

RELATING BEHAVIOR AND NEUROSCIENCE: INTRODUCTION AND SYNOPSIS

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Background

B. F. Skinner, in a chapter on “Behavior and the Nervous System” in his seminal work, *The Behavior of Organisms* (1938, pp. 418–432), expressed both strong interest in and considerable concern about relating behavior and what he termed “neurology.” On the positive side, he subscribed to a unified reductionist science: “One of the objectives of science is presumably the statement of all knowledge in a single language.” He treated this objective as a fundamental reason to intensely cultivate a behavioral approach because it would produce “. . . more rapid progress toward an ultimate synthesis [of the laws of behavior and the laws of the nervous system].”

At the same time Skinner spoke strongly against “. . . proceeding from a behavioral fact to its neural correlates instead of validating the fact as such, and then proceeding to deal with other problems in behavior.” In short, his goal was: first, to establish an independent science of the control and dynamics of behavior, separate from neural, physiological, and cognitive references and speculations; and then, to bridge the gap between behavior and neurobiology by a comprehensive integration. Skinner also placed strict preconditions on both sciences. He argued that neurobiological concepts had to be adequate to account for the complexity of the dynamics of behavior, and that numerous behavioral issues needed to be resolved, among them: distinguishing Type R (Operant) and S (Pavlovian) conditioning; clarifying the basis of temporal dis-

crimination; finalizing distinctions among stimulus functions; grouping reflexes by drives and emotions; and establishing the dynamics of reinforced behavior.

Thirty-six years later in a chapter on “What is Inside the Skin?” in *About Behaviorism* (1974, pp. 207–218), Skinner reaffirmed the importance of a reductionist framework, and again rejected attributing the cause of a behavior to a single neurobiological entity, whether it was a synapse, an anatomical structure, an emotion, or a motivation. The possible exception he noted was appealing to neural events to fill inevitable gaps in an operant account. For example, because behavioral accounts of reinforcement are “necessarily historical,” they leave gaps between events that might be filled in by neural processes related to memory. It was clear, though, that any large-scale integration remained far in the future, following the establishment of comprehensive and independent behavioral and neural sciences.

From the publication of *The Behavior of Organisms* to the present, the analysis and control of behavior has proliferated in academic and applied settings around the world. The Association for Behavior Analysis has grown to around 4700 members spread among 43 countries. The study of neuroscience has expanded even more rapidly. The Society for Neuroscience is a thoroughly international organization numbering over 37,000 members. Most relevant for our interest in relating behavior and neuroscience, Skinner’s methods have been widely adapted by neuroscientists. In fact, Skinner and his students played crucial roles in founding psychopharmacology, a field pursued in medical schools, drug companies, and multiple academic departments (Laties, 2003). Other scientists influenced directly or indirectly by Skinner adopted operant procedures and apparatus to measure the effects of brain lesions or brain stimulation on learning, discrimination, and motivation (e.g., Grossman, 1979). Still others have used operant techniques to study drug addiction, memory, the molecular basis of

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reinforcement, and effects of environmental pollutants on learning and behavior.

In short, there is considerable evidence for the existence of independent sciences of behavior and of neurobiology, *and* there is research that combines aspects of both. What is missing is the broad conceptual integration that Skinner began pointing toward in 1938. It might be argued that the time is not yet right because neuroscience has yet to account for the fine-grained dynamics of operant behavior (or because operant conditioning has yet to resolve the majority of the behavioral problems Skinner laid out in 1938). But such objections, however reasonable they may appear, ignore research that already has begun to integrate neuroscience and behavior.

What seems clear at this point is that there has not been (and will not be) one obvious moment when scientists agree to pursue full integration of neuroscience and behavior (or among neuroscience, behavior, and cognition). Neither will there be a single set of experiments, or a single experimental question, that seamlessly joins these approaches. Instead, there have been (and will continue to be) specific instances when enough is known about neurobiological and behavioral phenomena to integrate levels successfully (e.g., Schaal, 2003). Further, the potential for integration will be greater as experimenters use causal manipulations and analyses that consider both neuroscience and behavior. At the least, operant procedures can distinguish among effects of motivation versus discrimination or memory disruption, while increased knowledge of the involvement of specific brain mechanisms can direct experimental attention to specific manipulations, behaviors, and the timecourse of effects.

Purpose and Organization

The purpose of this special issue of the *Journal of the Experimental Analysis of Behavior* is to present experimental and conceptual articles that illustrate recent efforts to relate neuroscience and behavior in individual subjects. In abstract terms, this issue is intended to illustrate mappings between behavior and neuroscience that range from simple to complex. In concrete terms, this issue focuses on four areas: I. Effects of Drugs and Genetics on Common Operant Tasks; II. Complex Stimulus Relations; III. Discrimina-

tion, Choice, and Cortical Brain Activity; and IV. Neural and Behavioral Analyses of Learning-Related Brain Circuitry and Addiction. We begin this issue with a historical preface to the problem of reductionism by the philosopher William Bechtel, and finish with a book review by David Schaal of Bennett and Hacker's *Philosophical Foundations of Neuroscience*.

SYNOPSIS

Preface: Issues in Bridging Levels of Analysis

William Bechtel (*The challenge of characterizing operations in the mechanisms underlying behavior*, pp. 313–325) notes two problematic tendencies that need to be overcome in relating phenomena across levels of analysis. The first tendency is to presume that causal workings (Bechtel uses the term “operations”) at a lower level of analysis are of the same sort as those analyzed at higher levels. Bechtel draws an example from physical chemistry and the phenomenon of fermentation. As a parallel we might consider the concept of reinforcement. By analogy to Bechtel's example, attempts to reduce behavioral reinforcement to lower-level mechanisms typically are based on concepts of behavioral reinforcement, which, instead of referring to behavior-level operants, discriminative stimuli, and reinforcers, are used to designate parallel elements at the level of circuits, individual neurons, transmitters, ion channels, and/or molecules.

The second tendency Bechtel calls attention to is that of skipping levels of analysis when invoking causal connections. Applied to reinforcement, his warning calls attention to the multiple levels of mechanism that are omitted when we attribute the reinforcement of lever pressing to, say, GABA release. Such a correlation, even if present, does not specify the mechanisms that connect the multiple levels of organization separating GABA release and lever pressing. As an engineering problem, we would be unable to duplicate the effect in a realistic model of an organism.

A simple example may help illustrate both of Bechtel's points. Consider accelerating a car. At the level of the driver, the cause involves pressing down on the gas pedal. At the level of production of energy, the cause is the igniting of gasoline under pressure. In between are multiple workings including: throttle linkage,

carburetor, gas tank, fuel pump, spark plugs, valves, timing rotor, pistons, cam shaft, drive train, clutch, transmission, axles, wheels, and tires. There are no "accelerators" to press at lower levels, and no "explosions" at higher levels. The mechanisms differ at each level, and they all are necessary for the car to accelerate. We cannot expect links between behavior and neurobiology to be any less complex.

Section I: Effects of Drugs and Genetics in Common Operant Tasks

The experiments reported in Section I use well-developed operant tasks to reveal multiple effects of drugs and genes on behavior. Researchers report on the role of reinforcement schedules in clarifying drug effects on extinction (Leslie, Shaw, Gregg, McCormick, Reynolds, & Dawson); mouse strain effects on lever pressing for food (McKerchar, Zarcone, & Fowler); the developmental effects of drug-induced seizures on hearing (Neill, Liu, Mikati, & Holmes); the role of dopamine agonists in reinforcement matching (Bratcher, Farmer-Dougan, Dougan, Heidenreich, & Garris); and the effect of morphine on stimulus control by color and time (Ward & Odum).

(1) Leslie, Shaw, Gregg, McCormick, Reynolds, and Dawson—*Effects of reinforcement schedule on facilitation of operant extinction by chlordiazepoxide*. (pp. 327–338)

These researchers test the effects of chlordiazepoxide (a GABAergic drug) on the extinction of discrete-trial fixed-ratio or fixed-interval responding in the inbred mouse strain C57Bl/6 (a standard strain used in research). Extinction under all schedules was subject to facilitation by drug injections of chlordiazepoxide, but only if a number of extinction sessions had already occurred, and more so on FI than on FR schedules. The authors suggest that their effects are due to multiple processes in extinction.

(2) McKerchar, Zarcone, and Fowler—*Differential acquisition of lever pressing in inbred and outbred mice: Comparison of one-lever and two-lever procedures and correlation with differences in locomotor activity*. (pp. 339–356)

The authors examine the potential usefulness of testing for behavioral and procedural differences among multiple mouse strains using the standard operant task of lever

pressing for food, but they add additional measures, including: pressing an inoperative lever, locomotor activity, and the time required to move from lever to food hopper and back to lever.

(3) Neill, Liu, Mikati, and Holmes—*Pilocarpine seizures cause age-dependent impairment in auditory location discrimination*. (pp. 357–370)

Following pilocarpine injections at 20 or 45 days of age, rats were tested on auditory location and sound/silence discriminations beginning at 105 days of age. Pilocarpine injections at day 20 moderately impaired subsequent auditory location discrimination, but injections at day 45 produced subsequent failure to acquire either type of discrimination. The results are related to clinical cases of humans with a history of seizures and impaired auditory location discrimination.

(4) Bratcher, Farmer-Dougan, Dougan, Heidenreich, and Garris—*The role of dopamine in reinforcement: Changes in reinforcement sensitivity induced by D1-type, D2-type, and nonselective dopamine receptor agonists*. (pp. 371–399)

These authors are concerned with the specific actions of D1 and D2 receptors in facilitating rewarded behavior in rats. They studied the effects of injections of specific and general dopamine agonists using the matching paradigm, because this well-developed procedure provides measures of sensitivity to reinforcement. They obtained dose-dependent changes in sensitivity produced by D1 and general agonists, but not by a D2 agonist.

(5) Ward and Odum—*Effects of morphine on temporal discrimination and color matching: General disruption of stimulus control or selective effects on timing?* (pp. 401–415)

The authors used a three-component multiple schedule to compare the effects of morphine on temporal discrimination and accuracy of color matching. Their intent was to clarify the mechanisms by which morphine affects timing. Psychophysical analyses of schedule behavior showed that morphine decreased overall stimulus control by time, rather than selectively affecting timing abilities or ability to respond to the key color associated with the different schedules.

Section II: Complex Stimulus Relations

The studies in Section II focus on the relation of brain activity and complex stimulus discriminations (equivalence classes, analo-

gies, transitive inference, and biconditional discriminations involving context). The techniques used to assess brain activity include: evoked potentials in prefrontal cortex (Barnes-Holmes, Staunton, Whelan, Barnes-Holmes, Commins, Walsh, Stewart, Smeets, & Dymond; and Barnes-Holmes, Regan, Barnes-Holmes, Commins, Walsh, Stewart, Smeets, Whelan, & Dymond), fMRI in hippocampus (Dickins), and relative lesion damage to anterior cingulate and prelimbic areas of the cortex (Haddon & Killcross).

(1) Barnes-Holmes, Staunton, Whelan, Barnes-Holmes, Commins, Walsh, Stewart, Smeets, and Dymond—*Derived stimulus relations, semantic priming, and event-related potentials: Testing a behavioral theory of semantic networks*. (pp. 417–433)

(2) Barnes-Holmes, Regan, Barnes-Holmes, Commins, Walsh, Stewart, Smeets, Whelan, and Dymond—*Relating derived relations as a model of analogical reasoning: Reaction times and event-related potentials*. (pp. 435–451)

These authors use operant Matching-to-Sample discrimination training and subsequent testing procedures with humans to establish and test for the conceptual “frames” relating multiple stimuli (forming an equivalence class) or stimulus pairs (forming similar or different “analogies”). Both measures of reaction time and bilateral event-related potentials in prefrontal cortex provide support for the development of complex relations based on simpler discrimination training.

(3) Dickins—*On aims and methods in the neuroimaging of derived relations*. (pp. 453–483)

This author reviews the use of neuroimaging studies of the hippocampal area of the brain as a means of analyzing learned phenomena related to the emergence of transitive inference from the study of both stimulus equivalence and serial learning. He also briefly discusses the potential roles of evolution and ethology in relating brain and behavior.

(4) Haddon and Killcross—*Medial prefrontal cortex lesions abolish contextual control of competing responses*. (pp. 485–504)

These authors focus on the effects of medial prefrontal cortex damage on the behavior of rats trained in biconditional audio and visual discriminations. In the experiment, the lever associated with each audio (or visual) cue was correct in one context, but not in another. The test consisted of one video and one audio

cue designating either the same or different lever. Sham-control rats picked the lever predicted by the context. In lesioned rats, impairment in using the context was proportional to the amount of damage to anterior cingulate and prelimbic areas. Presumed effects of anterior cingulate damage decreased across a conflict test trial, whereas effects tied to prelimbic damage continued through the trial.

Section III: Discrimination, Choice, and Cortical Brain Activity

The researchers in Section III are concerned with the relation of fMRI and single-cell recording from prefrontal and parietal cortex to standard choice tasks such as the training of discriminative stimuli in humans (Schlund & Cataldo); delayed go/no-go discriminations in pigeons (Kalenscher, Güntürkün, Calabrese, Gehlen, Kalt, & Diekamp); choosing between small, short-term rewards and larger, long-term rewards in humans (Yarkoni, Braver, Gray, & Green), and specialized matching tasks using visual responses to a simulated foraging environment in rhesus monkeys (Lau & Glimcher; and Corrado, Sugrue, Seung, & Newsome).

(1) Schlund and Cataldo—*Integrating functional neuroimaging and human operant research: Brain activation correlated with presentation of discriminative stimuli*. (pp. 505–519)

These researchers train human subjects by rewarding a button press in the presence of one set of discriminative stimuli, and rewarding no responding by terminating the trial in the presence of another set of discriminative stimuli. The subjects simply memorize a third set of (control) stimuli. Subsequent exposure to all three sets of discriminative stimuli during fMRI scanning showed greater activation in frontal and striatal brain regions for both sets of discriminative stimuli than to the control stimuli. These results support attributing differences between brain imaging effects in human and nonhuman animals to the use of a required operant response with nonhuman animals.

(2) Kalenscher, Güntürkün, Calabrese, Gehlen, Kalt, and Diekamp—*Neural correlates of a default response in a delayed go/no-go task*. (pp. 521–535)

These researchers study pigeons trained on a delayed go/no-go task in which an initial cue signals the appropriate response. Retention

functions diverged across intervals indicating that the pigeons retained the specifics of the go stimulus, but not of the no-go stimulus. Single-cell recording from the avian nidopallium caudolaterale (similar to the mammalian prefrontal cortex) supported the view that the no-go response is a default response that is not stored in the same way as the go response.

(3) Yarkoni, Braver, Gray, and Green—*Prefrontal brain activity predicts temporally extended decision-making behavior*. (pp. 537–554)

The authors use fMRI to explore neural activity underlying behavior during a task requiring the subjects to select small, short-term rewards to ultimately receive larger, long-term gains. Choice behavior is predicted by neural activity in a surprisingly specific area of the right lateral prefrontal cortex, a region previously reported to be related to cognitive effort. In contrast, activity in the insular cortex responded to fluctuations in amount of reward but did not predict choice behavior.

(4) Lau and Glimcher—*Dynamic response-by-response models of matching behavior in rhesus monkeys*. (pp. 555–579)

These researchers manipulate frequency and amount of reward in a discrete-trials matching procedure with rhesus monkeys. Their goal is to identify brain areas relevant to integration of past reinforcers and choices. They minimize neurophysiological recording problems by using eye rather than hand movements for responses, and they minimize possible recording artifacts from jaw movements by using water rather than food reinforcers. Using linear models of response-by-response behavior, they find it necessary to weight recent reinforcers more heavily and to consider patterning of choice responses to predict steady-state behavior, fluctuations in responding during transitions between densities of reinforcement, and response-by-response patterns.

(5) Corrado, Sugrue, Seung, and Newsome—*Linear-nonlinear-Poisson models of primate choice dynamics*. (pp. 581–617)

These investigators also study the performance of rhesus monkeys in a matching paradigm using liquid rewards (juice, in this case) and eye movements in a dynamic video simulation of a foraging environment. Their aim also is to model the effects of past rewards on future choice. Their mathematically specified strategies make contact with known

characteristics of choice behavior (hyperbolic discounting, differential comparisons of option value, and empirical maximizing of feeding). The strategies also produce local scalar value metrics highly correlated with the firing of individual neurons in the lateral intraparietal area of the cortex.

Section IV: Neural and Behavioral Analyses of Learning-Related Brain Circuitry and Addiction.

The papers in the final section focus on integrating multiple neural cells and circuitry with learning in circumstances that include: relating activation of a set of hippocampal neurons to tasks tapping episodic memory effects in rats (Eichenbaum & Fortin); relating complex cerebellar circuits to eyeblink conditioning phenomena in rabbits (Villarreal & Steinmetz); and establishing the relation of single neurons in nucleus accumbens and prefrontal cortex to drug-seeking relapse in rats (Rebec & Sun). The final paper in Section IV (Winger, Woods, Galuska, & Wade-Galuska) raises the cautionary point that strictly neurobiological accounts of drug addiction may not be as useful for understanding and treating addicted behavior as approaches based on an analysis of drugs as reinforcers.

(1) Eichenbaum and Fortin—*Bridging the gap between brain and behavior: Cognitive and neural mechanisms of episodic memory*. (pp. 619–629)

These researchers analyze behavioral and electrophysiological evidence supporting the view that critical features of episodic memory (recollection, as opposed to recognition, of stimuli and places) are readily shown in studies of rats using olfactory stimuli. These features include thresholds for retrieval effects (instead of continuous functions) and memory for sequences of events. Their data show that a particular set of neurons in the hippocampus is selectively and reliably activated across a variety of tasks, thus providing the basis for networks of neurons activated by retrieval cues, including sequences of behavior.

(2) Villarreal and Steinmetz—*Neuroscience and learning: Lessons from studying the involvement of a region of cerebellar cortex in eyeblink classical conditioning*. (pp. 631–652)

These investigators outline the methods of basic neuroscience used to explore the relation between behavioral learning and the brain, including brain lesions, stimulation, pharmacology, anatomy, imaging, and record-

ing. They review the results of these techniques in working out the complex neural circuitry involved in classical conditioning of the eyeblink, and show how the technique of temporary brain inactivation combined with single-cell recording can clarify the contribution of a specific region of the cerebellar cortex (Larsell's lobule HVI).

(3) Rebec and Sun—*Neuronal substrates of relapse to cocaine-seeking behavior: Role of prefrontal cortex*. (pp. 653–666)

These researchers review animal models of drug addiction relapse (reinstatement) based on electrophysiological analysis relating the nucleus accumbens and the prefrontal cortex as a final common pathway. They then use single-unit recording in behaving animals to distinguish whether the activity of individual neurons in these brain structures reflects cues that signal the drug, the drug itself, or the motor sequence producing the drug. They provide preliminary findings that prefrontal cortex processes information related to cocaine seeking but not information about the hedonic effects of the drug.

(4) Winger, Woods, Galuska and Wade-Galuska — *Behavioral perspectives on the neuroscience of drug addiction*. (pp. 667–681)

These authors point out that neurophysiological accounts of drug addiction presume that addiction is based on long-term brain changes caused by chronic administration of drugs. They suggest the usefulness of the alternative perspective, namely that drug addiction is a behavioral disorder in which drugs are preeminent reinforcers. The authors argue that advances in treating drug addiction and understanding mechanisms related to excessive drug use will occur more rapidly by assessing the reinforcing effects of drugs.

Book Review

Schaal—*Naming our concerns about neuroscience: A review of Bennett and Hacker's Philosophical Foundations of Neuroscience*. (pp. 683–692)

The authors of the book under review present a thorough critique of the tendency of cognitive neuroscientists to commit the *mereological fallacy*, the tendency to “explain” psychological phenomena by ascribing to the brain (or its parts) psychological powers justifiably applied only to whole animals. For example, it is a fallacy to say that our forebrain “plans” when attempting to explain why

humans show planning. Much of what the authors of the book write will have a familiar ring to behavior analysts who long have criticized similar conceptual tendencies.

POSTSCRIPT

There appear to be two reasonable strategies in bridging the gap between behavior and neuroscience. A pure strategy is to stay primarily on one side or the other until the science on both sides has developed more fully. If you are a behaviorist, focus your efforts on amplifying the sophistication of your measures, manipulations, and analyses. If you are a neuroscientist, focus on *in vivo* preparations of brain cells, working out circuitry, neuronal functioning, and cellular processes. This strategy appears related to the initial “separate but equal” approach Skinner outlined in 1938. The gap between behavior and neuroscience should be maintained until the two sides produce parallel structures of concepts and relations that can be easily integrated. This solution simplifies the questions to be asked on each side and the models developed. The difficulty is that it does not make clear how to identify the proper time for integration, what constitutes parallel development, exactly how integration should occur, who will do it, and how the science might be different.

An alternative, mixed strategy, the one seemingly favored by most researchers in this issue, is to develop specific, albeit limited, bridges relating behavior and neuroscience. Given a focus on specific bridges, experimenters can focus more readily on areas where bridges appear interesting, possible, and most likely to be successful. As is evident from the present articles, some bridges are based on relating well-controlled tasks to manipulations of drugs, transmitters, lesions, and measures of brain activity. To increase the explanatory or causal traffic the bridge can bear, it should be anchored to multiple locations both in behavior and in the brain. For example, the classic and continuing studies of how barn owls localize and react to sounds in space provide wonderful examples of how knowledge gained about sensory neurobiology of the face feather structure and the brain clarifies how to perform better experiments, which in turn reveal more about how the sensory-motor mechanisms work (e.g., Carew, 2000). Such

interactive complexity is gradually developing in areas with better-established bridges (e.g., the articles here by Eichenbaum & Fortin, Rebec & Sun, Villarreal & Steinmetz; see also the review by Thompson, 2005).

Certainly, rapidly constructed, poorly conceived bridges often have drawbacks (e.g., see the discussion by Winger et al.). Researchers caught up in the excitement of relating measures of neurobiology and behavior may find that their anchors on one side or the other do not bear the weight of their predictions or assumptions. Skinner's warning against attributing causality to weakly anchored, neurobiologically tinged concepts is still good advice. However, his concern about causal anchoring applies also to the behavioral side. We should not forget that the causal interpretation of an operant reinforcement contingency itself is firmly anchored only in the sense that we can manipulate its components and observe regular results (Skinner, 1938; Timberlake, 2004). It is not clear what is to be done with phenomena such as autoshaping, misbehavior, and superstitious behavior, which are not similarly anchored in typical operant manipulations. Such phenomena might profit from more secure causal connections with behavior and with well-defined neurobiological processes.

The articles in this issue suggest that bridging the gap between behavior and neu-

robiology with eyes wide open is an important direction for operant conditioning, and learning in general, to proceed. It also is important to recall Skinner's goal of fully understanding both sides of the behavior-neurobiology gap, as well as Bechtel's compatible point about the necessity of filling in the working mechanisms that stitch together levels of analysis.

REFERENCES

- Carew, T. J. (2000). *Behavioral neurobiology: The cellular organization of natural behavior*. Sutherland, MA: Sinauer Associates, Inc.
- Grossman, S. P. (1979). The biology of motivation. *Annual Review of Psychology*, *30*, 209–242.
- Latties, V. G. (2003). Behavior analysis and the growth of behavioral pharmacology. *The Behavior Analyst*, *26*, 235–252.
- Schaal, D. W. (2003). Explanatory reductionism in behavior analysis. In K. A. Lattal & P. N. Chase (Eds.), *Behavior theory and philosophy* (pp. 83–102). New York: Kluwer Academic/Plenum Publishers.
- Skinner, B. F. (1938). *The behavior of organisms: An experimental analysis*. New York: Appleton-Century-Crofts.
- Skinner, B. F. (1974). *About behaviorism*. New York: Alfred A. Knopf.
- Thompson, R. F. (2005). In search of memory traces. *Annual Review of Psychology*, *56*, 1–23.
- Timberlake, W. (2004). Is the operant contingency enough for a science of behavior? *Behavior and Philosophy*, *32*, 197–229.