The highlight for January, 2008 is by James C. Smith, the Robert O. Lawson Distinguished Professor of Psychology at Florida State University. There are few individuals in the field with as extensive and extended history in food aversion learning as Dr. Smith. As outlined in the current highlight, his work over the past 50 years has focused on ionizing radiation, having its roots in his early association with Winthrop Kellogg. During this period, Dr. Smith and his colleagues explored radiation in the context of conditioning (both as a CS and US) and demonstrated the nature of radiation-induced taste aversions conditioning and the varied parameters under which it occurred. Dr. Smith's research spans an eclectic array of topics in this field, ranging from assessments of radiation-induced taste aversions to demonstrations of backward conditioning to reports of long-delay learning in animals exposed to X-rays. The fact that much of the findings from this workparalleled those reported with toxins and other drugs helped to give credibility to the phenomenon of taste aversion learning at a time when it was being challenged. Dr. Smith not only characterized radiation-induced taste aversion learning, but he also implicated its possible application as he and his colleagues demonstrated the conditioning of food aversions in cancer patients undergoing radiation therapy (and tested its generalization in animal models). More recently, he has joined with Dr. Tom Houpt to assess the basis for aversions induced by high intensity magnetic fields. In this work, which parallels that of his research with ionizing radiation, he has demonstrated the ability of such exposure to induce aversions and has examined the role of vestibular stimulation in its induction. Since his initial research in the early 1960's, Dr. Smith has used his expertise in learning, comparative psychology, sensory physiology and psychophysics to bring together a research program that is both comprehensive in scope and detailed in its analysis. Dr. Smith has simply been eclectic in his approach. It is interesting that Kenneth Roeder, an individual who had a major influence on Dr. Smith and who Dr. Smith called the greatest psychobiologist he ever met, shared this very characteristic. I have known Dr. Smith for over 30 years, and this eclecticism was evident at the outset of our association. His breadth remains clear and impressive, and his work stands out as being innovative, interesting and important.

Taste Aversion Learning: The Backbone of a Career

James C. Smith

I am most pleased with the invitation from Professor Anthony Riley to contribute my "highlight" on taste aversion learning. Tony has made a major contribution to this field with his own research, but I particularly want to point out his significant contribution to all TA researchers by his biographical work for more than 30 years. Starting with a publication of the first comprehensive list of TA references in Animal Learning and Behavior in 1976, he has continued to keep us up to date on what is new in TA learning. Going from laborious research in the abstracts to the current and most useful WEB Page, Tony has provided us with an invaluable contribution. I personally thank him for helping me for many years.

"In the history of science, nothing is more true than that the discoverer, even the greatest discoverer is but the descendent of his scientific forefathers; he is always essentially the product of the age in which he is born." This quote is from Sylvanus Phillips Thompson, a 19th Century Physics Professor. My story about my professional career and my work with conditioned taste aversion is a story of my scientific forefathers, my professors, my colleagues and ultimately my students.

I was born in the latter part of 1928 in Birmingham, Alabama. My mother and father were college educated people and it was expected that I would follow that course. My father was a mathematician with an emphasis in geometry. It was not unexpected that I majored in mathematics in college and was certified to teach at the high school level. At the time of my graduation from Auburn University, I was inclined not to make teaching my profession. The Korean War had started, and I was registered with the local draft board to enter the military. After graduation, I enrolled in a program in counseling psychology at The Florida State University (FSU) and I was deferred from the military for two years.

After arriving at FSU, my advisor requested that I enroll in a Psychology of Learning course which was to be taught by a "new" professor, Winthrop Niles Kellogg. I complied with his wish, and my life was changed forever. Professor Kellogg had moved from Indiana University to The Florida State University in the fall of 1950. Professor Kellogg was well known for his work in comparative psychology (<u>The Ape and the Child</u>), for his studies of in spinal conditioning in dogs and his later work on echolocation in dolphins and the human blind. He was a dynamic teacher, and I was spellbound by his work. In addition to taking Kellogg's courses, I continued some work in the Mathematics Department with more emphasis on statistics. Professors Howard Baker and Lloyd Beidler also joined the faculty at FSU that same year, and they also were to become an integral part of my education. I completed the M.S. Degree in Psychology in one year and knew that my future was to be in the Experimental/Comparative area. During my second year at FSU, my roommate, Art Orgel, and I finished collecting the data for our first publication on the sensitivity of pigeons to magnetic fields (1).

Exhausted from my continued negotiations with the draft board, I accepted a commission in the Air Force and took leave from my studies for slightly over three years (1953-56). During that tour of duty, I was assigned to a Human Resources Laboratory which was directed by the late Robert M. Gagne.

Upon my release from active duty, I returned to The Florida State University where Professor Kellogg agreed to accept me as a doctoral student in the Psychobiology Program. I also studied with Professor Baker (vision psychophysics). Inspired by a visit from Professor Keffer Hartline, I set up a program to see if I could condition a horseshoe crab to respond to a visual stimulus. This work led to my first NSF Grant (17K/year for two years) and a paper in JCPP (2).

In Kellogg's Neuropsychology Course, he assigned each of the graduate students a topic and we were to write a review manuscript and give a series of lectures to our fellow students. The topic he gave me was "X-rays and Behavior”. In later years I often wondered why Kellogg made these various assignments. I think he looked at topics that interested him, and he let us do the work to go through the abstracts and find the appropriate research reports. My review of this literature on ionizing irradiation was to determine the course of my professional life for many subsequent years. A second product of that seminar was that I met a fellow student, Don Tucker, who was studying with Professor Lloyd Beidler. Tucker was to become a close colleague some years later.

In my review of "X-rays and Behavior", most of the research I encountered was directed toward investigations of behavioral and cognitive skills following exposures to X- or Gamma Rays (often lethal doses). Following the development of the hydrogen bomb and the apprehensions about radiation exposure during the Cold War with Russia, it is not surprising that there was this emphasis in the literature. However, buried among the large number of such studies were some reports that living organisms could "detect" the presence of ionizing radiation, most likely through the sense of vision. Needless to say, this work was not without controversy, because Wilhelm Roentgen in 1895, describing his discovery of X-rays stated, "The retina of the eye is insensitive to our rays; the eye brought close to the discharge apparatus registers nothing, although according to common experience, the media contained in the eye must be sufficiently transparent to the rays." Many people read this important paper (published in 1895 and translated to English and published in ***Science*** in Feb. 1896. His second paper was also published in ***Science*** in May of 1896). Apparently only a few people read his third paper (1897; only an abstract was published in English). In this paper he retracted the finding that these rays were imperceptible. He stated "The fact observed by Mr. G. Brandes that X-rays can produce a light sensation in the retina of the eye, I have confirmed". Roentgen noted that he had once made such an observation earlier, but had thought it was subjective. He went on the describe his confirmation "if one holds a vertical metal slit, a few tenths of a millimeter wide, as close to the open or closed eye as possible, and if one holds the head, enveloped in a black cloth, near the discharge apparatus, one observes after some practice a weak and not uniformly bright strip of light, which according to the position of the slit in front of the eye has a different shape: straight, curved or circular. By a slow motion of the slit in a horizontal direction one can progressively make these forms pass into one another. An explanation of this phenomenon is easily found if one considers that the eyeball is intersected by a laminated beam of X-rays, and if one assumes that x-rays can produce fluorescence in the retina". The sensitivity of the eye to ionizing radiation exposures was "rediscovered" in the 1950's by Leo Lipetz and others.

By far, the most exciting reference that I found on detection of ionizing radiation was the 1955 paper by Garcia, Kimeldorf and Koelling in ***Science.*** I am sure that this seminal research was the starting point for most of the early investigators in TA research. Here was clear evidence that ionizing irradiation could be used as an unconditioned stimulus in conditioning an aversion to saccharin flavored water. As has been pointed out by others, this phenomenon was not accepted as "learning" by most of the traditional learning researchers at that time and that doubt was compounded by the use of ionizing radiation as the unconditioned stimulus.

The Biology Department at FSU had a deep therapy X-ray machine, and I ran several pilot experiments and was able to replicate the earlier work by Garcia, Kimeldorf and Koelling, using X-rays to condition an aversion to saccharin. I did not publish any of these efforts. For my dissertation, I conducted an experiment testing the effects of X- and Gamma Rays on operant behavior, which yielded very little significant information.

By the time I finished my PhD, I held an Instructor's appointment at FSU and the University offered me a tenure track position as an Assistant Professor. I held that position for a year and continued working on procedures for radiation-induced TA conditioning. After one year at FSU I left for an appointment at Colgate University in Hamilton, New York. The emphasis at Colgate at that time was much more on teaching than research. I stayed in New York for only one year because FSU made an offer to me to return, and the possibilities for developing a research program were strong. They had remodeled a nice laboratory and offered me a joint appointment in Psychology and the Institute of Molecular Biophysics (IMB). In addition, there was the promise for a new Psychology Research Building (which was actually kept 4 years later) and a new IMB Building (which materialized in only 2 years). The new Psychology Building (which was subsequently named for Kellogg) came with a built-in Cobalt 60 source and the IMB Building had a deep therapy X-ray machine.

There was a further driving force in my return to FSU. Shortly after I had finished my degree, Professor Beidler came to my laboratory one Saturday morning with a distinguished looking visitor. In typical Beidler manner, he did not introduce me, but simply said, "Smith, tell this man what you do." I began relating to "this man" the X-ray work (initiated by Garcia, Kimeldorf and Keolling) that had caught my interest and I outlined a program of study that I had planned. After finishing my story, "this man" said "I believe that we can support you". "This man" turned out to be Leroy Augenstein, Head of the Biophysics Group at the Atomic Energy Commission (AEC). During the year before I went to Colgate, I prepared a proposal to AEC and after a year of deliberation, they offered me a contract. Coming back to FSU, where I had the space and the equipment was the correct thing to do in order to accept the contract with the AEC. The original contract with the AEC was for three years. However, the work went well and they supported me for a total of 15 years.

Although I was only there for one year, there were many lasting things from the Colgate experience. While there I made frequent visits to Syracuse University, where Matthew Wayner was my host. I will be ever grateful to Matt for those visits. On one such visit, I met Professor Kenneth Roeder who had come to give a colloquium. He lectured on the predator/prey relation between the bat and the moth. He described his technique for recording from the tympanic nerve of the moth to natural high frequency sounds, such as those emitted by the flying bat. I was interested in this technique for this auditory recording and engaged him in conversation after his lecture. He invited me over to Tufts, and I accepted his invitation. I spent several days with him and in subsequent years he made many trips to Tallahassee with his charming wife, Sonja. During those visits to FSU, Roeder taught me many techniques with insects. I learned how to record from the tympanic nerve in the moth, how to measure motor behavior and Ken and I developed procedures for recording electroretinograms in these insects. I have subsequently taught these techniques to many students and I used them in subsequent research projects. I will describe two of these projects presently. My friendship with Ken and Sonja Roeder enriched my life. Ken Roeder, in my estimation, was the greatest "psychobiologist" I ever met. He knew anatomy, physiology and behavior and was competent and comfortable in all three areas. His book "Nerve Cells and Insect Behavior" is a must read for all neuroscience graduate students.

Before I left for Colgate, I attended my first meeting of the Radiation Research Society at Northwestern University in September, 1960. There I met Dr. Donald J. Kimeldorf. At that time, I had no idea of the impact that Kimeldorf would have on my life. Dr. Kimeldorf gave a paper entitled "Radiation Conditioned Behavior". He described conditioning effects with quite low doses of irradiation. This work was not well received for two reasons. 1. TA learning had not been accepted as "real learning" and 2. Few researchers believed that radiation doses that low could have any biological effect. The pilot work that I had done at FSU made me believe Kimeldorf's findings without doubt. I spoke with Kimeldorfafter his talk and over the next few months we had a lively correspondence. At the bottom of one of his letters in January, 1962 he penciled (in red) "A thought has just occurred to me. I wonder if you would be interested in spending next summer at San Francisco?" He went on to describe the laboratory there and other details. Needless to say, I accepted his invitation and went to the U. S. Naval Radiological Defense Laboratory (USNRDL) that summer and also the following summer in 1963. My intent was to work with Don and Ed Hunt in the area of radiation induced TA conditioning. That did not happen. Instead, we worked on immediate detection of X-rays by the Noctuidae moth.

When I amved at USNRDL I was relating to Don and Ed all I had learned from Ken Roeder. I actually caught a "California" Noctuidae moth and recorded from its tympanic nerve adjacent to their new deep therapy X-ray machine at USNRDL. This X-ray machine had a specially built shutter that was reported to operate without any noise. Since no tests had been run to detect if the shutter made high frequency sounds, the moth told us that movement of this shutter resulted in significant high frequency emissions. This finding disturbed Kimeldorf, but he found it fascinating that such recordings were possible. When I demonstrated an electroretinogram preparation, Kimeldorf left the room and returned with a strontium-90 source and waved it about in front of the moth's eye. Waving a piece of metal in front of the eye revealed no response. That day we clearly showed that the dark adapted moth eye responded to ionizing radiation stimuli. In subsequent work, we showed that the course of dark adaptation to light and to beta ray stimulation was quite different and we spent the two summers determining the cause of this difference (see 3and 4).

Donald J. Kimeldorf, along with Ed Hunt and John Garcia, had made an observation that led to the 1955 TA conditioning paper. They were observing the eating and drinking behavior of rats during a prolonged exposure to a low dose of gamma rays. Eating and drinking was reduced during the exposure period. To their surprise, after several such exposures they found a similar reduction in food and water intake during a sham exposure. Kimeldorf described the conditioned stimulus as a "complex of stimuli that normally accompany exposures (e.g., handling, confinement to exposure chambers, room cues)." This astute observation led to the idea of gamma ray-induced taste aversion learning. Kimeldorf was an extremely competent scientist. He was also an outstanding mentor. He was a particularly good science writer, and I was fortunate to have published two papers with him. In subsequent years, he read and gave me critique on many other of my writings on radiation-induced taste aversion learning and I always was better for seeking his advice. Anyone who had the chance to work with Kimeldorf was fortunate. His book with Ed Hunt entitled "Ionizing radiation: Neural function and behavior" is a thorough description of the physiological and behavioral effects of exposure to ionizing radiation and the 9th Chapter contains some good background on the development of radiation induced TA.

In my newly established laboratory at FSU, my first graduate student, Dale Morris, and I began to study some factors that contributed to radiation-induced TA learning. In the original paper in 1955 by Garcia, Kimeldorf and Koelling, they stated "The processes through which radiation is capable of operating as an unconditioned stimulus are unknown. Since consummatory behavior is partially a reflection of gastric function, it is plausible to suspect gastrointestinal disturbances as the physiological events that motivate the animal in the learning situation. Gastrointestinal functions are known to be disturbed during irradiation and are responsive to the same magnitude of radiation dose". One of the references that they quote was Conard, who had measured intestinal motility at the onset of X-ray exposure. Conard showed that he could enhance this motility with doses of physostigrnine and inhibit the motility with doses of atropine. It seemed to me if intestinal motility was the basis for the unconditioned response to radiation exposure, then atropine would reduce and physostigmine would enhance radiation-induced TA conditioning. The first experiment that Dale and I conducted was to see if atropine would deter the formation of a radiation-induced TA to saccharin flavored water. It did not (5). In later experiments, we tested to see if physostigmine would enhance TA learning and it did not (6). We did see a taste aversion in our control rats that got saccharin paired with the injection of physostigrnine and no radiation. I guess this was one of the first demonstrations of a drug-induced TA.

We had some quite old rats around, so Morris and I showed that one could produce this TA in senile rats (7). By this time, the IMB Building was completed and we had a GE deep therapy X-ray machine installed (250 kv). We could now manipulate the rate and wavelength of the radiation. We conditioned rats with dose rates from 100 to 828 R/minute and got comparable TA to saccharin among the groups. The wave length of the ionizing radiation exposures did not seem to matter as long as it was short enough to penetrate the rat (8).

We began a series of studies where we varied the time between tasting of the saccharin solution and the radiation exposure. When we began to give the radiation exposure before the rat was allowed to taste the saccharin, we found ourselves in serious trouble with the traditional learning colleagues because they knew that "backward conditioning" was not possible. We had to call this phenomenon "post exposure" conditioning in order to get the results published (9, 10 11 12). We found that one could get very good conditioning if the saccharin was presented to the rat as long as an hour after the radiation exposure. At that time, we had no clue as to the nature of the unconditioned response, but it was apparent that it was long lasting.

By the mid 60's, largely from the work of Harold Carroll who was working with Ed Hunt and Don Kimeldorf at USNRDL, it became apparent that the unconditioned response to ionizing radiation exposures was mediated through the circulating blood. Using parabiotic rat preparations that shared a common blood supply, they showed that one member of the pair could be irradiated while the second member drank saccharin flavored water and this second member would have a taste aversion to the saccharin. Something was being formed in the irradiated rat that was transmitted to its partner via the exchange of blood. Soon thereafter, Garcia published a paper in ***Nature*** demonstrating a TA to saccharin by pairing saccharin intake with an injection of irradiated serum fiom a donor rat.

A behavioral measure of the time course of the "aversive aspect of the irradiation" was demonstrated in the Master's Thesis of Marilyn Carroll at FSU (12). Marilyn (now on the faculty at Univ. of Minnesota Medical School) exposed a thirsty rat to 100 R fiom a Co60 source and then observed the rat drinking a saccharin solution. The rat drank for about 90 minutes and then stopped. A sham exposed rat continued to drink after the 90 minute period. When she imposed a 30 minute period between the irradiation and the onset of the drinking, the rat stopped after 60 minutes. When the delay was extended to 60 minutes, the rats stopped drinking after 30 minutes and when the delay was 90 minutes, the rats would not drink the saccharin solution at all. It seemed fiom her results that the unconditioned response peaked at 90 minutes following the 100 R exposure to the radiation source. With delays longer than 90 minutes, the rats started drinking again at the onset of the test. From the literature, we observed that this 90 minute time course mimicked the time course of the build up of histamine following similar radiation exposures. We then showed that injections of antihistamine could block the formation of a TA to saccharin and that we could produce a TA with histamine phosphate injections (13). Antiemetics did not block the formation of a TA.

The conditioned TA's where the irradiations preceded the tasting of the saccharin were beginning to make some sense. One other example of this "backward conditioning" helped to explain a persisting problem with radiation-induced conditioned TA. Dr. Barron Scarborough and his co-investigators at FSU had continued to report that they got TA to saccharin in rats that received water, not saccharin during the initial pairing of the taste with the irradiation. Their standard procedure was to pair the saccharin (or water) with the irradiation and then to immediately thereafter start the preference test between saccharin and water. Their rats that received the water/radiation pairing were drinking saccharin in the immediate post-exposure period at the initiation of their preference test. When looking at the intake 24 hours later, the rats had developed a strong TA to saccharin. Bob Shaffer and I replicated their findings by using separate groups of rats that had their preference test initiated immediately after the pairing or a preference test initiated 24 hours later. Water/radiated rats developed a TA with the immediate preference test and did not develop the TA when the test was delayed for 24 hours (14). It seemed obvious that what Scarborough's group had been showing was a "backward" pairing of irradiation and saccharin that was available in the immediately initiated preference test.

The delay between tasting the novel solution and a later radiation exposure was a different matter. Ed Hunt had done an experiment where he gave rats saccharin to drink, anesthetized the rats with ether and exposed them to X-rays. The rats quickly recovered from the ether and therefore were not anesthetized during the post exposure period when the UCR would be peaking. My graduate student, Dave Roll, and I wanted to repeat Ed's experiment, but to anesthetize the rats with a longer lasting drug, so that they would be out at least for the first couple of hours during and after the radiation exposure. Knowing that anesthetization would be much slower with a drug than with ether, we wanted to see if one could place a delay after the saccharin period and still get robust TA. We started with a 15 minute delay between saccharin and radiation. We got a profound aversion, so we extended the time to 30 minutes. Still getting an excellent aversion, we proceeded to extend the time further. We could get good TA with a delay of three and even six hours (15). Only a few people believed this finding, but it was being done in other labs at the same time. We published these results in Psychonomic Science, a journal that required little, or no, editing. We had more reprint requests for this finding than any other report from this laboratory.

Even into the late 1960's, many of the traditional experimental psychologists did not accept TA learning as "real learning". I had colleagues here at FSU who advised me to change the direction of my studies so that I would not ruin my career. One important skeptic was Professor Eliot Stellar. Stellar was the editor of the Journal of Comparative and Physiological Psychology at that time. He came to Tallahassee to visit Professor Beidler, and Beidler brought him over to the Psychology Department to spend an hour with me. He stayed almost the entire day. We had an intense dialog, but he listened. I smothered him with data, and he left my office thinking. Later, he called me and suggested that I write a review article on my findings with ionizing radiation. Because the book by Kimeldorf and Hunt had just been published, I thought this was not necessary at that time. Over the next few years, Stellar and I continued the conversation and ultimately became good friends. As true with many other young investigators, Stellar became a loyal supporter of my work. In 1970, Stellar and Jim Sprague asked me to contribute a chapter on our ionizing radiation findings to the 4th edition of *Progress in Physiological Psychology* (29).

Throughout the 60' and 70's, my laboratory also spent considerable time studying ionizing radiation as a conditioned stimulus. Jean Hendricks, my second PhD student had developed a conditioned suppression method for measuring sensory thresholds in pigeons. She borrowed from Howard Baker an apparatus that allowed her to present flickering and fused light to the bird. She measured Flicker Fusion Thresholds with great precision (45). Dale Morris used this procedure to measure the dose rate threshold for X-ray detection in rats (46). We, along with others, studied the role that olfaction and vision played in the early detection of X- and Gamma rays. We showed that pigeons could also detect the onset of an X-ray exposure via olfaction, and this caused quite a stir because of the traditional belief that birds could not smell. We were side tracked for several years working on bird olfaction (with Wendon Henton, Jim Walker and Don Tucker). Tucker, Walker and I also became involved in research involving the plasticity and reconstitution of the primary olfactory nerves. The conditioned suppression procedure was used for a variety of other stimuli in addition to X-rays over the next few years in our lab (29, 47).

In 1975, I was contacted by the National Cancer Institute and asked to develop a protocol to test if radiation-induced TA played a role in eating problems in radio-therapy patients. Did eating too close in time to the radiation therapy result in a conditioned TA to that particular taste? We had no local teaching hospital, so I turned down this request for two years. Finally, Dr. Frank Bilek, a local radiation therapist and I initiated several experiments with human patients (with support fiom NCI). We did not have a large population and our patients suffered fiom a variety of diseases and received radiation therapy concentrated on several bodily areas. We did produce what looked like a taste aversion to a common fruit juice, and we published our results in *Cancer Treatment Reports* and in a text. Needless to say, we had no "sham radiation" control group with the patients and had to use healthy volunteers (16, 17, and 18). As many of the readers know, Ilene Bernstein collected similar data with children undergoing chemotherapy.

While we were collecting data on the cancer patients, we were also working on a "rat model" for a radiotherapy patient. We postulated that tastes sampled by therapy patients would not likely be novel, they would have many exposures over several weeks and they would have only partial body exposures. We collected data on several groups of rats that had extensive experience with the saccharin, along with many conditioning trials and they were given partial body exposures (head, thorax and abdomen). TA's could be conditioned with small repeated partial body doses (19, 20).

Two other TA experiments with radiation proved to be interesting. Alan Spector's Master's Thesis compared measures of TA such as single bottle tests, two-bottle tests and extinction from the radiation-induced aversion. He had four groups (n = 32 per group). Group 1 had a saccharin/radiation pairing, Group 2 had a water/radiation pairing, Group 3 had a saccharin/sham exposure pairing and Group 4 had a water/sham exposure pairing. There were no differences among the latter three groups. They all drank large amounts of saccharin, had saccharin preference scores in the 90% range and had no aversion to extinguish. The saccharin/radiation group showed a profound TA on the initial single bottle test and on the first day of the 2-bottle test. Because of the large number of subjects in the saccharin/X-ray group, Alan observed that the variation in the extinction curves of the 32 rats in the Sac-Radiation group was profound. A few of the rats extinguished in a couple of days, another group extinguished in about 5-6 days and another small group never showed any signs of extinction. Most of the rats extinguished in about 14 days. We have not been able to determine if this broad difference in extinction times was the result of variation in saccharin preference, sensitivity to the X-rays or differences in the rats' ability to form the association. This variation, which we also saw in our magnet-induced TA, remains a mystery to me.

The last observation that I will describe regarding radiation-induced TA is published in *Physiology and Behavior*. Alan Spector and my loyal technician, Glee Hollander, and I gave rats a single pairing of saccharin and radiation. Following the pairing, we gave six groups of rats a single bottle of saccharin for 0, 3, 6, 12, 24 or 48 hours. 48 hours after the original saccharin/radiation pairing, we began a 24 hour two-bottle preference test between saccharin and water. Rats that had 24 or 48 hours of the saccharin alone during the post-exposure period showed no taste aversion during the subsequent two-bottle test. Rats that had zero or three hours of saccharin in the single bottle period had the typical taste aversion on the first day and gradually extinguished this aversion over the next 14 days. Rats that had 6 or 12 hours of saccharin alone showed intermediate effects on the aversion and the extinction process (22). Significant experience with the CS following the pairing of saccharin and radiation wipes out the subsequent aversion.

Additional research on radiation-induced TA was conducted in this laboratory during the 60's, 70's and 80's (23-32).

In August of 1990, The National High Magnetic Field Laboratory was awarded to FSU. (see http://www.magnet.fsu.edu) Very large magnets were built and bought, and the mission included the support of science including behavioral and biological work. My good colleague, the late Bruce Masterton, goaded me almost daily to see if a magnet could induce a taste aversion. In the summer of 1994, Ben Kalovitch, a high school senior, came to FSU in the NSF Summer Program which was designed to encourage bright students to choose math and science for their studies. Ben was assigned to my laboratory, and Masterson saw this as the chance to get me to try TA conditioning with a powerful magnet. Masterton made the arrangements for us to use a 9.4 Tesla wide-bore super-conducting magnet. With much skepticism, I agreed to try.

We gave a few rats 10 minutes access to saccharin flavored water, placed them in a capsule and inserted them into the core of this magnet for 30 minutes. They developed a strong aversion to the saccharin. Sham magnet exposures were conducted by placing the rats in the same capsule and inserting them in a PVC pipe of comparable bore. They developed no aversion to the saccharin. With the assistance of Ross Henderson, our engineer, we constructed a "boom" so we could pull the capsules in and out of the magnet numerous times allowing the rats to cross and re-cross the strong gradient of the magnet, but not stopping as the rat passed through the core. These "gradient exposed" rats developed no taste aversion. By the end of the summer, Ben and I had a good demonstration that 30 minutes in the core of this 9.4 Tesla magnet would induce a significant saccharin aversion.

Since I was busy with other research projects, I did not follow up on these findings for several years. Two graduate students, Chris Nolte and David Pittman, did a rotation through my laboratory and asked if they could use a larger group of rats and repeat the work that Ben and I had done. I agreed with the condition that if their work culminated in a publishable paper they would include Ben Kalovitch and Ross Henderson as co-authors. That paper was published in 1998 (33).

In the fall of 1998, Tom Houpt joined the faculty of FSU in the Department of Biological Sciences. I had met Tom when he was a postdoctoral student with Dr. Gerry Smith at the Bourne Laboratory of Cornell University Medical School. When I first met Tom I asked him if he knew Kathy Houpt. He did, for Kathy is his mother. Kathy Houpt co-authored a chapter with Donna Zahorik in the "first" TA book {edited by Lewis Barker (my 14th doctoral student), Mike Best and Mike Domjan in 1975). Needless to say, after that first meeting with Tom, I took an interest in his future. When Tom came for his second visit to FSU, I asked him what I could do to insure that he would accept the position here. He replied that I should revive my interest in magnet- and radiation-induced taste aversion learning. I replied, "you are easy". My only constraint was that I would no longer be a PI and I would not be first author on any publication we would submit. He had no trouble accepting those terms.

Tom Houpt has been my close colleague for nine years and he has given me "eternal life" after I formally retired in 2003. We have not yet revisited ionizing radiation as the UCS in a TA problem, but we have submerged our energies in high intensity magnetic fields. We received a substantial grant from FSU’s Research Office and are now one year in our second NIH Grant. We have nine published papers (34-42) and a chapter (ed. Reilly and Schachtman) in press.

We have characterized the conditions under which magnetic field-induced TA occurs. We get strong conditioning and slower extinction with field strengths of 9 Tesla and above and milder conditioning with 7 Tesla fields. Passing through or remaining in the gradient of the magnet does not produce strong and lasting TA as compared to being exposed in the core of the magnet. Magnitude and duration of the TA is related to time in the core of the magnet, with 30 minute exposures as optimal.

The unconditioned response to the magnet involves the vestibular system. We have found that if the vestibular system is chemically destroyed, the rats will not develop a magnet-induced taste aversion. We typically measure the locomotor activity of the rat following a 30-minute exposure in the core of the magnet. Rats run in circles, the direction of which is determined by the pole of the magnet that the rat faces during exposure. If the rat is oriented toward the South pole in these vertical magnets, it will circle in a counterclockwise direction for up to 2 minutes after exposure. In contrast, if the rat faces the north pole of the magnet it will circle in a clockwise direction. We have now exposed hundreds of rats in our 14T super conducting magnet, and no rat has ever turned in the "wrong" direction. There is, however, considerable variation in the number of turns the rats make following the magnet exposure. Animals exposed in the magnet tend to remain on all four feet following exposure as compared to sham exposed rats that rear and place their front feet on the cage side. These short lived locomotor disturbances do not occur if the rat has undergone a labyrinthectomy. The same directionality holds if the rat swims in a pool after exposure. Two prior 30-minute exposures to the magnet eliminate a subsequent attempt to condition a saccharin taste aversion. Our current research is directed toward understanding how (and how long) the vestibular system is altered by the magnet exposure.

Related to the continued gustatory research in my laboratory, we have used TA conditioning experiments to determine the generality of taste experiences to a rat (29). For example, rats conditioned with a mixture of glucose and saccharin show a much stronger aversion to the saccharin than to the glucose. More recently, we have used TA procedures to study the "taste of fat". For example, we blended corn oil (CO) with a mixture of glucose and saccharin and used this blend as a CS that was paired with an injection of LiCl. The rats show a subsequent aversion to G + S + CO, G + CO, S + CO and CO alone, but show no aversion to either G, S or the mixture of G + S. From this, we postulated that the salient feature of mixture of G, S and CO was the CO (43). We found similar results when we blended CO with sucrose, i.e., an aversion to CO, but not to sucrose (44).

Finally, in the laboratory, Pat Smith did his dissertation on conditioning TA's to the temperature of a solution. Ross Henderson designed and constructed a testing chamber that allowed for precise control of the temperature of two separate sipper tubes. The tubes passed through aluminum blocks that were heated or cooled by Peltier refrigerator units. Pat found that rats normally preferred cold water in comparison to warm water. By pairing cold water with an injection of LiCl, he could condition an aversion to cold water and the rats would then drink the warmer water. In these studies, Pat did several experiments that showed the strong influence of the temperature of a solution. His dissertation is not yet published, but a complete copy of the dissertation can be found at http://www.psy.fsu.edu/faculty/smith.dp.html

Conditioned Taste Aversion procedures have played a major role in the research I have done over the past 50 years, and my students and I are deeply indebted to many mentors and colleagues.

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