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Energy Dynamics in Seizure Disorder: Reexamining the Sacred Disease

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INTRODUCTION

In the Hippocratic work *On the Sacred Disease* the anonymous author critiques superstitious, magical beliefs surrounding epilepsy and, instead, attempts to establish a natural basis for its occurrence. At the time, epilepsy was believed to be of divine origin, mediated by malefic influences, and curable only by rituals and incantations. This profound 5th century Hippocratic shift in perspective reflects a transition in the evolution of human consciousness from its mythic roots to objective knowledge and rationality. At least one writer has commented that, while our ancient author rejects superstitious beliefs pertaining to epilepsy, he never denies the divine nature of the disorder but, rather, simply modifies the context by which 'divine' was to be understood [1]. Rather than being sent by the gods as punishment, epilepsy was part of an overarching natural order, exhibiting fixed patterns of cause and effect and subordinate to determinate laws and regularity.

The Greek word for sacred, *hieros*, as in 'hierarchy,' imputes a causal layer beyond the physical world, a supra- or metaphysical order as it were, in which agency and power flow downward into the material realm. Ancient thought, as typified in the Earth, Water, Air, Fire cosmology, was vertical in orientation and stratified hierarchically. In a rational sense, ancient notions of the sacred disease impute a supra-physical causal source that remains, in large measure, shrouded in mystery.

Twenty-five centuries after the colossal leap from mythos to logos, the origins of epilepsy remain as perplexing and ill-defined as in pre-Socratic times. Modern science-based knowledge is exhaustingly long on description and distressingly short on explanation. The age of rationality has thoroughly transformed human consciousness, not to mention the natural world, but to date it seems modernity has simply exchanged one set of beliefs for another.

Globally, epilepsy remains the second most common neurological disorder affecting 1-2% of the population or about 50-70 million individuals [2, 3]. In up to two-thirds of cases the underlying cause is never determined. Anti-epilepsy drugs have burdensome side effects and fail to control seizures in up to 30-40% of cases [4, 5]. Rational science has cultivated little insight into the essential nature of epilepsy. Perhaps ideas concerning the sacred disease need to be reconsidered.

In this paper we explore the dynamic basis of epilepsy, the sacred disease, and show, surprisingly, that in all cases its manifest signs and symptoms correspond to the four-tier vertical framework – material, efficient, formal and final causes – advanced by Aristotle a half-century after the Hippocratic works surfaced. Specifically, impaired energy dynamics during the seizure state transiently disrupt the couplement between the material and formal causal layers of the body precipitating the behavioral alterations that define epilepsy.

Unfortunately, a longstanding error regarding the relationship between brain and mind advanced by Enlightenment philosopher René Descartes precluded scientists from making rational sense of phenomena in front of their very eyes. Had they familiarized themselves with Aristotle's biological framework the significance of seizure events would have become apparent by now.

After briefly exploring the phenomenology of epilepsy we examine Descartes' monumental error and its deleterious impact on 20th century neuroscience. We catapult the flawed Cartesian perspective and replace it with Aristotle's correct formulation after which the physiological events surrounding the seizure state will become more obvious.

SEIZURE PHENOMENA

It is not our intention to chronicle the various seizure types or introduce a new classification system. Nor will we split hairs as to where anatomically the different seizure types happen to originate. There can be little question that seizures are initiated and propagated by the brain. But beyond such conventions a multitude of inconsistencies in the brain-centered narrative leads one to raise questions as to the actual nature of seizures and their mode of presentation.

The term epilepsy, from Greek, meaning to be forcefully seized or set upon, is used to denote abrupt interruptions in the flow of conscious experience, usually over a period of seconds to minutes, followed by either an equally abrupt return to the previous conscious state or a variable period of post-seizure somnolence and dimmed awareness. Seizures may involve the contents of consciousness, i.e., sensory aberrations, altered emotions or feelings, loss of voluntary motor control, cognition or any combination thereof, or, on the other hand, primarily impact conscious awareness giving rise to a spectrum of interior states in which the subject is completely unaware or immersed in a dreamy, liminal state [6-9].

In the 19th century neurologists introduced the terms 'grand mal' and 'petit mal' to describe what later became known as 'generalized' and 'focal' seizures but the distinction between the two was never so clear-cut. In any given subject seizures may begin as focal discharges and then secondarily generalize. Such behaviors led

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neurologist Roland Mackay in the 1960s to argue that all seizures were variations on a similar theme. Electroencephalography (EEG) has done little to clarify matters. Many generalized seizures are not so general and supposedly focal seizures can have general effects. Moreover, seizures may occur without obvious electrical changes as detected by conventional methods [10, 11].

By the late 19th century researchers had discovered that when areas of the cerebral cortex were electrically stimulated discrete movements or focal seizures were generated depending on the strength and location of the 'irritation'. English neurologist John Hughlings Jackson argued that seizures result from excessive neuronal discharge in local brain areas which then spreads trans-cortically into adjacent regions as the seizure evolves. As the location of the discharge focus varies so too do symptoms [12-14].

By the same token, Jackson argued that while the anatomical discharge site and attendant symptoms may vary, the underlying pathophysiology driving seizure events is always the same. The discharge focus, he claimed, was 'over-unstable', i.e., hyperirritable, and prone to release its energy more readily than normal cells.

In the 1940s physiologists, observing that electrical activity in cortical neurons became readily synchronized, deduced that the expanding wave of simultaneous discharge was mediated by side-to-side spread of rhythmic activity into nearby cells. Known as ephaptic coupling, it occurs as a result of electromagnetic interactions between adjacent neurons with merging and expansion of the discharge field. Ephaptic coupling was ignored for decades and only recently has drawn more attention [15-23].

In 1960 Mackay, in an illuminating essay entitled 'All Epilepsy is One', described two primary attributes of all seizures, 'autorhythmicity' (hyperexcitability), now recognized to result from loss of membrane threshold potentials, and 'hypersynchrony', the simultaneous firing of larger neuronal populations in the same rhythm and frequency, aka neuronal recruitment, which occurs by ephaptic coupling [24]. Epilepsy thus became conceived as a neurologic syndrome resulting from excessive, spontaneous electrical discharges at a particular site or generally throughout the brain.

EEG revealed a range of electromagnetic frequencies which, for classification purposes, were divided into supposedly discrete bands said to correspond with various states of function. Traditional waveform frequencies include delta, in the 0.5 to 4 Hz range, typical of sleep; theta, 4-7 Hz, found in deeply relaxed or drowsy states in which attention is inwardly focused; alpha, 8-12Hz, which characterizes the awake, relaxed state; sigma, 11-16 Hz, bursts of activity during non-REM sleep; beta, 13-30 Hz, characteristic of the active, externally oriented state; and gamma, 35-100 Hz, found during states of intense concentration and problem solving [25] (**Figure 1**). But studies reveal inconsistency underlying these definitions and 'shocking variability' in terms of frequency windows used to define each band [26, 27].

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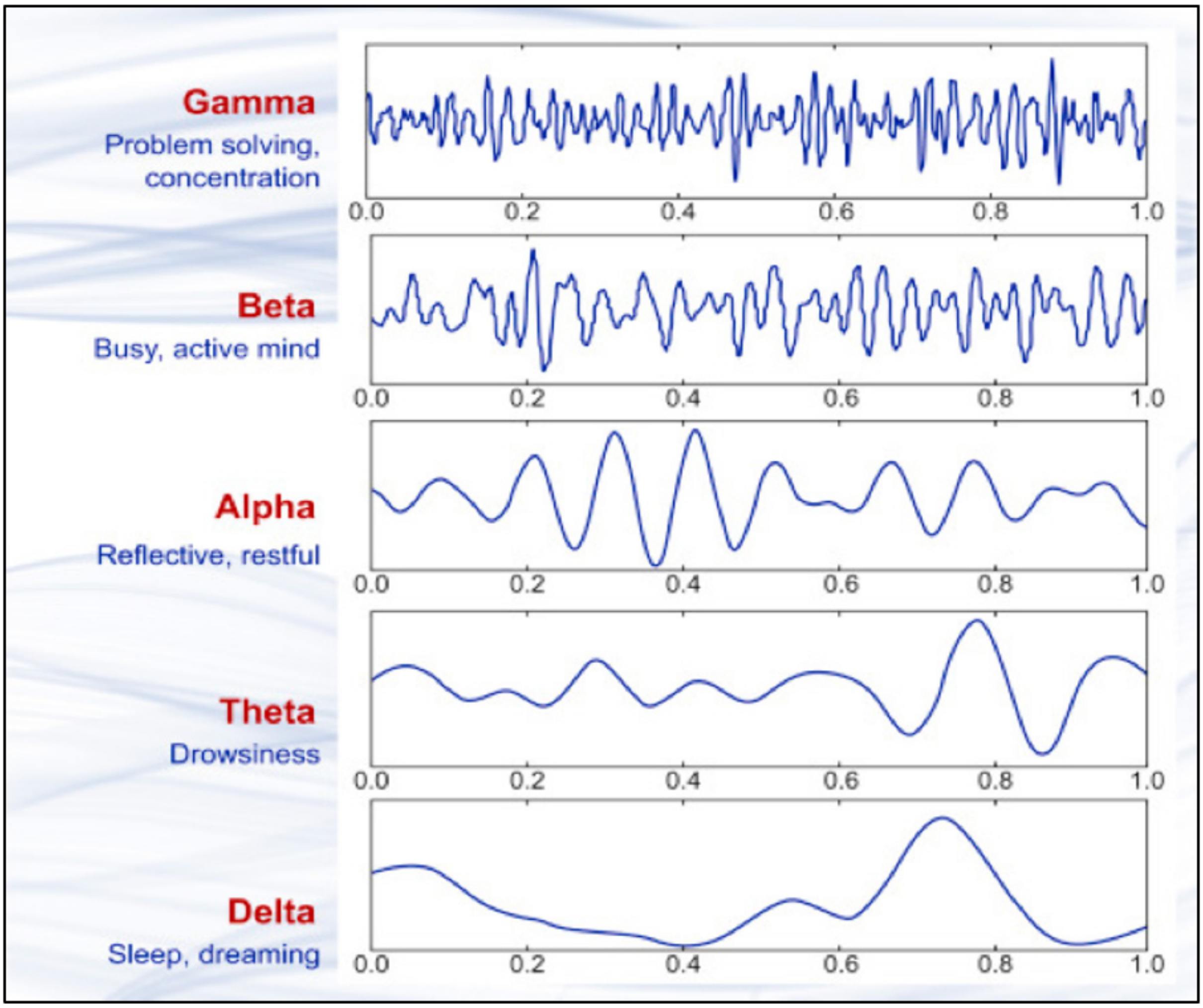

Figure 1: Conventional EEG frequencies and their relationship to states of activity in the sleep-wakefulness spectrum. (From: *Introduction to EEG- and Speech-Based Emotion Recognition.* Priyanka A. Abhang, Bharti W. Gawali, Suresh C. Mehrotra. Academic Press, 2016).

Practical difficulties with EEG abound. Its sensitivity for detecting pathology is only in the 25-60% range [28]. EEG tracings are but surrogates for a very poorly understood and highly complex set of processes that underlie brain function. Not only have scientists never explained how or from where neuronal electrical signals arise, they cannot account for how or why, in any given brain region, frequencies normally fluctuate up and down or change in amplitude in accordance with the mode of activity. We are led to question whether EEG rhythms drive functional activity or whether the functional state determines the frequency. Is causation top-down, bottom-up or somewhere in between?

Equally problematic is the conventional frequency range itself. In the 1950s researchers described 'infra-slow' cortical oscillations in the .02-.2 Hz range but the report was ignored for nearly a half-century [29]. More recently such slow, cyclical frequencies were detected throughout cortical regions during sleep and found to be tightly synchronized with higher frequency rhythms raising questions as to whether any of the conventional frequencies have independent existence [30].

The problem was compounded in recent decades by discovery of a wide range of frequencies at the upper end of the spectrum, so-called high frequency oscillations (HFOs) or 'ripples', in the 80-

600 Hz range. HFOs in the 80-250 Hz range are now recognized to play a key role in synchronization of neuronal activity and memory consolidation [31-34]. And higher frequency oscillations in the 250-600 Hz range, aka 'fast ripples' or pathologic HFOs, are believed to be involved in seizure generation [35-38]. Clearly scientists did not anticipate such developments when they embraced EEG nearly a century ago. This explains why the epilepsy classification system must continually be revised [39-41]. We briefly examine some of the common seizure types.

Absence seizures, first described in the 1700s, represent brief, usually 5-10 second periods of 'absence', during which the individual becomes unresponsive and stares blankly into space [42-44]. At seizure onset there is arrest of ongoing activity with lack of response to questions and commands (**Video Clip 1**). Subjects usually have no memory of events. Absence seizures, typically abrupt in onset and termination, may occur dozens and occasionally hundreds of times per day. Comparisons to the minimally conscious or persistent vegetative state, in which 'the lights are on but nobody home,' have repeatedly been drawn.

Video clip 1: Absence seizure. (From: https://www.youtube.com/shorts/6AeylCBOREk).

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Originally called petit mal they were later classified as general but more recent evidence suggests they selectively involve the thalamic and frontal regions. On EEG highly synchronized 'spike wave' discharges in the 3-4 Hz range involving bilateral thalamic and frontal regions are said to be characteristic. Scientists have no satisfying explanation for the sudden shift of cortical frequencies, from the dominant alpha-beta rhythms (8-30 Hz) of the waking state into the delta-theta (3-4 Hz) range. And why the symmetric bilateral pattern of involvement?

So-called ‘focal impaired awareness seizures’, formerly called ‘complex partial’ and before that ‘psychomotor’ seizures, often begin with a vacant stare and/or cessation of activity followed by various ‘automatisms’, i.e., hand movements, gestures, garbled speech, eye movements, or other reflexive movement patterns (**Video Clip 2**). The subject may appear as if in a dream-like trance. They usually have no memory of events [45-49]

Video clip 2: Complex partial seizure. (From https://www.youtube.com/watch?v=7l4_JhYo1Fo)

The qualifier 'partial' imputes a focal epileptogenic source, most often in one of the temporal lobes, but they can also begin in other areas. Correspondingly, EEG tracings tend to localize in a particular region often appearing as repetitive rhythmic discharges. But in up to one-third of such seizures characteristic EEG changes are not detectable. Similar behavioral changes may be seen in various psychological disorders, dementia, early stroke, fugue states, acute drug and alcohol intoxication, and metabolic encephalopathies.

Compared to the sheer diversity of focal seizures one is struck by the relative uniformity of grand mal seizures and yet they too display a degree of variability suggesting they don’t involve the entire nervous system uniformly [46-50]. Behavioral changes, described since the time of Hippocrates,

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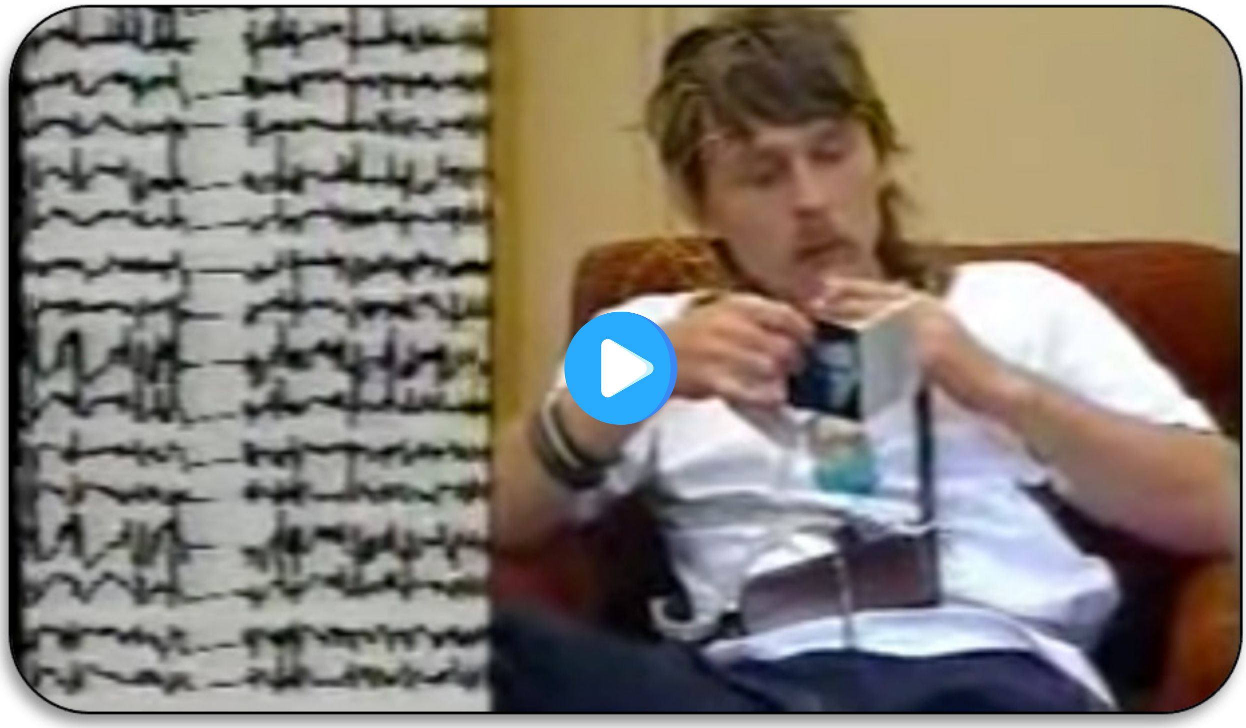
are said to progress through a series of stages: the aura, the cry, sustained tonic limb extension followed by rhythmic clonic jerking movements, salivation, incontinence, and deep post-ictal confusion and sleep. During attacks the subject is unresponsive and afterward has amnesia of events. Despite open eyes the level of consciousness resembles the coma state. The EEG pattern is typically synchronous, symmetric bi-hemispheric generalized spike-wave activity often punctuated by bursts of irregular discharge (**Video Clip 3**).



Video clip 3: Generalized clonic-tonic seizure. (From: https://www.youtube.com/watch?v=zyRea7rglF8)

But all seizures are not electrical in origin. A condition known as 'psychogenic non-epileptic seizures' can mimic various seizure types, including grand mal, in the *absence* of abnormal electrical activity (**Video Clip 4**). Said to be common, accounting for up to 30% of cases in tertiary epilepsy units, they are associated with psychological states like post-traumatic stress disorder, depression, anxiety and more [51-56]. All of this points to the inescapable conclusion that seizure disorder is not what it has been made out to be. But then neither is brain function.

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Video clip 4: Psychogenic non-epileptic seizure.
(From https://www.youtube.com/watch?vAXGTy3q8oJo)

CONSCIOUSNESS FIELD

Emerging evidence has turned conventional ideas about the brain upside down. Twentieth-century concepts of a sophisticated network of electrical micro-circuits has proven untenable [57]. It is now widely accepted that the brain generates a complex resonance field. First hinted at in the late 90s, researchers remain tenuous as to how it mediates conscious experience.

It is highly improbable that the brain spontaneously creates either conscious awareness or the contents of consciousness. Instead, its role appears limited to generation of a resonance field which interfaces these entities. Its function can be likened to that of a receiver-transmitter device, generating a field which, in turn, interacts with a supra-physical causal principle acting hierarchically 'above' the brain which, traditionally, has been called 'mind'. The necessity of such a directive entity was repeatedly raised by 20th-century neuroscientists, including Nobel laureates Charles Sherrington and, later, John Carew Eccles, but was never integrated into the formal theory structure. Historically its roots extend back to Plato and Aristotle.

None of the spectral frequencies identified by EEG have independent existence. All emerge from a commonly shared resonance field 'on demand' in relation to execution of various consciousness functions [58-60]. It should be understood that this field in no way explains the mental functions themselves but only how they are translated and expressed physically (**Figure 2**).

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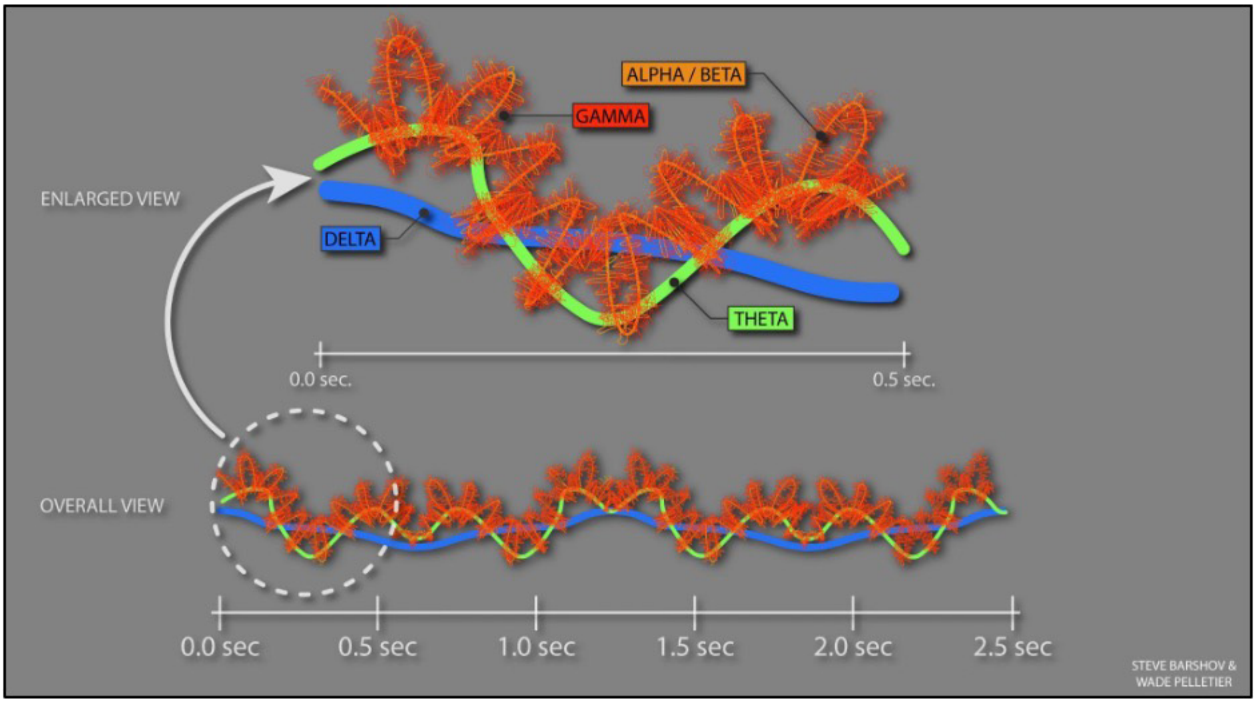

Figure 2: Graphic depiction of nested electromagnetic wave frequencies generated in the cerebral cortex that contribute to the brain's functional resonance field.

To underscore how impossibly complex the resonance field is: higher frequency rhythms like gamma and the HFOs are energetically intertwined with slower theta rhythms, aka 'cross-frequency coupling' [61-70]. Moreover, the amplitude (power) and frequency of the gamma waves regularly fluctuate in relation to the phase of the theta rhythm, aka 'phase amplitude coupling' [71-76]. Characteristic 'sharp-wave ripple' complexes often appear spontaneously during intentional activities such as concentration, memory, or anticipation of future events [77-82]. Researchers remain uncertain as to the purpose of these dynamic structures. In which direction is causation moving?

To add yet another layer of complexity, each of the frequencies is generated by a different population of cells in the cortex [83-93] (Figure 3). This is to say that discharge or firing of cells in the different cortical layers must be precisely timed based on some preexisting logic. The resonance field is built into the very neural architecture. And cells firing at the same frequency may, during certain activities, undergo phase-shifting, aka 'phase precession', with respect to nearby cells or cells in different cortical layers [94-100]. It is inconceivable that such highly intricate activities could be orchestrated by the brain itself.

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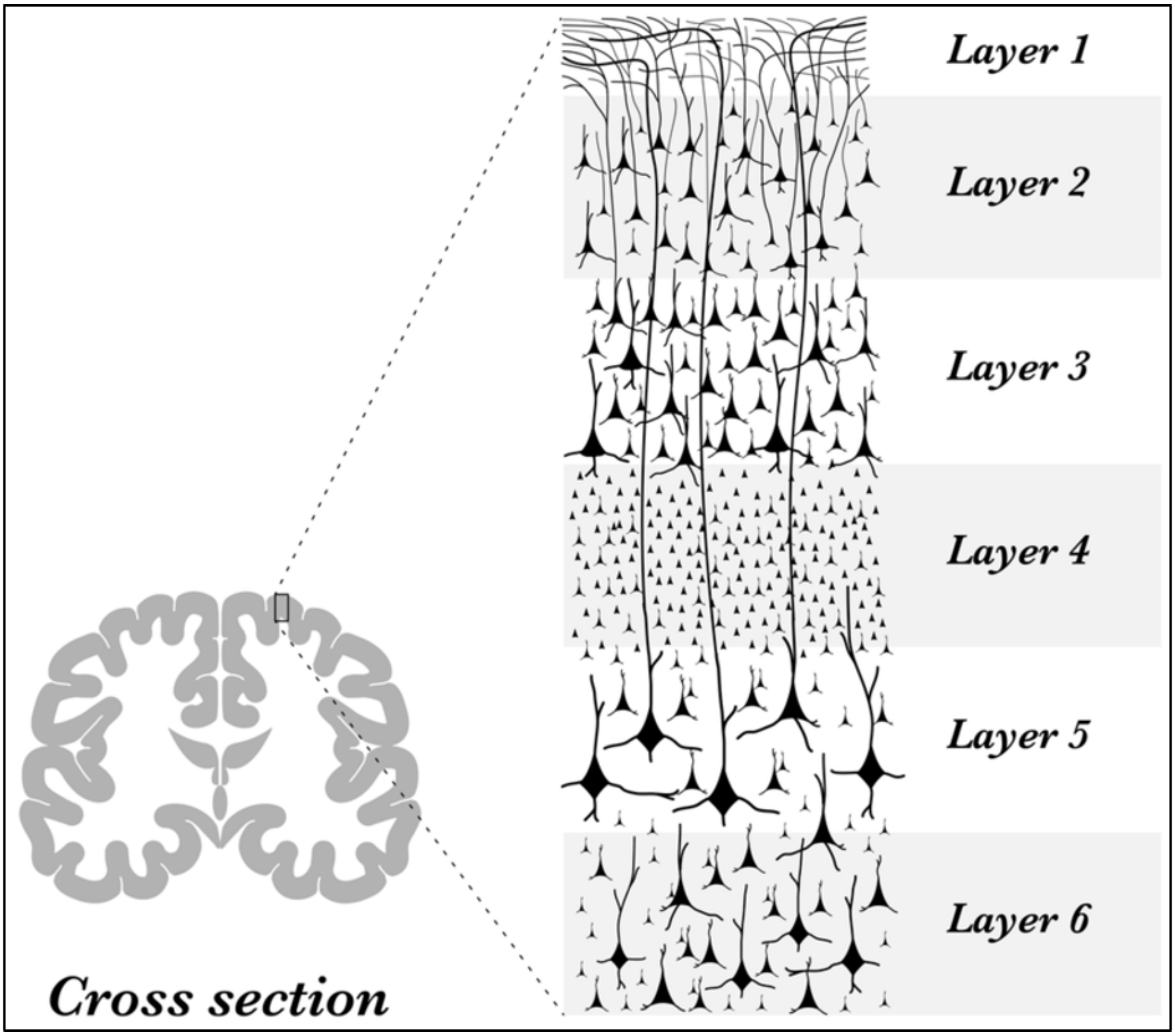

Figure 3: Depiction of the six layers of the cerebral cortex. 1 = molecular (dendritic) layer; 2 = external granular layer; 3 = external pyramidal layer; 4 = internal granular layer; 5 = ganglionic layer; 6 = multiform cell layer. (From: https://sevenandahalflessons.com/notes/Cerebral_cortex)

Oscillatory synchronization, i.e., simultaneous discharge of neurons in the same frequency range in various brain regions, is thought to play a role during attentional states [101-121]. Synchronized firing is seen between areas of the visual and parietal cortex, and between areas of the parietal and motor cortex in awake animals when visual patterns change [122, 123]. Synchronization occurs with 'zero time-lag' between areas mediating related functions [124]. Once again such coordinated activities would seem to demand not only a resonance field but a supra-physical directive entity.

Yet another example: the hippocampus, in the medial temporal lobe, organizes memory functions for various activities including spatial orientation. When rats are placed in a maze and EEG measurements obtained, neuronal firing patterns are temporally and spatially organized in a manner related to their location in the maze [125-135]. Different neuronal groups, aka 'place cells',

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are active only when the animal is in a particular location. Oscillations, mainly theta and gamma frequencies, begin in a particular phase relationship as the animal enters the field but continuously shift during transit. Place-specific neuronal firing results in precession of gamma rhythms with respect to the underlying theta wave. Researchers are unable to explain the tight linkage between events but believe theta and gamma complexes form a signaling or coding scheme.

It only stands to reason that memory functions guide the animal's passage through the maze. Moreover, the appearance of characteristic resonance patterns in the field having direct relation to the rat's location once again imputes top-down causality. The fact that amnesia frequently occurs in certain seizure forms, and that in between episodes individuals have relatively intact memory functions, suggests that seizures, with their chaotic discharge patterns, temporarily disrupt or attenuate the couplement between this supra-physical directive entity and physical brain structure.

Overwhelming evidence indicates that living organisms, including humans, exist in a vertically stratified functional system of 'causes' that interact hierarchically in a manner described by Aristotle in the 4th century BCE (**Figure 4**). This account was accepted as definitive for nearly two millennia until it was discarded in the 17th century by Enlightenment scientists.

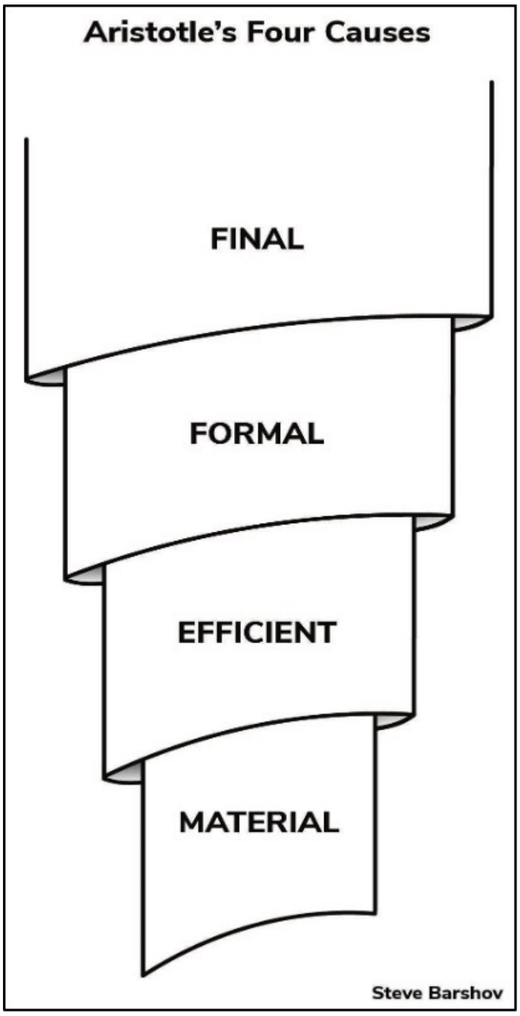

Figure 4

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The brain, the physical architecture of which consists of an assemblage of billions of neuronal elements possessing a staggeringly complex macromolecular organization, represents Aristotle's base-layer of 'material' or physical cause. Without material causes the upper layers cannot be expressed but without the 'upper' the 'lower' would not exist at all. Causation is bi-directional. Scientists have spent centuries attempting to construct a credible science from material causes alone with little success. This philosophical orientation has traditionally been called atomism.

Immediately 'above' we come across efficient causes, the fluidic layer of moving, dynamic forces as seen in the neural resonance field. This integrated nexus has a dual purpose, providing energy substrate to drive cellular functions as well as generating a resonance field that couples with the upper formal layer of cause. Distributed throughout the entire body, the energy field takes origin in the cardiovascular system through the motions of the heart, which we have documented in earlier writings [136-138]. It is no coincidence that the upper range of frequencies of the cardiovascular field and lower range of frequencies of the neural field overlap as the neural derives from the cardiovascular. One need only observe that during fainting spells or cardiac arrest there is immediate cessation of conscious awareness.

Formal cause, aka the life principle, described by Aristotle in *De Anima*, and traditionally known as 'soul', represents an upper tier of pure function in which the characteristic attributes that define the human species 'imprint' themselves on an undifferentiated mass of cells during morphogenesis. He described three phases of conjoined function: the vegetative (morphogenic) soul which directs development of the body proper; the sensitive (sentient) soul concerned with conscious awareness or mentality; and the rational (intellective) soul, possessed only by humans, and related to cultivation of insight and understanding (Figure 5).

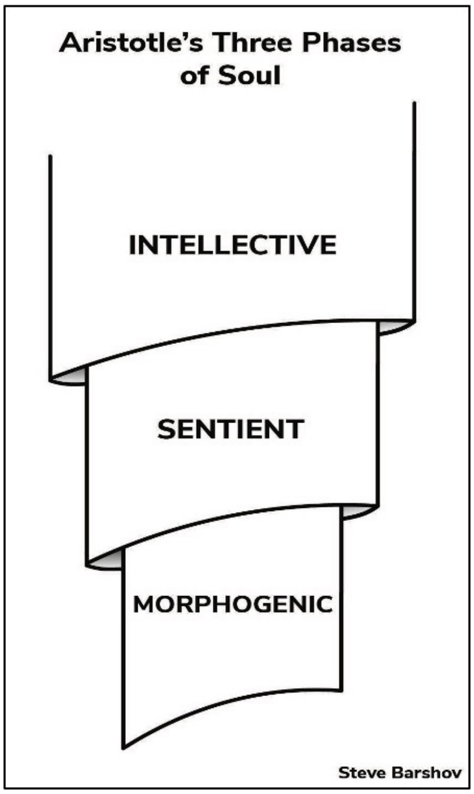

Figure 5

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In *Essay Concerning Human Understanding*, 17th century Enlightenment philosopher John Locke introduced a metaphor that would have fateful impact. He compared the human mind to the *camera obscura* and, furthermore, likened the senses to the small openings through which light enters its darkened space. The camera obscura, used by early scientists to study the behaviors of light or events like eclipses, consists of a box or room with a small hole in one side. Light from an external source passes through the hole and strikes the opposite inside surface whereupon the outer scene is displayed. The reproduced image possesses correct color and depth perspective but is mirror-image reversed and upside-down. Before long however the camera obscura became conceived as a mechanism by which consciousness was created in the brain [139].

Using dissected ocular globes from oxen or 'newly deceased' humans, Descartes let sunlight pass through the pupil and observed light patterns on the back wall of the eye implying the camera obscura effect (Figure 6). From his experiments he surmised that the eyes created an image of the outside world and, furthermore, relayed this image to the pineal gland where it was viewed *in camera* by the rational soul. And with the aid of memory in conjunction with the imagination, he surmised, these images could be recalled at will by the mind for further examination and reflection.

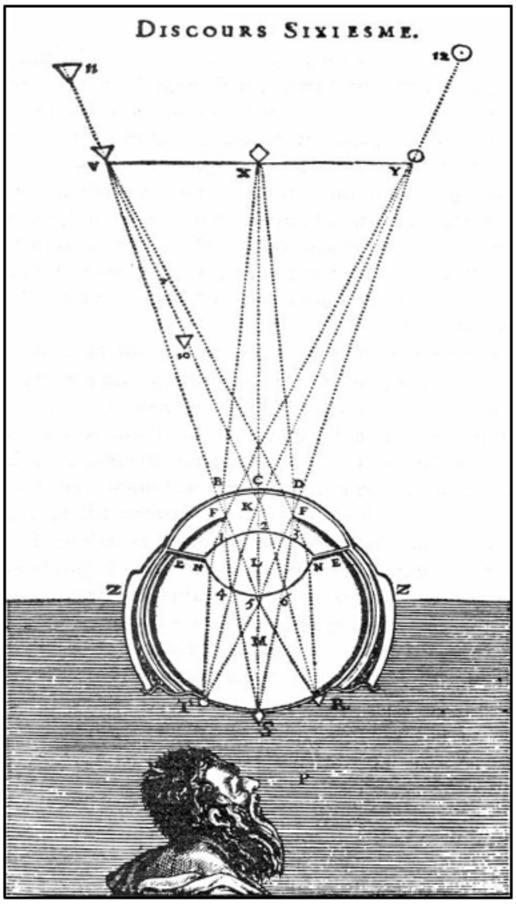

Figure 6: The eye as camera obscura. Illustration from Descartes' Optics (1637).

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Descartes' two-tier hierarchical model is obviously flawed but there is a phenomenological basis for his logic. Consciousness is an entirely private affair. While we have the subjective sense of gazing outwardly at objects in our surround, in reality we view a reconstructed image generated from within. How this happens remains a complete mystery.

Descartes alludes to the existential chasm between the individual and the outer world, i.e., between subjective and objective states. Sense experiences, feelings, perceptions and cognitions take place within this private space now known as 'conscious ego'. Called the Cartesian theater by philosophers, it forms the basis for all modern conceptions of brain and mind. It spawned the notorious mind-body problem and inaugurated a line of speculative theories that now inform the contemporary scientific brain myth. The Cartesian camera obscura set into motion a 350-year odyssey in search of mechanisms by which the brain ostensibly creates consciousness. Descartes' mechanistic speculations were never supported by factual evidence. In fact, quite the opposite.

In *The Integrative Action Of The Nervous System* (1906) neurophysiologist Sherrington argues that the brain cannot be responsible for the integration of sensory experience or conscious awareness [140]. There is no single structure or area in the brain where everything comes together and is unified. He points to the widely distributed nerve pathways throughout the brain. Each eye sends nerve tracts into both hemispheres and, far from converging, become more widely divergent. And yet each eye contains its own distinct image.

Integrative functions, Sherrington claims, must be ascribed to a hierarchical entity he calls 'mind'. But he unwittingly steps into the two-tier Cartesian brain-mind trap. If Sherrington is correct then how does one explain interactions between mind and the rest of the body? If this supra-physical directive entity attaches solely to the brain doesn't that imply the brain must control the body? Apparently so. With little recourse Sherrington advances his concept of the 'dominant brain'. Without the brain, he asserts, the body has all the determinacy of a 'penny-in-the-slot machine'. Certainly, we must admit, his dominant brain hypothesis goes a long way toward explaining some of the automatic behaviors seen during seizures. But are there other explanations?

J. C. Eccles spent his early career studying neuronal function for which he was awarded the Nobel Prize in 1963, but his interests gradually shifted toward mind and consciousness. *The Self and Its Brain* (1977), penned with philosopher Karl Popper, and *How the Self Controls Its Brain* (1994) set the groundwork for his 'three-world' hypothesis which, like Aristotle's four-tier causal hierarchy, consists of a ground layer of physical objects directed by an upper layer of mental events like thought, feeling and emotion, i.e., conscious ego, and a third tier comprising pure knowledge and the subjective Self, not dissimilar to Aristotle's rational soul or Plato's realm of Ideas. But in the manner of Descartes and Sherrington, Eccles associates mind with brain and once again leaves the body out of the equation [141, 142].

Eccles claims that conscious mind exists in and around the neural architecture, in the fluid-containing medium between neurons. Mind and brain, Eccles claims, interact through 'subtle communications' in the cortical grey matter based on quantum physics. As we saw these subtle communications represent a resonance field. His three-tier hierarchical framework ignores Aristotle's efficient causal layer and sidesteps any mention of an organized energy field. From where does the resonance field originate that mediates these subtle communications? We must look elsewhere for answers.

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HEART FIELD & FORMAL CAUSES

We awaken into an unfathomable state of awareness and inhabit this perceptual space throughout life. The consciousness field is the medium through which all experience manifests and is assimilated. Like a flower it blossoms and then, finally, vanishes into nothingness. Consciousness, like the life principle itself, is inexplicable and defies rational analysis.

When considering formal causes, mechanistic dissection and analysis no longer suffice; phenomena can be described only on the basis of their functional attributes and by the context in which they appear. Their irreducible facticity forms the basis for cultivation of all understanding into this mysterious but not unknowable layer of cause.

Form, the true anterior that engenders all bodily attributes as well as consciousness itself, supersedes the complex nest of relations we have just examined. Form represents the prior before any experiment or analysis is ever anticipated. Before *this* there was *that*. As Merleau-Ponty analogizes in *Phenomenology of Perception* (1945), form is the darkness of the theater through which the performance is revealed, i.e., the medium through which bodily phenomena manifest [143]. Form permits the intelligible to be perceived as intelligible. Form announces its presence early in human development.

All morphogenesis, says Aristotle, begins with the interaction between form and matter and consists of form imprinting its shape and function on matter. Form represents the active principle while matter is acted upon [144]. Early 20th century embryologists, like Hans Driesch and Hans Spemann, recognizing the purposive unfolding of events, deduced the necessity of this directive entity and devised ingenious experiments to affirm its presence [145]. The field concept was advanced independently by multiple researchers using terms like 'induction field' and 'determination field'. By the 1930s morphogenic fields were widely accepted and had become the subject of books. With the rise of the genetic movement the field concept was discarded in favor of material causes.

Early in morphogenesis form organizes the body's coming-into-being as the conceptus develops its own efficient means of generation, i.e., the heart and circulatory system, which begins to function autonomously. Described by Aristotle as the *punctum sanguineum* or point of blood, the beating heart, as the seat of efficient cause, is one of the most conspicuous and striking features of the early fetus (**Video Clip 5**). Aristotle regarded the circulatory system as a scaffolding around which the rest of the body developed. What comes into being first, he claimed, are first principles, after which everything else follows [146, 147]. As pointed out in an earlier piece, the centrality of the heart in morphogenesis, as seat of efficient causes, lies in the generation of a complex resonance field [148].

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Video clip 5: Fetal heart motion. From: https://www.jordmorklinikken.no and https://www.facebook.com/ultrasound.ie/videos/baby-heart-motion-at-12-weeks-%EF%B8%8F-this-video-clip-was-captured-during-the-advanced/204675227780605/

There is no more compelling affirmation of form and the morphogenic field than the phenomenon of situs inversus, mirror-image reversal in spatial orientation of organs in the chest and abdomen (**Figure 7**). Usually found incidentally on physical examination or by radiographic imaging, it is said to occur in about 1 in 10,000 births. In the majority of instances situs inversus occurs spontaneously and does not seem to be inherited. To date, no genetic cause has been identified [149, 150].

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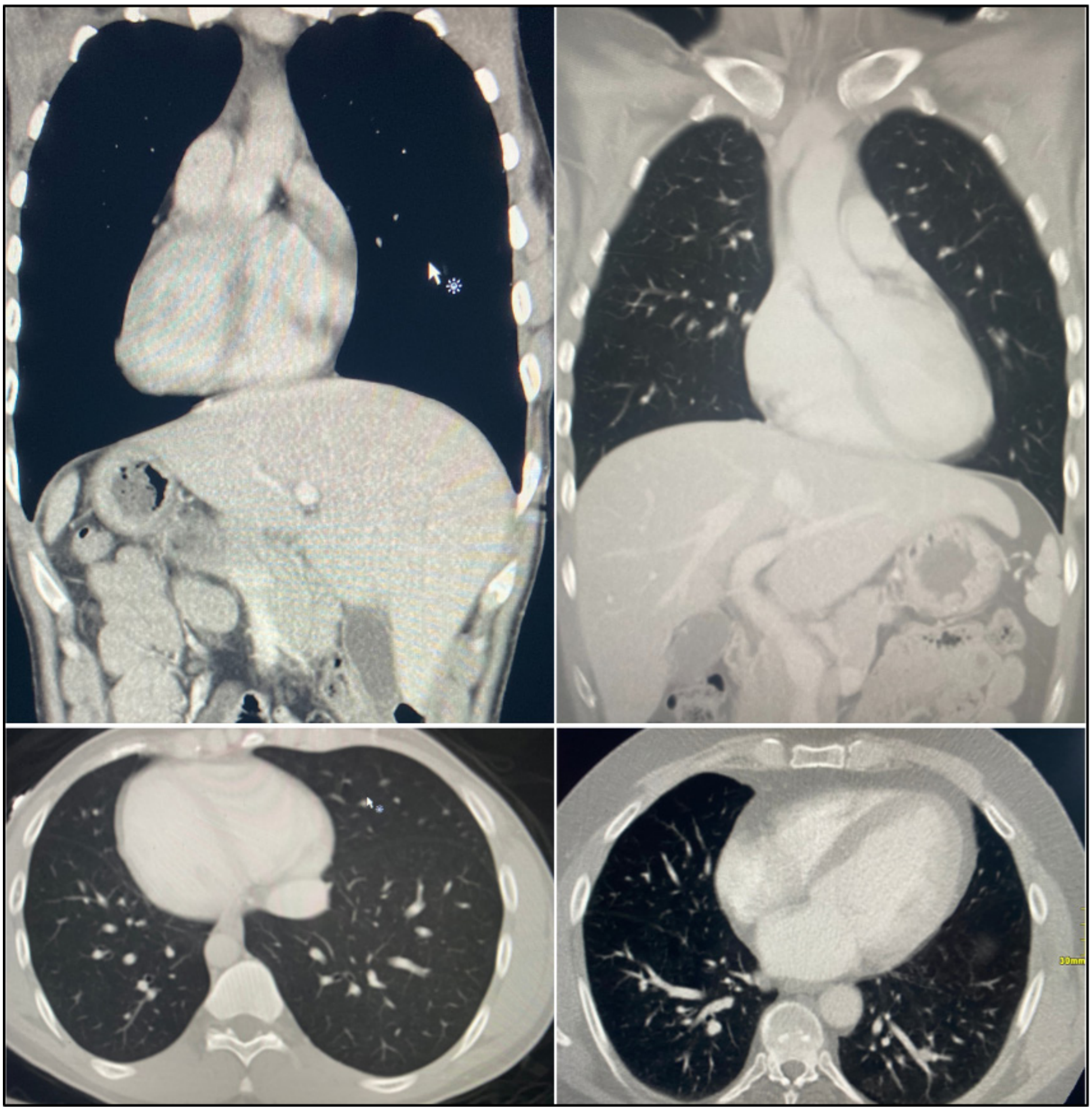

Figure 7: Coronal and axial CT images of situs inversus. Left upper and lower images show mirror-image reversal of the heart and aorta resulting in dextrocardia and right-sided aortic descent. In the abdomen the liver is in the left upper quadrant where the spleen usually resides. Right upper and lower coronal and axial images show normal situs of chest and abdominal viscera.

The mirror-image anomalies of situs inversus present as a dynamic continuum that takes origin in the heart and arterial system: while many have dextrocardia in the absence of situs inversus, few have situs inversus without dextrocardia. There is no mechanism by which a random genetic mutation could cause the embryonic structures to spontaneously 'flip' in the left-right axis. Such mirror-image phenomena more likely originate at the interface between efficient or formal layers of causation.

Sometime around 8-10 weeks of gestation the fetus begins to move: course truncal and head movements at first, followed by yawns, mouthing movements, stretches, as well as organized limb and finger motions not unlike the patterned automatisms seen in various seizure states

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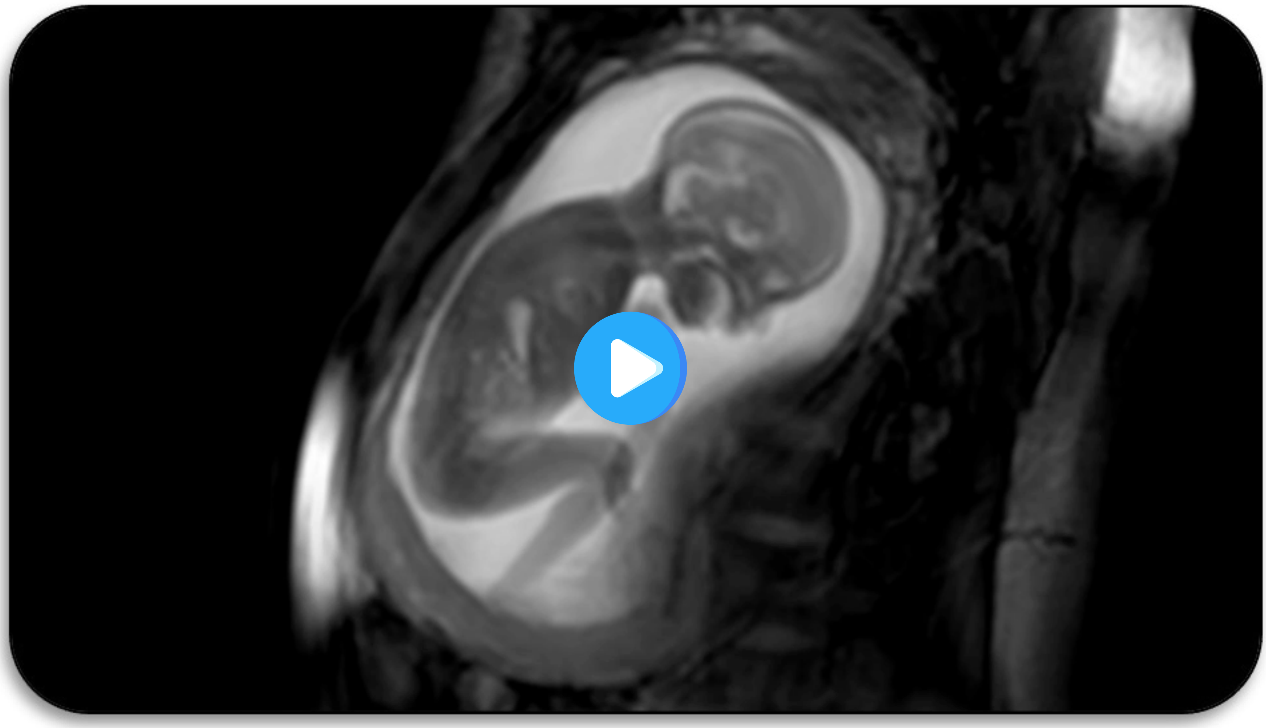
(**Video Clip 6**). These primal events mark the emergence of the consciousness field which requires a pre-existing, intact neural substrate as well as the continued function of the cardiovascular system. Absent either and there is no conscious awareness or automatic movements.



Video clip 6: MRI of early fetal development circa 16 weeks gestation.
(From: https://www.youtube.com/watch?v=djJnsC_Cddl)

The consciousness field, well-described by ancient writers and known as *psuche*, meaning 'living being', corresponds to Aristotle's sentient soul. Contrary to Descartes' mind, the sentient soul/consciousness field is distributed throughout the body, entering via the heart and attaching itself to the entire nervous system. Its functions include sensation (*aesthesis*), feelings and emotions (*pathé*), and cognition. But this compels us to redefine exactly what we mean by the terms 'consciousness' and 'awareness'.

According to the dominant brain model, sensory nerves relay their impulses to the brain where, by unknown means, it generates representations of the event and incorporates them into the consciousness field while at the same time creating this overarching state of awareness. In the case of pain, say, in an arm or leg, the nerve impulses supposedly ascend to the brain where the event is registered and assigned to its proper bodily location; somehow through this process one becomes aware not only of the pain but its quality and cause. How is this so different from Descartes' camera obscura?

The most confounding example is phantom limb syndrome. After the traumatic loss of a limb, many individuals, up to 70-80%, continue to feel distressing sensations associated with the lost limb. Often, they perceive movement [151-153]. Neuroscientists claim that after amputation a remapping of neuronal relationships in the cortex, mediated by a mysterious property they call

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'neuroplasticity', leads to reconstitution of the lost sensation. The phantom sensation, essentially, is nothing more than an illusion created by the brain [154].

But this dominant brain logic is riddled with inconsistency. Rather than an apparition manufactured by the brain, it seems more likely that the phantom sensations originate in the sensory field that still resides where the limb used to be. What one is feeling is pure primal awareness which registers events in real-time exactly when and where they arise. Sensation represents a primary and irreducible attribute of being.

The Aristotelian account, based on the sentient soul, would suggest there is a gradation in the refinement of sensory experience with touch or tactile sensation being the most immediate and concrete while higher sense faculties like vision and hearing mediate more general aspects of experience. And the brain itself is concerned with what we could call 'awareness of awareness', i.e., reflective consciousness, and mediates functions like thought and cognition.

Even more problematic for the dominant brain hypothesis are emotions which, since ancient times, were associated with the heart. When one is overcome by fear the body reacts suddenly and involuntarily: the heart beats rapidly, the stomach churns, muscles tighten, skin becomes cold and clammy, the body trembles. The responses to emotions like fear, rage, shame, or laughter are mediated through the movements of the heart and blood affecting the skin, muscles, and glands. Sherrington, perplexed by what he called the 'bodily resonance' of emotion, claimed they are excitations produced by a 'train of ideas' originating in the brain [155].

Decades earlier psychologist William James argued that feelings and emotions are inseparable from their bodily expressions [156]. He claimed that the temporal sequence science ascribes to feelings and emotion is backwards. Logic says we tremble because we are afraid. Rather, he contended, we are afraid because we tremble. James distinguished between the emotion-as-feeling, the subjective experience that resides in body, and emotion-as-idea, the awareness of experience centered in the head. One is mediated through unconscious processes, the other through conscious ego.

Given such considerations, what are we to make of pure sensory seizures, described lyrically by Mackay as 'the many queer attacks . . . the epigastric possession that rises and engulfs the mind . . . the clanging sound or the visual apparition . . . the inexplicable tingling that creeps from hand to elbow to shoulder . . . the unwilled twitching that marches on from joint to joint . . . the strange odor and weird affect . . . the paroxysmal waking dreams . . . the complex, inept bits of behavior, later unremembered' [157].

Or how do we regard emotional seizures characterized by sudden alterations in mood or emotion without accompanying subjective awareness of such affective expressions? Such automatisms may manifest as acute onset of fear or anxiety, bursts of laughter and giggling, or crying episodes accompanied by tears, sobbing, and facial expressions of sadness without conscious subjective awareness of the event [158-163] (**Video Clip 7**). To say the brain 'creates' these states is a bridge too far. They are properties of the sentient soul and their expression can only be related to disturbances in the conjoined resonance field generated by the heart and nervous system.

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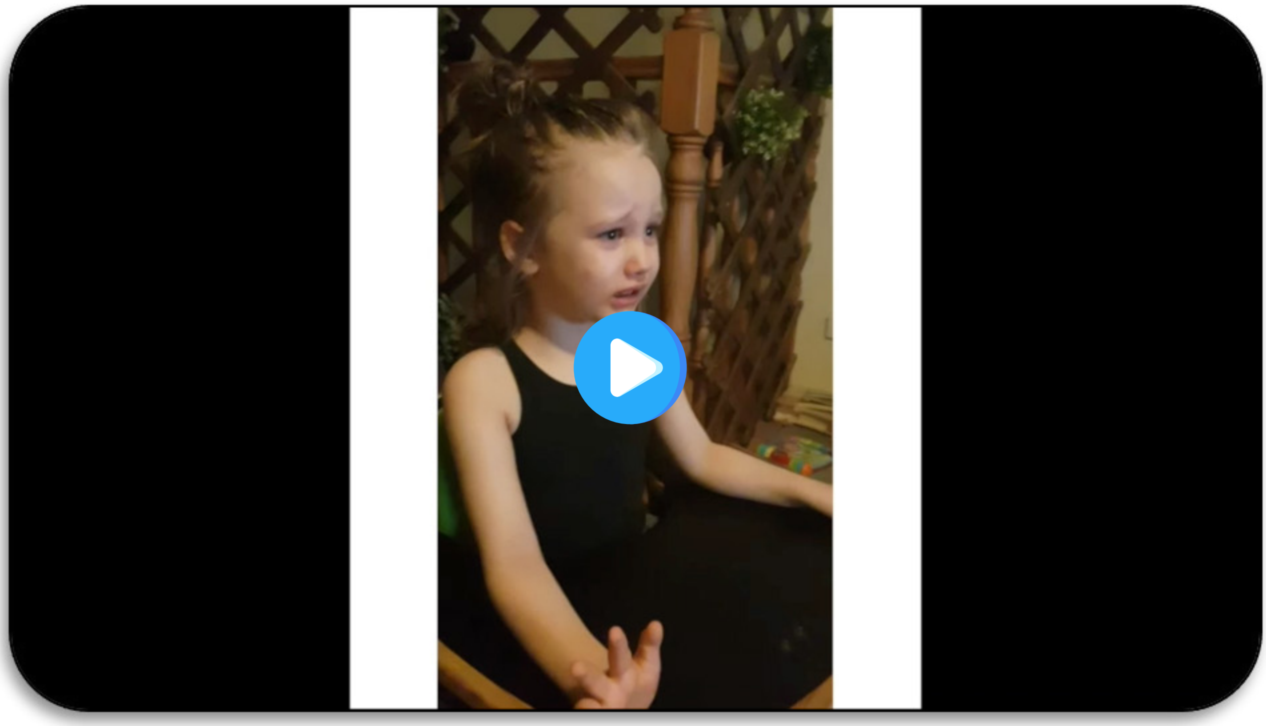

Video clip 7: Emotional seizure. (From: https://www.youtube.com/watch?v=qnjx_WOJmLs)

The coming together of awareness into a coherent 'space' centered in the head, i.e., conscious ego, was ascribed by Aristotle to the faculty he called *phantasia,* later known as imagination, also associated with the sentient soul. Imagination, i.e., the primary capacity to form representations of one's subjective and objective experiences, also mediates the appearance of images associated with memories and dreams. It likely plays a central role in most seizures particularly in auras and sensory events.

But left completely out of the picture by modern scientific accounts is any reference to how such attacks are related to and impact the individual's subjective layer of being, the Self. When conscious one is aware of being aware and consciousness assumes an identity all its own. Conscious experience is suffused with a sense of Self, of I-doing, I-feeling, I-thinking, I-remembering.

Self, the numinous center of being, what Merleau-Ponty calls 'the living nucleus of perception' descends into and inhabits the morphogenic and sentient layers of soul. In the 3rd century AD, Plotinus, 'first philosopher of the unconscious', called this primal core of being the Intellect and regarded it as distinct from the two lower phases of soul [164]. He claimed that while it attached to the heart, it never fully descended into the body. Both Aristotle and Plotinus agreed that Intellect was the only aspect of soul that persisted after death and regarded it as eternal.

The traditional function subsumed by the Intellect or Self has been cultivation of insight and wisdom. In *Phenomenology of Perception* Merleau-Ponty assigns to the Self a triad of functions: attention, reflection, and understanding, each of which also manifest in conscious ego. What has been thoroughly disregarded in modern commentaries on the nature of epilepsy is that, regardless of the many different outward forms by which seizures

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present, the single unifying feature that ties them into a coherent class is incapacitation or diminution of these very attributes. And with impairment of such directive functions the consciousness field is only able to express variably fragmented lower states of being. This may well be what the ancients hinted at in their denomination of epilepsy as the sacred disease.

HEART FIELD & SEIZURE FORMS

If seizures represent transient states of uncoupling between adjacent organized layers of function and this, in turn, is related to energy deficiency or alterations in the resonance field, it stands to reason, given that the heart and vascular system are the source of the field, that one would observe corresponding changes in the cardiovascular system during seizures. Put differently: does the heart field influence the expression of seizures or, conversely, is it affected by seizure activity? The answer is resoundingly yes.

Seizure research has advanced dramatically in recent decades with the use of functional MRI (fMRI) and single-photon emission CT (SPECT) imaging which, contrary to EEG, assess functional states in the brain associated with seizures. Instead of registering fluctuating electrical currents they reveal alterations in blood flow and metabolism. And by combining these modalities with EEG one can get a fairly accurate picture of what is going on from a dynamic standpoint.

Generalized and partial seizures don't exist and never did [165, 166]. Like the dominant brain they were based on pure speculation. Generalized seizures were supposed to involve the entire brain but evidence indicates they result from activation and deactivation of selected neuronal networks [167-169]. This is to say that observed seizure behaviors reflect a disjointed 'turning on' of some pathways and 'turning off' of others [170-172]. Even in focal seizures changes in network activity occur well beyond the primary affected area. Moreover, in all seizure forms global alterations in blood flow either precede or coincide with seizure activity. What is cause and what is effect? Provocatively, fluctuations in electrical frequencies detected by EEG seem to correlate with blood flow [173]. Certainly, the relationship between slow frequencies and decreased blood flow has been established [174].

The most dramatic implications of this involve the so-called consciousness system. Using quantitative blood flow mapping techniques researchers observed areas of the brain, mainly in the frontal regions, that became active when subjects were in a passive state [175, 176]. Paradoxically these regions were less active during goal-oriented, outwardly-directed tasks. Called the default mode network (DMN), it is also activated when subjects are asked to remember past events or imagine future possibilities. Researchers believe this network supports self-referential and introspective activities as well as playing a role in integration of memory and language functions [177-185] (**Figure 8**).

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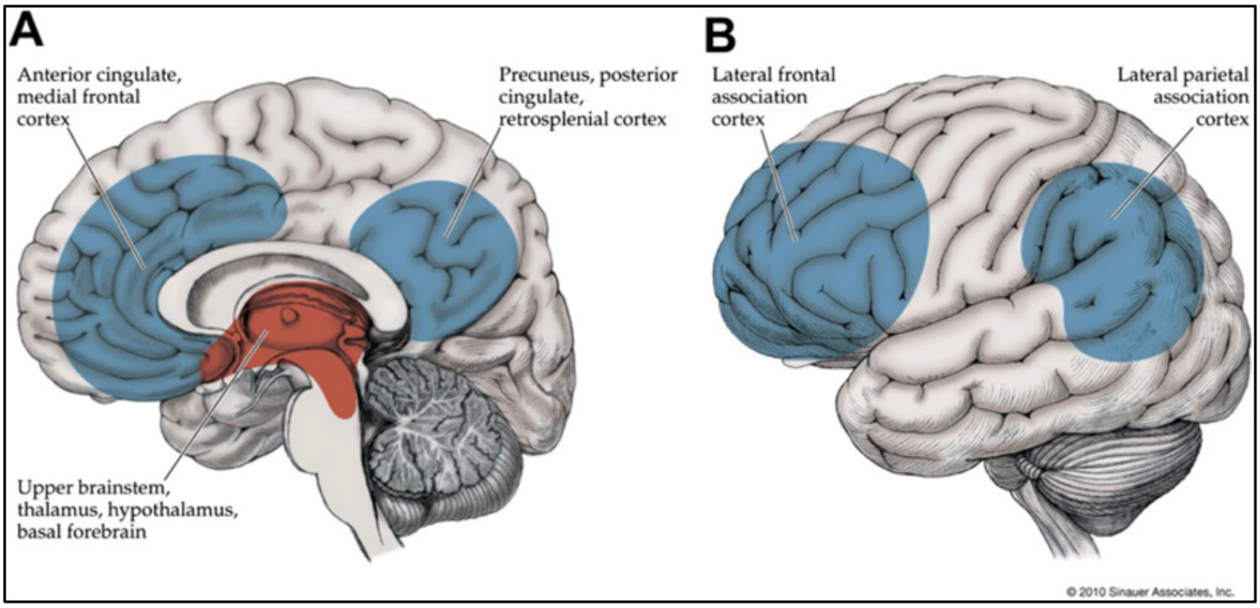

Figure 8: Anatomic regions involved in the so-called consciousness system that mediate such functions as attention, awareness, integration of memory and language, and aesthetic judgments. (A) Medial view of the hemisphere showing cortical (blue) and upper brainstem and thalamic (red) components of the system. (B) Lateral cortical components of the consciousness system. (From: Blumenfeld H. Neuroanatomy through clinical cases. 2nd edition. Sunderland (MA): Sinauer Associates; 2010)

Intriguingly, this region also appears to mediate aesthetic responses to visual art perceived by the individual as appealing and is associated with a sense of being moved or 'touched from within' [186-190]. In the *Enneads* Plotinus assigns the perception of beauty to the Intellect [191]. He also claims that Intellect mediates memory and intuition. As Plotinus (among others) seated the Self in the heart, one is led to question as to whether, during introspective states, activation of the DMN opens a direct communication with the Intellect, now widely referred to as the Unconscious.

Much has been made of the role of neural networks in consciousness functions while the contribution of arterial blood flow has been roundly ignored. The cerebral hemispheres are supplied by three distinct arterial divisions: the anterior cerebral arteries, which supply the frontal regions and the medial aspects of the hemispheres (including the DMN); the middle cerebral, which supply most of the outer surfaces of the temporal and parietal regions, encompassing mainly motor and sensory functions; and posterior cerebral, which supply deep interior structures like the upper brainstem and thalamic regions (**Figure 9**). It doesn't seem unreasonable to assume that as blood flow increases in one arterial territory there should be reflexive decreases another.

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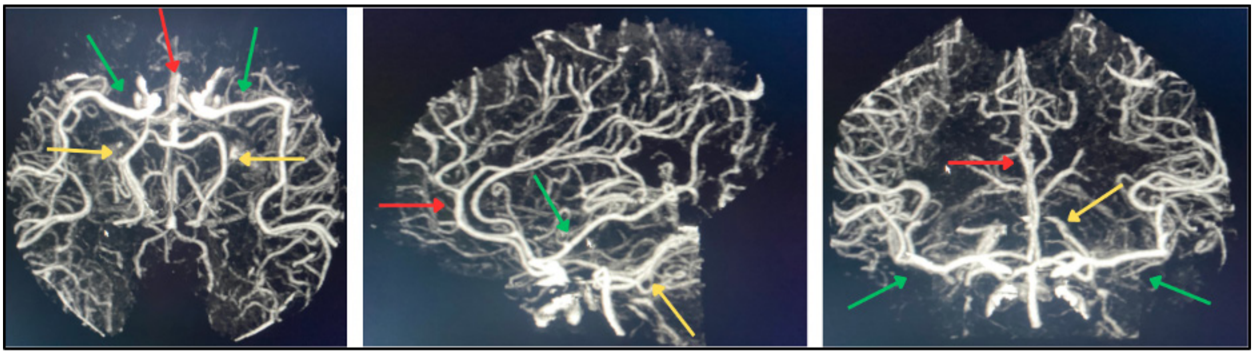

Figure 9: Reconstructed CT angiographic images of the intracranial circulation in (A) axial, (B) sagittal, and (C) coronal projections showing anterior cerebral (red arrow), middle cerebral (green arrow), and posterior cerebral (yellow arrow) arterial territories.

Researchers have long puzzled over why supposedly 'focal' temporal lobe seizures should impair consciousness [192, 193]. Dynamic alterations in temporal lobe seizures appear similar to those of absence and generalized tonic-clonic types: all have abnormal increased blood flow signal in the upper brainstem and thalamic regions and decreased signal in the DMN [194-212] (**Figure 10**). Researchers advanced the 'network inhibition hypothesis' which claims that temporal lobe seizures impair DMN activity by disrupting the thalamocortical arousal system which secondarily causes slow wave formation and impaired consciousness [213, 214]. But such phenomena can equally be explained on the basis of shifts in blood flow and energy distribution.

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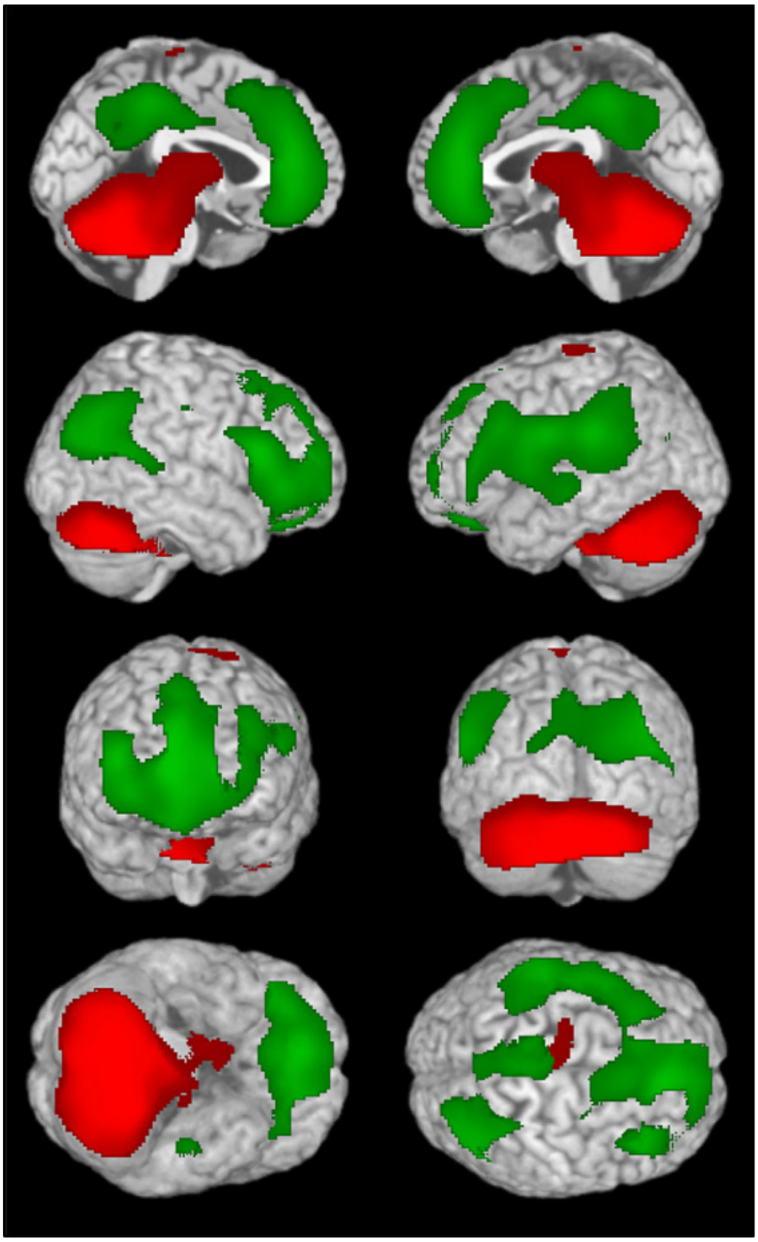

Figure 10: SPECT Imaging representations depicting hemispheric and cerebellar changes in blood flow distribution during and following generalized tonic-clonic seizures. Increases (red) in blood flow in cerebellar and thalamic regions correlate with decreased (green) flow in bilateral frontoparietal regions. Cumulative data obtained during 59 seizures in 53 subjects. (from: Blumenfeld H, Varghese G,Purcaro MJ, et al. Cortical and subcortical networks in human secondarily generalized tonicclonic seizures. Brain 2009;132:999–1012)

One of the peculiar findings seen with various seizure types is epileptogenic activity in the identical region of the opposite hemisphere, known as the 'mirror focus' phenomenon, the existence of which would seem to point in the direction of a vascular etiology [215-217]. And yet scientists continue to seek answers within the maze of neural networks. Here we encounter the problem science historian Thomas Kuhn called 'paradigm-induced blindness'. Scientists only 'see' what their conceptual framework conditions them to see. And as we just examined this pervasive brain-centered perspective has defined historical roots.

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In the early 20th century neurophysiologist J. N. Langley coined the term 'autonomic' to denote a distinct and independent system of nerves concerned with regulation of organ functions throughout the body. He recognized that the autonomic nervous system (ANS) functioned on an involuntary basis independent of conscious awareness. In his descriptions Langley was strongly swayed by Sherrington's dominant brain theory and posited a one-way outflow system that carried directive impulses from the brain to the body below. He specifically denied the presence of sensory nerves or reflex arcs in this system [218].

But Langley's formulation of the ANS, laden with inconsistency and error, has come under attack in recent decades. Researchers found both sensory and motor fibers in sympathetic nerves and the different nerve fibers communicate with one other indicating the presence of reflex arcs [219-230]. This indicates that processing, integrating, and responding to sensory information occurs throughout the body and not just in the brain.

Foremost among critics was Alberto Malliani who spent decades studying interactions between the heart and the ANS. In 1997 Malliani pointed a finger at contradictions in Langley's formulation: how can the ANS be considered at once independent while at the same time controlled by the brain? How can the reflex arc be considered a fundamental function of the nervous system and yet be excluded from the ANS? And if the brain is responsible for integrating functions in the body why is our knowledge of these processes so fragmented? Malliani argued that a radical revision of ideas was urgently needed [231].

More provocative yet is a rising tide of evidence supporting the central role of the heart in organizing ANS dynamics. Numerous studies document a network of sensory nerves in the heart corresponding to Aristotle's sense of touch [232-237]. In *Neurocardiology* (1994) J. Andrew Armour details a complex nervous system in the heart, what he calls the 'heart-brain', that initiates ANS reflexes [238]. The intrinsic cardiac nervous system regulates and modifies the motions of the heart during its cycles of contraction and dilation. It seems inescapable that seizure-related changes in brain blood flow patterns are mediated by the heart. Not only do such phenomena refute Langley's ANS hypothesis but overturn Sherrington's long-entrenched dogma of the dominant brain. Three decades later and scientists have yet to incorporate such evidence into their formal theory structure. It's all still cells, genes, and molecules. Atomism prevails.

Cardiovascular involvement during seizures is very common [239-247]. A rash of cardiac rhythmic disturbances, seen in up to 60-80% of seizures, have been described including tachycardias, bradycardias, asystole, A-V conduction blocks, as well as atrial and ventricular fibrillation. A wide range of autonomic symptoms not limited to the heart have been reported before, during, and after seizures, including difficulty in breathing, gastrointestinal disturbances, urinary incontinence, as well as skin and pupillary changes [248-257]. Seizures are systemic disturbances [258].

While the pre-ictal state is characterized by hyperexcitability and decreased electrical thresholds in susceptible regions, in recent years researchers have begun to grapple with another intriguing and counterintuitive question: Why do seizures suddenly stop? What effects their termination?

A 2009 study, using magnetoencephalography (MEG) stimulation, found marked reduction in cortical excitability following seizures that persisted for up to a day, suggesting a functional state of hyperpolarization [259]. EEG changes during the post-ictal state include appearance of slow delta

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waves which can persist for hours. During this period subjects often experience confusion and amnesia which can be more disturbing than the seizure itself. Hyperpolarization is a functional state that can only be explained on the basis of an influx of energy into affected networks. Once again, the question arises: from where does the energy originate?

That the post-ictal milieu is functionally hyperpolarized goes a long way in explaining post-ictal generalized EEG suppression (PGES) and sudden unexplained death in epilepsy (SUDEP), two common phenomena associated with the post-ictal state for which medical science has no compelling explanation [260]. PGES, absence of normal EEG activity following seizures, is associated with immobility, respiratory depression, and alterations in consciousness [261-265]. ANS changes associated with seizures correlate with the appearance of PGES [266]. This dynamic amounts to little more than robbing from Peter to pay Paul.

Even more compelling is the SUDEP phenomenon, the most common cause of death in the epileptic population, which usually follows generalized tonic-clonic seizures [267-271]. More common at night during sleep, it is said to result from autonomic dysfunction leading to respiratory or cardiac arrest. Underscoring its dynamic origins was a 1995 study linking SUDEP to abrupt, sudden increases in geomagnetic activity precipitated by solar flares [272]. A later study found a much higher rate of sudden death in epileptic rats exposed to nocturnal magnetic fields that simulated the lethal geomagnetic activity [273]. Given these associations it is difficult to refute either the energetic basis of seizures or the mediating role of the heart field in their expression.

THRESHOLD AND SUSCEPTIBILITY

The association between flashing lights, rapidly oscillating image patterns, and seizure induction has been recognized since antiquity. Platonic philosopher Apuleius, living in 2nd century Numidia, reported a seizure event while watching a spinning potter's wheel. Late 19th century neurologist William Gowers described a female subject who experienced seizures upon stepping into bright sunlight.

In the 1980s and 90s reports described a rash of seizures induced by video games, computers, and TVs which became known as 'video-game epilepsy' [274-276]. The most infamous of these, the Pokemon incident, named after a Japanese children's TV show, occurred in December, 1997. A cartoon depicting a rocket launch with rapidly oscillating red and blue colors is said to have induced seizures in some 500-600 school-age children, the majority of whom had no seizure history [277]. Photic-induced seizures are triggered by visual events, usually flashing lights, but also complex patterns like checkerboards, fencing and gridlines [278-281].

Even more common than photic-induced seizures is photosensitivity in which individuals, provoked by light stimuli, develop abnormal EEG responses with bursts of cortical spike wave discharges called photoparoxysmal responses [282-285]. When subjects with normal neuronal thresholds are exposed to pulsed light sequences they develop synchronized phase-locked EEG activity, known as visual-evoked potentials, in the occipital regions which do not extend beyond the population of activated sensory neurons.

Light-sensitive individuals, on the other hand, develop characteristic spike wave discharges that spread by ephaptic coupling into adjacent brain regions. Such hyperexcitability has been attributed

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to decreased threshold potentials in susceptible neuronal territories [286-288]. EEG screening programs conducted by various national Air Force agencies on prospective pilots suggest that ~0.4-2.4% of men aged 17-25yo develop abnormal PPR rhythms during a light stimulus test [289-291]. The rate is thought to be higher in the general population. The PPR can be elicited in 50-90% of epileptic individuals [292-296].

MEG studies report increased cortical excitability in the 24-48h period preceding seizure onset indicating periods of heightened susceptibility [297-299]. Once again, abnormal spike wave complexes, known as 'interictal epileptiform discharges' (IEDs), often appear during such periods [300-304]. First identified in the 1930s, IEDs are regarded as a hallmark of epilepsy and while researchers remain uncertain as to their significance they are widely believed to reflect cortical hyperexcitability. The frequency of IEDs increases after sleep deprivation and is higher during NREM sleep which also has the highest tendency for seizures during the sleep cycle [305-311]. Such heightened susceptibility, once again, is attributable to diminished amplitude of the electromagnetic wave function. We are thus justified in speaking of an epileptogenic or pro-seizure milieu.

Such EEG phenomena explain the relationship between sleep disturbances and seizure frequency [312-318] Epilepsy and sleep disorders are frequent bedfellows. Studies suggest that up to 40% of adult epileptics have sleep disturbances. The relationship is bidirectional. Sleep habits affect epilepsy just as seizure activity impacts sleep. Sleep architecture in epileptics is altered by frequent awakenings and shifting of sleep stages. Nocturnal seizures decrease total sleep time and REM sleep in some instances by up to 50%. The flip side of sleep fragmentation is excessive daytime drowsiness and decreased vigilance. This implies decreased amplitude of the cyclical wave function between deep sleep and full wakefulness. As this deteriorates seizure frequency increases.

Loss of threshold also explains the long-recognized relationship between stress and epilepsy [319-325] Emotional stress consistently ranks as the most commonly reported seizure precipitant independent of the type of epilepsy. Subjects with refractory epilepsy report stress more frequently than individuals whose seizures are well-controlled. It has been reported that prolonged stress early in life predisposes to the development of epilepsy [326]. This relation is exacerbated by stress hormones like cortisol which impacts neuronal excitability. Stress alters gene functions critical in the maintenance of brain regeneration [327].

Loss of threshold also mediates the complex interaction between epilepsy and depression [328-333]. Hippocrates alluded to this bidirectional relationship when he wrote 'melancholics ordinarily become epileptics and epileptics melancholics'. Depression is the most common comorbid psychiatric condition associated with epilepsy affecting up to 60% of epileptics. A study of newly-diagnosed adult-onset epileptics found that a history of depression was 6-fold more frequent than in the general population. Another study found that epileptics were 3.7-fold more likely to have experienced depression prior to their diagnosis than the general population.

With regard to the threshold question, then, the clustering of epilepsy, sleep and behavioral states such as stress and depression suggests that far from being a disturbance of local neuronal populations, seizure disorder and epilepsy represent a defect in the functions responsible for the transition between sleep and wakefulness, i.e., the same processes involved in the generation and maintenance of the consciousness field.

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Phenomena like photosensitivity suggest there is a large pool of susceptible individuals in the population prone to seizures and emphasize the need to develop new therapeutic strategies. The recognition that light, when administered at certain frequencies, is capable of inducing neuronal instability or seizures raises the intriguing question as to whether, when applied under different conditions and frequencies, it is capable of stabilizing membranes and diminishing or preventing seizure occurrence.

Population-based studies found significantly higher epilepsy rates in subjects born during winter months in the northern and southern hemispheres compared to those born at other times [334, 335]. Another study tracked seizure occurrence patterns over the course of a year at an inpatient epilepsy ward and found that seizures were less likely to occur on bright, sunny days than on cloudy days independent of season [336]. This raises questions as to the potential benefits of light treatment in subjects with refractory epilepsy. Studies already support the efficacy of phototherapy in conditions like seasonal affective disorder and depression not to mention neonatal hyperbilirubinemia.

Perhaps no single idea in the history of medicine has held a more powerful sway on therapeutic practices than the notion that all disease phenomena are composed of two distinct sets of processes, the direct effects of injury, i.e., the predisposing cause, and the healing response. In traditional therapeutics injurious agents were to be eliminated while the corrective response was to be stimulated by imitation of the conditions that produced the dominant symptom, a doctrine known as 'similars cure'. As symptoms result from natural causes it only made sense they should be treated by natural means [337].

Since the time of Hippocrates, the notion of the simile and similars cure, that like cures like, was a central tenet in medical therapeutics: diseases were provoked and healed by the same mechanism. The ancients regarded disease and health as contrary states, like hot and cold, day and night. The fact that seizures can be elicited through photic stimulation suggests that light or electromagnetic fields might be used in their treatment. No longer just metaphor light becomes simile, directly impacting the dynamics of seizure generation as well as pointing to the orchestrating role of light in the transition between sleep and waking states, which amounts to illumination of the consciousness field.

SACRED DISEASE REVISITED

Evidence we have examined suggests that the ancient appellation 'sacred disease' was fitting and appropriate given its manifest signs and symptoms and, furthermore, corresponds to the stratified vertical causal hierarchy elaborated by Aristotle and later Plotinus that came to rationally define the ancient cosmology. This organic knowledge tradition thoroughly influenced ancient ways of thought for centuries and persisted well into the 17th century until Enlightenment scientists rejected it without ever refuting its authenticity.

For over three centuries' scientists, armed with their prized experimental method, have fumbled and bungled their way, experiment by experiment, to construct what is now regarded as their highest achievement, the 20th century molecular/cellular paradigm, the sole basis of which resides in the piecemeal analysis of material causes.

Littered with inconsistency and contradiction, therapeutic strategies based on suppression and inhibition, it has utterly failed to meaningfully impact the problem of human disease. Indeed, one might argue that, on the basis of its flawed understanding of human nature, spawned by a rash of interpretive errors, medical science has very much facilitated and encouraged this expanding

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human dilemma. Epilepsy is prima facie evidence of the dismal failure of the experimental method and the scientific form of inquiry which, in the end, benefits few apart from those who propagate and wield this artificial and useless system of knowledge.

Given the miserable track record of current therapies in the treatment of epilepsy as well as the burgeoning epidemic of chronic disease that now spreads unchecked across the globe, contemporary societies would be well served to channel their resources into cultivation of new forms of knowledge as well as treatment modalities which more effectively address the dynamic nature of human disease states.

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