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Why EdgeScience? Because, contrary to public perception, scientific knowledge is still full of unknowns. What remains to be discovered —what we don't know — very likely dwarfs what we do know. And what we think we know may not be entirely correct or fully understood. Anomalies, which researchers tend to sweep under the rug, should be actively pursued as clues to potential breakthroughs and new directions in science.

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The Society for Scientific Exploration (SSE) is a professional organization of scientists and scholars who study unusual and unexplained phenomena. The primary goal of the Society is to provide a professional forum for presentations, criticism, and debate concerning topics which are for various reasons ignored or studied inadequately within mainstream science. A secondary goal is to promote improved understanding of those factors that unnecessarily limit the scope of scientific inquiry, such as sociological constraints, restrictive world views, hidden theoretical assumptions. and the temptation to convert prevailing theory into prevailing dogma. Topics under investigation cover a wide spectrum. At one end are apparent anomalies in well established disciplines. At the other, we find paradoxical phenomena that belong to no established discipline and therefore may offer the greatest potential for scientific advance and the expansion of human knowledge. The SSE was founded in 1982 and has approximately 800 members in 45 countries worldwide. The Society also publishes the peer-reviewed Journal of Scientific Exploration, and holds annual meetings in the U.S. and biennial meetings in Europe. Associate and student memberships are available to the public. To join the Society, or for more information, visit the website at scientificexploration.org.

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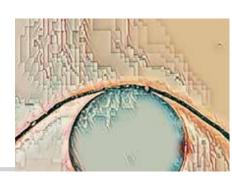
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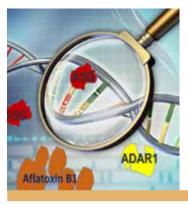


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Cover: A composite image of a captured Saddam Hussein and a remote viewer's drawing of the compound where he was captured.

### THE OBSERVATORY

**Manuel Matas** 

# It's Perfectly Normal

# I refuse to commit the fashionable stupidity of regarding everything I cannot explain as a fraud. —Carl Jung

have been a clinical psychiatrist for 40 years. For most of my professional career I worked in university teaching hospitals. I published peer-reviewed articles in psychiatric journals and presented papers at national psychiatric conferences. I was seen as a fairly traditional, medical-model psychiatrist.

My primary concern throughout my psychiatric career was always to provide the best possible care for my patients and the best possible education for my students. I was not a proponent of talking about spirituality in psychiatry, with patients or with students, although I was always open to discussion. Throughout my life, however, I have had many experiences that could be called strange, weird, unusual, extraordinary, paranormal, anomalous, psychic, spiritual, mystical, or mysterious, depending on your point of view.

These experiences were all completely spontaneous, neither planned nor desired. One time I saw an apparition in my bedroom. Another time I left my body and found myself floating on my bedroom ceiling. When I was a second-year medical student, I dreamt the Respirology exam the night before the exam. Many years later, I saw the angels at my father's funeral.

I have almost died many times. Although I have not had a typical near-death experience, I can say, in all humility, that I have had glimpses into the world beyond space and time. Without even trying, I saw, heard, and felt things that lit up my mind. I did not go looking for Spirit. Spirit came calling for me.

These events inspired a quest in me and set me on a spiritual path. I could not ignore the strange and mysterious things that were happening to me. I wanted to know what was causing them. Every once in a while something startling happens to us which shakes us up and wakes us up from our nine-to-five, humdrum, routine existence. As we live our lives, we often suspect there must be more to this life than meets the eye. We are not wrong. My quest confirmed my suspicion.

### Other Worlds

It is a fact that we have the ability to contemplate other worlds which co-exist and overlap in time and space with our own physical plane of existence. We know that mental, emotional, and spiritual realms are out there, but most of us don't usually think about them as we go about our busy lives. We are aware of the world of ideas, the world of emotions, and the world of spirit. How many other worlds are out there?

There are many paradigms describing the various levels, dimensions, or planes of existence that surround us. To name a few: the astral, causal, and etheric planes; personal consciousness, the personal unconscious, and the collective unconscious; the intermediate state between this world and the next world, which precedes life and follows death, known as Bardo in Indian and Tibetan Buddhism; the four worlds or spiritual realms of Kabbalah, which in descending order are: Atzilut (Emanation), Beriah (Creation), Yetzirah (Formation), and Asiyah (Action); the seven heavens through which the Prophet Muhammad ascended; and the nine circles of Hell in Dante's Inferno.

Just outside conscious awareness, many of us have had a sense of other worlds which, from time to time, intrude and make their presence known. There is often a conspiracy of silence that discourages a frank and open discussion of these ideas, which are often dismissed out of hand. It is well past time to draw back the veil of silence that surrounds these other worlds.

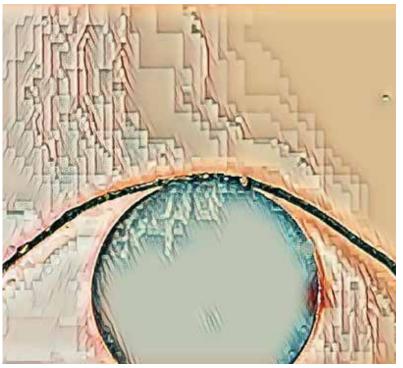
Paranormal and psychic experiences are not necessarily spiritual or supernatural in origin. They may be interpreted in many ways. Atheists, agnostics, and believers all experience paranormal, psychic, spiritual, and mystical phenomena, which



Manuel Matas

may arrive bidden or unbidden. These experiences can occur once in a lifetime or repeatedly. Even if such an occurrence happens only once, it can have a life-long impact.

For some, words like "psychic" or "paranormal" are fraught with negative baggage engendered by an assortment of fakes, frauds, and charlatans. Still, what people today call "paranormal" is actually quite normal, and being psychic or sensitive or intuitive is simply another way of being in the world.



Manuel Matas

### Meta-Psychiatry

My new book, *The Borders of Normal*, deals with the field of study known as meta-psychiatry (literally: "beyond psychiatry"). Meta-psychiatry represents the confluence of psychiatry with spirituality and metaphysics, which is the philosophy of being and knowing.

Just as there are various schools of psychiatry, there are also different schools of meta-psychiatry. I see meta-psychiatry as a field of study that does not conform to any particular religious dogma, ritual, or belief. Stanley R. Dean, clinical professor of psychiatry at the University of Florida and editor of *Psychiatry and Mysticism* (1975), used the word meta-psychiatry to describe the branch of psychiatry that studies psychic phenomena. He saw meta-psychiatry as the base of a pyramid whose other sides were psychiatry, parapsychology, philosophy, and mysticism. Meta-psychiatry includes elements of both transcendental and transpersonal psychology as it involves the study of our need for transcendence and also explores the meaning of experience beyond the personal.

Transcendental psychology is the field of study that deals with self-knowledge and self-actualization. In Abraham

Maslow's hierarchy of universal human needs, our need for transcendence is crucial. It is universal, found at all times, in all cultures. Transcendental psychology has its roots in transcendentalism, an American 19th-century philosophical movement whose major writers included Henry David Thoreau, Ralph Waldo Emerson, Emily Dickinson, and Walt Whitman. These writers believed that we acquire knowledge not just through our five senses, but also through our sixth sense, intuition. They combined contemplation of nature with direct knowledge of the world of spirit and were skeptical of established religions. They thought a church hierarchy was unnecessary as each individual has the capacity to attune to the divine within.

Transpersonal psychology is the branch of psychology that explores the nature of experience beyond the personal, extending outward towards the world, the cosmos, and all of humanity. It studies mystical experiences, trance states, peak experiences, and cosmic consciousness.

I have always been more drawn to the joy and beauty of life than to the mundane world of weights and measures. The idea that there is more to this life than meets the eye is not just idle speculation. It is a longing, an outcome fervently to be desired. Until recently, I kept my personal experiences mostly to myself; however, after surviving a life-threatening illness, leukemia; after a successful stem cell transplant from an anonymous donor; and after seeing the angels at my father's funeral, I decided to go public and share my experiences, in order to fight the stigma surrounding paranormal phenomena that is so prevalent in our society. I wanted people to know that it's OK to have these experiences and it's OK to talk about them. It's perfectly normal. There is no reason to feel embarrassed or ashamed. Nor is there any reason to feel proud or special. All in all, it's simply part of life.

Excepted with permission from *The Borders of Normal: A Clinical Psychiatrist de-Stigmatizes Paranormal Phenomena* by Manuel Matas, published by Friesen Press.

MANUEL MATAS, M.D., obtained his Medical Degree from the University of Manitoba and his Diploma in Psychiatry from McGill University. He has worked in a variety of settings, including the Scarborough Board of Education, the University of Toronto and the University of Manitoba teaching hospitals, and more recently, in private practice. He has served on the Board



and the Scientific Council of the Canadian Psychiatric Association, as well as the Boards of Physicians for Social Responsibility, Psychiatrists Against Psychiatric Abuse, the Manitoba Satir Institute, and the Learning Institute for Growth, Healing, and Transformation.

### Stephan A. Schwartz

# Finding Saddam Hussein: A Study in Applied Remote Viewing

On April 9, 2003, shortly after the American invasion of Iraq, Saddam Hussein, who had been president of that nation from July 16, 1979, was deposed and went into hiding. For the next several months, in spite of one of the most intense manhunts in history, his whereabouts remained unknown.

On November 3, 2003, an applied remote viewing experiment was carried out with the explicit purpose of locating and describing the circumstances and conditions of Saddam Hussein whereabouts. The experiment took place at the Edgar Cayce organization headquarters in Virginia Beach. I was teaching a workshop on remote viewing as part of a larger conference I had organized with almost all the founders of remote viewing including Russell Targ, Harold Puthoff, Ingo Swann, James Spottiswoode, Paul Smith, Skip Atwater, Dale Graff, as well as Edgar Evans Cayce, youngest son of Edgar Cayce, the most carefully documented remote viewer in history, and psychologist Henry Reed. It was a unique conference never again duplicated, and it attracted a large audience of some 500 people, including, as it turned out, a number of individuals from the military and intelligence world. Virginia Beach is relatively proximate to Washington, D.C. and Langley, Virginia, where the CIA is located.

At the end of the conference I put on a two-and-a-half-day workshop on remote viewing and 64 people self-selected to attend, both men and woman. They ranged in age from early 20s to early 70s. A number of them self-identified as active members of the military-intelligence community. They had heard about remote viewing and were, they said, very interested in understanding how it worked and actually experiencing a remote viewing session.

During the course of the first two morning sessions, after describing the process of remote viewing in some detail, I took the workshop participants through several triple-blind precognitive remote viewing sessions, asking them to describe a target image they would later be shown. There had been, as there usually is, considerable success. This constituted the training of the viewers.

At the midday break, a group of individuals, including three whom I knew to be involved with the military-intelligence community, came up to me and asked, "Can we do something real, something that has a real-world application, not just another target?"

During lunch I thought about how I could fulfill their request. I picked up a newspaper, and one of the above-the-fold stories was on the search, at that point fruitless, to find Saddam Hussein. I thought about that. Here was a highly numinous

target, one that was truly blind and that surely would have some kind of public ending. Millions of dollars were being spent to find Saddam Hussein with no success so far. It was a classic remote viewing challenge.

When the workshop group gathered again, I asked them, "Would you like to find Saddam Hussein?" and received a very positive response. So using the standard Mobius Consensus protocol<sup>1–14</sup> I have been using for decades to locate archaeological sites and solve crimes, I asked again, "How many would like to participate as viewers?" Forty-seven men and women chose to participate.

The experiment was double blind, that is neither the viewers, I, nor anyone in American government or armed forces, knew the answer; only Saddam Hussein himself and possibly some group of followers knew where he was.

In essence, when all of the geopolitical and media aspects are stripped away, the experiment was just a standard precognitive outbound protocol experiment, essentially the same as the hundreds of experiments Mobius and SRI carried out over three decades. <sup>15,16</sup>

### **Experimenter Bias and Instructions**

For over half a century there has been evidence in studies that nonlocal perception task performance can be influenced by the beliefs and expectations of the researcher. <sup>17,18,19,20,21</sup> For that reason I feel it is appropriate to say a word here about my own quite strong bias going into this experiment.

Saddam Hussein was a man noted for his fastidious personal hygiene. He had lived the sybaritic life of an autocrat for decades, and he had unlimited money. I assumed he would do what the violent dictator Idi Amin, President of Uganda from 1971 to 1979, had done. Amin's exit hatch was a compliant Saudi government that let him set up a quiet but luxurious life in Jeddeh, Saudi Arabia. And that is where he remained untouched and unpunished until his death of kidney failure in the King Faisal Specialist Hospital and Research Centre in Jeddah, on August 16, 2003. Why, I thought, would Saddam Hussein not do the same? I assumed he would eventually be found somewhere in Saudi Arabia in a similar situation. I said nothing about this to the viewers, but that was my experimenter bias.

The task instruction for the remote viewing session was: "Please describe the location and circumstances of Saddam Hussein at the time his location becomes known to American forces. Please describe his appearance, his mind set, and any

other relevant details that come to mind." For the next 20 minutes I would augment this by sayings things like, "Saddam Hussein is standing before you. Look at him in your mind's eye. Make a drawing. Write down the details of his clothing."

The individual remote viewers each independently recorded their impressions in answer to the stated task and my subsequent questions in accordance with the process they had been taught. At the end of the session, this session data documentation was turned in to me. It was photocopied, and the originals were put aside for later notarization and archiving.

There were not, as would usually be the case, audio records of the sessions. The written words and drawings each viewer had created constituted the record of the remote viewing data produced by the 47 viewers.

Projects like this are different than archaeology projects, and are more akin to Mobius' criminal and SRI's spy work. In an archaeology project, each concept can be painstakingly evaluated, a process that can take months, even years. In a military crisis or criminal situation like the Saddam Hussein search, one knows going in that almost certainly it will never be possible to assess the accuracy of each concept, as one can do in an archaeology experiment. The strategy in a situation such as this one is to define the task to a narrow parameter. What task is being attempted? In this case, the task was to locate Saddam Hussein, to give military troops a kind of Google map they could follow that would lead them to him, and that would also tell them what to expect when they got there, as well as what he would be like. To achieve that, a great deal of data of necessity was discarded, and just two things were considered:

- 1 Points of consensus concerning the physical location and its description;
- **2** What are called low *a priori* observations (things which are very unlikely to be predictable, such as specifics about Hussein's appearance on the day of his capture).

Additionally, because a number of viewers brought it up, I also assembled from their session data a sense of his state of mind at the time of his capture, although validating it seemed very improbable to me at the time. This analysis was then transformed into a series of hypotheses with which to guide subsequent fieldwork by a search team. That said, this was the analysis.

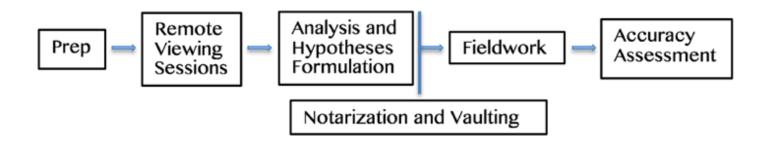
### **Hypotheses**

Seven consensual hypotheses emerged from my analysis of the data. The text in quotes is taken from the session records of the viewer participants as examples of how the consensus emerged:

- 1) LOCATION: Saddam will be found "beneath an ordinary looking house." "It is on the outskirts of a small village," "near Tikrit." "The house is part of a small compound." It is "bordered on one front by a dirt road and, on the backside, by a nearby river." "The house can be identified because it has a large tree growing at either end, and it has a strange kind of partial second floor over the front door."
- 2) SADDAM HUSSEIN HIDING PLACE: "Saddam Hussein has a hiding place." "It is like a cavern or a 'carved out space." It is "not visible but hidden underneath something." "Breathing is possible in this small hidden space because there's a vent tube built into this buried hiding space."
- **3) SADDAM HUSSEIN APPEARANCE:** "Saddam won't look anything like he normally does." "He looks like a homeless person." He will be "dressed in dark clothing." He will have a "ratty," "unkempt" "salt and pepper beard." His hair will be "wild." In general, his "appearance will be disheveled."
- **4) SUPPORTERS:** At the time of his capture Saddam Hussein will have only "two or three supporters with him at the time of his discovery."
- **5) FIREARMS:** Saddam would have a gun, "but would put up no resistance when captured."
- **6) MONEY:** He would "have a quantity of money with him."
- 7) **SADDAM HUSSEIN ATTITUDE:** "He will be defiant but will not put up any resistance; in fact he will be tired, and dispirited."

### **Unimpeachable Chronology**

From a research perspective the key to an experiment like this is that it must have an unimpeachable chronology. The sequence of events has to be absolutely clear and documented for any assessment of nonlocally derived information to be achieved. The chronology is established in this way.



Pursuant to the protocol, the following morning, the originals of all the session documentation, as well as the hypotheses derived from an analysis of the session data, were put into two envelopes and turned over to the Cayce Foundation archivist. The archivist sealed the envelopes, signed across the flap, put her notary stamp on the envelopes, and put them in the Foundation's archives under her control.



The Cayce Foundation Archive Vault



Envelopes containing original material. Note Notary seal and signature across flap.

In the workshop's final session, to give the viewers some minimal feedback, I outlined for them the operational hypotheses that had arisen from the consensus protocol analysis. I explained that if this were an archaeological project the next step would be to go to the location selected and expect to find there what had been described. I stressed that using remote viewing information there is no searching, just finding, or not.

In this case, I told them, we would just have to follow the media to learn how it all came out. For further feedback, an article about the experiment would appear in the Cayce organization's magazine, *Venture Inward*.<sup>22</sup>

### **Outcome and Assessment**

More than a month would go by, until December 13, 2003, when a small force of Americans aided by some Iraqis, operating under what the military called Operation Red Dawn, discovered and captured Saddam Hussein. In the following days declassified material appeared in the media that allowed the accuracy of the seven hypotheses developed from the remote viewing session data to be evaluated. The question to be assessed was: Could the information provided weeks earlier in the remote viewing sessions have been used to locate and capture Saddam Hussein?

HYPOTHESIS ONE: LOCATION: Saddam will be found "beneath an ordinary looking house." "It is on the outskirts of a small village," "near Tikrit." "The house is part of a small compound." It is "bordered by a dirt road and by a nearby river." "The house can be identified because it has a large tree growing at either end," and "it has a strange kind of partial second floor over the front door."

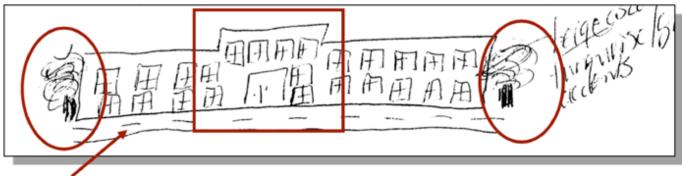


Compound new village of Ad Dawr, Iraq

### POST FIELDWORK ACCURACY ASSESSMENT:

"Saddam was found near the village of Adwar in the Tikrit area in a small compound...a river runs nearby, and a road is in front of the compound." *CNN*, December 16, 2003

The drawing at the top of the next page was made by one of the viewers, which embodied the most consensual elements. Note the two distinctively large trees at either end of the compound. Note also the odd little partial second floor in both the drawing and the image released by the government to *CNN*. And, of course, there's a gravel road that runs in front of the compound as described by the viewers.

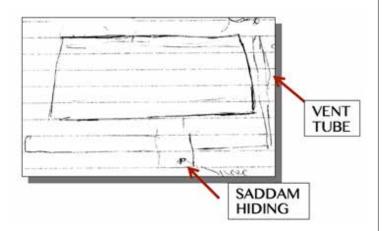




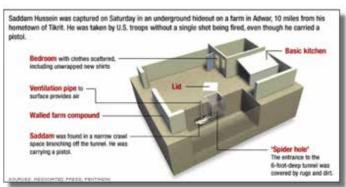
Picture released by the Department of Defense of the compound where Saddam Hussein was located and captured. Note the correlations between the drawing and the photograph.

### HYPOTHESIS TWO: SADDAM HIDING PLACE:

"Saddam Hussein has a hiding place." "It is like a cavern or a 'carved out space." It is "not visible but hidden underneath something." "Breathing is possible in this small hidden space because there's a vent tube built into this buried hiding space."



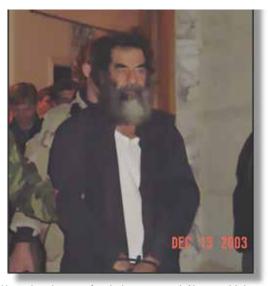
POST FIELDWORK ASSESSMENT: In the RV session drawing, Saddam Hussein is down in a hole, as he is in the image released by the Pentagon (next column). Note the low *a priori* RV observation about the vent pipe, shown in the drawing and the confirming image.



Picture released by the Department of Defense of the compound where Saddam Hussein was located and captured. Note the correlations between the drawing and the photograph.

**HYPOTHESIS THREE: SADDAM HUSSEIN APPEARANCE:** "Saddam won't look anything like he normally does." "He looks like a homeless person." He will be "dressed in dark clothing." He will have a "ratty," "unkempt" "salt and pepper beard." His hair will be "wild." His "appearance will be disheveled."

### POST FIELDWORK ASSESSMENT:



Saddam Hussein minutes after being captured. Note multiple correlations with the remote viewing session data.

**HYPOTHESIS FOUR: SUPPORTERS:** At the time of his capture Saddam Hussein will have only "two or three supporters with him at the time of his discovery."

**POST FIELDWORK ASSESSMENT:** "Troops took two other unidentified Iraqis affiliated with Saddam into custody." *New York Times*, December 16, 2003

\* \* \*

**HYPOTHESIS FIVE: FIREARMS AND RESISTANCE:** "Saddam will have a gun," "He will put up no resistance when captured."

**POST FIELDWORK ASSSESSMENT:** "Saddam was armed with a pistol, but showed no resistance during his capture." *Virginian Pilot*, December 16, 2003

\* \* \*

**HYPOTHESIS SIX: MONEY:** Saddam Hussein will "have a quantity of money with him." "Like a box of money."

### POST FIELDWORK ASSESSMENT:



The box of money found with Hussein containing U.S. hundred-dollar bills. The photo was obviously taken at the time of Saddam Hussein's capture. It was one of the pictures that mysteriously appeared in my mailbox. (see Final Comments)

\* \* \*

**HYPOTHESIS SEVEN: SADDAM HUSSEIN ATTITUDE:** "He will be defiant but will not put up any resistance." "He will be tired, and dispirited."

**POST FIELDWORK ASSESSMENT:** "He was a tired man, and also a man resigned to his fate." — Lt. Gen. Ricardo Sanchez, commander of U.S. forces news conference in Baghdad, December 16, 2003

### **Final Comments**

Workshops produce surprisingly good data in my view because people have no real idea what to expect, and nonlocal awareness is a highly numinous experience, particularly when you get positive feedback, even if that feedback lies in the future, as with the archaeological studies, which often did not produce feedback until months later. Numinosity, not time, is the operative variable.

There is even a name for this; it is called the First Time Effect, and it has been reported since the earliest days of remote viewing research. I believe this general success rate is the reason remote viewing has gone from being an obscure laboratory protocol used in research at SRI, Mobius, and PEAR, to an avocational interest on the scale of scuba diving or ballooning, with conferences, magazines, and newsletters.

The purpose of this experiment was to provide a set of hypotheses that could guide a field unit to Saddam Hussein and prepare them for what they would find when they got there. Was this accomplished? I think it is clear that the remote viewing data and the hypotheses it generated could in fact have accomplished that task. Did this information in fact play any role in his apprehension? The answer is, I do not know.

What I can say is this: About three weeks after Saddam Hussein was caught I went out to my mailbox to get the day's mail, and in the box was a standard manila envelope. There was no address on it, nor any return address. When I opened it, it contained no note, only the two photographs you see in this paper: one of Saddam Hussein at the time of his capture; the other of the money box he had with him. These pictures obviously were taken by a member of the team that located and captured Saddam Hussein. How they came to be in my mailbox in a blank envelope I cannot say.

Stephan A. Schwartz is a Distinguished Consulting Faculty of Saybrook University; a Fellow of the William James Center for Consciousness Studies, Sofia University; and a Research Associate of the Cognitive Sciences Laboratory of the Laboratories for Fundamental Research. He is the columnist for the journal Explore, and editor of the daily web publication *Schwartzreport.net* in both of which he covers trends that are affecting the future. He also writes regularly for *The Huffington Post*. His other academic



and research appointments include: Senior Samueli Fellow for Brain, Mind and Healing of the Samueli Institute; founder and Research Director of the Mobius laboratory; Director of Research of the Rhine Research Center; and Senior Fellow of The Philosophical Research Society. Government appointments include: Special Assistant for Research and Analysis to the Chief of Naval Operations, consultant to the Oceanographer of the Navy. For 40 years he has been studying the nature of consciousness, particularly that aspect independent of space and time. Schwartz is part of the small group that founded modern Remote Viewing research, and is the principal researcher studying the use of Remote Viewing in archaeology.

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# SAVE THE DATE! The 2019 Society for Scientific Exploration conference will be held June 5–8 at the Omni Interlocken Hotel in Broomfield, Colorado. Details will be available soon on the SSE website.

### **Larry Wile**

# Reissner's Fiber: The Gateway to Higher Consciousness

elief in the *prisca theologia*, the one Dtrue religion divinely revealed to man, is justified only if extraordinary ancient ancestors were endowed with suprasensory perceptions of the Infinite. Because such purported revelations are buried beneath the dust of fallen Babel, and have been distorted, disguised, fragmented, and embellished along a chain of mystical whisperers, belief in them requires a leap of faith that seemingly leaves reason and evidence behind. However, the earliest prophets were not only endowed with suprasensory perceptions of the Infinite, but also with interoceptions of their neural basis, Reissner's fiber.



Reissner's fiber is a hollow threadlike

structure that originates from the center of the brain, just below the pineal gland, and travels through the fluid-filled passageways of the cerebral ventricles and the central canal of the spinal cord, ensheathing the central axis of the central nervous system. It was discovered in 1860 by Ernst Reissner (pictured above) in the central canal of a lamprey. Three years later, Karl Kutschin confirmed Reissner's discovery, naming it "Reissner's fiber." However, in 1868, Ludwig Steida asserted that the spinal fluid and the chemicals used to preserve specimens had coagulated, creating a viscous thread—which had been mistakenly identified as a biological structure. Other neuroanatomists embraced Steida's opinion and the fiber fell into oblivion.

In the spring of 1899, Porter Sargent, a 27-year-old doctoral candidate at Harvard observed the same curious, glistening fiber in the central canal of a lamprey that Reissner had seen. Perusing the scientific literature, he found it "remarkable that so peculiar and conspicuous a structure as Reissner's fiber, which is of such great importance in the nervous anatomy as to persist throughout the vertebrate series, should have remained so little known for forty years after its discovery." Similarly, he was dismayed that the ventricles, their lining and content, had been "dismissed with a few words." His neuroanatomical studies and behavioral experiments convinced him that the fiber is a novel, "highly specialized conduction path" for the high-speed transmission of signals that mediate an "optic reflex apparatus" for the "short circuit transmission of motor reflexes."

Sargent (Sargent, 1905) concluded his 1905 paper by



saying, "The conclusions and the discussion of the results and bearings of this research are reserved for the second part of this paper dealing with the higher vertebrates. This is already well advanced, and it is hoped will appear in about a year." However, Sargent never published the second part of his paper. He abruptly abandoned his academic career and spent the next decade traveling the globe, "reeducating myself and others, studying and interpreting peoples, their arts and

For several years Sargent's hypothesis was widely accepted. However, he had mistakenly concluded that the fiber is formed by a coalescence of axons originating from various nuclei in the brain rather than an aggregation of secretions. His error was understandable. Rudolph Albert

von Kölliker, who coined the term axon in 1898, was unable to decide if Reissner's fiber is an axon, an artifact of preservation, or a "crystallization of biological secretions." It was not until 1975 that electron microscopy confirmed that the fiber is formed by an aggregation of secretions. Although Sargent distinguished the "axons" that form Reissner's fiber from "ordinary axis cylinders," described the fiber as a "highly specialized conduction path," and contrasted the "very thin medullary sheath" surrounding the fiber with the sheath surrounding "ordinary nerves," his identification of the fiber as an axon, nevertheless, eventually led to the rejection of his hypothesis.

In 1910, Dendy and Nicholls (Dendy, Nicholls, 1910) proposed that the fiber is an elastic cord. Varying tensions of the fiber resulting from movements of the body are relayed to sensory cells, which, in turn, regulate those movements. As the conceptualization of Reissner's fiber transformed from a novel high-speed transmitter of signals to an elastic cord, it became invisible to neuroscientists.

While Nicholl's inglorious hypothesis has been rejected, the fiber is still excluded as a neural correlate of consciousness. The discovery that the fiber binds neurotransmitters was interpreted with another inglorious hypothesis: the fiber detoxifies the cerebrospinal fluid. Currently, the few researchers who investigate the fiber are focused on its role in embryogenesis.

Pushing the fiber further into oblivion is the consensus of the few textbooks and articles that do mention the fiber that it does not exist in humans. However, the fiber has been

observed in a 14-year-old teenager (Agduhr,1922) and in 15and 16-week human embryos (Keene, 1935). Also, a successful immunoreaction against a proteinaceous compound secreted by the fetal human, the main source of the fiber, has been performed (Galarza, 2002). The subcommissural organ, the main source of the fiber, typically regresses during infancy, but a fully developed organ has been observed in a 60-year-old man (Gomez, 1962). The central canal typically occludes during childhood but sometimes persists into adulthood. Surprisingly, the occlusion is not the result of age-dependent degeneration but of inflammation of the canal's cellular lining.

Reissner's fiber undergoes rapid post-mortem degeneration and soon becomes undetectable. Other rare anomalies, therefore, might have gone undetected. The words of the French investigator of Reissner's fiber, Etienne-Jules Legait, remain true today: "when its existence is denied, this fact should be carefully analyzed and discussed: one could not take it into account if fixation is uncertain." Current neuroimaging techniques such as magnetic resonance imaging or positron emission tomography lack sufficient resolution to detect the fiber in living subjects.

In spite of the fact that the fiber has been conserved along

all the branches of the known 550-million-year-old protovertebrate and vertebrate phylogenetic tree from amphioxus to *Homo sapiens*, and occupies the most strategic location in the central nervous system, it remains so little known since its discovery that it has been dubbed the "Devil according to Baudelaire" whose "loveliest trick is convincing us that he doesn't exist" (Olry, Haines, 2003).

### "Wile's Hormone"

I arrived at the hypothesis that Reissner's fiber is the neural basis of suprasensory perceptions by exploring the possibility that ancient mystics perceived realities that are grasped by physicists as unvisualizable abstractions. In 1972, as a first-year medical student under the mentorship of Charles Loeser, Chairman of the Neurosciences Department, University of Connecticut Medical School, I explored the possibility that the anatom-

ical basis of suprasensory perceptions described by kundalini yoga is real. Is there a pathway from a triangular-shaped region at the base of spine through a hollow passageway in the center of the spinal cord to the center of the brain?

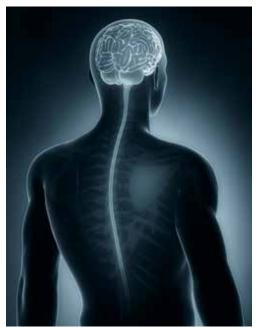
Loeser quickly informed me that there is a passageway called the central canal. It is regarded as an occluded remnant of the embryological neural tube from whose inner surface the cells of the central nervous system originate. While modern yoga is generally practiced as a form of physical exercise, its postures (asanas), muscular contractions similar to the Valsalva maneuver (Bandhas), and breath retention and rhythmic

breathing (*Pranayama*) can create "water hammer" pulsations through the central canal and thereby open it (Gardner, 1965). In kundalini yoga, the process of opening the occlusions in the central canal is known as untying knots, *granthis*, in the *Sushumna* nadi.

Encouraged by learning about the central canal, I turned my attention to its base. To Loeser's surprise, we learned from *Grey's Anatomy* that there is a triangular-shaped structure at the base of the central canal called the terminal ventricle. Curious, we examined specimens under the microscope and discovered previously unreported clusters of cells characteristic of endocrine glands. Loeser dubbed the mysterious substance "Wile's hormone." Turning my attention to the central canal's connection to the center of the brain, I learned that it opens into irregularly shaped cavities, the cerebral ventricles. On the roof of the uppermost cavity, the third ventricle, is the pineal gland, which has been identified with the "mystical third eye," the *Ajna chakra* of kundalini yoga. It had recently been proposed as a site of hallucinogen synthesis.

As I contemplated the psychedelic brew of hallucinogens synthesized by the pineal gland mixing with "Wile's hormone," I felt that something was missing. It was not until

a year later that I discovered what it was. A colleague of Loeser's, who had bemusedly followed our quixotic quest for something more substantial running from the terminal ventricle to the pineal gland than a flow of psychedelics, excitedly waved an article as I approached him in the hallway, "You dreamed it! Here it is!" he exulted. The article, titled "Studies concerning the function of the complex subcommissural organ-liquor fibre: The binding ability of the liquor fibre to pyrocatechin derivatives and its functional aspects" (Hess, 1973) introduced me to Reissner's fiber.



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### **Mystical Traditions**

The elusive fiber had played its role as the Devil according to Baudelaire so well that it not only had it eluded our search for more than a year, but it was not until

40 years later that I learned I had not been the first to identify the fiber with the central pathway of kundalini yoga. In 1927, Vasant Rele (Rele, 1927) identified Reissner's fiber with one of the concentric sheaths surrounding the central axis of kundalini yoga, the *Vajra* nadi. However, his proposal appeared in a confused glossary entry that was disconnected from the main text, which identified the central pathway of kundalini yoga with the right vagus nerve. In 1939 Theos Bernard (Bernard, 1939) made the first clear identification of the fiber with the central pathway of kundalini yoga. In *Heaven Lies Within Us*, he wrote, "Inside this central (*Sushumna*) nadi, the Yogi identifies an invisible nadi known in the West as the fibre of Reissner, but which is known here as *Chittra* (the Heavenly Passage,

in Sanskrit)." At the time, Bernard was a national celebrity. However, at the height of his fame, he died under mysterious circumstances in the hills of Spiti, India, while searching for lost manuscripts linking Jesus to yoga. Allegations that he was a fraud and an imposter, and his reputation for flamboyant self-promotion, eclipsed his proposal.

Shortly after my initial encounter with the fiber, I learned that it had previously been identified with a structure described by Chinese mystics that corresponds to the *Chittra*. In 1960, a North Korean scientist named Kim Bonghan (Bonghan, 1963) began an investigation to see if the meridians of acupuncture are real. He injected radioactive phosphorous (P<sup>32</sup>) into acupuncture points on a rabbit's abdomen. He found that injections into these points followed meridians along a novel network of ducts. Injections into other sites dispersed. Injections into the acupuncture point corresponding to the Governing Vessel—the central "extraordinary meridian" that corresponds to the *Chittra nadi*—label a threadlike structure inside the central canal. Bonghan made no reference to Reissner's fiber and named the labelled structure the "neural Bonghan duct."

Bonghan was praised by the North Korean government for discovering a "monumental theory in global science" and elevated to a high position in the government. However, amidst political intrigue and allegations that he'd withheld details of his methods, he was discredited and banished. The scientific community dismissed Bonghan's findings for several decades. In 2005, neuroscientists "rediscovered" the network of Bonghan ducts and proposed that they act as optical channels for coherent biophotons (Soh, 2004). In 2008, his team reported the discovery of a novel thread-like structure in the cerebral ventricles and central canal in a rabbit. They claimed the "novel thread-like structure" they had observed was different from Reissner's fiber yet occupies the same space (Lee, 2008)!

Another mystical tradition that traces its origins to the mists of prehistory is Kabbalah. The kabalistic counterpart to the Chittra and Governing Vessel is the central pillar of the Sephirot (right), the divine image in which man was created. While the Zohar, a foundational Kabbalistic text, predicted that the turning point in humankind's cosmic redemption would occur in 1840, "In the six hundredth year of the sixth millennium (5600 = 1840 C.E.) the gates of wisdom above [Kabbalah] together with the wellsprings of wisdom below [science] will be opened up, and the world will prepare to in the seventh millennium," the first explorations of the Kabbalah from a neuroscientific perspective have just begun (Shahar, 2015).

The identification of Reissner's fiber and the central axis of the *Sephirot* currently exists as a poetic metaphor (Ponce, 1978): "There's an Adam within each of us...in exile from the Garden. The aim of Kabbalah is the restoration of the divine man in the medium of mortal man...We are the laboratory...If one can

learn to connect the thread dangling free from the *Sephirot* with the thread of one's own being, one may begin the work of restoration."

Perhaps the "silver cord" described by near-death experiencers, another circuit between the human and the divine, is an interoception of a virtual Reissner's fiber perceived as the brain's energy drains centripetally toward its phylogenetically ancient core (Wile, 1994).

While the eyes are generally assumed to be the only generators of visual percepts, there is a sensory system surrounding Reissner's fiber that might generate them as well. Cilia resembling the rods and cones of the retina, which respond to single photons, line the brain's inner surface (Vigh, 1998). In 1913, Dimitri Tretjakov (Tretjakov,1913) dubbed the sensory system surrounding Reissner's fiber the "central sense organ." William Kolmer (Kolmer,1931) elaborated on Tretjakov's proposal, comparing Reissner's fiber to the gel-like tectorial membrane of the inner ear. Mystical practices, especially meditation, are well suited for shutting off external sensory input so that Reissner's fiber's input could be perceived like stars on a dark night. Interoceptions of the fiber could explain how ancient mystics described it thousands of years before it was objectively observed.

Prophetic visions and suprasensory perceptions eclipsed visual perceptions of the fiber. Those that were noted were deemed insignificant because the heart and lungs were believed to be the seats of consciousness. But now, looking through the lens of modern neuroscience, we might rediscover lost neuro-anatomical secrets.

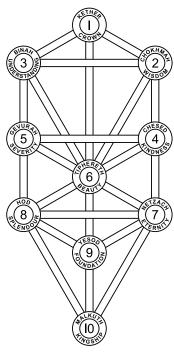
### **Neuroscience**

Filaments extending from Reissner's fiber to naked nerve endings projecting from neural systems that mediate the action of entheogens, opioids, and cannabinoids suggest that the fiber

can generate mystical experiences. However, while drugs can induce transformative ecstatic, noetic experiences, they fall short of realizing the mystics' claim of suprasensory perceptions of the Infinite. Specifically, drugs do not open the doors of perception to the quantum world.

The 5-nanometer filaments that comprise the fiber are, according to quantum orthodoxy, beyond conception or perception. Quantum physics is a "mystery without mysticism" (Plotnistsky, 2003). Niels Bohr famously declared, "There is no quantum world. There is only an abstract quantum description." Warned Werner Heisenberg: "The use of classical concepts is finally a consequence of the general way of thinking. There is no use in discussing what could be done if we were other beings than we are." However, the regeneration and reawakening of Reissner's fiber could make us beings other than we are.

We are denied perceptions of the quantum world because during interactions leading to conscious perception, the wave function



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collapses, decoheres, or splits into a classical reality. However, direct consciousness of Reissner's fiber as a quantum system could open the doors of perception to the quantum world.

Weighing against this hypothesis is the long-held belief that quantum effects are trivial in the warm noisy brain. However, the recent discoveries of quantum coherences in photosynthetic systems (Engel, 2007), the retina (Tscherbul, 2015), and the avian compass (Hamish, 2016), and new understandings of quantum feedback and control, suggest that nontrivial quantum effects in the brain are possible (Lambert, 2013, Mohseni, 2014).

Recent experiments involving quantum feedback and control of quanta inside a cavity have shown that the barriers to the creation of macroscopic quantum systems, such as "Schrodinger's cats," are technical, not conceptual. Reissner's fiber, floating within the brain's ventricular cavities, is uniquely well-suited to function as a biological analog of a cavity quantum electrodynamic system. Photosensors with afferent pathways connected to the most complex information processing system in the known universe, the human brain, could measure biophotons emitted from the fiber. Conservative estimates suggest that the brain operates 100 times faster than the fastest supercomputers, one exaflop (a quintillion floating point operations per second) versus 10 petaflops (10 quadrillion floating point operations per second). If speculations about quantum computations by microtubules or other neural structures are correct, then current estimates of brain computational power based on action potentials would represent an infinitesimal fraction of its true powers. Efferent pathways could inject electromagnetic signals and thereby control the quanta comprising the fiber. Such a quantum feedback and control system could operate nonconsciously as a self-organizing quantum-dissipative system or consciously as a biofeedback system using next generation neuroimaging devices to enhance the quantumness of fiber.

Because all the circuits of the brain originate from neural stem cells influenced by Reissner's fiber and its effects on the extracellular matrix, the fiber's stimulation of the inner-directed sensory system could produce neural activity equivalent to that produced by stimulation of the external senses, the basis of consensual reality. Reissner' fiber could generate a new perception of reality. According to mystical lore, the vibrations and geometries of the languages that communicated that reality resonated with the subtlest levels of physical reality (Holdrege, 1996). Without Reissner's fiber we are like blind aphasics in a library.

### My Research

To begin testing the hypothesis that the fiber exhibits quantum effects, my team of scientists, led by Professor Vasili Kharchenko, Harvard-Smithsonian Center for Astrophysics and Harvard Physics Department, and Professor Alexander Sergienko, Department of Physics, Boston University Photonics Center, have developed a novel micro-spectrometer to analyze biophotonic emissions from the fiber in living zebrafish larvae and similarly transparent adult zebrafish mutants (Caspar

line) using the technology of correlated photon counting with superconducting single-photon detectors coupled to a time-correlated counting system with picosecond resolution. Our apparatus is equipped with femtosecond pulsed infrared lasers to perform photon echo-based experiments similar to those recently used to reveal the quantum mechanisms involved in light harvesting during photosynthesis. We have also begun searching for electron spin coherences using nitrogen vacancy diamonds. Thus far, the signal-to-noise ratio has been too low to draw meaningful conclusions.

We are also developing mathematical models based on string theory that might lead to observable predictions. An intriguing possibility is that the compacted higher dimensions of string theory, which are conventionally thought of as either too small to be observed or parts of equations that are not parts of physical reality, might manifest themselves by their interaction with exotic states of the fiber. Another intriguing possibility is that  $(10^{-35})^2$  meter pixels of information covering the two-dimensional surface of the universe, which have been proposed to holographically encode the three-dimensional observable universe, might be holographically encoded by the one-dimensional thread ensheathed by the fiber (Stojkovic, 2013). The ancient precept that man is the microcosm of the cosmos would be realized mathematically. While infinities are erased from quantum field equations by the dubious methods of renormalization, it is possible to include them in a hierarchy of transfinite planes of reality culminating in what Georg Cantor, the originator of a hierarchy of infinites, called a "completely individual unity in which everything is included, which is the Absolute, incomprehensible to the human understanding. This is the Actus Purissimus, which by many is called God."

Confirming evidence for the hypothesis that Reissner's fiber confers suprasensory perceptions could include predictions of the fiber's activity beyond the limits of quantum uncertainty, or volitional control of its quantum effects. Correlations of the fiber's activity with telepathy, psychokinesis, precognition, or remote viewing would also provide confirming evidence. Correlations with reports of "peak experiences" and "cosmic consciousness" would also be corroborative. But noninvasive measurements that could provide such confirming evidence might require 22nd century technology.

### The Lost Circuit to Heaven

Perhaps Reissner's fiber's typical regression in the womb mirrors its recent evolutionary epigenetic suppression. Perhaps that loss is the biological basis of the evolutionary leap that set us on the road toward creating an expanding world of knowledge that liberated us from genetically programmed, stimulus bound behaviors.

According to the Kabbalah, the thread connecting us to the *Sephirot* snapped following the first bite from the fruit of the Tree of Knowledge on October 12, 3761 B.C.E. We were exiled from Paradise and sent on a mad, brutal journey to Redemption. Perhaps our journey ends in a unified neurocosmology organized around Reissner's fiber, fulfilling the prophesized union of the origin of the past with the final destiny of

the future. On that day, Reissner's fiber would no longer be the Devil according to Baudelaire, but the circuit to heaven.

Perhaps the lost circuit to heaven is an illusion derived from ancient hallucinatory confusions and wishful thinking. But now, for the first time in history we can investigate it as a scientific hypothesis. Our thoughts and beliefs can influence neural activity and genetic expression and might, thereby, regenerate the fiber. We can follow a path of pragmatic mysticism.

LAWRENCE WILE received a B.S. in physics from Union College (1971), an M.D. from the University of Connecticut (1976), a post-doctoral fellowship in psychiatry from Yale University (1979), and a M.A. in philosophy from the University of Massachusetts (1991). He is a Diplomate of the American Board of Psychiatry and Neurology. His essay "Reissner's Fiber and the Neurobiology of Mysticism" won



first prize in the John Templeton Foundation's "Ideas for Creative Research in Neurobiology" competition." His work has been published in the Journal of Near-Death Studies, Journal of Consciousness Exploration and Research, Journal of Consciousness Studies, Asian Journal of Social Science Studies, and Annals of Behavioral Neuroscience. His new book is The Jaynes Legacy: Shining New Light Through the Cracks in the Bicameral Mind (Imprint Academic, 2018). He is President of the Chaikin-Wile Foundation and is leading a multidisciplinary team at Boston University dedicated to the exploration of Reissner's fiber.

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for our own evolution?

### Robyn A. Lindley

# A New Treaty Between Disease and Evolution Are deaminases the "universal mutators" responsible

As we enter a new evidence-based era driven by Next Generation Sequencing (NGS), a revolution in our understanding about the source of mutations and their association with disease is overwhelming the traditional neo-Darwinian view of evolution based on the idea of "random" mutations. The new "big data" algorithms being developed in this "Age of Google" are forcing us to fundamentally alter our assumptions about genes, disease, and how genetic variability is generated. The recently discovered genetic mechanisms giving rise to mutations and disease depend on environmentally-driven and dynamic epigenetic gene regulation. These are coupled to highly targeted mutator mechanisms. This article describes the latest understanding of how these genetic mechanisms work together to pave a path to new evolutionary thought.

### The Weismann Barrier

In 1809 Jean-Baptiste de Lamarck published his Zoological Philosophy with his often controversial yet enduring idea that as an organism rubs up against the environment and adjusts, for example, to new habits and goals, new diseases, and new physical and nutritional challenges, some of the new acquired somatic adaptations are inherited to benefit the survival of their offspring. These environment-coupled steps of course violate a fundamental pillar of modern Neo-Darwinism termed the Weismann Barrier. It was erected by August Weismann in 1885 shortly after Darwin's death. The goal was to protect the germline from adaptations in the somatic body of an organism.<sup>1-4</sup> This concept thus erected a type of intellectual chastity belt around our germline genes never to be violated. Its emotive negative power has effectively suppressed any genuine research in acquired inheritance for over a hundred years. Of course, in his time, Lamarck could only justify acquired inheritance by keen comparative observation. Sixty years later Darwin also used similar arguments and observations to justify his acquired inheritance mechanism in his theory of Pangenesis.<sup>5</sup> A modern description would go something like this: as somatic cells are induced and stimulated by environmental signals, they emitted gemmules with new "pangenes," which in the course of their circulation around the organs registered newly acquired adaptations on the germline for transmission to progeny. In the context of the immune response to pathogens, we have previously pointed out that the body's harmless endogenous retroviruses are modern exemplars of Darwin's "pangenes" as types of somatic vectors or vesicles shuttling adapted genes into our germlines.2,6

In the modern genetic era, the first example describing the clear direct penetration of the Weismann Barrier was based on the antibody variable (V) genes of the immune system.<sup>7</sup> These germline V genes are inherited as "inactive" genetic elements with highly similar DNA sequences (they are only made "active" in the white cells of the body). The variations between germline V genes define the hundreds of different antigenbinding pockets so that different foreign invading pathogens can be recognized. They alter the antigen-binding pockets by introducing new somatic mutations: The new mutations are generated by the action of a family of endogenous proteins called "deaminases" that act in direct response to the foreign antigens on the invading pathogen. In humans, there are around 14 different deaminase proteins that change the structure of a gene by altering a single base unit in our DNA. For example, the result may be the mutation of an "A" (adenosine) to a "G" (guanosine) in a particular gene.

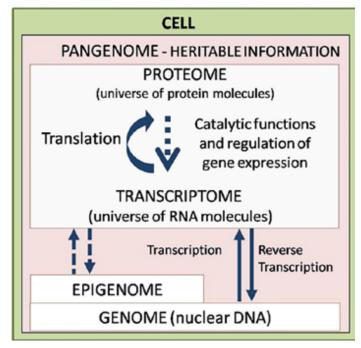
As a next step, a newly mutated V gene is then "clonally selected" in a true Darwinian manner if it produces the "best fitting" antibodies to protect against the disease. This step is also Lamarckian in the sense that the invading pathogen from the "environment" provides the trigger for initiation of the cascading immune response. Some of these new strongly selected somatic antibody V mutants are predicted to be transferred back to the germline for the benefit of future generations. Thus, the antibody V gene clusters are regularly updated following the body's immune response to foreign microorganisms. In the case of smallpox or polio, for example, previously exposed generations might then confer some genetically acquired resistance to future generations.

But current research on the origins of all types of mutations is now providing us with new molecular evidence for a far more general deaminase-based mutator mechanism. This evidence supports the idea that environment-driven genetic and epigenetic changes, which when combined, target new sites for non-random mutation in many other genes across our genome. It is this genetic-epigenetic coupling that now underpins new evolutionary thought.

It has been known for over two decades that a number of processes write additional "regulatory" information onto the surface of the genes without altering the genome sequence, a process termed the "epigenetic" or "soft" re-wiring of the genome. These epigenetic events make "surface footprints" on the gene sequences (composed of A,T,C,G nucleotides) making up a part or all of the genetic regions targeted. Many epigenetic changes triggered by the environment have been shown to be stably inherited by offspring for several generations. 3.4

### **Environmental Triggers**

What has been discovered since then is that environmentally triggered epigenetic markers also target genomic regions for deaminase action. Thus, environmentally triggered epigenetic changes *directly mark* potential gene sites for possible new gene mutations. (A schematic representation of the linkages implied by these coupled events is shown in Figure 1.) Scourzic and associates<sup>9</sup> have recently reviewed many of the potential molecular steps we think are important in these environmentally triggered epigenetic-genetic mutation paths.



Schematic diagram showing the main links between the proteome where many environmentally triggered pathways may actively direct epigenomic and genomic changes during transcription. Source: Fig 3 in Lindley 2011b *G.I.T Lab Journal* 

A key question is: How do natural instincts arise in evolution? Ever since Samuel Butler's Luck or Cunning?<sup>10</sup> simple logic for some implied that strong survival instincts based on fear responses must have arisen in our ancestors—not by chance, but in a Lamarckian manner, which were then passed on to their progeny. A recent report by Dias and Ressler<sup>11</sup> bears directly on how instinctual responses arise. Parental mice were subjected to Pavlovian odor fear conditioning before conception. It was then observed that subsequent generations had an increased specific behavioral sensitivity to the specific chemical odor used to condition the parents. That is, unrelated chemical odors did not trigger a fear response. They also did other breeding experiments that established that these specific acquired transgenerational effects are indeed inherited via parental gametes. Thus, both direct genomic and indirect epigenetic odorant receptor gene targeting appear to act together to establish what we now recognize as specific instinctual responses involving odorant receptor genes and behavior.

We do not know all the molecular steps involved, but current data suggests that environmental triggers direct specific families of proteins and associated molecules to introduce the epigenetic changes needed to open up specific genes for enhanced expression, and to identify the part of a gene that is potentially available for mutation. These epigenetic changes then permit susceptibility to deaminase action that may lead to permanent genetic change.<sup>9</sup>

This new understanding of epigenetic-genetic coupling that is required to introduce new genetic variants also helps us to better explain some other previously reported Lamarckian results. The now classic Lamarckian experiments of 1918–1924 by Guyer and Smith<sup>12</sup> on maternally induced eye defects in rabbits can be viewed as a complex combination of the antibody V gene soma-to-germline feedback process, and transgenerational epigenetic modifications involving both genomic access and targeted gene expression.<sup>9</sup> This new reality also reminds us of the work of Frederic Wood Jones. He emphasized many years ago<sup>13</sup> that coupled associated experiences together with acquired habits are powerful drivers of organic change.

As these and some other Lamarckian-like occurrences can now be explained using molecular genetics, many mainstream biologists have in recent years openly supported the idea of Lamarckian modes of inheritance as a key mechanism underpinning our current view of evolution. 14,15

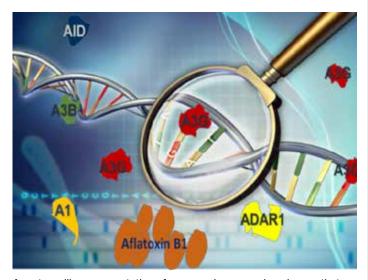
### The Role of the Deaminase Proteins

The present story involving the role of the deaminase proteins began about eight years ago when we asked: "What are the primary causes of the direct genetic changes guided by epigenetic gene expression and regulation?" In 2010, it was shown for the first time that the distinctive mutation patterns of antibody genes was also observed *in toto* (or in part) in all of the non-lymphoid cancers examined. From these *in silico* results, it was speculated that the same deaminase-dependent mutator processes known to be active in antibody genes must also be actively involved in the accumulation of mutations in the tissues where cancer was identified.

Just one year later, it was also discovered that the gene target sites of individual deaminases are far more specific than previously thought. An early analysis of the somatic mutations occurring in breast cancer showed that many mutations appear to be caused by a particular set of deaminases.<sup>17</sup> The unique mutation signatures left in the genome by each deaminase also provided us with some new information about the molecular processes causing cancer progression.

Are deaminases the "universal mutators" responsible for our own evolution? From yeast to man, deaminases have now been found in most animal species. Their mutational activity is highly targeted, and our understanding of their mutational role has resulted in a paradigm shift away from the idea that mutations arise randomly. While some mutations are also generated directly by external physical sources, such as ionizing radiation and hazardous chemicals, the deaminases are truly endogenous. They are activated in all cells, mainly by invading pathogens, viruses, bacteria, and fungi. <sup>18</sup> Thus, they appear to

play a pivotal role in the cause of gene mutations coupled to environmental signals. Together, these two processes support an updated view of adaptive evolution via endogenous genetic mechanisms involving epigenetic changes and deaminase mutational activity across the genome. The "Darwinian" roles of cell death and organism survival will continue to ensure that natural selection also plays a part in choosing those cells or individuals who will survive long enough to produce progeny of their own.



A cartoon-like representation of some endogenous deaminases that are produced to mutate and damage the DNA or RNA of invading pathogens before they replicate. While being produced in the body to fight pathogens, some deaminases may attach themselves to our DNA and leave behind new mutations. These new mutations are identified in the next generation of cells, and some may be passed on to the germline. Also included is Aflatoxin B1, which is an example of an environmental toxin that may directly cause mutations in next generation cells, and possibly alter the genome of subsequent generations.

As well as causing genetic damage to our body cells that may result in a diagnosis of cancer, there is also very recent evidence that the deaminase mutators have helped to shape the genetic landscape of the human germline over evolutionary time, that is the genomes encased in the cells of the eggs and sperm of the reproductive organs. 19 It has been shown that the genetic variations in the human germline known as "single nucleotide polymorphisms" (SNPs, pronounced as "SNIPS") occur at specific genetic signatures associated with deaminase mutational activity. This suggests that the original source of many SNPs was the result of deaminase-linked mutation processes, and that these have been inherited from ancestors and continue to persist in human sub-populations. The environmental trigger for some of the SNPs arising in our ancestors' genes could be the result of deaminase anti-viral activity. Some deaminases are widely known as "virus smashers." Unfortunately, in the process of their mutational action intended to kill and destroy a virus, our genes may also take an unintended mutational "hit" as collateral damage. 20 While lethal SNPs may arise, only a small number of SNPS cause lethal genetic diseases. Most are more benign highly adapted modifications of protein structure and function. The finding that many human SNPs occur at known deaminase genomic signatures is difficult to explain without the invocation of a soma-to-germline feedback loop as part of their primary cause in a previous generation.<sup>19</sup>

As far back as 2011, it was speculated that "... It may well be that the SHM mechanism (viz. somatic hypermutation in antibody V genes) is an important mechanism that is co-opted in some way to update the DNA of a large number of genes in healthy tissues and germline cells." It now appears that this speculation has since been confirmed by analyzing mutation patterns in thousands of non-immune system genes across both cancer genomes, 17,21 and the germline genomes of patients suffering a wide range of inherited genetic diseases that we now associate with "SNP" tests—some serious, the majority somewhat benign. 19

But what function do the deaminases perform in normal healthy cells? They have been recognized as potentially dangerous mutators for some time. It would have to be a regulated process of targeted somatic "mutation" that is beneficial to the cell and organism, otherwise cancer might easily develop. We know that the different types of deaminases are expressed to variable levels across the different tissues of the body. 22,23 During pathogenic virus infections such as the flu or HBV (hepatitis B virus) infection, the deaminase-mediated mutations literally riddle the viral genes with lethal mutations.<sup>20</sup> In a normal healthy person, many of the mutations occurring in the cell's genome are repaired to limit the number of unwanted new mutations being introduced to the genome as "collateral damage" while fighting an infection. Clearly, a healthy person needs to be able to mount an effective deaminase response to viral infection, and then ensure that the mutations are repaired for the next generation of cells—or offspring. One would therefore expect and hope that these processes imply that the action of deaminases themselves is safely regulated in the various tissues of the body.

Thus, as our papers continue to be published in respectable peer-reviewed journals, we can now legitimately ask: "What has been the *primary reason* for the massive recent cut-through in the tacit acceptance of the deaminase origins of gene mutations displaying a distinct Lamarckian-like flavor?"

The influx of massive quantities of whole genome DNA sequence information via Next Generation Sequencing technology (NGS) has been decisive. It is the overwhelming driver in this changed conceptual understanding. We now confidently talk of the "genomic landscape in cancer,"<sup>24</sup> and this is now applied on a significantly wide scale in the clinic. Hundreds of thousands, if not millions of whole genomes or their significant protein-coding sub-portions (the "exome" component encompassing 2% of the genome) have now been sequenced.

The NGS technological revolution has therefore utterly changed all aspects of biomedical research, particularly clinical personalized medicine. Numerous "big data" algorithms and bioinformatics pipelines come to the fore. Indeed deaminase-specific algorithms now allow for the identification

of which deaminase mutator is likely to have caused the identified somatic mutations during cancer development, or to identify the likely origin of an inherited germline mutation. The conservative estimate is that 30–40% of all somatic and germline genetic variations can be accounted for by just four or so members of the 14 known human deaminases.

### **Our Evolutionary Future**

At this historical juncture, learning to control the unintended mutational consequences of a deaminase response to an invading pathogen forces us to renew our thinking about how to manage health and disease, and thus direct our evolutionary future for "wellness." It is therefore important to further develop our knowledge of the complex interplay between the environment and evolution, and to understand the likely deaminase source of new somatic mutations as cancer progresses so that we may prevent cancer in the future. We also need to develop our understanding of how *de novo* deaminase associated mutations are inherited in the germline. Together, these new learnings will continue to reveal just how important the role of deaminases is in understanding our own health, the health of our ancestors, and our relationship with the environment in which we live.

From an evolutionary perspective, it is likely that NGS technologies will continue to provide an unstoppable torrent of new evidence supporting a Lamarckian-like view of how we both adapt to changes in our lifetimes and over evolutionary time. Many scientists and clinicians now overtly and tacitly entertain such views. As writers like Henry Bauer have written, the scientific process is not the "epitome of evidence-based, evidence-respecting knowledge and understanding." In the case of accepting evidence for Lamarckian-like inheritance, this is indeed more a myth than reality. Despite a gradual collapse of the old order based on "random mutations" and the longheld view of an inviolate germline, we expect that there will continue to be deeply entrenched pockets of resistance shaped and justified by many of the trenchant old-guard

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#### **ENDNOTES**

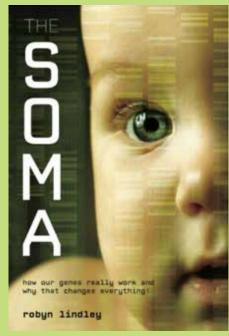
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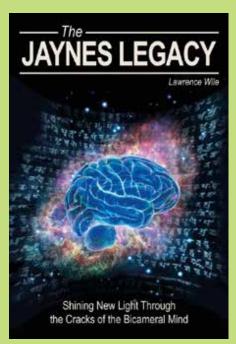
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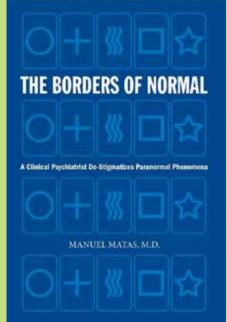
### **Noteworthy Books**



The Soma by Robyn A. Lindley CreateSpace, 2010



The Jaynes Legacy: Shining New Light
Through the Cracks of the Bicameral Mind
By Lawrence Wile
Imprint Academic, 2018



The Borders of Normal: A Clinical Psychiatrist
De-Stigmatizes Paranormal Phenomena
By Manuel Matas, MD
Friesen Press, 2017