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EXPERIMENTAL ANALYSES OF GENE–BRAIN–BEHAVIOR RELATIONS: SOME NOTES ON THEIR APPLICATION

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The fields of genetics and neuroscience are yielding findings useful in understanding complex behavior–environment relations. We believe that these developments in interdisciplinary basic research are of interest to applied behavior analysts because of the long history of basic findings being used by the readership of the *Journal of Applied Behavior Analysis* to improve everyday human activities. An awareness of contemporary developments in a range of basic research disciplines may facilitate the systematic replication of those functional relations in applied settings. In this context, we selectively review papers published in the *Journal of the Experimental Analysis of Behavior* and other basic research journals that relate to gene–brain–behavior relations.

DESCRIPTORS: genetics, neuroscience, applied behavior analysis, experimental analysis of behavior

The *Journal of the Experimental Analysis of Behavior* (*JEAB*) and the *Journal of Applied Behavior Analysis* (*JABA*) are replete with functional relations between behavior and environment. These relations include a multitude of basic processes, including positive reinforcement, negative reinforcement, response classes, stimulus control, stimulus equivalence, and establishing operations, to name only a few. Fundamental parameters of behavioral processes have been extensively explored in *JEAB* and applied to a wide range of human concerns in *JABA*.

Concurrent with developments in behavior analysis have been advances in two other areas that bear on human psychology: genetics and neuroscience. During the 1990s advances have occurred in neuroimaging and neuropharmacology that allow real-time analysis of brain activity in relation to environmental events and the selective pharmacological targeting of brain chemistry believed to be related to changes in behavior. Similarly, with the sequencing of the human genome, opportunities have emerged to relate alterations in genetic makeup to changes in responding and the sensitivity of behavior to environmental stimulation.

Intersections among genetics, neuroscience, and behavior analysis have occurred with increasing frequency over the past decade. The most frequent locus for this intersection has been in the laboratory, where operant conditioning techniques have been used across a range of disciplines (e.g., pharmacology, psychiatry, and psychology) to study behavior and biology. For example, the behavioral phenotyping of mutant mice (i.e., animals that have had specific genes either deleted or added to their genome) is becoming routine for identifying genetic influences on behavior (Hen, 1999).

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Indeed, novel areas of research, such as psychopharmacogenetics, are emerging from the integration of research on genetics, neurobiology, and behavior (Cook, 1999). The goal of psychopharmacogenetics is to study the interaction of brain chemistry and environmental and genetic influences to understand how they influence behavior. Research in such emerging disciplines is revealing how phylogenetic variables interact over the course of development with environmental events to determine behavioral phenomena. For example, recent research has shown that alterations in the gene that transports the neurochemical serotonin back into cells from the synapse predict differential treatment outcomes for people with psychiatric conditions, such as depression and anxiety disorders (e.g., Weizman & Weizman, 2000).

Findings like these should lead to a closer integration of genetics and the selection of specific interventions—pharmacological, behavioral, or both—to increase treatment efficacy. A predictable result of this research will be a greater appreciation of the functional interactions among a person's genotype, brain chemistry, and behavior. Further revealing how behavior–environment relations change, and are changed by, biological influences will provide a more complete account of human psychology. For applied behavior analysts, one benefit of studying gene–brain–behavior relations is the potential for improved treatment outcomes through a better understanding of the environmental and biological determinants of behavior.

We will review two areas in which gene–brain–behavior relations seem most relevant to behavior analysis through a review of papers published in *JEAB* and related basic research journals. The first section focuses on brain chemistry and behavior. In this section we will discuss research analyzing the role of neurotransmission in mediating the reinforcing effects of stimuli. The second section focuses on the interaction of genes and behavior; that is, how a person's genotype can differentially affect the types of behavior he or she engages in, and how sensitive various behavioral processes are to environmental events. Our goals are to provide a review of several laboratory studies relating to gene–brain–behavior analyses and provide some suggestions for how these findings may be of interest to applied behavior analysts.

Brain Chemistry and Reinforcement

Dopamine is a neurochemical of particular interest to behavior analysts because it is involved in phenomena such as positive reinforcement, movement, and remembering (Schultz, Dayan, & Montague, 1997). Dopamine antagonists—that is, drugs that decrease dopaminergic activity (e.g., haloperidol [Haldol])—have been used since the 1950s in the treatment of schizophrenia; elevated levels of dopamine have been hypothesized to be a critical feature of this disorder. Interestingly, dopamine agonists—that is, drugs that increase dopaminergic activity—are involved in the addictive effects of drugs like *d*-amphetamine, cocaine, and methylphenidate (MPH [Ritalin]).

Researchers have been interested for decades in how neurochemicals such as dopamine are involved in behavioral processes. Early research published in *JEAB* suggested that dopaminergic agonists like the amphetamines served a stimulant function on behavior. In the first volume of *JEAB*, Verhave (1958) analyzed the effects of methamphetamine on free-operant avoidance behavior. Rats were taught to lever press to postpone electric shocks that otherwise occurred at fixed intervals. A contingency such as this establishes negatively reinforced behavior by avoiding noxious stimulation. The overall outcome from a series of experiments was that administration of methamphetamine increased rates of negatively reinforced re-

sponding. Studying a qualitatively different reinforcement process, Dews and Morse (1958) reported that *d*-amphetamine increased the positively reinforced responding of humans. Using a differential-reinforcement-of-low-rate schedule, responding of typical adults was positively reinforced by monetary rewards. The schedule established intermittent responding consistent with the reinforcer contingency in effect, with response rates increasing following administration of the dopamine agonist. These findings replicated an earlier finding by Dews (1958) that showed that methamphetamine increased rates of positively reinforced behavior in nonhumans.

The behavioral effects of dopamine agonists just reviewed are more complex than simply stimulating an overall increase in activity. An illustration of this point is provided by J. Dougherty and Pickens (1973), who analyzed the effects of cocaine (a dopamine agonist) on positively reinforced responding. These authors established the lever pressing of rats on a fixed-interval schedule of intravenous cocaine administration. The result was a stable pattern of responding characteristic of fixed-interval schedules with cocaine administration as the consequence. This study is consistent with numerous subsequent studies that have shown that dopamine agonists such as *d*-amphetamine, cocaine, and MPH function as positive reinforcers for operant behavior. However, administration of dopamine antagonists (e.g., haloperidol) contingent on responding has shown that these compounds do not maintain responding (i.e., they do not function as positively reinforcing stimuli) (White, 1996).

The interrelation between dopaminergic activity and the effects of stimuli as positive reinforcers is shown in two studies using different pharmacological strategies. A classic approach to studying the effects of a presumed agonist for a particular neurochemical is to preexpose the subject to an antagonist for the same neurochemical. Winsauer and Thompson (1991) used such an approach to study the role of dopamine receptors in the positively reinforcing effects of cocaine. In one of these experiments, pigeons' key pecking was reinforced with either food or cocaine on a fixed-ratio multiple schedule, alternating between components with food or cocaine delivery. Animals were administered haloperidol prior to some sessions. When animals were preexposed to haloperidol, food continued to function as a reinforcer, but cocaine stopped functioning as a reinforcer. Once the dopamine antagonist was removed, both food and cocaine functioned as positively reinforcing consequences for responding.

The effect of dopaminergic agonists like cocaine, MPH, and the amphetamines at the cellular level is to block the reuptake of dopamine once it has entered the synaptic cleft. This process increases concentrations of dopamine at postsynaptic receptors, which stimulates increased activity in cells with postsynaptic dopamine receptors. The effect of dopamine antagonists is to occupy the postsynaptic dopamine receptors so that dopaminergic agonists cannot affect postsynaptic neurotransmission.

One important element of how dopamine agonists function as positive reinforcers is missing from the analyses just reviewed. All of the previous studies manipulated neurochemistry in the entire brain. Such whole-brain manipulations are important analytical tools, but they do not help to identify the specific brain regions that are involved in these effects other than, in this case, dopamingeric systems throughout the central nervous system. Recent research, some of which has appeared in *JEAB*, is helping to identify not only the brain chemicals involved in how dopamine agonists functions as positive reinforcers but also the neural substrates of

the brain that are involved in this behavioral process (Caine & Koob, 1994).

An area of the brain that has received a great deal of attention from researchers interested in positive reinforcement is the nucleus accumbens. The nucleus accumbens is part of a subdivision of the brain called the limbic system that is densely innervated by dopamine-producing neurons. This system has been implicated in psychological phenomena such as reward, remembering, and learning. If the nucleus accumbens is destroyed by lesions, dopamine agonists stop functioning as positive reinforcers (Robins & Koob, 1980). One issue that arises from studies of dopamine agonists functioning as positive reinforcers and the localization of specific brain regions is whether the lesioning studies selectively alter the effects of dopamine agonists or affect all stimuli that might function as positive reinforcers.

A study by Caine and Koob (1994) analyzed whether lesioning the nucleus accumbens produced effects that were selective to the dopamine agonist (cocaine) or more robustly affected positive reinforcers not involving dopamine. Caine and Koob established the lever pressing of rats under a multiple schedule of reinforcement that alternated between the delivery of food pellets and intravenous cocaine. Once stable baselines were established, the nucleus accumbens was destroyed to assess its role in reinforcement. A methodological improvement over previous studies by Caine and Koob was the lesioning technique. Previous research had typically used methods that destroyed all the cells in the nucleus accumbens and any nerve fibers that traveled through that area. As an alternative, these authors used a neurotoxin that selectively destroys only neurons that contain dopamine, thus preserving other cells and nerve fibers. Animals that received sham lesions (i.e., using saline rather than the neurotoxin) continued to respond to obtain food or cocaine. Animals who received the neurotoxin lesions continued to respond to obtain food, but their responding for cocaine greatly decreased. An additional control technique was used in another set of animals that, following sham lesions, were given intravenous saline rather than cocaine (a type of extinction procedure). The responding of the lesioned rats and saline rats showed the same selective reductions during the "cocaine" component of the multiple schedule. These findings suggest that the nucleus accumbens is selectively involved in the positive reinforcement effects of dopamine agonists.

Basic research findings suggest that drugs that are agonists of the dopaminergic system function as positive reinforcers, and that effect is mediated by the limbic system in the brain. So, what does all of this have to do with applied behavior analysis? In general, these findings illustrate the interrelation between reinforcement and neurobiology. Basic research is providing evidence of the brain chemistry and neural circuits that are involved in specific types of reinforcer functions and stimulus types. Another means by which the findings just reviewed are relevant is that they provide insights into how particular types of disabilities may be manifested at a neurobiological level and how those changes may affect behavior–environment relations. Yet another way in which neuroscience research is of relevance to applied behavior analysts is the potential for understanding interconnections among brain activity, behavioral functioning, and the effects of psychotropic medications.

One area of application for the findings discussed above is attention deficit hyperactivity disorder (ADHD). Hallmarks of ADHD are impulsivity, hyperactivity, difficulties in attending to task, and a lack of sensitivity to classroom-related positive reinforcement contingencies. Not surprisingly, students with ADHD are at greater risk for

school failure than are typically developing students.

There is evidence that people with ADHD have altered dopaminergic brain activity (Cook et al., 1995; Daly, Hawi, Fitzgerald, & Gill, 1999). Specifically, research suggests that these differences are related to the gene that transports dopamine back into the terminal button following release into the synaptic cleft. Dysregulation of the dopamine transporter (DAT) gene may result in an increased expression of DAT in the brain, thus increasing the reuptake of dopamine into presynaptic cells (D. Dougherty et al., 1999; Krause, Dresel, Krause, Kung, & Tatsch, 2000). The result is decreased indopaminergic activity that, given the neuromodulatory role that dopamine serves, may result in alterations in a number of related brain circuits. For example, some researchers have postulated that disruptions in DAT genes may result in stimuli functioning less effectively as positive reinforcers via lowered dopaminergic activity in the limbic system (Koob, 1996). However, more research is needed to clarify how DAT gene anomalies are manifested in humans. Interestingly, a common drug used to treat ADHD is MPH. At the cellular level, MPH blocks the reuptake of dopamine into presynaptic cells, increasing extracellular levels of dopamine (Volkow et al., 2001). This suggests that the neurobiological effect of MPH is that it stabilizes disruptions in dopamergic activity produced by a defective DAT gene.

Possible implications of these findings for behavioral analyses of ADHD might include (a) interactions between operant function and neurochemistry, (b) medication-induced shifts in preference hierarchies, and (c) research on treatment efficacy identifying optimal levels and combinations of behavior-analytic and psychotropic interventions. We will briefly discuss each of these areas.

Applied behavior analysts are only beginning to look at how psychotropic medications affect operant behavior (Kennedy & Meyer, 1998; Schaal & Hackenberg, 1994; Thompson, Egli, Symons, & Delaney, 1994). Although there are numerous basic studies of drug–behavior interactions conducted in operant laboratories, only recently have behavior-analytic studies begun to emerge with specific human populations. The drug compound that has been most frequently analyzed is MPH. Recent research has focused on the effects of MPH on altering sensitivity of behavior to reinforcing consequences in students with ADHD. For example, Murray and Kollins (2000) found that the behavior of students with ADHD was more sensitive to reinforcement schedule parameters under MPH than compared to a placebo condition. Such findings suggest that MPH alters the sensitivity of behavior to environmental events, consistent with laboratory findings.

Yet to be studied is how drugs like MPH alter different behavioral processes and particular types of stimuli (see Northup et al., 1999). For example, does MPH, which primarily alters dopamingeric neurotransmission, have its effect through increased efficacy of rewards offered under positive reinforcement contingencies, or does it also alter the negatively reinforcing properties of instructional contexts? The basic literature we have reviewed appears to suggest the former process, but an answer to this question in applied contexts awaits a behavioral analysis. Similar questions could be raised for a range of psychotropic compounds commonly prescribed to treat problem behaviors that are known to affect a variety of neurochemicals and brain systems. Laboratory research has repeatedly shown that compounds selective for specific neurotransmitter systems have selective effects on behavioral processes (e.g., Caine & Koob, 1994). Experimental analysis of behavioral functions and how they are altered (or left unchanged) by psychotropic

medications is an area that awaits further development in applied research.

Drugs like MPH have been demonstrated in the laboratory to differentially affect the reinforcing properties of certain stimuli. For example, Caine and Koob (1994) showed that eliminating specific dopamine neurons resulted in a dopamine agonist that no longer functions as a positive reinforcer, but food as positive reinforcement was unaffected. Could similar effects be seen in humans as a result of altered dopaminergic functioning? One test of this hypothesis would be to establish preference hierarchies across a range of stimuli with differing "hedonic" properties and then test whether dopamine agonists like MPH or dopamine antagonists like haloperidol alter preference hierarchies and stimulus functions. Basic research findings suggest the possibility that compounds like MPH or haloperidol may cause a change in reinforcer valence for some stimuli that would result in shifts in preference hierarchies. Such findings would help practitioners to predict how behavior support plans might be affected by a person beginning or terminating a particular drug regimen.

Finally, by gaining a better understanding of how particular drugs alter brain chemistry, affect the operant function of behaviors of interest, and cause changes in reinforcer effectiveness, the potential for a new generation of targeted interventions is created. Tremendous gains have been made in the last decade by linking the assessment of variables maintaining problem behavior with interventions based on operant function. If applied behavior analysts could develop similar functional assessment techniques for identifying how particular topographies of behavior might be affected by particular drugs and, similarly, how the reinforcing valences of stimuli are affected, further refinement in interventions would be expected. Treatment efficacy research might focus on optimizing behavioral and pharmacological interventions for people with behavior problems on an individual basis as a result of assessment profiles. Currently, behavioral interventions are linked to the functions of behavior, but without an understanding of how pharmacological interventions may change, eliminate, or create operant functions for a range of behaviors. Similarly, the prescription of psychotropic medications could be matched to the operant function of behavior, rather than the current practice of basing drug prescriptions on psychiatric diagnosis or "off-label" treatment.

Genes and Behavior

A variety of deprivation operations increase the reinforcing value of specific events. In *The Behavior of Organisms*, Skinner (1938) noted that one of the important properties of food deprivation was to increase the reinforcing value of food (p. 351). Other examples of operations that increase the reinforcing value of events include (a) injecting salt solution into rats to increase the reinforcing value of drinking water (Fregly, Rowland, & Cade, 1993; Scobie & Jensen, 1973), (b) injecting an opiate antagonist into an opiate-dependent monkey to increase the reinforcing value of morphine (an opiate agonist) (Thompson & Schuster, 1964), and (c) social deprivation enhancing the reinforcing value of adult attention for children (Gewirtz & Baer, 1958). These establishing operations have a strong genetic basis and are "hard-wired" into an animal's behavioral repertoire (Catania, 1993).

Indeed, the genesis of many events that function as positive or negative reinforcers has a phylogenetic basis and is expressed as behavioral phenotypes with unique topographies of behavior–environment patterns. For example, access to the specific visual image of a conspecific Siamese fighting fish is a powerful positive reinforcer for operant responding by *Betta splendens* (Grabowski & Thompson, 1969), a stimulus that is genet-

ically unique to this particular species. Another example of a genetic role for determining specific behavior–environment relations is the spontaneously hypertensive rat. Several behavioral characteristics that are unique to this strain of rat make it of interest to applied researchers because they mirror those seen in people with ADHD. Such hypertensive rats are more active, are less reactive to novel stimuli, and have a shorter freezing response compared to other strains of rats (McCarty & Kopin, 1979). In addition, these rats require more trials to learn various tasks and show greater baseline variability across tasks, whether or not variability is reinforced (Hunziker, Saldana, & Neuringer, 1996). Findings such as these illustrate the importance of an organism's genome in influencing behavioral characteristics and responsiveness to the environment.

The proliferation of information about genetic causes of specific phenotypic features, including behavioral features, has spawned interest in genetic variables as mediators of behavioral phenomena. In the field of developmental disabilities, there has been growing interest in several disabilities in which a role for genetic mechanisms has been identified, including Down syndrome, Fragile X syndrome, and Prader-Willi syndrome (see Hodapp & Dykens, in press).

In the remainder of this section, we will focus on gene–behavior relations in Prader-Willi syndrome because several recent developments related to this syndrome might be of particular interest to the *JABA* readership. Prader-Willi syndrome is a genetic developmental disability characterized by a group of specific behavioral features of which an insatiable appetite is the most striking. It is the most common known genetic cause of obesity. The eating disorder associated with Prader-Willi syndrome can be so severe as to be life threatening, including eating to the point of stomach rupture and death. Although a cluster of commonly covarying clinical features are exhibited by people with this syndrome, only the eating disorder is common to all affected individuals.

Prader-Willi syndrome shares behavioral features with other disorders and disabilities, such as obsessive compulsive disorder and autism, but only Prader-Willi syndrome includes the unique combination of characteristics that distinguish this syndrome. Because eating disorders such as bulimia and anorexia nervosa also share features with Prader-Willi syndrome, understanding the causes of the eating disorder in Prader-Willi syndrome could potentially have implications for other eating disorders.

Prader-Willi syndrome was first described in 1956, and since that time over 800 papers on the topic have been reported in the research literature (see Donaldson et al., 1994). The main clinical features include poor muscle tone during infancy with improvement by 9 months of age and obesity with onset between 6 months and 6 years of age. Although people with Prader-Willi syndrome have a developmental disability, they do not necessarily have mental retardation. Slightly less than half of the people with Prader-Willi syndrome function in the low-to-average range of intellectual functioning, and somewhat more than half test in the mild to moderate range of mental retardation. Roughly 60% to 70% have a partial deletion of a section of the long arm of Chromosome 15. Prader-Willi syndrome affects about one in every 10,000 to 20,000 individuals (Butler, 1990; Greenswag, 1987).

The specific genes that determine the relative reinforcing properties of food for people with Prader-Willi syndrome are not known, although several candidate genes in the Chromosome 15q11-13 region have been identified that appear to play a role in obesity and the eating disorder associated with Prader-Willi syndrome. One strategy for identifying the genetic basis of obesity

has been to use animal models. An often-used animal model of obesity is the OLETF rat, which lacks CCK_A receptors. Rats that lack CCK_A receptors exhibit hyperphagia, obesity after weaning, late-onset hyperglycemia, and chronic diabetes (Moran, 2000). CCK_A release is stimulated by rises in free fatty acids after a meal and mediates within-meal satiety. In normal individuals, rises in free fatty acids are correlated with rises in CCK_A (Guimbaud et al., 1997). Although baseline resting levels of plasma CCK_A in people with Prader-Willi syndrome are not significantly different from control participants, they do not demonstrate the correlational rises in CCK_A and free fatty acids after meals noted in control subjects (Butler, Carlson, Schmidt, Feurer, & Thompson, 2000). Thus, differences in response of peripheral CCK_A to free fatty acid levels may result in an altered satiety response in individuals with Prader-Willi syndrome. This altered satiety response in turn affects the reinforcing value of food.

Attempts have been made to better understand the nature of food motivation in Prader-Willi syndrome using a choice or "delayed gratification" model (Rachlin, 2000). To study this, a choice procedure was used, in which participants with and without Prader-Willi syndrome selected one of two stimuli, each associated with its own delay and food amount (Dimitropoulos et al., 2000). Each participant was presented with two horizontally adjacent squares, distinguishable by color, on a computer display. Touching one square was followed by the immediate presentation of one piece of sugarless candy; touching the other was followed by the presentation of three pieces of candy following a delay. During the first four trials of each block, only one of the two squares was presented, with each appearing exclusively on two of these four trials. These forced-choice trials served to acquaint the participant with the delay conditions in effect during each block of trials. The subsequent 10 trials consisted of free-choice trials in which both response options were available (i.e., immediate access to one piece of candy or delayed access to three pieces of candy). Over a range of delays, the participants with Prader-Willi syndrome tended to choose the larger delayed food presentation, regardless of the length of the delay. The control group tended to choose both outcomes equally often. The participants with Prader-Willi syndrome were more likely to select the larger delayed food reward than were the control participants. This is contrary to what is often reported anecdotally about people with Prader-Willi syndrome, in that they are often said to be impulsive (i.e., that they are unable to delay food choices). It appears that people with Prader-Willi syndrome are capable of self-control when there is sufficient incentive. The control participants appeared to be indifferent to reward size, in that they tended to choose both the small and large reward magnitudes nearly equally. This may have implications for treatment. People with Prader-Willi syndrome are especially sensitive to food reinforcer magnitude relative to intellectually matched peers, suggesting that appropriate choices may be optimized by employing larger delayed healthful edible consequences.

Bakke (1990) studied the relation between magnitude of food reinforcement and the distance cycled by people with Prader-Willi syndrome using a stationary exercise bicycle. Bakke found that the distance participants were willing to cycle was directly proportional to the caloric value of the food reinforcement provided. Using a slightly different approach, Keefer, Jackson, and Pennypacker (2000) developed an exercise program for individuals with Prader-Willi syndrome. Seven individuals were given the choice to exercise or not. Participants earned higher levels of caloric intake for meeting individualized exercise criteria. Interestingly,

for all participants, intensive aerobic exercise was established and maintained when these behaviors provided access to increased food intake. Keefer et al. also found that providing food choice increased the participants' cooperation with the daily exercise protocol and enhanced weight loss and subsequent weight maintenance.

The genetic mechanisms that increase the reinforcing value of food in Prader-Willi syndrome appear to turn on between 12 and 24 months of age (Dimitropoulos et al., 2000). But unlike laboratory food deprivation, once food reinforcement value has increased in Prader-Willi syndrome, it does not gradually decline, as does typical food satiation. But this difference in time course of some establishing operations is not unique. Sexual reinforcement is enhanced by the genetically regulated hormonal changes that occur at puberty, which although not permanent, are certainly long lasting. We believe that applied behavioral analysts could benefit from considering a broader array of genetically regulated factors in arriving at a further understanding of the mechanisms that underlie behavioral phenomena such as food intake in Prader-Willi syndrome.

Conclusion

Efforts to establish relations between behavior and biology continue to increase in basic research across a range of disciplines (Strumwasser, 1994). This research is integrating content among three key areas: behavior, neurobiology, and genetics. These three areas mutually influence each other and provide a complex set of linkages for broadening our understanding of human behavior. As research progresses on how behavioral development is influenced by brain development and genetics, and vice versa, a more robust analysis of the causes of behavior will be forthcoming.

Basic research on gene–brain–behavior relations may also have important applied implications. In this paper we have discussed two potential areas that could benefit from an expanded view of variables analyzed in applied behavior analysis. In the area of ADHD there is growing evidence that altered dopaminergic neurotransmission plays a role in the behavioral characteristics of this disorder. In addition, research on dopamine functioning at the cellular level may explain why drugs such as MPH can be effective pharmacological interventions for ADHD in some cases. In the area of Prader-Willi syndrome there is increasing evidence that genetic variables can influence the occurrence of specific behaviors. For example, people with a paternal 15q11-13 deletion or maternal uniparental disomy of Chromosome 15 express the characteristics that define Prader-Willi syndrome. Perhaps of greater interest to behavior analysts is the finding that small genetic variations involved in Prader-Willi syndrome are associated with different topographies of problem behavior, such as excessive food intake, relative to other disabilities.

The research reviewed in this article is only a small sampling of topics that await further integration between behavior analysis and biology. Other possible areas include a better understanding of how specific psychotropic medications differentially affect behavioral processes that are related to problem behavior. For example, how do antiepileptic medications alter positively versus negatively reinforced behavior, and how do the effects of a certain drug on brain chemistry relate to these changes in behavior? Or, how do changes in brain development lead to the expression of behavioral characteristics in autism, and how do certain behavioral interventions result in improved behavioral functioning?

When *JABA* was founded as a journal in the 1960s, such questions could have been dismissed as science fiction. However, we predict that such questions will increasingly

occupy the attention of basic and applied researchers who are interested in behavior analysis. We are not suggesting that behavior–environment relations will no longer be a focus for behavior-analytic researchers, only that with developments in neurobiology and genetics there will be increasing opportunities to relate these different fields to the causes of behavior. Such interdisciplinary efforts may result in an increased understanding of why behavior does or does not occur, and possible strategies for improving human development in cases in which the prognosis for a typical life is questionable.

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