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EVOLUTIONARY ORIGINS OF BRAIN DISORDERS IN *HOMO SAPIENS SAPIENS*

Patricia A. Helvenston and Robert G. Bednarik
IFRAO, Caulfield South, Australia

Abstract

This paper proposes a relatively recent advent of the brain disorders such as schizophrenia, obsessive compulsive disorder and bipolar illness, in anatomically modern humans. We will systematically demonstrate that the phylogenetically newest areas of the brain, including those containing von Economo neurons, are also the areas that are involved in these illnesses as well as other neurodegenerative brain disorders such as Alzheimer's, Parkinson's and Huntington's disease. The evolutionary preservation of these disorders is imputed to conditions similar to those that gave rise to the recent neotenization of *Homo sapiens*; which is attributed to breeding mate selection becoming influenced by cultural constructs.

We consider some recent failed models of biological natural selection and conclude that as hominin evolution became increasingly moderated by non-Darwinian criteria (i.e. niche construction and developmental systems theory possibly overriding the effects of natural selection) towards the end of the Pleistocene, disadvantageous features were tolerated, both of a somatic and neurological nature. Since anthropologists are concerned with human behavior, they should care deeply about the future directions of *Homo sapiens sapiens*' evolution, which is proceeding adversely with respect to the prevalence of serious brain illnesses.

1. Introduction

Homo sapiens is subject to an alarming number of brain disorders (this includes what formerly were thought to be 'mental illnesses' such as schizophrenia, bipolar illness, obsessive compulsive disorder), as well as autism spectrum disorders, Huntington's disease, Alzheimer's disease, Parkinson's disease and fronto-temporal dementia (Bednarik and Helvenston forthcoming). Recently Ghika (2008) published an excellent study demonstrating that many neurodegenerative diseases are age-related diseases of specific brain areas recently developed in *Homo sapiens* and we refer the interested reader to that study. None of these illnesses are found in the great apes, with the exception of what resembles obsessive

compulsive behavior evidenced by animals in captive environments without environmental stimulation and conspecifics present.

Although some authors have speculated that phylogenetically recent higher cortical functions may carry a risk of brain disease (Damasio et al. 1990; Hodgson 2003; Keller and Miller 2006; Keller 2008), few have systematically explored the depth of the relationship between newer cortical developments, brain disorders, and phylogenetic evolution, although a number of authors have proposed that schizophrenia is best understood as a deleterious side effect of the newly expanded social brain areas during hominization (Farley 1976; Crow 1995, 2000, 2002; Brüne and Brüne-Cohrs 2007; Cosmides and Tooby 1999; Burns 2006, 2004). We will consider schizophrenia, as an age-related neurodegenerative disorder and bipolar illness and obsessive compulsive disorder, which do not appear to be degenerative, in some detail. Keller and Miller have reported the heritability of schizophrenia to be 80% and its prevalence about 1% of the population in the U.S.A. Since schizophrenia is such a disabling and maladaptive disorder (Keller and Miller 2006: 2) its prevalence in the general population is said to be a *paradox*, because natural selection should have eliminated this illness. (Recently Adriaens 2008, has argued that there is no evolutionary paradox regarding schizophrenia, a position with which we disagree). But natural selection has not eliminated schizophrenia—if anything, the frequency of schizophrenia may be increasing, although this is difficult to document because diagnostic techniques and treatment options have improved dramatically over the past 50 years.

Not only are brain disorder susceptibility alleles being preserved in the human genome, our species harbors numerous other deleterious and maladaptive genes. But while the molecular bases of over 1,700 Mendelian (single gene) disorder phenotypes were identified by 2006, the loci of the polygenic conditions we are concerned with here have proved to be much harder to detect. Keller and Miller's seminal work considered three evolutionary models but the results remained inconclusive. Here we will present a vigorous explanation for their paradox, one that derives from Pleistocene archaeology, recent findings of genetics, and a revolutionary model explaining the recent gracilization of our species. We begin by exploring the relevant neuropsychology.

2. The Role of von Economo Neurons

There has been relatively little attempt to focus upon the unique aspects of the human brain aside from size (Jerison 1973) and reorganization patterns beginning with australopithecines (Holloway 2008 [2001]) until quite recently (see Allman 1977; Kaas et al. 1979; Stephan et al. 1981; Aiello and Dean 1990; Semendeferi 1994, 2001; Changeux and Chavaillon 1996; Schoenemann 2006; Ghika 2008; Bednarik and Helvenston in press for a more complete discussion). One of the major differences in the brains of great apes and *Homo sapiens sapiens* is the fact that the latter are subject to a number of brain disorders. Damasio et al. (1990) provisionally implicated the ventromedial or orbital prefrontal cortex of humans in both our rapid cognitive evolution and the attendant pathologies but they did not systematically develop the evidence across numerous diseases as we do. Some of the specific cells that appear to be most afflicted in brain pathologies are von Economo neurons (VENs). VENs are relatively newly evolved, being present in the great apes and humans. Also known as spindle cells, these have been the subjects of much recent interest (Nimchimsky et al.

1999; Watson et al. 2006). VENS have huge cell bodies but only one apical axon and one dendritic appendage. They are found in layer 5b of the human cortex. They are larger and far more numerous in the human anterior cingulate cortex and the frontoinsular cortex (Sridharan et al. 2008) than they are in the brains of great apes, and they appear to participate in very rapid signal transmissions (Allman et al. 2002; Allman et al. 2010; Hayashi 2006;). Recently, VENs have also been found in the dorsolateral prefrontal cortex, Brodmann area 9 (Fajardo et al. 2008). VENs also occur in sperm whales, bottlenosed dolphins, Risso's dolphin and beluga whales, and in the brains of African and Asian elephants (Coghlan 2006; Hof and Van der Gucht 2007; Butti et al. 2009; Hakeem et al. 2009; Seeley et al. 2006). This distribution suggests that they may be restricted to large animals with large brains and extensive social networks and have been especially evolved to rapidly transfer information to various areas of the brain and spinal cord.

In humans, VENs are barely present at birth and increase in number until eight months after birth, and there are significantly more VENs in the right hemisphere than the left, which may be related to asymmetries in the autonomic nervous system (Allman et al. 2010). The activity in the inferior anterior insula (which contains the frontoinsular cortex) is related to physiological changes in the body during decision making, error recognition and focused awareness (Allman 2010). The fact that VENs are developing after birth suggests that disruptive traumas or neglect can influence their development and thus they may be implicated in disorders such as schizophrenia and bipolar illness- both of which can be significantly effected by the environment during early developmental periods in childhood. Since VENs develop postnatally they may be relevant to the pathogenesis of other brain disorders because there is evidence that the survival of other populations of postnatally generated neurons is heavily influenced by environmental factors. For example the neurons in the dentate gyrus of the hippocampus are vulnerable to many stress-related events and their survival can be enhanced by enriched environments, physical activity and serotonin-mediated mechanisms (Gould et al. 1997; Jacobs 2000).

In extant humans, VENs are implicated in several brain illnesses. For example, frontal-temporal dementia (formerly known as Pick's disease) involves primarily VENs in the anterior cingulate cortex (Mayo Clinic 2010; Allman et al. 2010). This term represents a diverse group of uncommon disorders primarily affecting the frontal and temporal lobes of the brain—the areas we associate with complex human personality, behavior and language (Seeley 2008). These dementias are not of old age, often beginning in the 40s to 50s. The VENs are specifically and selectively attacked in the variant of these illnesses known as behavioral frontal-temporal dementia and some 74% of the VEN population is destroyed. What remains of the VEN population is severely dysmorphic (Allman et al. 2010). In Alzheimer's disease (Nimchinsky et al. 1999) the cingulate cortex is reduced (although this is disputed in Allman et al. 2010); and the anterior cingulate cortex is diminished in both size and metabolic activity in autistic patients (Haznedar et al. 2000). Both the size and activity of the ventral part of the anterior cingulate cortex are reduced in depressed patients (Drevets et al. 1997). Both schizophrenia and bipolar illness have abnormalities in the anterior cingulate cortex, but it is unclear as to whether VENs are involved in bipolar illness. The protein encoded by the gene DISC1 is preferentially expressed by the VENs and it is disrupted in schizophrenia. DISC1 has undergone rapid evolutionary change in the line leading to humans, and since it suppresses dendritic branching it may be involved in the distinctive VEN morphology (a bipolar shape with only one apical dendrite).

Recent work indicates that the anterior insula (frontal insular cortex) is involved in awareness (Ploran et al. 2007, 2010; Craig 2010; Nelson et al. 2010). For example, Ploran 2010 found that in an experiment where subjects were asked to note when they became aware of the identity of an object that had been masked by noise the 'aha' moment was the same moment activity in the anterior insula was most strongly indicated. The frontoinsular cortex seems to be critical, especially the right hemisphere, in switching between distinct brain networks across various tasks and stimulus modalities (Sridharan et al. 2008). Such skills are virtually a hallmark of much of human cognitive ability and these authors believe that their findings have important implications for a unified view of network mechanisms that underlie both exogenous and endogenous cognitive control; such switching is certainly a meta-level cognitive capacity.

VENS have been found to subserve a number of other functions in the past few years. Allman et al. (2005; 2010) speculate that they also play a role in intuition, which like perceptual recognition involves immediate effortless awareness rather than the activity of deliberative processes. For example, VENs are active during social situations, when we experience humor, trust, empathy, guilt, when we engage in deception and when we determine another's mental state. These VENs are located in the frontoinsular cortex and the anterior cingulate cortex. Interestingly, intuition often implies our 'gut' feeling about some situation, and these are precisely the areas of cortex that mediate sensations from the viscera.

Aziz-Zadeh et al. (2009) found that when subjects were solving anagrams and arrived at the 'aha' moment, both the anterior insula and anterior cingulate cortex were activated. These aspects of awareness are not limited to body states, but involve visual and linguistic experiences, suggesting that the role of insular cortex in awareness may include most or all aspects of perception and cognition. Perhaps the VENs in the frontoinsular cortex serve as a rapid relay of this information to the frontal cortex and other areas.

The frontoinsular area and the anterior cingulate cortex in anthropoid primates receive differential innervation for pain, itch, cooling and sensual touch. These brain regions are central components of highly evolved mechanisms for physiological homeostasis (Craig 2003, 2009). Perhaps the VEN-containing areas of both brain areas should be considered as a further elaboration of these homeostatic mechanisms. While they retain some aspects of their basic physiological functions, such as appetite regulation, they have extended their functions to the regulation of social interactions and the homeostasis of interpersonal relationships (Allman et al. 2010). Allman et al. cite a number of experimental studies that suggest the insula and cingulate cortex are involved in the recognition of error and the initiation of adaptive responses in error and negative feedback situations. Both areas are major components of the system for the flexible control of goal-directed behavior (Dosenbach et al. 2007). Furthermore, the brain disorders to be discussed have devastating consequences for complex social interactions involving these two brain areas.

3. Common Brain Illnesses Found Only in *Homo Sapiens*

There are a number of brain illnesses that singularly afflict human beings, i.e., schizophrenia, bipolar illness, obsessive compulsive disorders, Huntington's disease, Parkinson's disease, Alzheimer's disease, autistic spectrum disorders. Other illnesses such as multiple sclerosis, temporal lobe epilepsy, and middle cerebral artery disease (causing a

stroke in the language areas of the brain; see Bednarik and Helvenston in press for a discussion), also afflict humans, whereas epilepsy and stroke can also affect the great apes, although the incidence is extremely rare. In order to narrow our consideration of these disorders we will limit our discussion to those which affect younger individuals and are thus not complicated by the general factors of old age interacting with more specific disease processes that may have remained incipient in the individual until senescence. For example, it should be noted that Alzheimer's disease also involves VENs, as schizophrenia does. The most common dementia in humans is Alzheimer's, and movement disorders such as Huntington's and Parkinson's diseases also have a dementia (not Alzheimer's) component. Humans also suffer a number of neurodegenerative disorders in addition to the former illnesses and one of the most devastating is multiple sclerosis, wherein the visual system shows a high degree of susceptibility to degeneration (see discussion of Parkinson's disease, Huntington's disease, Alzheimer's disease, multiple sclerosis, temporal lobe epilepsy and middle cerebral artery disease in Bednarik and Helvenston in press). Here we will consider only three of these illnesses as one of the costs of a very large brain with the highest encephalization quotient and massive interconnections—the results of hominization.

3.1. Schizophrenia

In both schizophrenia and bipolar depression the anterior cingulate cortex is affected with reductions in the density of layer 2 (Benes et al. 2001). Recently, it has been shown that the density of VENs in the anterior cingulate cortex is reduced in early onset schizophrenia (Brüne et al. 2010). In most cases, schizophrenia is an end result of a complex interaction between hundreds of genes and multiple environmental risk factors—none of which on their own causes schizophrenia (Gilmore 2010) and which include family history/genetic predisposition, season of birth, urban birth, lower socioeconomic status, prenatal or birth complications, and known and unknown infectious agents. Arguably, schizophrenia is an age-related, neurodegenerative disorder in a way that manic depressive disorder and obsessive compulsive disorders are not. There is clearly evidence that infections of certain kinds in utero or postpartum play a role (Niebuhr et al. 2008), as do genes because the highest risk factor is a first degree relative with schizophrenia. Earlier onset schizophrenia is much more virulent as a disorder than later onset (Douaud et al. 2010). Schizophrenia delays and alters maturation of the brain in adolescence (neoteny of cerebral areas) leading to several neuropathological changes in the brains of those afflicted. Schizophrenia is characterized by complex cognitive deficits including hallucinations, delusions, working memory and attentional deficits, incoherence, catatonic behavior, severe amotivational syndromes, inability to care for the self, hallucinations, delusions, emotional blunting and difficulty finding a mate (DSM IV 1994). The fertility estimate for schizophrenia stands at about 47% (Keller 2008: 15).

As a mnemonic device there is a triad of the most consistent neuropsychological findings in schizophrenia, which consists of ventricular enlargement, reduced hippocampal volume and hypofrontality. Thus temporal and frontal lobes and related subcortical limbic structures are especially affected (Bradshaw 2001, reprint 2006: 128). At the first episode of schizophrenia in the third decade, there are already gray matter volumetric changes in the right and left middle and inferior temporal gyrus which worsen with chronicity (Kuroki et al.

2006; Hershfield et al. 2006). Hippocampal volume is reduced in schizophrenia and there is lateral ventricular enlargement (Harrison 1999). Moreover, schizophrenia is also associated with frontal lobe dysfunction and disconnectivity (Mathalon and Ford 2008). The probable proximal explanation for decreased cortical volume is reduced neuropil (axons, glial cells and dendrites that occupy space between neurons) and reduced neuronal size, rather than a loss of neurons, but this is a contested opinion (see Tamminga et al. 1992). These morphometric changes are in turn suggestive of alterations in synaptic, dendritic and axonal organization, a view supported by immunocytochemical and ultrastructural findings. Pathology in subcortical structures is not well established apart from the dorsal thalamic nuclei, which are interconnected with the dorsolateral prefrontal cortex (possesses VENs). The anterior cingulate cortex containing large numbers of VENs is also involved. In schizophrenia, reductions in the number of small neurons in layer II and reduced cerebral blood flow in the anterior cingulate have been noted (Tamminga et al. 1992), as well as reduced VEN density in the anterior cingulate cortex in early onset schizophrenia as mentioned.

The cognitive impairments of schizophrenia are not due to an Alzheimer's dementia (Harrison 1999). In schizophrenia the frontal lobes are afflicted by connectivity problems, the neurons are small, contributing to the appearance of atrophy and the cingulate cortex; temporal lobes and hippocampus are all adversely affected, i.e., the very structures that modulate the memory skills across immediate, short-term and long-term memory storage and emotions related to diverse social behaviors. The disconnections in projections to and from the frontal lobes result in poor planning, poor judgment, and lack of motivation. Finally, the dorsal medial nucleus of the thalamus, interconnecting with the dorsolateral prefrontal cortex is affected: all these structures are involved in schizophrenia and they are also uniquely developed in humans.

Schizophrenia appears to be a relatively recent illness as it is absent from historical descriptions. E. H. Hare (1988) has argued there is no historical record describing a condition consistent with that of schizophrenia until the 17th or 18th centuries, although some psychiatrists disagree. For example, one anonymous reviewer of this paper ascribed Joan of Arc's visions to schizophrenic hallucinations. The alleged 'hallucinations' or visions of medieval mystics such as Joan of Arc, Hildegard of Bingen, Margery Kemp etc., are difficult to interpret and we believe many psychiatrists have been in error jumping to the conclusion that they suffered from schizophrenia. Attributing schizophrenic hallucinations to medieval saints who routinely used trance-inducing techniques and experienced 'visions' is beyond the scope of this paper and we refer the reader to Kroll and Bachrach (2005) for a serious discussion of these complex issues. Hare believes that some 200 years ago a new virus appeared that led to the development of the new disorder. This view is consistent with recent viral and neurodevelopmental models of the etiology of schizophrenia. Finally, although attempts have been made to create animal models of schizophrenia using brain lesions or selected drugs, schizophrenia or any similar disorder is unknown in the great apes.

Schizotypic personality disorder is sometimes referred to as a milder form of schizophrenia because some individuals with this personality disorder become actively psychotic and develop full-blown schizophrenia. It too has a high heritability but it also confers some positive benefits such as creativity, which is viewed positively by prospective mates. Nettle and Clegg (2005) investigated the relationship between schizotypal personality traits, creative activity and mating success in a British population and found that schizotypal traits are maintained in the human population at significant levels because the negative effects

in terms of psychosis and other psychopathology are offset by enhanced mating success. Two factors seemed to attract mates, increased recklessness and creativity, both of which directly enhanced mating success. Related to the advantages of creativity, Crow (2000) has postulated that schizophrenia is the price *homo sapiens* pays for language.

3.2. Bipolar or Manic-Depressive Illness (BD)

Bipolar or manic-depressive illness is a chronic, relapsing, remitting neuro-psychiatric disorder that is characterized by disordered moods alternating between extremely euphoric (manic) mood and extremely depressed mood. Moods that are not as severe are known as hypomanic and dysphoric states and constitute cyclothymic disorder. About 1% to 1.6% of the population has manic-depressive disorder and close to 4% has cyclothymic disorder.

Bipolar patients spend about 1/5 of their life in either manic or depressed moods with 'normal' or euthymic moods being experienced in between episodes. Both men and women are equally susceptible and the age at onset varies from childhood to 50 years of age with a common onset date at age 15 16. BD is not accompanied by dementia as schizophrenia sometimes is and the 'normal' personality between episodes may be highly creative and productive (Goodwin and Jamison 1990).

BD has been studied extensively for 50 years using twin studies, family studies and adoption studies and the concordance rate for monozygotic twins is higher than for fraternal twins, pointing to a high degree of heritability. There are several genetic regions of interest identified in linkage studies that include chromosomes 18, 4p16, 12q23-q24, 16p13, 21q22 and Xq24-q26 (Craddock and Jones 1999).

Advances in neuroimaging suggest distinct differences in BD in the dorsolateral prefrontal cortex, limbic system, third ventricle, cerebellum, temporal lobe, basal ganglia, and subcortical white matter. Vawter et al. (2000) mention a number of other findings, such as reduced gray matter in the left subgenual prefrontal cortex and amygdala enlargement in BD. VENs are found in the dorsolateral prefrontal cortex and this represents the first description of these neurons in granular cortex (Fajardo et al. 2008) and suggests that VENs may be involved in BD, although further research is needed. The reader will recall that abnormalities in many of the same regions are also found in schizophrenia. However, in schizophrenia there is increased neuronal density in the prefrontal cortex whereas in BD there is decreased neuronal and glial density in association with glial hypertrophy (Rajkowska 2009). That author concludes that the neuropathological distinctions between BD and schizophrenia are indicative of separate mental illnesses, each with a unique morphologic disturbance of specific neural circuits.

In one of the most thorough postmortem investigations (Ongur et al. 1998) there was significant reduction in glial density in the subgenual prefrontal cortex, but the authors did not identify which type of glial cell, astrocytes, oligodendroglia or microglia were involved. A 50% reduction in glial density is striking for BD patients. Decreased cortical thickness in both bipolar and depressive disorders has been found in the rostral orbitofrontal and middle orbitofrontal cortex, whereas caudal orbitofrontal and dorsolateral prefrontal cortex appeared normal. Areas of neuronal densities were significantly decreased in the CA2 sector of the hippocampus of patients with both BD and schizophrenia, compared to control subjects.

Entorhinal cortex malformations were found in the architecture of clusters of medium to large-size stellate nerve cells in BD as compared to controls. In fact, the malformed architecture was observed in the entire rostral entorhinal area laterally up to the perirhinal area and to the temporal isocortex. These preliminary observations of abnormalities are suggestive of a disturbance of young neurons migrating in the deeper layer, and patients with schizophrenia also show some similar abnormalities (Beckman and Jacob 1991).

An important finding seen recently is that there are significant shape differences present in striatal structures (caudate and putamen) in BD, thus implicating the basal ganglia (Hwang et al. 2006) although the volumes were comparable. Finally, the signs and symptoms of bipolar illness are very dramatic and obvious, and the sufferers are often highly intelligent, creative and verbally communicative people which is likely one reason why these mood disorders have been recognized, described and linked together since at least the Hippocratic Corpus in Western civilization (Helvenston 1999).

There are anecdotal reports of animals mourning the loss of their mothers and becoming so dysphoric they died from grief. Goodall documents dysphoric behavior and behavioral disorders and death in young chimps that have lost their mother (1986: 101–104). No doubt some animals in restricted environments, isolated from conspecifics appear dysphoric, although their overt behavior more closely resembles obsessive compulsive disorder. It is also possible to create animal models of BD using surgical lesions or assorted neuroleptic drugs but no spontaneous illness such as BD is known in captive chimpanzees or other apes.

3.3. Obsessive Compulsive Disorder (OCD)

In this illness insistent thoughts and images and incessant urges to perform puzzling rituals are experienced, often to such a degree ordinary living is completely disrupted. A persistent feeling of dread or that something is wrong pervades the sufferer's consciousness. These feelings are generated by an overactive inferior prefrontal cortex (Schwartz and Begley 2002: 21–95).

OCD afflicts about 3.3 million adults and about 1 million children and adolescents in the U.S.A. The disorder usually first appears in childhood, adolescence, or early adulthood. It occurs about equally in men and women and affects people of all races and socioeconomic backgrounds. It is considered an anxiety disorder and thus has a genetic component as well as an environmental component in its etiology (Mayo Clinic Staff 2010). The areas of the brain comprising the 'worry circuit', to be discussed shortly, are modulated by the neurotransmitter serotonin, so an imbalance in this substance is believed to contribute to OCD (WebMD 2/20/10). This disorder has recently been effectively treated using specific cognitive behavioral techniques that modify both behavior, and the underlying neural substrates involved in causing and alleviating the disorder have been well documented (Schwartz and Begley 2002: 21–95).

Damage to the inferior prefrontal cortex produces persons who are unable to generate intuitive solutions to problems like planning and executing complex behaviors such as the manipulation of mental images. Excessive activity of the same area leads to an intrusive feeling that 'something is wrong'. This area of cortex is overactive in OCD patients who constantly have a gut feeling of doom (these feelings are accompanied by visceral symptoms such as racing heart rate, sweating, and overactive sympathetic nervous system signs). This

leads them to develop many obsessive stereotypical behaviors that provide some temporary relief from dread and thereby reinforce maladaptive behavioral sequences. A second area of over-activity in the OCD person's brain is the striatum (includes two structures, the caudate nucleus and the putamen). The inferior prefrontal cortex, orbitofrontal cortex and the cingulate cortex project to the striatum, causing the caudate to be overactive in an area known as the striosome area, thus bringing emotional tones and valences into the experience via the amygdala because it also projects into this same striosome area, leading to the constant feeling of doom and gloom.

The caudate thus represents a mosaic of reason (from projections from the dorso-lateral prefrontal cortex to the caudate in the matrisome area) and passion (from projections to the caudate from the cingulate gyrus and amygdala ending in the striosome area in the caudate, which is located close to the matrisome area). Sitting in between the matrisome and the striosome areas are the TANs, tonically active neurons, and these integrate the input from the inferior orbital frontal cortex via the strisomes with the input from the amygdala and orbitalfrontal region, also via the striosomes. In other words, the TANs are a gating mechanism between the matrisome and the striosome regions.

From the striatum, projections go to the globus pallidus, thalamus and motor and premotor cortex—this is known as the direct route by which the striatum projects to the cortex. In the indirect route fibers project from the striatum to the globus pallidus (known collectively as the basal ganglia), the subthalamic nucleus to the thalamus and then to motor and premotor cortex. The direct output from the striatum quiets the cortex, whereas the indirect pathway stimulates it. The gating TANs determine which pathway, the direct or indirect, will be taken. These interconnections make up the 'worry circuit' or the OCD circuit. When this circuit is working properly, the result is a finely tuned TANs area that can precisely modulate the orbital frontal cortex and anterior cingulate by adjusting the degree to which the thalamus drives both areas (Schwartz and Begley 2002: 54–95). When that modulation is faulty, as it is when OCD is acting up, the error detector centered in the orbital frontal cortex and anterior cingulate can be over-activated and thus locked into a pattern of repetitive firing. This triggers an overpowering feeling that *something* is wrong, accompanied by compulsive thoughts or behavioral attempts to somehow make it right. Because any action provides a few seconds or minutes of temporary relief, strange strings of thoughts and behaviors become reinforced.

The specific cognitive behavioral therapy utilized in these studies for the treatment of OCD patients is termed 'mindfulness'. It teaches patients to realize that when they experience the doom and gloom sensations it is a faulty brain signal and to suppress acting on that signal. Patients can learn to control the worry circuit with this treatment. For example, eighteen OCD patients were given PET scan imaging studies before and after they underwent a ten-week therapeutic regimen. After treatment the PET scans showed significantly diminished metabolic activity in both the right and left caudate with the right-side decrease particularly striking. All of the 18 patients showed major reductions of symptoms.

Therapy had altered the metabolism of the OCD 'worry circuit' and the severity of the symptoms (see also Heimer et al. 2008 for an extensive discussion of the forebrain neuroanatomy and neurophysiology of frontal and prefrontal structures and mental illness in humans). OCD is at least a relatively treatable disorder, much more so than schizophrenia and bipolar disorder, which are treated primarily with psychotropic medications. Older treatments of OCD have also relied upon anti-anxiety or antidepressant medications.

Animals confined in sterile cages or small spaces and isolated from conspecifics frequently develop a large variety of stereotypic behaviors. These include obsessive pacing, over-grooming, self-injury, repetitive behavior such as brushing the head against the cage, repetitive attempts to unlock the cage, etc. These behaviors are clearly similar to OCD in humans and may involve some similar neural circuits. Of the brain illnesses discussed in this paper, except for epilepsy and stroke, OCD is the only one that occurs spontaneously in captive animals not provided with complex, stimuli-filled, rich environments and members of their own species with which to interact (Mason and Rushen 2006).

3.4. OCD and the Price of Excellence in the Fossil Record

Obsessive compulsive disorder is certainly the ultimate price of striving for excellence. Since the initial introduction of concepts of perfection, the demands of excellence culture—especially recent literate and now scientific culture—has exacted from humans have mushroomed to the extent that modern societies would not function without them. The deliberate and conscious pursuit of performance, unknown to all other animals, has not only become the fulcrum of the neurology of our species, it has perhaps also demanded its toll.

The key measure of the cultural sophistication of hominin societies is provided by the growing role of symboling, expressed especially in palaeoart production. It begins during the Lower Paleolithic technocomplexes (several hundred millennia ago), in the form of beads or pendants, portable engravings, pigment use, proto-figurines, very early petroglyphs and manuports (Bednarik 1992, 1995, 2003a et passim). Of particular interest here are those productions of these exograms (Donald 1991, 1993, 2001) that can, by replication, be demonstrated to have made such demands of perfection that obsessive behavior is manifested by them. Some of them, especially beads, demonstrate advanced self-consciousness and thus essentially modern cognition (Bednarik 2008a). These exograms include Acheulian ostrich-eggshell beads (Bednarik 1997) and cupules of Mode 1 stone tool industries (Bednarik et al. 2005). The extraordinary investment of labor in essentially useless artifacts indicates the involvement of value judgments entirely different from those determining natural selection. Even some of the early stone tools, most particularly hand-axes, have been suggested to possess perfection far beyond the utilitarian (e.g. Gamble 1997; Wynn 2002).

Such a quest for perfection is an obsessive trait, offering little if any Darwinian benefit, yet it is highly time-consuming and demanding on resources. On the other hand it is central to our cognitive and technological advancement. There is no sense of perfection apparent in anything extant non-human primates make. Their sleeping nests or tools reveal no compulsion to go beyond the crudely functional, and have very probably remained completely unchanged for a long time. Nor is any such obsession apparent from the tools of australopithecines or early Homo (up to late *H. erectus*). Evidence for these impulses seems to appear roughly mid-way through the Acheulian technocomplex, or close to a million years ago. This coincides with the introduction of seafaring and the evidence for reflective language (Bednarik 2003b), i.e. clear evidence of symboling. Therefore it seems reasonable, at least until contradicting evidence comes to light, to attribute the rise of exograms—of storage of symbolic information external to the brain—essentially to the Middle Pleistocene period. It is here that the origins of human modernity become apparent on the empirical record.

Neurologically, the over-activation of the gating TANs between the matrisome and the striosome areas, on the orbital frontal cortex and anterior cingulate, could conceivably result from over-stimulation by the spiraling demands for perfection. However, since the rise of extreme OCD is clearly a detrimental development for humans, we can only assume that, at any one stage, the advantages of the development of the 'worry circuit' must have significantly outweighed its detrimental effects. Which might suggest that the latter were negligible initially, otherwise they could have selected against cognitive sophistication. At what stage should they be assumed to have become significant phylogenetic encumbrances cannot now be answered by empirical observation, but if we consider the hypothesis attributing final Pleistocene human neoteny to cultural selection, a realistic explanation offers itself. Just as evolutionary determinants could not prevent the deleterious changes from robust to gracile forms, because they were overruled by cultural determinants (Bednarik 2008b), mental disorders arising from burgeoning prefrontal cortex complexity may have escaped natural selection in much the same way. The development and persistence of these disorders suggests that selection against them was somehow suppressed.

4. Natural vs Cultural Selection

One of the mysteries in paleogenetics or evolutionary genetics is the conundrum of why evolutionary processes apparently failed to select against the degenerative genetic predispositions of extant humans. In the perhaps most comprehensive debate of this topic, Keller and Miller (2006; also Keller 2008) defined it as that field's unresolved paradox. Although their discussion and the contributions by thirty-five of the foremost specialists in the field considered every possible aspect and perspective of this veritable Gordian knot, they failed in providing more than a selection of weak and inconclusive hypotheses. Keller and Miller propose three evolutionary models – ancestral neutrality, balancing selection and mutation-selection balance—but in the end cannot implicate any one of them. Why the maladaptive mental disorder susceptibility alleles have not either fixated (for which they would need to be adaptive) or gone extinct has therefore remained entirely unsolved so far. Here we not only provide a realistic and logical explanation for this evolutionary puzzle; we can even explain why it has for so long remained unsolved. By promoting the replacement hypothesis as aggressively as Pleistocene archaeologists have done over recent decades, neuroscientists had to conduct their deliberations within a false paradigm, i.e. the notion that today's humans are a distinctive species and their characteristics are attributable to natural selection alone. Within that framework, the selection in favor of numerous deleterious traits is indeed a paradox. Within the domestication hypothesis (Bednarik 2008b), by contrast, it is not only readily explained, it is entirely predictable and logical. Domestication promotes unfavorable alleles (e.g. Horrobin 1998, 2002; Andolfatto 2001; Lu et al. 2006), and it can even account for other unexplained features, such as the abolition of estrus in females, which is as typical of domestication (and extremely rare in placental animals) as are so many detrimental traits.

The hitherto dominant archaeological notions of a replacement of all robust hominins have recently been replaced by the domestication hypothesis, which postulates that the somatic changes from robust to gracile types were primarily driven by culturally moderated selection (Bednarik 2008a; 2008b). The process of selecting genetic traits by means other

than Darwinian evolution is domestication, a radical hereditary reorganization of the genetic constitution of a species. In the case of robust *Homo sapiens*, it significantly accelerated the fetalization of the species that had already begun earlier, promoting behavioral and other plasticity. While it is reproductive success that determines phylogenetic direction in any species, processes of natural selection have been largely suspended in our recent evolution, having at some point in time been replaced by cultural mating imperatives. All other animals show no preferences in mate selection of youth or specific body ratios, facial features, skin tone or hair; yet in present humans these are strongly established. Facial symmetry, seen to imply high immunocompetence (Grammer and Thornhill 1994; Shackelford and Larsen 1997), is preferred, and male humans favor neotenous facial and other features in females (Jones 1995; 1996). Anecdotal evidence and focused observation reveal that young females also prefer Hollywood/Bollywood heroes who have a juvenile rather than a manly appearance. The rapid and universal human fetalization during the final third of the Late Pleistocene indicates that cultural practice had become such a determining force in human society that breeding mate selection became increasingly moderated by factors attributable to learned behavior. These could have included the application of cultural constructs in such choices, such as social standing, language skills, body decoration (which becomes notably prominent 40 ka [40,000 years] ago; Bednarik 1992), and most especially culturally negotiated constructs of physical attractiveness (Laland 1994), apparently expressed in art by up to 40 ka ago, in such figurines as those from Galgenberg (Bednarik 1989) and Hohle Fels (Conard 2009). The rapid gracilization towards the end of the Pleistocene begins with the females, while the males lag many millennia behind (Bednarik 2008b), and it continues to accelerate today.

Domestication, occurring in many forms and species, is the collective genetic alteration of physiology, behavior or life cycle through selective breeding. It does not necessarily yield a population of better-adapted organisms, as natural selection would be expected to evolve. Rather, it shows that selection for a single trait results in changes in numerous traits. For instance domestication of mammals typically yields decreased cranial volume relative to body size, a decrease that can be as much as 30–40%; *H. sapiens sapiens* fared better, with only ~10% reduction. Domestication typically decreases robusticity, increases susceptibility to detrimental changes, including neurological, and negates the effectiveness of estrus. The domesticators eliminate natural selection through their guardianship, but the patronage for the human domesticates is provided by their culture and technology: they need no protector. Thus the self-domestication of humans only became possible at a specific Rubicon of cultural and technological development. Apparently this occurred with the advent of the Upper Paleolithic 40 ka ago and was enhanced and further developed during the Neolithic farming period.

Developmental systems theory challenges the focus of natural selection on the genes with a model of interacting systems (Oyama 2000; Oyama et al. 2001), emphasizing non-genetic inheritance of traits and the cybernetic feedback from organism-environment systems changing over time. In niche construction (Odling-Smee et al. 2003), organisms modify the evolutionary pressures acting on them through culture. Laland et al. (2000, 2010) and Mesoudi et al. (2006) see much of niche construction as guided by socially learned knowledge and cultural inheritance (cf. Silk 2007). Other proposed non-genetic dimensions of evolution are epigenetic, behavioral and symbolic inheritance systems (Jablonka and Lamb 2005). Epigenetic inheritance refers to physiological/biological processes above the level of DNA that are impacted during ontogenesis by environmentally provided experience.

Behavioral inheritance is found in most species, defining the transference of information or behavior through learning rather than genetically. Thus evolution is not a simple genetic process relying on the appearance of mutations (Dobzhansky 1962: 18; 1972). The notion of a developing moderation of human evolution by culture is at the core of the gene-culture co-evolutionary model (Cavalli-Sforza and Feldman 1973; Feldman and Cavalli-Sforza 1989; Aoki and Feldman 1991; Durham 1991; Boyd and Richerson 2005; Richerson and Boyd 2005). Fuentes (2009), too, has sought to reconcile the pronounced duality of evolutionary biology and socio-cultural anthropology, pointing out that symbolic and other cultural processes influence behavior and potentially physiological and even genetic factors.

Evolutionary change occurs either through Darwinian or sexual selection. In the first, specific phenotypes representing aspects of morphology or behavior are preferentially reproduced across generations of a given population. In the second, phenotypes become over-represented either through mate choice or intra-sexual competition. In all sexually reproducing species, all characteristics of individuals are said to be inherited through genes, but it does not necessarily follow that all inheritance must be encoded in DNA. The principles and mechanisms of genetics apply to the molecular structure of cells and tissues, the development of individuals and the evolution of whole populations. Selective breeding defies natural evolution in the sense that it can rapidly change the characteristics of a population without any natural selection in the Darwinian sense.

If the rise of brain disorders is attributable to the same factor, which is the central proposition of this paper, it might suggest a similar timing. In their most consequential forms, these disorders can also only have become widespread after cultural imperatives had developed to the level of being able to provide the required existential shelter, except those affecting only the old. Once individuals have already contributed to the gene pool, their loss from it no longer influences phylogenetic direction. But this is very different with those affecting younger people, especially the very young. During most of hominin evolution these disadvantageous genetic predispositions would have been vigorously selected against. This includes not only the disorders we have discussed, but also a whole raft of other genetic disorders humans are now subjected to. We have illustrated how we propose to detect traces of these developments in the archaeological record with one of these disorders, OCD, and presented a possible scenario for its establishment.

To assist us in parceling out the factors that would clarify the influence of life expectancy on the heritability of brain disorders we will consider the common causes of death for hominins, hominoids, and *H. sapiens*.

5. Mortality Rates in Humans and Susceptibility to Neurodegenerative Disorders

Humans have unquestionably the longest lifespan of any primate. Infections cause most of the mortality in wild chimpanzees and in traditional forager-farmers. Even under the conditions of high mortality experienced by human hunter-foragers, the human life expectancy at birth is twice that of wild chimpanzees (Finch 2009). According to tooth wear, early *H. sapiens sapiens* and the best known of their robust predecessors, *H. sapiens neanderthalensis*, had a larger proportion of older adults than prior Homo species and

australopithecines (Caspari and Lee 2006). The greater survival to later ages allowed the evolution of stable multigenerational support of the young, which is a uniquely human trait among primates. Perhaps the expansive development of the human limbic system which is so involved with social and emotional aspects of life resulted in the grandparents being prominently involved with infants and young children, thus leading to higher survival rates of the family or small groups of families (Hawkes 2004; Gerven and Kaplan 2007; Coall and Hertwig 2010).

In healthy populations of humans and laboratory animals, the acceleration of mortality is preceded by increasing morbidity from chronic degenerative diseases (Finch 2007; Finch et al. 1990). For wild chimpanzees, typical early mortality rates are 20% per year in infancy, within the range of hunter-foragers, then decreasing to a q_{min} of about 3.5% per year in pre-adult ages. The chimpanzee life expectancy at birth is about 13 years, whereas those reaching adulthood (age 15) have about 15 more years of life expectancy (Kaplan et al. 2000; Hill et al. 2001). Very few have survived beyond age 50, even in captivity with modern veterinary care (Rosen 2008). In contrast, human mortality after the early years is much less, with a >2-fold longer life expectancy even with lower access to medicine. A definitive proportion of forager-farmers aged 60 or older die from nonspecific senescent causes, whereas chimps tend to die more frequently from infections (Finch 2009), which humans are eliminating in themselves in industrialized countries with relentless determination.

Increased longevity of humans facilitates the described processes of neoteny and further lowers the q_{min} thus prolonging the human life span even further; it is an autocatalytic factor. The neotenization of the human brain and the low q_{min} allow for developmental mechanisms to unfold, conferring an advantage on those aging slower, in terms of adaptations such as grandparents assisting grandchildren to prosper. The question is, do these newly evolving mechanisms also enable more degenerative diseases of aging, diseases that may lie incipient in the individual until senescence, such as Alzheimer's, Huntington's and Parkinson's disease? This question, while of great importance, is beyond the scope of the present paper but see Ghika (2008) for a reasonable hypothesis. The second question is, do brain illnesses unique to humans develop mainly from newly developed brain areas or neurons in humans? That hypothesis is supported by the data considered in this paper. Here we have only pondered some of those brain disorders affecting younger individuals, but there is some evidence that at least one disease of senescence, Alzheimer's, also involves VENs, as does fronto-temporal dementia (Seeley et al. 2006). This suggests that some of the differential neuronal susceptibility that occurs in the human brain in the course of age-related dementing illnesses may have appeared only recently during primate evolution. Schizophrenia, bipolar disorder, and obsessive compulsive disorder tend to set in relatively early, and even Parkinson's, Alzheimer's, and especially frontotemporal dementia and Huntington's are not limited to the old (Bednarik and Helvenston in press). Autism and Asperger's are typically manifested in early childhood, as are Rett and Down syndromes and dozens of other known genetic impairments endemic to humans. The most debilitating or prominent brain illnesses, such as schizophrenia, bipolar disorder, autism, multiple sclerosis and so on are basically absent in the great apes. Therefore it can be assumed that these primates do not share our genetic predisposition in that respect, and that the enlarged and newly evolved brain areas and neurons such as VENs primarily developed after the Miocene separation of our respective phylogenies. If the uniquely human brain illnesses developed in our recent history, at what point in our genetic past should we expect to find them appearing first?

6. Implications of the Findings

As a species we are fond of perceiving ourselves as the pinnacle of evolution, preferably ignoring that the purpose of evolution– a 'blind' random process –is merely to adapt living organisms to ever-changing environments. For instance in the last few decades, the most favored interpretation of our recent evolutionary history has us emerging in sub-Saharan Africa, rising to unprecedented sophistication, overwhelming all 'inferior' other humans of the world, having somehow distanced ourselves from them so much genetically that we could not have interbred with them. This fantasy (Bednarik 1992; 1995; 2003a) has been maintained until very recently, despite being devoid of any genetic, cultural or skeletal evidence (Bednarik 2008a). The realistic explanation of how *Homo sapiens sapiens* acquired its current characteristics is significantly less popular. Rather than some evolutionary pinnacle, we are a fetalized ape, a neotenous creature and quite probably not the likeness of a deity (Bednarik 2008b).

The species *Homo sapiens* can be traced back on the paleontological record for some hundreds of millennia. The recent mutations leading to its sole extant sub-species have to a significant extent been deleterious. Its brain volume has decreased by about 10% in a geological instant, reversing the process of encephalization our ancestors had experienced for millions of years. This occurred during a time of presumably unprecedented demands on the hominin brain engendered by a rapidly increasing complexity of our societies (Bradshaw 1997). During the very same time, the last quarter of the Late Pleistocene, the skeletal robusticity of our lineage waned so dramatically that many researchers perceive different species. Not only is the skull of a robust human several times as resistant to fatal impact as that of an extant gracile, the differences in robusticity of the post-cranial skeleton are almost as dramatic. The fossil evidence relating to muscle attachments also suggests that robusts, such as the much-maligned 'Neanderthals', are thought to have possessed up to twice the physical strength of modern graciles. But the perhaps most dramatic development separating our robust ancestors from us is the process of neotenization, i.e., the retention into sexual maturity of physical characteristics previously seen only in juveniles. Modern humans resemble chimpanzees anatomically most closely in the latter's fetal stage (Haldane 1932; De Beer 1940; Ashley-Montagu 1960; Bednarik 2008a). But while neoteny of a species is in some respects detrimental to it, it also involves evolutionary advantages. Most importantly, it facilitates the retention of plasticity or 'morphological evolvability' (de Beer 1930: 93; cf. Fuentes 2009). Adaptively useful novelties can become available as maturation genes are freed by pedomorphosis (juvenilization of the body morphology).

However, the deleterious somatic effects accompanying the change from robust to gracile humans, occurring roughly over the past 40 ka, are not the only detriments we have experienced in our most recent 'evolution'. There can be no doubt that they left us more susceptible to injury, physically weaker, and with a smaller brain than our robust ancestors. But what is worse, our brain has become vulnerable to a range of neurodegenerative pathologies, which other extant primates are largely free of (Walker and Cork 1999; Olson and Varki 2003). These range from dementia to bipolar illness, from obsessive compulsive disorder to sociopathic or antisocial personality disorders and diseases involving demyelination or dysmyelination of axons. Significantly they affect largely the very same

areas of the brain that are involved in its higher cognitive functions (Damasio et al. 1990; Bednarik and Helvenston in press).

Perhaps our much-cherished 'advanced' cognition came at a price. The presently unfolding genetic evidence has provided first empirical indicators that the predispositions for a variety of neurodegenerative or otherwise deleterious mutations are of recent phylogenic origins (Green et al. 2010). For instance, the DYRK1A gene, implicated in causing Down syndrome, seems absent in robust *Homo sapiens*. The genes CADPS2 and AUTS2, responsible for autism, also appear to be limited to modern Graciles. Perhaps more dramatic is the proposal that schizophrenia is of late historical origin and might have been introduced by a virus as recently as 200 or 300 years ago (Jeste et al. 1985; Hare 1988). Be that as it may, the NRG3 gene, associated with schizophrenia, also seems to be absent in so-called Neanderthals. Using the human haplotype map to test for selective sweeps in regions associated in genome scans with psychosis, such as 1q21, is promising (Voight et al. 2006). Again, such selective sweeps tend to yield relatively recent etiologies, of less than 20 ka, as predicted by the domestication hypothesis. While the genes SLC6A4 and NRG1 have been implicated in schizophrenia, and MAOA linked with bipolar disorder (Cho et al. 2005; Li et al. 2006; Andres et al. 2004; Preisig et al. 2005; Jansson et al. 2005), few other such loci have been identified for polygenic conditions (but see Saito et al. 2001; Yoshikawa et al. 2001; Ding et al. 2002; Enard et al. 2002; Muglia et al. 2002; Zhang et al. 2002; Kitano et al. 2004; Spinks et al. 2004; Stopkova et al. 2004; Abdolmaleky et al. 2005; Costas et al. 2005; Harrison and Weinberger 2005; Gardner et al. 2006; Sanjuan et al. 2006; Xu et al. 2006, which collectively link schizophrenia or bipolar disorder with APOL1, APOE, DRD4, FOXP2, GRM3, HOPA, IMPA2, MAOA, MAOB, NRG1, SLC6A4 and SYNJ1). This contrasts with the successful identification of more than 1,700 Mendelian (single gene) disorders, as noted. Continuing research is likely to locate more evidence that neurodegenerative illnesses are the burden specifically of modern sapienoids, just as other 'modern' human genes such as RUNX2 and CBRA1 (causing cleidocranial dysplasia or delayed closure of cranial sutures, malformed clavicles and dental abnormalities) and THADA (associated with type 2 diabetes) are certainly deleterious. In a species fully subject to the canons of natural selection such disadvantageous mutations would surely tend to be suppressed.

How did these pathologies initially develop; at what time in our evolution did they appear; and, most especially, why did evolutionary processes apparently fail to select against the relevant genetic predispositions? Without some appreciation of these issues the diseases concerned have no causal context or explanation. In this endeavor it is essential to ignore recent fads in paleoanthropology, such as the replacement hypothesis (e.g. Protsch 1975; Bräuer 1980; Stringer 1984; Stringer and Andrews 1988; Wainscoat et al. 1986; Cann et al. 1987), and reconsider the issues outside these models. The gradualist model of symbolic and cognitive evolution (Bednarik 1992; 1995), which is in opposition to the replacement or 'short range' model, enjoys increasing support from various disciplines (Lock and Peters 1996; Hodgson 2000; 2003; Bloom 2001; Dunbar 2003; Sedikides et al. 2006; Krause et al. 2007; Falk 2009). 'Neanderthal' genes persist in recent Europeans, Asians and even Papuans (Green et al. 2010; Gibbon 2010; Reich et al. 2010), but are absent in Africans. The frequency of African alleles in non-Africans averages only 13%, which implies very limited African introgression in Eurasia (or vice versa), whereas outside of Africa, populations may derive largely from Neanderthaloids. Thus the African Eve model has become an absurdity.

Generational mating site distance (Harpending et al. 1998) and reticulate introgression or introgressive hybridization (Anderson 1949) easily account for genetically observed changes in human populations over the past 50 ka.

The refutation of the model placing the origins of 'anatomically modern' humans either exclusively or largely in Africa requires an alternative explanation for the relatively rapid change from robust to gracile *H. sapiens*. A more realistic and better-supported explanation for this universal change in four continents is provided by the alternative domestication hypothesis (Bednarik 2008b). It proposes that culture-induced mate choice began having an effect on hominin breeding patterns roughly 40 ka or 30 ka ago, gaining influence over time and accelerating the rate of human neotenization and other inexpedient somatic changes. Here we argue that the development of our species' neurodegenerative pathologies is also related to the developing modernity of Late Pleistocene hominins. The very same areas of our brain that enable our unique cognitive abilities are also those affected by these brain illnesses, and this fact has huge implications which are far beyond the scope of this paper to explore.

Conclusion

The study of the hominization of the human brain is severely hampered by the dearth of empirical evidence, which has so far focused on the examination of endocasts and biological reasoning or comparisons. Some of this work has become available only relatively recently, through imaging techniques such as MRI, fMRI and PET scans. Preuss (2000: 1219) even refers to our species as 'the undiscovered primate'. Here we have taken a different approach, based on testable evidence and informed by recently acquired data and ideas. In this we have greatly benefited from the realization that the size and interconnectivity of the human brain (Semendeferi 2001: 107–120), which confers *H. sapiens*' superior cognitive abilities, also appears to have given rise to certain brain disorders, which are essentially endemic to humans. Thus, with the expansion of the human frontal insular cortex, dorsolateral prefrontal cortex, anterior cingulate cortex and temporal and parietal lobes, limbic system and basal ganglia, hominins have also developed brain illnesses that predominantly affect these same areas. Our present knowledge seems to point to a very late, essentially final Pleistocene—if not, in some cases, even Holocene –development of these pathologies. We have discussed schizophrenia, bipolar illness, obsessive compulsive disorder. We have also highlighted the areas of the brain involved in each of these illnesses, along with a discussion of the genetic underpinnings.

After having demonstrated the prevalence of brain disorders in the more highly evolved areas of the human brain one of our primary concerns was the question why natural selection should have permitted the development of these often severely debilitating illnesses in *Homo sapiens sapiens*. Here we noted that somatic 'modern' features of humans also contradict the canons of evolution: our subspecies is more susceptible to injury, physically weaker, and has a smaller brain than our robust immediate ancestors. These changes characterizing hominins of the final part of the Pleistocene and the Holocene define us as a neotenous adaptation, which was introduced through the rise of culture as the determinant of breeding patterns, through culturally mediated mate choice. If evolutionary processes were supplanted by cultural selection, the same mechanism can explain why degenerative susceptibility alleles have not either fixated or gone extinct, perhaps during the same period. The enhanced

connectivity that led to man's most brilliant achievements has apparently also led to brain disorders that are relatively common, but it needs to be explained why they were not selected against. In Darwinian evolution deleterious factors should be eliminated from a species' genome, but domestication defeats evolutionary canons (Bednarik 2008b). We posit that our explanation for human susceptibility to such pathologies is the most economical and forceful, on the basis of the current, very limited evidence.

We have also illustrated how this hypothesis could be applied to the specific example offered by the rise of OCD. An incipient sense of perfection can be detected during the Middle Pleistocene, being traceable to deliberate practices of people with Lower Paleolithic technologies. We have suggested that this behavior trait, unique in biology, marks the advent of incipient obsessive behavior, which, through over-stimulation of phylogenetically recent neural adaptations, may have eventually led to the development of OCD, in much more recent times.

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