A short history of latent inhibition research

R. E. Lubow

The first latent inhibition (LI) paper was published 50 years ago (Lubow & Moore, 1959), and the present book marks that anniversary. As such, it offers a convenient time for providing a historical perspective to a phenomenon that was born by accident, barely survived the first several post-parturitional years, and yet developed into a flourishing research enterprise, with activities cutting across such diverse fields as learning theory, schizophrenia, and even creativity. Indeed, in the weekly episodes of “Prison Break” on American TV, the concept of LI has even reached prime-time television.

In spite of the relatively widespread use of the LI paradigm in the laboratory, and, in particular, because of its adoption in research areas that are far removed from its origins, the present editors felt that there was a need to acquaint the larger audience with both the history and recent advances in LI research and theory.

Before describing the serendipitous discovery of LI, this apparently simple, yet ubiquitous, phenomenon requires a definition and a description of its adaptive function. Specifically, LI is a name for the decrease in the ability to acquire or express a new association to a stimulus that has previously received passive, non-reinforced preexposures, as compared to a stimulus that is either novel (not preexposed) or one that has been reinforced or attended. Importantly, LI is not a process. It is an effect that, as will be seen, is in search of a process that generates it. In short, at least according to one explanation of LI, some types of familiarity may not breed contempt, but rather an adaptive neglect. And, for that, we have much to be thankful!

When one considers that at any wakeful moment there are countless packets of stimuli that flood our sensory surfaces, it is astonishing that we are so successful at separating the relevant from the irrelevant, the trivial from the potentially useful. Undoubtedly, without the means to accomplish this partition, our lives would be unbearable, buried in an unsurvivable, undifferentiated Jamesian blooming, buzzing confusion, “...the consciousness of every creature would be a gray chaotic indiscriminateness, impossible for us even to conceive” (James, 1890/1950, pp. 402–403).

The manner in which organisms accomplish the survival-essential task of selecting the important from the insignificant has been a central concern of psychology over the entire course of its history. In the early years of modern experimental psychology, Gestalt psychologists appealed to the innate ability of the brain to organize information, and behaviorists to reinforcement-based learning. More recently, cognitive psychologists have placed the burden of stimulus selection on various somewhat homuncular models of selective attention (many of which tell us more about how the mind of the scientist works rather than the minds of the subjects that generated the data). Yet, from all of this activity, there appears to be one basic conclusion. As one might expect for a fundamental condition for survival, selection is supported by a variety of mechanisms, some probably complementary and overlapping, and others operating quite independently.

Nevertheless, until fifty years ago, with the exception of studies of response habituation, processing of unattended, irrelevant events and how they fostered adaptive behavior was largely ignored, particularly in regard to their subsequent fate when they became relevant. How then did researchers in psychology come to attend to the unattended?

The early years (1959–1973)

The idea for the initial experiments, the unexpected results of which came to be called “latent inhibition”, grew out of my interest in associative learning theory, which in the late 1950s was still identified with the competing models of Hull (1943, 1952) and Tolman (1932). At that time, I was a graduate student at Cornell University, working as an assistant to Howard Liddell at his animal behavior farm, an institution devoted to using classical Pavlovian procedures to induce so-called experimental neuroses in goats and sheep (and earlier, also in dogs and pigs). This was a particularly gloomy period for me, not only because of animal welfare concerns, but also because of my inability to observe the pathological behaviors that were apparently so clearly visible to other members of the laboratory (the sheep always seemed forlorn).

In that era, five decades ago, the exemplar of scientific psychology was to be found in the hard-floor mazes of associative learning theory and not in the straw-strewn barns of psychopathology. Indeed, one of the salient Hull–Tolman controversies concerned whether or not it was possible to learn without reinforcement. An extensive series of experiments by Tolman and his followers established that when a rat is allowed to explore a complex maze without receiving any overt reinforcement, and then later made hungry and rewarded with food when it reached the goal box, it will learn the correct path faster than one that did not have the opportunity to explore the maze (e.g., Tolman & Honzik, 1930). The superior learning of the group that was preexposed to the maze, but without reinforcement, as compared to a control group that was not preexposed to the maze, was called “latent learning”, latent because there was no evidence of learning during the exploratory phase.

R. E. Lubow
Today, it is generally accepted that although learning can benefit from reinforcement, reinforcement is not a necessary condition for learning. Even in the late 1950s, with the recognition of the distinction between learning and performance, the controversy was losing its significance. Nevertheless, to keep myself from following the assigned course of our animals into “neurosis” (the major conceptual variable for producing experimental neurosis was monotony), I began a project to try to demonstrate latent learning, not in a maze with rats, as all of the previous studies had done, but with sheep and goats in a purely classical conditioning paradigm. A classical conditioning procedure, with its clearly defined punctate conditioned stimuli, as opposed to the diffuse stimuli that constitute a maze, might, I thought, provide a clearer appreciation of what actually was learned during the non-reinforced stimulus preexposure stage.

With the help of Ulrich Moore, I constructed an experimental set-up for sheep and goats (Figure 1.1), and we began to search for a facilitatory effect of simple preexposure of the to-be-conditioned stimulus on subsequent conditioning. In that first experiment (Lubow & Moore, 1959, Experiment 1), the animals were exposed to
10 non-reinforced presentations of either a flashing light or a turning rotor. In the immediately following test stage, the subjects received alternating trials with the light and the rotor (CSs), each paired with a mild shock (US) to the right foreleg. With repeated CS–US pairings, such a conditioning procedure produces an anticipatory leg flexion (CR) during the presence of the CS. Thus, in this within-subject design, each subject generated CRs to the preexposed stimulus and to a novel stimulus. To our enormous disappointment, conditioning to the CS that had been preexposed was significantly slower than to the novel CS, exactly the opposite from what was expected.

However, I knew the reason for these unforeseen results, or so I thought. Unintentionally, the layout of the experimental context was such that the preexposed stimulus of stage-1 and the CSs of stage-2 were presented to the right of the animal, and the US was delivered to the right foreleg. During preexposure, stimulus presentations elicited a noticeable turning of the animal’s head to the right, what Pavlov (1927) had called an investigatory reflex. Sherrington’s (1906) earlier analyses of reflex patterns had indicated that turning the head to one side is accompanied by an increase in extensor muscle tonus of the limb on that same side. Thus, the preexposed stimulus in our experiment was reliably paired with leg extension, a response that would be in competition with the conditioned flexion of the CR. Wonderful! The same analysis yielded the prediction that, if the preexposed stimulus and the CS in test are presented to one side of the animal, and the US to the opposite side, then the preexposed stimulus will produce a flexion of the to-be-conditioned limb. Since flexion is the to-be-conditioned response, then we certainly should be able to obtain the facilitatory latent learning effect that we originally had set out to demonstrate.

We hurried back to the laboratory to test this sure-bet prediction (Lubow & Moore, 1959, Experiment 2). Except for the placement of the CSs and US on opposite sides of the animal, the procedure was exactly the same as in Experiment 1. By now, you can guess the outcome. Our prediction not only failed to be confirmed, but once again we obtained the opposite effect. Conditioning was poorer to the preexposed stimulus than to the novel stimulus.

Evidently, we had stumbled on to a new behavioral phenomenon, to which we gave the name “latent inhibition”. Importantly, but often misunderstood, the freshly coined term was not meant to have any theoretical meaning. It simply was adopted as a complement to the latent learning phenomenon. The LI effect was deemed latent because there was no behavioral evidence of its presence during the stimulus preexposure stage. As for inhibition, it was only meant to describe that stimulus preexposure produced relatively poor learning, as opposed to the better learning of the latent learning studies.

In retrospect, these first LI experiments had two conditions that made it surprising that we generated any effect at all. Firstly, the number of stimulus preexposures, ten, was relatively small. Secondly, the within-subject design of the test stage, with alternating presentations of the reinforced preexposed and novel stimuli, promotes
stimulus generalization. As such, it would be expected to reduce the differences in conditioning to the two stimuli. Indeed, as can be seen in Figure 1.2, the LI effects in Experiments 1 and 2, although reliable, were quite small.

Upon finishing my graduate studies, I accepted a position with the General Electric Co. in Ithaca, New York. As a consequence, for five years I was unable to follow up on the initial LI experiments. Not surprisingly, the 1959 article also languished, neither noticed nor cited, well on its way to becoming another fatal drowning in the publication ocean.

We (the publication and I) were rescued in 1963, when I was fortunate to receive a five-year NIH Career Development Award. The purpose of the grant was to investigate the role of eye movements in the development of visual form perception. The idea was to use a contact lens to mount a stable retinal image projection system on the eye of a new-born goat. Since goats are fully alert and ambulatory at birth, this technique would allow one to get at some of the basic nature/nurture interactions in perceptual development. North Carolina State University provided the needed animals, and I accepted an appointment in their Department of Psychology. Although the required equipment was developed, for a variety of reasons the research program became stalled. However, the sheep and goats were still on hand, and I returned to the still-puzzling phenomenon of LI.

Given that the LI effects in the first experiments were completely unexpected, quite small, and generated from sheep and goats, I had two concerns. Most importantly, I was apprehensive that it might be difficult to replicate the effect. Secondly, I was troubled by the possibility that LI might not be generalizable beyond our idiosyncratic farm subjects, or beyond the classical conditioning defensive leg flexion paradigm. These issues occupied me for the next five years.

It was with considerable relief that the next experiment (Lubow, 1965), also with sheep and goats, but with a between-subject design and with larger numbers of stimulus preexposures, produced a robust LI effect. Having replicated the basic LI effect, my students and I proceeded to address the problem of generality. In fairly short order, we demonstrated LI in rats with conditioned tail flexion (Chacto & Lubow, 1967) and conditioned suppression (Lubow & Siebert, 1969), and in rabbits with classical conditioning of the pinna response (Lubow, Markman, & Allen, 1968).

During this same period, we made several unsuccessful attempts to produce LI in adult humans with the then-popular eyelid conditioning paradigm. Later, one of the students involved in this project, Paul Schnur, then at Indiana University, recognized the relevance of Kenneth Spence’s (1966) use of a masking task to slow the extinction of a classically conditioned response in humans, and thereby to make the adult extinction curve similar to that obtained with animals. Schnur and Ksir (1969) presented subjects with the masking task, an unsolvable guessing game that was initiated in the preexposure phase and continued through the acquisition phase. While engaged in the masking task, the subjects received the critical to-be-CS, later followed by the CS–US pairings. The stimulus-preexposed group displayed poorer
Figure 1.2. Percent conditioned responses to the preexposed stimulus and to the non-preexposed stimulus as a function of blocks of trials: Panel A, Experiment 1; Panel B, experiment 2 (data from Lubow & Moore, 1959; graphs were not included in the original article; data were presented in tabular form as the number of trials before reaching a learning criterion of ten CRs).
conditioning than the groups that were not preexposed or preexposed to a stimulus that was different from the CS in the test stage. Thus, for the first time, stimulus-specific LI in humans was demonstrated, an effect that apparently required a masking task.

In 1971, after moving to Israel, and after a brief stay at Bar-Ilan University, I accepted a position at Tel Aviv University. In the meantime, Bob Rescorla and Allan Wagner published their influential model of associative learning (Rescorla & Wagner, 1972; Wagner & Rescorla, 1972), for which it was important to define the relationship between the LI effect and conditioned inhibition. They demonstrated that the stimulus preexposures prior to standard conditioning trials produced LI but not conditioned inhibition (Reiss & Wagner, 1972; Rescorla, 1971). Those two papers served to place LI outside the standard associative learning domain, and they led to accepting the idea that unreinforced preexposure of the to-be-conditioned stimulus results in a loss of stimulus salience.

As a consequence of the novelty of the LI phenomenon, the awkwardness with which it fit into extant learning theories, and the interest of two of the major figures in the field, LI was on its way to becoming an active area of research. By the early 1970s, there was enough literature on LI and related effects to warrant a review article (Lubow, 1973). Essentially, the paper provided evidence for the robustness of the LI effect, summarizing research with different species and learning paradigms, as well as the effects of a number of variables. It was shown that LI was stimulus-specific, increased as a function of the number of stimulus preexposures, survived relatively long delays between preexposure and acquisition, and was marked by important differences between human children and adults. In addition, the case was made as to why LI could not be explained by means of habituation of the orienting response (e.g., Sokolov, 1963), selective filters (Sutherland & Mackintosh, 1971), competing and complementary responses (Lubow & Moore, 1959), or, as already noted, by conditioned inhibition. The paper concluded with a call for a model of LI that combined attentional and learning constructs, a theme that has remained current.

The middle years (1974–1991)

Although one anonymous referee of the 1973 article harshly proclaimed that the “... review of the literature on latent inhibition is, unfortunately, much ado about practically nothing”, it, together with the Rescorla and Wagner papers, provided...
a turning point for LI research, both empirical and theoretical. Following their publication, numerous behavioral experiments examined LI as a function of a diverse array of variables, including duration, intensity, and inter-stimulus interval of stimulus preexposures. LI also was assessed as a function of retention interval, various additions of other stimuli during preexposure, and most importantly of context change from preexposure to acquisition/test (for summaries, see Lubow, 1989).

Accompanying the experimental research, ways were sought to encompass the new phenomenon within a general associative learning framework (e.g., Mackintosh, 1975; Pearce & Hall, 1980; Wagner, 1976). Although these theories continued with the Rescorla–Wagner position that stimulus preexposure produced a loss of stimulus salience (attention) and a subsequent reduction of stimulus associability (acquisition deficit), they differed from each other in regard to what is learned during preexposure and how that learning is transferred to the acquisition/test phase so as to reduce associability.

My colleagues and I also accepted the general attention/associability position (A-theories), but we developed an account of LI that was specific to the results from the unattended stimulus preexposure paradigm, namely Conditioned Attention Theory (CAT; Lubow, Schnur, & Rifkin, 1976; Lubow, Weiner & Schnur, 1981; Lubow, 1989). We posited that non-reinforced stimulus preexposures retard subsequent conditioning to that stimulus because the subject learns not to attend to the irrelevant stimulus. However, unlike other A-theories, attention was treated as a response that was subject to all of the empirical laws of classical conditioning, with the absence of a consequence following the to-be-CS serving as a US for the conditioning of an inattentional response. As noted, like other A-theories, CAT accepted the position that the reduced attention/salience of the to-be-CS decreased the ability to acquire a new association to that stimulus.

Ironically, early on, we had published a paper that would later provide a basis for undermining the acquisition-deficit position (Lubow, Alek, & Rifkin, 1976). In two experiments, one with children and one with rats, both using a two-stage preexposure and acquisition/test procedure, a comparison between the PE and NPE groups showed that a change of context from the preexposure stage to the acquisition/test stage destroyed the LI effect. In other words, LI was context-specific. The results were readily interpretable in terms of modulated attention, namely that an old stimulus in an old context attracts less attention than a new stimulus in an old context, the consequence of which is poorer acquisition of any new association with the familiar stimulus.

The attenuated-LI that accompanied a change of context that we had demonstrated in a two-stage procedure was soon confirmed in a variety of three-stage experiments (preexposure, acquisition, and test) where the context change occurred from the preexposure to the conditioning stage (e.g., Hall & Channell, 1986; Lovibond, Preston, & Mackintosh, 1984). However, the attentional/perceptual interpretation of context-specificity of LI (Lubow, Alek, & Rifkin, 1976), particularly as
A short history of latent inhibition research

expressed in modulations of subsequent associability, was challenged by Ralph Miller and Mark Bouton, both of whom contended that LI did not represent a failure of acquisition, but rather that it was the result of retrieval/competition processes (R-theories; e.g., Miller, Kasprow, & Schachtman, 1986; Bouton, 1993; also see Escobar & Miller, this volume). A similar conclusion was reached by Weiner (1990) from a review of the psychobiological data. Accordingly, unlike for A-theories, the acquisition of a new association to an old preexposed stimulus proceeds normally. However, when the subject again encounters the target stimulus in the test stage, two competing associations are retrieved: the earlier stimulus–no consequence association from the preexposure stage and the stimulus–US association from the acquisition stage. In such a situation, the non-preexposed group would gain an advantage because, at the time of test, it had not been previously confronted with a competing association.

Although this is not the place to compare and evaluate theories of LI, it is of interest to note that the controversy is yet another version of a broader division that has a long history, namely learning versus performance. Although there is compelling evidence for both sides of the argument, no experiment has been designed that explicitly formulates and tests the contrasting predictions. This suggests that these apparently conflicting theories may either lack sufficient preciseness, or deal with different data domains, or overlap in meaning, or even suffer from some combination of these possibilities. These issues are still alive (see Westbrook & Bouton, this volume; De la Casa & Pinedo, this volume; Hall & Rodriguez, this volume; Escobar & Miller, this volume; Lubow & Weiner, this volume; Schmajuk, this volume).

Thus far, the overview of LI activity has focused on behavioral experimentation and theory, which, indeed, dominated the field. However, just as neuroscience was beginning to affect many other aspects of experimental psychology, so too it was on its way to becoming a dominant factor in LI research. The earliest work in this area took several directions. Two of these tracks, namely lesions of the septo-hippocampal system and administration of drugs that modulate dopamine uptake, which evolved directly from interests in attentional processes, were later linked in an effort to understand anomalous LI effects in schizophrenia.

In the first of these studies, Ackil, Mellgren, Halgren, and Frommer (1969) reported that aspiration lesions of the hippocampus abolished LI of two-way active avoidance learning. The next several years saw a number of replications of this effect with a variety of different preparations (e.g., Kaye & Pearce, 1987; Solomon & Moore, 1975), as well as with septal lesions (e.g., Burton & Toga, 1982; see Gray & McNaughton, 1983, for an early review of the similar affects of septal and hippocampal lesions on LI). LI also was examined as a function of manipulations of noradrenergic (e.g., Tsaltas, Preston, Rawlins et al., 1984), serotonergic (e.g., Solomon, Kinsey, & Scott, 1978), and cholinergic systems (e.g., Moore, Goodell, & Solomon, 1976).

The facts that amphetamine, a dopamine agonist, can produce schizophrenia-like symptoms in humans and that schizophrenia is characterized by high distractibility
(attending to irrelevant stimuli) led to several critical studies of the effects of that drug on LI. Beginning with Ina Weiner’s master’s thesis (1979) and doctoral dissertation (1983), a series of experiments in our laboratory (Weiner, Lubow, & Feldon, 1981, 1984, 1988) and that of Paul Solomon (Solomon, Crider, Winkelman et al., 1981; Solomon & Staton, 1982) established that d-amphetamine attenuates LI. Importantly, Solomon et al. (1981) also found that the disruptive effects of d-amphetamine were eliminated by concomitant administration of chlorpromazine, a powerful neuroleptic. Shortly afterwards, Weiner and colleagues reported that haloperidol, a newer dopamine antagonist, actually potentiated LI (Weiner & Feldon, 1987; Weiner, Feldon, & Katz, 1987), and with that LI became a focal point for research relating attentional dysfunction to schizophrenia. This thrust was accelerated by two characteristics of the LI paradigm. Firstly, the same procedure for generating LI could be employed with animals and humans, including those with various pathologies. Secondly, attenuated LI is indexed by better learning in the test phase. Consequently, a reduction of LI in patient groups cannot be attributed to the nonspecific decremental effects which have plagued much of the research on schizophrenia.

By the close of the 1980s, there was enough published LI research to warrant two books (Lubow, 1989; Hall, 1991), both of which reviewed much of the material described above, but in considerably more detail.

The current era (1991–2008)

It is appropriate to begin this latest period with Jeffrey Gray (1934–2004), a visionary neuroscientist whose broad interests and knowledge made him the quintessential interdisciplinary researcher (see Schmajuk, this volume). Although he had already made a significant contribution to LI research in the previous era (e.g., Baruch, Hemsley, & Gray, J. A. 1988a, 1988b), his widely cited Behavior and Brain Sciences article (Gray, J. A. et al., 1991), which drew from the results of experiments on behavior, pharmacology, neurophysiology, and psychopathology, provided a coherent model for LI deficits in schizophrenia patients with acute, positive symptoms (also see Gray, J. A., 1998). Gray’s influential publications, together with our earlier work on the opposing influences of dopamine agonists and antagonists on LI (e.g., Lubow, Feldon & Weiner, 1982; Weiner, Lubow, & Feldon, 1981, 1984; Weiner & Feldon, 1987), and Lubow’s (1989) book summarizing the burgeoning LI literature, set the stage for much of the more recent developments in LI research and theorizing, and for their applications to schizophrenia.

Contemporary LI-schizophrenia research, much of which is summarized in the chapters of the present volume (e.g., Kumari & Ettinger; Swerdlow; Weiner), has continued in a number of the older areas, including behavioral studies with patients and healthy subjects who score high on self-report schizotypal questionnaires (for a