The Behavior Analyst 2004, 27, 231–238 No. 2 (Fall)

# A Behavior-Analytic Conceptualization of the Side Effects of Psychotropic Medication

Maria G. Valdovinos and Craig H. Kennedy
Vanderbilt University

A range of behavior—much deemed problematic by society—is treated with behavioral methods or psychotropic medications. Although the processes associated with behavioral interventions have been investigated using conceptual, experimental, and applied analyses, less is known about the behavioral processes associated with the use of psychotropic medication. Psychotropic drugs produce at least two types of effects of behavioral interest: (a) primary effects of drug action on target behaviors and (b) side effects that change the target or other behavior. Although an empirical literature exists regarding the former effects, little attention has been given to the latter topic. In this paper we offer a conceptual analysis of the side effects of psychotropic medication. We propose that the side effects of various drugs can influence behavior by functioning as motivating operations, conditional or discriminative stimuli, or by establishing new response–reinforcer relations. This conceptualization may facilitate the empirical analysis of how psychotropic drugs change behavior.

*Key words:* side effects of medication, motivating operations, discriminative stimuli, reinforcer, punisher, psychotropic medication, behavior analysis

Practitioners in psychology and related fields, such as psychiatry, pediatrics, and education, use two primary means of changing client behavior. The first is the use of environmental manipulations to rearrange the reinforcers, stimulus control, and motivating operations that maintain specific behavior. The second is the use of psychotropic drugs to bring about change in behavior. Both approaches are used with a wide variety of clinical populations, including people with anxiety disorders, developmental disabilities, or schizophrenia. In this paper we focus on psychotropic medications, the approach that is less familiar to behavior analysts. An extensive basic literature in behavioral pharmacology has described drug effects on behavior (e.g., Barrett, Thompson, & Dews, 1990). There is also an emerging literature on the use of psychotropic medications to change the behavior of various clinical populations (Kennedy, Caruso, & Thompson, 2001; Reiss & Aman, 1998).

The pharmacological literatures (both behavioral pharmacology and clinical psychopharmacology) have primarily focused on one aspect of psychotropic medication: the direct and therapeutic effects of drugs on behavior. There is, however, another set of effects that drugs can have on those who take them: side effects. *Side effects* refer, in general, to an "undesirable, unintended, or unwanted reaction because of the known pharmacological effects of a [medication]" at a therapeutic dosage (Kalachnik, 1999, p. 350). This definition is based on observable effects such as changes in overall status and physiological reactions (e.g., sweating, diarrhea, or tremors). Although this definition may aid physicians in making decisions about medication use, it does not explain why behavior may change when using these medications or what behavioral process influences the occurrence of responding as a result of side effects. Side effects are often considered to be deleterious, but, as we hope to show,

Preparation of this article was supported, in part, by NICHD Grant 1620476822A2 and OSEP Grant H324C020060. We thank Jennifer Zarcone for her discussion of these issues, and Edward Morris, Mark Harvey, Michael May, and Celeste Roberts for their comments on a previous version of the manuscript.

Address correspondence to Craig H. Kennedy, Box 328 – Peabody, Department of Special Education, Vanderbilt University, Nashville, Tennessee 37203 (e-mail: craig.kennedy@vanderbilt.edu).

**TABLE 1**

**Psychotropic medication classes and associated side effects**

| Class | Side effects |
|---|---|
| Antipsychotics | Sedation, weight gain, rashes, and movement disorders such as tardive dyskinesia and akathisia |
| Antiepileptics | Vertigo, drowsiness, unsteadiness, increased appetite, nausea, vomiting, and dizziness |
| Antidepressants (SSRIs) | Slighter and sometimes shorter term side effects, increased agitation, hypomania, insomnia, headache, dry mouth, appetite suppression, decreased libido, drowsiness, and gastrointestinal symptoms |
| Anxiolytics | Sedation, disinhibition, hyperactivity, irritability, and possible cognitive impairment |
| Mood stabilizers | Finger tremors, vomiting, chronic nausea, severe diarrhea, ataxia, coma, convulsions, edema, hypothyroidism, weight gain, and polyuria |
| Stimulants | Insomnia, anorexia, headache, stomachache, nausea, irritability, nervous tics, and increased talkativeness |
| Other medications | |
| Beta blockers | Depression, hypotension, vomiting, nausea, diarrhea, insomnia, and dizziness |
| Opiate blockers | Difficulty sleeping, anxiety, stomachache, nausea, low energy, sedation, headaches, and muscle or joint pain |

*Note.* Side effects reported for each class do not necessarily apply to all medications within each class, and our listing is not exhaustive.

some of their behavioral effects may also be beneficial.

There are seven major clinical classes of psychotropic medications: antipsychotics, antiepileptics, antidepressants, anxiolytics, mood stabilizers, stimulants, and other (see Kennedy & Meyer, 1998). Each medication class has known side effects; however, all medications within a class do not necessarily share the same profile (see Table 1). Although a great deal is known about the physical manifestations of side effects, less is known about how these side effects influence behavior. Many psychotropic drugs prescribed to change behavior have side-effect profiles that might affect behavior in ways that are difficult to predict. This is a particular concern when the clinical population who receives the medication, such as people with developmental disabilities, has a limited ability to communicate about public or private events associated with the side effects (Bond, 1998; Christian, Snycerski, Singh, & Poling, 1999; Harbord, 2000). These concerns may be further compounded if there is no behavioral conceptualization of side effects to guide assessment and subsequent intervention.

In what follows, we offer a conceptualization of side effects of medication that might assist behavior analysts in understanding how these phenomena relate to behavior. Such an understanding may assist in the development of interventions that reduce the negative side effects of psychotropic medication and facilitate the identification of positive effects on responding.

We will discuss possible behavioral processes involved in medication side effects via three fundamental operant processes: (a) motivating operations (MOs), (b) stimulus control, and (c) response–reinforcer relations. Both MOs and discriminative stimuli ($S^D$s) are antecedents to responding. However, unlike $S^D$s, MOs alter the value of reinforcers and punishers, whereas $S^D$s signal the availability of reinforcement contingent on responding. These antecedent processes can be distinguished from the most basic of behavioral

units, response–reinforcer relations. Such a conceptual framework provides an analytic model for discussing possible behavioral changes associated with side effects of medication. We will discuss each of these separately to describe how psychotropic drugs might affect each behavioral process.

## SIDE EFFECTS AS MOTIVATING OPERATIONS

Laraway, Snycerski, Michael, and Poling (2003) defined an MO as an event, operation, or stimulus condition that alters the effectiveness of reinforcers and punishers and thus alters the frequency of behaviors associated with these consequences. This alteration in reinforcer effectiveness can be either establishing (increasing the effectiveness of a stimulus) or abolishing (decreasing the effectiveness of a stimulus; Michael, 1982).

The integration of MOs into behavioral analyses is becoming increasingly prevalent (e.g., Kennedy & Meyer, 1998; McGill, 1999). Much of the research on MOs has focused on socially mediated reinforcers (i.e., positively or negatively reinforcing events that occur via the responding of another individual). For example, a person with developmental disabilities might engage in self-injury that results in gaining attention from others. If that person has not interacted with another person for a period of time, social interaction may increase in value as a positive reinforcer (Klatt & Morris, 2001). Conversely, if that person has had an extended social interaction, these events may no longer function as positive reinforcers.

In addition to MOs associated with socially mediated stimuli, recent research has also focused on nonsocial reinforcers and MOs. For example, research has shown that sleep deprivation can function as an MO, increasing rates of negatively reinforced responding (Kennedy & Meyer, 1996). Kennedy, Meyer, Werts, and Cushing (2000) found that when nonhumans were REM-sleep deprived, response rates increased on an avoidance schedule compared to response rates during free access to sleep. May et al. (2003) have shown this increase in response rate to be a function of hyperalgesia induced by REM-sleep deprivation. Other researchers have studied the effect of inner ear infection (otitis media) on responding in humans. O'Reilly (1997) found that when a person had otitis media, problem behavior was more prevalent in noisy environments. However, when the person was not infected, there was no problem behavior in the presence of the same noise. Thus, the infection served to establish noisemaking as a noxious stimulus.

*Establishing operations.* One type of effect that MOs have on positive or negative reinforcers is to increase the reinforcing effectiveness of stimuli, an effect referred to as "establishing." This effect includes deprivation for positive reinforcers and an increase in the noxiousness of stimuli that function as negative reinforcers. For example, side effects of medication may alter stimuli by increasing the reinforcing value or increasing the effectiveness of stimuli that already function as positive reinforcers. For instance, many people who take the antiepileptic valproic acid (Depakote®) experience increased hunger (Biton et al., 2001). In this instance, food becomes a more potent positive reinforcer. The rate of those behaviors that have a history of food reinforcement, such as aggression to gain access to food, may increase as a result of the side effect.

Similarly, side effects may also have establishing effects on negative reinforcers. Here, the side effect may make a particular event more aversive, thus establishing negative reinforcement for escape or avoidance. For example, consider a child who begins taking clomipramine (Anafranil®), a tricyclic antidepressant. One possible side effect of this drug is headaches. If such a side effect occurs, the child may seek to avoid or escape noisy situations that previously would have been tolerated,

such as a beginner's music class. In this example, the presence of a headache as a side effect has established loud sounds as aversive stimuli.

*Abolishing operations.* Although abolishing effects of MOs are not as often discussed in the behavioral literature as the establishing effects of MOs, side effects may also serve as abolishing operations to diminish the effectiveness of stimuli as reinforcers. In this case, stimuli that functioned as positive or negative reinforcers would no longer function, or have diminished function, as reinforcing stimuli. For positive reinforcers, abolishing operations could render stimuli neutral; hence, their effect on behavior would no longer be positively reinforcing.

When considering abolishing functions of side effects, the alteration of positive reinforcement functions could occur if a child's appetite is reduced after taking the stimulant methylphenidate (Ritalin®). If the child's teacher uses edible items as reinforcers, the reduction in appetite would diminish the effectiveness of food as positive reinforcement. Conversely, if an adult with developmental disabilities engages in aggression that functions to obtain food as a positive reinforcer, the same side effect produced by methylphenidate could reduce or eliminate aggression because of a diminution in the effectiveness of food as a reinforcer. Again, medication can have beneficial as well as detrimental side effects when viewed from a behavioral perspective.

Medication may also alter the effectiveness of negative reinforcement through an abolishing function. One way is to neutralize the noxiousness of a stimulus. An example of this is the anxiolytic side effect sometimes produced by the antiepileptic drug carbamazepine (Tegretol®). A university student with epilepsy may experience severe "test anxiety" that occasions avoidance of certain classes, even though they are part of the student's major area of study. A side effect of taking carbamazepine could be that the student is not anxious about this class or the possibility of being tested on the subject matter. In this instance, the medication has neutralized noxious stimuli, reducing the probability of escape or avoidance behavior.

Another example of altering the effectiveness of negative reinforcement could involve carbamazepine producing a side effect, such as nausea, that competes with a response that is negatively reinforced. As a result of experiencing nausea, an individual is more likely to allocate his or her behavior to an alternative response rather than the desired response. For example, consider an individual for whom a differential negative reinforcement contingency is being used to facilitate the completion of work as a means of escaping it. Nausea could potentially be more aversive than engaging in work, and escape from work would no longer be negatively reinforcing because it competes with escaping or avoiding nausea. As seen in the above examples, abolishing effects associated with medication may be direct or mediated through an intervention such as a differential negative reinforcement contingency.

## MEDICATION THAT AFFECTS STIMULUS CONTROL

Although MOs may be a primary behavioral process of interest in relation to side effects of medication (the answer to this assertion is empirical and cumulative), it is important to note that side effects may serve other operant functions. As previously mentioned, side effects might serve as stimulus control for response–reinforcer relations. That is, the presence of a side effect may serve as a stimulus that occasions responding as either a discriminative or conditional discriminative stimulus. In a three-term contingency, it is the discriminative stimulus that occasions the response by signaling the availability of reinforcement. In a four-term contingency, the original three-term contingency (discriminative

stimulus, response, and reinforcer) is in effect only in the presence of the conditional stimulus (Sidman, 1986). In this section, we illustrate how medication side effects might serve as stimulus control.

*Discriminative stimulus control.* Medications may alter the discriminative stimulus control exerted by members of a stimulus class previously associated with established response–reinforcer relations (e.g., Lubinski & Thompson, 1987). For example, consider an individual who is greeting acquaintances in a large social gathering. Typically in such situations, the individual would greet only those individuals whom she had previously met. However, while taking the antipsychotic thioridazine (Mellaril®), her vision becomes blurred and discrimination between familiar and unfamiliar faces becomes more difficult, resulting in her greeting strangers as well as previous acquaintances. In this example, the stimulus control gradients that influence the discriminative stimulus control of her greeting others have been broadened by the psychotropic medication.

*Conditional stimulus control.* It is also possible for a side effect to have a history of differentially predicting the availability of reinforcement under other stimulus conditions. The availability of reinforcement, signaled by an $S^D$, is contingent on the presence of a conditional discriminative stimulus. For example, while taking the antidepressant venlafaxine hydrochloride (Effexor®), an individual has muscle tension as a physical side effect. In the past, when swimming (a preferred activity), this person may have had muscle spasms and tension that led to near drowning (i.e., an aversive event). As a result of this history, when muscle tension occurs, the individual may refuse to engage in any activity in which water is involved (e.g., swimming, bathing, or showering). However, when there is no muscle tension, water activities are tolerated. In this instance, the private event of muscle tension serves as a conditional discriminative stimulus for water to serve as an $S^D$ for avoidance or escape behavior, even though the stimulus is produced by the medication.

## SIDE EFFECTS THAT AFFECT NEW RESPONSE–REINFORCER RELATIONS

Finally, we propose that medication may affect response–reinforcer relations. That is, the presence of side effects may result in the emergence of novel stimuli that directly reinforce or punish behavior. What follows in this section is an illustration of how medication affects reinforcer–response relations.

*Reinforcing effects.* First, medication may produce stimuli that function as positive or negative reinforcers, thus increasing the probability of behavior. For example, a side effect may create a new response/positive-reinforcer relation if, after taking lorazepam (Ativan®; an anxiolytic often used to treat seizure disorders), a person experiences muscle relaxation. As a result, this individual may begin to increase his or her use of the medication beyond the requirement for seizure control (i.e., medication abuse). In this example, a side effect of a drug can function as a positive reinforcer, increasing the use of the medication.

Side effects may also serve as negative reinforcers. An example of this effect is an overweight person taking the antidepressant medication bupropion hydrochloride (Wellbutrin®), which has a side effect of appetite suppression. As a result, the individual eats less and experiences weight loss. Continuation of the medication, possibly regardless of the therapeutic effect, is more likely to occur given that it results in the suppression of appetite and resulting weight loss.

*Punishing effects.* Side effects may also function as punishers for behavior. In this instance, the defining characteristic is the probability that a behavior will decrease as a consequence of the

medication. An example of positive punishment can be illustrated with a person who is taking the opiate-blocker naltrexone (ReVia®). The blocking of opiate receptors in the central nervous system limits the body's natural ability to attenuate pain, and as a result, when a person is hugged tightly, pain is produced. This pain, which would not be experienced were it not for the medication, punishes, thereby decreasing particular physical interactions with others. An example of negative punishment would be a man taking sertraline (Zoloft®) who experiences decreased libido or impotence. As a result, he discontinues treatment with this drug despite its therapeutic effects.

## CONCLUSION

Considering the prevalence of psychotropic medication use among the range of populations with whom behavior analysts work, the likelihood of individuals experiencing side effects of psychotropic medication is high (Kalachnik, 1999). Researchers should study and identify potential changes in functional relations between the environment and behavior that occur as a result of medication. In all the examples we have provided—for motivating operations, stimulus control functions and response–reinforcer relations—functionally evaluating behavior–environment relations prior to and during the administration of medication is the most likely means of identifying the side effects of medication on behavior.

Currently, professionals take a topographical approach to side effects of medication. A practitioner looks for the physical manifestation of a potential side effect for a particular medication and notes its tolerability to the patient and his or her social milieu. Often, when side effects are observed, more medications are prescribed to treat the side effect (Valdovinos, Caruso, Roberts, Kim, & Kennedy, in press). The result is medications being prescribed to treat side effects of medications prescribed to treat behavior. Although a great deal is known about potential interaction effects of medication, prescribing medications to treat side effects may still result in interaction effects between the psychotropic medication and the medication prescribed to treat the side effect.

An alternative approach may be for behavior analysts to conduct a functional assessment of the side effects in relation to the behavior of concern. Functional assessments could be beneficial for understanding exactly how side effects influence behavior and for indicating whether environmental manipulation could either alleviate negative aspects of changes in behavior or facilitate positive changes. For example, consider an individual who is taking risperidone (Risperdal®), experiences an increase in appetite, and subsequently begins to behave aggressively to gain access to food. Once the results of a functional assessment indicate that access to food is a reinforcer, an intervention might consist of modifying an individual's diet to include an opportunity to eat more often but to eat healthy snacks to prevent weight gain. Another approach would be to use medications with a lower side-effect profile that may be amenable to behavioral treatment. For example, if an individual experiences sedation on one particular medication, a different medication that is associated with insomnia may be substituted, with modifications made to the environment to treat the insomnia.

The implications for applied researchers are in the assessment and treatment of behavior of social concern and the concurrent use of psychotropic medication. When conducting assessments of the maintenance or worsening of behavioral conditions during treatment with psychotropic medication, three questions should be considered. First, what is the side-effect profile of the medication being administered and, if more than one medication is prescribed, what is the side-effect profile for drug interactions? Second, does the individual show actual signs of side ef-

fects? Third, what possible interaction could these side effects have with the person's current environments and behavioral repertoire? If functional relations between side effects and behavior are identified, the likelihood that successful interventions will be developed and implemented is greater. We hope that the current conceptual analysis of side effects of medication will serve to improve the probability that such effects will be assessed and functionally analyzed to improve behavior.

In summary, there are many behavioral functions of side effects of medication. They can alter the effectiveness of stimuli as consequences through establishing or abolishing operations, making stimuli either more or less reinforcing or punishing. Side effects may also serve as stimulus control for behavior under discriminative or conditional stimulus control. And, finally, side effects may serve to reinforce or punish behavior that establishes response–reinforcer relations. Conceptually analyzing the potential behavioral functions of side effects provides behavior analysts with a more complete understanding of how medication affects the relation between environment and behavior.

## REFERENCES


Barrett, J. E., Thompson, T., & Dews, P. B. (1990). *Advances in behavioral pharmacology* (Vol. 7). Hillsdale, NJ: Erlbaum.

Biton, V., Mirza, W., Montouris, G., Voung, A., Hammer, A. E., & Barrett, P. S. (2001). Weight change associated with valproate and lamatrigine monotherapy in patients with epilepsy. *Neurology, 56,* 172–177.

Bond, A. J. (1998). Drug-induced behavioural disinhibition: Incidence, mechanisms, and therapeutic implications. *CNS Drugs, 9,* 41–57.

Christian, L., Snycerski, S. M., Singh, N. N., & Poling, A. (1999). Direct service staff and their perceptions of psychotropic medication in non-institutional settings for people with intellectual disability. *Journal of Intellectual Disability Research, 43,* 88–93.

Harbord, M. G. (2000). Significant anticonvulsant side-effects in children and adolescents. *Journal of Clinical Neuroscience, 7,* 213–216.

Kalachnik, J. E. (1999). Measuring side effects of psychopharmacologic medication in individuals with mental retardation and developmental disabilities. *Mental Retardation and Developmental Disabilities Research Reviews, 5,* 348–359.

Kennedy, C. H., Caruso, M., & Thompson, T. (2001). Experimental analyses of gene–brain–behavior relations: Some notes on their application. *Journal of Applied Behavior Analysis, 34,* 539–549.

Kennedy, C. H., & Meyer, K. A. (1996). Sleep deprivation, allergy symptoms, and negatively reinforced problem behavior. *Journal of Applied Behavior Analysis, 29,* 133–135.

Kennedy, C. H., & Meyer, K. A. (1998). The use of psychotropic medication for people with severe disabilities and challenging behavior: Current status and future directions. *Journal of the Association for Persons with Severe Handicaps, 23,* 83–97.

Kennedy, C. H., Meyer, K. A., Werts, M. G., & Cushing, L. S. (2000). Effects of sleep deprivation on free-operant avoidance. *Journal of the Experimental Analysis of Behavior, 73,* 333–345.

Klatt, K. P., & Morris, E. K. (2001). The Premack principle, response deprivation, and establishing operations. *The Behavior Analyst,* 173–180.

Laraway, S., Snycerski, S., Michael, J., & Poling, A. (2003). Motivating operations and terms to describe them: Some further refinements. *Journal of Applied Behavior Analysis, 36,* 407–414.

Lubinski, D., & Thompson, T. (1987). An animal model of the interpersonal communication of interoceptive (private) states. *Journal of the Experimental Analysis of Behavior, 48,* 1–15.

May, M. E., Harvey, M. T., Valdovinos, M. G., Klein, R. J., Wiley, R. G., & Kennedy, C. H. (2003). *Age and nociceptor specfic effects of REM sleep deprivation induced hyperalgesia.* Manuscript submitted for publication.

McGill, P. (1999). Establishing operations: Implications for the assessment, treatment, and prevention of problem behavior. *Journal of Applied Behavior Analysis, 32,* 393–418.

Michael, J. (1982). Distinguishing between discriminative and motivational functions of stimuli. *Journal of the Experimental Analysis of Behavior, 37,* 149–155.

O'Reilly, M. F. (1997). Functional analysis of episodic self-injury correlated with recurrent otitis media. *Journal of Applied Behavior Analysis, 30,* 165–167.

Reiss, S., & Aman, M. G. (1998). *Psychotropic medications and developmental disabilities: The international consensus handbook.* Columbus: Ohio State University.

Sidman, M. (1986). Functional analysis of emergent verbal classes. In T. Thompson & M. D. Zeiler (Eds.), *Analysis and integration*

*of behavioral units* (pp. 213–245). Hillsdale, NJ: Erlbaum.

Valdovinos, M. G., Caruso, M., Roberts, C., Kim, G., & Kennedy, C. H. (in press). Prevalence of side effects associated with psychotropic medication use in people with developmental disabilities. *American Journal on Mental Retardation.*