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A Gene x Meme x Environment Interaction Model of Mental Illness

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Abstract

Background/Aims: Memes, like genes, are replicating packets of information. Genes make proteins, memes make thoughts and behaviors. Memes are memory that became portable in the course of evolution through speech and written words.

Methods: Memes consist of both memory formed by experience and information the brain absorbs. Memes reside as reinforced neural clusters in the brain, and undergo Darwinian natural selection. Genes do not interact with environment directly, but through memes.

Results: In vulnerable individuals, childhood stress may introduce pathogenic memes (e.g. helplessness) that take up residence in the brain. Exposure to stress memes in adulthood may induce a brain state favorable to the proliferation of resident pathogenic memes, which then may overwhelm the brain, resulting in a mental illness. Treatment of mental illness should be both biologic (gene-oriented) and memetic, i.e., detoxifying and neutralizing the toxic memes. Psychotherapies may be meme-specific (e.g., cognitive-behavioral) or broad-spectrum anti-meme therapies (e.g. relaxation, meditation).

Conclusion: The concept of gene x meme x environment interaction opens up avenues for further development of both gene and meme-oriented therapies including the use of music, exercise, and virtual reality, etc. It also puts into perspective the role of early nurturance and the teaching of critical thinking in the prevention of mental illness.

Introduction

There has recently been controversy concerning the gene x environment interaction model of depression. Since the elegant demonstration by Caspi et al. of gene x environment interaction [1,2], other studies including a meta-analysis [3] failed to support the interaction. There is, however, abundant evidence that early experiences affect gene expression in the brain, affecting both morphology and physiology [4,5].

These data suggest that external environment does not directly interact with genes, but rather an individual's experience of the environment, i.e., memories of past experience interact with perception, forming new information that interact with genes in the brain. Such information resides in the brain as reinforced neural clusters, and their activity causes epigenetic changes of vulnerability genes. We will first discuss how information that interacts with genes has evolved to become the powerful replicator, meme, in this information age.

Evolution of memes from memory

In the course of evolution, the brain evolved as a specialized organ dedicated to processing memory, both learned and intrinsic (DNA), which in turn facilitated learning, survival, reproduction, and further enlargement of the brain. Learning through trial and error created memories that facilitated individual and species survival, and resulted in building bigger brains, but the memories themselves died with the organism until the brain developed imitation as a learning tool [6].

With imitation, which is robustly in evidence in primates and in songbirds, learned behavior (memory) could be transferred from one brain to other brains in the form of memes (which is a term coined by Dawkins [6], which I use here to denote any portable memory, i.e., information.) Chimpanzees could observe a bright chimpanzee cracking a nut with a stone, and this information could spread, but only to a limited degree. First, they had to be in visual contact with the bright chimpanzee, and second, the bright chimpanzee must engage in the behavior for the meme (how to crack a nut) to spread, and this presupposes that there are nuts and stones around. If chimpanzees had language, one who observed the behavior could describe it even when there were no nuts and stones, and such a meme could spread much faster and wider. Such was the case with humans.

With the development of written word, memes found an abode outside of brains. Now they could reside in patterns of indentations in clay or stone, or ink on paper, and eventually as electronic signals in magnetic tapes and optical media. Now, more memes reside outside of human brains than inside them, in printed form in libraries and homes, in electronic media, and in digital form in computers, CDs and DVDs, and in the cloud. The acquisition of language by homo sapiens was instrumental in memes' attaining dominance over genes for the first time on planet earth. In fact, memes in the form of moral codes have suppressed gene-derived sexual drive in many cultures, and memes in the form of scientific knowledge provides humans with the ability to control gene propagation.

Neural memes and evolution of memes in the brain

How exactly does a meme reside in the brain? Kandel described a sequence of events in long term memory formation in aplysia. With repeated stimulus of a neuron, a sequence of chemical reactions causes gene activation in the nucleus of the neuron, resulting in release of messenger RNA in a dormant form. Further stimulation of the neuron causes a prion-like protein, CPEB (Cytoplasmic Polyadenylation

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Element-Binding Protein), which is present in all synapses, to become activated (to an infectious form), which in turn activates dormant messenger RNA, which in turn makes protein to form a new synapse. The prion-like infectious form of CPEB infects adjacent CPEB, and thus perpetuates itself and the protein synthesis, maintaining and re-enforcing the new synaptic connection [7].

In higher organisms, the stimulus that reaches a neuron resulting in this series of events is itself modified in several interneurons which have their own connections, i.e., stimulus (perception) is modified by existing memory (memes). Furthermore, neurons are capable of generating impulses without external stimulus, which may stimulate and reinforce connected neural clusters.

Memories thus formed and residing in reinforced neural connections are the basis of memes. A reinforced neural cluster may be represented as a binary neural code [8,9]. In this sense, memory in the brain may be similar to memory encoded in the hard drive of a computer. How does memory become portable and thus a meme?

Originally, Dawkins pointed out that through imitation, memes are replicated in the brains of the imitators. As the replications are not always exact, memes undergo Darwinian natural selection and evolution by being copied inexactly by different brains. How about the memes within an individual's brain?

Edelman described Darwinian natural selection of certain clusters of reinforced neurons in the brain in somatic time [10]. Neuronal groups may be reinforced by signals from other similarly firing neuronal groups (forming memes) and thus gain survival advantage. One might say that neurons thrive on memes. When a competing meme becomes dominant, neural clusters underlying it are enhanced, i.e., better fed, with more synapses. Thus, some memes will become dominant with repeated exposure and rehearsal and proliferate, i.e., recruit other neuronal groups; others will become dormant, not forming new connections or recruiting others. The process resulting in new parallel connections may be seen to be a process of replication of the meme, a prion-like replication by contact through synaptic and/or dendritic connection. This is not to imply that one neuron serves only one meme. In fact, a neuron has many connections and may be a component of a number of different memes and mimetic connections. Meme replication in the brain, therefore, does not involve reproducing new neurons, but rather occurs through recombination of component memes in existing neuronal groups. Such replication may occur through meme-processing mechanisms such as cognition, often stimulated by the entry of new memes into the brain.

The brain, in my view, is more like the Internet than a computer, with redundant storage and constantly changing connections and storage, in which memes are constantly created, propagated, combined, disintegrated, mutated, and evolved. Like the Internet, there are many interconnected processing centers that execute these functions. Some of these functions may involve a threshold number of processing units and reach consciousness, others functions occur without reaching consciousness. Just like information on the internet, some memes stay dormant and others become activated and spread.

Cognition as meme processing

When a problem is perceived, that perception arouses interconnected memes that may be in some way related to or resembles it, be it temporal, sonal, visual, semantic, or symbolic. Then, the problem is recognized, and a process of meme manipulation occurs to deal with it – the process of cognition.

Cognition is the brain's activity of processing memes. This may involve comparing new memes with existing ones, juggling existing memes to make way for new memes, rearranging memes by combining or breaking down memes and reassembling them. When memes combine to form memeplexes, i.e., neural clusters forming a meme develop strong connections to another, these memes may become synergistic and powerful.

Most of our memes are unconscious, and have migrated into our brains through auditory (verbal and sound), visual (books, images), and other senses. In fact, the unconscious may be likened to a meme pool where memes generated from our genes, as well as memes that have invaded our brains, percolate vying to surface.

Many of our memes are mutually supportive and coherent; others are in conflict with each other. Some may be frankly toxic, e.g. "Die for me (the meme may be a god, a cause, a clan); Kill for me".

Some memes, such as clichés, jingles, rhythms, and melodies propagate particularly well because they are adaptive memeplexes, i.e., the rhythm or melody is coupled with words that by themselves may not be as catchy. Earworms, melodies that keep on recurring in the head to the annoyance of the individual, are an example.

Gene-based life has evolved over some 3.7 billion years to the present splendor and diversity. The rapid increase in memes parallels the rapid increase in brain size that began in earnest some 2.5 million years ago when *homo habilis ("handyman")* began to use stone tools [11]. *Homo sapiens* emerged some 200,000 years ago, and in this eye-blink of geologic time, memes have built cultures, language, ethics, religions, ideologies, art, and science that have all evolved in a Darwinian fashion.

Memeplexes, development, and psychopathology

Why are our brains full of thoughts? According to Blackmore [11], the answer lies in the fact that memes are replicators, and the thoughts we have are expert replicators that survived Darwinian selection.

While most of the memes in our brains come from outside of the brains, some memes are created or cobbled together in new combinations within our brains in the form of new memeplexes. Our brain is full of memes and memeplexes that we have acquired over time. Some examples of memeplexes include : "I am intelligent", "good", "evil", "health", "God", "Devil", "socialism", "psychiatry", etc. Memeplexes may be complexes of ideas, sounds, and other perceptual memories, e.g., songs, scenes, posters, jingles.

A person is the net result of gene x meme x environment interaction that we call development. Except in rare cases where the environment interacts directly with genes as with environmental toxins and climate, genes interact with memes in the brain, which may have been absorbed directly from the environment as information, or may have been induced through experiential learning. Some newly introduced memes may conflict with existing memes in the brain, and may either die or become dormant (unconscious). Others may combine with existing dormant memes and activate them.

While the aggregate of these memes and memeplexes constitute our personalities, some such acquired memes are pathogens, and in interaction with genes and other "host factors" may cause mental illness. Treating such an infection may require the equivalents of either

a pathogen-specific antibody or a broad-spectrum antibiotic therapy. Prevention may also be possible through appropriate immunization.

Gene x Meme x Environment Interaction in the Pathogenesis of Mental Illness

Depression

Genes may create an environment in the brain that is more hospitable to certain types of memes than others. For example, in the presence of the short allele of the serotonin transporter promoter gene (5HTTLPR), the amygdala tends to be more sensitive to threatening stimuli (memes) [4,5]. In spite of the gene, if the child experiences abundant nurturance, the gene may be turned off. On the other hand, if the child is mistreated, the brain will respond with increased fear, anxiety, and helplessness, generating corresponding memes, which are likely to epigenetically activate the vulnerability gene. Such a brain would be more susceptible to infection by depressive memes and memeplexes coming from social interactions, learning, and even the media. A stressful event in adulthood may then infuse the brain with a massive dose of depressive memes. Thus, a brain that is already inhabited with a large number of depressive memes (most of which may be unconscious) may be overwhelmed by addition of new infection resulting in a depressive syndrome, a state of total control by the depressive memes (Figures 1 & 2).

In drug-induced depression, the drug attenuates the brain's ability to suppress already resident depressive memes which then multiply as well as making the brain to be more accepting of new depressive memes.

Bipolar disorder

Here we have an example par excellence of two groups of memes vying for control, and when a permissive physiologic environment occurs, takes over. The permissive physiologic brain state is of course dependent on gene x meme interaction. When each group is held in check, euthymia prevails.

Anxiety

Anxiety is an evolutionarily adaptive danger-signaling mechanism essential for survival. Like a smoke-detector, genes for anxiety sensitivity would have been selected for in ancient times [12]. It is natural, then, that memes associated with anxiety would easily replicate, such as

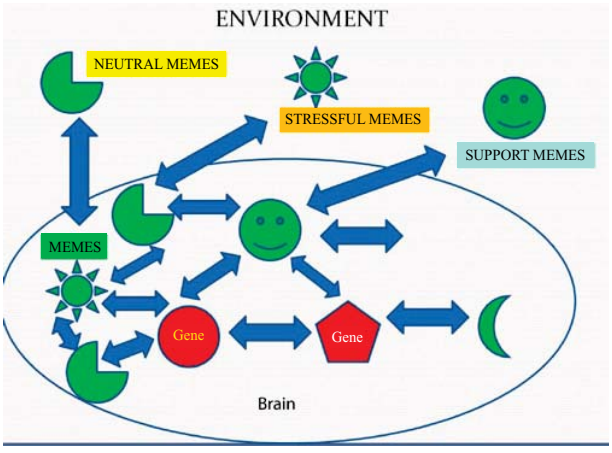

Figure 1: Gene x Meme x Environment Interaction.

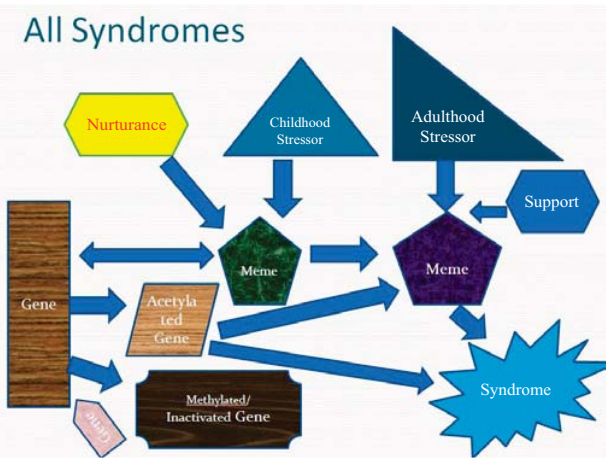

Figure 2: All Syndromes: Genes interact in childhood with memes formed by stress and nurturance, resulting in their being turned on (acetylated) or off (methylated). In adulthood, the active vulnerability gene interacts with memes influenced by stress and support, potentially resulting in syndrome.

"avoid the dark (jungle)", "avoid people with angry expression", etc. The meme would be particularly abundant in individuals who grew up in an environment where such memes thrived, as in poor and violent neighborhoods. Children with vivid imaginations may also replicate anxiety memes transmitted through folklore and media. Such memes may lie latent until a stressful event awakens them.

Paranoia, delusion, psychosis

A proliferation of anxiety memeplexes coupled with hypervigilance, which may also be genetically selected for [13], as well as influences by stress hormones, may give rise to paranoid memeplexes, i.e., the cause of the anxiety is rationalized and externalized, as "The FBI is watching me", "The Mafia is out to get me", etc.

Delusions, paranoid or otherwise, represent rampant proliferation of belief memes that provide an explanation for bodily sensations (e.g. discomfort, pain) or anxiety that may have arisen from stress, either from a conflict among resident memes attempting to achieve dominance or from the environment.

In psychosis, memeplexes concerning how an insane person behaves determines the form and content of psychotic symptoms. Psychosis is a final common pathway phenomenon where the brain state determined by gene x meme interaction and stress sets the stage for the functional takeover by the non-dominant primary process mode of being, as in a dream state. The content of the hallucinations and delusions are determined by the latent meme population, and naturally conforms to the cultural norms concerning psychosis. Thus, in cultures where religious memes are predominant, god and devil delusions and hallucinations predominate; the space age brought the extraterrestrial aliens into our delusions and hallucinations, and the computer age, computer chips implanted in our brains.

Obsessive compulsive disorder

As in the case of neoplasm, some memes and memeplexes may multiply uncontrollably under favorable brain conditions, such as a dysfunction of the basal ganglia. Such memes may be mutations, for example, when a conscious meme forms a memeplex with an unconscious meme, both may multiply uncontrollably. Compulsions

may be memes that form memeplexes with the obsessive memes, often to hold the obsessive memes in check (but resulting in mutual reinforcement and replication).

Posttraumatic stress disorder

This may be likened to a tumor of event-related memes. In massive traumatic stress, there may be an invasion of massive amounts of memes both representing the trauma (visual, auditory, tactile perceptions) as well as the meaning of the trauma (anxiety/fear memes, anger memes, regret memes, guilt memes). The massive infusion of memes results in massive stress hormone activation.

Hippocampus plays an important role in shutting off the HPA activation – any damage or atrophy of the hippocampus attenuates this, resulting in a prolonged HPA activation to stress [14]. Certain types of acute stress and many chronic stressors suppress neurogenesis or cell survival in the hippocampus. Glucocorticoids, excitatory amino acids acting on NMDA receptors, and endogenous opioids mediate the suppression [15]. Stress also affects the shape and abundance of dendrites in the hippocampus, amygdala, and prefrontal cortex. Generally, stress results in retraction and simplification of dendrites.

Thus, stress hormones tend to disconnect incoming memes from existing memes (memories) containing resident protective memes, allowing unchecked replication of newly introduced stress memes. These unchecked stress memes find every opportunity to reinforce them and replicate as in flashbacks and nightmares. Hypervigilance and avoidance in PTSD (Post Traumatic Stress Disorder) may be compensatory mechanisms to reduce the stress meme replication.

Psychosomatic illness

Ross postulated that a person becomes vulnerable to "psychosomatic memes" when in distress [16]. He writes, "the anguish of distress compels the sufferer to give it a name…a meaning…Like a virus that incorporates into a cell by fitting a forged protein into a cell receptor, a psychosomatic meme incorporates into a host by providing the "key" to the suffering".

Explanatory concepts of symptoms and disease are all memeplexes and undergo evolution within and across cultures.

Somatic sensation may be amplified by memes ("I have a serious disease") to the point of hypochondriasis. Psychosomatic memes may be epidemic, as in the case of pseudo hypoglycemia in the 1970s [17].

Personality disorders

Genetic personality disposition may be particularly hospitable to certain memes and not others. In Borderline Personality, epigenetically determined selective processing bias of the amygdala and hippocampus toward negative emotions and fear [18-20] may provide fertile ground for anxiety and depressive memes, and belief memes such as "the world is unpredictable", "people are all good or all bad."

In antisocial personality, the predominant memplexes are "Rules be damned, my needs come first no matter what." "Other people are there to be used" "I am not responsible for what I do", etc. These memes may find a favorable environment in the physiology of the individual whose genes require greater than normal stress for anxiety activation [21]. In schizotypical personalities, there may be epigenetic environment conducive to a moderate proliferation of psychosis memes.

Multiple personality and dissociation

There may be genetic predisposition to dissociation, which may be an adaptive trait co-evolved with memes, i.e., non-dominant memes can spread during a period of dissociation. We all have competing memeplexes within us, but they are in a state of equilibrium so that we maintain a sense of self, drawing from the dominant memeplexes. Dissociation, or takeover by latent or non-dominant memeplex, may result when such an equilibrium is unstable, which may be in part due to developmental influences on brain structures as well as the infection of mutually contradictory memes that prevented the formation of moderating memeplexes, e.g., being good and bad is a matter of degree.

Chemical dependence

Memes that indicate drugs cure distress are perhaps one of the most successful memes. With the explosion of mass media and the internet, memes about drugs abound. A subset of these memes are the memes that suggest drugs are the means of escape from stress and daily worries, and are the means of finding ecstasy.

Memetic diagnosis and possible future developments

Cultural factors are known to be important in mental illness, but so far little more than lip service was given to them. The conceptualization of memes allows us to concretize cultural factors as the memes in the environment, and those that have taken up residence early in the brains of patients, often unconsciously. The task is then to take an inventory of the memes (especially those that are salient and pathogenic) and to deal with them appropriately, which may include neutralization, desensitization, augmentation, reciprocal inhibition, sanitization, etc.

A memetic conceptual framework suggests new diagnostic procedures, perhaps meme-analysis, meme-scan, and memography, which maps out the patient's conscious and unconscious resident memes. Such a procedure could utilize words, melodies, rhythms (anything that is a meme) presented in rapid succession calling for word association, at the same time measuring physiologic activation (e.g. skin conductance, heart rate) and functional brain imaging. In a sense, projective tests such as Rorschach and psychoanalytic free association already serve some of this role. Unlike psychoanalysis, the meme-analysis could be utilized directly in determining the need for specific meme-neutralization therapies as well as broad-spectrum therapies. Novel meme-oriented therapies may develop, such as particular tones or rhythms counteracting specific toxic memes.

Computerized meme-analysis should make this procedure efficient and cost-effective, and may suggest one or a combination of meme-oriented therapies for an individual.

Treatment in the light of gene x meme x environment interaction

Treatment should be geared to 1. Attenuating or reversing the brain state that is hospitable to pathologic memes, 2. Attenuating or eradicating the strength of the pathologic memes that have taken control of the brain, and 3. Regulating the memes in the environment is reducing noxious memes and increasing therapeutic memes.

Pharmacologic and surgical (e.g. deep brain stimulation) treatments are primarily geared to changing the brain state. Psychotherapies are essentially treatment modalities geared toward memes, but without the conceptualization of memes, they tend to be haphazard and imprecise and seem mutually exclusive or contradictory. Cognitive-Behavioral Therapy (CBT) comes closest to a more explicit understanding of

the memes, particularly when the underlying "delusions", which are pathogenic memes, are identified.

As with antibiotics, meme-oriented therapies may be classified into broad spectrum and specific therapies. Broad spectrum anti-meme therapies suppress replication of all memes through activities such as meditation, mindfulness, music, dance, and exercise. Specific anti-meme therapies include extant psychotherapies specifically geared to delusions, phobias, conflicts, etc. The concept of memes may lead to more specific and direct methods of identifying and neutralizing specific memes, for example, through introduction of counter-memes which may be in the form of images, melodies, or sounds. Virtual reality may be used to create conducive memetic environments, and avatars, images of oneself, may be used as memetic identification figures [22,23].

In this gene x meme x environment interaction model of epigenetic development, prevention must play a key role. Prevention of epigenetic changes that cause vulnerability to illness, such as childhood abuse, as well as prevention through strengthening of the effective meme-filtering activity of critical thinking through education is essential measures in preventing mental illness [24].

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