Chapter 21
Attention-Cognition Spectrum Syndromes: Delirium, Dementia, Impulse Control Syndromes, ADHD, Antisocial Personality, Obsessive-Compulsive Personality Traits, Obsessive-Compulsive Syndrome

Contents

21.1 Gene × Meme Interaction, Evolutionary Adaptation, and Syndromes

Attention is a basic brain function necessary for any action from finding food to fight/flight reaction. Attention to internal physical stimuli such as distended bladder is also important to maintain health. Cognition is essentially the brain's meme-processing function and developed extensively with the growth of the neocortex.

Attention system seems to be separate from the data-processing systems of the brain and involves specific neural networks that carry out specific functions related to attention (Posner and Petersen, 1990). Posner and Peterson (1990) describe the components of the attention system as (1) orienting to sensory stimuli involving the parietal lobes and midbrain structures, (2) detecting signals for processing involving the parietal lobes and their connection to the frontal lobes and the anterior cingulate gyrus, and (3) maintaining an alert, vigilant state, involving the locus ceruleus and the right hemisphere.

There are normal degrees of attention and inattention depending on the nature and amount of external and internal stimuli, physiologic state, and the amount of internal processing of data that may require attention. It is obvious that well-functioning attention system has evolutionarily adaptive value, but the ease of shifts

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of attention vs. ability to stick to a task without distraction may have differential adaptive value depending on the habitat. When one is in constant threat of being attacked by a predator, easy shift of attention to a footstep may be lifesaving, on the other hand, if one has to concentrate to sharpen a sword before a battle, being able to ignore distractions may be all important. Thus, attention-regulating genes adapted for one environment may prove to be maladaptive for another.

Thinking, or cognition, is mainly a function of the frontal cortex with contributions from the sensory and association cortices. Working memory, associated with the dorsolateral prefrontal cortex and its connections (see Chapter 9) plays an essential part in cognition. The left brain is generally considered to be involved in logical, linear thinking, while the right brain is more involved with global, holistic, and intuitive thinking. Cognition is greatly affected by attention and arousal, as well as by emotions.

With the rapid growth of the neocortex with hominids that parallels the development and multiplication of memes, our brain's activity has become increasingly that of cognition. With ever increasing influx of memes in the form of language and information, the brain is challenged with the need for ever increasing efficiency in meme processing that we call cognition.

Prolongation of human life through technologies developed by memes may be responsible for the prevalence of degenerative dementias. As evolutionary adaptation functions exclusively during the reproductive period, there is no evolutionary disadvantage for diseases of the post-reproductive period in life.

In discussing treatment for syndromes in this section, we will first briefly deal with global dysregulation of meme processing associated with clear physiologic and/or structural aberrations, i.e., delirium and dementia, as it is beyond the scope of this book to discuss this large and important area in detail. Then, we will discuss in some detail the conditions associated with attention-deficit hyperactivity, impulse control problems, obsessions, compulsions, and preoccupations in two separate subsections.

21.1.1 Global Dysregulation of Meme Processing: Delirium and Dementia

Global dysregulation of meme processing occurs when there is a metabolic or toxic dysfunction of the brain as a whole. In delirium, which is characterized by relatively acute fluctuations in global brain function, the memetic content is confused and erratic. Because of the disturbances in neural circuitry and in neural firing and conduction due to electrolyte imbalance, toxins, etc., there are disturbances in the functions they serve, including perception, memory, thinking process, judgment. Hallucinations, delusions, preoccupations, etc., are common as well as emotional lability, agitation, and altered levels of awareness, e.g., sleepiness and stupor.

In dementia, there is often progressive degeneration of brain structures and thus reduction in their meme-processing function. Higher cortical functions necessary

for higher level meme processing, such as logical thinking and judgment are often impaired, and often results in disinhibition of normal memetic demands such as following social conventions of dress and behavior. Delirium is often superimposed on dementia resulting in more impairment and confusion.

The memetic diagnosis for delirium and dementia is based on recognizing the global deficits in meme processing, and the treatment should be geared to providing a nonthreatening and easy to comprehend memetic environment. Memetic treatment should be accompanied by drugs as needed. In delirium, the underlying metabolic or toxic cause must be identified and treated. Drug treatment may be geared toward immediate agitation and confusion as well as possible specific dementias.

21.1.2 Dysregulation of Infrastructure for Meme Processing: Attention-Deficit Disorder (ADHD), Impulse and Aggression Dyscontrol, Antisocial Personality

This dysregulation spectrum involves the infrastructures for meme processing, i.e., the tools needed to think and behave normally. This involves being able to shift and maintain attention, recognize and modulate impulses that may arise from gene- or meme-determined needs and to modulate and channel aggression which may also be determined by genes, memes, or both.

Neuropsychological and imaging studies indicate that attention-deficit hyperactivity disorder (ADHD) is associated with alterations in prefrontal cortex (PFC) and its connections to striatum and cerebellum. PFC is critical for utilizing representational knowledge in the regulation of behavior, attention, and affect. PFC is involved in sustaining attention, inhibiting distraction, and dividing attention, while more posterior areas are necessary for perception and allocation of attention. The right PFC seems especially important in behavioral inhibition as its lesions produce distractibility, forgetfulness, impulsivity, poor planning, and motor hyperactivity. PFC is very sensitive to levels of dopamine and norepinephrine. Norepinephrine may enhance signals through postsynaptic alpha-2A receptors in PFC, while dopamine decreases noise through D1 receptor stimulation (Brennan and Arnsten, 2008).

A number of candidate genes for ADHD have been identified, including the dopamine transporter gene (DAT1 or SLC6A3), the dopamine D2, D4, and D5 receptor genes, the serotonin transporter gene (SLC6A4 or 5-HTT), the serotonin 2A receptor gene (5-HT2A), and SNAP25. Other genes that have received significant study include the norepinephrine transporter (NET), catechol-*O*-methyltransferase (COMT), and the nicotinic acetylcholinereceptor alpha 4 subunit (CHRNA4).

Gene–environment interactions have been studied in ADHD. Interestingly, given childhood abuse, the long allele of the serotonin transporter promoter gene, rather than the short allele which is associated with neuroticism and later depression, was associated with ADHD (see Chapter 1 for further discussion of serotonin transporter promoter gene). It is possible that individuals with the long allele might cope

with stress through inattention while those with the short allele might be unable to cope and thus become more fearful and depressed. The short allele was associated with more severe ADHD pathology if the stresses were early in life (Muller et al., 2008). 5-HTTLPR thus may act as a moderator of environmental influences in ADHD (Muller et al., 2008).

Smoking seems to contribute to gene–environment interaction in the risk of ADHD and impulsive behavior (Wallis et al., 2008). Child hyperactivity–impulsivity and oppositional behaviors were associated with a DAT polymorphism but only when the child also had exposure to maternal prenatal smoking. In addition, interaction between DAT1 genotypes and maternal use of alcohol during pregnancy suggests that DAT1 moderates the environmental risk. Prenatal exposure to smoking and variations in the DAT1 and DRD4 loci seem to interact in children with the ADHD combined subtype. CHRNA4 gene polymorphisms interacted with prenatal smoking exposure on risk for severe combined type ADHD. Gene–environment interactions have been reported for DRD2 genotypes as well as COMT polymorphisms for ADHD and conduct disorder.

The short allele of the MAOA (MAOA-uVNTR) has been associated with aggressive behavior, violence, and antisocial behavior (Reif et al., 2007).

Carrying a short allele of the MAOA-uVNTR acted as a true and independent risk factor for later-life aggression, further adding to the risk conveyed by childhood maltreatment. Other behavioral traits such as disruptiveness and cluster B personality traits (dramatic, colorful, histrionic, antisocial, borderline) but not cluster C (shy and fearful) may be contributed to and regulated by the MAOA gene as well.

MAOA short allele has also been associated with hyperreactivity of the amygdala in response to emotional arousal, associated with impaired response of the prefrontal and anterior cingulate cortex in fMRI studies. In fact, stronger coupling between amygdala and the ventromedial prefrontal cortex through the rostral cingulate cortex predicted increased harm avoidance and decreased reward dependence (Buckholtz et al., 2008).

In pathologically aggressive individuals, serotonin transporter concentration was significantly reduced in the anterior cingulate cortex (Frankle et al., 2005). As the short allele of the 5-HTTLPR is associated with decreased levels of serotonin transporter, it may play a role in aggression. Homozygotes for the long allele have been shown to be less likely to develop later-life aggressive behavior, while the short allele homozygotes do. Most interestingly, only heterozygotes were influenced by environmental factors, that is, this polymorphism might have a role in balancing aggressive behaviors in differing societies (Reif et al., 2007).

21.1.3 Dysregulation of Meme-Processing Loop: Preoccupations, Obsessions, Compulsions

An evolutionarily important event was the development of romantic love, which serves as an example of memetic preoccupation, obsession, and compulsion, usually but not always within normal range. Helen Fisher studied romantic love

extensively. She states, "The sex drive evolved to motivate individuals to seek a range of mating partners; attraction evolved to motivate individuals to prefer and pursue specific partners; and attachment evolved to motivate individuals to remain together long enough to complete species-specific parenting duties. These three behavioural repertoires appear to be based on brain systems that are largely distinct yet interrelated, and they interact in specific ways to orchestrate reproduction, using both hormones and monoamines. Romantic attraction in humans and its antecedent in other mammalian species play a primary role: this neural mechanism motivates individuals to focus their courtship energy on specific others, thereby conserving valuable time and metabolic energy, and facilitating mate choice" (Fisher et al., 2006).

The neural circuit underlying romantic love involves the right ventral tegmental area of the brain stem and right posterodorsal body of the caudate nucleus. The dopaminergic reward and motivation pathways contribute to aspects of romantic love.

The complex neurotransmitter network of the cortico-striatal-thalamo-cortical (CSTC) circuit involving dopamine, serotonin, glutamate, and gamma-amino butyric acid (GABA) may be dysfunctional in obsessive-compulsive syndrome (Harvey et al., 2001). The dysfunction in this loop may arise from an attenuation of feedback signal indicating reward which results in compulsive lever pressing in rats, which is further enhanced by lesions of the orbitofrontal cortex (Joel et al., 2005). Compulsions may also develop from an operant conditioning (memetic) paradigm as in compulsive gambling, which in turn may result in functional changes in the brain such as impairment of decision-making capacity (Fellows, 2007; Hariri et al., 2006; Kalenscher et al., 2006).

Tourette's syndrome is an example of brain dysfunction that involves dysregulation of both meme processing and motoric function illuminating the role of the basal ganglia in both. In this syndrome, there are simple and complex motor tics, vocal tics, and frequently obsessive-compulsive symptoms. Its onset occurs before the age of 21 and the course is waxing and waning. Tourette's syndrome occurs mainly in boys and is genetically transmitted with variable penetrance but it has also been associated with various infections and immunological conditions such as the PANDAS (pediatric autoimmune neuropsychiatric disorder associated with streptococcal infection). The neuropathology seems to involve a disturbance of the dopaminergic system in the basal ganglia.

Gene–environment interaction involving the serotonin transporter promoter gene (5-HTTLPR) has also been reported in OCD, i.e., those with the *s/s* allele and childhood trauma were more likely to develop OCD with dissociative experiences (Lochner et al., 2007). Clearly, same gene–environment interaction may lead to multiple vulnerabilities in the CNS, including OCD, dissociation, anxiety, and depression.

In our discussion above, it seems that we are at a threshold of understanding the neurobiological mechanisms of normal functioning such as attention, thinking, aggressivity, and impulse control. Normal thinking process may become abnormal if stuck in a loop, as in preoccupations, obsessions, and compulsions. Structural and metabolic change in the brain may cause temporary or permanent

loss of the ability to perceive and process memes in the form of information and memory.

Attention deficit and hyperactivity are behavioral observations, i.e., what do the patients look like and how do they behave? Individuals with these problems may not initially complain of any distress, but their grades may suffer, and family and friends may be frustrated. The memetic content may be those of puzzlement and bewilderment. "Why do I forget so easily? I can't focus" Low self-esteem memes are introduced and proliferate, "I am not good at studying, math, . . ." With hyperactivity and impulse control problems, "badness" memes will be introduced and replicate – "I am a trouble-maker" "I am bad" "Nobody likes me."

With ADHD, however, the individual often fails to store sufficient variety and number of memes in the brain to function well, as well as being distracted by differing memes in the environment vying for attention to get into the brain. Many such memes may be poorly processed in the brain, and thus poorly integrated with existing memes.

With aggression, violence, and antisocial personality, the environment in the gene × meme × environment interaction infuses abuse and neglect memes that cause the epigenetic changes for poor impulse control through attenuation of meme-processing abilities. Furthermore, the abuse and neglect memes take up residence in the brain providing a model for future selfplexes – to be uncaring and abusing.

Preoccupations are excessive memetic replications in the brain. By replication, I do not mean that the neurons are replicating themselves – rather, the intensity of the firing of the neuronal cluster that makes the meme is increased, it recruits other clusters of neurons to fire and develop long-term potentiation like themselves, which is how memes replicate (Chapter 9). The enhanced firing may recruit the motor neurons to fire, thus expressing the meme to the outside, and when this is in the form of language, it is likely to infect the receiver. In other words, if I am preoccupied with love, I may say it aloud, may write an e-mail, and perhaps a poem. All of these will transmit my "love" meme to myself, my beloved, my friends, and the world at large.

Preoccupations, obsessions, and compulsions may occur unwantedly and unexpectedly, depending on the state of the brain and the memetic nature of the thought. In the obsessive-compulsive disorder (OCD), there may be a primary dysfunction of the cortico-striatal-thalamo-cortical network involving dopamine and serotonin discussed above. Symptoms of OCD may also occur because the meme representing the thought may be particularly strong because it is fed by energies from related preexisting memes in the brain. For example, a suicide meme may be introduced by seeing a film to a depressed brain that has many preexisting self-punishment and guilt memes, thus the suicide meme may gain strength, proliferate, and recruit the motor neurons to carry out suicide. Other memes, like earworms which are unwanted melodies or sounds that keep on occurring in the mind, may replicate because of the strength of their vehicles (the rhythm, melody, form of presentation, color, smell, texture, etc.). Some such memes may represent "supernormal stimulus," the kinds of stimuli that are evolutionarily

determined to elicit strong preferences, or results of early imprinting (Burkhardt, 2005).

The diagnosis of obsessions, compulsions, and OCD is made on the basis of the severity of the phenomena and the degree of distress. Earworms are nuisances but not necessarily distressing, ego-alien obsessions can be very distressing, and compulsions may be disabling.

21.2 Treatment

Genetic and pharmacologic treatment should be geared to the suspected or demonstrated brain dysfunction, and may include SSRIs, often in high doses, and surgical interventions including deep brain stimulation and capsulotomies have been used successfully in treatment-resistant OCD (Cecconi et al., 2008; Dowling, 2008; Nuttin et al., 2008). Treatment of delirium and dementia involves providing memetic environment that is stable and protective and appropriate medications. For ADHD, stimulants are effective as well as meme-oriented broad spectrum and specific therapies enhancing positive selfplexes.

Several symptom subtypes of obsessive-compulsive disorder (OCD) have been identified on the basis of the predominant obsessions and compulsions. Overt compulsions have been associated with a relatively good response to the exposure and response prevention (ERP) therapy and with poorer response to serotonin reuptake inhibitors (SSRIs). Washing and cleaning and checking compulsions tend to respond well to ERP, but and rather poorly to SSRIs. Patients with symmetry, ordering, and arranging subtype do tend to respond equally well to ERP and SSRIs. Some studies suggest that obsessions might respond to SSRIs somewhat better than to ERP. Hoarding and the subtype characterized by sexual or religious obsessions and absence of overt compulsions have been associated with poor response to ERP and SSRIs (Starcevic and Brakoulias, 2008).

Cognitive–behavioral therapy and antipsychotic medications have also been used effectively in OCD.

The memetic approach to preoccupations, obsessions, and compulsions should involve an analysis of the memetic content of the thoughts, and their memetic connections (and vehicles) such as the visual, auditory, olfactory, gustatory, and tactile associations. One might find that the energy for replication of the obsessive meme may indeed come from a conflict with a nondominant (repressed) meme that is associated with it.

Treatment should then include, in addition to cognitive behavioral and exposure and response techniques, direct memetic neutralization of the replicating thought (obsession) through infusion of new memes and/or strengthening of existing ones as with repetition of a word or phrase, visualization, and music therapy. Such specific treatments may be in conjunction with broad-spectrum anti-meme therapy (see Chapter 17) to reduce the unchecked proliferation of memes seen in OCD.

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