

*The highlight for January, 2009 is by Dr. David C. Riccio from Kent State University. As described in the highlight, Dr. Riccio's interest in taste aversion learning began with his early work on the assessment of motion sickness in the rat and the conditions effective in inducing and abating it. While his initial interest focused on this unique US in aversion learning, his work soon turned to the memorial aspects of conditioned taste aversions. In a recent review with Susanne Meehan, Dr. Riccio asks a poignant question about taste aversions and the study of memory in this learning process. The question focused on why might one be interested in such a process given that taste aversion is a phenomenon characterized by its rapid acquisition and the robust nature of its display, i.e., memory of such learning is a given. In fact, as early as 1954, Rzoska and his colleagues noted studies in which rats displayed the retention of poison-based food aversions almost a full year after its acquisition. In a recent review by Dr. Riccio (see Meehan and Riccio, 2009), the memory processes associated with aversion learning are eloquently described and the similarity and differences with traditional learning noted. Such issues as the influence of age on the acquisition and retention of aversions, how stimulus generalization functions vary with retention interval, how context interacts with the retention interval in the display of aversions, the demonstrations of memory for extinguished responding, of retrograde amnesia and age effects in delay learning, how taste attributes change over long delays, how electroconvulsive shock, anesthesia and hypothermia during the CS-US delays affect aversion learning and memories of latent inhibition and UCS preexposure are all described and illustrate the richness of memorial processes in aversion learning. Dr. Riccio's highlight reviews the role of his laboratory and students in assessing many of these issues and how memory processes shape this phenomenon. Aversion learning, while robust, provides a range of questions regarding memory, illustrating the multiple processes embedded in its acquisition and display.*

## Meandering Through the Gardens of Conditioned Taste Aversion

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I was flattered to be invited to write a paper about my research in the area of conditioned taste aversion (CTA), especially as my contributions have been both far less extensive and more sporadic than those of others in this series.

I finished my PhD in 1962 under Byron Campbell at Princeton, where my interests on the effects of early stress and behavior led to some related work on

developmental differences in adaptation to cold stress in rats (Campbell and Riccio, 1966; Riccio and Campbell, 1966). Graduate work was followed by a three year tour of military service. Most of my active duty was spent in the U.S. Navy at the Naval Aerospace Medical Institute in Pensacola, FL. The unit I was with had a major focus in the vestibular system and motion sickness. The standard view among the research physiologists was that rats, while desirable as subjects for all the usual reasons, could not be used to study motion sickness because they lacked the criterion response, i.e., they could not vomit.

### Behavioral Assessment of Motion Sickness in Rats

But from a psychologist's point of view, perhaps a behavioral change could be used to assess illness, and this turned out to be the case. A simple way to produce motion sickness is by exposing subjects to rotation, and the Navy had some very sophisticated rotation turntables. Initially, a co-worker, Arnold Eskin, and I (Eskin and Riccio, 1966) showed that spontaneous activity of rats in an open Plexiglas arena in a semi-darkened room decreased nicely as the angular velocity (rpm) of the turntable increased. Unfortunately, the activity measure required on-line observation of the rats on this "merry-go-round", which nearly produced nausea in the experimenters as well. But Jack Thach had arrived from an operant learning oriented program at the University of Maryland so our next strategy was to use operant procedures rather than eyeballing the activity levels of our subjects. The Skinner boxes were mounted over the center of the table (to eliminate any centrifugal forces) and were electrically connected to the non-rotating world by slip rings. Rats trained to stable levels of responding on FR or VI schedules showed orderly declines in bar pressing as the rotation speed was increased by one RPM every five minutes (Riccio and Thach, 1968). This was certainly consistent with the interpretation that a nauseous rat is not interested in working for food. In a manipulation confirming the vestibular-motion sickness view, we demonstrated that the rats, like people, were not sensitive to rotation effects if they had suffered damage to the vestibular system (Riccio, Igarashi, and Eskin, 1967).

With respect to CTA, the next step would seem obvious. Unfortunately, to me it wasn't, even though important studies on CTA were beginning to appear in the literature. It was not until some years later at Kent State University that I thought of re-visiting the motion sickness issue in rats in terms of CTA. Although I no longer had a sophisticated rotation device, I did have a sophisticated and clever grad student, Vahram (Harry) Haroutunian. Harry purchased a record turntable from a junk store, and we proceeded to study motion sickness resulting from rotation at 72 rpm. By that time, others had beaten us to the punch, but we extended their findings by exploring delays between the taste and the rotation exposure. Under our conditions, a single trial was sufficient to produce CTA if the CS to UCS interval was less than a minute, but several trials were required for an aversion to develop when a 30-minute delay was used. Furthermore, consistent with the Garcia effect, the same rotation treatment apparently failed to produce

learning to non-gustatory cues in either a CER or a punishment paradigm (Haroutunian and Riccio, 1975). That the CTA was related to vestibular stimulation from rotation was confirmed by showing that rats with damage to the system did not acquire the taste aversion (Haroutunian, Riccio and Gans, 1976). In that same study, we also found that CTA was alleviated in rats with a prior history of rotation exposures, a pre-exposure effect now commonly seen with many types of reinforcers.

Perhaps our most intriguing finding in that line of research came from our suspicion that motion sickness might be qualitatively different from other forms of malaise with respect to associability with exteroceptive stimuli. As mentioned above, we had found no evidence that rotation “worked” to produce learning when paired with external cues. But might the Garcia effect represent, at least in part, an example of the learning vs. performance distinction that we so often pointed out in courses on Learning? To test this possibility, we used a transfer test in search of a savings effect (Riccio and Haroutunian, 1977). If rats had associated external stimuli (black cues of a compartment) with rotation effects, then even if those same cues did not produce suppression of a response such as drinking, perhaps the animals would acquire suppression more rapidly than unpaired controls if those same cues were later paired with mild shock. That was what we found, but after the paper was rejected by a major journal, and Haroutunian was about to leave for a postdoc, we published the study (“Failure to learn in a taste aversion paradigm: Associative or performance deficit?”) in the *Bulletin of the Psychonomic Society*. We took some pleasure in knowing that Garcia’s classic cue-to-consequence paper had been published in the same journal (Garcia and Koelling, 1966).

### Potpourri

At various times, we did studies that just happened to strike our fancy. Casey Cole got interested in contextual control of the UCS pre-exposure effect. He found that novel contexts produced a much stronger pre-exposure effect, presumably because a highly familiar context was latently inhibited, that is, it would be more difficult to develop an association between the context and the UCS. An interesting twist was that a familiar context could be made to function like a novel one if an unfamiliar odor was added to the context (Cole, Van Tilburg, Burch-Vernon and Riccio, 1996).

With reports that a Ketamine-Xylazine (Ketaset-Rompun) combination produced a particularly effective deep anesthesia, the question of behavioral effects arose. Mitchell Metzger and Rob Flint showed that the drug administered after sucrose consumption resulted in a taste aversion, and did so quite strongly even with a 2 hour taste-to-anesthesia delay (Metzger, Flint and Riccio, 1997). The finding indicated a caveat for studies that employed this agent where flavor presentations might be involved.

If one wants to obtain a selective taste aversion, how might this discrimination be accomplished efficiently? The problem arises from the fact that substantial generalization often occurs and that in CTA the subject controls its exposure to any generalized flavors (as well as to the target CS, of course). Angie Burch-Vernon, using a strategy suggested by Mike Domjan in studying neophobia some years earlier, found that pre-exposure (latent inhibition) to a CS- facilitated discriminative learning between two similar tastes. Indeed, just one pre-exposure to the CS- was sufficient to yield the effect. She also found that the enhanced flavor discrimination persisted for at least two weeks after the CTA conditioning trial. However, in examining the retention of the pre-exposure effect she found some reduction in the enhancement of discrimination when a three week interval was interpolated between pre-exposure to the CS- and the subsequent conditioning episode (Burch-Vernon and Riccio, 1997).

By the 1990's, there was substantial evidence that NMDA receptor antagonists could impair acquisition in a number of learning tasks, but relatively little information on the effects of agonists of the receptor site. Cantey Land, who knew more about these issues than I did, got interested in the problem. As a few reports indicated that D-Cycloserine (DCS), a type of NMDA agonist, enhanced learning, but none had examined CTA, she proceeded to do so. The general findings of relevance here were that low doses of DCS did increase the strength of CTA (Land and Riccio, 1997). Her study also included a control experiment indicating that the enhancement was not likely due to an artifact of a larger UCR from the combined effects of LiCl and DCS. (Had I only thought to look at whether DCS might enhance extinction of CTA or, more generally, extinction of fear motivated conditioning, a topic that has now attracted considerable attention because of its potential implications for therapy!)

### Memory Interests

Somewhere along the line, my research shifted toward more memory-oriented issues, and this was true for CTA as well. Vic Guanowsky, who had been an undergraduate in Jim Misanin's lab at Susquehanna University and was now a graduate student in mine, along with Misanin and me, took another look at age related differences in retention of CTA. Consistent with findings on "infantile amnesia" from other tasks, weanling rats (23 days old) showed substantial memory loss after 4 weeks relative to either adults or aged (about 2 years) animals, although acquisition appeared comparable for all age groups. A somewhat surprising outcome was that old rats retained their aversion as well as young adults (Guanowsky, Misanin and Riccio, 1983). Later, at Misanin's invitation, I joined forces with them again to address another interesting developmental question. It had been found that young rats were deficient in acquiring CTA with a long CS-UCS interval, but was the impairment based on the failure to remember the taste, or, following a notion of Kalat and Rozin (1973), might it reflect the acquisition of latent inhibition to the CS during the interstimulus interval? We found that not only was latent inhibition obtained in

weanling rats, but that the effect was stronger than in adults (Misanin, Guanowky and Riccio, 1983). This outcome suggested that the impaired acquisition with long delays is not due simply to the loss of memory for the flavor stimulus.

By the 1980's, sparked by investigators such as Norman (Skip) Spear and Ralph Miller, among others, a growing interest had developed in whether some types of performance deficits (e.g., amnesia, Kamin blocking effect, overshadowing) were based on failures to express information rather than associative or memory impairments. In this connection, Kraemer and Roberts (1984) had reported the intriguing finding that rats showed latent inhibition of CTA when tested after a short but not a long interval following conditioning, the so-called "Kraemer effect". How could this occur if LI were an associative impairment? As certain features of that study were challenged, Lee Bakner along with several other graduate students conducted a slightly modified study on retention of LI. (Bakner, Strohen, Nordeen and Riccio, 1991). Our findings were consistent with Kraemer and Roberts: The pre-exposure effect was obtained at short intervals (2 and 5 days) after conditioning, but not after 21 days. This outcome was consistent with the view proposed that the LI at short intervals reflected a failure to retrieve the CTA memory, rather than a failure to acquire it.

As with LI, pre-exposure to the UCS can also impair performance in the CTA paradigm. Casey Cole asked if a similar recovery of the aversion might be found with a long interval after pre-exposure and conditioning. The pre-exposure to LiCl substantially reduced the level of CTA, as expected. In this case, however, there was no evidence of an increase in the aversion after retention intervals of either 11 or 21 days (Cole, Bakner, Vernon and Riccio, 1993). While negative results always leave the door open to other possible interpretations (e.g., a longer interval was needed), it appears that either the salience of the UCS memory made it very persistent or that this manipulation did, in fact, block acquisition of CTA.

Several studies in the literature indicated that latent inhibition was weakened when a long interval was interpolated between pre-exposure and conditioning. If the latent inhibition effect was subject to forgetting, could a reminder bring it back? A number of studies had shown that memory losses could often be alleviated by procedures designed to promote retrieval (see Spear and Riccio, 1994, for review), but these findings had typically dealt with decrements in conditioned responses. Would a similar recovery be obtained where the target memory was the effect of stimulus exposure per se, rather than performance of an explicitly learned response? That is, could the LI effect be recovered? To address this issue, Jen Ackil and several of her fellow students pre-exposed rats to a sucrose solution and 2 or 10 days later gave them a sucrose-illness pairing. The CTA was stronger in the long retention condition, indicating some forgetting of the stimulus pre-exposure treatment. At the 10-day interval, some rats received a "reminder cue" in the form of a brief exposure to the target flavor one day before conditioning. Relative to their non-cued controls, the reminder group

showed a substantial increase in latent inhibition. Importantly, in the absence of the original pre-exposure, the reminder cue itself failed to produce a latent inhibition effect (Ackil, Carman, Bakner and Riccio, 1992).

### Memory for Stimulus Attributes

There is another aspect of memory that has intrigued me ever since Debbie Ebner, then a graduate student, asked me one of those “simple” questions that went something like this: If generalization gradients flatten over time, why do you say that stimulus (context) change is one of the sources of forgetting over a retention interval? As soon as I started to explain, I realized that I was stumped. Some 25 years later, I still don’t really have the answer, although along the way the issue generated several *Psychological Bulletin* papers on the “contextual cues paradox” (Riccio, Richardson and Ebner, 1984; Riccio, Richardson and Ebner, 1999) and on some related methodological implications (Riccio, Ackil and Burch-Vernon, 1992). But I began to think more about how “forgetting of stimulus attributes” might be a useful way to conceptualize the findings that over time generalized stimuli were responded to as if they had become functionally more similar (Riccio, Rabinowitz and Axelrod, 1994)

At that time, there was still some argument over whether CTA followed all the principles of learning, so Rick Richardson decided to look at stimulus generalization in that paradigm. Having found a generalization gradient, he went on to show that the gradient flattened rather rapidly as the training to testing interval increased (Richardson, Williams and Riccio, 1984). Thus, CTA seemed to conform to some other aspects of learning situations. Some years later, Cantey Land, Steven Harrod and I returned to this issue in a somewhat different way. We wondered if forgetting of attributes might be detected if there were a long interval between the CS and the UCS, and obviously CTA seemed a perfect paradigm for asking about a long trace interval. Our major finding was that, as expected, with a 2-hour interval there was less aversion to the target flavor than with an immediate pairing, but that the differential responding to the generalized test flavor obtained at the short interval was largely eliminated at the long interval (Land, Harrod and Riccio, 1995). This outcome suggested that the rats forgot the specific features of the target CS during the interval; consequently, only a more general flavor representation was present at the time the association was formed.

Might there be other ways to examine forgetting of attributes of the CS prior to the conditioning episode? To ask this question, Mitchell Metzger took advantage of the latent inhibition paradigm. Using a pre-exposure to the flavor that was sufficient to produce LI after a one week interval, he compared the strength of LI to the target and a generalized stimulus. Pairing a similar, but not-pre-exposed flavor, with illness 1 day after pre-exposure to the target resulted in stronger conditioning than with the original flavor, i.e., LI was reduced. However, when the conditioning was given one week after pre-exposure both the original and the generalized flavor were now effective in producing LI. Thus, the loss of memory

for attributes occurred prior to the formation of the taste-illness association (Metzger and Riccio, in press). It is worth mentioning that in his dissertation Metzger also tried to ask a more difficult question: Are the attributes of the UCS forgotten over time? The problem here is that the UCS itself determines performance, so the generalization test cannot be used. The strategy was to take advantage of the UCS pre-exposure effect, using one illness-inducing agent and a different but somewhat similar toxin at conditioning. Again, the pre-exposure to training intervals were varied. Unfortunately, the data, while suggestive, were not clear cut, but I have always thought this is an interesting issue to pursue.

Our latest foray into memory issues has taken the form of a literature review. Susanne Meehan, a former doctoral student in my lab who had worked on other topics, was kind enough to team up with me to write an invited chapter for Steve Reilly and Todd Schachtman's book on behavioral and neural processes in CTA (Meehan and Riccio, 2008).

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