphine in Pigeons (*Columba livia*): Blockade by the D_1 Dopamine Antagonist SCH-23390. Behavioral neuroscience, 118, 1080.

Acerbo, M. J., Výboh, P., Košťál, Ľ., Kubíková, Ľ., Delius, J. D., 2005. Repeated apomorphine administration alters dopamine D1 and D2 receptor densities in pigeon basal telencephalon. Experimental brain research, 160, 533-537.

Ahearn, W., Hineline, P. N., David, F. G., 1992. Relative preferences for various bivalued ratio schedules. Learning & behavior, 20, 407-415.

Anselme, P., 2015. Does reward unpredictability reflect risk? Behavioural Brain Research, 280, 119-127.

Anselme, P., Robinson, M. J., 2016. "Wanting,""liking," and their relation to consciousness. Journal of Experimental Psychology: Animal Learning and Cognition, 42, 123.

Anselme, P., Robinson, M. J., Berridge, K. C., 2013. Reward uncertainty enhances incentive salience attribution as sign-tracking. Behavioural brain research, 238, 53-61.

Anselme P, Edeş N, Tabrik S, Güntürkün O., 2018. Long-term sensitization to apomorphine is independent of conditioning and increases conditioned pecking, but not preference, in pigeons, Behavioural Brain Research.

Bateson, M., Kacelnik, A., 1997. Starlings' preferences for predictable and unpredictable delays to food. Animal Behaviour, 53, 1129-1142.

Bateson, M., 2002. Recent advances in our understanding of risk-sensitive foraging Preferences. Proceedings of the Nutrition Society, 61, 1–8.

Battisti, J. J., Uretsky, N. J., Wallace, L. J., 1999. Sensitization of apomorphine-induced stereotyped behavior in mice is context dependent. Psychopharmacology, 146, 42-48.

Berridge, K. C., 2007. The debate over dopamine's role in reward: the case for incentive salience. Psychopharmacology, 191, 391-431.

Berridge, K. C., Robinson, T. E., 1998. What is the role of dopamine in reward: hedonic impact, reward learning, or incentive salience?. Brain research reviews, 28, 309-369.

Berridge, K. C., Robinson, T. E., Aldridge, J. W., 2009. Dissecting components of reward:'liking','wanting', and learning. Current opinion in pharmacology, 9, 65-73.

Bloise, E., Carey, R. J., Carrera, M. P., 2007. Behavioral sensitization produced by a single administration of apomorphine: implications for the role of Pavlovian conditioning in the mediation of context-specific sensitization. Pharmacology Biochemistry and Behavior, 86, 449-457.

Braga, P. Q., Dias, F. R. C., Carey, R. J., Carrera, M. P., 2009. Low dose apomorphine induces context-specific sensitization of hypolocomotion without conditioning: support for a new state dependent retrieval hypothesis of drug conditioning and sensitization. Pharmacology Biochemistry and Behavior, 93, 128-133.Brunelli, M., Magni, F., Moruzzi, G., Musumeci, D., 1975. Apomorphine pecking in the pigeon. Archives italiennes de Biologie, 113, 303-325.

Cannon, C. M., Palmiter, R. D., 2003. Reward without dopamine. Journal of neuroscience, 23, 10827-10831.

Caraco, T., 1980. On foraging time allocation in a stochastic environment. Ecology, 61, 119-128.

Caraco, T., 1981. Energy budgets, risk and foraging preferences in dark-eyed juncos (*Junco hyemalis*). Behavioral Ecology and Sociobiology, 8, 213-217.

Caraco, T., 1981. Risk-sensitivity and foraging groups. Ecology, 62, 527-531.

Caraco, T., Blanckenhorn, W. U., Gregory, G. M., Newman, J. A., Recer, G. M., Zwicker, S. M., 1990. Risk-sensitivity: ambient temperature affects foraging choice. Animal Behaviour, 39, 338-345.

Cardinal, R. N., 2006. Neural systems implicated in delayed and probabilistic reinforcement. Neural Networks, 19, 1277-1301.

Childress, A. R., Hole, A. V., Ehrman, R. N., Robbins, S. J., McLellan, A. T., O'Brien, C. P., 1993. Cue reactivity and cue reactivity interventions in drug dependence. NIDA research monograph, 137, 73-73.

Cocker, P. J., Hosking, J. G., Benoit, J., Winstanley, C. A., 02012. Sensitivity to cognitive effort mediates psychostimulant effects on a novel rodent cost/benefit decision-making task. Neuropsychopharmacology, 37, 1825.

Collins, L., Young, D. B., Davies, K., Pearce, J. M., 1983. The influence of partial reinforcement on serial autoshaping with pigeons. The Quarterly Journal of Experimental Psychology, 35, 275-290.

Cousins, M. S., Atherton, A., Turner, L., Salamone, J.D., 1996. Nucleus accumbens dopamine depletions alter relative response allocation in a T-maze cost/benefit task. Behav Brain Res, 74, 189–197.

Crombag, H. S., Badiani, A., Chan, J., Dell'Orco, J., Dineen, S. P., Robinson, T. E., 2001. The ability of environmental context to facilitate psychomotor sensitization to amphetamine can be dissociated from its effect on acute drug responsiveness and on conditioned responding. Neuropsychopharmacology, 24, 680-690.

Day, J. J., Jones, J. L., Wightman, R. M., Carelli, R. M., 2010. Phasic nucleus accumbens dopamine release encodes effort-and delay-related costs. Biological psychiatry, 68, 306-309.

de Lafuente, V., and Romo, R., 2011. Dopamine neurons code subjective sensory experience and uncertainty of perceptual decisions. Proc. Natl. Acad. Sci. U.S.A. 108, 19767–19771.

Delius, J. D., Acerbo, M. J., Krug, I., Lee, J., & Leydel, R. (2015). Sensitization to apomorphine in pigeons: a multifactorial conditioning process. Behavioural pharmacology, 26(1 and 2-Special Issue), 139-158.Dodd, M. L., Klos, K. J., Bower, J. H., Geda, Y. E., Josephs, K. A., Ahlskog, J. E., 2005. Pathological gambling caused by drugs used to treat Parkinson disease. Archives of neurology, 62, 1377-1381.

Estle, S. J., Green, L., Myerson, J., Holt, D. D., 2006. Differential effects of amount on temporal and probability discounting of gains and losses. Memory & Cognition, 34, 914-928.

Evenden, J. L., Ryan, C. N., 1996. The pharmacology of impulsive behaviour in rats: the effects of drugs on response choice with varying delays of reinforcement. Psychopharmacology, 128, 161-170.

Ferrario, C. R., Gorny, G., Crombag, H. S., Li, Y., Kolb, B., Robinson, T. E., 2005. Neural and behavioral plasticity associated with the transition from controlled to escalated cocaine use. Biological psychiatry, 58, 751-759.

Field, M., Cox, W. M., 2008. Attentional bias in addictive behaviors: a review of its development, causes, and consequences. Drug and alcohol dependence, 97, 1-20.

Fiorillo, C. D., Tobler, P. N., and Schultz, W., 2003. Discrete coding of reward probability and uncertainty by dopamine neurons. Science 299, 1898–1902.

Franken, I. H., 2003. Drug craving and addiction: integrating psychological and neuropsychopharmacological approaches. Progress in Neuro-Psychopharmacology and Biological Psychiatry, 27, 563-579.

Godoy, A.M., Siemann, M., Delius, J.D., 2000. Dose shift effects on an apomorphine induced response. Medical Science Research, 28, 39–42.

Guillemette, M., Himmelman, J.H., Barette, C., Reed, A., 1993. Habitat selection by common eiders in winter and its interaction with flock size. Canadian Journal of Zoology, 71, 1259-1266.

Güntürkün, O., 2012. The convergent evolution of neural substrates for cognition. Psychological research, 76, 212-219.

Hasin, D. S., Liu, X., Alderson, D., Grant, B. F., 2006. DSM-IV alcohol dependence: a categorical or dimensional phenotype?. Psychological medicine, 36, 1695-1705.

Hurly, T. A., Oseen, M. D., 1999. Context-dependent, risk-sensitive foraging preferences in wild rufous hummingbirds. Animal Behaviour, 58, 59-66.

Hwang, J., Kim, S., Lee, D., 2009. Temporal discounting and inter-temporal choice in rhesus monkeys. Frontiers in behavioral neuroscience, 3.

Ikemoto, S., Panksepp, J., 1996. Dissociations between appetitive and consummatory responses by pharmacological manipulations of reward-relevant brain regions. Behavioral neuroscience, 110, 331.

Jenkins, H. M., Moore, B. R., 1973. The form of the auto-shaped response with food or water reinforcers. Journal of The Experimental Analysis Of Behavior, 20, 163-181.

Johnson, P. S., Madden, G. J., Brewer, A. T., Pinkston, J. W., Fowler, S. C., 2011. Effects of acute pramipexole on preference for gambling-like schedules of reinforcement in rats. Psychopharmacology, 213, 11-18.

Joutsa, J., Johansson, J., Niemelä, S., Ollikainen, A., Hirvonen, M. M., Piepponen, P., Hietala, J., 2012. Mesolimbic dopamine release is linked to symptom severity in pathological gambling. Neuroimage, 60, 1992-1999.

Kalcelnik, A., Bateson, M., 1996. Risky theories-the effects of variance on foraging decisions. Amer. Zool, 36, 402-434.

Kacelnik, A., El Mouden, C., 2013. Triumphs and trials of the risk paradigm. Animal Behaviour, 86, 1117-1129.

Kalenscher, T., van Wingerden, M., 2011. Why we should use animals to study economic decision making - a perspective. Front Neuroscience.

Kaufman, J., 2012. The Personal MBA: Master the Art of Business.

Keller, S., Delius, J. D., Acerbo, M. J., 2002. Apomorphine sensitization: evoking conditions, context dependence, effect persistence and conditioned nature. Behavioural pharmacology, 13, 189-201.

Knight, F. H., 1921. Risk, Uncertainty, and Profit. Boston, Houghton Mifflin Company.

Ljungberg, T., Ungerstedt, U., 1977. Apomorphine-induced locomotion and gnawing: Evidence that the experimental design greatly influences gnawing while locomotion remains unchanged. European journal of pharmacology, 46, 147-151.

Lima, S.L., Dill, L.M., 1990.Behavioral decisions made under the risk of predation: a review and

prospectus. Canadian Journal of Zoology, 68, 619-640.

Linnet, J., Peterson, E., Doudet, D. J., Gjedde, A., Møller, A., 2010. Dopamine release in ventral striatum of pathological gamblers losing money. Acta Psychiatrica Scandinavica, 122, 326-333.

Linnet, J., Møller, A., Peterson, E., Gjedde, A., Doudet, D., 2011. Dopamine release in ventral striatum during Iowa Gambling Task performance is associated with increased excitement levels in pathological gambling. Addiction, 106, 383-390.

Lubman, D. I., Peters, L. A., Mogg, K., Bradley, B. P., Deakin, J. F. W., 2000. Attentional bias for drug cues in opiate dependence. Psychological medicine, 30, 169-175.

Mattingly, B. A., Gotsick, J. E., 1989. Conditioning and experiential factors affecting the development of sensitization to apomorphine. Behavioral neuroscience, 103, 1311.

Mattingly, B. A., Hart, T. C., Lim, K., Perkins, C., 1994. Selective antagonism of dopamine D 1 and D 2 receptors does not block the development of behavioral sensitization to cocaine. Psychopharmacology, 114, 239-242.

Mayack, C., Naug, D., 2011. A changing but not an absolute energy budget dictates risk-sensitive behaviour in the honeybee. Animal behaviour, 82, 595-600.

Mazur, J. E., 1987. An adjusting procedure for studying delayed reinforcement. Commons, ML.; Mazur, JE.; Nevin, JA, 55-73.

McDermott, R., Fowler, J. H., Smirnov, O., 2008. On the evolutionary origin of prospect theory preferences. Journal of Politics, 70, 335–350.

McGlone, M.S., 1983. Polynesian deforestation of New Zealand: A preliminary analysis. Archaeology in Oceania, 18, 11–25.

Mishra, S., 2014. Decision-making under risk: Integrating perspectives from biology, economics, and psychology. Personality and Social Psychology Review, 18, 280–307.

Moeller, F. G., Dougherty, D. M., 2002. Impulsivity and substance abuse: what is the connection?.

Addictive Disorders & Their Treatment, 1, 3-10.

Nagaoka, L., 2002. The effects of resource depression on foraging efficiency, diet breadth, and patch use in southern New Zealand. Journal of Anthropological Archaeology, 21, 419-442.

Nei, M., Xu, P., Glazko, G., 2001. Estimation of divergence times from multiprotein sequences for a few mammalian species and several distantly related organisms. Proceedings of the National Academy of Sciences, 98, 2497-2502.

Osuide, G., Adejoh, P. O., 1973. Effects of apomorphine and its interaction with other drugs in the domestic fowl. European journal of pharmacology, 23, 56-66.

Peck, H. L., Pringle, H. E., Marshall, H. H., Owens, I. P., Lord, A. M., 2014. Experimental evidence of impacts of an invasive parakeet on foraging behavior of native birds. Behavioral Ecology, 25, 582-590.

Pinkston, J. W., Lamb, R. J., 2012. Reinforcer magnitude attenuates apomorphine's effects on operant pecking. Journal of the experimental analysis of behavior, 98, 273-282.

Post, R. M., Lockfeld, A., Squillace, K. M., Contel, N. R., 1981. Drug-environment interaction: context dependency of cocaine-induced behavioral sensitization. Life sciences, 28, 755-760.

Poulson T.L., 1964. Animals in aquatic environments: animals in caves. American Physiological Society.

Preuschoff, K., Bossaerts, P., and Quartz, S. R., 2006. Neural differentiation of expected reward and risk in human subcortical structures. Neuron 51, 381–390.

Rachlin, H., Raineri, A., Cross, D., 1991. Subjective probability and delay. Journal of the experimental analysis of behavior, 55, 233-244.

Riba, J., Krämer, U. M., Heldmann, M., Richter, S., Münte, T. F., 2008. Dopamine agonist increases risk taking but blunts reward-related brain activity. PLoS One, 3, e2479.

Real, L.A., 1980. Fitness, uncertainty, and the role of diversification in evolution and behaviour. The

American Naturalist, 115, 623-638.

Real, L. A., 1981. Uncertainty and pollinator-plant interactions: The foraging behavior of bees and wasps on artificial flowers. Ecology, 62, 20-26.

Real, L., Caraco, T., 1986. Risk and foraging in stochastic environments. Annual Review of Ecology and Systematics, 17, 371-390.

Robinson, T. E., Berridge, K. C., 1993. The neural basis of drug craving: an incentive-sensitization theory of addiction. Brain research reviews, 18, 247-291.

Robinson, M. J. F., Robinson, T. E., Berridge, K. C., 2013. Incentive Salience and the Transition to Addiction. In Biological Research on Addiction, 391-399.

Robinson, M. J., Robinson, T. E., Berridge, K. C., 2014. Incentive Salience in Addiction and Over-Consumption. The interdisciplinary science of consumption, 185.

Saarikko, J., 1989. Foraging behaviour of shrews. In Annales Zoologici Fennici, 411-423.

Schultz, D. P., Schultz, S. E., 2015. A history of modern psychology. Cengage Learning.

Steadman, D. W., 1995. Prehistoric extinctions of Pacific island birds: biodiversity meets zooarchaeology. Science, 1123-1131.

Stephens, D. W., Krebs, J. R., 1986. Foraging theory. Princeton University Press.

Subramony, J. A., 2006. Apomorphine in dopaminergic therapy. Molecular pharmaceutics, 3, 380-385.

Thomsen, K. R., Fjorback, L. O., Møller, A., Lou, H. C., 2014. Applying incentive sensitization models to behavioral addiction. Neuroscience & Biobehavioral Reviews, 45, 343-349.

Tremblay, M., Silveira, M. M., Kaur, S., Hosking, J. G., Adams, W. K., Baunez, C., Winstanley, C. A., 2017. Chronic D2/3 agonist ropinirole treatment increases preference for uncertainty in rats regardless of baseline choice patterns. European Journal of Neuroscience, 45, 159-166.

Van Andel, T.H., Zangger, E., Demitrack, A., 1990. Land use and soil erosion in prehistoric Greece. Journal of Field Archaeology, 17, 379–398.

Vilà, M., Bartomeus, I., Dietzsch, A. C., Petanidou, T., Steffan-Dewenter, I., Stout, J. C., Tscheulin, T., 2009. Invasive plant integration into native plant–pollinator networks across Europe. Proceedings of the Royal Society of London B: Biological Sciences, 276, 3887-3893.

Volkow, N. D., Fowler, J. S., Wang, G. J., 2003. The addicted human brain: insights from imaging studies. Journal of clinical investigation, 111, 1444.

Võikar, V., Soosaar, A., Volke, V., Kõks, S., Bourin, M., Männistö, P. T., Vasar, E., 1999. Apomorphine-induced behavioural sensitization in rats: individual differences, role of dopamine and NMDA receptors. European Neuropsychopharmacology, 9, 507-514.

Weintraub, D., Koester, J., Potenza, M. N., Siderowf, A. D., Stacy, M., Voon, V., Lang, A. E., 2010. Impulse control disorders in Parkinson disease: a cross-sectional study of 3090 patients. Archives of neurology, 67, 589-595.

White, B., Gilman, A., Hunter, B., Fiebiger, S., Hill, D. J., Horsma, B., 2007. U.S. Patent Application No. 11/923,306.

Winterhalder, B., Lu, F., Tucker, B., 1999. Risk-senstive adaptive tactics: Models and evidence from subsistence studies in biology and anthropology, Journal of Archaeological Research, 7, 301–348.

Wynne, B., Delius, J. D., 1995. Sensitization to apomorphine in pigeons: unaffected by latent inhibition but still due to classical conditioning. Psychopharmacology, 119, 414-420.

Zald, D. H., Boileau, I., El-Dearedy, W., Gunn, R., McGlone, F., Dichter, G. S., Dagher, A., 2004. Dopamine transmission in the human striatum during monetary reward tasks. Journal of Neuroscience, 24, 4105-4112.

Zarrindast, M. R., Shokravi, S., Samini, M., 1992. Opposite influences of dopaminergic receptor subtypes on penile erection. General Pharmacology: The Vascular System, 23, 671-675.