The Journal of Undergraduate Neuroscience Education (JUNE), Spring 2017, 15(2):R29-R35

MEDIA REVIEW
The Missing Manuscript of Dr. Jose Delgado´s Radio Controlled Bulls

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ABSTRACT
Neuroscience systems level courses teach: 1) the role of neuroanatomical structures of the brain for perception, movement, and cognition; 2) methods to manipulate and study the brain including lesions, electrophysiological recordings, microstimulation, optogenetics, and pharmacology; 3) proper interpretation of behavioral data to deduce brain circuit operation; and 4) the similarities, differences, and ethics of animal models and their relation to human physiology. These four topics come together quite dramatically in Dr. Jose Delgado's 1960s famous experiments on the neural correlates of aggression in which he stopped bulls in mid-charge by electrically stimulating basal ganglia and thalamic structures. Technical documentation on these experiments is famously difficult to find. Here I translate and discuss a Spanish language article written by Dr. Delgado in 1981 for an encyclopedia on bull fighting published in Madrid. Here Dr. Delgado appears to give the most complete explanation of his experiments on microstimulation of bovine brains. Dr. Delgado's motivations, methods, and his interpretation of the bull experiments are summarized, as well as some accompanying information from his 1970 English language book: "Physical Control of the Mind." This review of Dr. Delgado's written work on the bull experiments can provide a resource to educators and students who desire to learn more about and interpret the attention-calling experiments that Dr. Delgado did on a ranch in Andalucía over 50 years ago.

INTRODUCTION
You may remember the moment when you first learned about Dr. Jose Delgado's "remote controlled bulls," -the 1960s era experiment where a Spanish scientist used a radio transmitter to electrically stimulate a part of the brain of a bull, stopping the bull in full charge. For me, it was spring of 2002 in the first year of graduate school at the University of Michigan during the systems neuroscience class. The experiment was discussed to demonstrate an eye-catching bizarre mix of neuroanatomy knowledge (role of electrode placement on behavioral effect), technology of neural interface construction (the design of the stimulating and receiving circuits), and bravado (testing on a charging bull). The photograph (Fig. 1) and experiments serve as a very effective hook to draw students into the subtleties of neuroanatomy and brain circuits and are included in undergraduate textbooks (for example, see Watson and Breedlove, 2016).

When the photograph is shown in a classroom, hands immediately pop up in a "wait, what?" moment, but we cannot give more information. Little is available in the literature beyond a New York Times article from 1965 that brought the experiment to international attention (Osmundsen, 1965). Details are lacking. Where exactly did Dr. Delgado place the electrodes? How did the electronics work? Was the experiment done systematically over years, or was it a one-off? There was never a formal publication, leaving the experiment to be only mentioned in passing as an oddity in the history of neural interfaces and neuroscience. Usually spoken about for 30 seconds in the classroom, we can only say: "Here is something weird from the 1960s, where the Spanish scientist Dr. Delgado wirelessly electrically stimulated the brain of a bull in mid-charge, and the bull stopped."

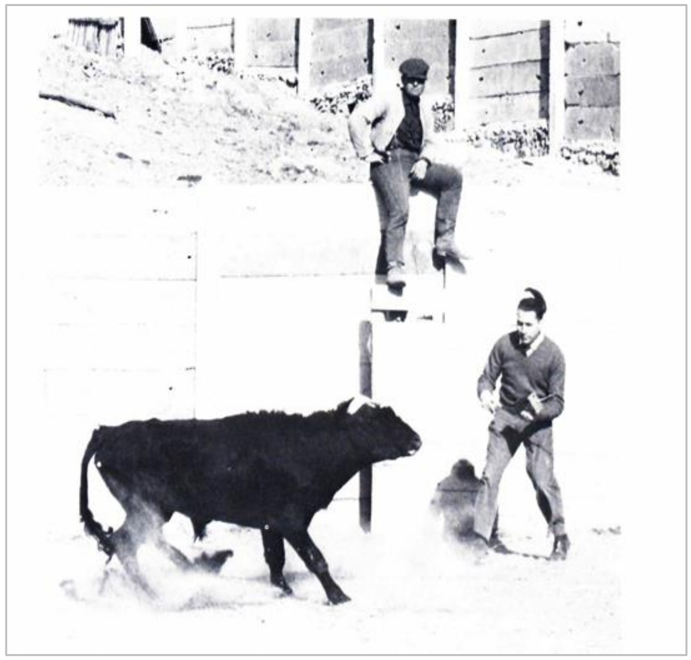

Figure 1. The famous photo - Dr. Delgado the scientist radio electrically stimulating the brain of the bull "Lucero" and stopping the animal in mid-charge. All photos and book excerpts by Dr. Delgado in this article are reproduced courtesy of the Delgado estate (see acknowledgements).

In an attempt to learn more, we can read Dr. Delgado's book "Physical Control of the Mind" (Delgado, 1970) summarizing his experiments on brain stimulation and neural recording in human patients and colonies of cats and rhesus monkeys. Disappointingly, his experiments on bulls are discussed only in passing in two paragraphs on pages 167-168, showing the same famous photographs and the same basic information as the New York Times article. Various archival videos can be found online, but they can be difficult to analyze and are sparse on technical details (Hunter, 1984). Searches of the literature do not reveal any further published details by Dr. Delgado.

Fourteen years after first hearing about this experiment, my curiosity was finally answered when neuroscientist colleague Professor Scott Currie, upon hearing I was in Spain for a science diffusion event in June 2016, graciously sent me some of his personal correspondence with Dr. Delgado from 1999, which included an article in Spanish entitled:

"Toros Radiodirigidos
Una Experiencia Científica con el Toro de Lidida
por José Manuel Rodríguez Delgado"

Or

"Radio Controlled Bulls
A Scientific Experience with the Bull of the Bullfight
by José Manuel Rodríguez Delgado"

In my hands was a 21-page treatise providing extensive details on the bull brain stimulation experiments (Delgado, 1981). This "missing manuscript" was an invited chapter Dr. Delgado wrote for a 9-tome encyclopedia on bullfighting published in Spain and only available through rare booksellers.

Reading the manuscript (see Supplemental Material) was illuminating, but some exposition is necessary before we dive into the experimental results and summarize what Dr. Delgado observed.

José Manuel Rodríguez Delgado was a Spanish-born, medically trained scientist who worked at Yale University. He is often considered the "proto" neural engineer due to his expertise in building custom microelectronics that interfaced with the nervous system. Quite remarkable for the time, and remarkable even today given how little wireless neural interfaces have advanced, Dr. Delgado did experiments on colonies of brain-implanted cats, rhesus monkeys, gibbons, chimpanzees, and bulls. He explored the neural roots of aggression, pain, passivity, and social behavior. His wide-ranging experiments are discussed in his numerous publications (over 500 published scientific articles and five books) and notably in his book "Physical Control of the Mind" (1970). This book is famous for a highly speculative final chapter discussing how electrical brain stimulation could be used to enable a peaceful, harmonious society and temper human behavioral and mental problems.

While grandiose sounding, this is not as strange as it seems. It is called "Electroceuticals" today or "Electrical Microstimulation," the most famous of which has been deep brain stimulation for Parkinson's disease and cochlear implants for treating types of deafness. Brain stimulation is now increasingly used in clinical experiments for treating depression and other disorders (DeLong and Wichmann, 2012).

Dr. Delgado's experiments on brain control in bulls can appear eccentric to contemporary students, but we should view these investigations in the context of early 20th century history. Dr. Delgado was born in 1915 in Ronda, Andalucía, Spain, and lived through the Spanish Civil War when he was 21-24 years old. He supported the losing side, the Republicans, and spent time in a Franco prison camp (Blackwell, 2012). The devastation of the events in Europe in the 1930s and 1940s, the Spanish Civil War, World War II, and the Holocaust led to obvious soul-searching in the psychology and sociology fields. How are humans capable of such terror and destruction towards their fellow beings?

After World War II, many psychologists, neuroscientists, sociologists, and funding sources in the United States and Europe began investigating the roots of violence, aggression, and group psychology when following orders. The two most famous of these investigations into the human psyche are Stanley Milgram's "Electric Shock Experiment" at Yale in 1961 (Milgram, 1965) and Philip Zimbardo's "Stanford Prison Experiment" in 1971 (Haney et al., 1973). Included as part of this zeitgeist are Dr. Delgado's experiments on the neural circuits of aggression culminating in his 1964 experiments with bulls and his 1970 book.

Under this historical context we can better understand Dr. Delgado's motivations. In the opening of the 1981 article, Dr. Delgado states that whereas most bulls are bred to be docile with large, supple muscles for meat production, Spanish "toros" have been bred to be athletic (agile, fast, and strong) and, importantly, aggressive. Since Dr. Delgado was interested in the neural correlates of aggression, the Spanish toro made a unique (Dr. Delgado would say ideal) preparation.

Upon reading Dr. Delgado's manuscript, one is struck by a peculiar mix of Techno-Rural-Classical Spanish culture, as if the experiments were conjured up more by a steampunk novelist rather than real investigations done by a talented scientist. We picture Dr. Delgado as a type of international technically brilliant investigator who spent much of his scientific life in the USA designing advanced neural electronics and doing controversial, influential experiments. However, as the article reveals, he is also a Spaniard from rural Andalucía, a land with a rich tradition in bull-fighting, lyricism (Garcia Lorca, Flamenco), the Islamic past (Al-Andalus and the Umayyad Caliphate), ranches of rolling yellow hills of encina trees, and for also unfortunately being on the losing side of the Spanish Civil War (the Málaga–Almería road massacre occurred near Dr. Delgado's hometown).

Summary of Article and Experiments

Note: All quotes made by Dr. Delgado (apart from "Physical Control of the Mind," written in English) are my translations of his Spanish text.

The bull experiments were done in 1964 in Córdoba, Spain on the ranch La Alamirilla owned by Don Ramón Sánchez whom Dr. Delgado heartily thanks in the text for allowing the experiments to occur on his hacienda. Figure 2 depicts the ranch hands present that day preparing the bull for the surgery while Don Ramón observes.

Dr. Delgado unfortunately does not state exactly how many bulls were involved in these experiments, but in his 1981 article he focuses his attention on the results of two bulls he implanted; one named "Cayetano" and another named "Lucero." Both bulls were approximately 3 years old and weighed 200-280 kg.

Approaching toros is highly hazardous even for trained bullfighters. To anesthetize the bulls, they were shot with a compressed air tranquilizer gun containing a syringe of Sernylan (also known as PCP or its street name - angel dust). This drug is an NMDA receptor antagonist and was a commonly used anesthetic for animal surgeries until ketamine, another NMDA receptor antagonist, was developed. Both anesthetics have dissociative hallucinogenic properties that can lead to abuse in humans (Lodge and Mercier, 2015). About 15 minutes after injection, a bull becomes sedated enough to approach, shown in a picture of two well-dressed people conversing near a bull who is sinking into a more profound anesthetic state (Figure 3).

Figure 2. Ranch hands prepare the bull for the surgery while ranch owner Don Ramón Sánchez (hand on hip) interacts with famous bullfighter El Cordobés (man in white jacket).

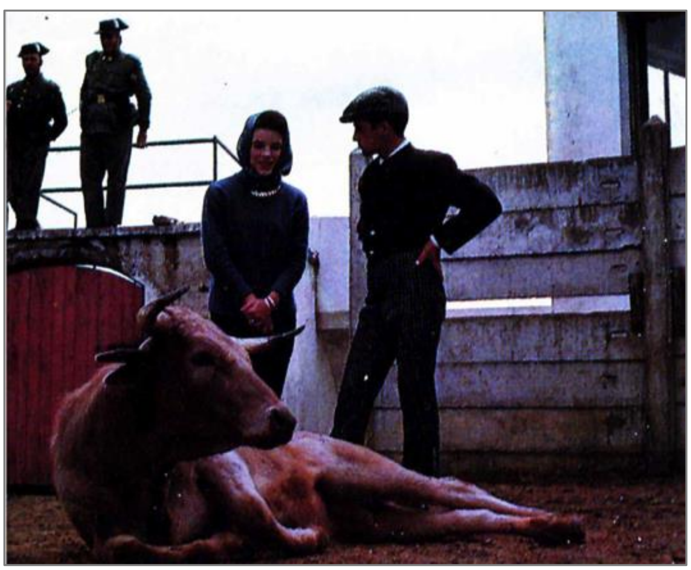

Figure 3. A bull entering anesthesia.

Once the animal was sufficiently anesthetized, Dr. Delgado and the ranch hands exposed the cranium and made a 2 cm diameter craniotomy (opening in skull) with a hand-trepanning tool in each hemisphere over the frontal bone. After exposing the brain, and with the bull´s head in a stereotaxic device (Fig. 4), the electrodes were inserted.

Figure 4. Head of a bull in the stereotaxic device.

The electrodes were 0.1 mm stainless steel wires insulated to the tip, collected in a seven-electrode bundle with each electrode separated by 5 mm in depth. Thus, each electrode bundle had a span of 7 locations across 30 mm allowing access to the primary motor cortex, caudate nucleus of the basal ganglia, and the optic thalamus. One to two such electrode bundles were placed in each craniotomy, such that each animal had 14-28 total electrodes inserted. This is technically impressive for the epoch. In my graduate work during the 2000s in the University of Michigan Neural Engineering Lab, microelectrode arrays of 16-32 sites were common in normal experiments (Marzullo et al., 2010). Advanced electrode arrays of 100-512 sites were becoming available but required complex custom hardware and software to use (Berényi et al., 2014). Equally impressive at the time of these experiments is that there was no published bull brain atlas. The awake freely-moving bovine electrophysiology preparation was (and continues to be) highly novel.

The electrodes were maintained in the bone with dental cement (as is common practice today in research labs), the skin sutured back around the cement, and wire connectors were attached to bandages around the horns. Figure 5 shows the attachment points for the electronics. Note the excessive salivation; normally animals now are given atropine, a parasympathetic antagonist, to counter this during surgery. The red spots on the horns are not wound bleeding but rather interface points that just happen to be red. How the wireless electronic stimulator circuit actually works and mounts on the bull's head is not explicitly stated other than being "*small and complicated*" and "*under a bandage*."

The stimulation trials began after a few days. To electrically stimulate the various anatomical points in the brain, Dr. Delgado used a radio transmitter he had invented in which the transmission channel, electrical stimulation pulse frequency, and electrical stimulation amplitude could be controlled. The hand-held radio transmitter had dimensions of 14x6x6 cm, and he could send electrical impulses ranging from 20-100 times per second (Hz) and up to 1-20 V (0.1-1 mA of current in the brain). Unfortunately, more details on the design of the transmission circuit the experimenter controlled and the receiving circuit on the bull are lacking. It is unclear whether the experimenter had access to all 14-28 electrodes at the same time or whether the receiver had to be "plugged-in" manually to different electrode array locations (a hazardous endeavor considering the animal involved).

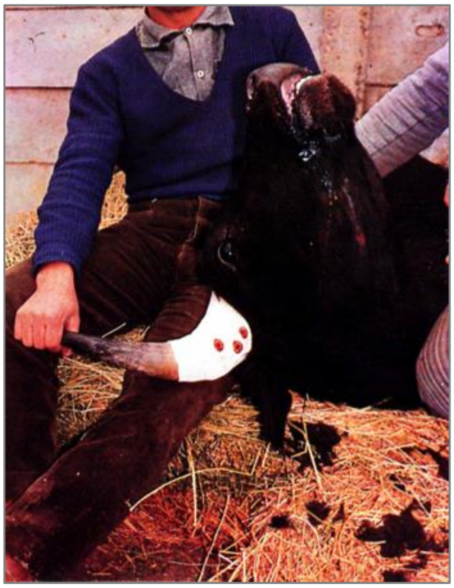

Figure 5. Animal post-surgery in recovery. Attachment points for the brain stimulation electronics are the three red plugs in the bandage on the horn.

Dr. Delgado writes in vivid and highly lyrical Spanish of the experience of doing neurosurgery on the ranch, acknowledging the oddity of it all.

"The ambience, of course, was not completely orthodox, given that we were operating in a bucolic, romantic science environment below the Andalusian sky accompanied with cowboys and foremen, moreover with songs of birds and distant mooing."

A number of pages of the 1981 manuscript are devoted to the first-discussed bull "Cayetano," in which Dr. Delgado set the stimulation frequency to 100 Hz, duration to 10-15 seconds (by manually pressing the button down for such length of time), and increasing the stimulation amplitude from 0.1 mA to 1 mA in the left caudate nucleus location. At 0.1 mA, there was no effect on the animal. At 0.5 mA, the animal moved its head to the left and then maintained it in the leftward position for the duration of the stimulation (Fig. 6**)**. At 0.7 mA, the animal moved its head to the left and spun in a complete circle. Dr. Delgado notes that the bull did not "*moo, flee, nor show signals of agitation*" in response to the stimulation, suggesting that the electrical stimulation was not hurting the animal. Dr. Delgado also states that given the caudate's proximity to limbic structures, stimulation might even cause the contrary effect where the animal may experience "*not pain but pleasure.*" Dr. Delgado is referring to monkey and rat medial forebrain bundle experiments where an animal will voluntarily hit a lever to electrically stimulate this part of the brain (Olds and Milner, 1954).

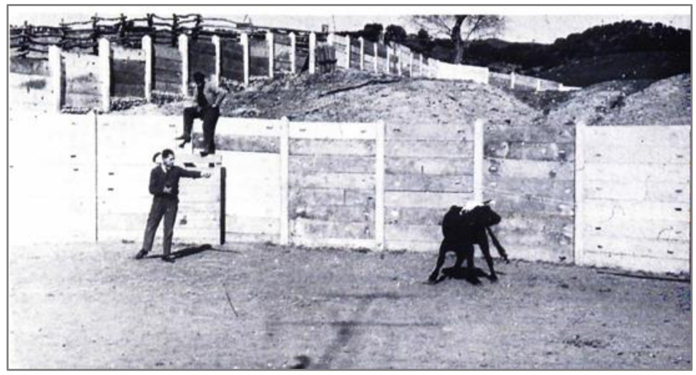

Figure 6. The bull Cayetano showing its left head turn upon stimulation of the left caudate nucleus.

At 0.9 mA stimulation, the animal continued to turn in circles but at a higher velocity. During this stimulation, the animal appeared "*surprised in its own conduct, but not irritated*" and would explore another area of the arena when the stimulation ended. When the stimulation was applied to the caudate location on the right side of the brain, similar behavior was observed, but the bull turned in the opposite direction- to the right. Dr. Delgado remarks that the investigators could then predict left versus right circular movement depending on which caudate side they stimulated.

Dr. Delgado then leaves Cayetano and returns to discussing the neural roots of aggression and passivity in the brain, explaining attempts to make docile bulls more aggressive. This was based on his previous experiments (summarized in Physical Control of the Mind) on aggression in cats. Passive, tame house cats would show "*false rage*" during stimulation of the anterior hypothalamus (that is, showing aggressive facial expressions, but not attacking other animals, and showing submissive behavior when cagemates responded to the false aggression with an attack). On the contrary, stimulation of the lateral hypothalamus caused "*true rage*" with cats manifesting attack behavior towards their cagemates during the stimulation (pages 123-133; Delgado, 1970) (Fig. 7). Dr.

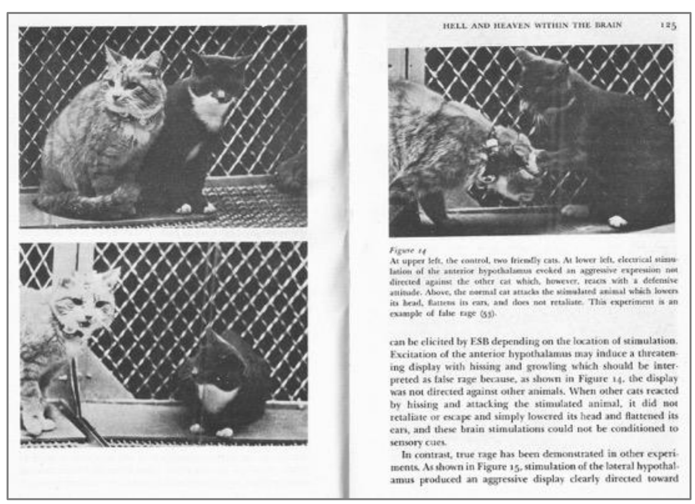

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Figure 14
At upper left, the control, two friendly cats. At lower left, electrical stimulation of the anterior hypothalamus evoked an aggressive expression not directed against the other cat which, however, reacts with a defensive attitude. Above, the normal cat attacks the stimulated animal which lowers its head, flattens its ears, and does not retaliate. This experiment is an example of false rage (53).

can be elicited by ESB depending on the location of stimulation. Excitation of the anterior hypothalamus may induce a threatening display with hissing and growling which should be interpreted as false rage because, as shown in Figure 14, the display was not directed against other animals. When other cats reacted by hissing and attacking the stimulated animal, it did not retaliate or escape and simply lowered its head and flattened its ears, and these brain stimulations could not be conditioned to sensory cues.

In contrast, true rage has been demonstrated in other experiments. As shown in Figure 15, stimulation of the lateral hypothalamus produced an aggressive display clearly directed toward

Figure 7. Excerpt from pages 124-125 of "Physical Control of the Mind" discussing the cat thalamic stimulation experiments.

Delgado also studied similar effects in rhesus monkey colonies, observing that stimulation of the periaqueductal grey (in the midbrain) increased aggression but that stimulation of the septum and caudate increased passivity.

Dr. Delgado in his 1981 Spanish manuscript discusses trying to replicate these experiments in docile bulls, attempting to make them more aggressive by stimulating thalamic structures. Beyond noticing motor responses (distinct body movements in response to the stimulation), he did not observe increases in aggression. He hypothesized that the electrodes may have been incorrectly placed.

Again, this experiment seems bizarre today, but it was part of the cultural-historical context of over 50 years ago of investigating destructive behavior in social groups. Indeed, in 1972, Michael Crichton, a science fiction author who was attentive to novel biomedical engineering research and the ethical issues therein, wrote "The Terminal Man," in which the central plot twist was brain stimulation in the main character Harry Bensen for treating his form of epilepsy that caused aggressive behavior (Crichton, 1972).

Dr. Delgado then focused in his 1981 manuscript on a second bull named "Lucero," which is the one always shown in the famous photos (Fig. 1), as this was perhaps the most dramatic result of the bull brain stimulations. Lucero continued demonstrating robust charging behavior after the surgery, allowing for full investigation of Dr. Delgado's ideas about aggression and brain circuits. When he stimulated at 100 Hz and 1 mA in the caudate and thalamus locations when the bull was charging a bullfighter, the bull immediately stopped and was still during the stimulation, although blinking its eyes and breathing regularly (Fig. 8). Since no obvious motor effect was observed as in the first bull Cayetano (turning of the head, moving in a circle, etc.), Lucero had the most compelling response- the halt of the charge. We can see and analyze Lucero's response during some brief video footage on a PBS documentary available online (Hunter, 1984).

Although the animal's attack was halted by the stimulation, "*detained in his aggressiveness,*" the bull returned "*furiously*" to a full charge when the electrical stimulation ceased. This appears to be the best result of the bull implantations and the reason why the experiments are still remembered and discussed today. Most of Dr. Delgado's 1981 text on Lucero (3 of 5 paragraphs) deals with his personal experience in the ring stopping the bull in mid-charge (Figs. 1 and 9), provocatively written in his Andalucían culture-infused Spanish.

"My personal ability with the cape had been tested sometimes in the rural festivals of my youth and is limited, but an investigator must accept the responsibility of his own methodology and for this I felt obligated to confront the experimental animal, perhaps driven by the memory of my birthplace, Ronda, with a long taurine history and tradition…. With the cape in my right hand and the radio transmitter in the left, I met with the bull "Lucero," trying to keep my blood cool, although my heart beat with greater violence than I desired. In the arena and in front of the bull, the novice's impression is exciting enough. The size of the bull and its horns appear to grow, one perceives its smell, one hears its snorts, and one becomes conscious of its power."

When Lucero was charging Dr. Delgado and had reached within 2 or 3 meters of him, Dr. Delgado would turn on the stimulation, and the animal would "*stop violently*," causing a "*cloud of dust with his legs halting suddenly, his tail lowering, his head raising*" and maintaining a state of *"disappeared aggressiveness."* Dr. Delgado would then back away, seek shelter behind a wooden barrier in the ring, turn off the stimulation, and the bull would immediately charge again and ram the barrier. Dr. Delgado closes the description of his experience with Lucero mentioning a momentary error in the electronics:

"As an anecdote I can tell you that one time there was a failure in the transmission circuit, and the bull managed to reach me, fortunately without more consequence than a good scare."

Dr. Delgado does not state how many bulls were tested, but summarizes his experiments by stating that stimulation amplitudes of 0.8 mA (and one assumes 100 Hz) in the anterior thalamus and the caudate nucleus would cause a "*general inhibitory response.*" If the animal was eating, it would stop chewing. If the animal was walking, it

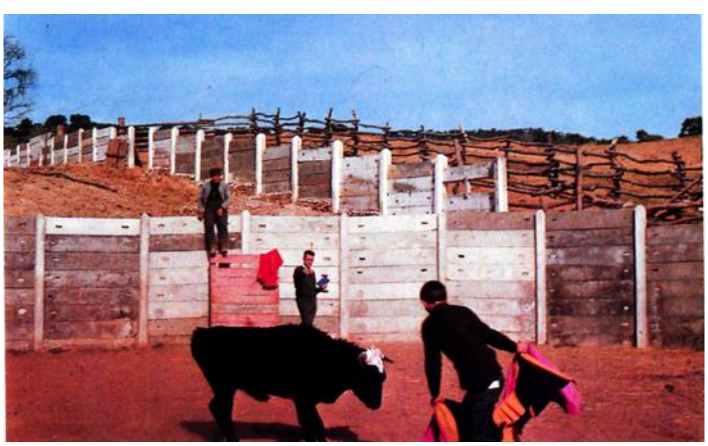

Figure 8. Lucero being halted in its charge to a bullfighter with thalamic or caudate stimulation.

Figure 9. Dr. Delgado himself personally testing his neural electronics interface on stopping Lucero's charging behavior via stimulation of the caudate or thalamus.

would detain. Though not in the article (Delgado, 1981), but included in "Physical Control of the Mind" (1970), Dr. Delgado notes in the one of the two paragraphs in the book discussing the bulls:

"Upon repeated stimulation, these animals were rendered less dangerous than usual, and for a period of several minutes would tolerate the presence of investigators in the ring without launching any attack."

Dr. Delgado spends the last pages of the 1981 manuscript remarking on the press caused in the Spanish bullfighting world as well as the international attention brought on by the New York Times front-page article. He notes purists of the sport accused him of "*placing a bomb at the fundamental pillars of bullfighting,"* the idea that bulls could be secretly implanted with such electronics by bullfighters attempting to gain a competitive edge. Dr. Delgado's enumeration of reasons why this is not feasible gives a glimpse into the limitations of the experiment.

1) It is too difficult and requires too many experts to implant the bull with the custom electronics.
2) It would be impossible to hide the fact that the animal had been implanted due to the electronics on its head.
3) Critically, the effectiveness of the stimulation varies from bull to bull.

Scientific Legacy of Dr. Delgado's Bull Experiments

Upon carefully reading the 1981 Spanish manuscript and finally having more extensive details, one reasons that the caudate and thalamic nuclei, being important in motor planning and pathways, would cause a change in motor behavior upon electrical stimulation and not necessarily reduce aggression. As all behavioral neurophysiologists know and struggle with, isolating cognitive intent and observed motor output is experimentally tricky. How does one separate out the effect of motor inhibition versus reduced aggression? For example, you intend to throw a punch at an unfortunate soul, you begin this action, and someone stimulates a motor circuit in your brain inhibiting this motor plan. Has your aggression been reduced or has simply the manifestation of that aggression, the punch, merely been stopped?

This is a tough but not insurmountable methodological problem, as one could measure other signals of aggression such as blood pressure, skin sweating (galvanic response), heart rate, eye dilation, etc., to provide more support for a reduced aggressiveness rather than simply an inhibited motor plan. It is acknowledged though that all these other physiology recordings would be rather tough in a freely moving very active and healthy bull using 60s (and even modern) technology. However, Dr. Delgado would certainly appreciate such experiments on aggression being born again using optogenetic technology in rodent models (Han et al., 2017).

Though indeed the caudate nucleus is part of both motor and limbic (emotional) circuits and Dr. Delgado could be affecting aggression, the interpretation of reduced aggression is limited. This is due to the above methodological problems, scarce published details (unexpected given Dr. Delgado's prolific publication history from the 1950s-2000s), and the lack of experimental information such as:

1) Quantification (behavioral scoring) of stimulation effects on bulls implanted
2) Data tables and summaries showing numbers of bulls implanted and discussion of variability
3) Schematics for both the transmitter and receiver circuits, and characterization of input/output functions
4) *Post mortem* examination of electrode locations. It does not appear that the brains of the bulls were examined histologically. Given that no bovine brain atlas existed at the time of this experiment, showing histological electrode location would have been valuable and unique data. Perhaps logistical issues of obtaining the brains at a later date from the ranch prevented this, as Dr. Delgado includes histology in many of his earlier published experiments (Delgado, 1952).

We thus leave this experiment rather close to where we began with it: a rather nebulous and ambitious demonstration of expertise in neuroanatomy and neural interface construction. While there is no doubt electrical stimulation of structures in the brain caused an effect on the motor behavior of the bulls, stating a reduction of aggressiveness is rather over-arching. One is left with the impression that the results were highly variable (which Dr. Delgado above confirms in his comments on relation to bullfighting politics).

One cannot, however, criticize Dr. Delgado for his lack of vision about the importance of brain neuroanatomical mapping and understanding how brain circuits function, which is why we continue to discuss his experiments today. In the closing passage of Dr. Delgado's 1981 article, filled with passion, you can see his desire to use this technology for benefit.

"The radio stimulated bulls underscore the classic symbolism of the bullfight, that is -- the triumph of intelligence over brute force, the supremacy of skill and grace over aggression and ferocity. The radio directed bulls also teach us that ancestral instincts of attack and destruction can be pacified by technology and human intelligence, giving a hope of peace that perhaps could benefit future humanity."

Dr. Delgado's active research dwindled in the late 1970s and 1980s while he helped found and teach at a medical school in Madrid, though he continued inventing, building a wireless human transcranial magnetic stimulator prototype (Horgan, 2005). He retired in the 1990s, living out his final years in San Diego, California, passing away in 2011 at 96 years of age. Dr. Delgado remains admired for being a pioneer in neural interface design and investigating difficult topics in social cohesion in controversial preparations of monkeys, cats, and, of course, bulls. His neural interfaces were 30 years ahead of his time, developing techniques that are still in active investigation and used today to treat human affictions such as motor disorders, deafness, and depression. Neural engineers of the world continue the mission to build tools to improve our knowledge of brain function in all its diverse and curious roles.

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Acknowledgements

Una gracias gigante (large thank you) goes to Professor Scott Currie of the University of California at Riverside for providing his personal correspondence with Dr. Delgado from 1999 which included the 'lost manuscript' and for critically reading versions of this article. Dr. Currie also agreed to have his letter from Dr. Delgado reproduced that appears at the end of the Supplementary Material file. Muchos agredecimientos (many acknowledgements) as well goes to the Delgado estate, specifically Dr. Delgado's son José Carlos Delgado, for reviewing this article and providing permission to reprint the photos and the 1981 article of the famous experiments (copy provided by Dr. Currie). Final thanks goes to the staff at Editorial Planeta (Toros RadioDirigidos) and Harper-Collins (Physical Control of the Mind) for assisting with permissions and reproductions of works cited here.

Disclosure

Author TM is co-owner of the company "Backyard Brains" that develops and sells neural stimulation and recording equipment for use by universities, high schools, and the general public.

Received October 01, 2016; revised March 26, 2017; accepted April 07, 2017.

This work was supported in part by the Spanish Television Program "El Hormiguero" that graciously invited the author to Madrid for various science outreach events, causing the chain of occurrences that led to receiving Dr. Delgado's rare manuscript as well as the opportunity to explore Andalucía.

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